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BOOK OF ABSTRACTS

IAEA-CN-185
CONTENTS

CLINICAL PET ONCOLOGY

IAEA-CN-185/104 ............................................................................................................ 2
Feasibility of biopsy guided by FDG-PET/CT in oncolical patients
J.J. Cerci, C.C. Pereira Neto, J.V. Vitola

IAEA-CN-185/105 ............................................................................................................ 3
Importance of 18F-FDG PET/CT imaging in patients with lymphoma and residual
CT mass after treatment
D. Sobic-Saranovic, V. Artiko, M. Todorovic-Tirmanic, V. Obradovic

IAEA-CN-185/106 ............................................................................................................ 4
PET/CT in diagnosis of metastases and recurrences of colorectal carcinomas
V. Artiko, D. Sobic-Saranovic, N. Petrovic, V. Obradovic

IAEA-CN-185/107 ............................................................................................................ 5
Pitfalls encountered in 1500 hybrid PET/CT studies
V.E. Soroa, J. Arashiro, M.M. Volpacchio, G. Rank, C. Giannone

IAEA-CN-185/113 ............................................................................................................ 8
Results of initial FDG PET/CT staging in recently diagnosed breast cancer
patients
S. Ozguven, F. Dede, T. Ones, B. Gulluoglu, S. Inanir, T.Y. Erdil, H.T. Turoglu

IAEA-CN-185/114 ............................................................................................................ 9
Morpho-metabolical changes at the operation site in recently mastectomized
patients: Impact of staging FDG PET/CT
S. Ozguven, F. Dede, T. Ones, B. Gulluoglu, S. Inanir, T.Y. Erdil, H.T. Turoglu

IAEA-CN-185/115 .......................................................................................................... 10
Synchronous metastases in recently diagnosed breast cancer: Role of staging FDG
PET/CT
S. Ozguven, F. Dede, T. Ones, B. Gulluoglu, S. Inanir, T.Y. Erdil, H.T. Turoglu

IAEA-CN-185/117 .......................................................................................................... 11
The value of FDG-PET/CT imaging in dermatomyositis as a paraneoplastic
syndrome in malignancy suspicion
M. Aras, T. Ones, F. Dede, F. Novruzov, S.S.C. Omercikoglu, S.Ozguven, S.
Gungor, S. Inanir, T.Y. Erdil, H.T. Turoglu

IAEA-CN-185/121 .......................................................................................................... 13
Radiological response evaluation of oncolytic virus treatment in patients with
advanced cancer
A. Koski, K. Kairemo, M. Oksanen, A. Koskela, K. Partanen, A. Hemminki

IAEA-CN-185/123 .......................................................................................................... 14
FDG PET in nephrourinary cancer: Our experience in 60 cases
Valdebenito

IAEA-CN-185/125 .......................................................................................................... 16
Significant impact of mid treatment 18-F FDG PET-CT as a prognostic indicator
in the management and follow-up of metastatic breast cancer
P.S. Choudhury, M. Gupta, A. Chaturvedi, A. Dogra

IAEA-CN-185/126 .......................................................................................................... 17
Usefulness of FDG-PET in the evaluation of sarcomas from diverse origin
Gallegos, R. Valdebenito, A. Quenaya
Evaluation of somatostatin receptors in prostate cancer lesions with Ga-68-DOTATATE PET-CT

Clinical study of 18F-FDG PET/CT in diagnosis and management of lung cancer
Y.P. Dang, Q. Wang

Evaluation of 18F-FDOPA PET-CT and its comparison with 99mTc- GHA SPECT/CT in detection of recurrence in patients with high grade primary glioma
S. Karunanithi, C.S. Bal, A. Malhotra, G.P. Bandopadhyaya

Role of 18F-FDG PET/CT in response evaluation of metastatic gastrointestinal stromal tumours to Imatinib Mesylate: Indian experience
S. Jeph, R. Kumar, C.S. Bal, A. Malhotra

Application of PET/CT simulation in radiation planning at the nuclear medicine and oncology centre, Bach Mai Hospital, HANOI, Vietnam

Clinical utility of FDG PET/CT in patients with lymphoma
J. Mihailovic, S. Goldsmith, R. Killeen, A. Abi Ghanem

Reliability of 18F-FDG PET/CT after 2 cycles of chemotherapy for prognosis prediction in patients with Non-Hodgkin lymphoma
L. Henzlová, M. Mysliveček, P. Koranda, T. Papajík, E. Buriánková, Z. Kapitáňová

18F-FDG PET/CT under TSH stimulation in patients with differentiated thyroid carcinoma
H. Crhakova, P. Koranda, L. Henzlova, M. Dockal, M. Myslivecek

Identification of cancer metastases using the combination of PET and viral vectors
P. Brader, Z. Gil, Y. Fong, T. Helbich, H. Hricak, C. Herold

PET/CT examinations with 68Ga -DOATATE in neuroendocrine tumours - Characterization of physiological uptake in organs in diagnosis of primary tumours
J. Kunikowska, L. Krolicki, D. Pawlak, I. Zerizer, L. Grabowska, R. Mikołajczak

PET/CT with 11C-acetate in prostate cancer: Appropriate diagnostic tool
F. Martínez-Preciado, M. Patiño-Zarco, E. Estrada-Lobato, O.F. García-Pérez, I. Soldevilla-Gallardo

Utility of 18 F-FDG PET-CT in the evaluation of orbital tumours
M.A. Maltez Cruz
Diagnostic and prognostic value of 18F-FDG PET/CT on cancer of unknown primary
S. Carmona, J. Santos, L. Oliveira, P. Colarinha, A.L. Bastos, A.I. Santos
IAEA-CN-185/188.......................................................................................................... 35
Intra-abdominal neoplasms – MRI versus 18F-FDG-PET/CT
J. Santos, S. Carmona, C. Bagulho, L. Oliveira, P. Colarinha, A.L. Bastos, A.I. Santos
IAEA-CN-185/190.......................................................................................................... 36
Clinical characteristics and 18F-FDG PET/CT imaging in differentiated thyroid carcinoma patients with negative 131I whole-body scan and elevated serum thyroglobulin
L.N. Ha, L.M. Ha, L.D. Hung, N.T. Huong
IAEA-CN-185/191.......................................................................................................... 38
PET/CT imaging with 68Ga-DOTATATE in the evaluation of neuroendocrine tumours (NET): Our leading experience in Chile
IAEA-CN-185/192.......................................................................................................... 40
Cost-effectiveness analysis of 18F-FDG PET/CT in detecting suspected recurrence or metastasis in thyroid carcinoma patients with negative diagnostic total body scan in Thailand: A decision analysis
K. Benjapa, N. Cherdchai, P. Pawana, T. Pongpija, T. Napaporn
IAEA-CN-185/195.......................................................................................................... 41
18FDG PET-CT role in management of dedifferentiated thyroid cancer
P. Kundu, Snehlata, A. Malhotra, C.S. Bal
IAEA-CN-185/197.......................................................................................................... 42
Role of 18F-FDG PET-CT in medullary thyroid carcinoma and correlation with serum calcitonin
C.B. Khangembam, C.S. Bal, R. Kumar, A. Malhotra
IAEA-CN-185/199.......................................................................................................... 43
Early assessment for suspected recurrent ovarian cancer - optimizing PET/CT performance using a tumour marker based analysis
K. Gourevich, K.A. Busing, A. Amit, Z. Keidar
IAEA-CN-185/202.......................................................................................................... 44
Impact of the 18F-FDG PET/CT on the treatment and management of oncological patients at the National Institute of Cancerology of Mexico
R.B. Belén, E. Estrada Lobato, I.F. Vega González
IAEA-CN-185/209.......................................................................................................... 46
The role of FDG-PET in the evaluation of treatment for lymphoma: Philippine setting
P.A. Bautista
IAEA-CN-185/214.......................................................................................................... 47
Clinical study on multiple traces PET/CT in gliomas
S. Gao, L. Cai, Y. Li
IAEA-CN-185/217.......................................................................................................... 48
F-18 FDG PET-CT in follow-up of patients with lymphoma
N.N. Mkhize, M.D.T.H.W. Vangu, N.S. Perumal
68Ga-DOTATATE PET/CT imaging: Preliminary findings in Johannesburg, South Africa
N. Malan, N.N. Mkhize, M.D.T.H.W. Vangu

IAEA-CN-185/220

Relationship of quantitative measures derived from (18)F-FDG PET/CT and diffusion-weighted MRI in patients with squamous cell carcinomas of the head and neck
J. Fruehwald-Pallamar, C. Czerny, B.S. Halpern, M.E. Mayerhoefer

IAEA-CN-185/225

Role of immediate [18F]FDG-PET/CT after tumour percutaneous ablation as a predictor of local recurrence-free survival

IAEA-CN-185/230

18F-FLT for stereotactic radiotherapy treatment planning of recurrent brain tumours: experience of the National Institute of Neurology and Neurosurgery of Mexico
M.A. Celis, J.M. Lárraga-Gutiérrez

IAEA-CN-185/232

Usefulness of 18F-FLT PET/CT in the differential diagnosis of radiation changes vs. tumour recurrence in the follow-up of patients with primary brain tumours
M. Patiño-Zarco, I. Soldevilla-Gallardo, O. García-Perez, E. Estrada-Lobato, F. Martínez-Preciado

IAEA-CN-185/233

Additional value of PET/CT-based radiotherapy planning in patients diagnosed of head and neck malignancy
R. De Juan, P. Cotrina, S. Ruiz, A. Ruiz

IAEA-CN-185/234

Clinical and cost-effectiveness of FDG-PET in preoperative staging of non–small cell lung cancer (NSCLC) in Brazil: A study in the context of Brazilian public health system

IAEA-CN-185/236

Usefulness of 68Ga-DOTATOC PET/CT in the evaluation of patients with medullary thyroid cancer and suspected recurrence
O.F. García-Pérez, E. Estrada-Lobato, M. Patiño-Zarco, I. Soldevilla-Gallardo, F. Martínez-Preciado

IAEA-CN-185/238

Non-invasive characterization of adrenals masses using 18FDG-PET/CT in patients with lung cancer
R. Chirico, G. Bruno, C. González, Y. Blumenkrantz, P. Parma

IAEA-CN-185/239

Clinical impact of PET/CT in detecting distant malignant compromise in patients, thought to have early and locally advanced stages breast cancer
C. González, G. Bruno, R. Chirico, Y. Blumenkrantz, M.E. Azar, C. Noblia, P. Parma
Impact of FDG PET/CT in the initial staging of patients of non-small cell lung cancer: 4 year experience from a tertiary care referral cancer centre in India


FDG PET/CT in small cell lung cancer: Initial experience from a tertiary cancer referral centre in India


FDG uptake, glucose transporter type 1, and KI-67 expressions in non-small-cell lung cancer: correlations and prognostic values


Role of 18F-DOPA PET/CT in the evaluation of neuroendocrine tumours

A. Kumar, C.S. Bal, A. Malhotra, G.P. Bandopadhayaya

Role of [18F]FDG PET-CT and 99mTc(V)DMSA in the management of patients with osteosarcoma

P. Gupta, A. Singh, J. Shukla, R. Kumar, G.P. Bandopadhayaya

Role of serial 18F-FDG PET/CT in surveillance of patients treated for colorectal cancer

H.N. Aftab, R. Kumar, C.S. Bal, A. Malhotra

Efficacy of F-18 FDG PET/CT in detecting recurrence in patients with epithelial ovarian carcinoma

K. Agrawal, B.R. Mittal, R. Kashyap, A. Bhattacharya, F.D. Patel

Role of whole body PET/CT in detecting distant metastasis in head and neck cancer

M.L. Abrar, B.R. Mittal, K.K. Kamaleshwaran, A. Bhattacharya, J. Bakshi

Comparison of 18-FDG PET-CT with conventional imaging for detection of suspected recurrence in patients with endometrial carcinoma

P. Sharma, R. Kumar, C.S. Bal, A. Malhotra

3-Deoxy-3-18F-Fluorothymidine (18F-FLT) PET/CT in patients with primary brain tumours: Mount Lebanon Hospital initial experience

M. Haidar, M. Haddad

18F-FDG PET-CT in the management of differentiated thyroid cancer

M. Haidar, M. Haddad

Role of FDG-PET in the restaging and recurrent breast cancer

M. Haidar, M. Haddad
Correlation between estimated tumour dose and response to PRRNT as determined by SMSreceptor PET/CT using Ga-68 DOTATOC
H. Kulkarni, V. Prasad, C. Schuchardt, R.P. Baum

Testicular cancer assessment with PET-FDG

Usefulness of 18F-FDG PET/CT in the assessment of the response to treatment of patients with lymphoma
S.R. Paredes Fernandez, J.A. Serna Macias, O. Quiroz Castro, N.R. Sánchez Casas, J.L. Ramírez Arias

Usefulness of 68Ga-DOTA-d-Phe (1)-Tyr (3)-Octreotide (DOTATOC) PET/CT in neuroendocrine tumours
O.F. García-Pérez, E. Estrada-Lobato, M. Patiño-Zarco, I. Soldevilla-Gallardo, F. Martínez-Preciado

Prognostic value of metabolic tumour burden with 18FDG PET/CT in diffuse large B cell lymphoma
O.F. García-Pérez, E. Estrada-Lobato, M. Patiño-Zarco, I. Soldevilla-Gallardo, F. Martínez-Preciado

Diagnostic accuracy of FDG PET/CT in recurrent osseous and soft tissue sarcoma: Comparison with full-dose diagnostic CT
A. Al-Ibraheem, K. Hermann, A.J. Beer, A. Buck, M. Schwaiger

Improving detection and evaluation of gastric malignancies on PET/CT by gastric distention with both milk and diatrizoate
Z. Zhu, C. Wu, X. Li, W. Cheng, D. Zhong, F. Li

FDG PET-CT in pre op staging of breast cancer: Initial experience from a comprehensive care centre for breast diseases
L. Pushpalatha Sudhakar, P. Singa, J. Srikala, P. Amber, R. Ram

Histopathologic correlation of 18F-FDG uptake in thyroid malignancy
B.K. Das, J. Mantil

The role of 18F-FDG-PET/CT in the preoperative staging and post-therapy follow-up: Comparison with spiral CT
E. Özkan, M. Araz, Ç. Soydal, N.Ö. Küçük

The role of PET/CT in the evaluation of pancreatic cancer and suspected pancreas masses
E. Özkan, Ç. Soydal, M. Araz, N.Ö. Küçük

18FDG PET-CT in radiotherapy planning – Comparison of gross tumour volumes obtained using automated versus manual methods
V.H. Somasundaram, S.S. Palaniswamy, S. Goyal, R. Anjana
Usefulness of F-18 FDG PET in evaluation of adrenal lesions in patients with lung cancer

B.R. Mittal, K. Agrawal, R. Kashyap, A. Bhattacharya, B. Singh, N. Singh

Clinical use of 11C-CHO PET function imaging in tumor location and regimen


Feasibility and utility of assessment of myocardial viability using ‘Hybrid’ 99mTc-MIBI SPECT and 18F-FDG PET studies in a remote PET centre without access to cyclotron

N. Seshadri, A. Sreedasyam, I. Hufton, S. Vinjamuri

Impact of coronary artery disease (CAD) over myocardial blood flow (MBF), total perfusion defect (TPD) and summed differential score (SDS) evaluated with 13N-ammonia PET/CT

A. Meave, M.A. Peña, M. Jiménez, E. Aleksanderson

PET/CT in early diagnosis of Alzheimer’s disease and alcohol dementia: Case report

B. Chaushev, A. Klisarova, M. Arnaudova, P. Bochev

Evaluation of metastatic brain lesions in whole body F18FDG PET-CT of oncological cases in correlation with their fasting blood sugar


PET-CT in paediatric oncology patients in an initial experience in a university hospital


One day protocol: Dual tracer/dual isotope FDG-18 and Ga-68 DOTA-NOC PET/CT. Study of a child with neuroblastoma to determine the metabolic tumour status

J.P. Oliva, R.P. Baum

Value of FDG PET scan in the evaluation of skeletal infections

S.V. Solav, R. Bhandari
Is FDG uniformly distributed throughout the skeleton in females?

FDG PET/CT in cancer patients with fibrous dysplasia

FDG PET/CT appearance of multi-regional elastofibroma

Diaphragmatic schwannoma mimicking hydatid cyst depicted by PET/CT
S. Gungor, T. Ones, F. Dede, F. Novruzov, S. Inanir, T.Y. Erdil, H.T. Turoglu

Atypical presentation of bronchiolitis obliterans organising pneumonia on 18FDG-PET/CT
A. Samarin, L. Karusoo, R. Brand, I. Muoni, M. Paris, S. Nazarenko

Utility of PET/CT with 18F-FDG (Fluorodeoxyglucose)-labelled leukocytes in the diagnosis of infectious processes associated with oncological pathologies: First Mexican experience
I. Soldevilla Gallardo, L.A. Medina Velázquez, E. Estrada Lobato, M. Patiño Zarco, V. López Rodríguez

Evaluation of agreement between F-18 PET–CT and Tc-99m MDP bone scan findings in patients with suspected bone metastases: Initial Johannesburg experience
N.N. Mkhize, M.D.T.H. Vangu, N.S. Perumal, N. Malan

Role of whole body 18F-FDG PET/CT in the evaluation of fever of unknown etiology

Methods of normalization and factors affecting liver and mediastinal blood pool standardized uptake values: A multivariate analysis
M.L. Abrar, K. Manohar, A. Bhattacharya, B. Singh, B.R. Mittal

Comparison of micro PET/CT using 18FDG and Micro SPECT/CT imaging of glioblastoma αVβ3 Integrin expression using 99mTc labelled RGD peptide
G. Estrada, L. Gonzalez-Maya, J. Altamirano

Comparison of Ga-68 DOTATATE vs. Tc-99m HYNIC OCTREOTIDE scan in follow-up of cancer thyroid patients with raised thyroglobulin and negative I-131 WBS
Introduction of PET-CT scanning impacts treatment decisions in the management of cervix carcinoma patients in a public hospital

H.M. Simonds, J. Warwick, A. Ellmann

Efficacy of PET/CT in the management of TENIS syndrome: A case report

Y.A. Onimode, M.D.T.W.H. Vangu, B.O.A. Osifo

Focal accumulation of FDG in lung parenchyma without morphological correlate on CT

V. Ptacnik, S. Bakalarova, J. Kubinyi

Peptide receptor radionuclide therapy (PRRNT) in patients with carcinoid heart disease (Hedinger’s syndrome): Prognostication of efficacy by Ga-68 SMS receptor PET/CT


Efficacy of Ga-68 somatostatin receptor PET/CT and peptide receptor radionuclide therapy in the management of neuroendocrine tumours of the rectum


Brown adipose tissue metabolism in diabetic mice and weight-loss mice: A preliminary study with 18F-FDG micro PET

Z. Zhu, C. Wu, W. Cheng

Normal uptake value of 11acetate in some organs

M.C. Trinh Thi, N.V. Tan, V.K. Nam

18FDG conjugated magnetic nanoparticle probes: Synthesis and in vitro investigation on MCF7 breast cancer cells


FDG Embolus: Focal lung uptake without CT abnormality- potential pitfall in PET-CT fusion imaging

V. Agarwal, S. Pande, S.K. Garg, D.R. Jangid

Role of SPECT-CT in cancer patients for diagnosis of bone metastases

S. Sergieva, E. Alexandrova, G. Baichev, N. Nikolova, A. Milev, B. Dimitrov

SPECT with 99mTc-MIBI and 99mTc-(V)DMSA in the assessment of breast lesions: Comparative study with planar scintimammography

N.Y. Voit, O.I. Solodyannikova

SPECT in diagnostic of metastatic medullary thyroid cancer

O.I. Solodyannikova, G.G. Sukach
IAEA-CN-185/141........................................................................................................ 141
Sentinel lymph node scintigraphy & gamma probing in patients with early stage
Ca cervix
S.S. Palaniswamy, P. Subramanyam, D.K. Vijaya Kumar, P. Kumar
IAEA-CN-185/159........................................................................................................ 142
Our first experience with SPECT/CT in oncology
M. Havel, O. Kraft
IAEA-CN-185/173........................................................................................................ 143
177Lu-DOTATATE: Management of metastatic well differentiated
neuroendocrine carcinomas in the National Cancer Institute of Bogota
Colombia
M. Martínez, A. Martí, A. De los Reyes, A. Llamas-Olier, E. Angarita, N.
Delgado, A. Arciniegas
IAEA-CN-185/194........................................................................................................ 144
Early differential diagnostics of oncopathology of neck area and mediastinum,
with radiological methods of diagnostics
G.G. Khachatryan, K.V. Khondkaryan, R.G. Khachatryan, A.G. Karapetyan
IAEA-CN-185/210........................................................................................................ 146
The use of SPECT-CT in determining Y-90 microspheres distribution post
selective internal radiation therapy: Preliminary experience in the
Philippines
P.A. Bautista, E.B. Cruz
IAEA-CN-185/218........................................................................................................ 147
SPECT/CT: An essential adjunct in the routine management of differentiated
thyroid carcinoma
M.D.T.H.W. Vangu, N. Malan, N.N. Mkhize
IAEA-CN-185/228........................................................................................................ 148
Incremental value of SPECT-CT in tumour imaging
R. Soumendranath, S.K. Sharma
IAEA-CN-185/229........................................................................................................ 149
Usefulness of SPECT-CT 99mTc-Tetrofosmin scintigraphy for the diagnosis and
follow-up of patients with lung cancer
S. Sandoval Borrego, B. Rivera Bravo, R. Garibay Viruex, L. Villalvazo Gutierrez
IAEA-CN-185/235........................................................................................................ 151
Clinical usefulness of SPECT/CT with 99mTc-29-41 ubiquicidin in cancer
patients with suspected infectious process
F.O. García-Pérez, E. Estrada-Lobato, M. Patiño-Zarco, I. Soldevilla-Gallardo,
F. Martínez-Preciado
IAEA-CN-185/243........................................................................................................ 152
Incremental value of diagnostic 131I SPECT/CT fusion imaging in assessment of
patients with differentiated thyroid carcinoma
A. Mhiri, I. Slim, I. Meddeb, M.F. Ben Slimane
IAEA-CN-185/293........................................................................................................ 153
High dose 50 mCi or 100 mCi NaI-131 for preventive thyroablation of thyroid
remnant in patients with differentiated thyroid cancer
D.N.K. Prawiro, P. Eko
IAEA-CN-185/297........................................................................................................ 154
Incremental value of SPECT-CT over planar scintigraphy and SPECT for the
evaluation of suspected bone metastasis in patients with breast cancer
H. Singh, R. Kumar, C.S. Bal, A. Malhotra

xiii
Empirical high-dose I-131 therapy in patients with increased thyroglobulin and no detectable anatomical lesions
A. Llamas-Olier, M.C. Martínez, L. Rojas, E. Angarita, E. Cadena, A. de los Reyes, Á. Calderón, H. Varela

Using the hypoxia volume distribution for calculation of tumour control probability (TCP)
C.F. Calderón Marín, J.J. González González, J.P. Oliva González

CLINICAL NON-PET CARDIOLOGY

Functional and morphological parameters of the left ventricle in patients with and without coronary artery disease with gated myocardial perfusion SPECT
I. Berrocal, G. Castro, M. Paz Muñoz, N. Santos, P. Padilla, T. Massardo

Tc 99m mibi infusion and low dose dobutamine gated SPECT - A novel myocardial viability detection protocol in ischaemic cardiomyopathy
P. Subramanyam, S.S. Palaniswamy, S. George, V. Harish, P.G. Sujith Kumar

A dual isotope rest SPECT myocardial perfusion scintigraphy (DI-R-MPI): Improved efficacy in the detection of myocardial viability
A. Verma, A. Kumar, R. Jeyachandran, S. Balani

Coronary artery disease functional assessment with gated myocardial perfusion SPECT
A. Puente, C. Martínez, F. García, J.L. Aceves

Myocardial perfusion imaging in patients with Chagas disease; Utility
S. Merlano Gaitán, R. Murgueitio Cabrera, E. Rodríguez Ferro

Prognostic value of myocardial perfusion study on population over 75 years
R. Murgueitio Cabrera, G.S. Merlano Gaitán, E. Rodríguez Ferro

Incremental prognostic value of perfusion defects in patients with scintigraphic evidence of left ventricular dysfunction
A.P. Quinon, J.M. Obaldo

Quantification of left ventricular parameters in normal adult Filipinos using cardiac MRI, gated SPECT Thallium-201 and 2D echocardiogram
A.P. Quinon, A.G. Serna, R. Tenorio, F. Dianco et al

Scintigraphy evaluation of cardiac disorders in ant phospholipids antibodies syndrome
E. Garcia Nicacio, A.R. Rodríguez

Utility of the complete left bundle branch block (LBBB) as prognostic factor of cardiac failure in patients with defects of myocardial perfusion evaluated with gated-SPECT
M.C. Martínez, A. Puente, C. Trejo
Value of post-NTG left ventricular volume and ejection fraction by gated myocardial perfusion SPECT in assessment of viability in patients with myocardial infarction

L.O. Cabrera, K. Padrón, R. Carrillo, Y. Fernández, E. Mena, A. Peix

CLINICAL NON-PET NEUROLOGY

Clinical value of SPECT with post-stroke Dementia
L.B. Kuanova, G.O. Ryskulova, A.S. Kassenova

99mTc-TRODAT-1 SPECT imaging of dopamine transporter in early diagnosis of Parkinson's disease
L.M. Pabón Castilla, E. Manzi

Radionuclide Cisternography in the era of PET
Z.M. Jawa, A. Ellmann

Value of combined brain blood flow and dopamine transporter imaging in patients with Dementia
A. Sreedasyam, N. Seshadri, M. Carroll, S. Vinjamuri

Ictal SPECT in Paediatric Epilepsy of temporal lobe origin – Correlation with surgical outcome
L. Pushpalatha Sudhakar, S. Jayalakshmi Sita, P. Manas, D. Ravivarma

CLINICAL NON-PET PAEDIATRICS

Atypical bone scintigraphy patterns in a child with acute lymphoblastic leukaemia: A case report
K.M.C. Dela Cruz, T.N.B. Pascual, R.A.O. Conlu, V.P.O. Magboo

CLINICAL NON-PET OTHERS

Additional value of SPECT-CT in the diagnosis of primary hyperparathyroidism
M. Garcheva-Tsacheva, I. Kostadinova, N. Temelkova, G. Ganchev

Our impressions from application of SPECT-CT in patients with a suspicion of infection of joint prosthesis in comparison with those with combined method for leukocytes and bone marrow scintigraphy
I. Kostadinova

Leukocyte SPECT/CT for diagnosis of osteomyelitis in patients with diabetic foot
O. Lang, I. Kuníková

Strategy of bone metastases treatment in patients with impending cord compression or vertebral fractures: A pilot study
N. Rasulova, V. Lyubshin, K. Hwan Kim, F. Djalalov
123I-MIBG imaging cardiac autonomic neuropathy in the chronic Chagas cardiopathy


Whole body imaging with Lu[177]-EDTMP: Extended phase II clinical trial investigation of Lu[177]-EDTMP for the palliation of metastatic bone pain

C. Liu, X. Liu, Z. Luo, J.J. Zaknun

Adjuvant treatment with radioactive I-131 in malignant struma ovarii

M.F. Ben Slimene, I. Slim, I. El Bez, M. Ghzaiel

Value of SPECT/CT scintigraphy in the assessment of patients with Hyperparathyroidism

I. Slim, A. Mhiri, L. Zaabar, M.F. Ben Slimene

177 Lu-EDTMP for bone pain palliation in metastatic prostate and breast cancer: A phase II trial

X. Liu, C. Liu, H. Li, Z. Luoc, Y. Wang, J.J. Zaknun

Is there a correlation between peptide receptor radionuclide therapy associated hematological toxicity and spleen dose?

H. Kulkarni, V. Prasad, C. Schuchardt, R.P. Baum

Intra-arterial radioembolization with Y-90 for unresectable primary and metastatic liver tumours

N. Ozlem Kucuk, C. Soydal, S. Lacin, E. Ozkan, S. Bilgic

The prevention of sialadenitis post-therapy with I-131 in patients with thyroid cancer reduces the dose of radiation in the salivary glands

F.M. Quintero Alvarez, J.C. Ramirez Fontalvo, I.F. Vega Gonzalez, G.M. Camacho García

A multi-center prospective randomized study comparing Yttrium-90 Ibritumomab Tiuxetan (Zevalin) and high-dose BEAM chemotherapy (Z-BEAM) versus BEAM alone prior to autologous stem-cell transplantation in patients with aggressive lymphoma

A. Shimoni, I. Avivi, J. Rowe, M. Yeshurun, I. Levi, R. Or, P. Patachenko, A. Avigdor, A. Nagler, S.T. Zwas

SPECT bone scan limits

A. Guensi, M. Aitidir, H. Belfaik, M. Kebbou

Imaging cancer therapeutic Trastuzumab bound on breast cancer cells with 111In-Biotin-Bn-EDTA-Anti-Human IgG1 monoclonal antibodies followed by the injection of macroaggregated albumin-avidin conjugate chase

N. Watanabe, M. Yoshizumi, S. Tanada, Y. Sasaki
Phosphorus 32 (32 P) skin patch for the treatment of basal cell carcinoma
A. Malhotra, P. Gupta, U. Pandey, S. Saxena, M. Venkatesh, S. Gupta, P. Chaturvedi

Outcome of radioactive iodine therapy in hyperthyroid HIV positive patients
Z.M. Jawa

RADIOPHARMACY PET

Automated synthesis and quality control of apoptosis PET probe -18F-ML-10 with multipurpose platform
C. Gameiro-Paris, B. Lambert, C. Sauvage, D. Caron

Optimized production of beyond FDG 18F-labelled radiopharmaceuticals with automated platform
C. Gameiro, B. Lambert, J.J. Cavelier, C. Sauvage

Building a radiopharmaceutical cyclotron production center from greenfield
J.M. Geets, D. Blampain, C. Gameiro

Doubling the current on IBA PET cyclotrons and other enhancements
J.M. Geets, E. Kral, M. Ghyoot

Current status of PET radionuclides and radiopharmaceuticals production in Iran
A. R. Jalilian, M. Ghannadi-Maragheh

A fully automated radiosynthesis of 4-[F-18]fluorobenzaldehyde: A synthon for amine-oxy peptide labeling
S.K. Nandy, M.G.R. Rajan

A simple fully automated one-pot synthesis of 3′-deoxy-3′-[F-18]fluorothymidine
S.K. Nandy, M.G.R. Rajan

A single column purification technique for the fully automated radiosynthesis of [F-18]fluoroacetate: A potential acetate analog for prostate tumor imaging
S.K. Nandy, M.G.R. Rajan

A single column purification technique for the fully automated radiosynthesis of [F-18]ethyl fluoroacetate([F-18]EFA) as a proradiotracer of [F-18]Fluoroacetate([F-18]FA) for the measurement of glial metabolism by PET
S.K. Nandy, M.G.R. Rajan

[18F]-FLT purification by SPE method in a fully automated synthesis procedure using a commercial synthesizer
A. Speranza, S. Del Vecchio, B. Alfano, L. Pace, M. Salvatore
Preclinical evaluation of fluorine-18 labelled bombesin peptide analogs as potential PET radiopharmaceuticals for breast cancer imaging
I. Al-Jammaz, B. Al-Otaibi, S. Amer, J. Amartey, M. Subhani

Development of a novel Ge-68/Ga-68 generator for biomedical applications
A. Dash, R. Chakravarty, M. Venkatesh

Validation of the nano-ceria-polyacrylonitrile composite based Ge-68/Ga-68 generator for the routine clinical preparation of Ga-68-DOTA-TATE
R. Chakravarty, T. Das, A. Dash, M. Venkatesh

High yield reliable automated system for the production of 18F-choline

RADIOPHARMACY NON-PET

The quality control of 99Tcm-MAG3 radiopharmaceutical
T. Teixeira Guimarães, A. Bordim, M. de Souza Albernaz, R. Santos-Oliveira

Nanoradiopharmaceuticals for nuclear medicine

Quality control of labeled MDP-99mTc with different chromatographic systems
S. Malja, B. Daci, K. Schomaecker, M. Alikaj

Comparative evaluation of chromatographic methods for radiochemical purity control of 99-Mo generator eluate
B. Daci, S. Malja, K. Schomaecker, M. Alikaj

Good radiopharmacy practice in the preparation of radiopharmaceuticals: A practical implementation
M. De Marco, S. Maggi

TAEK proton accelerator facility and radiopharmaceuticals production
S. Ozvatani, A. Tanrikut, S. Unal, A.N. Yuksel

Design and building of the first hospital radiopharmacy with USP and GRPhP standard in Colombia
N. Delgado, A. De los Reyes, F. Arguelles, C. Villamil, J. Rada, O. Juan
INSTRUMENTATION AND QUALITY CONTROL

IAEA-CN-185/151........................................................................................................ 259
Use of a novel acquisition strategy to facilitate respiratory motion correction and
evaluation of potential impact in lung SPECT
M. Núñez, F. Mut, J. Cánepa, K. Erlandsson, O. Alonso, B. Hutton
IAEA-CN-185/189........................................................................................................ 261
GE Discovery 690 performance reference tests
A.T. Garcez, D. Yanikian Nersissian, C. Chow Robilotta
IAEA-CN-185/222........................................................................................................ 263
Implementation of quality assurance programme (QAP) in PET centre in Malaysia
A.H. Ng, Z. Kayun Farni, B. Sapiin, H.S. Soh
IAEA-CN-185/223........................................................................................................ 264
The importance of having a quality control program for a hybrid equipment
SPECT-CT, considering the financial cost and the equipment downtime
M.R. Herrera Rodríguez, X. López Rendón, H. Vera Hermosillo, S.L. Soto
Gutiérrez
IAEA-CN-185/224........................................................................................................ 265
Development of low-cost phantom for Positron Emission Tomography-Computed
Tomography (PET-CT) performance tests
H.S. Soh, A.H. Ng
IAEA-CN-185/237........................................................................................................ 266
An overview of the installation project of a SPECT/CT (BrightView XCT) in
Malaysia
A. Mohd Zain, S.A. Sarji, A. Mohamed, K.H. Ng, S.Z. Ismail, N.K. Taharim, A.S.
Ahmad Sobri, Y.K. Loong, L.Y. Ping
IAEA-CN-185/323........................................................................................................ 268
Measurement methods and realization of PET/CT image fusion accuracy
J. An, B. Yue
IAEA-CN-185/324........................................................................................................ 269
Quality management and artifact recognition of PET/CT in oncology
S. Chen

EDUCATION AND TRAINING

IAEA-CN-185/136........................................................................................................ 271
Planning and education of a multidisciplinary team to implement PET/CT in Peru
R. Morales, R. Cano Pérez
IAEA-CN-185/167........................................................................................................ 272
Biomedical imaging in the era of molecular medicine: PET-CT versus alternate
clinical modalities
F. Berger, M.F. Reiser
IAEA-CN-185/182........................................................................................................ 274
A tool to facilitate collaboration and training in nuclear medicine for Latin
America
C.L. Vetere, P.R. Gomiz, J.C. Furnari
IAEA-CN-185/257........................................................................................................ 277
Setting-up and implementing a nuclear medicine specialty training programme
in a service hospital and university set-up: Experience from Malaysia
M.A. Abdul Khader, F. Hamzah, S. Ibrahim Ludfi, W.A. Wan Kamil

xx
PLANNING/ESTABLISHING/EXPERIENCES PET CENTRES

IAEA-CN-185/140........................................................................................................ 279
Survey on the use of SPECT-CT and PET-CT devices in Finland in 2011
N. Rauhala, J. Niemelä, H. Korpela, R. Bly
IAEA-CN-185/145........................................................................................................ 280
Improving diagnostic accuracy in molecular nuclear medicine in Ghana
F. Hasford, E.K. Nani, J.H. Amausi
IAEA-CN-185/169........................................................................................................ 281
How to make PET-CT feasible in countries with limited economic resources:
Estonian experience
S. Nazarenko, A. Samarin, L. Karusoo, R. Brand, I. Muoni, M. Paris
IAEA-CN-185/171........................................................................................................ 283
FDG-PET/CT and mediastinoscopy in mediastinal staging of lung cancer: Case
report
L. Karusoo, A. Samarin, R. Brand, I. Muoni, M. Paris, S. Nazarenko
IAEA-CN-185/174........................................................................................................ 284
Implementing a hospital radiopharmacy in the Urugayan centre of Molecular
Imaging
J. Giglio Barossi, V. Trindade, L. Reyes, E. Valsiskis, P. Oliver, H. Engler, H.
Balter, E. Savio
IAEA-CN-185/179........................................................................................................ 285
Challenges in establishing PET/CT-cyclotron facility in a developing country-
Bangladesh experience
M.F. Kabir, K. Afroj, N. Islam, M.N. Hossain
IAEA-CN-185/183........................................................................................................ 286
The National Cancer Program of Belarus to increase capacity for oncology:
Barriers to implementation of new technologies in radiation oncology
E. Slobina, N.N. Alexandrov
IAEA-CN-185/206........................................................................................................ 287
Current status and perspectives of clinical PET in Korea
H.S. Bom
IAEA-CN-185/226........................................................................................................ 288
Over one decade of experience in PET imaging at KFSH&RC-Riyadh, Saudi
Arabia
A.A. Al-Sugair
IAEA-CN-185/269........................................................................................................ 289
Nuclear Cardiology in Tajikistan
A. Dustov
IAEA-CN-185/274........................................................................................................ 290
The experience of establishment of first PET/CT Centre in Kazakhstan
G.K. Kanafin, Y.A. Akhmetov, T.R. Konurbayev, Y.N. Ilin
IAEA-CN-185/277........................................................................................................ 291
Tumour markers investigation in every-day practice of reproductive health clinic
in Kazakhstan
N.V. Kravtsova, J.A. Utesheva
IAEA-CN-185/284........................................................................................................ 292
Reflection on the challenges of establishing PET in emerging countries
F.I. Peer

xxi
Challenges of licensing on clinical PET and molecular Nuclear Medicine in Indonesia
Z. Arifin

The impact of the establishment of the first nuclear medicine centre in Yemen in 2008: The challenges and its effect on medical management, treatment and outcomes
F. Mohammed, S. Asa'ad

Medical cyclotron project at the National Cancer Institute in Bogota Colombia: A successful partnership with the IAEA
A. De los Reyes, A. Llamas-Olier

Implementation of hybrid imaging in Morocco
N. Ben Raïs, H. Guerrouj, R. Ouboukdir, I. Ghfir

Modern technologies of logistics network creation for short-lived isotopes
C. Artner, A. Zipper, M. Nader

DOSIMETRY AND RADIATION SAFETY

Internal dosimetry hyperthyroid patients by quantification in live: Method of images conjugated
A.J. Cárdenas Solano

Radiation dose to the personnel handling 18F-FDG and dose reduction methods
P. Tandon, M. Venkatesh, S.A. Hussain

Practical radiation safety issues for ensuring safe working environment in a high volume PET Center in India
A. Gupta, P. Sharma, S. Tayal, R. Sengupta, P.S. Choudhury

Medical Physicist role for a nuclear medicine building project at “Hospital Regional de Alta Especialidad de Oaxaca” according to Mexican regulatory Agency and IAEA Human Health Reports No. 1, (2010)
F.E. Trujillo Zamudio

Extremity dosimetry in Nuclear Medicine: Results of the ORAMED collaboration

Measuring through the noise: Using Mean Raw Pixel counts to characterize the SUV’s bias on differing count statistics encountered in gating scenarios
A.L. Kesner, N.C. FreedmaN
Estimation of the effective radiation dose from Nuclear Medicine procedures in children and from SPECT/CT and PET/CT studies in the general population
C. Salgado-Garcia, F. Carrera-Magariño, A. Jiménez-Heffernan

Evaluation of patient radiation dose during Nuclear Medicine investigations at Dr.M.Djamil Hospital- Padang- Indonesia
A. Elliyanti, Y. Fitri, P.T. Wahyuni, E.Y. Mailinatri

Presentation of a practical tool for shielding calculation in PET/CT facilities
M.A. Arciniegas Alvarez, H. Alejo Martínez, C.A. de los Reyes

Measurement of radiation exposure in relatives of thyroid cancer patients in 131I treatment
CLINICAL PET ONCOLOGY
Feasibility of biopsy guided by FDG-PET/CT in oncological patients

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Aim: When implying institution of therapy, FDG-PET/CT positive results should be confirmed by histology whenever possible. We evaluated the feasibility of percutaneous PET/CT-guided biopsies to histological confirmation of PET/CT positive lesions.

Methods: We prospectively evaluated 20 patients who underwent PET/CT with positive results with indication of histological evaluation of lesions by the referring physician. Imaging was performed in a PET/CT scanner with 16 slices and a CT fluoroscopic imaging system. A total of 21 lesions were accessed by PET/CT-guided biopsy. Technical feasibility and clinical success rates of PET/CT-guided biopsies were evaluated.

Results: Patients with FDG-PET/CT suspected lesions of lymphoma, melanoma, breast cancer and non-small cell lung cancer were admitted for biopsy guided by FDG-PET/CT. PET/CT positive lesions were successfully accessed and representative tissue samples were obtained in all 21 lesions. No major complications or adverse effects occurred. In eight patients (38.0%) the metabolic information of PET was considered crucial in defining the location of the biopsy, four patients had only increased metabolism identified by PET, with no corresponding anatomic lesion on CT. Of the 21 lesions biopsied, histology showed that 16 (76.2%) were tumours while five (23.8%) lesion were benign (inflammatory cells or necrotic tissue). These five patients had no recurrence of disease on the follow-up period averaging six months.

Conclusion: PET-CT guided biopsy is feasible and may optimize the diagnostic yield of imaging guided interventions. Also, PET/CT positive lesions with no morphological correlation may now be accessible to percutaneous interventions.
Importance of 18F-FDG PET/CT imaging in patients with lymphoma and residual CT mass after treatment

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In up to 60% of patients with lymphoma the residual mass on computed tomography is present after treatment or during the course of treatment. Only 20% of these residual tissues are reported to be positive for lymphoma on biopsy. Differentiation of post-therapeutic scar tissue from active lymphoma is difficult with morphological imaging such as computed tomography (CT) or magnetic resonance imaging. On the other hand, it has been proven that 18F-FDG uptake in lymphoma tissue predicts therapeutic response during the course of treatment or after completion of therapy. The purpose of this study was to evaluate our first 18F-FDG PET/CT results in lymphoma patients with residual radiological abnormalities during or after completion of therapy and to determine its impact on further therapeutic management. Fifty-seven patients, 38 females, mean age 31±9 years, with lymphoma (35 with Hodgkin lymphoma –HL, and 22 with Non-HL: 15 diffuse large B-cell NHL and 7 follicular NHL) and residual tumor mass on CT underwent whole body 18F-FDG PET/CT for post therapy assessment (chemotherapy and/or radiotherapy and/or stem cell transplant) or early during chemotherapy (12 patients). Whole body PET/CT was performed 60 minutes after iv. injection of 370MBg of 18F-FDG, on PET/CT, 64 slices, Siemens, Biograph scanner. According to 18F-FDG uptake in residual mass the patients were divided in three groups: group I with no uptake – 35 patients, group II with low and/or partial uptake in residual mass (10 patients) and group III with enhanced 18F-FDG uptake in residual mass or distant involvement (12 patients). In group I, despite residual mass present on CT, patients were proved to be in remission without need for further treatment. In group II, 6 patients showed improvement early during the course of therapy, suggesting good therapy results after completion of the therapy, while in the remaining 4 patients studied, the completion of therapy reduction of tumor was achieved and FDG uptake was low but still present with mean standardized uptake value (SUVmax) 3.6±1.4. In these patients autologous stem-cell transplantation was planned. In group III all 10 patients had high 18F-FDG uptake with SUVmax (mean 13.2±4.0, ranging from 6.51 to 19.6) in the residual tumor mass or other distant involvement with clinical and radiologic relapse. In 4 patients autologous stem-cell transplantation was considered on the basis of 18F-FDG PET/CT finding of distant metastatic involvement. In other patients from this group 18F-FDG PET/CT finding confirmed that the therapy was ineffective and that another therapeutic approach is needed. Our first results indicate that 18F-FDG PET/CT helps in management of lymphoma patients with residual mass not only at the end of therapy, but also early in the course of therapy.
PET/CT in diagnosis of metastases and recurrences of colorectal carcinomas

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The aim of the study was the assessment of recurrences and metastases of colorectal carcinomas using 18FDG PET/CT. The total of 56 patients was investigated, 30 males and 26 females, mean age 52.2±5.7 years. Investigation was performed with PET/CT, 64 slices, Siemens, Biograph, during 25 min, started 45 min after i.v. application of 10 mCi 18FDG. All the patients were suspected of having recurrent or metastatic lesions, according to tumour marker (CEA and Ca 19-9) levels, physical examination, a clinical imaging work-up and endoscopy. The gold standard was clinical and imaging follow-up for at least 6 months, surgery, or biopsy. In 37/56 patients with recurrences, findings were true positive (TP), in 15/56 findings were true negative (TN), in 2/56 findings were false positive (FP) while in 2/56 findings were false negative (FN). In 2/56 FP finding was due to local inflammation on the region of anastomosis (both patients were investigated < 8 months after surgery), while in 2/56 FN findings, radiopharmaceutical was not taken by the tumour tissue (mixed tumours with the high mucin level). Sensitivity was 95% specificity was 88%, positive predictive value was 95%, negative predictive value was 88%, and accuracy 93%. PET/CT finding contributed to the patient management in 32 patients. FDG PET/CT is a valuable tool for diagnosis, staging and follow-up of metastases and recurrences of colorectal carcinoma, especially to distinguish recurrence or metastases from postoperative changes or other benign lesions in postoperative colorectal cancer and radiologically or clinically suspicious lesions.
Pitfalls encountered in 1500 hybrid PET/CT studies

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Aim: Report pitfalls encountered that should be taken into account when reading PET/CT scans.

Materials and Methods: The population studied consisted of 1500 cancer patients. Data was registered from a Philips PET/CT Brilliance, with MDCT 16 files, 3D. Patients were given 20mg of beta-blockers (BB) if young and thin, others benzodiazepines and all had glycaemic control. Among the derived patients were Hodgkin, non-Hodgkin Lymphoma, lung cancer, melanoma, colon cancer, thyroid, tongue, bladder, unknown primary, carcinoid, kidney, FUO and ovary for staging, re-staging and for therapeutic response evaluation. Metabolically active distributions were also registered at 2hs post FDG-F18 when required.

Results: Focal FDG-F18 uptake was seen in thoracic soft tissue of a melanoma patient (Figure 1), due to inflammatory vaccine response. High bone marrow signal correlated with colony stimulant injections, chemotherapy and radiotherapy. Brown fat visualization in a young thin woman obliged to repeat the PET scan which became negative with a higher BB dose plus the appliance of a localized electric blanket (see Figure 2-a,b). Known myocardial compromise was seen with high fatty diets and oral administration of caffeine. Wall bladder lesion required late acquisition post-intravenous diuretic injection. Peri-prosthetic aseptic loosening observed as discontinuous uptake, while isquemic cerebrovascular accidents were hypo metabolic. We reported positive findings in esophagitis, sinusitis, vocal cord paralysis, uterine fibroids, inguinal herniation with colonic or bladder contents and musculoskeletal contractions (Figure 3). SUVmax usually increased in late scans confirming suspected malignant process. Technologists should be careful when filling patient’s acquisition parameters which affect SUV calculation (weight, height, activity, time of injection).

Conclusions: We conclude that it is of utmost importance to obtain a detailed patient’s history (inflammatory, infective, granulomatous findings), and to ensure optimal technical preparation before PET/CT scan and always take into account physiological and non-physiological causes of probable uptake in order to optimize the scan interpretation.
FIG. 1. Nodal soft tissue FDG-F18 uptake, due to intradermal TBC vaccine injections in a melanoma patient with SUV 5.5 (fused image). Initial melanoma lesion on the left thigh was surgically removed.
FIG. 2. (a, b) a) Young, thin patient with Lymphoma. In the whole body image, high FDG-F-18 uptake is observed in brown fat distribution. b) Note absence of brown fat in the repeated scan, two days later.

FIG. 3. Diffuse FDG-F18 uptake in left arm due to musculoskeletal contraction. Low back spinal muscle contraction is also seen.
Introduction: Breast cancer is the most common cancer in women and the second most common cause of death after lung cancer. By correct staging and appropriate treatment we can achieve better survival and improve quality of life. In this study results of initial staging FDG PET/CT of recently diagnosed breast cancer patients were analysed.

Methods: A total of 103 female breast cancer patients who were diagnosed by biopsy or surgery and underwent initial staging PET/CT study between July 2008 and July 2010 were retrospectively investigated. Based on the medical and PET/CT reports, findings of operation site, primary tumour, lymph node status (axillary/extra-axillary) and distant organ involvement were analysed.

Results: 103 female breast cancer patients [mean age: 56.2 ± 13.6 years (25-88 years), mean tumour size: 31.3 ± 19.2 mm (range 2-115mm.), 80% ductal typed] were included. Diagnosis was performed by MRM (60%) or biopsy (40%, tru-cut or excisional). Overall, 61 cases (59%) had at least one FDG positive finding for malignancy. None of the mastectomized patients had malignant foci at the operation site. In axillary dissection group, 31 cases had axillary nodal involvement and PET/CT showed residual nodal diseases in 5 of these cases. In cases diagnosed by biopsy, PET/CT showed malignant focus at primary tumour in 90% and lymph node positivity in 53% of these patients. Extra-axillary lymph node involvement was present in 26 of 103 (25%) patients. Of these cases 69% had locoregional (supraclavicular and parasternal, 42% and 35%, respectively) and 54% had non-locoregional lymphatic diseases (mediastinal, cervical, anterior diaphragmatic and abdominal lymph node metastases, 42%, 15%, 4% and 4% respectively). Distant organ metastases detected in 35 cases and 51% of them had multiple organ involvement and the remaining 49% had single organ metastasis.

Conclusion: Initial staging FDG PET/CT study showed positive findings for malignancy in more than half of the cases. PET/CT is useful in management of recently diagnosed breast cancer patients by showing axillary residual disease in the operated group, by determining primary mass with high sensitivity in the biopsied group and by showing nodal and distant metastasis in both groups.
Morpho-metabolical changes at the operation site in recently mastectomized patients: Impact of staging FDG PET/CT

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Introduction: Due to FDG not being a tumour specific agent, in some situations, postoperative inflammation may decrease the diagnostic performance of oncological PET studies. The aim of this study was to define postoperative morphometabolic changes according to initial staging PET/CT.

Methods: A total of 61 female breast cancer patients who recently underwent modified radical mastectomy (MRM) and initial staging PET/CT were retrospectively investigated. After observing the medical record and PET/CT image analysis, morphometabolic changes at operation site were described and its relationship with postoperative period was evaluated.

Results: 61 female patients [mean age of 56.11± 14 years (range 25-88)] underwent MRM with axillary sampling (SLN biopsy and/or curettage) were included. CT images showed thickening of skin in anterior chest wall and increased density at subcutaneous fat tissue without a mass formation at operation site (anterior chest wall and axilla) in all cases. In 34 cases (55.6%) CT images showed fluid collection (hematoma or seroma) in operation site. For our group PET showed mild to moderate increased asymmetrical FDG uptake [average SUVmax: 2.67±0.77 (1.3 – 4.8)] at the operation site (except in fluid collection area) with no distinct focus. Mean postoperative time was 25.52±14.3 (6-90) days. Statistically significant inverse relationship between postoperative period and FDG uptake levels (r: -0.33, p: 0.01) was shown by linear regression analysis. Average SUVmax values were over critical threshold value (SUVmax> 2.5) in the first 30 days after surgery [first 15 days (n: 19) mean SUVmax: 3.1±0.9, 15-30 days (n: 30) mean SUVmax: 2.6±0.7] and it decreased to 2.2±0.5 (n:12) after 30 days (nonparametric ANOVA, p:0.0132).

Conclusion: Diffuse mild to moderate asymmetric increased metabolism with thickening of skin and increased density in subcutaneous fat tissue at operation site was observed in all recently operated breast cancer patients. Approximately in half of the cases hypometabolic fluid collections were detected. During the first month of surgery, asymmetric hypermetabolism over the critical threshold was observed at operation site and it declined over time.
Synchronous metastases in recently diagnosed breast cancer: Role of staging FDG PET/CT

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Introduction: Breast cancer is the most common cancer in women. Demonstration of distant metastasis at time of diagnosis is important in determining management of patient and prognosis. In this study we aimed to investigate the role of staging FDG PET/CT in newly diagnosed breast cancer patients, and to analyse the relationship between the stage of the disease and synchronous metastasis patterns.

Methods: In this study, a total of 103 recently diagnosed (biopsy or surgery) female breast cancer patients who had undergone initial staging PET/CT were retrospectively analysed. All medical and PET/CT reports of patients were examined and distant organ metastasis patterns were determined.

Results: 103 patients with a mean age of 56.2 ± 13.6 years (25-88 years) were included in this study. Distant organ metastasis was detected in 35 cases (34%). Of these cases, in 51% (18/35) had multiple and 49% had single organ metastasis patterns (solitary or multiple). In our group, metastasis was most commonly found in the skeleton (69%), the other organs were non-locoregional lymph nodes (40%), liver (26%), lung (20%), adrenal glands (11%), pleura (11%), soft tissue (muscle and subcutaneous fat tissue) (9%) and thyroid gland (9%). In patients with single organ involvement, metastasis was mostly in the skeleton (59%). Others were in the mediastinal lymph nodes (18%), liver (12%), adrenal glands (6%) and thyroid gland (6%). Non loco-regional distant lymph node metastasis was observed in 14 (14%) patients. Of these cases, involved lymphatic stations were mediastinal (79%), cervical (29%), anterior diaphragmatic (7%) and abdominal lymphatics (7%). In the mastectomized group (n: 63) distant metastases were observed in 27% of the cases. Rate of distant metastasis in these cases in accordance to the histopathological stage I, II and III were 0%, 16% and 34% respectively (p: 0.258). The frequency of detecting distant organ metastases were 45% in non-operated patients (n: 40) diagnosed by biopsy. In these cases, rate of distant metastases for clinical T1, T2, T3 and T4 tumour were 44%, 42%, 50% and 0% respectively (p: 0.517). Interestingly in the biopsy group, 4 cases (%10) had distant metastasis without any hot spot in the axillary region.

Conclusion: In one third of initial staging FDG PET/CT scans, single or multiple synchronous distant organ metastasis with similar frequencies were observed in patients with recently diagnosed breast cancer. Most commonly involved organs were skeleton and non-locoregional lymph nodes. Although it is not statistically significant, rate of synchronous metastasis had a tendency to increase with histopathological stage.
The value of FDG-PET/CT imaging in dermatomyositis as a paraneoplastic syndrome in malignancy suspicion


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Dermatomyositis (DRM) is a clinical syndrome of unknown cause involving the skeletal and myocardial muscles. Five basic diagnostic criteria of DRM are; symmetrical proximal muscle weakness, abnormal muscle biopsy, increased skeletal muscle enzymes, abnormal electromyography and typical skin findings with or without dysphagia and shortness of breath. The incidence of the disease is 1/1,000,000 in the population, and may be seen with various types of cancers as paraneoplastic syndrome. It is thought that in patients with malignancy, DRM develops due to a reaction against cancer cells, but the pathophysiology of DRM could not be fully explained yet.

FDG PET/CT has been extensively used in tumour imaging recently. Although the role of PET/CT in cancer screening is not well known, there are papers that recommended it as an alternative to conventional methods. In this case report, we aimed to underline the importance of FDG-PET/CT in cancer screening in DRM patients.

A 45-year-old male patient with symptoms of DRM as a paraneoplastic syndrome was admitted to the dermatology service. His diagnostic thoracic CT revealed nodular lesion located in the superior-posterior segment of the lower lobe of the right lung without any other pathology. FDG PET/CT imaging was planned for the metabolic characterization of this nodule. PET/CT demonstrated intense FDG uptake not only in the suspected pulmonary nodular lesion (Fig.1A), but also in multiple enlarged mediastinal lymph nodes (Fig.1B). Additionally symmetric hypermetabolism in the proximal muscles of the upper and the lower extremities was seen in maximum intensity projection images (Fig.1C) due to DRM which was later confirmed by muscular biopsy. Non-small cell lung cancer was verified by CT guided biopsy.

In DRM, various types of malignancies can be seen such as breast, uterine and ovarian cancers in women and lung, prostate and gastrointestinal cancers in men. Hematologic malignancies can be seen in both sexes. Previous reports discussed and concluded that the majority of connective tissue disease patients who developed cancer were diagnosed at an advanced stage and had poor survival rates. Additionally, the third most common cause of death in inflammatory myositis patients were found as malignancies. Cancer risk is greater than normal population in DRM patients and the risk is highest in the first year following the diagnosis. The rate of malignancy in DRM was found 9.4% and most of them were detected in the first year of observation. The recommended cancer screening in DRM patients includes CT of the thorax/abdomen in all patients, US of the pelvic region and mammography in women, US of testes in men under 50 years and colonoscopy in men and women over 50. In one study FDG PET/CT compared with conventional cancer screening methods in diagnosing occult malignant disease in patients with myositis and the authors found similar results.
Conclusion: In patients with DRM, one has to be careful of the probability of coexistence of cancer and thus further studies should be performed to detect malignancy. FDG-PET/CT seems to be a useful method for both cancer screening and revealing active involvement in this group of patients.

FIG. 1. PET/CT demonstrating intense FDG uptake not only in the suspected pulmonary nodular lesion (A), but also in multiple enlarged mediastinal lymph nodes (B). Additionally symmetric hypermetabolism in the proximal muscles of the upper and the lower extremities was seen in maximum intensity projection images (C) due to DRM which was later confirmed by muscular biopsy.
Radiological response evaluation of oncolytic virus treatment in patients with advanced cancer

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Evaluating the efficacy of oncolytic viruses for treatment of cancer is problematic as approaches developed for chemotherapeutics may be poorly applicable. Overall survival and quality of life are the most relevant end points. However, surrogate end points such as tumour imaging can be useful for product approval and for day-to-day treatment decisions. For example, continuing treatment would be most appealing in patients that benefit from it. Currently computer tomography (CT) is the most common method for radiological response evaluation. Yet, standard radiological criteria rely solely on tumour size and may thus not be able to capture potential responders as treatment related inflammation can enlarge tumours. Positron emission tomography (PET) measures metabolic activity and is emerging as a promising alternative for CT in the treatment of many types of tumours. In theory, metabolic criteria could be less susceptible to treatment related tumour swelling. Formal comparison of CT and PET imaging in the context of oncolytic virotherapy has not been conducted previously.

We collected retrospective imaging data from patients treated with oncolytic adenoviruses in a Finnish Medicines Agency approved Advanced Therapy Access Program. Radiological responses, assessed by CT (RECIST1.1), were compared to survival of patients (n=119) to evaluate the power of CT in predicting benefits from treatments. Patients with disease control (stable disease or better) in CT exhibit significantly extended survival and the positive predictive value of disease control with CT was 100\% for 200d survival. However, also a large proportion of patients with disease progression (according to RECIST1.1) seem to exhibit long survival and thus the sensitivity of CT was low.

In a test subgroup of 20 patients who were imaged with both diagnostic CT and [F18]-FDG-PET, CT responses (RECIST1.1), PET responses (PERCIST1.0), symptom relief, tumour markers and survival, were assessed. In general, PERCIST and RECIST were concordant, while disease control rates were higher in PERCIST. Using the training set of 20 patients, we evaluated which factors were best able to identify patients most likely to present extended survival and propose some small modifications to PERCIST to facilitate use with oncolytic viruses. The new PET criteria were used successfully to identify long-term survivors in 33 patients. Based on these results, PET is a routine procedure in the response evaluation of oncolytic virus therapy.
Introduction: Nephrourinary tumours have relatively low prevalence and they are less studied than other malignancies with glucidic metabolic imaging with fluorine deoxyglucose (FDG), in part due to the difficulties inherent to the presence of urinary tract activity. New therapies available for renal cancer increase the need for a reliable marker able to obtain a wide disease overview. Our goal was to recognize how FDG PET performs in renal and urothelial cancer patients.

Methods: Sixty cases corresponding to nephrourinary tumours were performed since 2003 with a dedicated Siemens Ecat Exact HR+ PET scanner. We analysed demographics and image concordance with anatomical data or biopsy, if available.

Group A: Forty-eight studies in 44 renal cancer patients, (55% of them hypernephromas and the rest other or not specified histology). Their mean age was 61 years; 64% males. They were studied for restaging in 92% and staging in the rest, all those with another prior or concomitant malignancy.

Group B: 17 studies in 16 urothelial cancer patients (81% of them bladder tumours, the rest in the upper tract or urethra). The mean age was 66 years; 75% males, mostly smokers; 2 patients presented with other synchronic cancer. The FDG indication corresponded to 35% for restaging, 35% for therapy control (mainly chemo and/or radiotherapy) and the resting 30%, for staging.

Results: In the whole group of patients, the median lapse between histological diagnosis and FDG performance was 15 months [range 0.5-188]. The mean FDG dose was 481±59 MBq and the plasmatic glucose level 97±12mg/dL.

Group A: Initially, 39% of the patients presented invasive, recidivated or disseminated disease. Seventeen out of 48 studies were positive for glucidic activity. One out of 4 staging cases with in situ renal tumour was positive for FDG as well as 4 cases with local/recidivated disease. Skeletal lesions present in 99m Tc-bone scan in 5 patients were also observed in 3 of them and new bone lesions were observed in 4 patients. The overall agreement between FDG and the rest of clinical antecedents was 77%, being 44% with positive concordance. New or non-suspected lesions were observed in 17% of the studies.

Group B: Initially, 50% of the patients presented invasive, recidivated or disseminated tumours. Eight out of sixteen studies were positive for glucidic activity. A staging case with in situ urethral tumour was positive as well as two cases with local disease; there were 3 cases with distant disease. The two cases with concomitant cancer had
hypermetabolic lesions related with their second in situ known malignancy. The overall agreement between FDG and other data was 94%, being 53% with positive concordance. New lesions were observed in 18% of the studies.

Conclusion: FDG PET is a tool that could be considered as helpful in the evaluation of renal and urothelial cancers, mainly for restaging and therapy control.
Diagnostic accuracy in detection and functional assessment of metastatic disease defines response adapted treatment and decision making strategies to ensure effective palliation, longer progression free survival and quality of life. The aim of the present study is to evaluate 18-F FDG PET-CT as a metabolic marker to monitor treatment, effect early treatment changes when indicated and most importantly its role in prognostication to predict outcome. 

57 women with an age range of 36-70 years (mean 52 years) previously treated for breast cancer, with suspected metastasis at presentation or on follow-up and having undergone at least 2 sequential studies between Jan 2008-April 2009 (114 studies in total) were included. Disease progression or follow-up of a minimum of 12 months were considered end points. 

Standard whole body PET-CT acquisition protocol, without IV contrast followed. Reporting was jointly done by a Nuclear Medicine Physician and diagnostic Radiologist in an integrated reporting format. Focal abnormal areas of metabolic activity (non-physiological) were taken as positive. Comparison of standardized uptake values (SUVmax), normalized to body weight was used for response evaluation. Bone pains, cough, lymphnodal enlargement, chest wall swelling or increasing tumour markers like CA15.3 were the main presenting complaints in 43/57 (76%) of cases. Based on the findings of a baseline study, patients were divided into two groups. 44/57 (77%) had evidence of metastatic disease mostly involving multiple organs (Group-I) Cytological confirmation was done from at least one accessible abnormal site.13/57 (23%) had no evidence of disease (Group-II). 

Mid treatment scan was performed predominantly post 3 cycles of chemotherapy (14% at other variable timings ) in Group-I & during the next visit in Group-II (4-6 months) Comparison with baseline scan was done in all cases and interval changes noted. Persistent metabolic activity in previously known sites of abnormalities was considered as residual disease. (< 50% fall in SUVmax). 29/44 (65%) had significant residual disease. Progression of disease was subsequently seen in all of them documented by additional PET-CT studies as and when required. Average time to progression was 4.8 months. 15/44 (34%) had complete or significant response. 11/15(73%) of these remained disease-free for an average period of 13 months. 4/15 (27%) had progression (1 stopped treatment after 3 cycles) with an average time to progression of 7 months. An average disease-free interval of 15 months was seen in Group II. Our results show that a mid-treatment PET-CT evaluation is the single most significant prognostic indicator for predicting outcome in metastatic disease. It is helpful in effecting treatment changes early thereby helping in developing individualized treatment strategies. Negative study is an indicator of longer disease-free survival.
Usefulness of FDG-PET in the evaluation of sarcomas from diverse origin

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Sarcomas are a relatively complex tumour entity regarding their classification, diagnosis and therapy, and the role of FDG in its evaluation is not well defined yet. Our goal was to assess PET FDG performance in sarcomas of diverse origin.

Methods: We included 152 studies performed with a dedicated Siemens system corresponding to 84 patients with diverse sarcomas. Age range: 2-82 years (23\% under 18); 56\% males. The classification was performed according to histology, clinical staging and also the indication for FDG. We compared the tracer uptake as reported originally with clinical, histological and concurrent anatomic images data if available, and calculated their agreement. Twenty-three patients have serial FDG scans with a mean of 2.8 studies; some of them with close metabolic follow-up only with FDG for chemo or radiotherapy, including intra-therapeutic images were excluded from the concordance analysis. New lesions reported as possibly malignant were also recorded.

Results: The most common sarcomas studied were musculoskeletal and then soft tissues. Only 2 patients have a non-related prior cancer (melanoma and non-Hodgkin lymphoma); we observed 2 germinal cancers in subjects with a prior seminoma and a non-seminoma; another presented hepatic metastasis of an undifferentiated sarcoma of unknown origin. Tumour surgery was present in 68\% of the studies (excluding biopsies); radio and chemotherapy in 47\% and 66\%, respectively. The mean time between sarcoma diagnosis and the FDG study was 23±31 months.

Table 1 shows the main findings; specifically, high concordance of FDG uptake with other available data and new possibly malignant unsuspected lesions in all subgroups.

Conclusions: We found, in this group of adults and children with sarcomas, that FDG PET is helpful for diagnosis, follow-up and therapy control, mainly in high-grade or those less differentiated tumours.
# TABLE 1:

<table>
<thead>
<tr>
<th>Patients (studies)</th>
<th>Age</th>
<th>Sex</th>
<th>Initially distant/local extension/recidivated</th>
<th>S/R/T</th>
<th>C</th>
<th>Positive FDG Result</th>
<th>Agreement FDG vs. available data</th>
<th>New FDG lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteosarcoma</td>
<td>27±11 [16-48]</td>
<td>84</td>
<td>7/12 (58%)</td>
<td>1/159</td>
<td>17/25</td>
<td>95% 15P+5N</td>
<td>8/25</td>
<td></td>
</tr>
<tr>
<td></td>
<td>23±14 [8-63]</td>
<td>77</td>
<td>9/14 (36%)</td>
<td>3/149</td>
<td>13/26</td>
<td>87% 11P+9N</td>
<td>6/26</td>
<td></td>
</tr>
<tr>
<td>Ewing's/PNET</td>
<td>36±24 [2-66]</td>
<td>77</td>
<td>7/14 (50%)</td>
<td>2/124</td>
<td>10/18</td>
<td>93% 7P+6N</td>
<td>6/18</td>
<td></td>
</tr>
<tr>
<td>M. Fibrous Histiocytoma/ Fibrosarcoma</td>
<td>13±14 [2-50]</td>
<td>72</td>
<td>69 (67%)</td>
<td>1/612</td>
<td>10/19</td>
<td>100% 5P+2N</td>
<td>5/19</td>
<td></td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>5±17 35-83</td>
<td>5/1</td>
<td>3/6 (50%)</td>
<td>2/52</td>
<td>5/9</td>
<td>100% 5P+2N</td>
<td>3/9</td>
<td></td>
</tr>
<tr>
<td>Liposarcoma</td>
<td>39±15 [23-61]</td>
<td>1/5</td>
<td>4/6 (67%)</td>
<td>0/51</td>
<td>4/7</td>
<td>86% 4P+2N</td>
<td>2/7</td>
<td></td>
</tr>
<tr>
<td>Chondro/synovial</td>
<td>41±13 [30-59]</td>
<td>3/2</td>
<td>4/5 (80%)</td>
<td>2/49</td>
<td>12/15</td>
<td>80% 7P+1N</td>
<td>8/15</td>
<td></td>
</tr>
<tr>
<td>Angiosarcoma</td>
<td>5±10 [46-73]</td>
<td>0/5</td>
<td>5/5 (100%)</td>
<td>2/30</td>
<td>5/6</td>
<td>100% 4P+1N</td>
<td>4/6</td>
<td></td>
</tr>
<tr>
<td>Uterine sarcoma</td>
<td>41±21 [19-71]</td>
<td>4/1</td>
<td>3/5 (60%)</td>
<td>2/97</td>
<td>12/18</td>
<td>90% 6P+3N</td>
<td>4/18</td>
<td></td>
</tr>
<tr>
<td>High-grade</td>
<td>55±19 [36-74]</td>
<td>1/2</td>
<td>2/3 (66%)</td>
<td>1/140</td>
<td>5/5</td>
<td>100% 3P0N</td>
<td>3/5</td>
<td></td>
</tr>
<tr>
<td>NOS Sarcoma</td>
<td>37±17 [23-65]</td>
<td>4/1</td>
<td>3/6 (60%)</td>
<td>1/14</td>
<td>26</td>
<td>100% 1P/3N</td>
<td>2/5</td>
<td></td>
</tr>
</tbody>
</table>

S: Staging; R: Restaging; TC: Therapy Control; NOS: No Other Specification
Evaluation of somatostatin receptors in prostate cancer lesions with Ga-68-DOTATATE PET-CT


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Aim: To evaluate DOTATATE-affine in vivo somatostatin receptor expression in advanced prostate cancer lesions using Ga-68-DOTATATE PET-CT.

Methods: We studied seven patients with advanced prostate cancer under hormone deprivation therapy who presented rising levels of PSA. All patients underwent bone scintigraphy with an average Tc-99m-MDP dose of 925 MBq, in a double-head, LFOV gamma camera. Within 3 weeks, a PET-CT study was performed with a mean Ga-68-DOTATATE dose of 90.7 MBq, using a 64-slice PET-CT with time-of-flight correction. The maximum SUV (SUVmax) was measured in the metastases and in normal bone and/or adjacent tissues. For focal lesions, the difference in SUVmax between the metastases and normal tissues was also calculated (ΔSUVmax).

Results: Four patients presented bone scans suggestive of metastatic disease (Group A). The bone scans of the remaining three cases were highly suspicious of benign non-specific pathology (Group B). PET visualized abnormal bone uptake areas in all patients of Group A: three with focal and one with diffuse tracer accumulation who also showed focal uptake in a normal sized pelvic lymph node. In two patients PET showed more lesions than bone scans: 28 vs. 24 lesions, respectively. Mean ΔSUVmax was 3.7 (range: 3.3-4.6; n=28). Group B patients did not present abnormal bone Ga-68-DOTATATE uptake. Bone lesions previously identified by bone scanning were defined as benign by means of CT. Besides, all 7 patients presented abnormal uptake in an enlarged prostate gland: mean ΔSUVmax of 5.9 (range: 3.5-6.8).

Conclusions: In advanced prostate cancer patients, Ga-68-DOTATATE PET-CT can identify DOTATATE-affine lesions expressing somatostatin receptors. More studies are needed in order to test for receptor-mediated therapies with appropriate ligands labelled with Y-90 and/or Lu-177.
Clinical study of 18F-FDG PET/CT in diagnosis and management of lung cancer

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Aim: To evaluate the clinical value of PET/CT in diagnosis, staging and monitor the response of lung cancer.

Materials and Methods: 209 patients were involved in the study of which 123 were pathologically proven, 86 of them clinically proven. Among those patients, 128 had lung nodules or masses, and 81 patients received different therapy. Radiotracer: 18F-FDG. Imaging instrument; Discovery LS PET/CT produced by the American company GE.

Results: 1) Differential diagnosis of SPN and masses: The sensitivity, specificity, accuracy, positive predictive value and negative predictive value were 97.92%, 93.75%, 96.88%, 97.92% and 93.75% for PET/CT; 94.68%, 53.13%, 84.13%, 85.58% and 77.27% for dual-modality scanner CT and 97.92%, 56.25%, 87.50%, 87.04% and 90.00% for PET, respectively. 2) PET/CT corrected (T) stage 9.6% for CT and 31.9% for PET; (N) stage (M) stage 36.2%, 31.9% for thoracic CT, and 29.8%, 10.6% for dual-modality CT, respectively. PET/CT could find 45.5% more lymph nodes involvement and 40.5% more distant metastases than dual-modality CT, 13.4% more distant metastases than PET, and confirm localization of sites of 12.0% with lymph node involvement and 28.2% with distant metastases on PET. 3) PET metabolizing images of 25% patients were inconsistent with the CT morphology, and PET/CT could give a clear judgment in 6% patients with pathological changes but CT was uncertain whether the lesion was due to the operation or radiotherapy or the tumours recurrence, etc. PET/CT detected more lymph node involvement (48.7%) and more distant metastases (31.6%) than CT. Moreover, it was also found that the primary tumour response of prior and post treatment was different by 60% among 40 patients between metabolism and anatomy imaging.

Conclusion: 1) PET/CT was more accurate than CT and PET in differentiating pulmonary benign diseases from malignant ones. 2) PET/CT significantly improved the accuracy of staging in lung cancer and this advantage translates into treatment plan change of the patient substantially. 3) PET/CT metabolizing and the anatomic modality images have proved that the change of the sizes of lesions is inconsistent with the metabolizing responses. Furthermore, PET/CT can perform better than CT in discovering new lesions.
Evaluation of 18F-FDOPA PET-CT and its comparison with 99mTc- GHA SPECT/CT in detection of recurrence in patients with high grade primary glioma

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Purpose of this study was to evaluate the role of 18F-FDOPA PET-CT (FDOPA) and its comparison with 99mTc- GHA SPECT/CT (GHA) in detecting recurrence in patients with high grade primary glioma. A total of 20 patients with histopathologically proven glioma of high grade tumours (WHO grade - GBM-14 patients and Grade III – 6 patients) were included in the study. All the patients received their primary treatment, had been treated with surgery, radiotherapy or both. They were referred from treating physicians for clinical suspicion of recurrence. They were evaluated using FDOPA and GHA. The images were interpreted positive for any abnormal tracer uptake noted in brain parenchyma. For FDOPA ratios of tumour uptake to normal tissue uptake were generated by dividing the tumour SUVmax by the SUVmax of the contralateral normal hemispheric brain tissue (T/N), the normal striatum (T/S), the normal white matter (T/W) and the normal cerebellum (T/C). For GHA to quantify the nature of uptake and to find out its correlation with outcome, lesion to background ratio (scalp, surrounding brain tissue, and nasopharynx) was determined. Final outcome was judged on the basis of biopsy report and/or clinical follow-up and serial MRI /MR spectroscopy imaging results. Fourteen patients were considered positive (death in 5, biopsy in 2, clinical progression in 6 and progression on imaging in 10) while 6 were negative for recurrence. When considering high grade tumours in general (GBM and Grade III glioma) sensitivity and specificity of FDOPA PET/CT are 100% & 100% respectively, whereas that’s 100% & 66.6% in GHA SPECT/CT. In GBM, sensitivity and specificity of FDOPA PET/CT are 100% & 100% respectively, whereas that’s 100% & 0% in GHA SPECT/CT. So FDOPA PET/CT had the highest sensitivity & specificity in GBM. Also it has the highest positive predictive value (100%), highest negative predictive value (100%) and highest diagnostic accuracy (100%). In Grade III glioma, both FDOPA PET/CT and GHA SPECT/CT had similar results with sensitivity and specificity of 100% and 100% respectively. So both FDOPA PET/CT and GHA SPECT/CT had comparable results in anaplastic gliomas, but this result cannot be extrapolated in general as the number of patients in this subgroup is less (six) in our study. Though both had good sensitivity, FDOPA was found to have excellent specificity. Also FDOPA has the highest positive predictive value (100% vs.87.5%) and highest diagnostic accuracy (100% vs. 90%). FDOPA was found to be superior in recurrence detection while GHA scores better than FDOPA only in tumour margin delineation for those tumours located adjacent to basal ganglia.
Role of 18F-FDG PET/CT in response evaluation of metastatic gastrointestinal stromal tumours to Imatinib Mesylate: Indian experience

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Introduction: Gastrointestinal stromal tumour (GIST) is the most frequent mesenchymal malignancy of the gastrointestinal tract. In patients with localized disease, surgery is the mainstay of treatment. Unresectable or metastatic GISTs exhibit a dynamic clinical course, with no evidence of benefit from any standard cytotoxic chemotherapy and an inevitably fatal outcome. After the introduction of Imatinib mesylate, inhibitor of the KIT receptor tyrosine kinase, several studies have demonstrated the effective use of adjuvant treatment with Imatinib mesylate for unresectable, metastatic or recurrent gastrointestinal stromal tumours (GIST).

Aims: We evaluated the role of 18F-FDG PET/CT for assessing response to imatinib mesylate therapy in patients with metastatic GIST.

Materials and Methods: Sixteen consecutive patients with metastatic GIST confirmed by surgery (with primary from stomach 6, small bowel 8 and rectum 2) underwent 18F-FDG PET/CT imaging before and after beginning imatinib mesylate therapy (400 mg/day). PET/CT study was acquired 60-90 minutes after the intravenous injection of 333-707 MBq of 18F-FDG. Visual and semi-quantitative (standardized uptake value [SUV]) analysis of images was performed. Response to therapy was assessed according to EORTC recommendations for PET. Complete resolution of 18F-FDG uptake within the tumour volume so that it was indistinguishable from surrounding normal tissue was considered as complete metabolic response (CMR). Reduction of a minimum of 15% + 25% in tumour 18F-FDG SUV after one cycle of chemotherapy, and >25% after more than one cycle of therapy was considered as partial metabolic response (PMR). Increase in tumour 18F-FDG SUV <25% or decrease < 15% and no visible increase in extent of 18F-FDG tumour uptake (20% in longest dimension) was considered as stable metabolic disease (SMD). Increase in 18F-FDG tumour SUV of >25% within tumour region defined on baseline scan; visible increase in extent of 18F-FDG tumour uptake (20% in longest dimension) or appearance of new 18F-FDG uptake in metastatic lesion was classified as progressive metabolic disease (PMD). Results were confirmed by clinical follow-up, contrast enhanced CT (CECT) findings and/or histopathology (when available).

Results: Out of 16 patients 10 were male and 6 females. The age range was from 43 to 57 years (mean age 48 years). Complete metabolic response to imatinib mesylate was observed in three patients. Partial metabolic response was noted in seven and stable metabolic disease in two patients. Four patient demonstrated progressive metabolic disease, two developed liver metastasis, one developed abdominal lymph nodal pathology and one had increase in size and uptake of tumour.

Conclusion: 18F-FDG PET/CT is a useful modality in evaluating the response to imatinib mesylate therapy in patients with metastatic GIST.
Application of PET/CT simulation in radiation planning at the nuclear medicine and oncology centre, Bach Mai Hospital, HANOI, Vietnam


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Introduction: Assessing exact tumour volume is the first goal in radiation oncology because any volumetric errors would affect treatment outcome. PET/CT is a combination of the two strongest imaging techniques: CT (anatomical) and PET (metabolic), so it could reveal a tumour earlier and more accurately than CT or PET alone. Using PET/CT for simulation in oncology radiation planning is especially valuable for patients with lesions that are indeterminate by CT criteria, or those with heterogeneous masses, or those whose clinical history is complicated due to previous malignancy.

Aim: To evaluate the advantages and disadvantages of this technique and to build a standard radiation planning protocol based on PET/CT simulation.

Material and Method: 56 cancer patients were randomly chosen to undergo both diagnostic and simulated PET/CT, by which a 3D CRT (three dimensional conformal radiation therapy) or an IMRT (Intensity modulated radiation therapy) was planned. Treatments have been conducted and followed in the Nuclear Medicine and Oncology Centre of Bach Mai Hospital, Hanoi, Vietnam from 9/2009 to 9/2010. Delineation in GTV-PET or BTV (Biological target volume) is based on an SUV (Standard uptake volume) threshold of 2.5.

Results: Locations of cancer that have been found include nasopharynx, hypopharynx, larynx, lung, oesophagus, and rectum. PET/CT found 26.8% additional lesions that CT missed, especially in the cases that involve small regional lymph nodes. All cases that cannot be distinguished by CT as tumour and benign tissue or atelectasis could be revealed by PET/CT. In our study, the primary results are promising and safe.

Conclusions: Application of PET/CT simulation can improve radiation planning. Additional well designed studies are needed to better understand long term impacts of treatment outcomes and to identify subgroups of patient which will benefit most from this technique.
Clinical utility of FDG PET/CT in patients with lymphoma

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Aim: The purpose of this study was to evaluate: 1) the role of FDG PET/CT in the response to treatment, and 2) the value of FDG PET/CT in the detection of the extent of disease necessary for initial treatment strategy in patients with lymphoma.

Patients and Methods: This study was performed in the Department of Nuclear Medicine, New York Presbyterian Hospital in New York City from July to August 2010. Thirty patients, diagnosed as lymphoma, underwent PET/CT: 15 women and 15 men, aged from 21 to 86 years, mean 52.2 years. PET/CT scintigraphy was performed on GE Discovery LS. Following at least four-hour fasting, the patients’ blood glucose was measured. One hour following the injection of 18-F-FDG, low dose CT images were obtained from the orbital meatal line through the pelvis. PET images were then obtained through the same region. Attenuation corrected images were constructed using the CT scan. Fused images of PET and CT were reviewed. Oral contrast was administered prior to imaging.

Results: The patients were divided in two groups: 12 patients who underwent this study aimed to evaluate for initial treatment strategy, and 18 patients who underwent this study for evaluating the treatment response. PET/CT detected in the first group of patients: lymphadenopathy in 5 patients; lymphadenopathy combined with liver or spleen involvement in 2 patients; normal finding (after lymph node extraction) in one patient; bone involvement in one patient; and lymphadenopathy combined with bone involvement in 3 patients. In the second group of patients, PET/CT detected: good response to treatment (no evidence of local or recurrent disease) in 4 patients; partial response to treatment (disease regression combined with persistent disease) in 3 patients; and no response to treatment (progression of disease) in 11 patients.

Conclusions: FDG PET-CT scintigraphy has a significant role in routine clinical practice with lymphoma patients. It is important to monitor the treatment response to enable a change of treatment course in the absence of treatment response. It is also helpful in the evaluation of disease extent and the decision making process.
Reliability of 18F-FDG PET/CT after 2 cycles of chemotherapy for prognosis prediction in patients with Non-Hodgkin lymphoma

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Aim: Several recent studies have demonstrated that early assessment of response during the first treatment cycles is important to appreciate chemosensitivity and may potentially guide further risk-adapted therapeutic strategies in aggressive lymphoma. Assessment of early response relies most often on visual analysis, which could be subjective to the dichotomous interpretation of an observer. The purpose of our study was to assess the prognostic value of interim 18F-FDG PET/CT after 2 cycles during first-line chemotherapy using standardized uptake value (SUV) semi-quantification in the group of patients (pts) with diffuse large B-cell (DLBCL) and follicular lymphoma (FL).

Methods: 50 consecutive patients, 27 M, 23 F, median age 52 years (range 28-70) with newly diagnosed and histologically proven DLBCL (38) and FL (12) were enrolled in the study. All patients underwent contrast enhanced 18F-FDG PET/CT examination before (PET/CT1) and after (PET/CT2) 2 cycles of chemotherapy (interim examination). After 6hrs fasting, blood glucose level determination (< 7 mM) and 60 min after in vitro administration of 400 MBq 18F-FDG/70 kg, 18F-FDG PET/CT images were performed using Biograph 16 HI-REZ in 3D mode from the base of the skull to the mid-thigh. Maximum SUV normalized to body surface area (SUVmax) was computed on the most intense uptake areas (graded colour-scaled parametric analysis applied in reconstructed coronal PET image) in accordance to standardly used formulas. The SUVmax changes overtime between PET/CT1 and PET/CT2 were used for prediction of patient prognosis. To evaluate the prognostic value of PET/CT2 examination, event-free survival (EFS) was chosen as an endpoint. EFS was defined as the date of enrolment to first evidence of progression, relapse, or death from any case. Data was censored if the patients were alive and free of progression or relapse at last follow-up.

Results: During a follow-up period, which was 11.7±12.4 months, 37 pts (74%) were in complete remission, whereas the remaining 13 pts (26%) relapsed, progressed or died. Median of SUVmax reduction in the group of 13 pts whose disease relapsed, progressed or who died was 53% (range 27-64) versus median of 83% (range 66-95) pts who remained free of disease. ROC analysis yielded an optimal cut-off value of 65.3% for predicting event free survival of pts after second cycle of chemotherapy. In case of SUVmax reduction ~ 65.3%, event free survival could be predicted with sensitivity, specificity, positive and negative predictive value and accuracy 86.5%, 61.5%, 96.5%, 61.5% and 80.0%, respectively.

Conclusions: Our findings indicate that SUVmax-based assessment of therapeutic response after second cycle during first line chemotherapy of patients with DLBCL and FL seems to have good prognostic value and is able to predict the risk of relapsed or progressive disease during the follow up with sufficient reliability. The optimal cut-off value for SUVmax reduction from baseline to interim examination for predicting EFS in our study was found to be 65.3%.
18F-FDG PET/CT under TSH stimulation in patients with differentiated thyroid carcinoma

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18F-FDG PET helps detect recurrence of differentiated papillary and follicular thyroid carcinoma in thyroidectomized patients with elevated thyroglobulin (Tg) levels and negative 131I whole-body scans. The aim of this study was to evaluate the diagnostic efficiency of thyrotropin (TSH)-stimulated 18F-FDG PET/CT scanning in these carcinomas, keeping in mind that TSH stimulates thyrocyte metabolism, Glut1 expression in thyroid cells, glucose trapping, and glycolysis.

Methods: A total of 63 patients with suspicion of recurrences or metastases of differentiated papillary and follicular thyroid carcinomas and negative 131I whole-body scans underwent thyrotropin (TSH)-stimulated contrast-enhanced 18F-FDG PET/CT (400 MBq 18F-FDG/70 kg body weight, TSH > 30 mU/L). The suspicion was based on elevated Tg level in 51 patients and on clinical signs (including ultrasonography) in 12 cases. Patients were subdivided into the following subgroups: Tg < 2 µg/L (12 patients), 2 µg/L < Tg < 10 µg/L (15), 10 µg/L < Tg < 100 µg/L (23), and 100 µg/L < Tg (13).

Results: Among the whole group of 63 patients, TSH-stimulated contrast-enhanced 18F-FDG PET/CT were positive in 35 patients - 33 true positive (52%), false positive 2(3%). 18F-FDG PET/CT correctly detected thyroid carcinoma mass in Tg-subgroups: < 2 µg/L - 4/12 patients (33%), 2 < Tg < 10 µg/L - 6/15 patients (40%), 10 µg/L < Tg < 100 µg/L - 13/23 patients (56,5%), and 100 µg/L < Tg - 10/13 patients (76,9%). The surgical removal of tumoral remnants was performed in 21 cases, 11 patients were considered as inoperable due to a metastatic spread of a tumour detected on PET/CT. Therapeutic strategy was changed according to TSH-stimulated contrast-enhanced 18F-FDG PET/CT in 21/63 patients (33%).

Conclusions: TSH-stimulated contrast-enhanced 18F-FDG PET/CT was an efficient diagnostic tool in this group of patients with significant impact on therapy. This study shows that PET/CT identified recurrences or metastases of differentiated thyroid carcinomas in the important part of patients with negative 131I whole-body scans and distinct elevation of Tg levels. The detection rate of recurrences is relatively low in persons with Tg < 10 µg/L or with only clinical suspicion of metastases, nevertheless the positive findings represent a significant part of these patients. Therefore, this series shows that one cannot determine the lower Tg limit to select patient candidates for TSH-stimulated contrast-enhanced 18F-FDG PET/CT examination to detect the recurrence of differentiated thyroid carcinoma.
Identification of cancer metastases using the combination of PET and viral vectors

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Cancer is a prevalent disease worldwide and a primary cause of mortality in the western world. There are three main ways for dissemination of solid tumours: direct invasion, lymphatic spread and hematogenic spread. The presence of metastases is the most significant factor in predicting prognosis and therefore evidence of metastases will influence the decision-making process regarding the treatment. The imaging modalities used in clinical practice for cancer staging include ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) scanning. These imaging techniques are limited in the evaluation and localization of metastases due to their restricted ability to identify sub-centimetre neoplastic disease. Hence, there is need for an effective non-invasive modality that can accurately identify occult metastases in cancer patients.

One such method is the combination of positron emission tomography with vectors designed for delivery of reporter genes into target cells. There are three main classes of reporter genes: receptors, transporters and enzymes. A membranous receptor, which is commonly used for imaging of endocrine cancers, is the somatostatin receptor (hSST\textsubscript{rs}). In the transporter group, the human norepinephrine transporter (hNET) transgene carried by a recombinant vaccinia virus (GLV-1h99) resulted in specific uptake of the radiotracer \[131\text{I}\]-meta-iodobenzylguanidine (MIBG) in orthotopic mesothelioma and pancreatic ductal carcinoma tumour models. In the enzyme group, the herpes simplex virus-1 thymidine kinase (HSV1-tk) gene and its mutation were extensively studied as candidate reporter genes for imaging of cancer.

Combination of HSV1-tk and PET imaging is based on the viruses of viral or non-viral vectors which can carry and selectively express the HSV1-tk reporter gene in a variety of cancer cells but not in normal cells. A radioactive tracer which is applied systemically is phosphorylated by the HSV1-tk enzyme, and as a consequence, the tracer accumulates in proportion to the level of HSV1-tk expression which can be imaged using PET.

In our studies we showed that the NV1023 herpes virus expressing the HSV-1-tk gene can track to draining lymph nodes following direct intratumoral injection and infect metastatic melanoma cells in the SLNs (sentinel lymph nodes). Nodal metastases can be then successfully identified by \[18\text{F}\]-2\textprime-\text{fluoro}-2\textprime-deoxy-1\textbeta-D-\textbeta-arabinofur anosyl-5-ethyluracil ([18F]FEAU) PET imaging (figure 2). In another animal model we demonstrated that this combined imaging system could also be used to allow in vivo imaging and detection of
cancerous neural invasion. Positron emission tomography with [18F] FEAU showed significantly higher uptake in neural invasion than in control animals.

These diagnostic paradigms introduce an advantageous new concept in non-invasive molecular imaging with the potential benefits for improving patient care by providing guidance for therapy to patients with risk of metastases.
PET/CT examinations with 68Ga -DOTATATE in neuroendocrine tumours - Characterization of physiological uptake in organs in diagnosis of primary tumours

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Introduction: Neuroendocrine tumours (NET) are a heterogeneous group of carcinomas which originate from the one kind of tissue. Most of these tumours are characterized by over expression of somatostatin (SST) receptors. 68Ga-DOTA-DPhe1, Tyr3-octreotate (68Ga-DOTATATE) is a somatostatin analogue that shows high affinity for somatostatin receptor subtype 2 (sst2) which is the most common presented on NET from GI tract. Novel techniques of PET/CT with 68Ga -DOTATATE open new diagnostic ways in the diagnosis of patients with NET. The knowledge of normal uptake patterns and potential pitfalls is necessary to interpretation of examinations. In disseminated NET the very important question is localizing of primary tumours.

The aim of the study was to define physiological uptake of 68Ga-DOTATATE and usefulness of this method in clinical diagnosis.

Method: 277 patients with disseminated NET were examined. Normal uptake calculation was done based on 164 examination preformed in 56 men and 119 women, with mean age 55 +/- 13.8 year referred to Nuclear Medicine Department. 58/277 (21%) patients were examined (24 men, 34 women; age range, 20-74 y; mean age +/- SD, 50.4 +/- 12.1 y for localization of primary tumours. Clinical history, previous imaging examinations and treatments were documented. PET imaging was performed on PET/CT scanner Biograph 64, 60-80 minutes post injection of 120-185 MBq of 68Ga -DOTA-TATE.

Results: The labelling yields in the range from 37.4 to 72.4% (median 61.6%) were obtained (calculated as percent of 68Ga-DOTATATE fraction radioactivity related to the radioactivity of eluate used for synthesis, no time correction). The biochemical purity after SPE purification was >99%. SUVmax (mean±standard deviation) was determined in: pituitary gland: 12±5, thyroid: 3 ±1.8, salivatory gland: 3.2± 1.8, normal liver: 6.5±2.2, spleen:18.7±6.5, adrenal: 10.8±6, kidney: 14.6±3.5. Additionally increasing uptake in processus uncinatus of pancreas was seen in 13 % of patients with SUV 7.1±2.5.

In the localization of primary tumours 68Ga -DOTATATE revealed 47/58 (81 %) primary foci. 6 foci were localized in lungs; retrospective analysis of CT revealed small nodule in the lung measuring 4-5 mm. 19 were observed in pancreas, only 3 were seen in CT. In intestine, PET/CT revealed 20 primary tumours, 14 localized in small intestine, 6 in colon; small
intestine polypus was seen only in 1 case in CT, thickening of wall was seen in colon in 2 cases. Additionally, primary tumours were seen in stomach - 1 patient and in pelvis - 1 patient, both seen in CT. Neither PET/CT with 68Ga -DOTATATE nor CT with contrast media found primary tumours in 11/58 (19%).

Conclusion: 68Ga -DOTATATE PET/CT is a useful non-invasive technique in the diagnosis of patients with NET in cases of unknown primary tumours. In our study 68Ga-DOTATATE PET/CT enables us to localize 80% of primary tumours site. Through the obtaining of 68Ga from germanium/gallium generators, procedures could be used in many PET centres without onsite cyclotron.
PET / CT with 11C-acetate in prostate cancer: Appropriate diagnostic tool

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Introduction: Molecular imaging in oncology has focused on the use of 18F-FDG PET, because many cancers are highly glycolytic even under aerobic conditions. However, in some malignancies such as prostate cancer, the degree of utilization of glycolytic metabolism as a pathway for energy production is limited. This problem diagnosis, has allowed the development of new tracers for the study of other metabolic pathways, such as the synthesis of amino acids or the synthesis of membrane lipids. It is known that prostate cancer has an increased rate of lipid metabolism for the synthesis of membrane, as well as energy synthesis through the citric acid route. In this context, the realization of molecular imaging through the use of 11C-acetate as substrate is useful in the assessment.

Aim: The present work is to present the initial experience of the institute.

Material and Methods: Patients with known diagnosis of prostate cancer in treatment with suspicion of recurrence due to elevation of PSA. We performed PET / CT whole body BIOGRAPHIC ® team SIEMENS 5mCi administered dose of 11C-acetate intravenously. We performed PET / CT whole body with equipment BIOGRAPHIC ® SIEMENS with administered dose of 5 mCi 11C-acetate intravenously

Results: All patients were abnormal areas of uptake of 11C-acetate and that correlate tomographically corresponded to regional lymph nodes of malignant aspect. In only one patient were found metastatic lesions, not lymph node (bone).

Conclusions: Despite the small number of patients on 11C-acetate is a promising radiotracer for the assessment of early-stage prostate cancer. Could be useful in patients not diagnosed with high suspicion and locate accurately the site of incipient neoplasia before anatomical changes occur therefore studies are needed to learn about all its possible applications.
Utility of 18 F-FDG PET-CT in the evaluation of orbital tumours

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Aim: To determine clinical utility of 18 F-FDG PET-CT in the evaluation of orbital tumours.

Material and Methods: This is a retrospective and descriptive study, a review of cases, performed at the nuclear medicine service of the Cancer Institute Mexico. In this study there were a total of 18 patients who had been referred to the ophthalmology department for orbital tumour diagnosis and had consequently undergone 18 FDG PET-CT.

Results: The predominant age range was 60 years and of the male gender. The most common tumour was choroidal melanoma, and was found in 7 patients. 13 patients showed ocular hypermetabolism also besides anatomical ocular injury. The average SUV was 3.3. 6 patients had distant metastases demonstrated through the PET CT, 4 patients developed cervical lymph node involvement outside the region, 2 with mediastinal lymph node involvement and 1 with distant disease at the liver, lung and diaphragm in a patient and the primary diagnoses were orbital in 2 patients MALT lymphoma, 2 choroidal melanoma, 1 with squamous cell carcinoma of conjunctiva and eyelid basal cell 1. Through PET-CT, a second primary thyroid malignancy was discovered in a patient with choroidal melanoma.

Conclusion: The 18 FDG PET-CT provides useful information in patients with orbital tumours, particularly T-type mucosa-associated lymphoma (MALT) and epidermiode carcinoma of the conjunctiva, and through PET CT, local disease, lymph node invasion and distant metastases were shown. In the staging of choroidal melanoma mediastinal lymphatic invasion was observed in 2 patients, excluding distant metastases and lymph node in most patients.
Diagnostic and prognostic value of 18F-FDG PET/CT on cancer of unknown primary

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Aim: The aim of this study was to evaluate the role of whole body 18F-FDG PET/CT on the detection of the primary tumour in patients with cancer of unknown primary (CUP). The prognostic value of 18F-FDG PET/CT findings was also evaluated.

Methods: We retrospectively analysed all the patients who have performed an 18F-FDG PET/CT for CPU in our institution (40 patients - 25 men and 15 women). All of these patients had histological evidence of metastasis of unknown origin, with clinical and complementary exams (CT, MRI, endoscopic techniques, ecography) negatives or inconclusive evidence for the primary tumour. The detection rate of the primary tumour was determined according to the final pathological result or clinical follow up. Median follow-up duration of all the patients was 8, 3 months (range: 2-30 months). Overall patient’s survival was evaluated to determine the prognostic value of 18F-FDG PET/CT findings.

Results: Considering the 18F-FDG PET/CT results for the primary tumour detection: the scan was able to correctly identify the primary tumour in 14 patients (35%; 14/40) – lung (n=6), pancreas (n=2), salivary glands (n=3), breast (n=1), colon (n=1) and ovary (n=1); in 8 (20%; 8/40) positive scans the primary tumour was never confirmed by pathological results or clinical follow up; 2 positive scans were false positive for a hyperplasic colonic adenoma and an endometriosis pelvic focus, respectively; in 15 patients the scan was negative (40%; 16/40) and the primary tumour was never identified; 1 negative scan was a false negative for an oesophageal tumour, detected less than one month after the 18F-FDG PET/CT scan. Considering 18F-FDG PET/CT results for metastasis detection: in 21 patients further metastasis were found - (M) distant metastasis (n=11), (N) ganglionar metastasis (n=5) and (N and M) distant and ganglionar metastasis (n=5). Analysing the prognostic value of 18F-FDG PET/CT: A significantly longer overall survival was found among patients with a negative or positive scan for localized disease, compared to patients with a scan showing disseminated disease (log rank p<0,001). A significantly shorter overall survival was found among patients in whom the primary tumour was correctly identified by scan, in comparison to patients in whom no primary tumour was identified (log rank p = 0,021).

Conclusion: Our results show that 18F-FDG PET/CT has a good detection rate for CUP, confirming its usefulness in this disease (taking into consideration that even at autopsy, the primary tumour is not identified in about 70% of the cases). Disseminated disease, documented by 18F-FDG PET/CT was associated with the worst survival rate, suggesting that...
18F-FDG PET/CT findings have prognostic value for life expectancy in patients with CUP. Surprisingly, the correct identification of the primary tumour by 18F-FDG PET/CT was associated with a shorter survival rate, contradicting other studies and suggesting that the prognostic value of primary tumour identification in CUP is not yet clear. Also, this confirms the idea that CUP represents a group of cancers with proper genetic characteristics, where primary tumour characteristics are diluted.
Intra-abdominal neoplasms – MRI versus 18F-FDG-PET/CT

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Aim: To compare 18F-fluoro-desoxiglucose positron emission tomography/computerized tomography (18F-FDG-PET/CT) and abdominal magnetic resonance (MRI) performances on the restaging of patients (pts) with intra-abdominal neoplasms.

Patients and Methods: We retrospectively evaluated exams of patients who were subject to both exams as restaging procedures of intra-abdominal neoplasms (n = 30; 14 M, 16 F). The histology of the primary tumours was colo-rectal carcinoma (n = 23), gynaecological neoplasm (n = 5) and GIST (n = 2). Both exams were performed within the time frame of one month (MRI was the first exam in 20 pts). The exams reports were compared with the follow up results, including pathology reports, surgical findings and further exams. The sensitivity, specificity, and accuracy of both techniques were calculated. The extended McNemar Chi-square test was used to compare both sensitivity and specificity.

Results: 18F-FDG-PET/CT presented a sensitivity of 95%, a specificity of 89%, and an accuracy of 93%. MRI had a sensitivity of 86%, a specificity of 44% and an accuracy of 73%. However, the differences between sensitivity and specificity of both exams were not statistically significant, as calculated by the extended McNemar Chi-square test (equal to 5, for a 95% significance level). Also, 18F-FDG-PET/CT documented extra-abdominal secondary lesions in 10% (n=3) of all pts.

Discussion: The overall performance of 18F-FDG-PET/CT was better than that of abdominal MRI, even if not in a statistically significant manner. Actually, the sensitivity, specificity and accuracy values calculated for MRI were lower than reported by other authors. This fact probably reflects a referral bias among pts whose exams were studied, since several pts were referred to an 18F-FDG-PET/CT examination based on equivocal findings by the MRI. In these cases, 18F-FDG-PET/CT supported better the clinical decision making. Therefore, even if the referral bias does not allow a wider comparison between these two procedures, our results support the concept that 18F-FDG-PET/CT brings clinical benefits in the restaging of abdominal neoplasms, when compared with state of the art anatomical imaging methods, especially when these latter procedures yield equivocal findings. Furthermore, the fact of 18F-FDG-PET/CT being a whole-body procedure, capable of detecting neoplastic lesions in multiple anatomical levels, increases its usefulness in supporting clinical decision making.
Clinical characteristics and 18F-FDG PET/CT imaging in differentiated thyroid carcinoma patients with negative 131I whole-body scan and elevated serum thyroglobulin

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Objectives: The purpose of this study was to assess clinical characteristics and 18F-FDG PET/CT findings in differentiated thyroid carcinoma (DTC) patients with negative radiiodine scan and high serum thyroglobulin (Tg) concentration.

Methods: Twenty-six histopathologically proven DTC patients with negative radiiodine scan and elevated serum Tg concentration were enrolled in the study. Whole-body and dedicated head-neck PET/CT scan was performed 60 min after injecting 0.16 – 0.20 µCi/kg of 18F-FDG. Abnormal uptake was defined as any focus of increased 18F-FDG uptake greater than the surrounding normal tissue, or when the standardized uptake value (SUV) was ≥ 3. Cervical lymph nodes were classified according to the American Academy of Otolaryngology Head and Neck Surgery. A lymph node was suspicious of metastasis if SUV ≥ 3 and/or ≥ 10 mm in diameter. The 18F-FDG PET/CT imaging results were compared with histopathologic findings and used for further clinical decision making.

Results: Patient’s mean age 45.6 ± 15.2; male 26.9%, female 73.1%; papillary thyroid carcinoma 92.3%, follicular thyroid carcinoma 7.7%. Average serum Tg was 113 ng/mL in negative FDG PET/CT group compared with 309 ng/mL in positive FDG PET/CT group (p<0.01). FDG PET/CT imaging revealed loco-regional recurrences or metastases in 17 of 26 the DTC patients (65.5%) including loco-regional recurrences 23.1%, cervical lymph node metastases 50%, distant metastasis 30.8%. Of the patients with metastatic lymph nodes, 76.9% was seen in level VI, 53.8% in level IV, 38.5% in level II. There was slight agreement (kappa coefficient = 0.14) between FDG metabolism-based and size-based diagnosis of metastatic lymph nodes on PET/CT images (Figure 1). FDG PET/CT is helpful to detect exactly and precisely the localization of recurrent/metastatic lesions, particularly cervical and mediastinal lymph node metastases. This consequently resulted in a change of therapeutic management in 50% of these DTC patients, mostly for surgical treatment including alone resection (34.6%), surgery and external radiation (7.7%), surgery and empirical 131-I treatment (7.7%).

Conclusions: FDG PET/CT can be used for detecting and localizing recurrences and/or metastatic lesions and the impact on management of DTC patient’s subset with elevated serum Tg and whose 131I whole body scans were negative.
FIG. 1: Distribution of SUV and size of cervical and mediastinal lymph nodes on FDG PET/CT
PET/CT imaging with 68Ga-DOTATATE in the evaluation of neuroendocrine tumours (NET): Our leading experience in Chile

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Aim: One of the main characteristics of NET is over-expression of somatostatin receptor (SR), especially subtype 2, which can be visualized with 111In-octreotide scintigraphy (SRS). Since the 80’s, SRS has been recognized as an icon for Molecular Nuclear Medicine for its capability to represent specific SR images. Until now the most used radiopharmaceutical (RP) for SR is 111In-Octreotide. Nevertheless, this RP has significant restrictions mostly due to intrinsic physical characteristics of the radionuclide (RN) such as half-life and single gamma emission. These facts create some limitations in image quality, either for planar or SPECT, due to gamma-camera detectors properties. Additionally, 111In-Octreotide has restricted availability in places without local production.

Nowadays, the revival of 68Ge/68Ga generator allows the use of 68Ga, a positron emitter RN with 68 minutes half-life, as an ideal agent to label somatostatin analogue peptides for PET/CT images. The aim of this communication is to present our pioneer experience in Chile and in Latin-American with this novel tracer.

Methods: In the last two years we carried out 271 whole body PET/CT studies in 201 patients, 105 males and 96 females (52.4 ± 15.1 years) with histologically proved NET origin. After elution of the 68Ge/68Ga generator, 68Ga-DOTATATE was labelled using a semi-automatic synthesis module and purified in C18 column. RP quality control (QC) was done by TLC-Al SG. Fifty minutes after i.v. administration of 3.6 ± 0.62 mCi of 68Ga-DOTATATE (CGM Nuclear) PET/CT images were acquired and processed, including SUV measurement, in a Siemens Biograph 6 HiRez P3D. The referring diagnosis was GEPNET in 159, medullary thyroid carcinoma in 12, bronchial carcinoid in 10, rectal carcinoid in 6, carcinoid syndrome with unknown primary in 6, Cushing’s syndrome in 3, MEN I in 2, GIST in 1, pheochromocytoma in 1 and thymic carcinoid in 1. The referring indication was: staging 37%, re-staging 21.1%, unknown primary 14.3%, follow-up 14.2%, therapy control 13.4%.

Results: Radiochemical purity of the RP was always over 99%. In all cases PET/CT images were of excellent quality allowing clear localization either for primary tumours or metastases. No side effects or adverse reactions were seen. Tumour sites localizations were: liver 28.4%, abdomen and lymph nodes 18.1%, pancreas 11.0%, bone 8.9%, Ileum/appendix 5.0%, mediastinum 5.0% and others 23.6%.

Conclusions: NET imaging with 68Ga-DOTATATE PET/CT has several pros over 111In-Octreotide planar or SPECT SRS in places where a PET/CT system is available. According to our experience the main advantages of this new technique are: 3D PET/CT images in less than 2 hours, semi-quantitative tumour activity evaluation by SUV measurement, permanent
availability of the RN from generator without need of a cyclotron, easy labelling process, lower radiation dose to the patient and lower radiopharmaceutical cost in places where $^{111}$In is not locally available.
Cost-effectiveness analysis of 18F-FDG PET/CT in detecting suspected recurrence or metastasis in thyroid carcinoma patients with negative diagnostic total body scan in Thailand: A decision analysis

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There are various management methods for thyroid cancer patients with high serum thyroglobulin (Tg) but negative total body scan (TBS). Even though PET/CT has the high accuracy to detect recurrence and metastasis, most of the patients in Thailand cannot reach the investigation because of its cost. The cost-effectiveness analysis of 18F-FDG PET/CT to detect recurrence or metastasis in thyroid cancer patients with high Tg but negative TBS will lead to proper treatment. A decision tree model was used to estimate the incremental cost and Quality Adjusted Life Year (QALY) gains associated with seven strategies approached. The first strategy is treatment with empirical high radioactive iodine. The second strategy is using CT scan and additional PET/CT scan in cases with negative CT scan, then surgery in operable cases and radiation therapy in inoperable cases. The third strategy is using CT scan and additional PET/CT scan in cases with negative CT scan, then surgery in operable cases and high radioiodine treatment in inoperable cases. The fourth strategy is using PET/CT scan, then surgery in operable cases and radiation therapy in inoperable cases. The fifth strategy is using PET/CT scan, then surgery in operable cases and high radioiodine treatment in inoperable cases. The sixth strategy is using 99mTcMIBI scan and additional PET/CT scan in cases with negative MIBI scan, then surgery in operable cases and radiation therapy in inoperable cases. The seventh strategy is using MIBI scan and additional PET/CT scan in cases with negative MIBI scan, then surgery in operable cases and high radioiodine treatment in inoperable cases. All strategies were adopted hospital perspective. Literature reviews for radioiodine, surgical and radiation therapy treatments associated with each strategy were used to estimate QALY gains. Direct medical cost was estimated based on the reference price of Siriraj hospital. Deterministic sensitivity analysis was conducted to investigate the effect of parameter uncertainty. The strategy using PET/CT scan to detect recurrence, then surgery in operable cases and high radioiodine treatment in inoperable cases gives the highest quality adjust life year of 28.03 years and acceptable incremental cost effectiveness ratio (ICER) of 191.34 US dollars per QALYs when compared to the strategy using MIBI scan and additional PET/CT scan in negative MIBI result. Other strategies were dominated by this PET/CT strategy. Deterministic sensitivity analysis (based on the willingness to pay (WTP) 11,675.42 US dollars) showed that the cost of PET/CT scan has no impact on the net health benefit. These findings should be proposed to the Society of Nuclear Medicine Thailand to improve the guidelines for appropriate and cost-effective use of FDG PET/CT scan for thyroid cancer. Moreover, this study supports the use of health care resources to improve Thai health care system and determine criteria for reimbursement in Thailand.
The aim is to evaluate the role of 18FDG PET-CT in recurrent thyroid cancer patients presenting with negative whole body radiiodine scan (WBS) and increasing serum thyroglobulin (Tg). In this prospective study 25 patients (male = 9, females = 16; mean age = 43 years, range = 18-68 yrs) with differentiated thyroid cancer (papillary 21; follicular 4) were included. All of them were initially managed with thyroidectomy and radiiodine therapy. On follow up, they presented with increasing serum Tg (>10ng/ml) and negative WBS. Stimulated 18FDG PET-CT was done in these patients with 370MBq (10 mCi) dose of FDG. Findings on 18FDG PET-CT were grouped as local recurrence, lymph nodal disease, lung metastasis and bone metastasis. A combination of histopathology and/or meticulous clinical examination, CT and follow up (minimum 6 months) was taken as reference standard. Impact of 18 FDG PET-CT on patient management was also evaluated. Out of 25 patients, 20 patients showed positive findings on 18FDG PET-CT. In 10 patients these findings were confirmed by histopathology reports. In other patients serial Tg measurement on follow up confirmed these findings. Two patients, however, had antibody titre positive (ATA). After starting re-differentiation therapy 7 patients showed decrease in serum Tg value and in 3 patients serum Tg value showed persistent increase despite therapy. Out of 5 patients showing negative findings on 18FDG PET-CT, 3 patients were true negative showing decrease in serum Tg values on follow up without any therapy. Two patients were falsely negative on 18FDG PET-CT confirmed by increasing serum Tg value on serial follow up. One patient with increased ATA was true positive and other was true negative. Therefore, sensitivity of 18FDG PET-CT for disease detection is 91%, specificity 100%, negative predictive value and positive predictive value are 60% and 100%, respectively. Sensitivity and specificity for lesion wise disease detection are - local (89.5%, 83.3%), nodal (92.3%, 100%) and pulmonary (83.33%, 100%), respectively. Mean of SUVmax for 18FDG PET-CT positive lesions is 5.7. By using ROC analysis, cut off value of SUVmax for showing response on re-differentiation therapy was 4.1 (sensitivity 40%, specificity 100%). Mean serum thyroglobulin value for patients with positive 18FDG PET-CT findings is 372ng/ml [range 20-3000 ng/ml]. For patients showing negative 18FDG PET-CT findings mean serum thyroglobulin value is 150ng/ml [range 59-252]. Distant metastases were identified in 24% of patients (pulmonary 20%, skeletal 4%). In 44% of patients treatment plan was altered after 18FDG PET-CT findings. Surgery was performed in 36% of patients who underwent 18FDG PET-CT. Additional 8% of patients were treated with radiotherapy. 18FDG PET-CT shows high diagnostic accuracy in identifying loco-regional and distant metastases in dedifferentiated thyroid cancer. It is also helpful in deciding further clinical management of dedifferentiated thyroid cancer.
Role of 18F-FDG PET-CT in medullary thyroid carcinoma and correlation with serum calcitonin

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The aim of the study was to evaluate the role of 18F-FDG PET-CT in medullary thyroid carcinoma (MTC) and the correlation with serum calcitonin. Retrospective analysis was done in 30 patients (19 males and 11 females) of MTC with a mean age of 42.80±10.98 years of whom, 27 had been treated previously and 3, referred for baseline study. The mean duration of disease prior to the FDG PET-CT was 43.69 months (range: 2-360 months) while the mean serum calcitonin was 2989 pg/ml (range: 5-19065 pg/ml). There were 5 patients with both primary and nodal disease, 7 with only nodal disease, 4 with liver, 5 with bone and 5 with lung metastasis on FDG PET-CT study. Sensitivity, specificity and positive predictive value of FDG PET-CT were 65.38%, 100% and 100% respectively. The mean serum calcitonin level was 756.91 pg/ml in PET negative patients in contrast to 4302.67 pg/ml in PET positive patients and this difference was statistically significant (p=0.002). Receiver Operating Characteristics analysis revealed a cut-off serum calcitonin level of 269.5 pg/ml at which sensitivity, specificity, positive predictive value and negative predictive value of FDG PET-CT was 88.24%, 80%, 88.2% and 80% respectively. The sensitivity of FDG PET-CT, however, did not correlate with the duration of the disease (p=0.507). The mean serum calcitonin levels in PET positive patients with nodal disease with or without primary disease and in those with systemic metastasis were 1599.3 pg/ml and 7343 pg/ml respectively. However, the difference was not statistically significant (p=0.122). There was no statistically significant correlation between the serum calcitonin level with respect to the duration of disease and SUVmax (p=0.434; p=0.836). The mean SUVmax of all the lesions of all the patients was 1.75±0.964. The mean SUVmax of patients with nodal disease with or without primary disease and patients with systemic metastasis were 1.8 and 1.7 respectively which was statistically not significant (p=0.816).

Conclusion: FDG PET-CT is a sensitive and specific investigation in patients of MTC with serum calcitonin level greater than 269 pg/ml, with little use below this level. There is predominance of systemic metastasis at high serum calcitonin levels (median=4220 pg/ml) as compared to nodal metastasis (median=472 pg/ml) on FDG PET-CT.
Early assessment for suspected recurrent ovarian cancer - optimizing PET/CT performance using a tumour marker based analysis

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Aim: Serum CA125 level measurements are used in the assessment of patients with ovarian cancer, with 35 μg/mL representing the upper normal value. This study aimed at determining the optimal cut-off value of CA125 levels for best PET/CT performance in early evaluation of suspected recurrent ovarian cancer.

Methods: 84 PET/CT studies of 49 patients with ovarian cancer were retrospectively reviewed. Indication for PET/CT included suspicion for recurrence due to increasing CA125 levels (n=34) or CT findings (n=11), monitoring response to treatment (n=35) or follow-up (n=4). All available Serum CA125 measurements at the time of the PET/CT study were recorded. Various CA125 values <35 μg/mL were correlated with PET/CT performance using ROC analysis and with clinical follow-up.

Result: CA125 levels ≥ 35 μg/mL were found in 43 studies (51%). Recurrent cancer was diagnosed in 41 of them (95%). PET/CT had a sensitivity, specificity, positive and negative predictive value and accuracy of 95%, 100%, 100%, 50% and 95% respectively. ROC analysis found the CA 125 lowest cut-off value of 23 μg/mL to correspond to a similar PET/CT sensitivity, specificity, positive and negative predictive value and accuracy of 96%, 100%, 100%, 50% and 96% respectively.

Conclusion: Yielding the same performance indices for PET/CT positivity, a lower Ca125 threshold value of 23 μg/mL, rather than the standard limit of 35 μg/mL should be used as a referral guide at the decision time point aiming at early diagnosis of recurrent ovarian cancer.
Objective: To evaluate the clinical impact of the 18F-FDG PET/CT (18Fluor-desoxiglucose Positron Emission Tomography/Computed Tomography) used as a diagnostic method in the treatment of oncologic patients of the National Institute of Cancerology.

Methods: A total of 1177 whole body 18F-FDG PET/CT scans evaluated from March to October 2007- the exclusion criteria were studies for no oncologic diagnoses and patients without following data. 672 studies were included, and each of them analysed the therapeutic decision or management before and after the 18F-FDG PET/CT scans. The results of the scans show local, recurrent or progressive disease as well as no disease detection. The scan result was confirmed by histopathology, clinical or imagenology follow up.

Results: Of the 672 studies, in 362 patients (53.8%) the specialist physicians changed the treatment and management of the patient based on the results of the 18F-FDG PET/CT scan.

In table 1 we describe the referral diagnoses for PET/CT (column A), the total number of studies carried out due to this diagnosis (column B), and the number of studies that changed the management of the patient (medical or surgical) according to the 18F-FDG PET/CT study result (column C).

TABLE 1:

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>Column A</th>
<th>Column B</th>
<th>Column C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervico-Uterine</td>
<td>70</td>
<td>40</td>
<td>57.1</td>
</tr>
<tr>
<td>Lung</td>
<td>51</td>
<td>37</td>
<td>72.5</td>
</tr>
<tr>
<td>Breast</td>
<td>39</td>
<td>22</td>
<td>56.4</td>
</tr>
<tr>
<td>Thyroid</td>
<td>11</td>
<td>7</td>
<td>63.6</td>
</tr>
<tr>
<td>Skin and soft parts</td>
<td>9</td>
<td>5</td>
<td>55.5</td>
</tr>
<tr>
<td>Melanoma</td>
<td>13</td>
<td>7</td>
<td>53.8</td>
</tr>
<tr>
<td>Colon and rectum</td>
<td>28</td>
<td>19</td>
<td>67.85</td>
</tr>
</tbody>
</table>
Conclusions: In almost half of the patients the results of the 18F-FDG PET/CT scans were decisive in order to change the therapeutic management of the patient, with a relevant clinical impact for the patient.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Count</th>
<th>True Positives</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>GIST</td>
<td>10</td>
<td>4</td>
<td>40</td>
</tr>
<tr>
<td>Others from digestive apparatus</td>
<td>13</td>
<td>6</td>
<td>46.5</td>
</tr>
<tr>
<td>Non Hodgkin lymphoma</td>
<td>269</td>
<td>134</td>
<td>49.8</td>
</tr>
<tr>
<td>Bone</td>
<td>5</td>
<td>1</td>
<td>20</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>38</td>
<td>13</td>
<td>34.2</td>
</tr>
<tr>
<td>Renal</td>
<td>7</td>
<td>2</td>
<td>28.5</td>
</tr>
<tr>
<td>Endometrial</td>
<td>4</td>
<td>2</td>
<td>50</td>
</tr>
<tr>
<td>Fallopian tube</td>
<td>1</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>Choriocarcinoma</td>
<td></td>
<td>3</td>
<td>100</td>
</tr>
<tr>
<td>Testicle</td>
<td>20</td>
<td>15</td>
<td>75</td>
</tr>
<tr>
<td>Germinal extra-gonadal</td>
<td>6</td>
<td>4</td>
<td>66.6</td>
</tr>
<tr>
<td>Penis</td>
<td>3</td>
<td>1</td>
<td>33.3</td>
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<tr>
<td>Prostate</td>
<td>5</td>
<td>2</td>
<td>40</td>
</tr>
<tr>
<td>Ovary</td>
<td>26</td>
<td>18</td>
<td>69.2</td>
</tr>
<tr>
<td>Bladder</td>
<td>1</td>
<td>1</td>
<td>100</td>
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<tr>
<td>Head and neck</td>
<td>22</td>
<td>8</td>
<td>36.3</td>
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<tr>
<td>Unknown primary</td>
<td>6</td>
<td>2</td>
<td>33.3</td>
</tr>
<tr>
<td>Leukaemia</td>
<td>1</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>Castleman disease</td>
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<td>1</td>
<td>100</td>
</tr>
<tr>
<td>Glioblastoma</td>
<td>1</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>Second primary</td>
<td>9</td>
<td>6</td>
<td>66.6</td>
</tr>
<tr>
<td>TOTAL</td>
<td>672</td>
<td>362</td>
<td>53.8</td>
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</tbody>
</table>
The role of FDG-PET in the evaluation of treatment for lymphoma: Philippine setting

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PET is essential for the post-treatment assessment of lymphomas because a negative PET scan after treatment is required for a complete remission and curative outcome. Functional imaging with 18F-FDG PET enables evaluation of the early metabolic changes rather than the morphologic changes of the lymphoma occurring later during therapy. Among 186 patients diagnosed with Hodgkin’s Disease (HD) or Non-Hodgkin’s Lymphoma (NHL) who were referred to the PET Centre in this institution from April 2002 to June 2010, 35 patients with at least two PET or PET/CT scans were included in this study. Twenty-six patients were diagnosed to have NHL whereas nine patients were diagnosed with HD. The patient group was composed of 17 men and 18 women with a mean age of 50 years. Descriptive frequencies were obtained to characterize demographic and prognostic data of the study population. Kaplan-Meier survival analysis was used to evaluate progression-free survival (PFS), defined here as the time interval without progression of disease from the start of treatment. The log-rank test was used to compare PFS between PET-negative and PET-positive patients. All 14 patients who only had end-of-chemotherapy scans without mid-cycle scans had no tumour recurrence on subsequent scan/s, with a median follow-up of 17.5 months. Of the remaining 21 patients, 11 patients had positive studies, 9 had negative studies and 1 had an indeterminate study on the mid-cycle scans. All the patients obtained similar results on the subsequent scans, excluding 5 with no follow-up scans, with median follow-ups of 13 months for the PET-positive patients and 23 months for the PET-negative patients. Patients with negative scans had higher survival probabilities and longer PFS period. Comparison of survival curves using the log-rank test yielded P = 0.0789, indicating no significant difference between the two groups. The strong prognostic value of PET for aggressive lymphomas is established, whether the imaging is performed at the end of therapy or after only a few cycles of chemotherapy. PET has consistently been shown to have a very high negative predictive value or NPV (a measure of the ability of a negative PET scan to exclude persistent disease or future relapse) averaging about 90% and exceeding 80% in virtually all reported studies.
Clinical study on multiple traces PET/CT in gliomas

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Objective: To explore the correlation between histopathologic features and metabolic activity of human gliomas using FDG, MET, CHO PET/CT

Materials and Methods: 159 patients with suspected primary glioma underwent PET/CT examination, 131 patients with FDG, 95 patients with MET, and 44 patients with both CHO and FDG, 87 patients with both MET and FDG, and 8 patients with three traces. Conventional and enhancement MRI were performed within 2 weeks before PET scanning. Pathologic diagnosis was obtained by biopsy or open surgery in all patients with tumours. The traces uptake in lesions were analysed in visual and semi-quantitative approaches (SUVmax and L/WM), and compared with tumour grade, tumour type, tumour Gd-DTPA MRI enhancement and tumour proliferation activity (Ki67).

Results: The lesions included 108 gliomas (3 WHO I tumours, 42 II tumours, 42 III tumours, 21 IV tumours), 18 other tumours and 33 non-neoplasm lesions. By visual analysis, the diagnosis accuracy of FDG, MET, CHO PET/CT in brain tumours is 71%, 92.6%, and 61.4% respectively. The accuracy of combination two traces PET/CT is no more than that of MET PET/CT alone. By semi-quantitative analysis, glioma grade influenced FDG, MET and CHO uptake, glioma type influenced FDG and MET uptake only. The L/WM (FDG and MET) of oligodendroglial tumours was significantly higher than astrocytic tumours. The best ratio to differentiate low to high grade tumours is L/WM (CHO) by ROC curve, and the cut-off value of L/WM (CHO) is 5.05. There were significant differences between high-grade tumours and non-neoplasm for three traces, but there was a difference between low grade tumours and non-neoplasm lesions only for MET. There were no significant difference of 3 traces uptake among high grade glioma, brain metastasis and lymphoma, but FDG PET/CT body scan is helpful to identify brain metastasis. In astrocytic tumours, there were significant correlations between L/WM ratios of each trace and Ki67 and Gd-DTPA MRI enhancement. However, for oligodendroglial tumours, significant correlations were not shown in all of the traces.

Conclusion: MET is more tumour-selective than FDG and CHO, CHO is not able to differentiate glioma with non-neoplasm lesion. Human glioma grade and type influenced FDG and MET uptake, but CHO uptake was influenced only by tumour grade, so CHO is better for glioma grading.
F-18 FDG PET-CT in follow-up of patients with lymphoma

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Introduction: Some malignancies such as lymphomas frequently have a residual mass/lymph node after completion of treatment, whether these harbour viable malignant tissue can only be assessed non-invasively by functional imaging such as F-18 FDG PET.

Methods: We retrospectively reviewed FDG PET-CT scans of 50 patients with lymphoma referred to our department. There were 27 females and 23 males; ages ranged from 16 to 77 years (mean 45). All the patients had at least 2 scans with initial abnormal PET-CT scans. Thirty-two patients had pre and post chemotherapy scans. Sixteen patients had no treatment between the scans based on clinical grounds. One patient had DXT and another had both chemotherapy and DXT. The 50 patients were classified into 4 categories based on the latest PET-CT scan findings: CMR (complete metabolic response), PMR (partial metabolic response), SMD (stable metabolic disease) and PMD (progressive metabolic disease), this is according to the EORTC (European Organization for Research and Treatment of Cancer) PET study group 1999 recommendations.

Results: CMR consisted of 8 patients: 4 females and 4 males; 4 HL and 4 NHL; all patients were treated prior to latest scan. PMR consisted of 10 patients: 5 males and 5 females; 5 HL and 5 NHL; all patients had treatment prior to latest scan. SMD consisted of 6 patients: 2 male 4 female; 4 HL and 2 NHL; none received treatment prior to the latest scan. PMD: consisted of 26 patients; 13 male and 13 female; 9 HL and 17 NHL; 16 patients treated prior to latest scan and 10 not treated.

Conclusion: PET monitoring helps to identify response to treatment by assessing the presence of active disease or not. The results showed that gender may not influence treatment outcome. The type of histology affected outcome in 2 categories: SMD which comprised more HL (67%) although the limited number, and PMD with more NHL (65%). The findings suggest that NHL is more resistant to treatment than HL which also correlates with the documented clinical literature.
IAEA-CN-185/219

68Ga-DOTATATE PET/CT imaging: Preliminary findings in Johannesburg, South Africa

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Objective: Imaging neuro-endocrine tumours (NET) continues to gain momentum in clinical practice. The availability of the long-lived 68Ge/68Ga generator makes PET/CT imaging an attractive option with great potential for use in developing countries, particularly those with limited access to nearby cyclotrons. The aim of this study was to assess the role of this technology in our clinical environment.

Methods: We retrospectively reviewed 25 68Ga-DOTATATE PET/CT scans that were acquired in 2010 since receiving our first 68Ge/68Ga generator. Patients that were referred included well differentiated neuro-endocrine tumours (NET) [n=8], poorly differentiated NET NOS [n=1], carcinoid [n=8], medullary thyroid carcinoma [n=1], neuroblastoma [n=1], pheochromocytoma [n=2], glomus jugulare tympanicum [n=2], gastrinoma [n=1] and MEN syndrome [n=1]. Diagnosis was based on relevant biochemistry and clinical presentation or incidental findings on routine biopsy. Indications for referral included localization of primary lesion, assessment of possible residual or recurrent disease following treatment and assessment of extent of disease. In subgroups of the studies that were reviewed, some patients also underwent 123I-metaiodobenzylguanidine (MIBG) [n=10] or 111In-pentreotide [n=7].

Results: Imaging with 68Ga-DOTATATE revealed increased lesion to background ratio when compared to 111In-pentreotide imaging, allowing better lesion detectability. When assessing findings in patients that underwent imaging with more than one tracer, concordance was noted. In addition, 68Ga-DOTATATE demonstrated more lesions. All lesions noted on 123I-MIBG or 111In-pentreotide were also visualized on PET/CT.

Conclusions: Our experience concurs with preliminary findings of limited published data in literature. 68Ga-DOTATATE appears to be a superior tracer for imaging NET patients. It is likely to become the standard of reference in NET imaging. Treatment with heavy metal peptide analogues are not currently available in developing countries but options may very well be explored, particularly in South Africa where both heavy metal isotopes are being produced and peptides are available but labelling experience is still lacking.
The relationship of quantitative measures derived from (18)F-FDG PET/CT and diffusion-weighted MRI in patients with squamous cell carcinomas of the head and neck

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The main goal of this prospective study was to determine, in patients with squamous cell carcinoma (SCC) of the head and neck, the correlation between maximum standardized uptake values (SUVmax) calculated from (18)F-fludeoxyglucose (FDG) positron emission tomography (PET) data, and apparent diffusion coefficient (ADC) values calculated from diffusion-weighted magnetic resonance imaging (DWI). Furthermore, it was of special interest to determine whether SUVmax and ADC values differ significantly between histological SCC grades. Thirty-one consecutive patients with biopsy-proven head and neck SCC (five G1, 22 G2, and four G3 tumours) were included in the present study, which was approved by the local Ethics Committee. In all patients, contrast-enhanced, whole-body (18)F-FDG PET/CT was performed using an integrated 64-row multi-detector hybrid PET/CT scanner. 300 MBq of (18)F-FDG were administered intravenously 50 minutes prior to PET data acquisition. PET images were reconstructed with a slice thickness of 5 mm, using the Ordered Subsets Expectation Maximization (OSEM) technique. Attenuation correction was based on the CT images, which were obtained with a tube voltage of 120 mA, a tube current of 230 kV, a collimation of 64x0.6 mm, a section thickness of 3 mm with 2 mm increment, and a 512x512 matrix. SUVmax was measured in 3D for every tumour, using a volume of interest that was based on an isocontour threshold method. MR images of the head and neck region were obtained using a 3.0T MR scanner, equipped with a dedicated 16-channel head and neck coil. In addition to morphological sequences, axial diffusion-weighted sequences were obtained using b-values of 0 mm2/s and 800 mm2/s, and ADC maps were calculated. The ADC values of the tumours were measured using manually defined ROIs that covered the entire tumour. Statistical analysis comprised two-way repeated-measures ANOVA and Spearman rank correlation. The specified level of significance was 0.05 for all tests. The mean SUVmax values were 26.5 ±12.1 for all SCC combined, 29.3 ±12.9 for G1 tumours, 26.6 ±12.3 for G2 tumours, and 22.5 ±7.9 for G3 tumours. Mean ADC values were 0.928 ±0.160 for all SCC combined, 0.922 ±0.123 for G1 tumours, 0.940 ±0.177 for G2 tumours, and 0.871 ±0.063 for G3 tumours. There was no significant difference between the tumour grades (p>0.05), with regard to either SUVmax or ADC values. There was also no significant correlation between SUVmax values and ADC values (p>0.05). We therefore conclude that there is no correlation between the FDG uptake (i.e. glycolytic activity) and the ADC values (i.e. restriction of hydrogen diffusion, which is associated with cellularity) in SCC of the head and neck. Neither SUVmax values nor ADC values appear to be suitable for distinguishing between histological SCC tumour grades.
Role of immediate [18F]FDG-PET/CT after tumour percutaneous ablation as a predictor of local recurrence-free survival

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Objective: Localised tumours may be treated with radiofrequency ablation (RFA) or Cryoablation, both low invasive methods yet limited by the lack of direct evidence of the radicalness of treatment. We evaluated the role of immediate [18F]FDG-PET/CT in RFA and cryogenic treatment success and early diagnosis of local relapse after procedure.

Methods: This is a single-centre retrospective, descriptive, exploratory study. Data set was acquired at our institution digital records between February/2008 and June/2009. Seven patients showed eight FDG-positive lesions (a patient had two lesions treated in different organs) in pre-interventional PET/CT. Immediate post-interventional PET/CT was performed 2 hours after procedure. We considered an immediate evaluation negative when two readers agreed there was no evidence of uptake on the treated margin area. Patients were followed up with PET/CT (six patients) and magnetic resonance (one patient) with a mean time of thirteen months.

Results: Female/male rate was 4:3. Target lesions were located at: liver (3), lungs (2), retroperitoneum (2) and peritoneum (1). Three were adenocarcinomas from colon (2), lung (1) and ovarium (1); two were melanomas, one hepatocarcinoma and one malignant fibrous histiocytoma. Six patients had a negative immediate post-interventional PET/CT and all follow up scans remained negative in the local ablation area, despite tumour progression in other sites in 4 cases. One case (colorectal liver metastasis) had a positive immediate PET/CT with uptake in the edge of the lesion and follow up scan confirmed local recurrence.

Conclusions: The immediate evaluation of tumour ablation with [18F]FDG PET/CT can be a good tool to detect viable neoplastic tissue within the ablated area margins, avoiding the misleading effects of the inflammatory changes related to the procedure in the glucose uptake analysis. Negative results possibly indicate complete ablation of the lesions and may predict effective local control. A positive result probably indicates incomplete ablation, allowing earlier complimentary sessions to obtain wider margins.
18F-FLT for stereotactic radiotherapy treatment planning of recurrent brain tumours: experience of the National Institute of Neurology and Neurosurgery of Mexico

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The most recent advances in nuclear medicine technologies in developing countries like Mexico arrived only some years ago. While, there are over 160 sites in the USA and over 120 sites in Europe as well as the access to many tracers, in our country there are about 8 sites with a positron emission tomography (PET)/computed tomography (CT) and the only tracer for neuro-oncologic studies was 2-deoxy-2-fluoro-D-glucose labelled with 18F (18FDG). The thymidine analog 3-deoxy-3-18F-fluorothymidine (18F-FLT) has been developed as a PET tracer to image proliferation in vivo. Recently, this tracer has become available in Mexico for imaging proliferation of brain tumours. Thirty six patients with previously diagnosed and treated brain tumours with stereotactic radiotherapy (SRT) underwent 3T MRI and PET imaging to evaluate tumour recurrence/progression. The distribution of cases was: 17 anaplastic astrocytoma and 19 glioblastoma multiforme (GBM). From these patients, 10 underwent both, 18F-FLT and 18FDG PET imaging. SUV uptake, contrast and tumour volume was compared for both PET imaging techniques. 18F-FLT visualized all tumours with a higher contrast than 18FDG. SUV uptake values for 18F-FLT was 1.28±0.61 with a contrast greater or equal than 3.2 (SUVtumor/SUVnormal tissue) for all cases. SRT treatment plan was based on the use of T1+T2 3T MRI + 18F-FLT or 18FDG. Except one case (see Figure 1), 18F-FLT based tumour volume was less than T1+T2 3T MRI + 18FDG outlining, resulting in normal tissue sparing. 18F-FLT PET was more sensitive than 18F-FDG to image recurrent high-grade tumours. SUV and contrast values are in agreement with those reported in the literature. With this new tool re-irradiation of recurrent brain tumours will be more selective with smaller target volumes and normal tissue sparing.

FIG. 1. Comparison of different image modalities for a recurrent grade II glioma. A. 18F-FLT PET, B. 18F-FDG PET, C. T2 3T MRI and D. T1 contrast enhanced 3T MRI. The SRT treatment planning was performed using 18-F FLT + T1 3T MRI for tumour outlining.
Usefulness of 18F-FLT PET/CT in the differential diagnosis of radiation changes vs. tumour recurrence in the follow-up of patients with primary brain tumours

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Introduction: Current imaging techniques, such as MRI, CT, FDG-PET have a limited role in the follow-up evaluation of patients with primary brain tumours (PBT), usually they cannot make an appropriate differentiation between radiation changes and tumour recurrence, which is critical for patient survival. (18F) fluorothymidine (FLT) is a relatively novel radiotracer aimed to identify sites with increased cellular proliferation, typical of primary brain tumour recurrence, without the inconvenience of high uptake by the normal brain as in FDG PET.

Material and Methods: 18F-FLT PET/CT was performed in 8 patients treated (chemo-radiotherapy) for high grade primary brain tumours; all the patients had inconclusive MRI results on follow-up.

Results: 12 lesions were identified, 11 showed high FLT uptake, corresponding with tumour recurrence, 1 lesion had no FLT uptake and represented radiation necrosis. The average background/lesion ratio for the FLT positive sites was 11.9 (range 4-24) whereas the ratio for the FLT negative site was 1 (P: 0.001).

Conclusion: 18F-FLT PET/CT is a promising imaging tool in the follow-up of patients with PBT, with highly specific findings that can differentiate radiation changes vs. tumour recurrence.
Additional value of PET/CT-based radiotherapy planning in patients diagnosed of head and neck malignancy

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Aim: To assess the additional diagnostic value of PET/CT versus standard diagnostic work-up investigations for clinical staging, clinical and therapeutic impact of radiotherapy planning (RTP) in patients newly diagnosed of head and neck malignancy.

Material and Method: 28 head and neck patients (24 men, 4 women; mean age 58 years) who were radiotherapy candidates were included prospectively. All underwent co-registered PET/CT F18-FDG with intravenous iodinated contrast and whole body volumetric acquisition in specific RTP positioning. The anatomic location of the primary malignancy was: lip and oral cavity (n=8, 29%), nasopharynx (n=5, 18%), oropharynx (n=3, 11%), hypopharynx (n=6, 21%) and larynx (n=6, 21%). Histology classification was: squamous cell (n=23, 82%) lymphoepithelioma (n=4, 14 %), other (n=1, 4 %). Clinical stage: I (n=1, 4%), II (n=3, 11 %), III (n=4, 14 %), IV a (n=16, 57%), IV b (n= 4, 14 %).

Results: Both visual and semi-quantitative analysis (SUVmax) were performed. The per-patient analysis showed disagreement in 9/28 cases (32 %), PET/CT upstaged 7/9 (78%) and down-staged 2/9 (22%). The per-lesion analysis showed T stage disagreement in 12/28 cases (43%), PET/CT upstaged 11/12 and down-staged 1/12. N stage was in disagreement in 10/28 (35 %) cases, PET/CT upstaged 5/10 and down-staged 5/10. PET/CT detected unexpected metastases in 3 patients, thus modifying therapy intent from radical to palliative.

Conclusions: The implementation of PET/CT allows for simultaneous initial staging and RTP within a single investigation, which may modify baseline clinical staging, thus altering clinical decision-making and therapeutic intent, potentially improving volume delineation. Most patients are under-staged by standard diagnostic work-up investigations.
Clinical and cost-effectiveness of FDG-PET in preoperative staging of non–small cell lung cancer (NSCLC) in Brazil: A study in the context of Brazilian public health system

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Aim: Lung cancer continues to be a major health problem worldwide. Previous studies have shown that positron emission tomography (PET) is more accurate than computed tomography (CT) for the staging of NSCLC. To date, there are no published prospective studies in Brazil evaluating the impact of FDG-PET on clinical management of patients with lung cancer. The clinical utility and cost-effectiveness of metabolic staging (MS) with FDG-PET was compared to conventional clinical staging (CCS) strategy for preoperative staging of NSCLC in the context of the Brazilian public health system.

Method: Two decision strategies were compared CCS and CCS coupled with FDG-PET in all 83 patients before the beginning of treatment. A standard of reference was determined with CT, FDG-PET, histology and follow-up exams. The results of the CCS were compared to the MS with FDG-PET results. Local unit costs of procedures and tests were evaluated.

Results: The incorporation of FDG-PET coupled with CCS in the staging procedure upstaged 72.3% (60/83) and down-staged 2.4% (2/83) of the patients. As a result of these changes in staging, 45.0% (38/83) of the patients would have received a different therapeutic regimen, and 42.1% (35/83) would not be submitted to surgery. Local average CCS costs without PET were $3,037 compared to $4,161 with PET. However, due to treatment modifications, average treatment cost per patient with CCS was $17,285 and with PET staging was $16,665, with a 3.6% decrease in costs.

Conclusion: FDG-PET is more accurate than CT in NSCLC staging. PET changed patient management and avoided unnecessary surgeries in 45% of the patients. Given observed probabilities, FDG-PET is highly cost-effective and would reduce costs for the public healthcare program in Brazil. This cost savings added to clinical effectiveness, justify PET reimbursement from Brazilian’s public health system in preoperative staging NSCLC.
Usefulness of 68Ga-DOTATOC PET/CT in the evaluation of patients with medullary thyroid cancer and suspected recurrence

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Introduction: Medullary thyroid carcinoma is characterised by high expression of somatostatin receptors, mainly SSRT2. Therefore, imaging with somatostatin analogs labelled with positron emission radionuclides such as 68Ga-DOTA-d-Phe(1)-Tyr(3)-octreotide (DOTATOC) can be used to detect occult tumour sites. The aim of this study was to describe the performance of this radiotracer in detecting metastasis from medullary thyroid cancer.

Methods: Five patients were included (1 man, 4 women, median age: 47 years) who had previously been diagnosed for MTC. Calcitonin levels were increased. We considered positive lesions identified by visual analysis, semi-quantitative analysis by calculation of maximum standardized uptake value and tumour/non tumour ratio. Corroboration diagnosis was made by clinical follow-up biopsy.

Results: Average levels of calcitonin were 564 ± 167. We identified 10 of 14 lesions (77%) by semi-quantitative analysis, 11 of 14 (78.57%) by visual analysis and 12 of 14 (85.7%) by determination of tumour/non tumour ratio. The SUVmax value had no statistically significant correlation, compared to calcitonin levels (pearson r=0.12), sites of metastases were bone structures (n = 5), hilar (n = 5), cervical nodes (n = 2), liver (n = 1), lung (n = 1). The 4 not identified lesions in the semi-quantitative analysis, were cervical lymph nodes (n = 2) and bone structures (n = 2). In visual analysis, two lesions corresponded to cervical lymph nodes and one bone (humerus), the two undetected lesions by visual analysis corresponded to cervical lymph nodes.

Conclusions: The 68Ga DOTATOC PET / CT is a reliable tool in detecting hidden sites of metastasis in patients with CMT. However, due to the bio-distribution and ubiquity of somatostatin receptors it is important not to base the assessment by automated methods. The tumour / no tumour ratio is capable of identifying more lesions than SUVmax or visual analysis in regions where the physiological distribution of somatostatin receptors may be high.
Non-invasive characterization of adrenals masses using 18FDG-PET/CT in patients with lung cancer

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Objective: To evaluate the ability of positron emission tomography (PET) to characterize adrenal masses in patients with lung cancer.

Materials and Methods: We evaluated retrospectively the incidence of adrenal masses in 478 patients with confirmed lung cancer. Sixty three patients (50 men and 13 women, aged 51 to 89 years old) had adrenal masses. The lesions smaller than 8 mm were excluded, due to them being below the spatial resolution of PET. All the patients were studied with 18FDG-PET/CT without IV contrast using GE Discovery STE 16 equipment. PET was performed in fasting patients 60 minutes after infusion of 0.11 mCi/kg (4 MBq/kg), of 2-[fluorine-18]-fluoro-2-deoxy-D-glucose (FDG). PET images were correlated with findings from computed tomography (CT). The 18FDG uptakes of the lesions were analysed using visual examination and semi-quantitative estimation of the maximal standardized uptake value (SUV). The adrenal masses that presented SUVmax higher than the liver background SUVavg (semi-quantitative estimation of the average standardized uptake value), were considered malignant by PET.

Results: The size of the masses ranged from 12 to 81 mm and the SUVs in the lesions suspicious of malignancy oscillated between 2.9 and 34.3 (mean: 9.18). Our entire patients were followed up clinically to confirm our findings and none of them underwent biopsy. From the 63 patients with adrenal lesions, 31 were interpreted as metastasis (14 on the left side, 8 on the right side and 9 were bilateral), and 30 of these patients also presented distant metastasis in different sites, and 1 patient had adrenal compromise only with an SUVmax of 13.5 and biopsy confirmation was considered unnecessary due to the intense FDG uptake of the lesion. The rest of the adrenal lesions with SUVmax uptake lower/equal than the liver background were considered benign and followed over time.

Conclusion: 18FDG-PET/CT could potentially be considered a non-invasive useful tool to discriminate benign from malignant adrenal lesions.
Clinical impact of PET/CT in detecting distant malignant compromise in patients, thought to have early and locally advanced stages breast cancer

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Objective: To determine the efficacy of PET/CT for the detection of metastasis in patients with breast cancer, in early (I and IIa) and locally advanced (III) stages and to compare the results with clinical examination and conventional methods of diagnosis.

Materials and Methods: We evaluated retrospectively 71 patients with biopsy proven breast cancer. All the patients were staged initially according to results of clinical examination and conventional diagnostic methods (Rx, ultrasound and bone scan). The patients were divided in two groups: Group 1: 48 patients were referred as early stage breast cancer (I and IIa) and Group 2: 23 patients as locally advanced stage breast cancer (III). Both groups were studied with 18FDG-PET/CT using GE Discovery STE 16 equipment and the FDG uptake of the lesions were analysed using visual examination and semi-quantitative estimation of the maximal standardized uptake value (SUVmax). The results were evaluated and compared between diagnostic methods.

Results: In group 1, only 2 of the 48 evaluated patients, presented distant compromise (in one case bone metastasis and in the other, pulmonary lesion)- representing 5 % of the patients, changing the initial stage (up-stage).

In group 2, 10 of the 23 patients showed metastasis (47 %). In 7 of these 10 cases were detected by 18 FDG-PET/CT (70 %) reporting 3 cases in the mediastinum, 2 in the lung, 1 in the liver and the last patient had bone affectation. The 3 remaining cases (30 %) had metastases that were identified by all methods (conventional imaging and 18FDG-PET/CT), showing bone metastasis in two patients and hepatic ones in the other.

Conclusion: 18 FDG-PET/CT revealed higher efficacy to detect distant lesions than conventional diagnostic methods in locally advanced stages of breast cancer. However it did not show significant advantages in early stages.
Impact of FDG PET/CT in the initial staging of patients of non-small cell lung cancer: 4 year experience from a tertiary care referral cancer centre in India


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Introduction: Non-small cell lung cancer (NSCLC) is the most common cause of cancer death in the developed world with less than 13% survival at the end of 5 years. The impact of FDG-PET and PET-CT is well documented from developed countries and an upstaging or a change in staging leading to change in treatment plan is documented in 15-28%. Reports from other Asian countries (Korea, Japan) have shown the above figure to be 19-22%. Here we present our 4-year experience using FDG PET-CT for initial staging of patients with non-small cell lung cancer.

Aim: To study the impact of 18 F-FDG PET-CT on potentially resectable patients of NSCLC presenting to a tertiary care cancer centre in India.

Materials and Methods: 606 patients were referred for a staging whole body FDG PET-CT study, they were deemed to be potentially resectable after a joint clinic decision based on the findings of conventional imaging work up (including CT chest-abdomen, bone scan & MRI brain). The study was performed with 5MBq/kg body weight FDG and scan obtained after 60 minutes of uptake from the base of the skull to the lower-third part of the thigh. The accompanying CT was contrast enhanced.

Patients were marked as inoperable when:

a) PET/CT showed contralateral mediastinal or supraclavicular lymphadenopathy (N3)

b) PET/CT showed distant metastatic sites (M1)

Lesions were considered to be due to disease involvement on the basis of pathological findings (obtained by a biopsy) and if there was accompanying morphological change on the CT component of the PET or any other correlative imaging. The FDG PET/CT studies were read by a Nuclear Physician and Radiologist and were also further subjected to a review by the Thoracic tumour board (comprising of a surgeon, radiation oncologist and a medical oncologist). A treatment decision of surgery or non-surgery was taken only after reaching a common consensus after considering the FDG PET/CT findings.

Results: Out of 606 patients who underwent the whole body PET-CT scan, 350 were considered to be potentially operable and there was no stage alteration after the conventional work up. 246 (40.5%) were upstaged and considered to be inoperable and were offered non-surgical treatment options. Of these 246 patients, 203 had N3 nodes, 26 had liver metastases, 47 had adrenal, 122 had skeletal involvement, 39 had metastatic lung involvement, 60 had pleural involvement, 8 had muscle and soft-tissue metastases and 3 had renal parenchymal deposits. Extra-thoracic metastatic disease was seen in 206 patients. Out of these, skeletal
metastases accounted for the highest number, followed by adrenal and then liver metastases. Contralateral or supraclavicular (N3) nodal disease accounted for more inoperable patients as compared to metastatic lung involvement.

Conclusion: PET/CT detects metastatic disease in a significant proportion of patients of NSCLC at initial staging (40.5%) after conventional work up deems them to be potentially operable. In our series, the inoperability in otherwise operable is significantly higher than that of the reports from the US, Europe, Japan and Korea.

Future impact: In developing countries like India where adequate screening programme of high-risk population is not evolved, the impact of FDG PET-CT would be higher in the initial staging of non-small cell lung cancer by preventing futile surgeries and radical therapies. This is bound to have a significant saving in public expenditure.
FDG PET/CT in small cell lung cancer: Initial experience from a tertiary cancer referral centre in India


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Introduction: Small cell lung cancer (SCLC) is a rapidly progressive, biologically aggressive form of lung cancer that has a short survival rate without timely treatment. The majority of patients present with extensive disease and treatment options are determined according to whether the disease is localised (limited stage) or disseminated (extensive stage). FDG PET/CT plays an important role in the initial staging work up as well as response assessment in patients of SCLC.

Objectives: To assess the utility of FDG PET/CT in SCLC for the following indications: 1) Initial staging 2) Assessment of treatment response 3) Restaging.

Materials and Methods: 67 patients of pathologically proven SCLC of the lung underwent 87 FDG PET/CT studies from 2005 to 2009. The FDG PET/CT scans were performed with 5MBq/kg body weight FDG and scan obtained after 60 minutes of uptake from the base of the skull to the lower-third of the thigh.

Scans were performed for the following indications:

a) Initial staging - 50 patients underwent baseline FDG PET/CT study for initial staging.

b) Response assessment – 20 patients underwent both pre & post treatment FDG PET/CT

c) Restaging – 17 patients underwent a restaging FDG PET/CT study after completion of treatment for suspected recurrence.

FDG findings were considered to be due to disease involvement if there was histopathological correlation and/or a corresponding morphological correlate on the CT component of the PET study or on any other correlative imaging study. The FDG PET/CT findings were read by a Nuclear Physician and a Radiologist and then reviewed again in a Thoracic tumour board meeting on the basis of which, the disease was labelled limited or in the extensive stage and treatment was planned accordingly.

Results: a) 32 patients who were deemed to be limited stage after a thoracic tumour board decision (after reviewing the findings from CECT chest-abdomen, bone scan & MRI brain) underwent a baseline staging FDG PET/CT study. 19/32 (59.3 %) patients showed extensive stage disease on FDG PET/CT. Conventional work up had showed limited disease in these 19 patients, 13 (40.7 %) patients showed limited disease on FDG PET/CT which was consistent with the conventional work-up. Remaining 18 patients who were labelled extensive stage on conventional work up (during thoracic tumour board) were referred for a baseline FDG PET/CT study. 20 patients showed extensive stage disease on FDG PET/CT. Conventional work up had showed limited disease in these 20 patients, 13 (40.7 %) patients showed limited disease on FDG PET/CT which was consistent with the conventional work-up. Remaining 18 patients who were labelled extensive stage on conventional work up (during thoracic tumour board) were referred for a baseline FDG PET/CT study.
PET/CT study. In these patients both PET & conventional work up findings were consistent for extensive stage disease.

b) In 20 patients, both baseline and post treatment PET/CT studies were performed and metabolic response was assessed. Complete metabolic response was seen in 5 patients. Progressive disease was noted in 8 patients. Residual disease was seen in 7 patients (partial response or stable disease).

c) 17 patients were referred for a restaging FDG PET/CT study after completion of treatment for suspected recurrence. Recurrence was confirmed in 15 patients. In two patients PET did not reveal e/o disease, however showed disease progression subsequently.
Purpose: FDG uptake mediated by glucose transporter type 1 (Glut-1) and tumour proliferative activity assessed by Ki-67 expression provide prognostic information in patients with non-small-cell lung cancer (NSCLC). Here, we compared the prognostic significances of FDG uptake, and of Glut-1 and Ki-67 expressions in patients with NSCLC.

Methods: NSCLC patients (n = 53, F:M = 16:37, age 61.9±12.1 years) who underwent curative resection after FDG-PET were enrolled. Thirty-one patients had stage I, 15 stage II, and 7 stage III disease. Patients were treated by surgery only (n = 12), surgery plus adjuvant oral chemotherapy (n = 32), or surgery plus adjuvant intravenous chemo- or radio-therapy (n = 9). Maximum standardized FDG uptake values (maxSUV), and the Glut-1 and Ki-67 expressions of resected tumors were analysed for correlations and relations with tumor recurrence. The median follow-up duration was 15 months.

Results: Thirteen (24.5%) of the 53 patients experienced recurrence during a median follow-up of 8 months and significant correlations were found between maxSUV, Glut-1, and Ki-67 expressions (r = 0.48–0.79, p < 0.001). Univariate analysis revealed that disease-free survival (DFS) was significantly correlated with maxSUV (<7 versus ≥7, p = 0.001), % Ki-67 expression (<25% versus ≥25%, p = 0.047), tumour size (<3 cm versus ≥3 cm, p = 0.027), and tumour cell differentiation (well/moderate versus poor, p = 0.011). However, multivariate Cox proportional analysis identified maxSUV as the only determinant of DFS (p = 0.005). Patients with a maxSUV of ≥7 (n = 14) had a significantly lower 1-year DFS rate (57.1%) than those with a maxSUV of <7 (n = 39, 89.7%).

Conclusion: FDG uptake is more valuable than Glut-1 or Ki-67 expression in terms of predicting prognosis in patients with resected NSCLC.
Fig. 1. Scatter plot of maxSUV vs. Glut-1.

Fig. 2. Scatter plot of maxSUV vs. Ki67.

Fig. 3. Scatter plot of Ki67 vs. Glut-1.

Fig. 4. Disease-free survival rate curves at maxSUV cut-off value of 7. Patients with a maxSUV ≥7 (n=144) had a lower 5-year disease-free survival rate (57.1%) than those with a maxSUV <7 (n=70, 89.7%).
Role of 18F-DOPA PET/CT in the evaluation of neuroendocrine tumours

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The aim of this study was to evaluate the role of 18F-DOPA PET/CT in the detection of neuroendocrine tumours. Thirty four patients with histologically proven neuroendocrine tumours were prospectively enrolled and scheduled for 18F-DOPA PET/CT. No carbidopa was administered to these patients prior to the 18F-DOPA PET/CT study. These 34 patients were divided into two groups based on their diagnosis. One group consisted of patients with carcinoids (n=22) and the other group of patients with medullary thyroid carcinoma (n=12). These patients were being evaluated for staging/restaging, recurrence and response to therapy. The scans were evaluated independently by two nuclear medicine physicians. PET/CT results obtained were compared with other investigations like CT, MRI, 68Ga-DOTANOC PET/CT, etc. and correlated with clinical history and biochemical markers for the establishment of gold standard. Results were analysed separately for the two individual disease groups. In the carcinoid patient group (n=22), the most common primary tumour site was the pancreas and the most common metastatic site was liver. However, 18F-DOPA did not identify all metastatic sites in liver as compared to the 68Ga-DOTANOC PET/CT and CECT. 18F-DOPA PET/CT identified 13 out of 18 positive patients with a sensitivity of 72%. 4 patients were identified as true negative on 18F-DOPA PET/CT and were confirmed to be the same on 68Ga-DOTANOC PET/CT and clinical follow-up at 6 months. In the medullary thyroid carcinoma (MTC) group (n=12) 18F-DOPA was positive in 8 out of 10 positive patients with a sensitivity of 80%. 18F-DOPA PET/CT was positive in primary disease, recurrent disease as well as in metastatic lymph nodes. Two patients were classified as true negative on 18F-DOPA PET/CT based on imaging findings, calcitonin assay and clinical follow up. Overall, 18F-DOPA PET/CT seems to be a very promising modality in the evaluation of neuroendocrine tumours. On lesions basis 18F-DOPA PET/CT showed inferior sensitivity in detection of metastatic liver disease and underestimated the actual total burden of disease in patients with carcinoids. In patients with MTC 18F-DOPA PET/CT showed an excellent sensitivity in detection of primary as well as metastatic disease. Whenever, available 18F-DOPA PET/CT should be used in the evaluation of neuroendocrine tumours.
The aim of this study was to evaluate the role of 99mTc(V)DMSA and [18F]FDG PET-CT in the management of patients with osteosarcoma. 19 patients (M:11, F:8, age 9-70yrs, mean 30yrs) with confirmed osteosarcoma were included in the study (17 untreated and 2 post chemotherapy). All patients underwent both 99mTc(V)DMSA and whole body [18F]FDG PET-CT scans within an interval of 1 week. 700-740 MBq of 99mTc(V)DMSA was injected in vitro and whole body planar & SPECT images of primary site and chest were performed after 120 minutes. [18F]FDG PET-CT images were obtained 60 minutes post intravenous injection of 370 MBq of F-18 FDG. Scan findings were interpreted in consensus with histologic reports, radiological imaging, and clinical findings which were used as the reference standard. Both FDG PET-CT (mean SUV max=7.4,) and DMSA(V) scan showed abnormal uptake at primary site in all the 19 patients (100% sensitivity for both). Whole body PET-CT detected metastasis in 10 pts (lung mets in 9 and lung + bone mets in 1 patient). Of these, 8 patients had b/l multiple lung nodules with variable degree of FDG uptake (mean SUV max.1.1) while 2 patients had solitary lung lesion. Whole body planar DMSA(V) detected bone metastasis in one patient, and SPECT of chest revealed lung mets in 6 patients and LN in 1 patient. HRCT of chest confirmed lung mets in 9 patients and inflammatory lesion in one patient with solitary nodule. 6 patients positive for mets on DMSA(V) scan had higher uptake in lung lesions as compared to FDG uptake on PET-CT. However the number of lung lesions with DMSA uptake was less in same patients and 3 patients who did not show any DMSA uptake had sub cm Lung Nodule. Both 99mTc(V)DMSA (whole body planar and SPECT imaging) and [18F]FDG PET-CT provide important information about local and distant metastasis in osteosarcoma. Results of both the scans were comparable in evaluation of primary site lesions and metastatic lesions greater than 1 cm. Though 99mTc(V)DMSA had higher uptake in the lesions as compared to[18F]FDG PET-CT, [18F]FDG PET-CT had an advantage as it could also detect sub cm lesions.
Role of serial 18F-FDG PET/CT in surveillance of patients treated for colorectal cancer

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Recurrence of colorectal cancer (CRC) occurs in about 30% to 40% of patients within initial 1 to 2 years. Overall diagnostic accuracy of 18F-FDG PET/CT is superior to that of conventional imaging for diagnosis of CRC. We aimed to find out the usefulness of serial 18F-FDG PET/CT study in the surveillance of patients who have been treated for CRC. Retrospective analysis was done. 18 patients (16 male & 2 females) were included in the study with median age 55.5 years (age: 32-72 years). A total of 44 PET/CT were performed over these 18 patients (11 patients underwent 2 scans, 6 patients underwent 3 scans and 1 patient underwent 4 scans). All the patients underwent some standard mode of treatment before the first 18F-FDG PET/CT study. Positive FDG PET findings were defined as focal accumulation of FDG above the normal level of surrounding tissue, excluding physiologically increased uptake. Clinical follow-up was the gold standard. Mean duration of follow up was 3 years. Out of the total 44 scans performed, 23 scans had positive findings on 18F-FDG PET/CT study. 21 scans were negative for any residual or recurrent disease. Out of 23 positive scans, 3 were found to be false positive. Of the total 21 negative scans, 2 were found to be false negative. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of 18F-FDG PET/CT for detection of residual/recurrent disease and metastasis was found to be 90.9%, 86.3%, 86.9%, 90.4% and 88.6% respectively. Serial 18F-FDG PET/CT performed in patients treated for colorectal cancer has an important role in follow-up and surveillance to find out residual/recurrent disease and distant metastasis.
Efficacy of F-18 FDG PET/CT in detecting recurrence in patients with epithelial ovarian carcinoma

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Surveillance in patients with ovarian carcinoma after primary treatment is not well defined. Validity of CA-125 marker as a guide for tumour recurrence is still controversial. We studied the accuracy of whole body fluorine-18 fluorodeoxyglucose (FDG) positron emission tomography (PET) in patients with epithelial ovarian carcinoma after treatment. 45 consecutive patients were retrospectively evaluated during follow-up after surgery and chemotherapy with CA-125 determinations and PET/CT study. In 14 patients with negative tumour marker, PET/CT performed due to suspicion of residual or recurrence was negative in 6 and positive in 8 patients. In remaining 31 studies, patients presented with progressively rising or high CA-125 levels. Out of these 31 patients, PET/CT was positive in 26 and negative in 5 patients. In all PET negative cases follow-up was done with clinical examination, CA-125 marker and conventional imaging for 6-12 months. 2/11 PET negative patients showed recurrence, one after 11 months and one after 4 months of PET/CT scan. Out of 34 PET positive cases, widespread metastases were detected in 15 cases, pathological confirmation was concordant in 7 cases and biopsy was negative in 4 cases. In remaining 8 PET positive cases, patients received chemotherapy and follow-up with CT, PET/CT and CA-125 was performed. True positive, true negative, false positive and false negative results with PET/CT were 30, 9, 4 and 2 respectively. Sensitivity, specificity, PPV, NPV and accuracy of PET/CT in identifying recurrence in post-treatment ovarian cancer was 93.75%, 69.23%, 88.23%, 81.81% and 86.66% respectively. This study showed that F-18 FDG PET/CT is a useful tool to plan the best treatment when CA125 level rises progressively. It can accurately detect the site of recurrence and is useful in deciding patient wise management. PET/CT also helped in identifying recurrence in CA125 negative cases. Thus, PET/CT should be considered in suspicion of recurrence in post-treatment patients of ovarian cancer.

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<th>PET positive (n=34)</th>
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<tr>
<td>Widespread metastases</td>
<td>15</td>
<td>Disease free on follow-up  9</td>
</tr>
<tr>
<td>Biopsy concordant</td>
<td>7</td>
<td>Recurrence 2</td>
</tr>
<tr>
<td>Follow-up with CT, PET/CT and CA-125</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Biopsy discordant</td>
<td>4</td>
<td></td>
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</table>
Role of whole body PET/CT in detecting distant metastasis in head and neck cancer

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Information: The incidence of distant metastases in patients with head and neck cancers (HNC) is smaller ranging from 4% to 25%, with the lungs, bones and liver being the most frequent sites. 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET)/computer tomography (CT) has shown more sensitivity in detecting unsuspected distant metastasis. Several reports indicate that for HNC a whole body scan may yield little additional information. So our aim was to evaluate the role of whole body PET/CT in detecting the distant metastasis in HNC.

Materials and Methods: An analysis of 82 consecutive FDG PET/CT data of various HNC (cancer from buccal mucosa: 13, pharyngeal: 6, laryngeal: 7, tongue: 23, oral cavity: 2, pyriform fossa: 3, alveolar: 7, ethmoid sinus: 2, maxillary sinus: 4, tonsil: 4, parotid: 1 and thyroid: 10) was performed to identify metastatic lesions. 26 underwent scan for initial staging and 56 for restaging. For initial staging (26), 4 showed abnormal FDG uptake, one cancer tongue showed abnormal uptake in lungs and adrenals which was confirmed as tuberculosis, second showed uptake in a lung nodule which was confirmed as metastasis. One alveolar carcinoma showed abnormal uptake in oesophagus which was confirmed as synchronous malignancy. One buccal carcinoma showed uptake in enlarged bilateral axillary nodes. Amongst those patients for re-staging (56), PET/CT scan identified unknown widespread metastasis in 10 patients, which upstaged the disease to M1. A case of maxillary sinus cancer showed FDG uptake in multiple nodules in the lung and hypo-dense lesions in the liver. A case of alveolar cancer showed uptake in lesions in the liver and spleen and lytic lesions in the right first rib and the left iliac bone. So therapy planning has been changed by whole body PET/CT in 2 during initial staging and 10 during restaging. A synchronous oesophageal carcinoma was identified in a patient who came for PET scan for initial staging.

Conclusion: The detection of distant metastases at the time of initial evaluation and during restaging changes the prognosis and influences the selection of treatment modality in patients with HNC. PET/CT also plays an important role in detection of secondary malignancies associated with HNC. While FDG-PET/CT had high sensitivity, specificity, and negative predictive value, it had a lower positive predictive value, suggesting that additional diagnostic methods are essential to rule out false positives and to avoid false upstaging to M1 for appropriate therapeutic planning.
Recurrent carcinoma endometrium has a poor prognosis. However, successful salvage with long-term survival has been achieved after hormone therapy, radical surgery and radiotherapy/chemotherapy in patients with recurrent disease. Conventional imaging and tumour marker have limited accuracy for detecting recurrence in these patients. The aim of the present study was to compare the role of 18 F- Fluorodeoxyglucose (FDG) positron emission tomography-computed tomography (PET-CT) and conventional imaging (CI)[contrast enhanced CT (CECT) and/or magnetic resonance imaging (MRI)] in patients suspected to have recurrence of carcinoma endometrium. In this retrospective study a total 63 patients were evaluated. All patients had undergone surgery with/without adjuvant therapy (chemotherapy/radiotherapy/both) for histologically proven carcinoma endometrium. They underwent 18-FDG PET-CT studies for suspected recurrence. All patients also had undergone CI within 4 weeks of FDG PET-CT. Imaging findings were divided into five regions: local recurrence, nodal, organ, bone and others (serosal/skin). Clinical and/or imaging follow up (minimum- 6 months) and/or histopathology was taken as reference standard. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were calculated for both modalities. McNemar test was used to compare the diagnostic accuracies of CI and FDG PET-CT. Statistical analysis was done using SPSS 11.5.The mean age was 56.9±8.6 years. Primary histopathology was adenocarcinoma in 56 patients, adenosquamous in 6 and poorly differentiated carcinoma in 1. FDG PET-CT was positive for recurrence in 35 (55.5%) patients and negative in 28 (44.5%). On FDG PET-CT loco-regional disease was seen in 15 patients, metastatic disease was seen in 7 and 13 showed both loco-regional and metastatic disease. The sensitivity, specificity, PPV, NPV and accuracy of FDG PET-CT were 87.1%, 95.8%, 97.1%, 82.1% and 90.4% respectively. The sensitivity, specificity, PPV, NPV and accuracy of CI were 81.5%, 56%, 73.8%, 66.6% and 71.4% respectively. Compared to CI, FDG PET-CT has much higher specificity (56% vs.95.8%) and accuracy (71.4% vs.90.4%) with comparable sensitivity (81.5% vs.87.1%). False positive findings were much more common with CI than FDG PET-CT (11vs.1). On McNemar analysis no significant difference was found between FDG PET-CT and CI on per patient analysis (p=210). However, distant organ recurrence is more likely to be detected by FDG PET-CT compared to CI (p=0.02). FDG PET-CT is a highly sensitive and specific modality for detecting recurrence in post therapy patients of carcinoma endometrium with suspected recurrence. It is more specific than conventional imaging and is especially useful for detecting recurrence in distant organs.
Introduction: 3-Deoxy-3-18F-fluorothymidine (18F-FLT) is a recently developed PET tracer to image tumour cell proliferation. We characterized 18F-FLT PET of brain primary tumours and compared 18F-FLT with 18F-FDG PET in side-by-side studies of the same patients.

Methods: 4 patients with newly diagnosed or previously treated brain tumours underwent PET with 18F-FLT and 18F-FDG on consecutive days. Uptake of 18F-FLT and 18F-FDG was quantified by the standardized uptake value (SUV) and the tumour-to-normal tissue (T/N) ratio. The accuracy of 18F-FLT and 18F-FDG PET in evaluating newly diagnosed and recurrent tumours was compared.

Results: 18F-FLT uptake in tumours was rapid, peaking at 5–10 min after injection and remaining stable up to 75 min. Hence, a 30-min scan beginning at 5 min after injection was sufficient for imaging. 18F-FLT visualized all tumours. The absolute uptake of 18F-FLT was low but image contrast was better than with 18F-FDG. 18F-FDG PET studies were negative or presented low uptake in 3 patients with recurrent brain tumours.

Conclusion: Thirty minute 18F-FLT PET 5 min after injection was more sensitive than 18F-FDG to image recurrent brain tumours. Thus, 18F-FLT appears to be a promising tracer as a surrogate marker of proliferation in brain tumours especially those of a high grade.
Aim: To evaluate the impact of 18F-FDG PET-CT (PET-CT) in the management of differentiated thyroid cancer (DTC) patients with negative 131I post-therapy whole body scan (WBS) and elevated serum thyroglobulin (Tg).

Material and Methods: This retrospective study included 20 patients with DTC (15 papillary and 5 follicular carcinoma). All patients were submitted to total thyroidectomy and to several 131I treatments (RAI) for thyroid remnant ablation or loco-regional and distant metastases. WBS was performed 5-7 days after RAI. Inclusion criteria were negative WBS, elevated serum Tg levels, and negative anti-Tg autoantibodies (AbTg) observed during the long-term follow-up. 18 patients were studied off L-T4 therapy and 2 after recombinant human TSH (Thyrogen®) administration. PET-CT scan was performed in fasting patients 60 minutes following in vitro administration of 18F-FDG.

Results: PET-CT was positive in 13/20 patients (65%). Loco-regional recurrences in thyroid bed (3 patients), and metastases in bone (3 patients), cervical lymph node (LN) (3 patients) and in multiple sites (2 patients) were found. The overall sensitivity and accuracy of PET-CT were 63% and 60%, respectively. In 4/13 patients (30%) PET-CT changed the therapeutic management. 3 patients with residual tumour in the neck were submitted to surgical dissection and/or External Beam Radiotherapy.

Conclusion: PET-CT identified residual neoplastic tissue in 65% of patients with high levels of Tg and negative WBS. PET-CT modified the therapeutic management in 30% of patients suggesting suitable modality of treatment.
Role of FDG-PET in the restaging and recurrent breast cancer

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Aim: To evaluate the impact of integrated 18FDG Positron emission tomography with computed tomography (PET/CT) on restaging and recurrent disease in the retrospective study of breast cancer (BC) patient follow-up.

Patients and Methods: 20 BC patients included PET/CT studies for restaging after long term follow-up (after the 6th month). All patients underwent whole-body PET/CT for diagnostic purposes PET/CT was performed approximately 60 minutes following 18F-FDG injection. CT portion acquired with low dose X-ray for localization and attenuation correction.

Results: 18F-FDG-PET restaged 15 patients with recurrence of the disease. PET/CT described loco-regional recurrences in 4 and distant metastases in 11 patients. Compared to the CT alone, PET/CT rejected recurrence of the disease in 5 CT FP results and correctly detected 2 more malignant lesions, equivocal on the CT. Integrated PET/CT showed 98% sensitivity, 90% specificity, 97% accuracy in the follow-up recurrences evaluation.

Conclusion: In breast cancer restaging, 18F-FDG PET/CT is more accurate than CT alone.
Correlation between estimated tumour dose and response to PRRNT as determined by SMSreceptor PET/CT using Ga-68 DOTATOC

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Aim: To evaluate a dose-response relationship, i.e. a relation between the doses delivered during peptide receptor radionuclide therapy (PRRNT) with Lu-177 labelled somatostatin (SMS) analogues (DOTATOC/DOTATATE) to liver metastases of neuroendocrine tumours, and the molecular response as determined by the change in SUVmax on subsequent Ga-68 labelled SMS analogue PET/CT (SMS PET/CT); and therefore to be evaluate a possibility of predicting the response based on the dose delivered.

Methods: 67 patients (40 males and 27 females; age 55 ± 16 years) of metastatic neuroendocrine tumours who underwent a cycle of PRRNT were selected for this study. A total of 96 liver metastases (1-4 in each patient) were analysed in all patients before and after PRRNT, with duration of between 3-10 months (median 5 months) between the pre- and post-therapy SMS PET/CT. Dosimetric calculations (MIRD scheme) were performed using OLINDA software. Up to 4 liver metastases in each patient well matched on the Lu-177 labelled SMS analogue whole body planar images and SMS PET/CT MIP images were selected for determining the dose delivered and the therapeutic response respectively. The response index (RI) was calculated in each of the liver metastases as the change in the SUVmax after PRRNT as follows: RI = (pre therapy SUVmax – post therapy SUVmax)/ pre therapy SUVmax. A dose-response curve was plotted with dose on x-axis and response index on y-axis. The lesions were divided into two groups - group 1 (n=24) showing more than 25% fall in SUVmax post therapy (minor response) and group 2 (n=18) showing 15% or more rise in SUVmax post therapy (minor progression or progressive disease).

Results: There was a logarithmic increase in response with increasing dose. No definite threshold of the dose was found to determine a measurable response and there was a wide variation in the degree of response. There was a significant difference (p<0.01) in the dose delivered between group 1, i.e. lesions showing minor therapy response (n=24; mean/median dose = 142.75 Sv/79 Sv) and group 2, i.e. lesions showing minor progression or progressive disease (n=18; mean/median dose = 22.99 Sv/20 Sv). This reconfirms the finding that a high dose delivered is associated with a better molecular response post PRRNT.

Conclusion: The preliminary results showed that there is a trend of logarithmic increase in molecular response (as determined with decrease in SUVmax on PET/CT) with increase in the dose delivered. The response cannot be predicted based alone on the dose delivered. Additional radiobiological factors must be taken into consideration using complex mathematical models to determine the dose-response relationship on PET/CT.
Testicular cancer is responsible for the highest mortality among the malignant diseases in the young adult male population. FDG is helpful in some histological types of testicular cancers and teratomas have a lower tracer uptake due to their very well differentiated status.

Objective: To evaluate PET-FDG imaging performance in patients studied for testicular tumour evaluation.

Methods: We studied 81 males with 96 FDG scans. Age range: 18-53 y.o. The test was performed with a dedicated PET Siemens System using 518±37MBq mCi of 18F-FDG. Whole body images were supplemented with a post delayed pelvis acquisition. The report was based mainly on visual analysis. We compared FDG results with anatomic imaging and all clinical available data, according to tumour histology.

Results: Forty-four patients have left tumour, and 35 right (p=ns); 2 of them had a prior testicular cancer. No pure teratomas were included. Four germ cell tumours were included in NOS group (No Otherwise Specified). Patients with carcinoembrionary tumours were significantly younger and with shorter time between orchiectomy and FDG performance. Initial staging corresponded to: Stage 1=13%; 2=34%; 3=25% and 4=23%. The most frequent FDG indication was therapy control (mainly chemotherapy) and then restaging (p=0.03). Only one seminoma patient had the primary tumour on site with a negative FDG scan. The overall FDG agreement with other images, tumoural markers and clinical data was 82% (kappa=0.628). The discordant results were all, but one, with negative FDG results. There was no significant difference in the agreement observed between groups even it was higher in seminomas. (See Table 1)

Conclusion: In this testicular cancer sample, without pure teratoma cases, we observed that PET-FDG was a useful tool for patient management such as therapy control and restaging.
Conclusions: In this testicular cancer sample, without pure teratoma cases, we observed that PET-FDG was a useful tool for patient management such as therapy control and restaging.

**TABLE 1:**

<table>
<thead>
<tr>
<th>Patients</th>
<th>Initial Age (years)</th>
<th>Time to Orchiectomy (months)</th>
<th>S/R/TC</th>
<th>FDG Positive</th>
<th>Agreement FDG vs. Other Data</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Seminoma</strong></td>
<td>28 (37)</td>
<td>38±9$^*$</td>
<td>27±28</td>
<td>1/16/20</td>
<td>17/37</td>
</tr>
<tr>
<td><strong>Embryonal Carcinoma</strong></td>
<td>9 (1)</td>
<td>24±7$^*$</td>
<td>6±4</td>
<td>0/6/4</td>
<td>5/10</td>
</tr>
<tr>
<td><strong>Non-Seminoma</strong></td>
<td>5 (6)</td>
<td>29±7$^*$</td>
<td>8±5</td>
<td>0/3/3</td>
<td>4/6</td>
</tr>
<tr>
<td><strong>Mix Germ Tumors</strong></td>
<td>26 (26)</td>
<td>32±8$^*$</td>
<td>23±24</td>
<td>0/19/7</td>
<td>9/26</td>
</tr>
<tr>
<td><strong>NOS</strong></td>
<td>13 (17)</td>
<td>33±12$^*$</td>
<td>46±53</td>
<td>0/11/6</td>
<td>4/17</td>
</tr>
</tbody>
</table>
Usefulness of 18F-FDG PET/CT in the assessment of the response to treatment of patients with lymphoma

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Objective: Assess response to treatment of patients with lymphoma by studying PET / CT with 18F-fluorodeoxyglucose (FDG).

Material and Methods: An ambispective, transversal and descriptive study. We reviewed records of 101 patients with lymphoma who came to Hospital Angeles Pedregal (59.4% men and 40.6% women, average age 47.0 + / - 16.2 years) for evaluation of treatment response by means of PET/CT analysis with FDG. We used labelled Fluorodeoxyglucose Fluor-18 (FDG); doses of 150 uCi per body weight/Kilogram. Computer: GEMINI-16 Power. Phillips PET/CT. For image analysis/findings, criteria NCCN/IWG was used (National Comprehensive Cancer Network/International Working Group) and the relation to histological subtypes, staging baseline, relapse, and disease free survival. Statistical analysis included Kolmogorov-Smirnov statistic: chi-square tests to compare associated variables; statistical parametric analysis of variance to compare 3 or more averages, and normal distribution, nonparametric statistics: Kruskal-Wallis test for survival and time free survival were used (SPSS version 15).

Results: The total (101 patients), diagnosis of non-Hodgkin lymphoma (NHL) accounted for 61.4% of the sample from 38.6% of Hodgkin’s Disease (LDH). 72.3% response to treatment was classified as a complete survival of 3.47 years and disease free survival of 2.36 years. 12.9% partial response 3.23 years survival and disease free survival of 0.69 years. 2.0% stable response with survival of 2.50 years and 0.23 years free of disease and 12.9% progressive disease 2.62 years, 0.23 years of survival and disease free. The complete responses were significantly associated with chemotherapy treatments 77.6% and 75% with chemotherapy plus radiotherapy. Cases with progressive response were treated mainly with chemotherapy (53.8%), 23.1% with chemotherapy plus radiation therapy, 15.4% with surgery only and 7.7% with surgery plus radiotherapy (p = 0.0001). Patients undergoing bone marrow transplant were located mostly in partial response. The relapse rate in LDH rose to 23.1% versus 8.2% for NHL (¬p=0.03). They were mostly in complete response after treatment, but paradoxically the LDH had a longer disease free 2.7 years to 1.2 years of NHL (p=0.04) and correspondingly greater survival period after diagnosis.

Conclusions: In the evaluation of treatment response of patients with lymphoma by studying 18F-FDG PET/CT, showed that most patients were classified as having complete response were located in the early stages with a large cell histological subtype, and most of these patients were treated only with chemotherapy, obtaining a longer survival and more disease free time. It was reported that there were more relapses in patients with LDH than NHL and paradoxically LDH patients were reported with a longer life span and disease free time, which differs from other author’s reports.
Usefulness of 68Ga-DOTA-d-Phe (1)-Tyr (3)-Octreotide (DOTATOC) PET/CT in neuroendocrine tumours

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Introduction: The initial assessment of neuroendocrine tumours has been regularly performed using somatostatin analogs labelled with 111In or 99mTc. Nevertheless, the arrival of positron emission tomography has revolutionized the diagnostic-therapeutic approach, due to the increase in specificity and sensitivity for this molecular imaging modality. The labelling of these new peptides with 68Ga is considered a highly accurate diagnostic study, and it provides a relatively low dosimetry and, as it is obtained by a generator, the availability has been improved.

Aim: To show the initial experience in the use of 68Ga DOTATOC in patients with neuroendocrine tumours in the Instituto Nacional de Cancerología and compare the effectiveness versus other conventional imaging methods.

Materials and Methods: The study included 27 patients with histo-pathological diagnosis of neuroendocrine tumour and imaging study for initial evaluation. Then, the restaging and assessment of therapy response were done using 68Ga-DOTATOC PET/CT. The regions of interest in the normal bio-distribution structures and the tumour lesions were drawn. The results were compared to other conventional imaging methods. The verification was carried out by endoscopic or surgical findings with histo-pathological study.

Results: We studied 27 patients (19 women and 8 men) with mean age 48 +/- 11.7 years old. The 68Ga DOTATOC PET/CT sensitivity was 86% (32/37) and contrasted CT sensitivity was 78% (29/37). 6 patients (4 high-grade, 2 low grade) had supplementary 18FDG PET / CT, showing a statistically significant difference p = 0.0442 (p <0.05). The SUVmax range of structures with normal uptake did not show any significant difference in all cases. Three patients with other molecular imaging studies (131I MIBG or 18 F-FDG) did not show the recurrence site, while using the 68Ga DOTATOC the detection was effectively performed.

Conclusions: It was observed that the 68GaDOTATOC PET/CT was useful in the evaluation of neuroendocrine tumours, since it has high sensitivity and specificity it provides additional information not shown in conventional imaging methods.
Prognostic value of metabolic tumour burden with 18FDG PET/CT in diffuse large B cell lymphoma

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Introduction: The diffuse large cell lymphomas (LNHDCG) have a variable course whose survival depends on the aggressive therapeutic regime according to the calculated prognosis. The tumour burden is an established factor indirectly calculated. However, the implementation of imaging technics such as positron emission tomography (PET/CT) using 18 Fluorodeoxyglucose (18FDG), have established the glycolytic activity measured in volume and thus the total metabolic burden tumour is accurately estimated.

Methods: The study included 29 patients with corroborated immunohistochemistry for diffuse large cells non-Hodgkin lymphoma and baseline 18FDG PET/CT study. The CMT was measured using the three dimensional outlining of the region of interest with the standardized uptake cut-off value (SUVmax) 2.5 to the positive lesion, the progression-free survival and disease-free survival were analysed versus other prognostic variables. The correlation indices between CMT, DHL and B2 microglobulin were obtained.

Results: The diagnosis average age was 49.1 +/- 18.2 years (range 23-82), 15 men and 14 women. The cut-off for characterizing prognosis according to the mean survival was <1900 cm3 (sensitivity 92% 95% CI 73.1-99.02%, specificity 100% 95% CI 39.7-100% p=0.005), and the probability index 12.5. The correlation index between VMT and DHL is 0.63 (p=0.0002) and between VMT and B2MG was 0.5664 (p=0.0014). In an unvaried analysis the CMT was significantly related to progression-free survival (LR=6.2, df=2, p=0.0430) and overall survival (LR=7.8, df=2, p=0.019). An increase of 731.4cm3 between 50 and 75 percentile, increases 1.9 times the progression risk. The actuarial curve analysis with the test for the overall survival results for LR=21, df=2, p<0.00001, SUVmax LR=12.75, df=1, p=0.0002, clinical stage LR 22.7 df=22.7 df=1, p<0.00001, DHL, LR=10.9 df=1, p=0.001, DHL, LR:10.9 df=1, p=0.001, extra nodal presentation RL=0.0004619, df=1, p=0.0458.

Conclusions: The calculated CMT using 18FDG PET/CT is an independent survival predictor more effective than some commonly used variables for patients with LNHDC, and also, due to the close correlation with the tumour serum markers, the amount of metabolically active tumour cells was measured.
Diagnostic accuracy of FDG PET/CT in recurrent osseous and soft tissue sarcoma: Comparison with full-dose diagnostic CT

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Objective: To compare the diagnostic accuracy of integrated positron emission tomography and computed tomography (PET/CT) using 18F-fluorodeoxyglucose (FDG) with full-dose diagnostic CT in restaging sarcoma. We also investigated the incremental impact of this integrated modality on management plan.

Methods: In this study, 30 patients (age range: 21-79 years, mean age: 42 years) with history of sarcoma (13 soft tissue sarcoma and 17 primary osseous sarcoma) underwent FDG-PET/CT examination and full-dose diagnostic PET/(contrast-enhanced)CE-CT (n=22) or separate diagnostic CE-CT within one month of the PET/CT study (n=8) for suspected recurrence disease, integrated PET/CT images and diagnostic CT alone were separately interpreted by two experienced reviewers by consensus. Imaging findings were validated on the basis of histopathology or radiological and clinical follow-up (> 6 months).

Results: Follow-up revealed local recurrence and/or distant metastasis in 18 patients (7 local). PET/CT was true positive in 16 and false negative in 2 patients. Local recurrence was detected in 6/7 patients by PET/CT. CT alone was true positive in 13 patients and false negative in 5 patients. Local recurrence was detected in 3/7 patients. In 12 patients without evidence of recurrence during follow-up, PET/CT was true negative in 10 patients and false positive in 2 patients. CT alone was true negative in 8 patients and false positive in 4 patients. In patient-based comparison between PET/CT and CT alone, corresponding sensitivity, specificity, and accuracy were 89%, 83% and 87% for PET/CT and 72%, 67% and 70% for diagnostic CT alone, respectively. Sub-analysis based on lesion-site revealed a PET/CT sensitivity of 100% and 71% for detection of bone and soft tissue lesions, compared to 78% and 57% for CT alone, respectively. PET/CT findings led to changes in the subsequent clinical management in 13% of patients (4/30) when analysed side-by-side with CT alone.

Conclusion: Integrated PET/CT is an accurate method for assessing recurrent sarcoma. Integrated PET/CT is more accurate for restaging sarcoma compared to diagnostic CT alone. Detection of bone and soft tissue lesions is the most evident advantage of integrated PET/CT over diagnostic CT alone. Keywords: sarcoma, restaging, recurrence, FDG PET/CT, full-dose diagnostic CT.
Improving detection and evaluation of gastric malignancies on PET/CT by gastric distention with both milk and diatrizoate

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Worldwide, gastric cancer is the second leading cause of cancer-related deaths, and the incidence is the highest in the Asian and African population. However, conventional FDG PET/(CT) in fasting status has shown limited value in diagnosis of primary gastric malignancies because of physiological uptake and vulnerable peristalsis of the crimple stomach. Based on the ideal of distending stomach with milk immediately before the scanning to increase the contrast of PET and using oral contrast for better visualization of the lesion on CT as well, we underwent a clinical study to prove its value for detection of primary gastric malignancies and in evaluation of tumour response to neoadjuvant chemotherapy.

Method: As a modified PET/CT protocol, the patients were suggested to ingest the mixture of 300ml milk and 300ml 1.2% Diatrizoate within 5 minutes before the PET/CT scanning. The study enrolled 55 patients with proved gastric malignancies and 63 patients with benign or negative finding by recent gastroscopy; 20 patients who underwent serial modified PET/CT scans to evaluate the neoadjuvant chemotherapy were also included. The maximum standardized uptake value (SUV) of the suspicious gastric lesions and the normal gastric walls were measured.

Result: Under the modified PET/CT protocol, the maximum SUVs for gastric malignancies were 9.14±7.50, which were significantly higher than those of the distended normal gastric walls and the benign gastric lesions (SUV 1.14±0.53, P<0.001). If a lesion with maximum SUV ≥ 2.5 was considered as a malignancy, the sensitivity, specificity, and accuracy of the modified PET/CT for diagnosis of gastric malignancies were 94.55%, 98.41%, and 96.30%, respectively. Even for the 3 false negative cases, the low dose CT with oral contrast in the stomach also delineated the suspicious gastric lesions (see Figure 1). For the 20 patients who underwent serial modified PET/CT during the neoadjuvant chemotherapy, 10 showed decrease of maximum SUV by >25%, while 3 showed increased uptake. These results corresponded well with the pathological findings after the surgery.

Conclusion: FDG PET/CT scanning under gastric distention by both milk and Diatrizoate shows high sensitivity and high contrast for the detection of gastric malignancies. It also warrants accurate response evaluation of gastric cancer to chemotherapy.
FIG. 1. In a 69-year-old man with poorly differentiated adenocarcinoma, gastric distention with both milk and Diatrizole helped for delineation of the lesion with mild 18F-FDG uptake (maximum SUV 2.1).
FDG PET-CT in pre op staging of breast cancer: Initial experience from a comprehensive care centre for breast diseases

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Aim: To evaluate the role of PET CT in pre-operative initial work up of breast cancer.

Materials and Methods: A total of 35 patients with clinical suspicion of breast cancer were included in the study. Digital mammography, Breast ultrasound (US) and FDG PET-CT were performed in all patients. Malignancy was confirmed by core biopsy. U/S and mammogram findings of lobulated mass with spiculations and pleomorphic calcifications were the diagnostic parameters. Lesion with max SUV value of > 5 was taken as malignant on PET CT. Metastatic disease was confirmed either with follow-up PET scans after neoadjuvant chemotherapy or with biopsy.

Results: Total number of patients was 35 with mean age of 36 yrs. Total of 39 breast lesions were analysed. When max SUV value of > 5 was taken as diagnostic criteria, PET-CT was 100% sensitive in diagnosing primary lesion. With max SUV value of > 7 the sensitivity was 97%. Conventional U/S and digital mammogram had a sensitivity of 95%. Bilateral breast cancer was seen in 4 patients (11.4%), out of which two were diagnosed by PET scan alone. All the three modalities picked up the axillary nodal involvement in 14 patients (40%) and PET scan helped in confirming by means of high metabolic activity (max SUV of > 5). PET scan showed metastatic disease in six patients (17%). Three patients with splenic metastases (1) and meditational nodal metastases (2) showed complete resolution of FDG uptake on follow-up PET CT following neoadjuvant chemotherapy. The rest of the 3 had pulmonary and skeletal metastases. All the six patients are on modified treatment protocol.

Conclusion: PET–CT is more sensitive than conventional ultrasound and digital mammogram in diagnosing primary breast lesions (100% vs. 95%). Added advantage in bilateral breast disease is highlighted. PET–CT upstaged the disease in 17% of patients which guided the oncologists to adjust and find the optimal treatment option for each patient.
Aim: With the large scale availability of PET and PET–CT in many centres world over in recent years, this technology has been increasingly used in the diagnosis and management of thyroid malignancy. Most published studies have emphasized the role of PET in patients with high Thyroglobulin (Tg) levels and negative radio iodine whole body scans (RIS). However, not much data is available on correlation of FDG uptake and histopathology in malignant disorders of the thyroid gland.

The purpose of this study is to analyse 18F-FDG uptake in different histopathological types of thyroid malignancy and to establish which type of thyroid cancer will benefit most from the FDG uptake study in addition to the conventional diagnostic procedures.

Material and Method: 69 consecutive patients with different histopathology were subjected to 82 studies of 18F-FDG uptake. In all patients conventional diagnostic procedures like radioiodine whole body scan (RIS), estimation of thyroglobulin (Tg) level and CT/MRI/US (wherever indicated) had been performed prior to FDG -PET study.

There were 50 females and 19 males in the age group between 11 and 91 years. 18F-FDG study was performed using the standard PET procedure either in, a dedicated PET Camera (ECAT, Siemens) or a PET / CT (Biograph, Siemens) machine. Standard uptake values (SUV) and maximum uptake values (SUV max) were registered in all suspected lesions. The results of the PET studies were correlated with various histopathological findings.

Results: In Papillary thyroid carcinoma (n = 51), 50 patients were clinically suspected of having recurrence or metastasis (all with high Tg levels, 6 positive, 44 negative RI). PET study failed to demonstrate any 18F-FDG uptake in 46% (23/50) of these patients. In Follicular thyroid carcinoma (n = 5) 4 patients were clinically suspected to have metastatic disease with high Tg levels and negative RIS. All showed multiple lesions with high FDG uptake. The one patient with Follicular carcinoma arising from Struma Ovarii in whom Tg was low did not show abnormal FDG uptake. All Hurthel Cell carcinoma cases (n = 4) had high Tg levels, negative RIS but very high FDG uptake (mean SUV: 31.47). In Medullary carcinoma (n = 6) 5 showed no FDG uptake with one with a doubtful lesion (SUV = 2.4). Both Anaplastic and Squamous Cell carcinoma (n=1 each) showed FDG uptake whereas the Adenocarcinoma patient did not show any FDG concentration although there was diffuse 131I uptake in both lungs. The SUV values in FDG positive cases of papillary carcinoma were generally low with maximum measured value of 17.6 in one patient. However, SUV values in Follicular and Hurthel Cell carcinoma were generally high with maximum value of 21.8 in Follicular and 62.1 in Hurthel Cell carcinoma.

Conclusion: 18F – FDG uptake study has a significant role to play in Follicular and Hurthel cell carcinomas with high rate of lesion detection. This is particularly important as in all cases radio iodine whole body scan was negative. In Papillary carcinoma FDG-PET study could not
demonstrate recurrence or metastasis in more than 52% of the cases with negative RIS and high Tg values and hence less likely to add significant additional information.
The role of 18F-FDG-PET/CT in the preoperative staging and post-therapy follow-up: Comparison with spiral CT

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Aim: The aim of this study was to investigate the role of F-18 fluoro-deoxy-glucose (FDG) positron emission tomography and computed tomography (PET/CT) in the preoperative and post-therapy restaging of gastric cancer and to compare with spiral computerized tomography (CT).

Method: A total of 42 PET/CT scans of 36 gastric cancer patients (28M, 8F; mean age: 56.0 ± 15) were included in the study. A retrospective analysis of the PET/CT results of the patients were compared with concurrent CT results. Confirmation was made by clinical course and serial imaging studies in the follow up. The compatibility ratios were calculated and the accuracy of the PET/CT was assessed.

Results: Patients were separated into 3 groups: the patients who were referred to our clinic for preoperative staging (4 patients), for post-therapy evaluation (24 patients) and for the suspicion of local recurrence and/or metastasis exploration after a disease free period (8 patients). Groups 1 and 3 included a small number of patients so they were omitted from the statistical analysis. Focusing on Group 2, the overall concordance rate was 50% (12 patients). Region based analysis showed the rates of concordance for local recurrence, local lymph node metastasis and distant metastasis were 91% (Kappa: 0.70), 95% (Kappa: 0.86) and 50% (Kappa: 0.26) respectively. Distant metastases were also investigated in detail and the two techniques showed a concordance of 91% (Kappa: 0.75) for liver, 79% (Kappa: 0.31) for distant lymph node, 79% (0.42) for lung, 87% (Kappa: 0.33) for bone and 95% for intestinal wall metastasis.

Conclusion: PET/CT is a complementary imaging method which can be successfully used in both preoperative and post-therapy evaluation of gastric cancer.
The role of PET/CT in the evaluation of pancreatic cancer and suspected pancreas masses

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Objective: The aim of this retrospective analysis was to compare the PET/CT findings with other conventional imaging modality in patients with pancreatic cancer or suspicious pancreatic masses and to evaluate the potential benefit of PET/CT imaging on diagnosis, primary staging and restaging.

Method: 20 patients with known or suspected pancreatic cancer who underwent both PET/CT and conventional examinations (CT and/or MRI) in 2007-2009, were evaluated retrospectively. Then, the findings of PET/CT and CT and/or MRI were compared in order to determine the contribution of PET/CT to primary staging and treatment management in this patient population.

Results: 8/20 patients with histopathologically proven pancreas had pathological 18F FDG uptakes (SUV max: 3.8-38.6) in pancreatic lesions. Moreover, focal increased uptakes in the right lung in 1/8, intra-abdominal lymph nodes in 4/8 and on ribs and spine in 1/8 patient were recorded in PET/CT where CT and MRI had failed. In another 1/8 patient, the disease upstaged to 4 from 1 with multiple bone metastasis detected by PET/CT. The other 1/8 patient did not have any increased uptake except pancreatic mass. 4/20 patients with suspicious pancreatic masses detected by conventional examinations underwent PET/CT imaging. 3/4 patients had normal PET/CT scans and are still in the follow-up period. In 1/4 patients with high serum Ca 19-9 levels and with normal 18F FDG/PET scans, consequent surgery was performed and the histopathology revealed the pancreatic malignancy. In 8/20 patients PET/CT referred to the restaging of known pancreatic cancer and a suspicion of recurrent diseases after Whipple surgery. 2/8 patients had normal 18-F FDG/PET scans also normal Ca 19-9 levels. In their follow-up evidence of recurrence or distant metastases were not detected. In 1/8 patient with normal CT and with high Ca 19-9 levels, PET/CT showed multiple increased uptakes in both lungs and spine. In another 2/8 patients with suspected pancreatic lesion in postoperative MRI and with high Ca 19-9 levels, PET/CT detected multiple metastatic foci, in addition to the pancreatic lesions (liver and lymph nodes metastases). Conversely, 1/8 patients had enlarged peripancreatic and mesenteric lymph nodes in CT and normal 18-F FDG scans, no recurrence or metastases was seen. 2/8 patients with recurrent disease detected by postoperative CT, MRI and PET/CT, were taking adjuvant chemotherapy treatment.

Conclusion: 18 F FDG PET/CT was found to be more sensitive than the conventional anatomic imaging in the evaluation of suspicious pancreatic masses and more accurate in staging and restaging of pancreatic cancer. However, the value of PET/CT in diagnosis of pancreatic cancer is still unclear, since further studies are required.
18FDG PET-CT in radiotherapy planning – Comparison of gross tumour volumes obtained using automated versus manual methods

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Purpose: Compare gross tumour volumes (for radiotherapy planning) on 18FDG PET-CT obtained using different segmentation algorithms and threshold limits versus manually contoured tumour volumes.

Materials and Methods: 20 lung lesions in 17 subjects with non-small cell lung carcinoma (NSCLC) and 20 lesions (primary/lymph nodal deposits) among 15 subjects with Head and Neck cancers (H&NC) (Squamous Cell Carcinoma) were contoured. All subjects underwent whole body diagnostic/staging 18FDG-PET/CT scans on Discovery 8 slice PET-CT (GE Healthcare) camera. PET and CT images reconstructed to 5mm slice thickness were transferred to the Advantage Workstation equipped with PET-VCAR (Volume Computer Assisted Reading) automated segmentation software. A set of 13 Gross Tumour Volumes (GTVs) were defined for each lesion. GTVCT—volume contoured manually by an experienced radiation oncologist using CT information independently on FOCALSIM contouring workstation. GTVP—volume contoured manually using the PET images independently on AdvantageSim workstation by an experienced nuclear medicine physician. 11 automated GTVs contoured using 3 different algorithms: GTVF (1-4) – volumes using fixed SUV (Standardized Uptake Value) threshold of 2.5, 3, 3.5, and 4g/ml; GTVT (1-3) – volumes using segmentation threshold at 40%, 42% and 45% of the maximum SUV (SUVmax) of lesion; GTVET (1-4) – volumes using Estimated Threshold algorithm at weighting factors 0.4, 0.5, 0.6 and 0.7 respectively. Estimated threshold algorithm is a mathematical function that identifies the gradient slope between SUVmax and background for a lesion, weighting factor defining tightness of the contour. GTVCT was taken as standard reference volume and rest compared using Wilcoxon Summed Rank test.

Results: NSCLC subjects: GTVCT values of 2 lesions were significantly greater than their GTVP values, for the rest they correlated- GTVF1 and GTVF2 (fixed SUV threshold at 2.5 and 3.0) showed good correlation with GTVCT and GTVP. Similarly, GTVET volumes obtained at weighting factors 0.5 and 0.6 correlated with both the manually contoured volumes. H&NC subjects: GTVP volumes were higher than the GTVCT volumes in 19 of the 20 lesions. GTVF2 and GTVF3 (fixed SUV thresholds at 3.0 and 3.5) correlated well with GTVCT for the respective lesion. GTVF2 matched the GTVP. GTVET at weighting factor 0.4 correlated with GTVP and at weighting factor 0.5 correlated with the GTVCT volumes. Volumes obtained at percentage threshold algorithms (GTVT) in both subject groups showed no statistically significant correlation with the manual contouring techniques.

Conclusion: Higher GTVCT volume in 2 NSCLC subjects corresponded to collapsed lung parenchyma contoured in CT. In H&NC subjects, higher volumes obtained by contouring the
PET images corresponded to bone and soft-tissue extension of lesions not producing CT signals, and lymph nodal deposits not identified on the CT. Percentage threshold algorithm is not a reliable algorithm for automated segmentation. Volumes for fixed threshold of 3.0g/ml correlated well with manually contoured volumes. The best correlation between automated and manually contoured tumour volumes was for the estimated threshold algorithm. This study recommends weighting factors 0.5 for lung and 0.4 for head and neck/nodal lesions.
Usefulness of F-18 FDG PET in evaluation of adrenal lesions in patients with lung cancer

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Introduction: The incidence of adrenal masses in clinical studies of patients with non–small cell lung carcinoma (NSCLC) varies from 4 to 18\%. However, not all adrenal masses can be assumed to represent metastasis, because 2–9\% of the masses may be benign adenomas. The aim of this study was to assess the role of PET/CT (positron emission tomography/computed tomography) with F-18 FDG (fluorine-18 fluorodeoxyglucose) in differentiating benign from metastatic adrenal masses in patients with lung cancer.

Methods: In this retrospective study, we analysed F-18 FDG PET/CT scans of 126 patients with lung cancer who had undergone PET/CT for metastatic work up. Of these 126 patients, only those patients who had a bulky adrenal on CT scan, or PET was positive with normal bulk of adrenals were included in the data analysis. 31 adrenal masses (size range, 0.7–3.9 cm) were evaluated in 25 patients. PET findings were interpreted as positive if the FDG uptake of the adrenal mass was greater than or equal to that of the liver, and as negative if the FDG uptake of the adrenal mass was less than that of the liver. All studies were reviewed and the results were then correlated with clinical follow-up or biopsy results wherever available.

Results: Of the 31 lesions, 26 were positive for FDG uptake. 23 of these patients after percutaneous biopsy (n=3) or clinical follow-up (n=20) proved to be metastatic adrenal disease. The remaining 3 patients showed no change in size on follow-up CT or PET/CT. In these three cases, SUV\textsubscript{max} was less than 3.7. Five lesions were negative for FDG uptake; all of these were eventually proven by clinical follow-up for at least 6 months to be benign.

Conclusion: F-18 FDG PET/CT is an accurate, non-invasive technique for differentiating benign from metastatic adrenal lesions in patients with lung cancer.

<table>
<thead>
<tr>
<th>Biopsy / Clinical Follow up findings</th>
<th>PET Positive</th>
<th>PET Negative</th>
<th>CT Positive</th>
<th>CT Negative</th>
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<tr>
<td>Positive</td>
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<td>17</td>
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</tr>
<tr>
<td>Negative</td>
<td>03</td>
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</table>
Clinical use of 11C-CHO PET function imaging in tumor location and regimen

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Background: The use of recent radio-chemotherapy technology requires the capability of identifying the appropriate regions to tumour target. This article focuses on the potential of the metabolic imaging techniques to refine our clinical target volumes and optimization of radio-chemotherapy treatment regimen of brain gliomas.

Methods: The 11C-Choline positive-emission tomography (CHO-PET) functional imaging of 23 cases of glioma confirmed by pathological examination from Jan. 2008 to Jun. 2009 were analysed and compared with MRI. Co-registered biology tumour volume (BTV) of CHO-PET imaging was used as an index for the choice of therapeutic treatment.

Results: CHO-PET imaging displayed clear boundaries between glioma and surrounding normal tissue. The diagnosis and the target treatment volume of 10 patients (43.5%) were changed because of the integrated CHO-PET. Results included 5 cases (31.3%) of per-radiotherapy (post-operation) and 5 cases (71.4%) of post-radiotherapy. Gross tumours volume (GTV) radiotherapy expanded in 1 case (grade III) because of the increase of target volume. The follow-up was changed to chemotherapy in 1 case (grade II) because of the recurrence. Clinical tumours volume CTV) radiotherapy was changed to CTV + GTV radiotherapy for post-operation tumour residue in 4 cases (1 case in grade III and 3 cases in grade II) and no recurrence of tumour occurred. CHO-PET changed treatment regimen of gliomas for grade II (88.9%, 8/9), grade III (22.2%.2/9), and grade IV (0%.0/5) respectively. The accurate diagnosis accuracy of MRI was 85.7% for WHO grade III/IV.

Conclusion: Integrated CHO-PET imaging displays the circumscribed glioma clearly. It is helpful for the diagnosis of glioma of grade II and III. The optimization of treatment therapeutic regimen has a greater value in judging the clinical effect and the differential diagnosis of recurrence and necrosis.
Feasibility and utility of assessment of myocardial viability using ‘Hybrid’ 99mTc-MIBI SPECT and 18F-FDG PET studies in a remote PET centre without access to cyclotron

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Introduction: 18F-FDG PET has been shown to be the most sensitive non-invasive means for the prediction of left ventricular functional recovery after coronary revascularization and has demonstrated beneficial outcomes in patients with left ventricular dysfunction and suspected coronary artery disease being considered for revascularization. Conventionally the assessment of viable myocardium is performed with 201Tl with a higher radiation dose (15mSv) and prolonged imaging up to 24hrs. PET imaging of myocardial perfusion and metabolism, identifies regional viability and assesses the risk for future cardiac events. Myocardial metabolism assessment can be readily performed using 18F-FDG. The assessment of myocardial perfusion using PET can be performed by using 13N-Ammonia or 82-Rubidium, but necessitates the need for a cyclotron/Rubidium generator to be situated in close proximity to the scanner which proves to be an expensive affair. However in nuclear medicine centres with a PET scanner but with no access to such facilities the combined hybrid imaging approach to evaluate myocardial viability using 99mTc-sestamibi SPECT looking at myocardial perfusion and 18F-FDG PET to assess myocardial metabolism can be a feasible approach with comparable results.

Materials and Methods: Six patients underwent viability assessment using the hybrid imaging approach. All patients had LV dysfunction with/without history of previous myocardial infarction. SPECT Perfusion imaging was performed at rest 45 minutes after injection of 99mTc-sestamibi. Images were acquired using a dual-headed gamma camera with 2 X 32 steps over 180° on a 128x128 matrix. Low dose CT was performed for attenuation correction. Attenuation and scatter corrected trans-axial, HLA and VLA slices were reconstructed using Flash3D.

After oral glucose loading 200MBq of 18F FDG was injected and 3D PET imaging was performed 60 minutes later. Low dose CT was performed for attenuation correction. Trans-axial images were reconstructed on a 128 X 128 matrix using a defined zoom factor to obtain the same in-plane pixel size as the SPECT images, and consecutive pairs of PET slices were combined to achieve an identical axial pixel size for both imaging techniques.

The images were classified by visual analysis as normal, mismatched or severe matched defect to define normal, viable or scarred myocardium respectively. Two nuclear medicine physicians interpreted the images independently and were blinded to the other person's report. Study results were divided into three categories based on how confident the observers were of the diagnosis: (1) Complete agreement (2) Agreement with minor differences in interpretation (3) No agreement.
Results: There was no disparity in the interpretation of results between the observers, showing excellent reporter confidence in interpreting myocardial viability studies. The average study time using the hybrid approach was around 2 hours and the overall radiation burden was <12 mSv.

Conclusion: ‘Hybrid’ imaging technique using 99mTc-sestamibi SPECT and 18FFDG PET is a quick and feasible approach with a greater degree of confidence for interpretation and lower radiation burden as well as quick turn-around time in the diagnosis of myocardial viability as compared to 201Tl chloride.
Impact of coronary artery disease (CAD) over myocardial blood flow (MBF), total perfusion defect (TPD) and summed differential score (SDS) evaluated with 13N-ammonia PET/CT

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Introduction: CAD is one of the main causes of mortality and morbidity all around the world. The cardiac study with positron emission tomography (PET) and cardiovascular computed tomography (CCT) can give us physiological and anatomical information of the heart. PET is the best method to evaluate myocardial perfusion and quantify the perfusion with the SDS, TPD, and it also allows us to measure the MBF. The CCT, known for its high negative predictive value for CAD, give us information about the characteristics of coronary plaques and stenosis. The purpose of using these 2 methods is to identify CAD and its impact in the myocardial perfusion.

Methods: We studied 18 patients, 9 with significant coronary artery lesions (stenosis > 50%) and 9 with normal arteries diagnosed by CCT. A two phase (rest and adenosine induced stress) 13N-ammonia cardiac PET was also realised in all the patients. The dynamic images were used to measure the MBF in rest and stress with the P-MOD software expressed in ml/g/min. The relation between the stress MBF and rest MBF is known as Coronary Flow Reserve (CFR), and it is considered normal when the value is > 2.5. The static images were analysed using the CSI QPS software to obtain the difference between stress and rest TPD, a value < 3 is considered as normal. The study was also analysed by two experts to obtain the SDS, that is the difference between the summed stress score (SSS) and summed rest score (SRS), and it is considered normal with values < 3.

Results: The difference between CFR in patients with significant coronary artery lesion compared with patients with normal arteries was significantly lower (2.01 ± 0.61 versus 3.28 ± 0.91, p=0.001). The TPD in patients with significant coronary artery lesions was significant higher compared with patients with normal arteries (9.89 ± 5.06 versus 1.89 ± 2.14, p<0.001), as well as SDS (12.33 ± 6.59 versus 2.22 ± 2.38, p<0.001).

Conclusion: We have found that patients with significant coronary artery lesions have a reduction in CFR, and higher values of TPD and SDS. This represents the impact of a significant coronary stenosis in the myocardial perfusion.
CLINICAL PET NEUROLOGY
PET/CT in early diagnosis of Alzheimer’s disease and alcohol dementia: Case report

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Introduction: Some of the detrimental effects of heavy alcohol consumption on brain function are similar to those observed with Alzheimer’s disease /AD/. Although alcoholic use may be a risk factor for AD, it is difficult to study this relationship because of similarities between alcoholic dementia and AD and because standard diagnostic criteria for alcoholic dementia have not been developed. Early and accurate diagnosis of dementia is crucial for patients and their families. It helps provide the best available courses of treatment according to the specific kind of dementia. A number of studies discuss the possible link between alcohol use and AD. Some diagnostic difficulties could arise because of clinical similarities between alcohol dementia and AD. There is significant data that a PET scan significantly improves the accuracy of diagnosing a type of dementia often mistaken for AD.

Subject of our study was a 46-year-old female with a history of heavy alcohol consumption, impaired memory and cognitive skills, decline in social and occupational functioning. In 2007 she was diagnosed with alcohol addiction. Computer tomography/CT at that time was described as normal. Hospital admission in Jun 2010 was due to states of anxiety. Clinical and neuropsychological examinations revealed severe dementia.

Method: Under conditions of ambient light and sound in the Division of Nuclear Medicine, the patient received an intravenous injection of 4.7 mCi FDG 18F- FDG and 60 minutes later, PET/CT imaging of the brain was carried out.

Results: Normal brain structure on native CT scanning. Diminished FDG uptake in the frontal, parietal and temporal zones bilaterally, which are compatible with Alzheimer’s disease.

Conclusion: PET scans enable physicians to identify the conditions underlying each patient’s mental decline and choose appropriate courses of treatment. But PET scans alone are not enough to confirm Alzheimer’s. A careful consideration of the medical history and examination will continue to be essential to dementia evaluation.
Evaluation of metastatic brain lesions in whole body F18FDG PET-CT of oncological cases in correlation with their fasting blood sugar


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Aim: To evaluate the metastatic brain lesions in the whole body F18 FDG PET-CT of oncological cases in correlation with their Fasting Blood Sugar.

Materials and Methods: It is a retrospective study of 2500 patients- whole body F18 FDG PET-CT including the brain between July 2008 and Dec 2010 indicated in various oncological cases were analysed. We have included 31 cases showing metastatic brain lesions (MBL) in various cancers of non CNS origin with their corresponding Fasting Blood Sugar (FBS) Levels (L) in mg/dl prior to F18 FDG injection; these were evaluated by obtaining SUV max of MBL and SUV max of contralateral cerebral grey & white matter (CGm &CWm) and Cerebellum (Ce) by using point curser region of interest (ROI) on PET with the aid of PET-CT images. The MBL to CGm, CWm & Ce FDG Uptake Ratio (UR) were grouped into A, B & C respectively. Mean (M) and standard deviation (SD) of each of them were correlated with their FBS levels broadly separated into Normal FBS(NFBS) & Abnormal FBS (AFBS) Latter was again subdivided based on their values into L-i<80 (hypoglycaemia), L-ii 110<150 (mild hyperglycaemia) L-iii150<200 (moderate hyperglycaemia) L-iv>200 (severe hyperglycaemia).

Results: Out of 31 patients with non CNS malignancies included 11 ca breast,10 ca lung and 10 others,15 male & 16 females aged between 54years to 66 years, number of NFBS were 13 and AFBS were 18 out of which L-i, L-ii, L-iii & L-iv were 1, 10, 5 & 2 respectively. There is a strong correlation with diminishing of FDG uptake with respect to AFBS levels observed in CGm (9.07+4.25), CWm (3.20+1.47) & Ce (7.70+3.02). The FDG UR in Group A (3.10+2.36) & Group B (2.00+2.31) and group C (1.41+0.93) in relation to AFBS appears increased in group A & B compared to group C (i.e., A>B>C). The FDG UR in relation to NFBS in Group A(2.26+1.00), Group B (2.37+2.31), Group C (1.44+0.81) appears below the AFBS and their p-value were 0.190, 0.669 and 0.903 respectively. Our results although appears statistically less significant (probably due to small samples) but expresses high clinical relevance.

Conclusion: Evaluation of glucose avidity in metastatic brain lesions estimated by FDG UR in relation to the FBS in our study reveals high positive predictive value in diagnosis of active metastasis despite abnormal FBS during whole body F18FDG PET-CT of non CNS malignancies. Mild to moderately elevated FBS significantly influences the MBL FDG UR than severely elevated FBS, since AFBS at 110<200 mg/dl show high differential uptake of FDG in MBL to rest of normal brain parenchyma compared to >200mg/dl. Regardless of FBS estimation of SUV max of MBL to Cerebral grey matter shows high differential glucose activity than white matter and cerebellum and hence the MBL to CGm FDG UR parameter may be proposed for use in pre and post treatment assessment.
TABLE 1: Correlations of max SUV of MBL / BGm (Group A) MBL/ BWm (Group B) and MBL/ Ce (Group C) Uptake Ration (UR) to FBS before FDG injection

<table>
<thead>
<tr>
<th>Fasting blood sugar (FBS)mg/dl</th>
<th>Total no. of MBL N=31</th>
<th>%</th>
<th>Group A Mean ± SD</th>
<th>Group B Mean ± SD</th>
<th>Group C mean ± SD</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Normal (NFBS) 13 80 &lt; 110</td>
<td>13</td>
<td>41.9</td>
<td>2.26 ± 1.00</td>
<td>2.37 ± 2.31</td>
<td>1.44 ± 0.81</td>
<td></td>
</tr>
<tr>
<td>Abnormal (AFBS) 18</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>hypo &lt;80</td>
<td>1</td>
<td>3.2</td>
<td>3.44 ± 1.20</td>
<td>1.20 ± 1.30</td>
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<tr>
<td>Mild.Hyper 110&lt;150</td>
<td>10</td>
<td>32.3</td>
<td>3.15 ± 2.45</td>
<td>2.32 ± 3.02</td>
<td>1.45 ± 1.11</td>
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</tr>
<tr>
<td>Mod.hyper 150,200</td>
<td>5</td>
<td>16.1</td>
<td>3.29 ± 3.06</td>
<td>1.51 ± 1.14</td>
<td>1.32 ± 0.93</td>
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</tr>
<tr>
<td>Severe hyper &gt;200</td>
<td>2</td>
<td>6.5</td>
<td>2.18 ± 1.01</td>
<td>2.09 ± 0.83</td>
<td>1.47 ± 0.11</td>
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<tr>
<td>p-value</td>
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<td>0.767</td>
<td>0.954</td>
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</table>

FIG. 1:
FIG. 2. PET CT of a female with Ca breast, 70yrs with FBS 149 mg/dl showing increased FDG uptake in primary tumour in the left breast, multiple metastasis in the skeleton, lung and solitary metastasis in the right cerebellum (SUV Max of MBL 12.26, CGm 16.77, CWm 7.10 and Ce 15.27).
PET-CT in paediatric oncology patients in an initial experience in a university hospital


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Introduction: PET-CT has become a very important imaging procedure, allowing the fusion of anatomic and functional information. It is especially useful in different steps of the evaluation in oncological patients; diagnosis of disease, allowing a more accurate tumour staging, differentiation between malignant and benign lesions, and the evaluation of therapeutic response.

Aim: To show our initial experience in the use of PET-CT in paediatric oncologic patients.

Method: Clinical data and images of all patients in whom PET-CT was performed in any time of their treatment, treated at the Paediatric Oncology Unit in our hospital, were retrospectively reviewed. This technique was implemented for child use in March 2009. The study period was March 2009 to August 2010.

Results: 27 PET-CT studies were performed, in a population of 21 patients (12 male, 9 female); the average age was 13.4 years (range 1.3-18 y.o). Twenty one of these studies were indicated for staging and/or therapeutic response evaluation of lymphoma patients, one for medullar thyroid cancer staging, one for melanoma staging, one child with papillary thyroid cancer staging and two children suspected to have a malignancy. All but one study were performed with F18-FDG and the other with Ga68-DOTATATE. There were no reported adverse effects or immediate complications. In all of them, the PET-CT gave very important information for clinical purposes.

Conclusion: PET-CT offers a wide range of useful applications in the oncological paediatric population.
One day protocol: Dual tracer/dual isotope FDG-18 and Ga-68 DOTA-NOC PET/CT. Study of a child with neuroblastoma to determine the metabolic tumour status

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We report on a 6 year-old boy with a history of neuroblastoma. The tumour was first diagnosed in March 2004, arising from the right adrenal gland as confirmed through fine needle aspiration biopsy, Ultrasound, CT scan as well as tumour markers. Due to the size and extension, the tumour was inoperable at the time and two cycles of chemotherapy (vincristin, cisplatin, etoposide, and cyclophosphamide altering with vincristin, carboplatin, etoposide and cyclophosphamide) were given. Then, the patient underwent retroperitoneal surgery and the right adrenal gland and the tumour were completely resected. After the operation, the patient received 4 additional cycles of chemotherapy until March 2005. During August and September 2005 the patient complained about abdominal pain and recurrence was suspected. Ultrasound and CT scan were repeatedly performed, but were unclear. In December 2005, a I-131 MIBG scan (148MBq, 4mCi iv, planar images and SPECT from 24 hours until 6 d p i) revealed only a normal left adrenal gland but no recurrence, proving that the tumour had no MIBG uptake. In January 2006 the child (121 cm height, weight 21 kg) was submitted to the PET/CT Centre of the Central clinic Bad Berka, Germany for receptor PET/CT using 68-Ga/DOTA-NOC, a high affinity pansomatostatin analogue. NSE was determined in serum prior to the PET/CT study and was elevated (24.8 ng/ml, cutoff 15). The patient received 46 MBq (1.24 mCi) Ga-68 DOTA-NOC in vitro and a whole-body PET/CT was performed 75 min p.i. There was no abnormal uptake proving that the recurrence had no somatostatin receptors. After this negative result it was decided to perform additionally an F-18 FDG PET/CT study (with contrast enhanced low dose CT scan). After a fasting time of 6 hours, the patient received 151 MBq (4.1 mCi) F-18 FDG. Whole-body PET/CT was performed 75 min.p.i and a recurrence was clearly depicted as a hyper metabolic tumour (SUVmax. 8.1, molecular tumour volume(MTV) 15.2 cm\textsuperscript{3}, 27x27x40mm in diameter, cranial-caudal extension 4.5 cm) between the vena cava inferior and the aorta with extension to the psoas muscle and infiltration of the right renal artery, see Fig. 1. Additionally, a weak hyper metabolic focus was detected in the right spina iliaca anterior superior (SUV 2.0). The results of the F-18 FDG study were confirmed by surgery performed 1 week later. To our best knowledge, this is the first report on a one day protocol applying two different PET tracers labelled with two different radionuclides in a neuroblastoma patient. This study confirms previous reports stating that some neuroblastoma recurrences may have undifferentiated cells that do not express somatostatin receptors, but show high glucose consumption which has also significant (adverse) impact on prognosis.
FIG. 1. Results of dual tracer/dual isotope FDG-18 and Ga-68 DOTA-NOC PET/CT study in a child with neuroblastoma.

Ga-68 DOTA-NOC PET/CT

No somatostatin receptor expression

18FDG PET/CT

Craniocaudal recurrence between the vena cava inferior and the aorta with extension to the psoas muscle and infiltration of the right renal artery. Additionally, a weak hypermetabolic focus was detected in the right spinailiac anterior superior. The results of the F-18 FDG study were confirmed by surgery performed 1 week later.
CLINICAL PET OTHERS
Value of FDG PET scan in the evaluation of skeletal infections

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Introduction: Bone scan is a useful tool to rule out skeletal infection in a non-violated bone. However in a violated skeleton, bone scan has limited specificity to document infection. In such a situation adding Gallium citrate scan helps to separate infection from inflammation. However, there are logistical issues with procuring Gallium citrate. Hence, we performed FDG PET (fluorodeoxyglucose) scan in these cases to look for evidence of infection. 48% of cases were positive for infection based on abnormal metabolic activity (incongruent increased uptake seen on PET scan as compared to the Bone scan.) 2 of these cases were negative for infection on both the studies. None of these cases had abnormality on PET scan in presence of normal bone scan.

Material and method: 43 cases with suspected skeletal infection were subjected to bone scan using 10 to 20 millicuries of Technetium-99m-MDP (methylene diphosphonate). Images were acquired on Ecam signature series gamma camera. All of these cases also underwent regional FDG-PET-CT scan using 3 to 10 millicuries of Fluorine18-Fluorodeoxyglucose administered in the fasting state. Images were acquired at 60 minutes on LSO based Biograph duo dedicated PET CT system.

Results: The cases were divided into following categories: 1) Increased MDP uptake with congruent uptake on FDG. 2) Increased MDP uptake with normal FDG uptake. 3) Increased MDP uptake with incongruent increased FDG uptake. 4) Negative MDP scan with increased FDG uptake. 5) Negative MDP as well as FDG. Categories 1, 2, 5 were classified as negative for infection and categories 3 and 4 were classified as positive for infection. Accordingly 21 of the 43 cases were positive for infection and 12 cases were negative for infection.

Conclusion: Bone scan per se has limited value in excluding infection in a traumatized skeleton. 48% of cases in the present study showed evidence of infection based on FDG PET scan as against 95% cases in which abnormal osteoblastic activity was seen on bone scan. Hence in post traumatized skeleton (such as prosthesis, internal fixation etc.) adding FDG scan helps in the documentation of infection for further treatment strategies.
Is FDG uniformly distributed throughout the skeleton in females?


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Introduction: FDG PET/CT has been extensively used for imaging primary or metastatic bone lesions. Although the relationship between SUVmax value and benign and malignant bone lesions were investigated in previous studies, the differential physiologic bio-distribution of FDG throughout the skeleton was not analysed before. The aim of this study was to investigate whether FDG was uniformly distributed throughout the skeleton in female patients.

Methods: A total of 100 female cancer patients, who were referred to our clinic for initial staging with FDG PET were included in this retrospective study. None of the patients had received prior treatment that directly affected bone marrow (chemotherapy, radiotherapy or colony stimulating factors) and the patients had no history of anaemia. The patients who had bone metastases were excluded from the study. The maximum standard uptake value (SUVmax) of the 24 different locations (the heads and proximal diaphysis of the bilateral upper and lower extremities, rib (10th rib) sternum (manibrium and corpus), vertebral column (C3, C5, T3, T7, L1, L3) and bilateral pelvic bones (sacrum and bilateral anterior and posterior parts of the iliac bones and acetabulum) were obtained and all the values were compared to each other.

Results: Although FDG uptake in the skeleton was not uniform (p<0.05), the mean SUVmax was 2.05 (SD: 0.39 and 95% Conf. limit: 1.98 – 2.13). While the highest FDG uptake was seen in L3 vertebra (mean SUVmax: 3.009), the least glucose metabolism was observed in the 10th rib (mean SUVmax: 1.432). The SUVmax of the bilateral heads of the upper and lower extremity were significantly higher than the neighbouring diaphysis (p < 0.05). The SUVmax of the manibrium of the sternum was significantly higher than the corpus (p < 0.05). For pelvic bones, while the highest FDG uptakes were detected in the sacrum (mean SUVmax: 2.73), the least FDG uptakes were seen in anterior iliac bones (SUVmax: 1.82), (p < 0.05). For vertebral column FDG uptakes were also non-uniform and the SUVmax gradually increases from cervical to the lumber part (C3-mean SUV max: 2.28, L3-meanSUVmax: 3.0), (p < 0.05). On the other hand, mean skeletal SUVmax was decreased by age (r: -0.20, p<0.05).

Conclusion: The FDG was not uniformly distributed throughout the skeleton in female patients. It had a tendency to increase from appendicular to the axial skeleton and from upper to lower regions in the vertebral column which may be related to the normal distribution of the red bone marrow. Additionally, through age, glycolytic metabolism of the whole skeleton showed a gradual decrease.
FDG PET/CT in cancer patients with fibrous dysplasia

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Fibrous Dysplasia of bone (FDB) is a slowly progressive bone disorder in which normal bone is replaced by abnormal fibrous tissue. Several FDG PET/CT reports suggest that the appearance of FDB could mimic a malignant process. Therefore, this case is presented with the aim of guiding physicians in evaluating bone lesions in cancer patients with FDB.

The subject was a 48-year-old male patient presented with an abdominopelvic USG which showed a tumor mass lesion in the urinary bladder. Transurethral resection of the mass was performed and revealed a transitional cell carcinoma. FDG PET/CT was requested and it showed multiple lytic, expansive bone lesions (Figure 1 A-P). The lesions showed heterogeneous hyper-metabolic activity and a clear distinction cannot be made for the probability of metastasis. When the past medical history of the patient was reviewed in detail, it revealed polyostotic FDB diagnosed 10 years ago. We obtained the patient’s previous bone scintigraphy which was made 10 years ago (Figure 1 R). It showed increased osteoblastic activity in the polyostotic FDB lesions. Later a new bone scan was requested to re-evaluate the polyostotic FDB lesions (Figure 1 S). When these three imaging studies were reviewed together, the PET/CT scan appearances of the lesions showed similarities to those on the scintigraphic ones. These overlapping findings were evaluated in favour of FDB. Additionally the costal lesion in the left hemi-thorax was biopsied and reported as FDB rather than metastasis.

Several case reports have described that FDB can have either intense FDG activity or can be metabolically normal without any increased FDG activity. These significantly increased FDG activities may mimic bone metastases or skeletal involvement of the primary malignancy in cancer patients with FDB. These findings may change the stage of the cancer. On the other hand, few studies showed that FDG PET/CT is useful for detecting and differentiating bone metastasis from FDB in patients with a malignancy. Malignant transformation may also be seen in some FDB patients. Previous reports discussed the role of FDG PET/CT in the diagnosis of malignant transformation of FDB and in a few studies the authors concluded that the local progressive increase of the SUVmax can contribute to an early detection of sarcomatous transformation.

In the light of the literature findings it may be concluded that FDG PET/CT scans need to be interpreted in the overall clinical context, on a patient-per-patient basis. In our case, new bone scintigraphy was performed instead of radiography, diagnostic CT or MRI to confirm the diagnosis. The recent bone scan showed the lesions that correlated with both, the previous bone scan and FDG PET/CT scan. The CT characteristics of the lesions on FDG PET/CT were also compatible with FDB.

Conclusion: If the FDG positive bone lesions are the only positive finding on PET/CT scan except for the primary tumour in cancer patients with a past medical history of FDB, then they
should not be misinterpreted as bone metastases. To improve the diagnostic accuracy, such lesions need to be correlated with the previous imaging studies and biopsied if they are equivocal.

FIG. 1:
FDG PET/CT appearance of multi-regional elastofibroma


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A 70-year-old woman with biopsy proven intracranial large B cell lymphoma was sent to a whole body F18-flourodeoxyglucose (FDG) PET/CT imaging for initial staging. Mild to moderate hyper-metabolic multiple soft tissue masses were observed between the inferior tips of the scapulae and chest wall and between the gluteal muscles (medius and maximus) and greater trochanters of femur bilaterally in FDG PET-CT (Figure 1). For the differential diagnosis of these findings, CT images were consulted by a radiologist and elastofibroma was considered according to characteristic appearances of multiple soft tissue masses. Because of its diagnostic CT pattern, neither invasive procedures nor further imaging was planned for this asymptomatic patient. Elastofibroma was first described by Järvi and Saxén in 1961. It is not a true neoplasm, and is generally considered to be a slowly growing, fibroblastic pseudo-tumour. It probably arises from periosteal fibroblasts with deranged elastic fibrillogenesis. It is not uncommon and was predominantly found in elderly patients (24% in women and, 11% in men). The pathogenesis of this lesion is unclear and thought to be related to repeated mechanical friction. Although in the majority of the cases (more than 80%), elastofibroma is located in the subscapular region as a mass, occasionally it can be presented as multiple foci in the various parts of the body as in our case. Fortunately more than half of the patients are asymptomatic and complete surgical excision is generally indicated in symptomatic cases. Conventional imaging methods such as plain radiography, computed tomography and magnetic resonance imaging have been used to diagnose elastofibroma. Plain chest radiographs may show a soft tissue density mass in the subscapular region. On MRI, the lesions show relatively low signal intensity (similar to muscle) on T1- and T2- weighted images. Interlaced fat is seen as strands of high signal intensity within these hypointense lesions. Enhancement after the administration of gadopentetate dimeglumine has been reported. Thoracic CT has a main role in the diagnosis. The classical pattern is poorly defined inhomogeneous soft-tissue density with attenuation approximately the same as that of skeletal muscle in the subscapular region. Normal structure can also mimic elastofibroma, like the fibers of the muscles, which has a globular appearance especially on CT images. Lesions with signal intensity similar to skeletal muscle such as extra-abdominal desmoid, neurofibroma, cicatrical fibroma and malignant fibrous histiocyotma should be considered in the differential diagnosis. Another helpful feature for differential diagnosis is bilaterality of the lesion. Presence of a similar periscapular lesion on the contralateral side strongly eliminates malignancy from differential diagnosis. Thoracic mass presented as an elastofibroma dorsi is well-known. However multi-regional bilateral elastofibromas are rare even for the radiologist. Although there are few FDG avid elastofibroma dorsi cases reported in the literature, to our knowledge, PET/CT appearance of multi-regional involvement especially including bilateral greater trochanteric regions has not been reported yet. Unnecessary radiological or surgical interventions and anxiety in oncology patients will be avoided by recognition of the PET/CT pattern of elastofibroma.
FIG. 1. Mild to moderate hyper-metabolic multiple soft tissue masses were observed between the inferior tips of the scapulae and chest wall and between the gluteal muscles (medius and maximus) and greater trochanters of femur bilaterally in FDG PET-CT.
Diaphragmatic schwannoma mimicking hydatid cyst depicted by PET/CT

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A 39-year-old man who was presented with cough and sputum was referred to the outpatient clinic for chest medicine. Diagnostic computed tomography (CT) was performed. It showed encapsulated, well-defined, round, heterogeneous cystic soft tissue mass that arose from the right diaphragm. The lesion was measured approximately 10 cm in diameter and extended from right dome of the diaphragm to superior pole of the right kidney. Since Turkey is an endemic country for Echinococcus infestation, it was initially misdiagnosed as a hydatid cyst according to its CT pattern. F-18 fluorodeoxyglucose (FDG) PET/CT was requested to exclude possible malignancy. (A) Axial, (B) coronal, (C) sagittal PET, CT and combined PET/CT images (Figure 1) demonstrated mild to moderate FDG uptake [maximum standardized uptake values (SUVmax): 4.1] at the solid components which were located in the peripheral and central zones of this cystic lesion. The total resection was performed and histological examination revealed a benign schwannoma. Schwannoma is a benign tumour that originates from Schwann cells surrounding peripheral and cranial nerves. It has a predilection for the head and neck and flexor surfaces of the upper and lower extremities. Schwannoma is most frequently present in patients aged 20 to 50 years, more frequently in men than in women. They comprise 5% of all benign soft tissue tumours. Schwannoma of the chest wall and diaphragm are rare. Schwannoma is often found incidentally or present with vague, non-specific symptoms. Schwannoma is almost invariably slow growing, non-aggressive neoplasm and it is solitary in the vast majority of cases. Malignant transformation is very rare. It is important for the radiologist to consider the diagnosis of benign schwannoma when presented with a retroperitoneal or pelvic mass, to avoid unnecessary surgery, because these lesions can be managed conservatively. On CT schwannoma typically reveals encapsulated, well-defined round, solid or cystic soft tissue mass. On T1-weighted MR the lesion shows a round mass of homogeneous low signal intensity. However, on contrast-enhanced T1-weighted MR imaging the characteristic pattern is a soft tissue mass that shows a high signal intensity in the central zone, with multiple degenerative areas and very low signal intensity in the peripheral zone of the tumour. The tumour has a characteristic target appearance on unenhanced T2-weighted image, with non-homogeneous decreased signal intensity in the central zone of the tumour and with markedly increased signal intensity in the peripheral zone. In PET/CT, a few reports have indicated that schwannoma has a diffuse and wide range of SUV uptake on PET imaging depending on the degree of its cellularity. Schwannoma can rarely be almost entirely cystic, in which case they may resemble benign entities such as retroperitoneal pseudo-cyst, abscess or lymphocele. In case of the similarity of their clinical and radiological findings, schwannoma should be included in the differential diagnosis of hydatid cysts especially in endemic countries as in our case. In conclusion, this is the first report of a primary diaphragmatic schwannoma which was evaluated with F-18 fluorodeoxyglucose PET/CT.
FIG. 1. (A) Axial, (B) coronal, (C) sagittal PET, CT and combined PET/CT images.
Atypical presentation of bronchiolitis obliterans organising pneumonia on 18FDG-PET/CT

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Introduction: A 72 year old male patient was submitted to 18FDG-PET/CT for the assessment of an undetermined nodule in the upper lobe of the left lung (Figure 1). The nodule was previously found on CT scan. The patient was known to have asthma and chronic pulmonary insufficiency.

Methods: Whole body 18FDG-PET/CT was performed on GE Discovery STE scanner. The study was performed one hour after injection of 282 MBq FDG. During the study low-dose CT was used for attenuation correction. Additionally, diagnostic CT with contrast media (Visipaque, 90ml) was done for enhanced morphologic evaluation.

Results: PET/CT scan showed 16 x 12 mm soft tissue lesion in the upper lobe of the left lung with intense FDG uptake (SUVmax 11) and contrast enhancement. No pathological FDG uptake in mediastinal lymph nodes or elsewhere in the body was found. The findings on PET and CT were highly suggestive for malignant lesions in left upper lobe. Therefore left upper lobectomy with removal of sub-aortic, para-aortic, left hilar and inter-lobar lymph nodes was performed. Pathologic findings were consistent with chronic inflammation characteristic for bronchiolitis obliterans organizing pneumonia (BOOP). Histologic evaluation of lymph nodes revealed inflammatory changes. No malignant tissue was identified in lung or lymph node specimens.

Discussion: This case highlights the fact that the imaging features and metabolic activity of inflammatory processes can be highly variable. Inflammatory disease may present itself as solitary lesion with intense FDG uptake. Typical presentation of BOOP also known as cryptogenic organizing pneumonia is multiple pulmonary infiltrates, however the disease may also manifest as solitary lesion. Intensity of FDG uptake in inflammation is in correlation with the activity of inflammatory process. In our case SUVmax was 11, this suggests a very active metabolism which is characteristic to cancer but in present study was seen in inflammatory process. It has been shown that FDG-PET/CT has high accuracy in assessment of solitary pulmonary nodules. Although intense FDG uptake in solitary pulmonary nodule is highly suggestive of a malignant process, one should always consider inflammation as a possible differential diagnosis.

Conclusion: bronchiolitis obliterans organizing pneumonia can mimic malignant disease on 18FDG-PET/CT if presenting a solitary lesion with high metabolic activity.
FIG. A 72 year old male patient submitted to 18FDG-PET/CT for the assessment of an undetermined nodule in the upper lobe of the left lung.
Introduction: Inflammation is a non-specific answer to damaged tissue and it serves as a protective process before the lesion; if the lesion involves pathogenic micro-organisms, the process ends in infection. The $^{18}$FDG, a glucose analog is a nonspecific tracer because it concentrates at sites of infection and inflammation and tumour cells. FDG metabolism is elevated in activated inflammatory cells (leukocytes, granulocytes and macrophages), so the marking of these cells may be useful to detect the source of infection. The mechanism of uptake of $^{18}$FDG leukocyte diapedesis of granulocytes is through chemotactic processes.

Objective: To determine the utility of the PET/CT with $^{18}$FDG (fluorodeoxyglucose)-leukocytes, for the diagnosis and localization of infectious processes in patients from the National Institute of Oncology. The microbiology studies were used as a comparative gold standard.

Material and Methods: Longitudinal, prospective, observational and descriptive studies performed at the Department of Nuclear Medicine, National Institute of Oncology (October 2009-January 2010). A total of 11 patients from the Division of Infectious Diseases, with diagnostic or suspicions of infectious processes, participated in the study. Leukocytes were obtained from 40-80 ml of blood from patients, using an erythrocyte-lysis technique. Leukocytes were labelled with 740 MBq (20 mCi) of $^{18}$FDG. We performed whole body PET/CT with equipment BIOGRAPHIC ® SIEMENS. The PET/CT images were carried out 1 hour after the injection. The labelling efficiency and leukocyte viability was determined. Statistical analysis was performed with Epidat 3.1 software.

Results: From the 11 patients, 5 were women and 6 men. The image interpretation was carried out by visual analysis in terms of a positive or negative diagnosis. The study was positive in 10 patients and negative in 1. Histopathological studies showed that the predominant microorganism associated with the infectious process was the staphylococcus aureus. The labelling efficiency half obtained was 48 %. The Sensitivity and specificity was 100 %.

Conclusion: The PET/CT with $^{18}$FDG-leukocytes is a promising technique for the diagnosis of infectious processes related to oncological diseases, showing high sensitivity and specificity. The technique is useful in orthopaedic, abdominal or intra-cerebral infection, endocarditis and fever of an unknown origin.
Evaluation of agreement between F-18 PET–CT and Tc-99m MDP bone scan findings in patients with suspected bone metastases: Initial Johannesburg experience

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Introduction: F18 Na F PET-CT has been reported in previous publications to have a higher sensitivity, specificity and accuracy for bone metastases than Tc-99m MDP (with or without SPECT), the latter has been widely used for bone scanning in the past 4 decades. We wanted to assess the agreement between the two modalities with the view of opting for PET-CT imaging whenever necessary in the current climate of worldwide Molybdenum shortage.

Methods: We reviewed 33 consecutive patients who had F-18 Na F PET-CT bone scans (FBS). They also had Tc-99m MDP bone scan (TBS) within 24 hours of PET-CT as part of a pilot study. Three patients were excluded because the clinical indication was to evaluate benign disease. Of the remaining 30 patients, 11 patients had only the FBS. Therefore the number of patients analysed for comparison to TBS was 19. They were referred with the following malignancies: breast cancer (n=12), prostate cancer (n=6) and 1 with bladder cancer. Whole body sweep or spot views for bone scan with Tc-99m MDP were followed by SPECT acquisition of the spine in patients with suspicious lesion/s on planar images.

Results: The final diagnosis was concordant in 17/19 (89%) patients and discordant in 2/19 (11%). In the 1 patient (with breast cancer) FBS was positive for bone metastases while TBS was negative and in the other patient (with prostate cancer) FBS was negative for bone metastases (the uptake in the ribs was due to rib fractures on the CT part of the PET-CT) while TBS was suspicious of bone metastases. Looking at the findings on lesion basis, FBS showed more sites of increased tracer uptake in 7/19 (37%) patients whereas TBS showed more sites in 2/19 (11%) patients. The rest of the patients, 10/19 (52%) showed concordance for all abnormal sites of increased uptake. FBS eliminated the need for X-ray correlation in 7/19 (37%) patients.

Conclusion: There is good agreement in the final diagnosis between the two modalities, 89% of the patients, therefore FBS is unlikely to modify management in these patients. However lesion based analysis shows concordance in only 52% of patients favouring FBS as more sensitive than TBS but the impact on patient management remains uncertain. It is our view that further prospective studies with a large number of patients as well as clinical follow-up are needed for more clarity regarding the impact of FBS on patients’ management and clinical outcome.
Role of whole body 18F-FDG PET/CT in the evaluation of fever of unknown etiology


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Introduction: Fever of unknown aetiology (FUE) is a diagnostic challenge encountered in clinical practice, the common causes of which are infection, malignancy and connective tissue disorders. Many patients (pts) remain undiagnosed receiving empiric therapy. Studies show that FDG PET/CT proves useful in diagnosis after the initial work up of history, laboratory tests and conventional imaging. We present our experience using 18F-FDG PET/CT in the work up of FUE in the small group of pts referred to our centre.

Aim: To evaluate the role of whole body 18F-FDG PET/CT in FUE.

Material and Methods: This is a retrospective analysis of FDG PET/CT reports of 31 pts scanned from the year 2007 to 2010. All pts had undiagnosed fever for a minimum period of 15 days and had undergone all routine investigations which were inconclusive. A whole body 18F-FDG PET/CT scan was requested, CT scan being of diagnostic quality with oral and intravenous contrast. The procedure was performed as per routine protocol and scans reported by a radiologist and a nuclear medicine physician. Clinical and pathological correlation was obtained wherever possible.

Results: Scans were negative for metabolically active FDG avid foci in 5/31(16%) pts, among which 1 showed ground glass opacities and sub-pleural fibrosis in both lungs on CT scan. PET/CT scan was helpful in localizing the abnormality in 26/31(84%) pts. Increased FDG concentration was noted in enlarged lymph nodes in 21/26(81%), skeletal lesions in 7/26(27%), spleen in 11/26(42%), lung in 5/26(19%), liver in 1/26(4%), aorta in 1/26(4%), thyroid gland in 1/26(4%), prostate in 2/26(8%), subcutaneous tissue in 2/26(8%) intestinal wall in 1/26(4%) and bone marrow in 5/26(19%) pts. CT helped in anatomical localization and characterization of lesions. In 2 pts, additional lesions were noted in the lungs and brain on CT scan which were non-FDG avid. Follow-up of pts with positive scan, which was obtained in 22/26(85%) pts showed that 12/22(55%) had tuberculosis(3 pulmonary & 9 extra pulmonary), 1/22(4%) had tuberculosis and systemic lupus erythematosus, 1/22(4%) sarcoidosis with nodal involvement and erythema nodosum, 1/22(4%) aortic dissection with aortitis & reactive lymphadenitis, 3/22(14%) lymphoma (1 Hodgkin’s and 2 Non-Hodgkin’s lymphoma), 1/22(4%) was diagnosed with Kikuchi Fujimoto disease, 1/22(4%) with pneumonia, 1/22(4%) with pyogenic abscesses in the subcutaneous tissue of the right leg and foot and 1/22(4%) had autoimmune granulomatous thyroiditis. Among pts with negative PET/CT scan, 1/5(20%) was subsequently diagnosed with ANCA positive connective tissue disorder and 1/5(20%) was treated empirically for pulmonary tuberculosis. The rest 3/5(60%) on follow up had an uneventful course.

Conclusion: FDG PET/CT proved useful in management of patients with FUE referred to our centre indicating a promising role in diagnosing the cause for FUE which was inconclusive by routine investigations, guiding intervention aimed at tissue diagnosis and providing assurance in pts with negative scans by excluding diseases that warrant further treatment.
Methods of normalization and factors affecting liver and mediastinal blood pool standardized uptake values: A multivariate analysis

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Introduction: The PERCIST criteria proposed by Wahl et al, suggested usage of SUL (SUV normalized to lean body mass) as quantitative parameter to assess response. According to PERCIST criteria normal background F-18 FDG activity is determined in the right hepatic lobe and consists of SUL and SD in a 3-cm-diameter spherical ROI. To define a measurable tumour each baseline (pre-treatment) tumour SUL peak must be 1.5 times mean liver SUL ± 2 SDs of mean SUL. If the liver is diseased, 2.0 times the blood-pool F-18 FDG activity ± 2 SDs in the mediastinum is suggested as minimal metabolically measurable tumour activity. Previous studies have shown that SUL is dependent on body weight and SUV normalized to body surface area (SUB) is least dependant on body weight and varies less from patient to patient.

Aim: This prospective study was carried out to assess the variability of Liver and mediastinal SUVs normalized to lean body mass (SULL, SULM), body surface area (SUBL, SUBM) and body weight (SUWL, SUWM) and their dependency on various factors which can uptake SUV values.

Materials and Methods: 88 patients who underwent FDG PET/CT for various oncological indications were prospectively included in this study. SUVs of liver and mediastinum were calculated by ROIs drawn as suggested in PERCIST criteria. Multivariate linear regression analysis was done to assess for the various factors influencing the SUVs of liver and mediastinum according to the normalization factors applied. Factors assessed were age, sex, weight, blood glucose levels at the time of injection of F-18 FDG, diabetic status and uptake period. P value less than 0.01 was considered significant.

Results: SULL, SULM, SUBL, SUBM, SUWL, SUWM were not affected significantly by any of these four factors-Age, Sex, Blood glucose levels, Diabetic status. Uptake period had statistically significant effect on SULL (p=0.007; range =1.2-2.8) and SUWL (p=0.008; range=1.5-3.5) with progressive decrease with increasing uptake time. Body weight showed statistically significant effect on SUWL (p=0.001; range=1.5-3.5) while SULL and SUBL were not dependant on weight. SUBL was least dependant on weight (p=0.851, range=0.5-0.9) when compared with SULL (p=0.425). However SULL was also not affected statistically significantly by variations in body weight (p=0.425). Mediastinal SUVs were also not significantly affected by bodyweight when normalized to bodyweight, body surface area of lean body mass.

Conclusion: Though SUBL appears to be least dependant on weight, SULL is also not significantly affected by weight and is close to SUWL. Uptake period appears to be the only factor which affects SULL significantly and this calls for acquisition of scans with standard uptake period with minimal variability in uptake times. In contrast mediastinal SUVs were not affected significantly by any of the factors and when normalized by any of the methods.
Comparison of micro PET/CT using 18FDG and Micro SPECT/CT imaging of glioblastoma αVβ3 Integrin expression using 99mTc labelled RGD peptide

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Introduction: Integrin αVβ3 played a significant role in tumour angiogenesis and is a receptor for the extracellular matrix proteins with the exposed arginine-glycine-aspartic (RGD) tripeptide sequence. Integrins αVβ3 are over expressed on the activated endothelial cells of tumour neovasculature and some tumour cells such as breast cancer and glioblastoma. Antiangiogenic therapy by usage of small peptide antagonists of αVβ3 integrins slows tumour growth and prevents tumour spread.

Methods: Glioblastoma xenografts were induced by subcutaneous injection of 2.5 x 106 C6 cells into the left back leg of female athymic nude mice. As a negative control cervix xenografts were induced by subcutaneous injection of 6.5 x 106 HeLa cells into the right back leg. Three weeks after inoculation of the tumour cells, when the tumour reached 1 cm in diameter, the mice were used for biodistribution and micro SPECT/CT and micro PET/CT experiments. The peptide HYNIC-RGD was labelled with 99mTc from a lyophilized kit formulation for distribution and micro SPECT/CT imaging studies in female athymic nude mice bearing subcutaneous C6 glioblastoma compared with subcutaneous HeLa cervix xenografts. Also receptor blocking experiments with the co-injection of cold peptide and immunohistochemistry were also performed to evaluate the αVβ3 binding affinity/specificity of the RGD peptide in vivo and in vitro. For biodistribution studies female nude mice bearing tumour xenograft of glioblastoma and cervix were injected with 700-950 µCi of 99mTc-HYNIC-RGD and 500-650 µCi of 18FDG (intraperitoneal). The mice were sacrificed and dissected at 1, 2, 3, 4, 6 and 24 h after injection of 99mTc-HYNIC-RGD. Blood, tumours, major organs and tissues were collected and wet weighted. The results are presented as the percentage injected dose per gram (%ID/g). Values are expressed as mean ± SD for each group.

Results: Rapid and high activity accumulation in the αVβ3 C6 tumours was observed at early time points. Tumour uptake persisted during the next 6 h with a peak at 3 h. The renal and liver activities were initially high, but fell at 4h. A significant decrease of radioactivity in the C6 tumour was shown. Uptake in tumour images was reduced most markedly from 84 cts/s to 28 cts/s. The tracer revealed receptor specific tumour accumulation which was confirmed by effective receptor-blocking experiments. Static micro SPECT/CT imaging showed strong contrast from the contralateral non positive αVβ3 tumour (cervix) and from 18FDG PET studies. The tumour-to-background (muscle) ratio at 1 h after injection was 5.47. Tumour uptake was 3.99 %ID/g at 1 h and 9.09 %ID/g at 3 h.

Conclusions: This study demonstrated that 99mTc-HYNIC-RGD is a tracer suitable for SPECT/CT imaging of αVβ3 integrin expression in glioblastoma tumours in xenograft models with clear contrast tumour-targeting, high receptor-binding affinity and receptor specific uptake. Because of the wide accessibility of the cameras and high availability and excellent
imaging characteristics of 99mTc, the 99mTc-HYNIC-RGD may be an attractive alternative to other radio labelled RGD peptides for angiogenesis research.
Comparison of Ga-68 DOTATATE vs. Tc-99m HYNIC OCTREOTIDE scan in follow-up of cancer thyroid patients with raised thyroglobulin and negative I-131 WBS

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Introduction: Somatostatin analogues labelled with 111In, 99mTc and 68Ga are used for the diagnosis of neuroendocrine tumours. There is evidence suggesting that they can be used in the evaluation of thyroid cancer patients, that have already undergone surgery and 131I therapy, and that in the follow up have high thyroglobulin levels and negative 131I whole body scan. These patients represent a diagnostic and therapeutic challenge. The objective of this paper was to evaluate these patients by means of 99mTc HYNIC Octreotide and 68Ga DOTA TATE.

Material and Methods: 68Ga DOTA TATE was performed in 11 patients bearing thyroid cancer that had already undergone surgery and 131I therapy. In the follow up these patients had high thyroglobulin levels and negative 131I whole body scan and a positive 99mTc HYNIC Octreotide scintigraphy. Median age was 43 years (29-70), 9 women and 2 men. Pathology after thyroid surgery revealed papillary thyroid cancer in nine of them and follicular cancer in two. Scintigraphy images were performed at 4 and 24 hours after injection of 900 MBq of 99mTc-HYNIC Octreotide performing a whole body scan followed by SPECT images of the region of interest. A double detector gamma camera equipped with LEHR collimators (Mediso Nucline Spirit DH -V, Hungary) was used for scintigraphy. PET-CT images were performed in a GE Discovery ST-16 at 30 minutes post-injection of 90 MBq of 68Ga DOTA TATE.

Results: 68Ga-DOTA TATE studies were able to correlate positively with 99mTc HYNIC Octreotide lesion localization in only 2 patients, being compatible with local relapse. One of these patients had a Hurthle cell carcinoma that was positive with both methods, underwent radioguided surgery with 99mTc HYNIC Octreotide. The other 9 patients were negative for thyroid cancer using 68Ga DOTA TATE and are now being followed-up.

Conclusion: Although both radiotracers are able to identify somatostatin receptors, the observed differences suggest that these patients should have a clinical and imaging follow-up in order to validate 99mTc HYNIC Octreotide findings.
Introduction of PET-CT scanning impacts treatment decisions in the management of cervix carcinoma patients in a public hospital

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The increasing use of PET-CT scanning in the staging of cervix carcinoma has shown that a significant number of patients are found to have nodal disease outside the pelvis, or distant metastases. Tygerberg Hospital gained access to PET-CT in late 2008. Consequently limited use was made for staging of a selected number of patients with stage IIIb cervix carcinoma who were able to attend for a scan. A retrospective analysis was made of the 12 patients scanned to date. The data collected included results of conventional staging with chest X-Ray (CXR) and abdominal ultrasound (USS), PET-CT results and change in treatment intent and therapy. One patient had a finding of a perirenal lymph node mass on USS; otherwise all CXR and USS reports were normal. Of the 12 PET-CTs six had no evidence of disease outside the pelvis, two showed pelvic and paraaortic nodal (PAN) involvement, three showed distant metastases or nodes above the diaphragm and one showed evidence of a renal mass and cerebral metastases. Consequently of the 12 patients, six received routine chemoradiation, two patients received additional extended field chemoradiation to treat the PAN and four patients were treated with appropriate palliative care. Thus, 50% of cases had altered treatment decisions as a direct consequence of the PET-CT results. In conclusion we found that the use of PET-CT had a significant impact on the treatment decisions made for this small cohort of patients with Stage IIIb cervix carcinoma. It is hoped to increase access to this staging modality for our patients with locally advanced cervix carcinoma, and a formal study to further assess the use of PET-CT in cervix carcinoma patients is under development.
Efficacy of PET/CT in the management of TENIS syndrome: A case report

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Thyroid carcinoma is the most common endocrine tumour, and papillary carcinoma is its commonest subtype in iodine-replete populations. It is more common in females and has a peak age incidence of thirty to fifty years. The tumour spreads to locoregional lymph nodes and to the lungs. Haematogenous spread to bone and central nervous system has also been documented. Prognosis is better for younger patients than for patients who are older than forty-five years of age. Patients diagnosed and treated with radioactive iodine for differentiated thyroid carcinoma are monitored with whole-body iodine scans and serum thyroglobulin levels, as well as cervical ultrasonography if experienced thyroid radiologists are available. It has been said that 10-15\% of patients may have elevation of serum thyroglobulin in the presence of a falsely-negative radioiodine whole-body scan, termed the TENIS syndrome (Truncated Expression of the NIS, where NIS represents the sodium-iodide symporter). The syndrome has been variously attributed to: small doses of radioiodine used for the diagnostic scan, possible ‘stunning’ of functional thyroid tissue, iodine loading, dedifferentiation of the carcinoma, or the absence of immune-reactive cytoplasmic thyroglobulin and thyroxine. Older patients might have a “loss-of-function mutation” of the symporter. The presence of anti-thyroglobulin antibodies must also be excluded as heterophile antibodies are a known cause of falsely elevated serum thyroglobulin. Alternative imaging with tumour-imaging agents has been advocated, for example, with radiolabelled sestamibi, octreotide, and fluorodeoxyglucose (FDG). A female Caucasian patient known with papillary thyroid carcinoma had been followed up at the Thyroid Cancer clinic. At presentation, a diagnostic scan with ten millicuries of radioiodine revealed the presence of residual thyroid tissue. RAI ablation of the thyroid gland was performed with eighty millicuries of radioiodine. Two- and five-year follow-up scans were clear. However, thyroglobulin levels demonstrated persistent low-grade elevation, with a spike noted that year. The patient was diagnosed with the TENIS syndrome. A PET-CT scan was performed which demonstrated inhomogeneous uptake in the liver, with focal increased activity in the right lobe (SUV more than six). A pedunculated inhomogeneous mass lesion arising from segment five of the liver was also noted (SUV five). A CT scan of the abdomen confirmed multiple liver metastases. Sonar-guided FNA of liver lesion revealed several groups of malignant cells. Persistently elevated thyroglobulin levels in the presence of a negative whole-body RAI scan are of great concern. FDG PET imaging is the most sensitive modality for detecting tumour spread and recurrence in such instances.
Focal accumulation of FDG in lung parenchyma without morphological correlate on CT

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Hybrid 18F-FDG PET/CT imaging provides functional and anatomical information important for oncological diagnosis and therapy planning. Assessment of the hybrid study requires correct differentiation of physiological and pathological findings from potential artefacts. Several previous reports describe focal lung uptake of FDG without structural alterations on CT. The foci were observed in various parts of the lung and tentatively interpreted as microemboli attributable to the intravenous injection of FDG, mostly due to extravasation. In one paper, the authors interpreted such a focus as FDG activity in the renal upper calyx. On CT, no structural alterations have been observed at FDG hot-spot sites. In all cases, abnormal focal lung uptake disappeared in the study repeated in 1-3 days. In case of activity deposited in the renal calyx, it disappeared on the scan repeated after 1 hour. Total number of cases reported by 5 groups of authors was 15 (7 men and 8 women of various age). However, no report indicates frequency of the finding in a routine PET/CT practice. We have observed this type of artefact shortly after starting PET/CT services in our department in a 67 years old woman examined for restaging of breast cancer. The patient was scanned 70 min after administration of 400 MBq of FDG and 100 ml of intravenous x-ray contrast through flexible cannula using automatic injectors. The PET study showed 3 foci in both left and right lung with highly increased FDG uptake (SUVmax - 11, 11, 17) with normal finding on CT (Figure 1). No manifest extravasation has been detected. The study focused on the lung was repeated in 3 days. The second study showed normal findings in both PET and CT scans. The foci observed in our scan were comparable with those reported in the literature. Since this single observation, similar findings were not experienced in the 300 patients that followed. In agreement with the authors of previous reports, we assume artificial etiology of the finding caused by microembolism due to microthrombi created by microcoagulation of the blood in the tubes or by micro-damage of a vascular wall. An alternative embolising particle can also be a microparticle from the stoppers and seals included in the tubing connections in either FDG application or production devices. This second tentative explanation may be more likely in the patients where there is no observable extravasation. Although this type of artefact is probably not too frequent, the readers should be aware of it to avoid possible misinterpretation.
FIG. 1. Maximum intensity projection of 3 observed hot spots on the FDG PET scan.
Peptide receptor radionuclide therapy (PRRNT) in patients with carcinoid heart disease (Hedinger’s syndrome): Prognostication of efficacy by Ga-68 SMS receptor PET/CT

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Aims: The objectives of the study were to determine the survival in patients with carcinoid heart disease (Hedinger's Syndrome, HS) and to analyse the efficacy of Peptide Receptor Radionuclide Therapy (PRRNT) with Y-90 or Lu-177 DOTATATE in these patients.

Materials and Methods: Out of 550 patients with progressive neuroendocrine tumours treated at our neuroendocrine tumour centre, 42 patients (mean age 59 years; female: male 19:23) were found to have HS (confirmed by 2-D echocardiography and Colour Doppler). Patients were treated with either Y-90 or Lu-177 DOTATATE at 3-4 months intervals under amino acid nephroprotection and 3-monthly serotonin level monitoring. Response was assessed by Ga-68 DOTANOC receptor PET/CT. Kidney function was assessed using renal scintigraphy (Tc-99m MAG3) and tubular extraction rate (TER), and glomerular filtration rate measurements using the single sample plasma clearance method.

Results: Out of the 42 patients with HS, 23 patients had NET of the ileum/jejunum/stomach, 14 had pancreatic NET, 4 with Carcinoma of Unknown Primary (CUP), and one had rectal NET. According to severity, 17 patients had grade I, 8 grade II, 4 grade III and 13 had grade IV tricuspid valve regurgitation (TR) - 9/42 (21%) patients died. Median/mean survival from time of first diagnosis (ToFD) in patients with high grade TR (grade 3 and 4) was 146/123 months as compared to a mean survival time of 233 months for low grade (1 and 2) TR from ToFD. Mean survival in patients with high grade TR was 33.8 months from the time of first PRRNT (42% died) vs. 69.3 months for low grade TR (7% died). Patients treated with 3 cycles of PRRNT achieved stable disease (SD) in 50% while the remaining had progressive disease (PD). Six patients had improvement in TR after PRRT (all with grade 1). Four patients with grade 4 TR underwent tricuspid valve replacement. Mean fall in TER (32.6%) was significantly higher as GFR fall (26%) suggesting that TER may be a better predictor of renal function in patients with HS. There was a significant correlation between the grade of TR and TER value (n=30); no correlation was observed concerning GFR and grade of TR. TER fall (16.2%) in low grade TR was significantly lower as compared to TER fall (37.5%) in patients with high grade TR; no such correlation was observed for GFR.
Conclusions: The probability of survival in patients with high grade HS is two times less when compared to those with low grade HS. Patients with carcinoid heart disease have poorer response to PRRNT in comparison to patients with normal heart function. Tubular extraction rate is the better parameter for assessment of renal function in carcinoid heart disease.
Efficacy of Ga-68 somatostatin receptor PET/CT and peptide receptor radionuclide therapy in the management of neuroendocrine tumours of the rectum

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Aims: To assess the role of Ga-68 somatostatin receptor PET/CT (SR-PET/CT) and Peptide Receptor Radionuclide Therapy (PRRNT) in the diagnosis and treatment of patients with neuroendocrine tumours of the rectum (rNET).

Material and Methods: 24 patients (Male: Female 13:11; mean age 55.2 years) with rNET were referred for staging or restaging with SR-PET/CT and for evaluating the possibility of PRRNT (using Y-90 or Lu-177 DOTATATE). SR-PET/CT was also used for response assessment after PRRNT.

Results: Median duration of follow-up from first cycle of PRRNT was 14.7 months (3-39 months). Sites and numbers of metastases detected on CT scan alone were the following: liver (15), lymph nodes (9), bone (1) and local recurrences (2). On the other hand SR-PET/CT detected 14 metastases in the liver, 9 lymph nodes, 10 in bone and 2 local recurrences in the same group of patients. Discordant results (SR-PET+ and CT-): bone 9/10 and lymph node 1. In 2 patients, SR-PET was negative and CT positive (1 liver and 1 lung lesion). 19 patients were treated by PRRNT (15 received >3 cycles). In total, 27\% of patients achieved a partial remission/minor response, 40\% had stable disease, whereas the remaining 33\% had progressive disease. 7 patients showed a fall in tubular extraction rate (TER) of greater than 20\% (Lu-177: n=3 and Lu-177 plus Y-90: n=4). Out of 7 patients with a TER fall of > 20\%, 3 had prior external radiation therapy (60 Gy), 2 had 5-FU/streptozotocin chemotherapy, and one patient had diabetic nephropathy and arterial hypertension. Anaemia grade 1-2 occurred in 14 patients (74\%), grade 3 in four (21\%), and grade 1 thrombocytopenia in one patient (5\%).

Conclusions: Ga-68 somatostatin receptor PET/CT is superior to CT alone for staging of rectal neuroendocrine tumours, and especially for the detection of bone metastases. PRRNT is safe and effective in patients with progressive neuroendocrine rectal tumours.
Brown adipose tissue metabolism in diabetic mice and weight-loss mice: A preliminary study with 18F-FDG micro PET

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Introduction: This study aims at using 18F-FDG microPET to evaluate several interventions related to Sympathetic Nerve System (SNS) in stimulation and inhibition of brown adipose tissue (BAT), and to study the role of BRL37344, an adrenergic β3 receptor agonist, in activation of BAT metabolism in normal mice, type 2 diabetes model mice, and obese model mice receiving weight-loss treatment (weight-loss mice).

Method: 6-7 week-old ICR mice were enrolled. To study the physical interventions, normal mice were exposed to cold (6-7°C, n=6), warm (35°C, n=6), cold and then warm (n=6), or constant temperature of 21±3°C (n=12) for 1 h. In pharmacological interventions, normal mice received either intraperitoneal injection of norepinephrine (NE, 0.4mg/kg, n=5), epinephrine (0.02mg/kg, n=5), isoprenaline (0.016mg/kg, n=6), or intragastric administration of propranolol (13.2mg/kg, n=3). To study the role of BRL37344, 24 mice were randomly divided into 3 groups: the normal control group (grp 1, n=12), the type 2 diabetes group (group 2, n=6), and the weight-loss group (group 3, n=6). Group 2 and 3 were bred with high fat diet for 8 weeks. We use Streptozocin (STZ, 100mg/kg) to build the type 2 diabetes model in group 2, and Sibutramine (8mg/kg) gavage for 2 weeks daily to build the weight-loss mouse model in grp 3. All the groups received peritoneal injection of either BRL37344 (2mg/kg) or saline half to half for each group. MicroPET scans were performed 1h after an intraperitoneal injection of 3.7 MBq 18F-FDG. The FDG uptake ratio (R) between interscapular BAT and liver (or brain) was calculated in each mouse for semi-quantitative analysis.

Results: Stimulation of SNS by cold or NE significantly increased BAT uptake (R: 10.22±4.13 vs. 4.08±1.32, P=0.0002, and 10.55±5.85 vs. 4.08±1.32, P=0.002, respectively), and much higher BAT uptake was observed under both interventions (R: 15.64±5.58 vs. 4.08±1.32, P=0.000002). Epinephrine and isoprenaline intervention did not show significant increase of BAT uptake of FDG (P=0.459 and 0.293, respectively). Inhibiting SNS by warming up or propranolol administration, could significantly reduce BAT uptake in mice (R: 2.48±0.88 vs. 4.08±1.32, P=0.017, 1.30±0.16 vs. 3.09±0.90, P=0.027, respectively). BAT metabolism could be significantly stimulated by BRL37344 treatment in normal mice and weight-loss mice (R: 30.0±23.3 VS 8.6±2.7, P<0.05, 16.8±5.07 vs. 5.4±3.92, P<0.05, respectively), but could not significantly activate the BAT in diabetes mice (R: 5.1±3.98 vs. 6.8±1.76, P>0.05). Under the stimulation of BRL37344, BAT metabolism was the highest in normal mice and the lowest in type II diabetes mice (R: 30.0±23.3 and 5.4±3.92, respectively, P<0.05).

Conclusion: BAT metabolism has a positive correlation with SNS activation; stimulation or inhibition of SNS by physical or pharmacological methods may increase or decrease BAT metabolism correspondingly. Type II diabetes coincides with BAT’s dysfunction or desensitization to stimulating factors such as BRL37344. Weight-loss treatment, using
Sibutramine for example, is related to the increase of BAT’s sensitivity to adrenergic β3 receptor agonist.
Normal uptake value of 11acetate in some organs

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Introduction: PET/CT with 11C-Acetate has been put into clinical practice in our centre. 11C-Acetate is used for the evaluation of the fatty acid metabolic activity of the tumours. We have performed initial cases of PET/CT with 11C-Acetate for diagnosis and follow-up of HCC and urological cancers. We wanted to assess the 11C-Acetate uptake in the normal-appearing tissue of some organs in the body.

Methods: All male patients fasted for at least 6 hours before 11C-Acetate PET/CT whole-body scanning (Biograph true D w/true V 64 slice, Siemens) at Cho Ray hospital, Viet Nam. 11C-Acetate was intravenously injected at 10 MBq/kg body weight (0.27 mCi/kg). Whole-body scanning was performed at 15 minutes after 11C-Acetate injection from the skull base to upper thigh. The uptake of 11C-Acetate in the normal-appearing tissue of some organs was semi-quantified by maximum and mean standardized uptake value (maxSUV and meanSUV) calculated by radioactivity in ROI (Bq/ml) x body weight (kg) / injected radioactivity (Bq).

Results: Nine male patients were included in the study. The mean age was 59±13.9 years (46 to 79). There were 7 patients with HCC, 1 with combined bladder and prostate cancers and 1 with resected renal cancer with bladder seeding. The maxSUV and meanSUV of the normal-appearing tissue of liver were 4.8±1.0 and 3.7±0.7, spleen were 5.6±0.9 and 4.7±0.8, pancreas were 11.4±3.0 and 8.9±2.9, prostate were 4.1±1.4 and 3.2±0.6, renal cortices were 3.8±0.7 and 3.3±0.6, parotid gland were 4.7±1.7 and 3.6±0.9 and bone marrow were 1.8±0.8 and 1.8±0.8, respectively.

Conclusion: PET/CT showed the normal highest uptake of 11C-Acetate in pancreas and the 11C-Acetate uptake in order of descending levels which were spleen, liver, parotid gland, renal cortices, prostate and bone marrow. These values could be used as the reference value necessary for the certification of normal uptake of 11C-Acetate in the human body and for clinical interpretation of PET/CT with 11C-Acetate.
Magnetite nanoparticles (MNP) are significant alternatives for hybrid imaging tools such as PET-MR when radiolabelled with PET radionuclides. In this work, 18F labelled magnetic iron oxide NPs were synthesized as PET-MR hybrid imaging agent. Mannose triflate, a precursor of 18FDG, was used to conjugate with cysteamine. The synthesized compound that will be referred to as mannose triflate-cysteamine (MC) was then labelled with 18F via nucleophilic fluorination. This reaction was also carried out using cold fluoride. 18F labelled mannose triflate-cysteamine (18FDG-CA) was then made to react with a solution of FeCl3. Subsequently, MNPs were synthesized by reduction of the resulting compound with NaBH4. SEM (Scanning Electron Microscopy) images demonstrated that MNPs are nano-sized. Synthesized and characterized MNPs as a model imaging agent were applied to MCF7 breast cancer cell line. As well as time dependent cell incorporation, apoptotic effects of synthesized compounds were examined. 18FDG-cysteamine bound MNPs (18FDG-CA-Fe3O4) exhibited the cell incorporation ratio up to 50%. It was also observed that cold FDG-CA-Fe3O4 had apoptotic effects and synthesized structures could have a potential as hybrid imaging agent in PET-MR imaging systems.
FDG Embolus: Focal lung uptake without CT abnormality- potential pitfall in PET-CT fusion imaging

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PET-CT has an important role in staging the patients in oncology because metabolic changes are detected before any anatomical changes are evident, and provide more accurate definitions of lesions and early lymph node involvement than conventional CT which relies on morphological criteria only. As PET/CT fusion imaging finds more and more clinical indications, novel conditions that pose interpretive problems, artefacts or pitfalls have been described, emphasising the need for careful evaluation of every hot spot abnormality without corresponding CT changes before assigning significance to it, a point which our study highlights. We present 4 cases with focus on 18F-FluoroDeoxyGlucose uptake in the lung without corresponding CT lesions. The first was a case of osteosarcoma in the right leg for pre-treatment evaluation. PET-CT scan for metastatic survey revealed focal hyper-metabolism in the left lung upper lobe without any anatomical abnormality on CT. Second was a follow up case of carcinoma rectum, in which an FDG avid nodularity was noted in the left lower lobe without any significant CT changes. This was suspicious, as patients with Ca. rectum are known to have isolated lung metastases bypassing the liver in rare instances. The third case was of lymphoma where also a solitary hyper-metabolic focus in the left lung upper lobe, not confirming to any CT abnormality, was noted. The last case was for initial staging for carcinoma lung. On PET-CT scan, besides uptake in primary neoplasm in left upper lobe, there was no metabolically active loco-regional lymphadenopathy or distant metastases, except a 'hyper-metabolic focus' in the right lung middle lobe without any CT changes. On repeating the scan the next day in all patients, these hyper-metabolic foci disappeared, proving correct our suspicion for possible FDG injection embolus. This had important implications on staging (from metastatic disease to local) and subsequent course of treatment in all the cases, except probably the third one. A possible explanation for the observed findings (injection embolus) could be that at sites of endothelial injury during radiopharmaceutical injection, platelets activate and adhere to the sub-endothelium, rapidly changing their shape and aggregating. Although anaerobic glycolysis is the major energy source for platelets at rest, the activation process is highly extracellular-glucose dependent via the most active glucose transporter, GLUT-3. The activation of platelets by thrombin induces a three-to-five fold increase in glucose transport via GLUT-3 which is mainly stored in the a-cyttoplasmic granules of platelets and translocate to the cell-surface after activation. Activated platelets and fibrin are major constituents of blood clots and may explain the high 18F-FDG uptake of the focal lesions observed on PET images. Clot formation at any level of the administration kit (including the needle, syringe cone, tip of the cannula), patients with abnormal peripheral venous system, difficult phlebotomy or the presence of a hypercoagulability state may also lead to microembolism. The possibility of pitfalls in the interpretation of high 18F-FDG uptake areas underline the importance of being cautious and watchful, and repeating the scan to rule out any embolus being labelled as metastases.
CLINICAL NON-PET ONCOLOGY
Role of SPECT-CT in cancer patients for diagnosis of bone metastases

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The combined application of baseline whole-body bone scintigraphy (WBBS), followed by more specific techniques such as SPECT-CT fusion is an advanced approach for diagnosis, differential diagnosis and staging of osseous metastases.

Aim: To evaluate the value of SPECT-CT for the detection of bone metastatic lesions in patients (pts) with oncological diseases.

Material and Methods: This study included 89 pts (54F, 35M; age 18-92 yrs) with different types of tumours. All pts underwent routine WBBS with 99mTc-MDP as well as target SPECT-CT imaging. The field of SPECT-CT images correlated with scintigraphycally visualized bone foci with abnormal uptake of the tracer and uncertain character. Double-headed SPECT camera with 2-slice CT scanner (Symbia T2, Siemens) was used.

Results: After retrospective review of WBBS and SPECT-CT fused images 141 bone lesions in 89 pts were analysed (Table 1):

<table>
<thead>
<tr>
<th>ANATOMIC REGION</th>
<th>BENIGN (n)</th>
<th>MALIGNANT (n)</th>
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<tbody>
<tr>
<td>1. CRANIUM</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>2. CERVICAL SPINE</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>3. THORACIC SPINE</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>4. LUMBAR SPINE</td>
<td>11</td>
<td>9</td>
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<tr>
<td>5. RIB</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>6. STERNUM</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>7. STERNOCLOACULAR JOINT</td>
<td>0</td>
<td>4</td>
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<tr>
<td>8. CLAVICULA</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>9. PELVIS</td>
<td>14</td>
<td>41</td>
</tr>
<tr>
<td>10. FEMUR</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>11. SHOULDER</td>
<td>0</td>
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</tr>
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The skeletal findings with previously uncertain character were classified as definitely benign, indeterminate or definitely malignant: 1) 47 (33\%) of all lesions in 36 pts could be correlated with benign degenerative findings on SPECT-CT images 5 (3\%) lesions in 3 of these pts were indeterminate on the SPECT-CT images. They were localized in the area of articulation parts and corpus of the thoracic vertebra and ribs. After additional MRT examination and 6 months follow-up these changes were considered degenerative. 2) 41 (28,1\%) single osseous metastatic spots (up to 3 foci) were scanned in 31 pts. They were localized mostly in the flat bones of the pelvis, vertebrae or the sternum.
3) 13 (10%) lesions caused by direct infiltration of bone structures was observed in 6 pts as a result of proximity to the neoplastic recurrent or metastatic process localized in the surrounding soft tissues.

4) 21 (15%) lesions with prevailing “cold” osteolytic component were observed in 8 pts with renal, endometrial, colorectal or urinary bladder cancer.

5) 17 (12%) “mixed-type” lesions - osteolytic and osteosclerotic were obtained in 6 cases with breast, prostatic and NSCLC cancer.

6) Two pts were with 2 (1.9%) single extraosseous lesions: one – with myositis ossificans in the region of the right femur and the second – with soft tissue calcifoid metastasis in the right abdomen due to appendicitis cancer.

Conclusion: SPECT-CT camera allows the precise correlation of functional and morphological data on the same image. CT is a valuable method for characterizing destruction of the bone spongy lesions, their consolidation or calcium accumulation. This fact allows differentiation of the osteolytic metastases from the sclerotic and mixed lesions and also from degenerative ones. WBBS followed by SPECT-CT studies enable to perform differential diagnosis between malignant and benign changes in the skeleton which is very important for future management of cancer patients.
SPECT with 99mTc-MIBI and 99mTc-(V)DMSA in the assessment of breast lesions: Comparative study with planar scintimammography

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Purpose: To evaluate and compare the diagnostic value of planar breast scintimammography (SMG) using 99mTc-MIBI and 99mTc - (V) DMSA with SPECT in detection of primary breast cancer (BC) and metastatic lymph node involvement.

Materials and Methods: 96 women referred for a suspicious BC on physical examinations or/and equivocal data of mammography underwent planar SMG followed by SPECT. Patients were divided into 2 groups depending upon the radiotracer which had been injected. In 1st group (65 patients) studies were performed with 99mTc-MIBI, in 2nd group (31 patients) - with 99mTc - (V) DMSA. The results of radionuclide diagnostic were compared with histological findings. BC were histologically confirmed in 75 patients (12 of them had lesion less than 10 mm). Benign lesions were found in 21 patients.

Results: In BC lesions less than 10 mm (6 patients) planar SMG in 1st group with 99mTc-MIBI was true positive in 4 out of 6 patients (66%) and SPECT – 5 out of 6 patients (83,3%), planar SMG and SPECT study showed equal sensitivity in 2nd group and was true positive in 5 out of 6 (83,3%)patients. Tumours greater then 10mm in the 1st group with planar SMG were revealed in 44 out of 49 patients (89,7%) and SPECT – in 46 out of 49 (93,8%), in 2nd group sensitivity of planar SMG was definitely positive in 10 out of 12 patients (83,3%) and SPECT – in 11 out of 12 patients (91,6%). In benign lesions planar SMG in both groups were true negative in 19 out of 21 patients (specificity 90,4%) and SPECT in 17 out of 21 (specificity 80,9%). Metastatic lymph node involvement was successfully imaged in 1st group with planar SMG in 13 out of 19 patients (68,4%) and SPECT 16 out of 19 patients (84,2%), while true negative planar scans were observed in 33 out of 36 patients (specificity 83,3%) with benign or malignant tumours without lymph node involvement and SPECT scans in 32 out of 36 patients (88,8%). In the 2nd group planar SMG was definitely positive in 6 out of 9 patients (66,6%) versus 8 out of 9 patients (88,8%) who underwent SPECT. Specificity of planar SMG revealed 81,8% (18 from 22 patients were true negative) and SPECT - 77,2 % (17 from 22 patients).

Conclusion: Diagnostic opportunities of both methods in detection of primary BC with both radiotracers are almost equal but 99mTc - (V) DMSA has a tendency to be more intensely localized then 99mTc-MIBI in lesions smaller than 10 mm. SPECT is more sensitive in detection of small lesions and has lower specificity in comparison with planar SMG. SPECT is more sensitive than planar SMG in detection of metastatic lymph node involvement in equivalent specificity. Thus, SPECT has a high diagnostic value in detection of lymph node involvement in comparison with planar SMG and can be used for adequate planning of treatment.
SPECT in diagnostic of metastatic medullary thyroid cancer

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Background: Medullary carcinoma is a relatively rare neuroendocrine tumour. According to some authors medullary carcinoma ranges from 3% to 7% of all thyroid cancers. Over 50% of patients may have local or distant metastases at the time of primary diagnostic of MTC. Several conventional radiological imaging modalities such as ultrasound, MRI, CT are routinely used in long-term follow-up of post-operative MTC-patients, but they often fail to localize the recurrent or metastatic disease of MTC. In the search for a more reliable method, SPECT study with 99mTc-carbomec was applied in post-operative work-up.

Purpose: To estimate the diagnostic value of planar and SPECT studies with 99mTc-carbomec in post-operative MTC patients.

Materials and Methods: 40 patients (22 females and 18 males) with MTC, aged 23 – 64 years, underwent planar scintigraphy with 99mTc-carbomec, followed by SPECT – study 1 month after surgery treatment (total thyroidectomy). Investigations were performed using dual-head gamma-camera "E - CAM - 180" (Siemens). The obtained results were compared to the clinical data and other employed imaging methods.

Results: Data of both diagnostic procedures (planar scintigraphy and SPECT) were true negative in 21 patients and revealed no regional and distant metastases. Metastatic lymph node involvement had been detected in 10 patients (3 of them had metastases in the mediastinal lymph nodes, and 7 - in the neck lymph nodes), 6 patients had distant metastases in lung, and 3 had multiple metastases in lung and liver. Metastases in lymph nodes were detected by both methods - planar scan and SPECT in all 7 patients. At the same time mediastinal lymph nodes were revealed only by SPECT. In 2 out of 6 patients distant lung metastases visualised by both planar scintigraphy and SPECT study, and 4 patients - only by SPECT. In multiple lung and liver metastases diagnostic value of planar and SPECT studies were equal and were definitely positive in all 3 patients. The diagnostic value of both - planar and SPECT studies - were assessed. The sensitivity of neck lymph nodes planar scintigraphy and distant multiple metastases in lung and liver was 100%, SPECT-100%. Planar scans were uninformative in patients with metastatic involvement of mediastinum lymph nodes, while the sensitivity of SPECT was 100%. Sensitivity of planar scintigraphy in lung metastases patients were 34%, versus SPECT-66%.

Conclusion: Thus, post-operative work-up in patients with MTC can be carried out using both planar and SPECT scintigraphy. SPECT is a more sensitive functional imaging modality for detecting regional and distant metastatic disease in MTC patients.
Sentinel lymph node scintigraphy & gamma probing in patients with early stage Ca cervix

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Single most important factor that predicts patient outcome in early Ca cervix is lymph node metastasis status. Systematic retroperitoneal lymph node dissection is “gold standard” for identification of lymph nodal metastases. Sentinel lymph node (SLN) biopsy are being increasingly used in oncology with good success. It minimizes regional lymphadenectomies, associated lymphatic complications. We aim to extrapolate this approach in cervical cancers, the second most common malignancy worldwide. Incidence of lymph node metastases in stage I A2 and stage I B1 is only 7% and 20%, thus Sentinel Lymphnode Scintigraphy (SLS) can be used to avoid unnecessary lymphadenectomy in SLN negative patients. Traditional imaging techniques may fail to identify nodal metastases with accuracy, as micro-metastases can be present in sub-centimetre sized nodes. We aim to study the following: 1) To assess feasibility and standardize SLS in early cervical cancers (2) To assess Negative predictive value (NPV) of SLN biopsy (3) Anatomic localization of SLN by SPECT CT (4) Micro-metastases rate in SLN by node sampling.

Materials and Methods: 23 proven early cervical cancer patients with tumour size < 4 cm were included. Patients mean age was 51.7 yrs (range 31 - 73 yrs), Stage IB 1: IA2 = 21:2. All cases were scheduled for radical hysterectomy, full para-aortic & pelvic lymphadenectomy. SLS performed on day of surgery. 3-4 injections of 0.1 ml each (total < 37MBq) of Tc 99m sulfur colloid (filtered) were given peritumourally. Planar imaging followed by SPECT CT and skin markings of SLN was done. Intra-operative SLN probing was performed using a cordless gamma probe. SLN were sent for serial sectioning and Immunohistochemistry analysis. All patients were on follow-up for 1 year.

Results: 22/23 patients (96%) showed SLN 30 min after injection. 1 patient showed delayed visualization at 90 min. 4/23 (17.3%) patients had SLN metastases (3 macro & 1 micro-mets). More than one node was identified in 5 patients. SLN distribution by SPECT CT was internal iliac in 73% patients, obturator in 23% and the remaining 4% were external/common iliac, paraaortic nodes. All positive nodes were identified by SLS. No skip metastases noted. NPV was 100%, (when SLN negative, all other nodes also negative for metastases). Follow-up of 4 patients with positive SLN & rest SLN negative patients was uneventful.

Conclusion: Our study shows feasibility of performing standardized SLS procedure in early Ca cervix with confidence. SLN biopsy with gamma probing is useful in identifying nodal metastases in these patients with excellent NPV. SPECT CT is essential in localizing exact group of SLN.
Our first experience with SPECT/CT in oncology

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In our Department of Nuclear Medicine in the Faculty Hospital Ostrava, a hybrid SPECT/CT camera was installed in January 2010. Since then, it has been used especially for the diagnosis of bone metastasis and also for some special application e.g. thyroid cancer post iodine therapy scans. This combined system helps to make more accurate diagnosis and also shows better, the anatomical localization of the lesions. In our poster we will present such cases – detection of iodine accumulating bone metastases and also complementary examination of post-iodine scintigraphy and 99mTc-MIBI scintigraphy in detection of thyroid cancer lymph node metastases.
We hereby report our experience in the radionuclide treatment of five patients (three men, two women) with metastatic non-resectable neuroendocrine tumours (NET) (three pancreas NETS, one mid-gut NET, one rectal NET) from August 2009 to February 2011 who were selected for systemic treatment using peptide receptor radionuclide therapy (PRRT), we radiolabeled a somatostatin analog (177Lu-DOTATATE) and administered it by intravenous route as an inpatient basis between three and four cycles, each cycle consisted of a 100-200 mCi dose. Acute treatment toxicity was observed in one patient and consisted of nausea and vomiting. No serious adverse events have been documented so far. After restaging, a partial remission was found in one patient, stable disease in two patients, and tumour progression in one patient and a complete response in one patient.

Conclusion: Although we have a limited number of patients our data compare favourably with the reports of the European literature; such therapy might become the therapy of first choice in patients with non-resectable metastasised well differentiated neuroendocrine carcinomas. The data suggests that therapeutic radionuclides might represent a promising new therapeutic tool, with fewer side effects than chemotherapy.
Early differential diagnostics of oncopathology of neck area and mediastinum, with radiological methods of diagnostics

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Introduction: Differential diagnostics of inflammatory and neoplastic processes in the neck and mediastinum areas remains a difficult clinical problem despite the introduction of a number of the newest diagnostic technologies into the clinical practice. Necessity to differentiate tumour and inflammatory processes, mixed pathologies of one organ, invasive growth into the adjacent anatomic structures can occur during the primary study as well as after surgical treatment, when there is a question of differential diagnostics of recurrence and inflammatory changes. For differential diagnostics of mixed pathology the methods of medical visualisation are used in a set, which prompts the best diagnostic result. From all the methods of ray diagnostics, radionuclide methods are the most functional and specifically directed, which allows us to study each organ and each anatomic structure separately, with the application of two and more examinations.

Objectives: Optimisation of diagnostics during oncopathologies of neck and mediastinum with the inclusion of 2 and more organs and with the corresponding shift and deformation of the adjacent tissues. 150 patients with pathology of various genesis were examined of different age and sex. Clinical characteristics of a researched group of patients:

1) Pathology of thyroid and parathyroid glands (malignant and benign) - 78 patients

2) Pathology of lymphatic nodes (of oncological and neo-oncological genesis) - 37 patients.

3) Oncopathology of soft tissues of the neck and mediastinum areas - 35 patients.

Methods: 1) US 2) CT 3) MRI - were researched based on the medical reports. 4) Radionuclide methods were carried out in the Scientific Center of Radiation Medicine and Burns laboratory of radionuclide diagnostics and RA Ministry of Health. The spectrum of envisaged radionuclide studies was based on the results of other studies. All the studies will be carried out on SPECT-camera of ‘Medico’ firm – Hungary. The analysis of obtained results will be carried out according to the standard programming packages of the IAEA. Main used radionuclide – radioactive technetium. Main sets – MIBI, pentatech, pirfotech, nanocoll.

Discussion: Patients with the oncological anamnesis can have other not oncological lesions. Specific radiodiagnostic scintigraphic characteristics for each clinical group are allocated: presence of hot and cold centres, recurrence of anatomic borders, a condition of surrounding tissues and their combinations. Practice shows that complex application of regular non-standard situational algorithm of the use of radiological method of diagnostics (taking into account histological research) could be the most effective.
Conclusion: Thus, salvation of differential diagnostics cannot be achieved via application of a standardised, universal approach, based on the utilisation of only one, even the most informative radiological method of diagnostics.

Practical importance of study: Possibility of early and precise diagnostics of a location of oncopathology is a necessary requirement of: 1) The choice of treatment measures 2) The quality and volume of not only treatment and diagnostic but also prophylactic measures and 3) The possibility of the discovery of predictive factors, especially in oncological practice.
Hepatocellular carcinoma and metastatic colorectal carcinoma are amongst the more common causes of cancer-related mortality worldwide. Selective internal radiation therapy (SIRT) with Y-90 microspheres, which is a relatively novel approach, is usually indicated in patients with nonresectable status and extensive colorectal liver metastases that are refractory to chemotherapy or target therapy. Several examinations, including CT, MRI or PET, serum chemical analyses, hepatic angiography and liver-lung shunting study with Tc-99m MAA, are done to ensure appropriateness and safety of therapy. Herein, three cases (first two with hepatocellular carcinoma and the third with metastatic colorectal cancer) who qualified for SIRT are presented. All of them underwent the necessary work-up pre-therapy. The CT and PET-CT scans identified the hepatic lesions. The blood tests showed nearly normal hepatic and renal functions, except for the third case with elevated bilirubin level. The hepatic angiograms revealed no significant gastrointestinal shunting. The liver-lung shunting studies computed <20% hepatopulmonary shunt fraction in all cases. The first patient had >10% hepatopulmonary shunt, hence he, together with the patient with an elevated bilirubin level, received a reduced dose of Y-90 microspheres by 20%. After SIRT, bremsstrahlung planar imaging and SPECT-CT were performed to localise the distribution of the Y-90 microspheres, the findings of which correlated well with the results of the pre-therapy Tc-99m MAA scans and with the location of tumour deposits demonstrated on CT scans. On follow-up, the first patient died of a cerebrovascular disease one year post-therapy after achieving a decrease in size of the hepatic lesions. The third patient with metastatic colorectal cancer died one month post-therapy due to the aggressiveness of the disease itself. The second patient survived and underwent another SIRT 20 months since the initial one. The added value of SPECT-CT was shown in the management of these patients. The tomographic images demonstrated areas of maximum tracer uptake which correlate anatomically with sites of maximum tumour density, unlike in traditional bremsstrahlung images which offer little anatomic detail. Indeed, the use of SPECT-CT is recommended for better anatomic localisation and functional correlation. It may also be utilized in therapeutic planning, especially in the learning curve or when the angiographic procedure is difficult.
SPECT/CT: An essential adjunct in the routine management of differentiated thyroid carcinoma

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Objective: The management of differentiated thyroid carcinoma (DTC) remains surrounded by controversies. DTC in low risk patients have a favourable prognosis with a low documented mortality rate. The role of Iodine 131/123 imaging is to detect residual neck disease as well as lymph node involvement and distant metastases. Accurate scan interpretation is crucial to ensure proper management. The addition of SPECT/CT will not only assist in improved localization of foci that are seen on planar images, but may also detect foci that were not apparent on planar images.

Methods: We routinely introduced the use of SPECT/CT whenever planar imaging demonstrated evidence of abnormal activity. Seventeen patients attending our clinic for follow-up during 2009 and 2010 underwent SPECT/CT as part of their management. We therefore reviewed these studies to assess the impact of SPECT/CT imaging on patient management.

Results: SPECT/CT localized foci of increased activity demonstrated on planar imaging to: tracheostomy site [n=1], pericardial effusion (secondary to hypothyroidal state) [n=1], bowel activity [n=2], thyroid bed with or without additional cervical lymph nodes [n=6], contamination [n=1], lung with or without mediastinal lymph nodes [n=2], mediastinal lymph node [n=1], bone [n=3]. The impact on management is profound, ranging from a patient that required urgent neurosurgical intervention for metastases in C2 vertebra, to patients that required no further treatment after SPECT/CT revealed apparent abnormal activity as physiological.

Conclusion: The use of SPECT/CT clearly assisted in improving localization of abnormal activity seen on planar imaging. It seems that this modality is a vital tool for optimal management of patients with DTC.
Incremental value of SPECT-CT in tumour imaging

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In this study we have evaluated the role of SPECT-CT in tumour imaging and underlined its incremental values in the overall management of the disease. A wide range of tumours were imaged starting from suspected solitary bone metastasis, non-small cell lung cancer, space occupying lesion in the liver, metastatic thyroid cancer, recurrence of brain tumour, bronchoalveolar carcinoma, chest wall recurrence of breast cancer, soft tissue sarcoma, spindle cell neoplasm and others. Radiopharmaceuticals used included $^{99m}$Tc-MDP, $^{99m}$Tc-MIBI, $^{99m}$Tc-Tetrofosmin and I-131. SPECT-CT studies were performed in GE Infinia Hawkeye II system. In a few cases CT imaging was performed in a GE 16 slice light speed scanner and software based perfusion was performed in the SPECT system after importing the images from the CT. SPECT-CT could reliably confirm or rule out solitary bone metastasis where the conventional planar bone scan was equivocal. $^{99m}$Tc-MIBI SPECT-CT showed focally intense uptake in a solitary pulmonary nodule where FNAC (fine needle aspiration cytology) was inconclusive and also showed increased uptake in mediastinal lymph nodes. Biopsy showed non-small cell lung cancer. Markedly increased concentration of $^{99m}$Tc-MIBI was demonstrated in a bronchoalveolar carcinoma which is usually not FDG avid. Dual tracer ($^{99m}$Tc-Sulphur Colloid and $^{99m}$Tc-Red Blood cell) confirmed a case of atypical haemangioma and ruled out focal nodular hyperplasia and metastases which were other differential diagnoses in CT. I-131 SPECT-CT confirmed a scalp swelling as the metastasis from a thyroid cancer with bone erosion and intracranial extension and also detected the primary in thyroid. Likewise in many other cases tumour avid scintigraphy with SPECT-CT gave incremental information over and above conventional nuclear imaging or other anatomic imaging modalities which had some positive impacts on the patient management. SPECT-CT was found to be a very effective tool in the evaluation of treatment response after chemotherapy and it was able to identify the right area of the lesion from where biopsy is to be obtained to increase the positive yield. PET-CT is yet to be available everywhere especially in developing countries. Tumour imaging with SPECT-CT can provide valuable incremental information in those situations. The cost of the investigation is also much less as shown in our study where we have mostly used commonly available radiotracers only. Even when PET-CT is available, SPECT-CT tumour imaging will be of value where FDG PET has limitations like in the case of bronchoalveolar carcinoma, thyroid cancer or other non FDG avid tumours.
Usefulness of SPECT-CT 99mTc-Tetrofosmin scintigraphy for the diagnosis and follow-up of patients with lung cancer

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Introduction: The 99mTc labelled Tetrofosmin was originally developed for myocardial perfusion studies; today it is also used for the evaluation of several oncological diseases. In our institute we use 99mTc- Tetrofosmin in combination with SPECT-CT as a non-invasive diagnostic method for the diagnosis and follow-up of lung cancer; regardless of the histologic type.

Objective: To determine the usefulness of the SPECT-CT studies with 99mTc-tetrofosmin in providing accurate and non-invasive diagnosis and the monitoring of lung cancer patients after surgical or medical treatment.

Materials and Methods: We retrospectively reviewed 555 clinical records of patients referred to our department between March 2008 and July 2009, among them 282 patients were selected, who fulfil the inclusion criteria of having had the SPECT-CT study and biopsy.

Discussion: In our department the Tetrofosmin SPECT-CT scintigraphy has a sensitivity of 95% and a specificity of 70% for the diagnosis and follow-up of lung cancer (regardless of histologic type). The specificity was due to the tetrofosmin uptake in non-neoplastic tissues, such as infectious or inflammatory processes thus confirming that histopathology, remains the gold standard for the diagnosis of lung cancer. The Tetrofosmin SPECT studies also prove to be useful in monitoring patients who already have been diagnosed with lung cancer and are undergoing treatment, monitoring or surveillance by means of detecting disease progression, response to therapy or tumour recurrence. The use of SPECT-CT provides metabolic information, coupled with the anatomic data which increases the diagnostic accuracy of both methods, improving the early diagnosis and the future non-invasive follow-up in the patient with lung cancer. 99mTc-Tetrofosmin SPECT/CT is an accessible, low cost imaging method, with low radiation exposure for the patient and for the staff. One additional advantage of the SPECT/CT is that it provides information about regional or distant metastatic sites. The high sensitivity and specificity of the SPECT/CT imaging method gives us a new tool that could be included in the diagnostic work-up of patients with clinical and radiological suspicion of lung cancer. Since this image method includes CT, we propose, that the CT (standalone) may be replaced by the SPECT-CT in the evaluation of lung cancer patients. It is a reliable imaging method that has advantages over other imaging techniques such as plain x-rays or CT alone. The 99mTc-Tetrofosmin SPECT/CT is a reliable imaging method with advantages over other imaging techniques such as plain x-rays or CT alone.

Conclusion: In our institute the 99mTc-Tetrofosmin SPECT-CT has a sensitivity of 95% and a specificity of 70%, for evaluation of lung cancer (diagnostic and follow-up). We believe it could be included in the diagnostic work-up algorithm of patients with clinical and radiological suspicion of lung cancer, monitoring and surveillance. It is an accessible,
reproducible, inexpensive study with low dose for the patient and staff. With this method of imaging, anatomy and physiology can demonstrate both locoregional metastases and distant.
Clinical usefulness of SPECT/CT with 99mTc-29-41 ubiquicidin in cancer patients with suspected infectious process

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Introduction: The tumour pathologies involve the immune system, thus the predisposition to suffer some kind of infection and consequently, a risk of complication is increased. Nuclear medicine has played a fundamental role as an assistant at the time of identification of infectious diseases by detecting cellular changes, the metabolic trapping by phagocytic cells and selective binding to live bacteria can be performed using radio labelled antibiotics or by chemotaxis of some peptides like ubiquicidin.

Methods: The study includes 56 patients with suspected infectious processes in the surgical wound on tumour layer, where there is infiltration and over-infection associated with the clinical history, symptoms and findings with other imaging methods. A semi-quantitative analysis was performed in the suspected sites of infection, and a cut-off point was determined in order to differentiate between the infection and inflammation process.

Results: The leukocyte count mean value in all patients was 9.0 +/- 8.2, ESR 36 +/- 15. The most prevalent pathological isolated agent was Stafilococo aureus (n=21), it was followed by Escherichia coli (n=8), Pseduomona aureginosa (n=7), Klebsiella oxitoca (n=2) and other rare agents (n=11). There was a false negative study associated to the poor tracing of the radiotracer, and a false positive in a highly vascularized tumour where the presence of bacterial infection cannot be proved by cultures. The overall sensitivity for detection of infectious disease was 97%, specificity 88%, PPV 97% and NPV 88%. The results were retrieved by ROC curves, using a cut-off of 2.55 (sensitivity of 100 (95% CI 63% -100), specificity of 97.8% (95% CI 82.47-99.94) of the tumour/no tumour rate, to differentiate an infectious process from inflammation. The difference between the tumour/no tumour patient rates considered as positives and negatives was statistically significant with p<0.0001 (U-Mann Whitney).

Conclusions: Detection of infectious diseases using SPECT/CT 99mTc ubiquicidin 29-41 is a highly efficient sensitive and specific tool, which can be used in a wide variety of clinical settings, without the risk of blood samples management.
Incremental value of diagnostic 131I SPECT/CT fusion imaging in assessment of patients with differentiated thyroid carcinoma

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Planar 131I scintigraphy is routinely used to detect radioiodine-avid metastases of differentiated thyroid carcinoma (DTC). However, the modality has limitations, such as low sensitivity and lack of anatomic landmarks. The purpose of our study is to determine the incremental value of the single photon emission computed tomography with integrated low-dose CT (SPECT-CT) over traditional planar imaging of patients with DTC.

Methods: We evaluated 40 thyroidectomized patients (papillary form in 80% of cases) with a mean age of 45 years. Planar imaging and SPECT/CT were performed after 3 weeks of L-thyroxine withdrawal and 4 days after oral administration of 3, 7-5, 55 GBq (100-150mCi) of I-131. The indication for treatment was remnant ablation or additional radioiodine therapy (in cases of metastatic disease) with rising thyroglobulin levels. SPECT/low dose CT of the neck and chest was acquired with a Symbia T camera with high energy collimators.

Results: Planar imaging showed 65 foci of uptake in 37 of 40 patients (92.5%), and SPECT/CT showed 79 foci in 38 of 40 patients (95%), confirming all foci seen on planar imaging but identifying an additional 14 occult foci in 12 of the patients (30%). SPECT/CT was a determinant in classifying as neoplastic 27 foci for which planar imaging seemed to exclude malignancy, discriminating in 29 cases between residue and lymph node metastases in the neck, or showing thoracic lesions in 9 cases. SPECT/CT information changed the proposed therapeutic indication in 23 cases (57.5%) of patients, on the basis of our department protocol.

Conclusion: According to our results, SPECT/CT enhances sensitivity for DTC lesions detection over planar scintigraphy with impact on therapeutic management. This equipment allows us to directly correlate functional and anatomical images, and should be used as a complementary to planar imaging in selected patients with DTC.
Differentiated thyroid cancer (DTC) was indolent cancer but can be aggressive especially for patients more than 50 years of age. Management of DTC includes surgical excision, preventive thyroablation with NaI-131, and thyroid hormone replacement therapy. Thyroidablation with NaI-131 destroys remnant thyroid left after surgery thus enhancing detection of recurrent neck disease and metastasis lesions, besides allowing monitoring of the disease with thyroglobulin estimation.

Aim: The aim of this study was to compare the efficacy of single high dose of 50 mCi versus 100 mCi NaI-131 for preventive thyroablation in post total thyroidectomy cases without regional node metastasis or distant metastases.

Materials and Methods: In this retrospective study, we had 34 subjects with DTC without metastases, post total thyroidectomy, and thyroid scintigraphy. 20 subjects were given 50 mCi NaI-131 (4 men, 16 women), aged 20 to 58 years, mean; 44 years and 14 subjects were given 100 mCi NaI-131 (4 men, 10 women), aged 23 to 71 years, mean; 48 years and then all subjects were given thyroid hormone with suppressive doses. Three months later, they were examined for evaluation with thyroid scintigraphy, TSHs, thyroglobulin and anti-thyroglobulin. The hormone thyroid was stopped three weeks before examination. The thyroablation therapy was considered successful if there was no residual thyroid tissue, the uptake thyroid was 0%, TSHs was high (>30 uIU/ml), thyroglobulin was low (<3 ng/ml), and anti-thyroglobulin was negative.

Results: Before therapy NaI-131 50 mCi: Thyroid scanning: It was thyroid remnant, uptake thyroid from 0.03 to 1.86 %, mean; 0.64 %. After therapy: Thyroid scanning: no residual thyroid tissue, uptake 0%, mean TSHs; 42.95 uIU/ml, mean thyroglobulin; 2.08 ng/ml and anti-thyroglobulin was negative. Before therapy NaI-131 100 mCi: Thyroid scanning: It was thyroid remnant, Uptake thyroid from 0.05 to 1, 86 %, mean; 0, 54 %. After therapy: Thyroid scanning: no residual thyroid tissue, uptake 0%, mean TSHs; 36, 95 uIU/ml, mean thyroglobulin; 2, 16 ng/ml and anti-thyroglobulin was negative. Therapy using NaI 50 mCi or 100 mCi showed the same result that there is no residual thyroid tissue; uptake thyroid 0%, high TSHs, low thyroglobulin and negative anti-thyroglobulin. We found no significant difference in two groups with high dose preventive thyroablation.

Conclusion: We did not find any difference between thyroablation with 50 mCi and 100 mCi NaI-131 to destroy thyroid remnant. The preventive thyroablation with 50 mCi dose seems to destroy thyroid remnant.
Incremental value of SPECT-CT over planar scintigraphy and SPECT for the evaluation of suspected bone metastasis in patients with breast cancer

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Introduction: Bone scintigraphy is used extensively in evaluating metastatic disease in patients with breast cancer. The aim of the present study was to evaluate the incremental value provided by SPECT-CT over planar scintigraphy and SPECT for the evaluation of bone scan lesions in patients with breast cancer.

Methods: This was a retrospective study. Thirty four patients with 41 equivocal lesions on planar scintigraphy underwent SPECT and SPECT/CT imaging of selected volume. All images were evaluated by 2 nuclear medicine physicians who were not given previous insight into any of the clinical findings. Planar, SPECT and SPECT-CT images were evaluated in separate sessions 1 week apart to minimise recall bias. On planar scintigraphy, SPECT and SPECT/CT, lesions were classified as malignant (score-1) likely malignant (score-2), indeterminate (score-3), likely benign (score-4) and benign (score-5). Follow-up (3-6 months) clinical information and radiological studies were used as a reference standard. Planar scintigraphy, SPECT and SPECT-CT were compared in terms of the number of equivocal findings and accuracy on a lesion by lesion basis. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) was calculated for each modality. For this purpose any lesion with a score of less than or equal to 2 was taken as metastatic and with a score of greater than or equal to 3 was considered benign. ROC analysis was done for calculating the area under the curves (AUC) and compared. All statistical analysis was done using SPSS 11.5.

Results: All 34 people in this study were biopsy proven carcinoma breast patients who underwent bone scan for staging (n=10), suspected metastasis (n=12) or response monitoring (n=12). There were 32 females and 2 males. The mean age was 48.5 ± 11.1 years (median-50; range: 25-73). There were 41 equivocal lesions mostly in vertebrae (n=19). Ribs were the next most common site (n=5). On clinical and/or radiological follow up (reference standard) 22 lesions were benign (18-degenerative; 4-traumatic) and 19 were metastatic. The sensitivity, specificity, PPV and NPV of planar scintigraphy were 77.7%, 91.3%, 87.5%, 84% respectively. Those for SPECT were 100%, 95.6%, 94.7% and 100%, while those for SPECT-CT were 100%, 95.6%, 94.7% and 100% respectively. The AUCs for diagnostic score were 0.932 (95%CI-0.808 to 0.986) for planar, 0.915 (95% CI-0.785 to 0.979) for SPECT and 0.978 (95% CI-0.875 to 0.996) for SPECT-CT lesions. Four indeterminate lesions on planar were correctly diagnosed as benign and four as metastatic on SPECT-CT. Three lesions reported as metastatic on SPECT were correctly diagnosed as benign on SPECT-CT. However, no significant difference was found between planar and SPECT (p=.739), planar and SPECT-CT (p=.299), and SPECT and SPECT-CT (p=.184).

Conclusion: SPECT-CT is more helpful than SPECT alone for the interpretation of equivocal skeletal lesions in breast cancer patients undergoing planar scintigraphy.
Empirical high-dose I-131 therapy in patients with increased thyroglobulin and no detectable anatomical lesions

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Purpose: To describe the immediate (diagnostic) results of empirical I-131 therapy in patients with elevated serum thyroglobulin (Tg) levels in the absence of detectable lesions in conventional imaging.

Methods: History charts of patients with differentiated thyroid cancer treated at the Colombian National Cancer Institute between January 2003 and December 2008 were retrospectively reviewed. Twenty-seven patients received empirical doses of I-131 because of elevated Tg levels without evidence of disease in neck ultrasound and chest CT scan/x rays.

Results: 27 patients (24 females), with mean age of 46 years, were included. All, except one (pT2), had locally invasive disease at the onset (pT3, pT4); 19 had lymph node metastases (pN1a, pN1b). Initial treatment included total thyroidectomy in all but 1 patient (subtotal) and I-131 ablation therapy with 50-200 mCi. Six patients needed additional surgery before ablation therapy and an additional 6 patients needed neck lymph node dissection during the first year after ablation (n=3) or more than 1 year after initial treatment (n=3). At the time of empirical I-131 therapy all patients had Tg>10 ng/ml (mean + SD: 63.5+82.5ng/ml) after thyroxine withdrawal (TSH>30 mUI/L). Seventeen patients were treated with an empirical I-131 dose of 150 mCi and the remaining 10 with 100 mCi. Post-therapy scans were positive in 16 (59\%) patients. Abnormal foci of uptake were found in neck lymph nodes (n=13 patients), mediastinum (n=8), lung (n=2) and thyroid bed (n=1). Patients with positive post-therapy scans had higher levels of pre-therapy Tg-on thyroxine (median, 2.3 ng/ml vs 1.0 ng/ml; KWallis 7.089 p=0.0078) and higher Tg-off thyroxine levels (50 ng/ml vs 18 ng/ml; KWallis 4.203 p=0.04) than patients with negative post-therapy scans.

Conclusions: Post-therapy scanning after an empirical dose of I-131 allowed detection of radiologically occult lesions in 59\% of our patients providing a means to diagnose and potentially treat them. Whether or not there is a therapeutic benefit is yet to be seen upon completion of follow-up, yet there was an upfront surgical chance for many of the depicted lesions (lymph nodes). It should be safe to assume that patients with negative post-therapy scans should not expect a therapeutic benefit. A PET-CT scan could then be warranted to search for resectable lesions.
Using the hypoxia volume distribution for calculation of tumour control probability (TCP)

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In the present work, a model to calculate Tumour Control Probability (TCP) considering the fractional volume distribution of hypoxic and anoxic zones in a tumour is presented. Considering the tumour as a sphere of radius R, an equation representing the radiopharmaceutical diffusion considering the ligand-receptor interactions was numerically solved. The oxygen concentration distribution was calculated based on the Krogh’s model and correlated with the vascular density. The spatial distribution of activity was considered dependent on radiopharmaceutical penetration by diffusion and the clearance rate of tumour. The vascular density was considered proportional with the radiopharmaceutical distribution at a fixed time (24hr or 48hr). The proportionality constant is function of fractional volumes representing the anoxic and hypoxic regions, keeping in mind that when oxygen partial pressure is below 5mm Hg the environment is considered as hypoxic. The spatial activity distribution obtained from the solution of diffusion equation was "voxelized" and several slices like a SPECT image were generated. Briefly, for the spatial interval which is represented by the voxel, it is assumed that the activity in the voxel will be equal to the mean activity calculated from the activity profile in the spatial interval. From the activity distribution the dose rate spatial-time distribution in the tumour was calculated using the voxel dosimetry approach. The linear-quadratic model (LQ) was used for the generation of the Biological Effective Dose (BED) spatial distribution, considering the oxygenation conditions in each region by modifying adequately the alpha and beta parameters of the LQ model using the Oxygen-Enhancement Ratio (OER) value for the cell population. The surviving fraction was calculated in two ways: (a) by integration of overall tumour volume or (b) by calculation of Equivalent Uniform BED (EUBED). Only cells in the anoxic region will be able to proliferate. The TCP was calculated by the Poisson model considering the contribution of each fraction (hypoxic and anoxic). Several activity distributions were simulated by generating some ligand-receptor magnitudes and diffusion coefficient considering a gaussian distribution for those parameters. All these profiles were used to estimate the effects of inter-tumour variations because of different uptake features. Similarly the influence of inter-tumour radiosensitivity was also analysed by generating a set of alpha radio-sensitivity with gaussian distribution. TCP vs. dose (TCP(D)) curves were calculated for uniform acute irradiation at high dose rate (HDR) and irradiation at low dose rate (LDR) like targeted radionuclide therapy and isoeffective relationships were plotted. The TCP(D) are influenced by the inter-tumour radiosensitivity and oxygen distribution in dependence of the diffusion proprieties. The model presented allows the use of functional images to evaluate the influence of oxygen distribution in tumour response for different irradiation schemes.
CLINICAL NON-PET CARDIOLOGY
Introduction: Different functional parameters are usually obtained during a gated myocardial perfusion single-photon emission tomography (gSPECT). Ischemia may produce left ventricular dilation and decreased left ventricular ejection fraction (LVEF). In advanced coronary artery disease (CAD) as well as in other cardiac diseases, the left ventricle changes and tends to form into a spherical shape.

Aim: The aim of this work was to compare left ventricular systolic function and a morphological parameter in adult patients with and without known CAD using gSPECT.

Method: Group A) 79 patients (61% males) with cardiovascular risk factors (CVRF) such as arterial hypertension, type 2 diabetes mellitus, dyslipidemia and smoking, all without left ventricular wall motion abnormalities at rest. Group B) 88 patients (73% males) with myocardial infarction (MI) and / or ischemic cardiomyopathy. LVEF and end diastolic and -systole volumes (EDV and ESV) were evaluated at rest and post stress using 99mTc-Sestamibi and QGS program. Stress was induced with Bruce protocol exercise test or using Dipyridamole i.v. in patients to enable reaching 85% of their maximal predicted heart rate. In addition, we compared those parameters in cases with and without ischemia using QPS automatic analysis (SDS> 5). We also measured with the software provided in our system the resting eccentricity index (EI), which assesses left ventricular shape (being the sphere = zero and the line=1). For that analysis, we selected semiautomatic processing when needed, performed by the same operators to assure the exclusion of extra cardiac activity. Gating signal was adequate in all cases; patients with severe or non-corrected motion during acquisition were excluded.

Results: Rest LVEF and left volumes were different in patients with MI or dilated cardiomyopathy compared with those with CVRF group as showed in the Table; there was also significant difference in post-stress changes. When we analysed patients with and without ischemia from groups A and B, according to SDS score, there was no significant difference in their functional parameters (p=ns). Rest EI was significantly inferior in group B (see also Table). No patients with CVRF had eccentricity index under 0.80, at rest.

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (years)</th>
<th>LVEF (%)</th>
<th>EDV (ml)</th>
<th>ESV (ml)</th>
<th>Delta Rest minus Post-stress LVEF</th>
<th>Delta Rest minus Post-stress EDV</th>
<th>Rest EI</th>
</tr>
</thead>
<tbody>
<tr>
<td>A: CVRF</td>
<td>59±7</td>
<td>55.6±9.8</td>
<td>71±20</td>
<td>32±13</td>
<td>1.1±8.2</td>
<td>-4.5±8.2</td>
<td>0.885±0.02</td>
</tr>
<tr>
<td>B: CAD</td>
<td>63±11</td>
<td>33.3±11.8</td>
<td>141±77</td>
<td>100±69</td>
<td>-1.9±5.2</td>
<td>8.7±19</td>
<td>0.836±0.04</td>
</tr>
<tr>
<td>p</td>
<td>0.006</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
<td>0.0057</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>
Conclusion: We observed that patients with MI or ischemic cardiomyopathy, regardless of the presence of ischemia, post-stress had a decrease in LVEF and ventricular dilation, compared with patients with CVRF. The former group presented greater left ventricular eccentricity, probably explained by pathological remodeling in those CAD patients that could be easily evaluated with gSPECT.
Tc 99m mibi infusion and low dose dobutamine gated SPECT - A novel myocardial viability detection protocol in ischaemic cardiomyopathy

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Many techniques such as nitrate enhancement, tracer administration as infusion and low dose dobutamine gating have improved myocardial viability detection sensitivity of Tc radiopharmaceuticals. We attempted to establish this novel imaging protocol of administering 99mTc MIBI as infusion and acquiring gated SPECT with Low Dose Dobutamine (LDD) augmentation.

Material and Methods: 50 patients with ischaemic cardiomyopathy referred for myocardial viability detection (M: F= 42:8, age 35-68y Mean 55.7 year, STE: NSTEMI = 29: 21) were enrolled for this study (Jan-Dec 09). All underwent Conventional nitrate enhanced rest Gated SPECT (CG SPECT) and on a separate day a low dose dobutamine augmented Gated rest SPECT performed 1 hour after 99mTc MIBI administration as infusion over 20 minutes. Rest myocardial perfusion defects, myocardial wall thickening in gated images were visually scored using a 4-point severity scale and myocardial MIBI uptake semi-quantitatively assessed (10 point colour scale). (a) Severity of myocardial perfusion defects at rest, (b) 99mTc MIBI semi quantitative myocardial uptake and (c) segmental wall thickening obtained during this Novel Gated SPECT (NG SPECT) were compared to (CG SPECT).

Results: Based on a 10 segment myocardial model, a total of 500 segments were analysed. 274/500 segments showed perfusion defects in CG SPECT and out of these 274 segmental perfusion defects 140 (51%) showed improvement in NG SPECT. A statistically significant number of segments showed improvement in perfusion defect severity score and MIBI semi-quantitative % uptake during NG SPECT (Defect score: % uptake= 140: 134, p < 0.01). Interestingly myocardial segments with > 40% MIBI rest uptake showed more significant improvement (i.e. 115/191 [60 %] segments with uptake of more than 40 % MIBI versus 25/83 [30%] segments with less than 40 % MIBI uptake, p < 0.001). On the wall thickening front the same trend was also reflected. Out of 230/500 segments with abnormal wall thickening in CG SPECT, 120 segments (52%) showed improvement in NG SPECT protocol.

Conclusion: This pilot study shows that a combined TcMIBI infusion and low dose dobutamine augmented gated SPECT is a practically feasible protocol and probably has better sensitivity in myocardial viability detection.
A dual isotope rest SPECT myocardial perfusion scintigraphy (DI-R-MPI): Improved efficacy in the detection of myocardial viability

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Aims: The assessment of myocardial viability continues to be a very important aspect in deciding the need of revascularisation in patients with gross left Ventricular dysfunction and cardiac failure. The revascularisation should be planned only when there is sufficient evidence of myocardial viability. Because of reperfusional kinetics, Rest-redistribution thallium201 (RRT) protocol remains the method of choice in our institute for myocardial viability assessment. A major drawback with this method is anterior/anteroseptal and apical walls photopaenicity as a result of over subtraction during image reconstruction because of severe lung uptake of thallium201. In such patients, a rest gated SPECT using Tc99m MIBI protocol (R-GMPI) was tried to overcome the drawback of the presence of lung uptake of Tl201 but was found to underestimate the myocardial viability in comparison to RRT. This is because Tc99m MIBI uptake depends on the presence of active mitochondria which is either less or scattered in myocardial hibernation. Thus a DI-R-MPI were aimed and performed to overcome the drawbacks of both the procedures.

Materials and Methods: Thirty six subjects with low LVEF (<25%) and Acute LV-failure irrespective of age and sex mainly from ICU and Heart commands were subjected to RRT & R-GMPI on separate days. On the first day RRT were performed after iv injection of about 110 MBq of Tl201 and imaging were performed immediately and about 4 hours post injection under a Symbia SPECT gamma camera. R-GMPI were performed the next day keeping all the parameters the same after iv. injection of 550 MBq of Tc99m MIBI. The patients were given nitrates pre injection. Segmental radiotracer uptakes were quantified. Also Myocardial contractility and centripetal excursion were assessed.

Observation and Results: After proper processing and image reconstruction, the total subjects were divided into two groups; Group I included severe lung uptake subjects and Group II included subjects with mild or no lung uptake of Ti201. Group I constituted 31 subjects where photopaenicity was seen in septal, anterior and apical walls on immediate post injection phase of RRT- out of these, 10 showed fixed defects even on redistribution imaging A R-GMPI and also showed gross reduction of radiotracer uptake of the same walls with akinesia on a gated SPECT study, suggestive of myocardial infarction with no viability; 18 subjects showed partial refilling on RRT comparable with Tc99m MIBI imaging and gross hypokinesia on a gated SPECT imaging, thereby suggesting myocardial infarction with residual hibernation; the remaining 3 subjects showed near total normalisation on redistribution imaging with maintained uptake and normal contractility on R-GMPI which suggests that the photopaenicity is exclusively because of excessive lung uptake rather than any perfusion defect. Group II included 5 subjects where maintained perfusion and myocardial contractility were observed in 2 cases which suggests maintained LV myocardial perfusion: 1 case showed reperfusional kinetics in inferolateral wall on RRT with hypoperfusion concordant with hypocontractility on R-GMPI, suggestive of Myocardial hibernation and remaining 2 cases showed maintained perfusion in all the LV myocardial
segments. However, a gated SPECT study shows akinesia in the septal wall in one case and akinesia of the anteroseptal wall in the remaining one subject, indicating myocardial stunning.

Conclusion: From the above observations and results, it has been observed that dual isotope R-MPI has a greater efficacy in the detection of myocardial viability than individual RRT and R-GMPI does and provides additional information like myocardial stunning.
Coronary artery disease functional assessment with gated myocardial perfusion SPECT

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Objective: To determine the relation of left ventricular function and myocardial perfusion defects, evaluated with Gated-Myocardial Perfusion Single-Photon Computed Tomography (G-SPECT) with the presence of significant Coronary Artery Disease (CAD).

Methods: G-SPECT myocardial perfusion studies and coronary angiography of 150 patients with a diagnosis of ischemic heart disease were analysed. Patients with valvular heart disease, dilated myocardiopathy and previous revascularization were excluded. The registered variables were: age, cardiovascular risk factors, rest and post-stress Left Ventricle Ejection Fraction (LVEF), End-Diastolic Volume (EDV) and End-Systolic Volume (ESV); severity of ischemia and significant coronary lesions (luminal obstruction >70%).

Results: The average age was 62 ± 10 years, 65% were women. All had at least two risk factors: systemic arterial hypertension (73%), diabetes mellitus (35%), dyslipidemia (47%) and smoking (21%). The G-SPECT showed moderate (29%) and severe (21%) myocardial ischemia; LVEF post-stress reduction (54±16 vs 47±15) and increase in EDV (125 ± 62 vs. 141 ± 72 ml) and ESV (63±4 vs 94 ±6 ml) from rest to stress. Sixty-three patients had multi-vessel CAD: two vessels 20% and three vessels 43%; right coronary artery lesions 37%, left anterior descending 36% and circumflex 70%. The Bivariate analysis showed significant association between LVEF decrease (8±1), ESV (31± 2) and EDV (19±2) post-stress increase, with significant coronary lesions (p<0.001) and moderate to severe ischemia (p<0.001). The sensitivity and specificity of LVEF decrease, EDV and ESV increase from rest to stress to detect moderate to severe ischemia and significant coronary lesions was 90% and 80% respectively.

Conclusions: The decrease in LVEF and increase in ESV and EDV in post-stress, has significant association and high predictive ability to detect high-risk abnormalities in G-SPECT study and presence of significant coronary lesions.
Myocardial perfusion imaging in patients with Chagas disease; Utility

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Background: Few studies have considered the appropriate use of myocardial perfusion imaging (MPI) in patients with Chagas disease and coronary artery disease (CAD) concomitantly.

Design: Historical analytical cohort. Diagnostic test evaluation.

Objective: To measure the prevalence of positive myocardial perfusion imaging in a group of patients with Chagas disease, and to measure the prevalence of concomitant CAD and the ability of myocardial perfusion to detect the presence of CAD in this group of patients.

Material and Methods: 39 patients who met the criteria 1+2 were included in the study from February 2005 to September 2009: 1) To have Chagas disease diagnosed and suspected CAD and 2) To have a myocardial perfusion study. Using as the gold standard, coronary angiography and follow-up, the operating characteristics for detecting concomitant CAD in patients with Chagas disease were obtained.

Results: There were 17 men and 22 women. Mean age 66 ± 11. 28 were followed for 22 ± 10 months. 22 MPI studies were interpreted abnormal: 10 with fixed defects, 8 with reversible defects and 4 with mixed defects. The prevalence of abnormal studies in patients with Chagas disease found was 56.4%. With a mix gold standard of angiography and follow-up we found a 75% sensitivity, LR (-) 0.4 (95% CI 0.08-2.62). The specificity was 54%. This low specificity can be explained by the characteristic microvascular arterial injury in Chagas disease increasing the number of ‘false positive’ results. The prevalence of CAD in this group was 14%. Compared with a control group of patients with non-Chagasic cardiomyopathy the odds ratio of MP (+) was 1.17 95% CI 1.07 to 1.27.

Conclusions: 1) The prevalence of CDA in patients with Chagas disease is important, modifies the treatment. Chest pain in this group of patients is not always related to significant coronary artery lesions. The neuropathic origin and/or microvascular lesions should be considered. 2) About 60% of the patients with Chagas Disease have abnormal MPI studies. However, most patients do not have CAD. The negative result excludes concomitant CAD. 3) We need to evaluate a greater number of patients to increase the accuracy of the values, and prognostic cohort studies must be encouraged.
Prognostic value of myocardial perfusion study on population over 75 years

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Objectives: Although myocardial perfusion is very useful in the diagnosis and risk stratification in patients with coronary disease, its prognostic value in the elderly has not been well defined. The aim of this study is to determine its prognostic value in this population.

Study Design: Cohort analytical observation.

Place of study: Bogota D.C. Colombia.

Patients: 363 patients (220 men, 143 women) aged 75 years with suspected coronary artery disease.

Interventions: We took a myocardial perfusion (99mTc - Sestamibi Gated SPECT), according to protocol one day, under physical stress treadmill belt or dipyridamole pharmacologic stress, depending on the patient's clinical condition.

Measurements: We determined the presence of a reversible defect, fixed or mixed with up to 13 ± 6 months recording outcomes defined as cardiac death, non-fatal myocardial infarction or need for myocardial revascularization.

Results: 348 patients (96%) completed the follow-up. There were 34 events in the entire group, 108 surveys (31%) were abnormal, of which 45 showed ischemia, necrosis 27 and 36 with mixed defects. The event rate among patients with normal myocardial perfusion was 2.4% per year (9 240), compared with 14.6% per year among patients with abnormal myocardial perfusion (25 of 108). Abnormal studies were more common in men, patients with chest pain and/or ST segment changes on baseline ECG or exercise. An abnormal study was significantly associated with the presence of cardiac events P <0.0001.

Conclusions: Myocardial perfusion study with 99mTc-Sestamibi under physical or pharmacological stress is a valuable prognostic tool in patients over 75 years with suspected coronary artery disease.
Myocardial perfusion imaging (MPI) is an established method in diagnosing patients for coronary artery disease. Single photon emission computed tomography (SPECT) thallium-201 is used to assess myocardial viability and ischemic burden. Coronary artery disease patients with impaired LV systolic function represent a high risk group, with a significantly greater annual mortality than those with preserved LV function, and thus a significant prognostic factor. Revascularization of dysfunctional but viable myocardium shows significant improvement in patient’s symptoms and final outcome compared with medically treated patients. The potential significance of the extent (severity and degree of non-viable segments (SSS)) or the ischemic burden (presence of inducible ischemia (SDS)) in its relation to the subsequent degree of prognostic benefit was not yet ascertained. The objective of the study is to determine the incremental prognostic value of perfusion defects in patients with scintigraphic evidence of LV dysfunction.

Method: Patients showing either transient ischemic dilatation or Tl-201 lung:heart ratio of >0.5 on exercise or dipyridamole SPECT Tl-201 myocardial perfusion scan were included in the study. Perfusion defects were scored semi-quantitatively using a 17-segment, 5-point scale (0 = normal, 4 = absent uptake). The extent and severity of defects were quantified using number of abnormal segments (NAS) and the summed stress score (SSS). Defect reversibility was quantified using the summed difference score (SDS) between stress and rest defects. Patients were followed up for the development of coronary events (myocardial infarction [MI] or cardiac death) over a period of 12 - 30 months.

Results: There were 6 cardiac deaths and 7 MIs in the 65 patients included in the study (20% overall event rate). The receiver operating characteristic (ROC) curve analysis of the scores revealed the following suggested cut-off values for predicting cardiac event: NAS ≥7 (85% sensitivity, 56% specificity), SSS ≥19 (77% sensitivity, 67% specificity) and SDS ≥7 (31% sensitivity, 60% specificity). Event rate was significantly higher above the cut-off value in SSS (<19 = 9%, >19 = 32%, p = 0.04). With NAS, the event rate was higher above the cut-off value, with the difference approaching significance (NAS <7 = 6%, NAS >7 = 26%, p = 0.06). There was no statistically significant difference in the event rate with high or low SDS (SDS <7 = 23%, SDS >7 = 16%, p = 0.32). The odds ratios for NAS and SSS (5.8, 4.9, respectively) were higher compared with SDS (0.56).

Conclusion: Left ventricular dysfunction is a prognostic predictor in patients with coronary artery disease. The differentiation of viable myocardium from non-viable myocardium is a relevant diagnostic issue being considered for revascularization or medical therapy alone. The extent and severity of stress perfusion defects provided incremental prognostic information in patients with LV dysfunction. Our data suggest that the degree of defect reversibility showed no prognostic value.
Quantification of left ventricular parameters in normal adult Filipinos using cardiac MRI, gated SPECT Thallium-201 and 2D echocardiogram

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The complete evaluation of heart disease requires the accurate characterization of both cardiac anatomy and function. Left ventricular volume and mass at end-diastole (ED) and end-systole (ES) are essential clinical parameters for the diagnosis and management of cardiac diseases. The study objective is to define the normal LV parameters (LVESV, LVEDV and LVEF) using 3 different modalities among normal adult Filipinos. Each procedure gives additional information not limited to LV function. The MRI gives anatomic structure of the heart and valve while 2D echo can add pressure gradients. The stress gated SPECT Thallium-201 will give perfusion imaging which rule out coronary artery disease and can prognosticate coronary events. These data are also needed to define the normalcy of the participants, with the likelihood ratio of less than 1% risk for cardiac event. The other criterion includes age ranging from 20 to 60 years old; normal physical, laboratory yearly examinations, resting blood pressure, resting and exercise ECG. The exclusion criteria includes symptomatic patient, recent intake of sympathomimetic drugs or alcohol, prior heart surgery and metallic implants that will hinder MRI procedures.

Material and Methods: A report of 17 normal patients who underwent any of the three modalities, Gated SPECT–Thallium, cine cardiac-MRI and 2D echocardiogram, was included in the study.

Results and Conclusion: The normal range of value for left ventricular ejection fraction (LVEF) were 49-62% in male and 61-71% in female for thallium studies while the 2D echo study showed 62-73% in male and 67-77% for female. The cardiac MRI range of value was 58-69% in males and 54-55% in females. The LVEDV (M: 67-114, F: 47-71; M: 91-174, F: 84-85; M: 92-110, F: 58-69) and LVESV (M: 26-59, F: 16-28; M: 28-70, F: 38-40; M: 18-32, F: 11-16) for gated SPECT thallium, cine cardiac MRI and 2D echo respectively. The percentage values on each parameter are wide; however, those are statistically elevated than the lower normal published range. Cardiac size is related to the weight, height, body surface, sex and age. Reference values on that subgroup may not be applicable to Filipino sizes. In a similar study done by Dominguez-Mejia et al on Kidney Measurements by Sonography on Normal Filipino Adults (Phil. J. Internal Medicine 2001), they concluded that the average kidney size of Filipinos is smaller than that of Caucasians for length and width. The cardiac MRI tends to have a closer ejection fraction values with the gated SPECT studies. In gated SPECT Thallium and 2D echocardiogram showed a higher female to male ejection fraction in contrast with the cardiac MRI. The 2D echocardiography results have higher ejection fraction values compared with the rest of the modalities. There is a great overlap in the left ventricular volumes for the three modalities.
The anti-phospholipids antibody syndrome is characterized by immunological abnormalities such as arterial and venous thrombosis. These abnormalities are the cause of some disorders such as valve disease, atherosclerosis, myocardial ischemia and cardiac myopathy, which are risk factors for developing impaired contractility. In order to evaluate the heart disorders, a group of 52 patients (group1) with diagnosis of antiphospholipids antibody were studied, as well as a control group of 30 healthy subjects (group2). All the patients underwent stress and rest gated single photon emission tomography (gated SPECT) by the administration of 99mTc SestaMIBI, using a Siemens camera according to international protocols to obtain regional wall motion, total and regional left ventricular ejection fraction (LVEF), and perfusion index to detect myocardial ischemia, through the program of 17 segments. In a second phase (resting phase) we calculated the right ventricular ejection fraction (RVEF) by first pass technique.

Results: Forty patients of the first group (77%) were female and 12 (23%) male and for the second group, 24 female and 6 male. The age range was 30-60 years for both groups. The average time between diagnosis and evaluation was 3.4 years. The dysfunction of motility was evident in 10 women (25%). Global LVEF was abnormal (LVEF < 45%) in 14 patients, in 3 of them (21%) abnormal RVEF was also observed (RVEF < 35%). With regard to myocardial ischemia, 3 patients showed this alteration; with respect to the regions affected, the septum, anterior and anterior septa segments were involved; there was no evidence of ischemia in female patients. In 4 (33%) of males patients, wall motions disorders were diagnosed, showing inferior lateral, inferior septa and anterior septa dysfunction with abnormal LVEF (<42%) and normal RVEF. Ischemia was detected in 2 of them. The segments affected by ischemia were the same than those found with disorders of motility.

Conclusion: Women are most commonly affected than man in a relation of 3:1 (77%). The cardiac changes most frequently observed were a decrease in global ejection fraction in 31% of all the patients studied, while myocardial ischemia was only evident in men (9.6%). Right ventricular ejection fraction is also affected in these types of patients but less frequently than LVEF. We conclude that Gated SPECT 99mTc MIBI is a useful and reliable method for early detection of cardiac abnormalities in these patients.
Utility of the complete left bundle branch block (LBBB) as prognostic factor of cardiac failure in patients with defects of myocardial perfusion evaluated with gated-SPECT

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Introduction: The complete left bundle branch block (LBBB) is associated with ventricular dysfunction in asymptomatic patients. It was observed that the LBBB is a marker for cardiovascular morbidity and mortality in individuals with congestive heart failure and dilated cardiomyopathy.

Objective: The aim of this study was to evaluate the prognostic value of complete blockage of the left branch bundle for developing heart failure in patients with myocardial perfusion defects assessed by gated-SPECT.

Material and Methods: In a retrospective analysis we selected 74 patients referred to nuclear medicine sent January 2007- January 2009 from the Centro Medico Nacional 20 de Noviembre with dilated cardiomyopathy and LBBB underwent myocardial perfusion SPECT with simultaneous evaluation of ventricular function GATED. We compared the clinical diagnosis, nuclear medicine and we reviewed the files with a follow-up to 2010 the evolution diagnosis, nuclear medicine and records were reviewed to monitor developments.

Results: For 74 patients referred to nuclear medicine, 67% had perfusion defects due to LBBB, 33% of patients had normal myocardial perfusion study with LBBB, multivariate analysis showed no differences between the two groups. For 50 patients with perfusion defect and LBBB the gated cardiac SPECT detected heart failure in 48 patients (94%). For the 24 patients without perfusion defect and LBBB, the gated SPECT correctly predicted the absence of heart failure in 21 patients (91%). The negative predictive value positive was 96% and 88% for negative predictive value.

Discussion: Perfusion defects on gated SPECT were predominantly in the anteroseptal and septal region and these were fixed. Most patients with perfusion defects and LBBB had reduced left ventricular systolic function, the patients without myocardial perfusion defects and LBBB showed a normal left ventricle, with statistical significance between groups.

Conclusions: This study establishes that the gated-SPECT myocardial perfusion imaging can identify patients with LBBB who will develop left ventricular systolic dysfunction and heart failure in the short run allowing a plan for prevention and treatment. Patients with LBBB and anteroseptal perfusion defect in the gated-SPECT are mainly associated with deterioration of the left ventricular ejection fraction (LVEF), so the studio gated myocardial perfusion SPECT identifies patients with LBBB that will develop left ventricular systolic dysfunction and heart failure in the short term allowing a plan for prevention and treatment.
Value of post-NTG left ventricular volume and ejection fraction by gated myocardial perfusion SPECT in assessment of viability in patients with myocardial infarction

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Purpose: The aim of the study was to evaluate how left ventricular volumes (EDV and ESV) before and after nitrate administration can increase the diagnostic of viability in myocardial infarction.

Method: We enrolled 56 patients with previous myocardial infarction (MI) and postischemic left ventricular dysfunction (gated SPECT [G-SPECT] ejection fraction ≤50%). Patients were divided into two groups based on the presence or absence of viability. Of the patients, 21 (37.5%) (Group 1) showed viability, whereas 35 (62.5%) (Group 2) showed no viability.

Results: Gated-SPECT mean ejection fraction was similar in both groups: Group 1 (29.43% ± 7%) and Group 2 (29.46% ± 6.8) at rest; (29.38% ± 8.9) and (30.49% ± 7.3) post NTG respectively. Analysis of left ventricular volume in systole and diastole at rest and post-NTG showed no significant difference in either group. Mean measurements of EDV (at rest and post NTG) were 235 ml vs. 227 ml in Group 1 and 232 ml vs. 235 ml in Group 2. Mean measurements of ESV (at rest and post NTG) were 164 ml vs. 163 ml in Group 1 and 169 ml vs. 167 ml in Group 2. Semi-quantitative scoring system of the stress myocardial perfusion pattern showed a significant difference between the summed rest scores (SRS) and summed NTG scores (SNS) in patients with viability and non-viability (P < 0.001). In the quantitative analysis of ventricular volume after NTG administration a significant reduction was found in EDV, in a greater number of patients with viability (P < 0.016). There was also a tendency to a reduction of the ESV (P<0.072). Of the patients with a decrease in EDV volume after NTG administration, mean SRS was 16.69 vs. 21.36 in the group without viability (P<0.54), indicative only a tendency to reduce the amount of risk myocardium; mean SNS was 11.85 vs. 21.14 in Group 2 (P<0.001), indicative a statistical significance in the reduction of the size of scar. On the other hand, in patients with an increase in EDV after NTG administration, the amount of risk myocardium (SRS) and scar tissue (SNS) is statistically significantly greater in Group 2 than in Group 1.

Conclusion: Post-NTG ventricular volume behaviour adds useful information to the perfusion Semi-quantitative analysis for the assessment of myocardial viability in patients with myocardial infarction and left ventricular dysfunction.
The preservation of cognitive functions after an ischemic stroke depends on the number of intact or minimally modified neurons in the cortex and subcortical brain structures. Modern non-invasive methods for assessing blood flow and metabolism in brain tissue may provide substantial assistance in assessing the degree of damage in post-stroke dementia.

Materials and Methods: 8 patients were tested to define regional cerebral blood circulation by using Single Photon Emission Computed Tomography (SPECT). Cerebral perfusion was studied with radiopharmaceuticals (RP) 99mTc - hexamethylpropilenaminoxim (HMPAO) («Ceretec» by Amersham Ltd) and expressed in ml blood/min/100g of brain tissue. State of cognitive function was assessed using standardized scales: a short scale of mental status (Mini-Mental State Examination - MMSE), a complex scale-level expression of Mattis, a scale of clinical evaluation of dementia (Clinical Dementia Rating), and also the test of frontal dysfunction.

Results and Discussion: Patients with dementia disorders were examined during clinical decompensation after overcoming an ischemic stroke. This is manifested by the exacerbation of cognitive deficits and caused the patient's complaints, changes in blood pressure or neurological symptoms in the form of growth of pseudobulbar syndrome, disorders in coordination, and the appearance of vestibular complaints. In a study of patients with hypertension (4), results allowed us to state that at the time of development of hypertensive crisis there are some changes similar to those for stroke. For patients with dementia disorders without ex-charged changes of blood pressure, on the contrary showed the presence of small areas of decreased blood flow at the location of vascular lesions and areas of leykoareoz with subsequent restoration of blood flow. Thus, in patients with post-stroke dementia there were observed two variants of pathological changes: in the form of multiple foci of hypometabolism in the cerebral cortex and basal nuclei or isolated areas to reduce metabolism/ametabolism in the so-called "strategic" areas of the brain (the parietal-temporal-occipital junction, thalamus, frontal lobes, and limbic structures). Zone of reduced metabolism and aperusive foci, are in fact manifestations of acute disorder of brain blood flow with development of ischemic and reperfusion injury of brain tissue. In the altered metabolic and hemodynamic conditions, acute events may occur without many symptoms demonstrating transient disorders clinic and frequently repeated, to create the foundation for the progression of dementia. At the same time reliable dependence of metabolic and clinical data were not available ($r = 0.25$, $p = 0.3$), which is possibly due to the small number of our observations.

From our point of view, neuroimaging techniques for the assessment of metabolic and perfusion changes in brain tissue could serve as a basis for the selection of an effective neuroprotective therapy of post-stroke dementia.
The diagnosis of Parkinson's disease (PD) based substantially on clinical symptoms, may be difficult when the symptoms are not fully typical of PD, particularly in the early stages when symptoms may be mild. Symptoms appear when 70% - 80% of neuronal tissue has been lost, resulting in a latent state before clinical manifestations.

Objective: To describe the experience with 99mTc-TRODAT-1 SPECT Imaging in differential diagnosis of patients with abnormal movements and PD de novo submitted to the Nuclear Medicine Unit.

Methods: A case series of patients with any of the following symptoms: resting tremor, rigidity, bradykinesia or akinesia, assessed by neurology, without diagnosis of PD, who underwent 99mTc-TRODAT-1 SPECT imaging. We reviewed the medical charts obtained demographic information, signs, symptoms and clinical course. SPECT imaging with 99mTc-TRODAT-1 was conducted in 73 patients and analysis of striatal 99mTc-TRODAT-1 binding was made by drawn of regions of interest (ROIs) in caudate nucleus (CN), putamen (P). We described the decreased uptake or the absence of tracer concentration and calculated the asymmetric index (ASI) in 69 patients. Clinical correlation with SPECT imaging was considered if abnormal SPECT imaging result was opposed to the predominant clinical symptoms.

Results: Between Dec-2006 to Dec-2010 73 patients were evaluated. The median age was 63 (IQR: 56 - 74) years, 53% were men. The median duration of symptoms was 1 year (IQR: 7.2 months-3 years). The most common symptoms were tremor at rest (81%), 44% bilateral with predominance in the right side, bradykinesia (53%), rigors (70%), gait disturbances (45%). Other symptoms present were depression (36%), impaired sense of smell (20%) and exposure to toxins (5%). SPECT imaging was abnormal in 93% of patients, 52 (71%) had decreased uptake the NC, 23/52 (44%) decreased uptake right and 7 / 52 (13%) bilateral. The putamen was involved in 93%, 24 (37%) right putamen, 22 (34%) left and 19 (29%) bilateral. The median and IQR for ASI were: striatum: 3.74 (1.9 - 5.7), NC: 2.77 (1.14 to 5.9), P: 6 (3.9 - 9 4). Final diagnosis was PD 51/62, Parkinsonism 4/62, Parkinson Plus 7/62. Clinical correlation was found in 60/63 patients (95.2%). 10 patients (14%) were not available for follow-up.

Conclusions: In this study group the SPECT imaging has clinical correlations with the side with the dominant symptoms. Similarly, there was correlation between the images and calculated index. The SPECT imaging with 99mTc-TRODAT-1 allows early assessment of nigral dopaminergic degeneration in patients with nonspecific symptoms, mild or inconclusive. It takes a cohort of asymptomatic patients to establish normal ranges of quantification in our environment.
Radionuclide Cisternography in the era of PET

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Introduction: Radionuclide Cisternography (RC) is a sensitive, reliable and safe technique that provides valuable information on CSF dynamics, which is particular useful in the localization of CSF leakage in patients with CSF rhinorrhoea, otorrhea or recurrent meningitis and also in determining CSF shunt patency (shuntography) in patient with CSF shunt.

Objectives: We report our experience with radionuclide cisternography preformed with Tc-99m-diethylenetriamine penta-acetic acid (DTPA) using SPECT/CT in the accurate localization of site of CSF leakage and planar Tc-99m shuntography for determining patency of a ventriculo-peritoneal (V-P) shunt tube in children with hydrocephalus.

Methods: CSF leakage was detected and localized after intrathecal administration of Tc-99m DTPA and using SPECT/CT fusion imaging, abnormal tracer accumulation could be accurately correlated to an anatomical structure, which had not been possible by evaluation of the planar studies alone. Shuntography was performed with Tc-99m pertechnetate injected into the shunt tube and dynamic/planar images acquired to demonstrated patency or tubal blockage in patients with hydrocephalus and V-P shunt

Results: CSF leakage was accurately detected and localised to an anatomical region using SPECT/CT fusion imaging in 5 patients with history of recurrent meningitis and CSF rhinorrhoea. CSF shuntography was performed in 16 patients with CSF V-P shunt tubes. Four patients demonstrated abrupt hold up of radiotracer at the thoracic portion of the tube suggestive of total obstruction in keeping with mechanical malfunction of the tube. In 3 patients the entire tube was visualised but there was delayed spillage of radioactive into the peritoneal cavity suggestive of partial obstruction from inflammatory debris. However, 9 patients showed normal functioning and patent tubes where the entire tube was visualised and there was free spillage of radiotracer into the peritoneal cavity.

Discussion: Even though radionuclide cisternography is not a routine procedure in most Nuclear Medicine departments, accounting for less than 1% in most centres, understanding of the clinical indication i.e. recurrent meningitis with suspected CSF leak, normal pressure hydrocephalus, and V-P shunt patency is important. Since the introduction of radionuclide cisternography in the early 1950’s, there has not been significant change in the technique and radiopharmaceuticals. However, with the introduction of PET imaging, there has been an attempt to utilize Ga-68-EDTA, but with little success. The most important evolution in the procedure is the introduction of hybrid systems which greatly improved the image quality and better anatomical localization of the abnormal site.

Conclusion: There is strong evidence to suggest that the introduction of SPECT/CT for radionuclide cisternography provides a unique and valuable tool in the accurate detection and localization of CSF leakage. Also planar Tc-99m shuntography is a simple and reliable
investigation for determining the functional status of V-P shunts. This is true even in this era of PET/CT imaging.
Value of combined brain blood flow and dopamine transporter imaging in patients with Dementia

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Purpose: To assess the utility of combined brain blood flow and Dopamine transporter imaging in patients with dementia.

Introduction: Dementia is becoming a growing global problem due to the expansion of the elderly population with significant financial implications on health care. Therefore, making a correct diagnosis and appropriate management strategies is very important. Besides financial benefits, making a correct diagnosis helps patients and family understand and accept the disease better. Diagnosing the cause of dementia has proven to be extremely difficult using clinical assessment and standard cross-sectional imaging studies of the brain alone. Meta-analysis of the literature regarding functional brain imaging in the dementias concluded that functional brain imaging provided critical information in the initial diagnosis of dementia. Despite this, on occasions it is difficult to provide the clinicians a conclusive diagnosis of specific dementia with greater confidence using either Tc99m HMPAO or I123 Ioflupane alone, due to inherent drawback of lower specificity of functional imaging. We tried to assess whether ‘Sequential Brain imaging’ would improve our diagnostic accuracy of various dementia disorders.

Materials and Methods: We reviewed 7 Patients with suspected clinical diagnosis of dementia in whom LBD was suspected based on either clinical or scan features. All of these underwent concurrent functional imaging using Tc99m HMPAO and I123 Ioflupane in 2010 (either test first based on clinical symptoms and clinical question). The subsequent functional imaging was justified when the scan diagnosis was inconsistent with clinically suspected diagnosis. Patients undergoing Tc99m HMPAO SPECT imaging were rested in a quiet room 10 minutes before and after 500 MBq Tc99m HMPAO injection, to avoid excessive neuronal stimulation that might affect pattern of Radio pharmaceutical distribution. Patients undergoing I123 Ioflupane study had Thyroid blockade prior to 185 MBq I123 Ioflupane injection. SPECT Brain images were acquired using dual-headed Gamma camera 10 min post injection for Tc99m HMPAO and 3 hour post injection for I123 Ioflupane. The raw data was checked for movement artefacts and the acquired data of projection views were reconstructed with ‘Filtered Back Projection’ using Metz filter. Reconstructed slices were realigned and masked if needed. The images were displayed in trans-axial, Coronal and Sagittal planes.

Results: In 6 of 7 patients with complex clinical symptoms, Tc99m HMPAO was performed first. 4 of these 6 patients had indeterminate diagnosis of dementia for which they underwent I123 Ioflupane study, which conclusively diagnosed Lewy body dementia (LBD). In 2 of 6 patients, the subsequent I123 Ioflupane study ruled out LBD.
In 1 of 7 patients with suspected dementia and symptoms consistent with Parkinson’s disease, I123 Ioflupane study was performed first. The study did not show scan features of LBD. A subsequent Tc99m HMPAO study confirmed vascular dementia in this patient.

Conclusion: In patients with complex clinical symptoms and signs of dementia, our study clearly showed the usefulness of sequential functional brain imaging in improving diagnostic confidence of our nuclear medicine physicians.
Ictal SPECT in Paediatric Epilepsy of temporal lobe origin – Correlation with surgical outcome

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Aim: To assess the role of ictal SPECT in paediatric Temporal lobe epilepsy (TLE) and to correlate ictal perfusion patterns with surgical outcome.

Methods: A retrospective analysis of Ictal & Interictal SPECT, Ictal Video EEG, MRI and surgical outcome was performed in 27 children of TLE. SPECT Perfusion patterns were classified as Typical (anteromedial, anterolateral, inferior) and Atypical (extra temporal). Surgical outcome was assessed according to Engel’s classification.

Results: Ictal and Interictal SPECT were done in 21, Interictal alone in 6. Sixteen had Hippocampal sclerosis (HS), while nonHS group had neuronal loss in four, Dual pathology in two, FCD in 2, ganglioglioma in 1, gliosis in one and normal in one. Sensitivity of ictal SPECT is 95 %, interictal is 78%. SPECT was diagnostic in 85.7 % of normal MRI patients. Typical pattern with anteromedial and lateral hyperperfusion is commonest in HS (75%). Atypical pattern is more commonly seen in nonHS group than with HS (45.4% vs 25%). 91.6 % of HS group with typical pattern are in Engel’s class 1 outcome. Whereas 80% of nonHS group with atypical pattern are in poor surgical outcome (p < 0.05).

Conclusion: Ictal SPECT is highly sensitive (95%) in pre surgical evaluation of paediatric TLE. The typical pattern is commonest in HS (75%) and shows good surgical outcome. Significant association of atypical pattern with poor surgical outcome is noted in nonHS group (p value<0.05) SPECT was diagnostic in 85.7% of normal MRI patients.
CLINICAL NON-PET PAEDIATRICS
Atypical bone scintigraphy patterns in a child with acute lymphoblastic leukaemia: A case report

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This is a case of a two-year old male with an eight-week history of generalized bone pains, reluctance to move and inability to ambulate. Patient was initially diagnosed with Juvenile Rheumatoid Arthritis. Progression of symptoms prompted consultation and subsequent admission. As part of initial work-up of unexplained bone pains, three phase bone scintigraphy study using Tc-99m HDP, showed patchy areas with poor tracer uptake in the growth plates of both proximal and distal tibiae, proximal shaft of both femora and distal forearms. Focal photopenic areas adjacent to the plates in the distal femora and in the talus bilaterally are also noted. Incidentally, prominent diffuse bilateral lung and renal parenchymal tracer retention was seen in the delayed phase. Chest X-ray showed interstitial infiltrates and chest CT showed interstitial pneumonia in both lungs with bilateral pleural effusion, multiple lytic bone changes and enlarged kidneys. Subsequent bone marrow biopsy confirmed Acute Lymphoblastic Leukaemia (ALL). Patient underwent chemotherapy and was able to stand alone unsupported with a wobbly gait after more than a month. Acute Lymphoblastic Leukaemia accounts for 80% of the cases seen in children. The first clinical manifestation of leukaemia may be musculoskeletal symptoms that may be difficult to differentiate with arthritis and other orthopaedic pathologies. Patients may be referred for bone scans before diagnosis is made. Abnormal bone scintigraphic findings may be due to leukemic infiltration, which are usually symmetrical, resulting in diffuse reactivity in cortical bones most commonly in the metaphysical regions of the lower limbs. Diffuse involvement of long and flat bones may also occur. Photopenic areas may also result from vascular compromise with avascular necrosis or osteonecrosis. Atypical findings in ALL on bone scintigraphy can also be observed. Diffuse tracer retention within the renal parenchyma on delayed images can suggest leukemic infiltration. The same tracer retention pattern in the lungs can be seen in cases of pulmonary calcinosis. This patient represents a case of severe ALL with bilateral pulmonary calcinosis and diffuse leukemic infiltration of the renal parenchyma on top of abnormal skeletal findings. Knowledge of reported skeletal scintigraphic patterns seen in leukemic patients can facilitate early diagnosis and therefore treatment. Another importance of bone scan is its capability to suggest the disease earlier than the blood examinations. Blood examinations such as peripheral blood smears may also be negative for acute lymphoblastic leukaemia in aleukaemic forms. Attention is drawn to the importance of bone scintigraphy as part of the initial work-up for paediatric patients who present unexplained musculoskeletal complaints in order to consider the possibility of leukaemia, its complications or other pathologies.
CLINICAL NON-PET OTHERS
Additional value of SPECT-CT in the diagnosis of primary hyperparathyroidism

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The visualization of parathyroid glands is difficult because of the very small size of both: normal and hyperfunctioning glands. Ultrasound examination is helpful by hypodense nodules detection, but it cannot be effective in cases with ectopy, retrotracheal localization of the parathyroid adenomas, or when a multi-nodular goiter coexists. Preoperative localization is very useful for the success of surgery. The aim of the study was to evaluate the role of SPECT-CT in the nuclear medicine examination of the hyperfunctioning parathyroid glands.

Material and Methods: A combination of subtraction planar scintigraphy (with application of 37 MBq 99mTc-pertechnetate and 740 MBq 99mTc-tetrofosmin) and SPECT-CT was performed in 59 patients with a proven hyperparathyroidism (level of parathyroid hormone 97 -3107 pg/ml). The SPECT-CT was done according to the zone with residual focal uptake after subtraction: neck and eventually upper part of the thorax. The images derived from SPECT were compared to the images from SPECT-CT. Surgery was undertaken in 25 patients and the information obtained from SPECT-CT imaging was verified.

Results and Discussion: In 52 of the patients an increased focal uptake in the hyperfunctioning glands was detected (in 59 glands) after subtraction. The SPECT images were used in fusion with CT images and separately for localization of the visualized gland (glands). The comparison demonstrated five advantages of SPECT-CT: 1) Precise localization in case of ectopy (2 patients with retrosternal and 1 with mediastinal localization). 2) Precise retrotracheal localization in 6 cases. 3) Recognition of retained vascular activity, which can mimic an ectopic adenoma. 4) Confidence in detection of multi-gland disease. 5) The combination of subtraction and SPECT-CT alleviate the differentiation of thyroid from parathyroid nodules (adenomas). The SPECT images without fusion did not give precise localization of hyperfunctioning glands and did not help the evaluation of the ectopic focal parathyroid adenomas. In operated patients the SPECT-CT derived diagnosis and localization were confirmed. We can conclude that SPECT-CT is a very promising pre-operative method for the visualization of hyperfunctioning parathyroid glands, especially in cases where ectopic or retrotracheal localization is anticipated.
Our impressions from application of SPECT-CT in patients with a suspicion of infection of joint prosthesis in comparison with those with combined method for leukocytes and bone marrow scintigraphy

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The disadvantage of leukocyte' scintigraphy (LS), when applied in patients (Pts) with a suspicion of infection of joint prosthesis is, the difficulty to localize and differentiate bone from soft tissue infection and additionally false positive results could be obtained in some cases if bone marrow scintigraphy is not performed. In total, between 2007 and 2010, we investigated 31 patients with hip or knee prosthesis, in whom infection was suspected, but final diagnosis, was proved with surgery or microbiological aspiration. The patients were divided in 2 groups. In the first group- 15 of them were included- 11 with hip and 4 with knee joint replacement, and the sequential LS- with in vitro labelled leukocytes with 370MBq 99mTc-HMPAO, scintigraphy was performed 2h p.i. and in the following days- bone marrow scintigraphy with 370MBq 99mTc-nanocolloid were applied. In 8 of the patients a right positive result was received 2 of them had additional soft tissue infection with fistulas, in 5- right negative result, in 1-false negative, without false positive result and with a sensitivity of 89%, specificity-100% and accuracy-93%. In a second group of 16 pts, 12-with hip and 4- with knee replacement, we have applied SPECT-CT technique low dose CT on Symbia T2- Siemens after injection of in vitro labelled leukocytes with 370MBq 99mTc-HMPAO without bone marrow scintigraphy. In 7 of the patients a right positive result was received and in 2 of them also fistulas were visualized, in 8-right negative results, in 1-false positive, with a sensitivity of 100%, specificity- 89% and accuracy-94%. When difficulties in interpreting of the results were encountered, because of the metal prosthesis artefact, non-attenuated corrected images were also considered. Having CT as a method for anatomical reference, it was also easy to localize and differentiate bone from soft tissue infection and to determine its extent. As a conclusion, after applying both techniques for a visualization of infection in pts with joint prosthesis, we suggest that they have comparable accuracy. The hybrid SPECT-CT technique is easier and quicker to perform and the patient has the possibility to achieve the result on the same day and respectively, to follow the therapeutic plan.
Leukocyte SPECT/CT for diagnosis of osteomyelitis in patients with diabetic foot

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Introduction: Osteomyelitis (OM) is a serious complication in the diabetic foot. Its diagnosis is usually challenging - X ray and bone scan provide information only about bone tissue, MRI about bone marrow. These modalities are non-specific and difficult to interpret, especially if Charcot’s foot is present. The only method specific for inflammation detection is scintigraphy with labelled leukocytes, and it is helpful in the differential diagnosis. In this procedure, scintigraphy provides information about the presence or absence of inflammation, but precise localization of the site of infection, which is crucial for distinguishing cellulitis from OM, is difficult. Hybrid imaging (SPECT/CT) is very useful in this regard.

Methods: We evaluated 9 patients (pts.) with the diabetic foot syndrome. There were 8 male and 1 female, average age 62 (48-79) years. We used monoclonal antibody against a surface antigen of leukocytes labelled with Tc-99m as a tracer (LEU). All pts were imaged with SPECT in combination with low-dose CT (LDCT). Findings were evaluated as a cellulitis or OM. Follow-up clinical examination was performed within 2 to 15 months. Healing of the foot was considered as a cellulitis, presence of ulcers or surgical removing of bone was considered OM.

Results: 2 pts considered cellulitis healed, ulcer persisted in one (2/3 truly negative). 6 pts were considered as OM; ulcers persisted in 3, bone was removed in 2, 1 pt healed (5/6 truly positive). Calculated sensitivity for OM was 83%, specificity 67% and accuracy 78%.

Conclusion: Image fusion of leukocytes SPECT with CT allows precise localization of inflammation. If the focal accumulation of leukocytes localizes to a bone structure on CT, OM can be confirmed. The challenge of interpretation is the presence of Charcot’s foot, where leukocytes can also accumulate. Bone marrow scan with colloids could be performed to distinguish this. SPECT/CT is a very useful imaging method for the diagnosis of OM in patients with diabetic foot syndrome. Scintigraphy with labelled leukocytes detects the presence of inflammation and CT helps in its precise localization, thus obviating the need for bone scintigraphy.
Introduction: Impending cord compression and vertebral fractures are considered as contraindications for radionuclide bone therapy. However, most of the patients with widespread bone metastases already have weakened vertebral segments that may be broken. Therefore, local field external-beam radiotherapy or percutaneous vertebroplasty should be considered to improve the patient’s quality of life and to enable suitable treatment, including radionuclide bone therapy.

Objective: To create a strategy for an effective treatment of bone metastases in patients with widespread bone metastases and intolerable pain associated with impending cord compression or vertebral fractures.

Material and Methods: 11 patients (5 female and 6 male, aged 32-62, mean age 53, 8+2, and 7) with multiple skeletal metastases from prostatic carcinoma (3), breast carcinoma (3) or lung carcinoma (5) were studied. Their mean objective pain score according to 10 score system was 8, 64+0, 15 (range 8-9) and the mean number of levels with impending cord compression or vertebral fracture was 2, 64+0, 34 (range 1-4). All patients underwent vertebroplasty and after 3-7 days received Sm-153 EDTMP therapy. Sm-153 EDTMP was administered at the standard bone palliation dose of 37 MBq/kg body weight. WB bone scan, CT and MRI were performed before and after treatment in all patients.

Results: Pain relief due to stabilization of vertebrae after vertebroplasty occurred within the first 12 hours (mean 4,8+1,2; range 0,5-12 hrs.), and the mean objective pain score was reduced to 4,36+0,39 (range 2-6). After subsequent Sm-153 EDTMP treatment further pain relief occurred after 3,91+0,39 days (range 2-6 days) and the objective pain score decreased to 0,55 +0,21(range 0-2). There is statistically significant difference according to pain score system before and after treatment P< 0, 0001

Conclusion: Spinal stabilization using vertebroplasty in patients with wide spread bone metastases and impending cord compression is an effective way to decrease disability with pain and to facilitate subsequent systemic palliation of painful skeletal metastases by administration of Sm-153 EDTMP.
123I-MIBG imaging cardiac autonomic neuropathy in the chronic Chagas cardiopathy


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Background: Cardiac involvement is the most frequent and serious manifestation in the chronic phase of chronic Chagas disease and has diverse clinical course. Identifying patients who are at risk of dying remains a challenge. At present, the role of the involvement of the autonomic nervous system (ANS) in the pathogenesis of chronic Chagas cardiopathy is highly controversial. Most previous studies have evaluated the parasympathetic ANS, showing that vagal impairment occurs early in the natural history of the disease, independently of deterioration of the left ventricular function. However, there are few studies on the involvement of the sympathetic ANS, as well as its association or not with the left ventricular function.

Objectives: The objective of this study was to clarify the involvement of the autonomic nervous system in the pathogenesis of chronic Chagas cardiopathy.

Patients and Methods: In order to investigate ANS involvement in the pathogenesis of chronic Chagas cardiopathy, nineteen patients (mean age, 48 years-old; 13 males and 6 females), 85% classified as NYHA I were studied. Blood samples were obtained to measure neurohormones such as brain natriuretic peptide (BNP), renin activity, noradrenaline, and angiotensin II; 24-hour Holter monitoring was performed to assess heart rate variability (HRV); Echocardiography (ECO) to assess left ventricular ejection fraction (LVEF). Stress/rest 99mTc-sestamibi quantitative gated imaging (MIBI) and MIBG imaging were used to analyse perfusion defects and the heart/mediastinum (H/M) ratios as well as the extent of cardiac washout rate (WR%), respectively.

Results: The early and late H/M ratio were 1.62 (1.46-1.71) and 1.46 (1.38-1.65), respectively and the WR% was 30 (25-37); 70% of the patients showed MIBG defects bigger than perfusion (MIBI) defects. The mean left ventricular ejection fraction was 35 (30-42) %. Simple linear regression analysis showed that WR% had a significant negative correlation to LVEF (rs=-0.456, p < 0.001).
FIG. 1. Relationship between 123MIBG cardiac washout rate (WR%) and left ventricular ejection fraction (LVEF) ($r_s = -0.456, p < 0.001$).

Conclusion: This study suggested that sympathetic innervation was closely related to LV function in Chagas cardiopathy. As such, the clinical role of 123I- MIBG imaging in the early diagnosis of ANS in Chagas Disease has yet to be investigated, as well as its role in assessing prognosis and developing management strategies.
**IAEA-CN-185/240**

*Whole body imaging with Lu[177]-EDTMP: Extended phase II clinical trial investigation of Lu[177]-EDTMP for the palliation of metastatic bone pain*

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**Objective:** Lu[177]-EDTMP, a beta-emitting bone-seeking therapeutic being assessed as an agent for palliation of bone pain, emits gamma-photons of 113 keV (6.4%) and 208 keV (11%), suitable for imaging. This investigation sought to characterize the ideal conditions for whole-body gamma camera imaging of Lu[177]-EDTMP in patients.

**Methods:** Eleven subjects suffering from metastatic bone pain from prostate or breast cancer underwent whole-body scans with a double headed gamma camera at three time points: 1hr, 24hrs and 48hrs after injection of Lu[177]-EDTMP (16.9~41.9 MBq/Kg BW). At each time point, scans were acquired with a multi-energy window setting of peak-energy A: 113 keV and B: 208 keV applying low energy high resolution parallel hole (LEHR) and medium energy all purpose (MELP) collimators, successively. All subjects underwent a bone scanning using Tc[99m]-MDP while screening. Region of interest technique was used to analyse tracer’s uptake in bone, soft tissue and metastatic bone lesions.

**Results:** The femur-to-muscle ratio (F/M) with 99mTc-MDP was 2.69±1.06. For Lu[177]-EDTMP, the highest F/M rations were found at 24hr (12.59±5.73) and 48hr (12.54±5.23) by applying MELP collimators and collecting the 208 keV photons. These two ratios were significantly higher than other combinations (P<0.05). In the same combinations of collimator and peak energy, the F/Ms at 24hr and 48hr are significantly higher than those at 1 hr., except the combination of LEHR collimator and 208 keV peak energy. The lowest F/M was 1.06±0.16, gained at 1hr with the combination of LEHR and 208 keV peak energy and there was no significant change in F/Ms of this combination from 1hr to 48hr. Lesion-to-normal bone uptake ratios (L/N) of 99mTc-MDP bone scan and images at 24hr and 48hr phases of Lu[177]-EDTMP were analysed. There was no significant difference in L/Ns of all these series of images among groups (P>0.05). Assessing image quality by means of femur-to-muscle uptake ratio and visual inspection, Lu[177]-EDTMP images we ranked from highest to lowest quality as follows: 208 keV with MELP > 103 keV with MELP > 103 keV with LEHR > and 208 keV with LEHR.

**Conclusions:** Lu[177]-EDTMP can provide good quality whole body images with best results when applying medium energy collimation and collecting the 208 keV energy photons alternatively by collecting both 208 keV and 113 keV photons for higher counts statistics. The most appropriate time point for imaging is between 24~48hr post-injection.
FIG. 1. Example of 12 series of whole-body images of 177Lu-EDTMP of a 73-year-old man (Subject 5, 2557MBq of 177Lu-EDTMP injected, scan length: 200cm) with prostate cancer acquired at three time phases of 1hr, 24hr and 48hr with various combinations of collimators and energy window settings. A: LEHR and 113 keV, B: LEHR and 208 keV, C: MELP and 113 keV, D: MELP and 208 keV.
Adjuvant treatment with radioactive I-131 in malignant struma ovarii

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Struma ovarii, a rare form of ovarian tumour, represents less than 3% of ovarian teratomas. It’s defined by the presence of thyroid tissue comprising more than 50% of the overall mass. The vast majority of struma ovarii are benign; however, malignant disease is found in a small percentage of cases. Only thirty cases of distant metastasis of malignant struma ovarii was reported in the literature. This is a case of a 67 years old woman who presented a tumour of the right ovary. A total hysterectomy with bilateral annexectomy was performed on June 1988. The histological examination showed prevailing thyroid tissue in very different sizes of vesicles without any histological signs of malignancy. The patient leaved with a diagnosis of benign struma ovarii.

On December 2006, 18 years later, the patient presented abdominal pain with dyspnoea. A pelvic sonography and a CT scan had already been performed and showed a huge right lateral cystic tumour. After surgical resection with pelvic washings, total abdominal hysterectomy, bilateral salpingo-oophorectomy and lymph node sampling, pathological examination revealed thyroid tissue as the major component of the mass, with papillary histology. Postoperative evaluation with uptake of sodium iodide I-131 demonstrated thyroid uptake in lymph nodes and pelvic masses. The bone scan with HMDP-Tc99m was normal. A thyroidectomy was suggested before any adjuvant treatment in order to potentiate the effects of radio ablation. After thyroidectomy, a total body scan with 720 MBq of Iodine 131 was performed on July 2007 and showed cervical metastases, macro-nodular pulmonary metastases and several abnormal uptakes in residual lymph nodes and pelvic masses. A first IRAtherapy with 5 GBq of I131 was performed. On November 2007, a second IRAtherapy with 7, 2 GBq of I131 was performed. The post-treatment whole body scan didn’t show any uptake of I131.

Conclusion: Currently, the pathological criteria used in diagnosing thyroid carcinoma are widely accepted as the standard in diagnosing malignant struma ovarii. However, there is still controversy over defining characteristics of a malignant struma ovarii tumour. Surgical resection remains the definitive treatment for benign disease, and surgery with adjuvant radioiodine therapy has been shown to be successful in treating metastatic and recurrent disease. The recurrence rate in patients with malignant struma ovarii who undergo surgery without subsequent radio ablation has been cited as high as 50%. Radioactive I-131 ablation has been shown to treat malignant disease in both its initial presentation and any subsequent recurrence with excellent efficacy, although the rarity of the disease and lack of data surrounding its long-term management prove challenging to clinicians.
Value of SPECT/CT scintigraphy in the assessment of patients with Hyperparathyroidism

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Despite progress in parathyroid imaging, detection and correct localization of hyperfunctioning parathyroid glands in patients with hyperparathyroidism remains a problem. The purpose of the present study was to evaluate the incremental diagnostic value of early single photon emission computed tomography with low dose CT study (SPECT-CT) in detection and localisation of abnormal parathyroid glands as compared with planar imaging alone.

Methods: We evaluated 30 patients with biochemical diagnosis of hyperparathyroidism: 16 patients (4 M, 12 F, age 56, 5±17 years) with primary hyperparathyroidism (PHP) and 14 patients (7 M, 7 F, age 43, 9±18 years) with secondary hyperparathyroidism (SHP). The mean intact parathyroid hormone level was 387, 8±266 pg/ml in patients with PHP and 1250±415 pg/ml in SHP cases. All patients underwent an optimized parathyroid scintigraphic protocol based on planar imaging with dual-phase, dual-tracer scintigraphy and an early SPECT-CT study. Scintigraphic imaging protocol included: thyroid exam with 50 MBq of pertechnetate and dual-phase parathyroid planar study (at 10 min and 150 min) post 99mTc-Sesta mibi (740 MBq) injection. SPECT/low dose CT of the neck and chest was acquired with a Symbia T camera at early phase (30-40 min after Sestamibi injection).

Results: Planar imaging identified hyperfunctioning parathyroid glands in 20 patients: 11 with PHP (69%) and 9 with SHP (64%), while SPECT/CT detected hyperfunctioning parathyroid glands in 24 patients: 14 with PHP (87, 5%) and 10 with SHP (71%). In 4 cases, pathologic glands were missed on planar scintigraphy but identified with SPECT-CT. Of these, 2 hyperfunctioning parathyroid glands in eutopic position did not show significant tracer uptake to allow differentiation from physiological thyroid uptake in planar acquisition. In further cases, SPECT/CT localized sestamibi uptake in ectopically located parathyroid in the mediastinal in one patient and in the submandibular salivary gland region in the other. In 3 patients, ectopic glands were detected by planar imaging and SPECT/CT study provided more precise localisation. Discordant planar - SPECT/CT information was obtained in 7 patients (24%).

Conclusion: According to our results, preoperative SPECT/CT enhances sensitivity for parathyroid detection over planar scintigraphy and also provides incremental anatomic information which is meaningful to the surgeon.
**177 Lu-EDTMP for bone pain palliation in metastatic prostate and breast cancer: A phase II trial**

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Objectives: To assess safety and efficacy of 177Lu-EDTMP in bone pain palliation in breast and prostate cancer patients with bone metastases.

Methods: Subjects were treated with 177Lu-EDTMP. The criteria for entry into the trial, was a positive 99mTc-MDP bone scan consistent with bone metastatic pain. Life expectancy is more than 3 months.

Results: Eleven patients, 6 prostate and 5 breast cancer, aged 65.5±13.8yr (38-84 yr). Seven and four received 1295 MBq (35mCi) and 2590MBq (70mCi) respectively. 11 patients mean bone lesion score was 14.18 (6-19). In platelet toxicity, 2(18%) of 11 patients developed grade I, 1(9%) developed grade III, 1(9%) developed grade IV. The mean nadir platelet count was 91, 1111/mm3at the 4th week and began complete recovery from the 6th week; 1(9%) patient developed grade II leucocyte toxicity. The median nadir leucocyte count was 4,352/mm3 at 2nd week and began complete recovery from the 6th week. Two subjects did not provide the hematologic counts from 2nd week. Large dose caused more marrow suppression. Table 1 depicts all 11 patients responding almost at the 2nd week by the observed trend of pain score, analgesic frequency, mobility, Karnofsky performance. Six, three and two of 11 patients had duration of palliation of 3, 2, and 1 month respectively.

Conclusions: This primary trial indicated that 177Lu-EDTMP is an effective treatment for palliation of pain from bone metastases. More cases are now being recruited into this study to further examine the efficacy of 177Lu-EDTMP.

Table 1: Observed efficacy of 177Lu-EDTMP during 3 months following-up.

<table>
<thead>
<tr>
<th>Observation\time point (week)</th>
<th>wk0</th>
<th>wk2</th>
<th>wk4</th>
<th>k6</th>
<th>wk8</th>
<th>wk12</th>
</tr>
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<tr>
<td>Pain score sum(n)</td>
<td>80(11)</td>
<td>43(11)</td>
<td>24(11)</td>
<td>19(11)</td>
<td>15(9)</td>
<td>28(9)</td>
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<tr>
<td>Analgesic Frequency sum(n)</td>
<td>8(4)</td>
<td>4(4)</td>
<td>3(2)</td>
<td>3(2)</td>
<td>3(2)</td>
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<td>Mobility sum(n)</td>
<td>32(11)</td>
<td>21(11)</td>
<td>18(11)</td>
<td>16(11)</td>
<td>12(9)</td>
<td>16(9)</td>
</tr>
<tr>
<td>Karnofsky sum(n)</td>
<td>630(11)</td>
<td>770(11)</td>
<td>840(11)</td>
<td>840(11)</td>
<td>690(9)</td>
<td>660(9)</td>
</tr>
<tr>
<td>Analgesic type sum(n)</td>
<td>5(4)</td>
<td>5(4)</td>
<td>2(2)</td>
<td>2(2)</td>
<td>2(2)</td>
<td>2(2)</td>
</tr>
</tbody>
</table>

n: patients number
Is there a correlation between peptide receptor radionuclide therapy associated hematological toxicity and spleen dose?

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The spleen receives the highest radiation dose during Peptide Receptor Radionuclide Therapy (PRRNT) using 177Lu or 90Y labelled somatostatin analogs. This is due to high somatostatin receptor density particularly in the red pulp. There have been no previous studies examining the effect of high radiation dose to the spleen during PRRNT. The spleen is a reservoir of erythrocytes and platelets, to be made available in the event of an emergency like haemorrhagic shock, and of leucocytes particularly undifferentiated monocytes, which are mobilized and deployed at the sites of inflammation.

Aim: The aim of this study was to correlate between the radiation dose to the spleen and the effect on the blood cell count after PRRNT.

Methods: The study included 53 patients having undergone a single cycle of PRRNT with 3.8 – 8.5 GBq of 177Lu-DOTATATE or DOTATOC. The time-dependent spleen activity was determined based on conjugated planar whole-body scans acquired 0.5h, 3h, 20h, 44h and 68h post injection and dosimetry calculations (MIRD scheme) were performed using OLINDA software. 11 patients who had undergone splenectomy before PRRNT were treated with 4.7 – 7.6 GBq of 177Lu DOTATATE or DOTATOC and were selected as controls. The patients in study and control groups were selected after excluding past history of chemotherapy. The RBC, WBC (total and differential) and platelet counts before and after each cycle of PRRNT were documented. Non-parametric sign rank tests were used to compare the post-therapy changes in blood cell counts in the study group and splenectomy group (control).

Results: The median dose to the spleen in the study group was 6.34 Gy (2.32 – 20.06). There was no significant difference in the post-therapy changes in the blood cell counts (RBC, WBC or platelets) between the study group and the control group. Mild haematological toxicity was found in 7 of the 53 (13.2%) patients in the study group and all of these patients presented mild erythrocytopenia. However, there was no correlation between the incidence and grade of haematological toxicity, and the dose to the spleen. In the control group, 1 out of the 11 patients (9.1%) had mild erythrocytopenia post PRRNT.

Conclusion: PRRNT with 177Lu-labeled peptides is safe and has minor adverse haematological effects, mostly mild erythrocytopenia. However, this is most likely due to the radiation dose to the whole body (including bone marrow) and most probably unrelated to the radiation dose to the spleen. Further studies are required to ascertain the somatostatin receptor expression by specific cells in the spleen.
Intra-arterial radioembolization with Y-90 for unresectable primary and metastatic liver tumours

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Aim: The aim of this study was to evaluate the success of SIRT treatment in liver metastases of different tumours. Also we interpreted the contribution of SIRT treatment to survival times according to responder- nonresponder and hepatic- extrahepatic disease.

Method: The clinical and follow-up data of 124 patients who were referred to our department for SIRT treatment between June 2006 and October 2010 were evaluated retrospectively. SIRT treatment has been applied in 78 patients who were suitable for treatment. All patients had unresectable liver metastasis of different malignancies (35/78 colorectal, 25/78 hepatocellular, 7/78 gastric, 4/78 breast, 1/78 malign melanoma, 1/78 pancreas, 1/78 renal cell, 1/78 esophagus and 3/78 neuroendocrine tumour patients). Treatment was repeated at least one more time in 5 patients to same or other lobe. Treatment response evaluated by PET/CT as metabolically 6 months after treatment. FDG-PET/CT was repeated in per six weeks periods. The response criterion which had been described recently was accepted as at least 20% decrease of SUV value. Also in patients with neuroendocrine tumour serial Ga-68 PET/CT was used for evaluating response. Patients were divided into 2 groups according to treatment response (R=responder, NR=non-responder) and also into two groups according to disease stage; patients have only liver metastases (H) and have metastases in other organs (EH).

Results: 68 patients received treatment for right lobe- seven patients received treatment for left lobe and 3 patients for both lobes. The mean treatment dose was estimated as 1.62 GBq. In the evaluation of treatment response; 43(55%) patients were responder (R) and 35 (45%) patients were non-responder (NR). Mean pre-treatment SUVmax value of R group was 11.6 and NR group was 10.7. While only 11 (31%) out of 35 NR patients had H disease, 30 (69%) out of 43 R patients had H disease (p<0.05). Mean overall survival time of R group was calculated as 25.63+1.52 months and NR group’s 20.45+2.11 (p=0.04). Mean overall survival time of H group was computed as 25.66+1.52 months and EH group’s 20.76+1.97 (p=0.09).

Conclusion: SIRT is a useful treatment method which can contribute to lengthening of survival times in patients with primary or metastatic unresectable liver malignancies. Also 18F-FDG PET/CT seems to be a successful imaging method in evaluating treatment response for predicting survival times in this patient group.
The prevention of sialadenitis post-therapy with I-131 in patients with thyroid cancer reduces the dose of radiation in the salivary glands

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One of the most common side effects of Iodine 131 therapy for thyroid cancer is the sialoadenitis, between 12 to 50% of patients who received the therapeutic doses for postoperative ablation of residual functioning thyroid tissue or the presence of metastasis, develop almost straightaway after therapy temporary swelling and pain with decreased salivary flow, this phenomenon is usually bilateral and involves the parotid glands. The post-therapy induced swelling causes increased periductal pressure with duct constriction thus resulting in salivary retention and adds to the swelling and pain. The effect is hasty and dose related. Within a few days, resolution of this inflammatory process occurs and symptoms recede. Unfortunately, no data are available regarding the frequency of this immediate post-131I sialoadenitis. In order to prevent the onset of sialoadenitis, we routinely use, in our institution, an appropriate hydration (1500 to 2000 ml/day between juice and water); furthermore we prescribe the consumption of candies and gum to increase the salivation process from the time of the I131 therapy administration and for a period of eight days. We also recommend frequent mouth wash (at least four times per day). There are reports in the literature on the use of sialogogues that are frequently used in the treatment of xerostomia (dry mouth), to stimulate salivary gland tissue to produce more saliva a process that could decrease the onset of inflammation of a salivary gland and reduce the radiation dose to the salivary glands. We retrospectively reviewed 200 patients treated in our institution with therapeutic doses of I131 (100 to 250 mCi) among them 40 (20%) developed unilateral or bilateral sialoadenitis over a period of six months despite the preventive measures of hydration and stimulation of salivation by intake of sweets and chewing gum.

The studied population comprised 170 females (85%) and 30 males (15%), ranging in age from 15 to 75 years who were referred for therapy with 131 I between January 2009 and July 2010. Among them 172 (86%) have Papillary thyroid cancer, 22 (11%) follicular thyroid cancer, and six (3%) Hurtle Cell Ca. Due to the presence of residual functioning thyroid tissue in the thyroid bed 160 (80%) patients received a therapeutic dose of 100 to 120 mCi (3700 to 4440 MBq); 30 (15%) patients received a dose of 120 to 200 mCi (4440 to 7400 MBq) due to metastatic involvements of the lungs (27 patients) and to the bones (2 patients). Due to the high incidence of sialoadenitis in our institution, we decided to design a prospective clinical study including 100 patients referred to our nuclear medicine department for evaluation and administration of 131 I therapy for ablation of residual tissue or treatment of metastasis. The population will be divided in two 50-patient groups with similar conditions mainly sex, age and I-131 administer dose. Group 1 will receive the common salivation stimulation and group two a sialogogue (pilocarpine) in addition to the salivary stimulation provided for group 1. A dosimetric evaluation of the neck and in the salivary glands at 8 and 24 hours of the I131 administration, at 7 days after the therapy, 8 weeks later and 5 months later will be performed. In addition patients developing inflammation symptoms of the salivary glands will be evaluated with a 99mTc syalography.
High-dose chemotherapy and autologous stem-cell transplantation (ASCT) is the standard therapy for refractory/relapsed aggressive lymphoma. In the era of rituximab-containing front-line regimens, it is becoming more challenging to salvage patients in this setting and novel approaches are required. Following initial experience at C. Sheba Medical Center the current randomized phase-II, two-arm study was designed to evaluate the safety and efficacy of standard-dose Ibritumomab Tiuxetan (Zevalin) combined with high-dose BEAM chemotherapy (Z-BEAM) and ASCT in refractory/relapsed aggressive lymphoma. Forty-three patients (pts) with CD20+-aggressive lymphoma eligible for ASCT were randomized to treatment arm (Z-BEAM, n=22) or control arm (BEAM alone, n=21). Zevalin treatment dose of 0.4 mCi/kg was given on day -14 prior to ASCT. The median age was 55 years (range, 23-67); 27 men, 16 women. Thirty-four pts had diffuse large B-cell lymphoma which was either refractory to first-line therapy (n=5) or recurrent (n=29). Nine pts had transformed follicular lymphoma, in first (n=2) or second remission (n=7). All pts responded to second-line therapy, however 17 pts had positive PET-CT prior to ASCT.

Twenty-six pts were scored as high-risk (relapse within 12 months of diagnosis and/or sIPI>2) and 17 as low-risk disease. Patient and disease characteristics were well matched in the 2 groups. All pts engrafted after SCT in a median of 10 days and 13 days for neutrophil and platelet recovery, respectively, with no difference between the 2 regimens and there were no early treatment related deaths. 2-year progression-free survival (PFS) was 42% (95%CI, 25-60%); 55% and 30% after Z-BEAM and BEAM alone, respectively (p=0.2). Multivariable analysis identified advanced age (HR 7.6, p=0.001), high-risk disease (HR 3.1, p=0.03), positive PET-CT pre-transplant (HR 2.4, p=0.07) and BEAM alone (HR 2.8, p=0.03) as poor prognostic factors. Patients with none of the first 3 factors had excellent outcome, while patients with all 3 factors had dismal outcome. Intermediate-risk patients with 1-2 risk factors had better PFS with Z-BEAM compared with BEAM; 62% and 17%, respectively (p=0.07).
In conclusion standard-dose Zevalin combined with BEAM high-dose chemotherapy is safe and possibly more effective than BEAM alone as conditioning regimen for ASCT. Larger studies with longer follow-up are needed to confirm these observations before the new Z-BEAM regimen can be accepted as a new standard of care for ASCT, in the era of rituximab containing chemotherapy.
Background: Bone scintigraphy is the most sensitive modality in detecting bone lesion however its lack of specificity makes differentiation between benign and malignant lesions difficult. Single photon emission computed tomography (SPECT), has improved specificity of bone scintigraphy to detect more lesions, especially in vertebra where metastasis are frequently seen.

Purpose: To evaluate contribution of SPECT bone scan in the determination of indeterminate bone planar scintigraphy abnormalities.

Patients and Methods: This retrospective study was done with 30 patients. These patients have had a whole body planar bone scan followed by SPECT acquisition between March 2009 and November 2010. The patients were 12 women and 18 men; the mean age was 54.5 years ranged 16-90 (59% ≥55 years old). All patients except 2 have malignant diseases. The patients investigated had breast cancers (10), lung cancers (6), prostate cancers (6), head and neck cancers (2), and osteosarcoma (1). Two patients had back pain and knee pain without any history of malignancy. A whole body bone scan (anterior and posterior) were done after more than 2 hours post injection of 500-750 MBq of Tc99m MDP/HMDP. SPECT: step and shot mode, 64x64 matrices, 64 projections, projections duration was 20-30 seconds. Images processing was done using iterative reconstruction. SPECT acquisition was done to define location of indeterminate uptake abnormalities seen in planar scan and to look after abnormalities when planar bone scan was normal in patients with pain. Bone SPECT was focused on vertebra in 27 cases and on pelvis in 2 cases.

Results: A total of 36 uptake abnormalities were seen in 27 patients (in SPECT focused region). SPECT bone scan showed abnormal uptake cortical bone in 15 patients. In two patients, SPECT eliminated doubt about bone abnormalities suspected on planar scan. SPECT bone scan found 2 new increased focal uptake. In ten patients, SPECT was able to determine if bone lesion was benign or malignant, confusion was related to increased uptake localisation near articulation.

Discussion: Bone scan is an accepted functional imaging technique for uncovering bone lesions. In our patients, the most frequent indication was looking after bone metastasises; both planar and SPECT bone scan had showed increased cortical bone uptake in 51% of our patients however in 41%, lesions remain indeterminate. The fact is that we need more specific results in bone scan findings to avoid false positive results related to degenerative and inflammatory lesions. The use of SPECT/computed tomography fusion and sodium F-18 fluoride PET/CT could help us improve accuracy of results and diagnosis confidence.
Imaging cancer therapeutic Trastuzumab bound on breast cancer cells with 111In-Biotin-Bn-EDTA-Anti-Human IgG1 monoclonal antibodies followed by the injection of macroaggregated albumin-avidin conjugate chase

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Binding of trastuzumab, a recombinant humanized IgG1 monoclonal antibody (MAb) against human epidermal growth factor receptor 2 (HER2) to breast cancer cells may activate antibody-dependent cell-mediated cytotoxicity (ADCC) as well as inhibit proliferation of the cancer cells. We have applied a macroaggregated albumin (MAA)-avidin conjugate chasing system in a functional imaging of the trastuzumab bound at the site of HER2 on breast cancer cells using two radiolabeled biotinylated anti-human IgG1 MAb. Methods: Biotinylated trastuzumab (4mg/g of mouse body weight) was intravenously administered to nude mice bearing BT-474 breast cancer cells xenografts overexpressing HER2 followed by MAA-avidin conjugate chase. 111In-biotin-Bn-EDTA-murine anti-human IgG1 (Fc specific) or (Fab specific) MAb was then injected to the nude mice at various times up to 24 hr. The biodistribution of radioactivity in nude mice was examined after MAA-avidin conjugate chase while the kinetics of cell-bound trastuzumab was investigated. As a control, other IgG subclass (Fc specific) or (Fab specific) MAb was used. Results: No significant difference in pharmacokinetics or therapeutic effect in nude mice was noted between trastuzumab and biotinylated trastuzumab. The amount of the trastuzumab bound to the tumor decreased with time and about 30% of the initial accumulation of trastuzumab remained at the tumor in the late stage. The bound trastuzumab could be significantly delineated at the early stage by radiolabeled anti-lgG1 (Fc specific) MAb but failed at the late stage, while it was significantly depicted by radiolabeled anti-lgG1 (Fab specific) MAb during the observation period. Conclusions: Cell-bound trastuzumab is able to be internalized and the remaining cell-bound (trastuzumab becomes gradually indemonstrable on the development with an antibody specific for the human IgG1 Fc region, suggesting that binding of trastuzumab to cells leads to interaction with immune effector cells.
Phosphorus 32 (32 P) skin patch for the treatment of basal cell carcinoma

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Introduction: 32 P with T ½ 14.3 days, emitting high energy beta particles (pure beta emitter) with max energy of 1.71 Mev, and decays to stable nonradioactive sulphur atom is an extremely useful but forgotten radioisotope in nuclear medicine. 32 P when incorporated into cotton skin patch of appropriate size, shape and dose can be very effectively used for the treatment of Basal Cell Carcinoma (BCC). Absence of gamma radiation reduces the dose to localized area and to the operator, besides it can be applied to the area not accessible to surgery or radiation.

Material and Method: 14 patients with histo-pathologically proven BBC in the age range of 45-74 (mean 57.25 years underwent this method of treatment after they had given a written consent to participate in a larger series. All patients had undergone detailed clinical examination, hemogram, liver, renal function tests, and skin biopsy. Skin patches of required size, shape and 32 P were applied at the tumour site for 3 hours which delivered a radiation dose of 3-4 K rads (30-40 Gy) to the lesion. Repeat patch was applied on 4th and 7th day. Follow-up was done at 1, 4 and 12 weeks post treatment for any skin reaction and to assess the efficacy of the treatment clinically, blood samples were also obtained to assess any side effects. Repeat biopsy was obtained at 12 weeks from the margins of the lesions to assess any residual disease.

Results: 32 P skin patches resulted in complete cure of superficial lesions from the skin with no evidence of malignancy in repeat biopsy. Radiation damage to the underlying and adjoin tissue was negligible because of ultra-short range of 2-3 mm of pure beta rays. There were no haematological, hepatic or renal toxicity.

Conclusion: Thus it has been shown that 32 P skin patches can be very effectively, safely, and conveniently used for treatment of BCC. The study is being enlarged to use 188 Rhenium skin patches and skin keloids.
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Outcome of radioactive iodine therapy in hyperthyroid HIV positive patients

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Radioactive Iodine Therapy (RIT) is a recognised permanent treatment option for hyperthyroid patients. This treatment option is becoming popular and is increasingly used in patients who are hyperthyroid and HIV positive.

Objective: The aim of this investigation was to determine the outcome in the first year following radioactive iodine therapy (I-131) in patients with hyperthyroidism who were tested positive for HIV-1 infection and are on antiretroviral medications. In the literature there is no data available on this patient cohort.

Methods: A total of 19 hyperthyroid HIV-1 positive patients were recruited in this study (13 female and 6 male), mean age 35±4 years. All patients were on antiretroviral therapy. Thyreostatic medication was discontinued for 3-5 days prior to I-131 treatment. An oral dose ranging between 10-20mCi of NaI I-131 given as a capsule was administered and patients were followed for one year.

Results: During the first three month post RIT, 11 patients (8 female and 3 male) developed hypothyroidism. Five patients became euthyroid and 3 patients, (all males) did not respond to the first RIT. The latter group received a second dose six months following the first RIT after which all patients became hypothyroid.

Conclusion: In this small cohort, it is suggested that HIV-1 infection and antiretroviral therapy have no effect on the outcome of RIT in hyperthyroid patients.
RADIOPHARMACY PET
Automated synthesis and quality control of apoptosis PET probe -18F-ML-10 with multipurpose platform

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Real-time imaging of apoptosis is of paramount importance in the assessment of tumour response to treatment improving personalized patient care. The apoptotic process is selectively tracked at its early stage by 18F-ML-10 (alpha\textsubscript{-}methyl-18F-alkyl-dicarboxylic acid). In this work, a fully automated and optimized method for the two-step synthesis and purification of 18F-ML-10 will be reported along with its quality control data. The analytical methods were validated according to ICH Q2. Complete process is supported by Synthera platform, comprising an automatic synthesizer and an HPLC system. The synthesizer employs single-use auto-ejectable cassette. Numerous (n=52) tests (up to 10 Ci) were performed to optimize synthesis parameters and purification conditions in order to enhance radiochemical yield and purity profile. Both fluorination of the tosylated precursor in acetonitrile and subsequent hydrolysis with aqueous HCl were performed at 110°C for approximately 10 min. Buffered reaction mixture was then purified by reversed-phase HPLC using 90 \% aqueous phosphate buffer/10 \% ethanol as mobile phase. This eluent system prevents the need of the time-consuming solvent replacement step. Radiochemical yields are > 40 \% after 60 min (total synthesis time including HPLC purification). Final product presents high radiochemical and chemical purity (> 99\%). In this work, we have described a fully automated and reliable synthesis and purification of the apoptosis PET tracer 18F-ML-10. This new synthesis procedure combines high and consistent yields, with the benefits of a disposable cassette system which is in line with GMP guidelines. The final product shows high radiochemical and chemical purity.
Optimized production of beyond FDG 18F-labelled radiopharmaceuticals with automated platform

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In this work, optimized syntheses for reliable production of highly specific probes such as [18F]-NaF (sodium fluoride) for bone metastasis detection; [18F]-FCH (fluoromethylcholine) for prostate cancer diagnosis and [18F]-FLT (fluoro-thymidine) for cell proliferation imaging were developed on IBA Synthera platform. The automated synthesis of each radiotracer takes place on single-use IFP (integrated fluidic processor). [18F]-NaF synthesis takes place in IFP Chromatography. For the [18F]-FCH, two synthesizers as well as two interconnected IFPs (IFP Distillation and IFP Alkylation) are necessary for the two-step synthesis. [18F]-FLT manufacturing employs the IFP Nucleophilic and the product obtained is purified via high performance liquid chromatography (HPLC) on Synthera HPLC unit. In neither of the applications hardware changes are required which is compatible with a multipurpose platform. [18F]-NaF is obtained in less than 10 minutes with quantitative yield. Analytical data show it complies with European Pharmacopoeia (Eur. Ph.). [18F]-FCH is produced in two steps: the first step is performed in IFP Distillation. It includes the fluorination of dibromomethane and purification of fluorinated volatile [18F]-fluorobromomethane by distillation through silica cartridges. The second step, in IFP alkylation, a solid-supported fluoromethylation of N,N-dimethylaminoethanol precursor is carried out resulting in [18F]-FCH which is then purified through a cation exchange cartridge. The use of adequate reversed phase cartridge for solid-supported alkylation maximized radiochemical yield (>20% EOS). The total synthesis time is < 50 minutes. Final product presents high radiochemical purity and chemical purity (>95 %). The synthesis of [18F]-FLT is accomplished in IFP Nucleophilic which supports several steps: [18F]-trapping and activation; nucleophilic substitution of the precursor; deprotection step (hydrolysis); dilution/neutralization. [18F]-fluorination of 3-N-Boc-5’-O-dimethoxytrityl-3’-O-nosyl-thymidine is carried out at 100°C followed by acid hydrolysis with diluted HCl. The resulting product is buffered and diluted with acetate solution before reversed-phase HPLC purification. Ethanol/ water is used as mobile phase. Typical retention time is approximately 23 minutes. Numerous (n=20) hot runs were performed in order to optimize all of the steps of the process resulting in a yield of >15 % EOS after HPLC purification. The total synthesis time is approximately 45 minutes. Final product presents high radiochemical purity and chemical purity (>95%). The automated platform has proven to be robust and reliable when it comes to routine production of promising radiopharmaceuticals beyond FDG such as [18F]-NaF, [18F]-FCH and [18F]-FLT for clinical applications. The radiochemical yields obtained are reproducible and stable and final products obtained show high radiochemical and chemical purity. All of the radiopharmaceutical syntheses are carried out within appropriate IFP cassettes (Chromatography, Distillation, Alkylation and Nucleophilic) in one single
platform set up with open software for customized applications. The IFP is a disposable, preventing cross-contamination and supporting line clearance which is in-line with GMP guidelines. The modules are fully interchangeable underpinning the platform multipurpose capability and flexibility. Synthera platform allows routine manufacturing, in a GMP environment, of a wide range of radiopharmaceuticals thanks to its proven consistency and reliability.
Building a radiopharmaceutical cyclotron production center from greenfield

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Objectives: Acquiring a cyclotron for radiopharmaceutical production is only the first step of a long and quite complex story. With its team of experts, IBA IntegraLab is streamlining the complete process towards a cGMP (good manufacturing practice) compliant radio pharmacy for PET and/or SPECT product.

Methods: Using the key steps of pharmacy development: Define, Design, Comply, Build and Run, the Integralab team will guide the future user to the completion of a radiopharmaceutical center which will be compliant to cGMP (pharmaceutical injectable drug) and radiation safety regulations. Both have constraints and usually provide guidelines for solutions that are totally in opposition. The users would like to compile as soon as possible a complete and detailed building file to call for local building companies and to apply for national license and permits. Such file will need first of all a consensus amongst the consultants, the user’s and the authorities (fire safety, radiation-atomic authority and Ministry of Health) as well as the local constraint of space and occupancy. In the first step, a good and exhaustive definition of the project is mandatory so as to get the most efficient design available. Special subjects such as radiation monitoring, ventilation and clean rooms, radiation shielding or waste handling must be covered by this file apart from the usual gas storage, electrical and fluid network in addition to a set of detailed requirements for room finishing and equipment (room data sheets and equipment requirements) which will reduce causes for failures or misinterpretation. After a kick-off meeting with architects and construction companies, global support during the construction phase is mandatory so as to quickly answer questions and provide expertise in building inspections key steps (before pouring concrete, before rigging, before installation). Overall project should have enough investment from the future user’s team as well as a Training program in the various fields for the new Centre’s Operation (chemistry, QA, logistics.)

Pitfalls and lessons to be learned: The first cause of failure is choosing a company without a track record of projects of the same kind or going with the smallest budget without having defined the extent of the work covered by the contract. Serious delays will occur during the re-discussion of the terms of the agreement, the budget or the scope between parties. Secondly, a poor definition of the goals of the Cyclotron Centre before design or changing too much the scope of work (addition of laboratories, new radioisotopes, changing available space) will certainly create frustration amongst the partners, delays and high costs for design. It is then better to define and design some space for ‘future development’ at the first stage of the process than adding it later to a greater cost. Other cause of failure is usually minimizing the extent of the Project Management for such projects and the need to co-ordinate and select various suppliers (besides cyclotron/chemistry; think about hotcell, analytical equipment, laboratory equipment, special techniques, etc.) answering the interface and requirement for each and dealing with the architect and the schedule of delivery/installation. Integration of radioprotection and radiation monitoring with the building management system and the cyclotron system must be based on a risk analysis of operation that cannot be done without
experience too. Finally the global extent of the support and availability of company experts during the construction phases, the documentation provided for the licenses and the training program must be clearly discussed in the global scope of the project to avoid delays. Having real experts around the table will ensure design with an efficient flow of people and material and enough ergonomy for the operation (how much bench length for a QC lab).

Conclusions: Everything is possible to a motivated investor but most of them have benefit of the IntegraLab consultancy and IBA Academy training to build rapidly and professionally their own centre. By streamlining the process, the duration gained is certainly a financial advantage; the moment to be operational on the market is definitely a key issue for users. A typical PET-center design and realisation is possible in 18 months. Long term support and development of new tracers is also covered by some companies with track records of successfully completed projects and a development roadmap.
Doubling the current on IBA PET cyclotrons and other enhancements

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Objectives: To reply to the strong demand of F-18 radio-tracer in PET (positron emission tomography) nuclear medicine and to enhance FDG production reliability, IBA has finished a development program on the Cyclone 18 PET cyclotron with the aim of increasing beam current and reliability. Reduction of human dose during maintenance was also considered.

Methods: This contribution will show the latest results that have been achieved on the IBA Cyclone 18. A new central region was designed to host two proton ion sources (Cyclone TWIN) in the cyclotron in order to achieve higher reliability and to reduce unexpected operation downtime especially for commercial FDG (fluorodeoxyglucose) suppliers. Doubling the extracted beam current from 80μA to 150μA has been done by developing a new RF amplifier of 16kW and by improvement to the central region and ion source system. Gamma cartography was done that leads to modification of some internal parts or use of other material to reduce activation.

Results: The new ion source improves lifetime and maintenance time. The stripper system has been reviewed in order to increase the foil lifetime and to make its replacement easier with a significant maintenance dose reduction. The beam current upgrade is proposed as factory upgrade but was also achieved on multiple machines in the field. The double proton sources (TWIN) has strongly increased uptime and production reliability on Customer’s sites, the concept was patented. The Twin proton source is now also available on the Cyclone 11. Modification of some internal parts showed a 5 to10 fold decrease in residual radiation field.

Conclusions: The latest development in PET cyclotron improved the fluor-18 production capacity from 10 to 18Ci in two hours in a reliable manner with both maintenance time and human dose reduction.
PET has been the most exciting modality in molecular imaging around the world. Apart from FDG, which is the most widely used tracer in PET nuclear medicine, research has continued on the creation and introduction of other PET radioisotopes and radiopharmaceuticals around the world. In this report, a review of recent works regarding production and preliminary studies of PET tracers has been introduced. FDG has been produced routinely for research studies and due to the installation of few PET cameras in the country. Regarding other radionuclides, ⁶¹⁶Cu an intermediate half-life PET tracer, has been prepared in curies and used in the production of important radiopharmaceuticals such as ⁶¹⁶Cu-ATSM, ⁶¹⁶Cu PTSM for diagnosis of hypoxia and perfusion studies respectively. ⁶⁴⁶Cu an interesting PET/therapeutic radionuclide was prepared in few hundred-millicurie amounts and used in the production of targeted therapy agents in our group successfully and used in the vast production of Cu-⁶⁴ ATSM for hypoxia tumour imaging. Gallium-⁶⁸, an important PET radionuclide, has been produced through an in-house developed generator in the country and soon would be released for possible demand. Rb-⁸²⁸m is another PET tracer used in PET cardiology as a K+ homologue and was produced in our centre using 30% enriched Kr gas. ⁶²⁶Zn/⁶²⁶Cu, an interesting PET generator has already been prepared by irradiation of natural copper and was used in radiolabeling of new tracers.
A fully automated radiosynthesis of 4-[F-18]fluorobenzaldehyde: A synthon for amine-oxy peptide labeling

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Direct and fast no-carrier added (n.c.a.) labelling of large and complex bio-molecules such as peptides with F-18 is very difficult for several reasons. As an alternative, several [F-18]-labelled synthons have been developed and used successfully for conjugation labelling of bio-molecules with F-18. Recently, a rapid and single step synthesis has been reported giving high-yields of [F-18]-labelled synthon, which can be chemoselectively conjugated to unprotected peptides in aqueous media and is stable against in vivo defluorination. The latter synthesis consists of a chemoselective oxime formation between an amine-oxy peptide and 4-[F-18] fluorobenzaldehyde. This methodology has been developed with the objective of large scale production of [F-18]-labelled peptides for supply to hospitals. In this abstract, we report the fully automated radiosynthesis of 4-[F-18] fluorobenzaldehyde starting from 4-nitro benzaldehyde using an adapted fluorination module similar to the GE TRACERlab FX-FDG module and single neutral alumina column purification. Satisfactory radiosynthesis yields with the desired purity were observed. [F-18]- produced in the Cyclotron [O-18 (p, n) F-18] is trapped in a small anion exchange column (Chromafix 45-PS-HCO3) and eluted as [F-18]TBAF (Tetrabutyl Ammonium Fluoride). Excess DNA-grade acetonitrile was added and the mixture distilled azeotropically until the [F-18]TBAF was dry. To this 5 mg 4-nitrobenzaldehyde in 1.0 ml DMSO was added and heated to 150°C for 15 minutes for radiofluorination. The reaction mixture is cooled to 65°C and passed through a single neutral alumina column. The reaction mixture is rinsed with 1.5 ml absolute ethanol passed through the column. Finally, 4-[F-18]fluorobenzaldehyde (4-[F-18]FB-CHO) was eluted with 8 ml 80% ethanol:20% water in the product vial. Finally, it was collected in multiple sterile and bacterial endotoxin free vials through 0.2µ filtration. The synthesized 4-[F-18]fluorobenzaldehyde is clear and light orange in colour. The RCP of 4-[F-18]fluorobenzaldehyde was >95% [Rf of 0.9 – 1.0 in MeCN: H2O (95:5)] and was confirmed by TLC of the reference standard 4-[F-19]fluorobenzaldehyde. Radiochemical purity was also confirmed by radio HPLC and comparing the retention time with the reference standard (Figure 1). The radionuclidic identity was confirmed to be F-18- by T1/2 measurements (110±5 minutes). All the batches produced passed the sterility and bacterial endotoxin tests. The total synthesis time is 35±1 minutes and the radiochemical yield is 30.1±1.1 % (n=10, without any decay correction). 4-[F-18]Fluorobenzaldehyde can be successfully synthesized using a general purpose fluorination module which in principle is identical with GE TRACERlab FXFDG with considerable yield in a short synthesis time. This method can easily be adapted in any commercial FDG synthesis module for routine production of 4-[F-18]fluorobenzaldehyde and subsequently for labelling aminox peptides.
FIG. 1. HPLC Spectrum of 4-[18F] Fluoro Benzaldehyde doped with reference standard 4-Fluoro-Benzaldehyde (Red Peak = UV peak of reference standard, Green peak = radioactivity peak of 4-[18F]-BZ, Radioactivity Peak, Rt = 12.50 min, UV (λ = 254 nm) Peak, Rt: 12.53 min) [C-18 RP (LiChroCART® 250-4), 0.5 ml/min flow rate, 80/20 Methanol/Water solvent].
A simple fully automated one-pot synthesis of 3'-deoxy-3'-[F-18]fluorothymidine

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[F-18]FDG is the most widely used PET-RP for tumour imaging using positron emission tomography (PET) technique. But the non-specific uptake of [F-18]FDG in brain as well as non-cancerous cells (macrophage, inflammatory cells) has shown the importance of 3'-deoxy-3'-[F-18]fluorothymidine ([F-18]FLT) as a proliferation tracer. [F-18]FLT has emerged out as a promising imaging agent for detection and assessing therapy response of lung cancer, brain tumour and other kind of cancer. During the last few years, several precursors as well as several novel methods have been developed for the synthesis of [F-18] FLT but they are either complicated or associated with low yield to be considered for routine production. More recently, semi-automatic synthesis of [F-18] FLT by using SEP PAK cartridges instead of HPLC purification at two-pot [F-18] FDG synthesis module (CTI Co., USA), with the radiochemical yield of 37.9% within a total synthesis time of 50 min, has been reported. Latest, a facile and rapid synthesis of [F-18] FLT with a decay uncorrected yield of 16-22% with SEP PAK columns purification has been reported in substantially modified PET-MF-2V-IT-I synthesis module (Beijing PET Company, China). Additionally FLT-Kit (Cartridge Version, ABX) are available for dedicated FLT synthesizers of different commercial companies (GE TRACERlab MS, BIOSCAN F-18 FLT LiteTM etc.). In this abstract, we report the synthesis of [F-18] FLT using an adapted general purpose fluorination module similar to GE TRACERlab FXFDG module and SEP-PAK® (WATER, USA) columns purification. A considerable radiosynthesis yield with the desired purity was observed. [F-18]F—produced in the Cyclotron [O-18 (p, n) F-18] is trapped in a small anion exchange column (Chromafix 45-PS-HCO3) and eluted as [F-18]TBAF (Tetrabutyl Ammonium Fluoride). Excess DNA-grade acetonitrile was added and the mixture distilled azeotropically until the [F-18]TBAF was dry. To this, is added 3N-BOC [3-N-t-butoxycarbonyl-(5’-O-(4,4’-dimethoxytriphenylmethyl)-2’-deoxy-3’-O-(4-nitrobenzenesulfonyl)-β-D-threo-pentofuranosyl)thymine] precursor, 30 mg in 1.0 ml acetonitrile and heated to 135˚C for 10 minutes for radiofluorination. After drying under vacuum under He-gas, 1ml HCl (1M) was added and heated to 105˚C for 10 minutes to knock out the protecting groups of the 3N-BOC precursor. The reaction mixture is cooled and passed through the series of properly conditioned SEP-PAK® (QMA Accell Plus→ C18 RP Plus→ ALUMINA N Plus). The reaction mixture is rinsed with 0.7 ml 15% ethanol containing water and passed through the columns. Finally, [F-18]FLT was eluted with 12 ml 10% ethanol containing water in the product vial already having 1.7 ml 10% NaCl and 0.7 ml 1(M)NaH2PO4 to maintain acceptable pH and isotonicity of the product. The final product is then dispensed through 0.2µ filter into sterile and bacterial endotoxin-free evacuated vials. Sterility and bacterial endotoxin tests were done on samples post radioactive decay. The quality of the [F-18]FLT synthesized is satisfactory from all respects. The final product is clear and colourless. The RCP of [F-18]FLT was >95% [Rf of 0.6 – 0.7 in MeCN: H2O (95:5) and 0.2-0.3 in Ethylacetate: heptane (60:30)] and was confirmed by TLC (Silica gel 60 F254, Merck) of the reference standard ([F-19]FLT). Radiochemical purity was also confirmed by radio HPLC and comparing the retention time with the reference standard (Fig.1). The radionuclidic identity was confirmed to be [F-18]F-
by T (½) measurements (110±5 minutes). All the batches produced passed the sterility and bacterial endotoxin tests. The total synthesis time is 45±5 minutes and the radiochemical yield is 18±2 % (n=5, without any decay correction). This does not include the trial batches to optimize the reaction conditions and the sequence of SEP-PAK®s. \( ^{[18F]} \)FLT can be successfully synthesized using a general purpose fluorination module which in principle is identical with GE TRACERlab FXFDG. This method can easily be adapted in any commercial FDG synthesis module for routine production of \( ^{[18F]} \)FLT.

FIG. 1. Radio-HPLC Spectrum of \( ^{[18F]} \)FLT (C-18 RP (250X4, 5µ, Machery Nagel Column), 7.5/92.5 (Ethanol/Water) solvent, 0.5ml/min flow rate) \( ^{18F} \)FLT, Rt = 31.8 min.
A single column purification technique for the fully automated radiosynthesis of [F-18]fluoroacetate: A potential acetate analog for prostate tumor imaging

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PET with [C-11]acetate ([C-11]ACE) has a high sensitivity for detection of prostate cancer and several other cancers that are poorly detected by [F-18]FDG. However, the potential for widespread use of [C-11]ACE is limited by a short half-life (20.4 min) of C-11, which necessitates production with an in-house cyclotron. Even with high yield synthesis, only a limited number of patients can be studied from a single-batch production. [F-18]fluoracetate ([F-18]FAC) is an analog of acetate with a longer radioactive half-life ([F-18]=110 min). In this abstract, we report, a novel fully automated radiosynthesis procedure for [F-18]-fluroacetate ([F-18]FAC) using a single combination column composed of neutral alumina and reverse phase resin, for purification in an adapted general purpose fluorination module. The developed procedure is very similar to [F-18FDG synthesis in GE TRACERlab FX-FDG module. A considerable radiosynthesis yield within a short synthesis time was observed. [F-18]F– produced in the cyclotron [O-18 (p, n)F-18] is trapped in a small anion exchange column (Chromafix 45-PS-HCO3) and eluted as [F-18]TBAF (Tetrabutyl Ammonium Fluoride). Excess DNA-grade acetonitrile was added and the mixture distilled azeotropically until the [F-18]TBAF was dry. To this, 10 mg ethyl (p-tosyloxy) acetate (precursor) in 1.0 ml MeCN was added and heated to 105°C for 7 minutes for radiofluorination. The reaction mixture is cooled to 65°C and then 1.5 ml 0.7 (M) NaOH for hydrolysis. Hydrolysis is carried out at the same temperature (65°C) in a closed reaction vessel for 10 min. After the completion of alkali hydrolysis, the reaction mixture is further cooled to 50°C and subsequently, the reaction mixture is passed through the properly conditioned combination purification column. The reaction mixture is rinsed with 1.5 ml 15% ethanol containing water and passed through the column. Finally, [F-18]-fluoracetate ([F-18]FAC) was eluted with 12 ml 15% ethanol containing water in the product vial. Lastly, it is collected in multiple sterile and bacterial endotoxin free vials through 0.2µ filtration. The synthesized [F-18]FAC is clear and colourless. The RCP of [F-18]FAC was >95% [Rf of 0.3 – 0.4 in MeCN: H2O (95:5)]. Radiochemical purity was also confirmed by radio HPLC (Figure1). The radionuclide identity was confirmed to be [F-18]F- by T (½ )measurements (110±5 minutes). All the batches produced passed the sterility and bacterial endotoxin tests (Tests have been carried out on post decayed samples). The total synthesis time is 40±1 minutes and the radiochemical yield is 47.2 ± 3.0 % (n=5, without any decay correction). [F-18]FAC can be successfully synthesized using a general purpose fluorination module which in principle is identical with GE TRACERlab FX-FDG with considerable yield in a short synthesis time. This method can easily be adapted in any commercial FDG synthesis module for routine production of [F-18]FAC for clinical use.
**FIG. 1**: Radio HPLC chromatogram of [18F]fluoroacetate, Retention time: 6.75 min.

LiChroCART® 250-4, HPLC cartridge, LiChrospher® 100 RP-18 (5µm), 30/70 MeOH/H2O solvent, 0.5 ml/min flow rate.
A single column purification technique for the fully automated radiosynthesis of [F-18]ethyl fluoroacetate ([F-18]EFA) as a proradiotracer of [F-18]Fluoroacetate ([F-18]FA) for the measurement of glial metabolism by PET

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Glial cells are the main effector cells of innate immune responses to neuronal damage in the central nervous system (CNS). Microglia and astrocytes are strongly activated in response to neuronal damage, producing an array of inflammatory mediators and performing phagocytic functions. Therefore, selective imaging of glial cell activity may be a valuable method to determine the extent and progress of disease and to access a therapeutic intervention. Furthermore, changes in glial metabolism in brain ischemia, Alzheimer’s disease, depression, schizophrenia, epilepsy and manganese neurotoxicity have been reported. Undisputedly, the measure of glial metabolism in vivo for the elucidation and diagnosis of these diseases has significant importance. [F-18] labelled fluoroacetate (FA) has been developed as a PET tracer for imaging of oxidative metabolism in various tissues. For brain studies, however, the low blood-brain barrier (BBB) permeability of anionic form like FA is a fundamental problem. It is well known that ethyl acetate penetrates easily in the brain, then, is hydrolysed to acetate rapidly in vivo, hence based on these characteristics, 18F-labelled ethyl fluoroacetate (EFA), ethyl-ester of FA, as a potential candidate of PET tracer of oxidative metabolism in the brain.

In this abstract, we report a novel fully automated radiosynthesis procedure for ethyl [F-18]fluoroacetate ([F-18]EFA) using a commercially available combination column, CHROMABOND® SET V (FDG-BASE-HYDR) for purification in an adapted general purpose fluorination module. A considerable radiosynthesis yield within a short synthesis time was observed. [F-18]F– produced in the Cyclotron [O-18 (p, n)F-18] is trapped in a small anion exchange column (Chromafix 45-PS-HCO3) and eluted as [F-18]TBAF (Tetrabutyl Ammonium Fluoride). Excess DNA-grade acetonitrile was added and the mixture distilled azeotropically until the [F-18]TBAF was dry. To this, 10 mg ethyl (p-tosyloxy) acetate (precursor) in 1.0 ml MeCN was added and heated to 105°C for 7 minutes for radiofluorination. The reaction mixture is cooled to 65°C and passed through a properly conditioned CHROMABOND® SET V (FDG-BASE-HYDR, ABX) column. The reaction mixture is rinsed with 2.0 ml absolute ethanol passed through the column. Finally, ([F-18]EFA) was eluted with 10 ml absolute ethanol in the product vial. Lastly, it is collected in multiple sterile and bacterial endotoxin free vials through 0.2µ filtration. The synthesized [F-18]EFA is clear and colourless. The RCP of [F-18]EFA was >95% [Rf of 0.9 – 1.0 in MeCN: H2O (95:5)] (Fig.1). Radiochemical purity was also confirmed by radio HPLC. The radionuclidic identity was confirmed to be [F-18]F- by T (½) measurements (110±5 minutes). All the batches produced passed the sterility and bacterial endotoxin tests. The total synthesis time is 32±1 minutes and the radiochemical yield is 44.0±1.5 % (n=5, without any decay correction). [F-18]EFA can be successfully synthesized using a general purpose fluorination module which in principle is identical with GE TRACERlab FXFDG with considerable yield in a short synthesis time. This method can easily be adapted in any commercial FDG synthesis module for routine production of [F-18]EFA for clinical use.
FIG. 1. Radio TLC of Ethyl [F-18]fluoroacetate in 95:5 MeCN/H2O.

TLC Shows RCP more than 99% Absence of free [F-18]F- (Rf : 0.02) and [F-18]fluoroacetate (Rf : 0.3).
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[18F]-FLT purification by SPE method in a fully automated synthesis procedure using a commercial synthesizer

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The aim of this work is to investigate the feasibility of purifying [18F]-FLT by SPE (solid phase extraction)

Method: [18F]-FLT purification procedure is commonly performed by Radio-HPLC method. This is highly effective and widely used in radiopharmaceutical preparation, however it is time consuming, it uses large amount of solvent, it requires expert personnel and to work in sterile conditions when required can be problematic. The idea of substituting the HPLC purification with a SPE (solid phase extraction) method aims to shorten the overall time of synthesis, to reduce the amount of solvent used and to implement a simpler methodology of synthesis. [18F]-FLT synthesis has been performed by a commercial available synthesizer (TRACER lab™ FXF-N) and it has been achieved with the following steps: a) enriched water recovery through a cartridge Chromafix Ps-H+ followed by elution, in the reaction vessel, of 18F- with 0.5 ml water solution (3 mg) of K2CO3; b) introduction in the reaction vessel of 15 mg Kryptofix 222 in 1 ml acetonitrile followed evaporation at 85 °C for 6 min; c) after complete evaporation introduction in the reaction vessel of 15 mg of 3-N-Boc-5′-O-dimethoxytrityl-3′-O-nosyl-thymidine in 1 ml acetonitrile. The labelling reaction is achieved at 105 min for 10 min; d) introduction in the reaction vessel of 1 ml 1 M hydrochloric acid for hydrolysis carried out at 105 °C for 5 min. After cooling, the crude product is purified by SPE. The implementation of this method of purification on the synthesizer does not require any hardware modification and it is based on the use of a copolymer cartridge (lipophilic-hydrophilic polymer balance), an AlN (Al2O3 column N type) and an anionic exchange cartridge type SAX. The purification steps are performed as following: The crude product is passed throughout AlN to remove all undesired compounds with polar function and unwonted aromatic compound, afterwards throughout the copolymer cartridge. Here, the [18F]-FLT is entrapped. Then, copolymer cartridge is firstly washed with 15 ml water for injectable solution and afterwards [18F]-FLT is eluted by 3.5 ml ethanol/water solution (30/70; v/v). The purified product is then diluted in water for injectable solution as required. Finally, the water solution is passed throughout an anionic exchange cartridge to remove any 18F-. The overall time of synthesis lasts about 40 min. It has achieved a RCY of about 10% decay corrected (n=3), with a radiochemical purity above 97%. Quality control was performed by HPLC with a C18 column (Econosil, 10 micron, I.D. 4.6mm, L 250 mm), 1 ml flow water/ethanol (90/10, v/v). [18F]-FLT retention time has been 10.2 min. The suggested method of purification of [18F]-FLT by SPE is reliable, simple and effective and it sensibly reduces the time of synthesis as well as the amount of solvent used. In addition, sterile working conditions are easier to be kept.
18F-FDG production experience at IPEN-CNEN/SP


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The most important radiopharmaceutical used routinely worldwide in clinical PET studies is the 2-[18F]fluoro-2-deoxy-D-glucose (18F-FDG), for brain, heart and tumour studies, as well as in basic research. This compound has provided a valuable tool for the study of the glucose metabolism in both normal and disease tissue. The synthesis is achieved by a nucleophilic substitution reaction in an automatic module available for production. The main advantages of this method are the high purity of the final product, the reduced synthesis time and the decreased radiation exposition to the workers. IPEN was the first 18F-FDG supplier in Brazil and started the production in 1998. In the last years an increase was observed in the number of PET/CT installed in Brazil. The objective of this work is to describe the improvement in the routine production and quality control of 18F-FDG at IPEN-CEN/SP. The present infrastructure consists in 02 cyclotrons (30 and 18 MeV from IBA), 03 synthesis modules (TraceLab GE) and the installation and qualification of new laboratory under GMP rules. The 18F- is obtained by the nuclear reaction 18O(p,n)18F using enriched H218O (97 %). At the end of bombardment the fluoride is transferred directly to the automatic module. All the reagents are with ultra-pure degree and provided as a “reagents kit” (ABX) that must be fit 15 - 20 minutes before the start of the synthesis. The automatic synthesis is achieved in 25 minutes. The impurities are trapped automatically and the labelled precursor is washed away and sterilized by 0.22 mm Millipore filter. The resulting neutral eluent (16 ± 0.6) ml of 18F-FDG is dispensing in a sterile glass vial. Thin layer chromatography system is carried out for radiochemical and chemical assays, in TLC using acetonitrile: H2O (95:5) and NH4OH: MeOH (1:9) as solvents, respectively. Stability of 18F-FDG is determined immediately and 10 hours at the end of synthesis (EOS). Sterility and pyrogen tests are performed by the microbiology procedures outlined in the pharmacopoeias in different culture medium. The apirogenicity is evaluated using the “in-vitro” Limulus test (LAL). In the year 2010, 567 irradiations were performed, in a total of 1,128 hours, producing 107.5 GBq of 18Ffluorine. The yield of synthesis was (47.0±9.4)% EOS. The radiochemical purity of 18F-FDG was (99.04 ±0.96)% and (95.91 ±4.09)%, immediately and 10 hours EOS, respectively. The Kriptofix level was below the detection limit of colour spot test. Sterility and pyrogen tests were negative in all delivered vials. During the last year (2010), the Radiopharmacy Centre has produced 92,500 – 110,000 MBq/batch of 18F-FDG at the end of synthesis (EOS) and distributed 11.67 GBq of 18F-FDG in 3,535 doses at nuclear medicine services in Brazil.
Critical factors for a successful installation of a cyclotron site

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By the end of 2006, Instituto de Radiologia do Hospital das Clínicas da Universidade de São Paulo, InRad-HC-USP, has decided to implement an entire cyclotron project. The main reasons being the lifting of restricted production of short-lived radioisotopes by the National Commission of Nuclear Energy (CNEN) and the planned installation of 4 to 5 PET/CT systems in the largest Brazilian public hospital complex. It was declared by the hospital administration as a turn-key project for the installation of a 16.5 MeV cyclotron. A turn-key project implies that the chosen accelerator supplier is also responsible for the entire project, including the construction of the bunker, the laboratories, offices and all others facilities, as well as the devices and third parties involved. In order to follow the entire installation process, the hospital set up a multi-disciplinary team of pharmacists, physicians, physicists, engineers and managers, among other professionals. This proved to be a correct decision as many of the difficulties were overcome by the joint effort of this group and the supplier. There are many reasons for contracting one project under a turn-key modality, and we choose to highlight two of them: 1) The high complexity involved and the managerial control of such a project. 2) The establishment of a partnership with Hospital Sirio Libanes, which is an important private health care organization in São Paulo. The partnership is guided by a document named “Technical - Scientific Agreement”, which allowed for the Hospital Sirio Libanes to participate with half of the required funds. This agreement also forecasts the pay back to the hospital by supplying Fluorodesoxyglucose, FDG-F-18, during the following five years. An additional important factor of the project is the location of InRad-HC-USP in a region where one can find several hospitals with PET facilities, most of them not farther than 10 kilometers away. This reduces the effects of F-18 radioactive decay. This report shows us that there many factors that can contribute to a successful implementation of a cyclotron site in public service. However, three of them are equally critical: the public institution has to be completely committed with the project, both at the financial and administrative level; the adoption of a turn-key project modality, to reduce handling of complex projects and to gain greater managerial control; and the establishment of partnerships with different health organizations that can provide part of the funding.
Nuclear medicine has grown exponentially owing to extensive research and technological advances over the past 65 years. Nuclear Medicine has propagated at varying pace in developed and developing countries mostly owing to high cost of equipment and radiopharmaceuticals involved. The concept of emission transmission tomography which was put forward in the early 1950s by Kuhl et al culminated in clinical use of PET in the 90s. PET-CT has revolutionized disease management. Growth of this modality is tremendous in developed countries. However, many developing countries like Pakistan are severely falling behind in introduction of this imaging technique. The perspective from a developing country is different from that of developed countries, as the health care is not the priority due to financial constraints. Pakistan like many other developing countries is spending less than 1% of the GDP on its health sector with the greatest expenditures on the basic health issues. For establishing a PET cyclotron facility initial investment was well outside the range of the country’s health care budget. The first government aided PET cyclotron facility in Pakistan will shortly start functioning. The astute use of this PET-Cyclotron facility is mandatory to enable PET to be applied in a reasonable and effective manner without risk of underutilization. Few practical steps to be taken in account to justify this expensive modality will be discussed. Running the centre as centralized cyclotron facility will distribute FDG to a number of PET scanners operating in parallel. The provision of FDG on commercial basis has some prerequisites like availability of PET scanner only facilities, in transportable range of cyclotron facility. The second step which can be taken to ensure proper utilization is to keep the cost of the PET scan in an affordable range for patients. As there is no concept of a health reimbursement system in the country, the costs of the test is usually born by the patient himself so keeping prices of the test too high will eventually result in a decrease of the number of patients. Accordingly, higher throughput offers cost efficiency advantages. Judicious use of PET also includes educating referring physicians about the legitimate and proper indication of test as it is an expensive modality and improper use will not only be burden to the patient but to the facility as well. More accurate and appropriate allocation of therapeutic resources can substantially counterbalance the cost of more expensive diagnostic and therapeutic procedures. Steps to reduce annual expenditure and costs can be obtained by adopting measures which extend the life of equipment and site expenditures. Last but not least, one of contributor of the capital cost is employing the staff to run the PET-cyclotron facility. This cost can be saved by utilizing ample qualified staff employed in PAEC.

The need for a carefully planned strategy for running the country’s first government owned PET centre is crucial in the pecuniary conditions prevailing in Pakistan, where the dissemination of PET may be impeded by a scarcity of financial resources and an inadequate understanding of the potential contributions PET imaging can play in a health care system.
**Synthesis and preliminary evaluation of a 68Ga-DOTA complex with a nitroimidazol moiety as potential radiopharmaceutical with selectivity towards hypoxic tissue**

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Tumour perfusion and oxygenation status have been recognized as important factors that may cause poor treatment outcome after radio and chemotherapy. In addition, hypoxic cells are very resistant to radiation damage and diffusional limitations also restrict the efficacy of cytotoxic drugs. The aim of this work is to develop a potential 68Ga-radiopharmaceutical with selectivity towards hypoxic tissue. The selected pharmacophore was a nitroimidazole, of recognized biorreductive capacity. This reduction is irreversible in hypoxic tissue resulting in entrapment of metabolites within the cells.

Metronidazole (commercial anti-parasitic bearing a 5-nitroimidazol moiety) was used as starting reagent. The metronidazole-OH-group was transformed into a primary amine in a two-step reaction and this intermediate was coupled to an activated DOTA unit: (N-hydroxy-succinimide)-DOTA ester). Identity of the final compound was confirmed by 1H-NMR spectroscopy and mass spectrometry. 68Ga-labeling was performed using a 68Ge/68Ga generator eluate, 5M acetate buffer (pH=4.6) and 18 nmoles of ligand under 10 minutes of heating at 95°C. Proposed complex structure is shown in figure. Radiochemical purity was determined by reverse phase HPLC using a C18 column and a mobile phase gradient consisting of trifluoroacetic acid (TFA) 0.1% in water and TFA 0.1% in acetonitrile. A single species with radiochemical purity above 99% was obtained with stability for at least 4 hours in reaction milieu. The complex is highly hydrophilic, as demonstrated by the logP in octanol:phosphate buffer pH=7.4 of -1.65±0.05. Additionally, this complex exhibited a low plasma protein binding (2.3±0.1%, at 60 minutes of incubation, determined by molecular exclusion). Biodistribution studies in C57 mice bearing induced Lewis carcinoma, 3 animals per group, were performed at 0.5, 1, 1.5 and 2 hours post-injection. Results show that this complex has a moderate tumour uptake (1.0 % at 1 h post-injection) and adequate retention (1.05±0.09% at 1.5 h). Favourable tumour/muscle ratio of 1.98±0.62 at 2 h post injection results from soft tissue depuration. Blood uptake is low during the studied period and a favourable tumour/blood ratio of 2.44±0.37% is obtained after 2 h. Liver uptake is also low, as expected from lipophilicity and protein binding studies. Urinary clearance is high at 0.5 h, 76.6±5.3%, reaching a value of 91.0±0.4% after 2 h. Other organs uptake is negligible.
In conclusion, synthesis of a new DOTA derivative bearing a nitroimidazole unit as active moiety was successfully achieved. Labelling with $^{68}$Ga was performed with high radiochemical purity. Biodistribution results show preferential uptake in tumour and high renal elimination. These results are promising and further biological evaluation is required to confirm the initial findings.
Optimization of 68Ga-DOTA-TATE labelling for the first PET clinical applications in Uruguay

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68-Ga-DOTA-TATE is a radiopharmaceutical suitable for molecular imaging of neuroendocrine tumours due to its high affinity for somatostatin receptors of subtype 2. First we characterized and optimized the elution of the 68Ge/68Ga IGG100 Eckert & Ziegler-50M generator. To reduce the radiation dose to the operator in the elution step the generator was connected to a peristaltic pump, in order to perform each elution with 5 mL of ultrapure 0.1 M HCl with a flow of 1.7 mL / min.

Labelling of DOTA-TATE with 68Ga was tested using different elution volumes starting with the complete elution of 5 mL up to the activity peak with different volumes of the fractionated elution. Radionuclidic purity was determined in 2.3 to 3.6 mL volumes peaks (containing 90 to 97\% of the total eluted activity) by solid scintillation NaI (Tl) (3x3", Ortec), resulting in a content less than 10E-05\% of 68Ge. In the labelling process we studied various parameters, heating time, pH and amount of peptide used in order to achieve the highest specific activity with suitable radiochemical purity in the shortest time. The heating time optimization was carried out using dry block at 100ºC, 28 nmol of DOTA-TATE, assaying the time between 1 and 15 minutes, 10 minutes was ultimately chosen as the optimum time. For pH adjustment we used 22.5 nmol of peptide, 100º C for 10 minutes in a pH range of 3 to 6, resulting that pH 4 was the more appropriate (using acetate buffer). At last, we analysed the amount of peptide in the conditions previously optimized, testing this between 60 and 12.5 nmol, 20 nmol being ultimately selected for use. Finally we studied the insertion of a final purification step for the labelled solution through Sep-pak C18 light cartridge, considering the 68Ge amount variation in the process. We obtained 10E-06\% of 68Ge activity in the labelled solution unpurified and an undetectable level of 68Ge in the purified solution, so we chose to perform this purification procedure to decrease the amount of impurities to inject the patient. Due to the need to fulfill the requirements for an injectable solution, the labelling process was ended by a sterile filtration (0.2 um), in a shielded laminar flow located in a clean area where all procedures were performed. Compliance was verified with sterility testing. The radiochemical purity of 68Ga-DOTA-TATE was determined by HPLC using a C18 column (4.6x150 mm), water: acetonitrile (76:24) with 0.1\% trifluoroacetic acid was used as solvent and a flow of 1 mL/min (68Ga-DOTA-TATE tr = 5.0 min; 68GaCl3 tr = 1.5 min). For the colloid determination ITLC-SG was used as support and 0.15 M ammonium acetate:methanol (1:1) as mobile phase (Rf (Colloid+68GaCl3) = 0, Rf (68Ga-DOTA-TATE) = 1).
The optimized procedure allowed the provision of 68Ga-DOTA-TATE in a reproducible manner, verifying the conditions required to inject patients. At the moment we have examined more than 90 patients with the first available positron emitting radiopharmaceutical in the country.
In recent years the interest in 68Ga labelled agents useful in diagnostic procedures in PET is increasing rapidly followed by the increasing number of 68Ga/68Ge generators users and suppliers. Previous studies on the 68Ga labelling of DOTA-chelated peptides revealed that labelling pH at the level of 3.5 – 4.0 has critical influence on the labelling yield. Hence, optimization of labelling procedures is required in order to reduce time necessary for efficient radiopharmaceutical preparation, involving automation of the process. The goal of this work was to establish a routine procedure for 68Ga labelling of DOTATATE using the SnO2 based 68Ge/68Ga generator for their further use in PET/CT diagnosis of patients with neuroendocrine tumours (NETs).

Methods: The SnO2 based generator (iThembaLABS) was eluted with 0.6 M HCl according to the instructions provided by the supplier. Only the first 3 mL of eluate (254 – 1640 MBq of 68Ga) were further used for labelling of 100 μg DOTATATE (piChem, Austria) dissolved in 2.4 mL 1,25 M AcONa, giving final pH of about 3.7. Incubation was carried out at 95°C for 15 mins using a heating oven. Final product was purified using solid phase extraction (SPE) C-18 0.1 mg minicolumn (Waters). Radiochemical purity was assessed by HPLC using C-12 Jupiter/Phenomenex column and gradient of 0.1%TFA/ACN and 0.1%TFA/H2O. Finally the product was sterilized by filtration. Content of 68Ge was assessed by gamma-spectrometry.

Results: Labelling yields in the range 37.4 to 72.4% (median 61.6%) were obtained in 106 consecutive labelling runs (calculated as % of 68Ga-DOTATATE fraction radioactivity related to the radioactivity of eluate used for synthesis, no time correction) in the labelling procedure lasting 20-25 min. After SPE purification the radiochemical purity was >99%. Gamma-spectrometry revealed not more than 5x10-4% of 68Ge in the 68Ga-DOTATATE.

Conclusions: High labelling yields and high radiochemical purity of 68Ga-DOTATATE allowed its use in patients. The labelling procedure has been validated in the hospital radiopharmacy. More than 300 patient doses of 120-185MBq were prepared. The clinical usefulness of 68Ga-DPTATATE PET/CT was proved in localizing primary tumour and disease staging of NET patients.
Development of the radiopharmaceutical 18F-acetate for detection of primary tumour of breast prostate

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The design of 18F-FAC (fluoroacetate) aims its production and its application on the detection of primary prostate and breast tumours, using PET-CT (positron emission computed tomography) techniques. Recent studies show the efficacy of the 18F-FAc in the detection of tumours that have low 18F-FDG (fluorodeoxyglucose) uptake. Fluoroacetate is a substrate for the enzyme acetyl-CoA synthase that metabolizes acid fluorocitrate that, not being metabolized, causes inhibition of aconitase and inhibition of tricarboxylic acid. The overexpression of FAZ (fatty acid synthase) is shown in many cancers, especially in prostate cancer where the degree of overexpression is related to tumour aggressiveness. Prostate cancer has a low avidity by 18F-FDG, as well as breast cancer. Renal elimination of 18F-FDG makes the visualization of lesions difficult in the pelvic area. Breast cancer is diagnosed by mammography because of the high sensitivity but it has low positive value for malignancy, leading patients to surgical biopsy that is often unnecessary. Furthermore, the low negative value for dense breasts, severe fibrocystic disease, implants, and patients who have undergone surgery or radiotherapy. Thus, fluoroacetate, in breast cancer, is useful in detecting small tumours leading to the decrease of the false-negative results. The aim of this paper is to present the initial results of the project for the production of 18F-acetate. The labelling of sodium fluoroacetate with 18F-(fluoride ion) is made by nucleophilic substitution of the precursor (ethyl O-mesyl-glycolate) by 18F\textsuperscript{-}, followed by hydrolysis. The fluoride ion will be produced at IPEN using the Cyclone 30 and 18 cyclotrons from IBA, by irradiating to enriched 18O water with protons. The step of labelling will be performed in the same synthesis module used in the production of 18F-FDG, using kits purchased from ABX. The optimization variables for labelling are: time, temperature, mass of precursor, pH, 18F-activity, the mass of solvent and kryptofix. The following controls will be performed: radionuclidic and chemical controls for 18F- and radiochemical, chemical and radionuclidic controls for 18F-FAC in order to evaluate the optimization of production and final product quality. The stability of 18F-FAC will also be studied. The initial results showed that the labelling yield is about 37\% for the 3 reaction temperatures studied (85\textdegree{}C, 95\textdegree{}C and 105\textdegree{}C). The radiochemical purity is higher than 99\% and the product is stable up to 5 hours.
Preparation and preliminary studies on 68Ga-labeled cyclic RGD peptide dimer as a potential PET radiotracer for tumour imaging

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Integrin $\alpha v\beta 3$ plays a significant role in angiogenesis during tumour growth and metastasis, and is a receptor for the extracellular matrix proteins with the exposed arginine(R)-glycine(G)-aspartic acid(D) tripeptide sequence. The overexpression of integrin $\alpha v\beta 3$ during tumour growth and metastasis presents an interesting molecular target for both early detection and treatment of rapidly growing solid tumours. The recent introduction of 68Ga-PET imaging into clinical practice has made a significant impact in the field of PET imaging which does not require the availability of a cyclotron. 68Ga is a positron emitter with a short half-life of 68 min, which is suitable for the pharmacokinetics of many peptides and other small molecules owing to their quick blood clearance and rapid target localization. In the present study the cyclic RGD peptide dimer E$[c(RGDfK)]_2$ (E = Glutamic acid, f = phenyl alanine, K = lysine) coupled to the bifunctional chelator DOTA is chosen as the targeting biomolecule owing to the improved tumour uptake and retention of the dimer compared to its monomeric counterpart. Taking these factors into consideration, an attempt has been made to prepare 68Ga labelled DOTA-E$[c(RGDfK)]_2$ as a potential PET radiotracer for tumour imaging.

E$[c(RGDfK)]_2$ was coupled to DOTA using DOTA-NHS ester. The conjugate was purified by semi-preparative HPLC and characterized by MALDI mass spectrometry. 68Ga was obtained from a 68Ge/68Ga generator developed in-house using nanoceria-polyacrylonitrile (PAN) composite sorbent. The 68Ga complex of DOTA-E$[c(RGDfK)]_2$ was prepared with > 98% radiochemical purity as determined by radio-HPLC technique and the complex exhibited excellent in vitro stability. Biological behaviour of the radiotracer prepared was studied in Swiss mice bearing fibrosarcoma tumours. The results of the biodistribution studies revealed significant tumour uptake within 10 min p.i. (4.14 ± 0.54 %IA/g). The activity accumulated in the tumour was observed to increase further (4.61 ± 0.31 %IA/g) at 30 min p.i. Initial accumulation of activity was observed in various non-target organs viz. liver, GIT, kidney, lungs etc. However, with the progress of time, the uptake in non-target organs was observed to reduce gradually. The tumour/organ ratio of the radiotracer at different time points p.i. for the major organs/tissue is shown in Figure 1. The tumour to blood ratio was observed to increase from 1.75 ± 0.42 at 10 min p.i. to 2.25 ± 0.20 at 60 min p.i., while the tumour to liver and tumour to muscle ratio increased from 2.71 ± 0.76 to 3.31 ± 0.84 and 5.37 ± 1.08 to 8.97 ± 1.32, respectively, between the same time points. The radiolabeled conjugate exhibited predominant urinary excretion, as more than 80% of the injected activity cleared via renal pathway within 60 min p.i.
These preliminary studies indicate the potential of the developed agent for possible use in early detection of the tumor by PET imaging. However, further studies are warranted in animal models to assess the potential applicability of the agent.

**FIG. 1.** The tumour/organ ratio of 68Ga-DOTA- E[c(RGDfK)]2 complex at different time points p.i. for the major organs/tissue in Swiss mice bearing fibrosarcoma tumours.
Methods of purification of 68Ga for biomolecules labelling

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The positron-emitting 68Ga (T1/2=68 min) obtained from the 68Ge-68Ga generator is a metallic radionuclide adequate for labelling biomolecules. However, the eluate from commercial generators still contains high levels of long lived 68Ge, besides other metallic impurities, which competes with 68Ga with a consequent reduction of the labelling yield of biomolecules. Moreover, the successful clinical application of peptides demands a high specific radioactivity, considering the limited amount of receptors, high binding affinity to receptor and the possibility of pharmacological side effects. Thus, the lower the amount of impurities in the eluate, the smaller the competition between the radiolabeled and unlabelled peptide by the receptor, the quality of imaging will be better. In order to reduce impurities, a subsequent purification step is needed after the generator elution. The aim of this work is to present the results of the preliminary steps of the purification of 68Ga and further radiolabeling with DOTATOC. A commercial generator based on a TiO2 phase adsorbing 68Ge was obtained from Cyclotron Co. (Obninsk, Russian Federation). The first purification column used was a standard syringe (1mL), containing 0.5 mL of the cation exchange resin AG50W-X8 (H+, 200-400 mesh). Pure 68Ga was eluted with 1mL of a mixture of acetone/12 mol L\textsuperscript{-1} HCl (97:0.4)\% and the elution yield was (52.0±0.6)\% (n=2). The DOTATOC (0.05 mg diluted in 5mL water) was labelled with 68Ga at 100\degree C during 10 minutes. The reaction mixture was passed through a Sep-Pak C-18 Light cartridge to purify the labelled peptide. The best labelling yield for 68Ga-DOTATOC was 26\% with radiochemical purity higher than 98\%. Nevertheless, the glass wool that served as a physical barrier to prevent the passage of the resin to the syringe was not sufficient and the eluate contained a small portion of the resin. In order to improve the quality of 68Ga, other purification methods were tested. First, the volume of cationic resin was reduced from 0.5 mL to 0.05 mL and the elution conditions were maintained. With this effort, satisfactory results of elution yield were obtained (70±10)\% (n=13); even so the levels of impurities were high (0.02mg for Zn, Ge, Fe and Ti). Therefore, another method was tested, the conventional method of purification using diisopropyl ether extraction with added TiCl\textsubscript{3}, which the advantage is obtaining purified gallium directly in aqueous solution. A solution containing 67Ga in 7 mol.L\textsuperscript{-1} HCl was extracted with satisfactory (73±0.1)\% (n=3), however this method was time consuming and not useful for the short half-life of 68Ga. For this reason, the purification studies shifted towards the preparation of extraction chromatography column based in the absorption of diisopropyl ether in XAD-16 (20-60 mesh), which was tested with both radionuclides. The preliminary results showed that the elution yield for 67Ga was (78±4)\% (n=7) and 67\% (n=1) for 68Ga (at pH 5). However, the total level of impurities, mainly Zn, for 68Ga was the same (0.02mg) and efforts must be done to decrease the levels of Zn in the 68Ga eluate.
Preparation and biological evaluation of 64Cu-CB-TE1A1P-LLP2A, a peptidomimetic ligand targeting α4β1-positive tumours with high affinity and stability

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Small peptide-based agents serve as cancer-targeting agents for diagnostic imaging and targeted therapy. N-[[4-[[[[2-ethylphenyl]amino]carbonyl]amino]phenyl]acetyl]-Ne-6-[(2E)-1-oxo-3-(3-pyridinyl-2-propenyl)]-L-lysyl-L-2-aminohexanediol-(1-amino-1-cyclohexane) carboxamide (LLP2A) is a high-affinity, high-specificity peptidomimetic ligand that binds the activated α4β1 integrin found on a variety of malignant lymphoid cell lines. It was reported that 64Cu-CB-TE2A-LLP2A had uptake in VLA-4 (very late antigen-4, also known as α4β1 integrin) expressing tumour, spleen and bone marrow. We conjugated LLP2A with CB-1, 4, 8, 11-tetraazacyclotetradecane-1-(methanephosphonic acid)-8-(methanecarboxylic acid) (CB-TE1A1P), a new developed copper chelator with high stability. In comparison with CB-TE2A-LLP2A, synthesized CB-TE1A1P-LLP2A was further investigated via biodistribution and microPET imaging. CB-TE1A1P-LLP2A was synthesized, purified via HPLC. Radio labeling of CB-TE1A1P-LLP2A with 64Cu had a purity exceeding 97% and the specific activity is 1 mCi/ug. Cellular uptake experiments were carried out in B16, RPMI 8226 and U266 cell lines. The cells were incubated with 10 nm 64Cu-TE1A1P-LLP2A with or without 1000-fold cold peptide for 1 h at 37 oC. Cell uptake studies validated the internalization to be a receptor-specific process. MicroPET studies were performed on mice bearing B16F10 tumours followed by biodistribution studies. MicroPET imaging performed on mice planted with B16 cells proved that CB-TE1A1P-LLP2A had a higher tumour to background ratio than CB-TE2A-LLP2A. Tumour uptake could be blocked by high doses of LLP2A. 64Cu-CB-TE1A1P-LLP2A was also evaluated in the mouse model of human multiple myeloma (MM) cells, RPMI 8226-luc-GFP and U266-luc-GFP by PET/CT. PET/CT imaging showed high tracer uptake in the legs and spleen, where MM tumour accumulated. In conclusion, 64Cu-CB-TE1A1P-LLP2A can effectively image VLA-4 on B16F10 and multiple myeloma cells and may be highly effective in monitoring therapy.

FIG. 1. Chemical Structure of CB-TE1A1P-LLP2A
We are a PET/CT- cyclotron centre from Argentina. We produce radiopharmaceuticals in our laboratories for internal use, as well as supply other PET centres with the latter. In Latin America, most of the PET centres are founded by the National State of each country. Our roots come from national entities (CNEA – National Commission of Atomic Energy). At the beginning of the habilitation process, we faced several controversies and vicissitudes in regulatory issues caused by the lack of experience in the field from the regulating authorities. In Argentina, authority requirements are the same as for multinational laboratories. There was a lack of experience and existing references at the time in which we were running the project.

Conclusion: We strongly believe that it is necessary to establish regional workgroups in order to combine efforts to face regulatory authorities’ requirements.
The aim of this work is to share our production experience at Fundacion Centro Diagnostico Nuclear (FCDN, Buenos Aires, Argentina) in the first four years, working with a Siemens RDS111 cyclotron and a GE Tracerlab FXFDG. In this period, more than 800 productions were run. About 1700 Ci of 18F and 1000 Ci of FDG were produced. Activities, radiochemical yield (average EOS yield 52%) and relevant QC data (average Radiochemical purity 99.2%) are presented and the importance of preventive maintenance is shown. All processes are conducted following GMP, attending both internal (PET Services) and external clients (local and regional).

In conclusion, in these four years we established a reliable and competitive radiopharmaceutical service, despite the fact that only one module is available. Due to the high maintenance needed for Tracerlab FXFDG, the acquisition of a new module is imperative, aiming to improve the reliability and throughput of activity that the near future market requires.
Preclinical evaluation of fluorine-18 labelled bombesin peptide analogs as potential PET radiopharmaceuticals for breast cancer imaging

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Introduction: Radiolabeled peptides continue to emerge as potential radiopharmaceuticals for targeting several diseases such as cancer. One of these peptides is bombesin’s analog (BN) a 14-amino acid peptide that has a high affinity for the gastrin-releasing peptide (GRP) receptor. A wide variety of human tumours, including breast cancer are known to express receptors specific for BN-like peptides. Recently, several analogs of BN-peptides radiolabeled with various radionuclides have been evaluated for the detection of BN/GRP receptors expressing cancers. In this study, we have synthesized and radiolabeled several potent BN-peptide analogs with fluorine-18 (F-18) using the conjugate approach N-succinimidyld activated esters of hydrophilic 18F-isonicotinic ([18F]SFP) and the lipophilic 18F-benzoic acids ([18F]SFB).

Experiment: Various BN-peptide analogs were synthesized by solid-phase synthesis according to standard Fmoc/HBTU methodology. In separate vials, BN-peptide analogs were added to [18F]SFP solutions which contain TEA. Mixtures were heated for 15 minutes at 95oC, diluted with water and passed through Sep-Pak cartridge. Finally, BN-peptide-2-[18F]fluoropyridine-4-carboxylate conjugates (BN-[18F]SFP) were eluted with ethanol. Similar procedures were used to produce the other BN-peptide-4-[18F]fluorobenzene-1-carboxylate conjugates (BN-[18F]SFB). For the stability determination, each radiofluorinated BN-peptide analog was incubated with human plasma followed by HPLC analysis. Cell-binding activities of these BN-conjugates were measured on human MDA-MB-231 breast cancer cell-line. The biodistribution was performed in normal and nude female mice bearing breast cancer cell-lines organs and tissues were assayed for radioactivity.

Results and Discussion: Several BN-peptide analogs were designed and synthesized by introducing the hydrophilic aspartic acid to the original sequence. The synthetic approaches for preparation of the BN-[18F]SFP and BN-[18F]SFB conjugates entailed several sequence of reactions and differences between the unlabelled peptide and the conjugates permitted simple isolation of the BN-[18F]SFP and BN-[18F]SFB conjugates. Hence, the simple purification technique is amenable to automation and holds considerable promise as a rapid and simple method for the radiofluorination of bioactive molecules with high specific activity. Radio-HPLC analysis showed that each of the BN-[18F]SFP and BN-[18F]SFB conjugates resulted in the formation of a single radioactive peak and radiochemical purities were greater than 98%. The overall radiochemical yields ranged between 40-60% with preparation time of about 80 minutes. Stability results indicate that all BN-[18F]SFP and BN-[18F]SFB conjugates are stable in human plasma. Measurement of cell-binding activity of these conjugates on MDA-MB-231 human breast cancer cell lines showed high affinity for GRP receptors especially the BBN-[18F]SFB conjugates. Moreover, biodistribution studies of the bombesin peptide radioconjugates in normal and nude mice bearing breast cancer cell-lines mice displayed fast clearance from the blood and elevated radioactivity accumulation mainly
in the liver, kidney, intestine and significant tumour uptake. Uptake was blocked by excess of
the unlabelled original sequence bombesin peptide suggesting a GRP receptor-mediated
process. The initial in vivo images of the nude mice bearing tumour using selected
radioconjugates using animal imaging modality confirmed in vitro and in vivo findings.
Development of a novel Ge-68/Ga-68 generator for biomedical applications

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Ga-68 is an excellent positron emitting radioisotope suitable for clinical positron emission tomography (PET) applications in nuclear medicine. The cyclotron independent availability of Ga-68 from a Ge-68/Ga-68 generator at a reasonable cost makes it an attractive and realistic option for countries with limited or no cyclotron facilities. However, most of the commercially available Ge-68/Ga-68 generator systems are not optimally designed for direct applications in a clinical context. The Ga-68 solution eluted from these generators is low radioactive concentration, often contaminated with residuals of matrix materials (such as TiO2, SnO2, Ti and Sn ions) and contains significant amounts of Ga-68. This necessitates tedious multiple post-elution processing steps for radiopharmaceutical applications. In view of these limitations, development of Ge-68/Ga-68 generators based on nanoparticle based sorbents such as nanozirconia seems to be an interesting proposition owing to their unique morphological features, pore structure and high surface areas. Nano-zirconia was synthesized by controlled hydrolysis of zirconyl chloride in ammonium hydroxide medium. The product obtained was granular in texture with adequate mechanical strength and insoluble in water, dilute mineral acids and alkalies. It exhibited free flowing characteristics in fixed-bed column operation. In order to explore the potential to use nano-zirconia for the separation of Ga-68 from Ge-68, distribution ratios (Kd) of Ge-68 and Ga-68 ions in solutions at different acidities were determined. In 0.01 N HCl solution (pH 2), the distribution ratio of Ge-68 ions were significantly high (~12000) while Ga-68 ions had distinctly lower Kd values (~0.1) and offers the separation from Ge-68. The breakthrough capacity of nano-zirconia column was determined to be as high as ~70 mg Ge per g and hence a 3.7 GBq (100 mCi) Ge-68/Ga-68 generator can easily be retained using only 200 mg of nano-zirconia. A 740 MBq Ge-68/Ga-68 generator was developed and its performance was evaluated over a period of 1 year. Ga-68 could be availed from this generator in 2 ml of 0.01 N HCl solution with >80% yield. The amount of 68Ge impurity in 68Ga eluate was <20 Bq (<10-5% of the total 68Ga activity) in all the elutions over the period of 1 year. The generator gave a consistent performance with respect to the elution yield and purity of 68Ga over a period of 1 year (Fig. 1). The presence of Zr ions in the Ga-68, possibly due to bleeding of the nano-zirconia column matrix was analysed by ICP-AES analysis, and was found to be as low as 0.05±0.01 µg/mL. The level of metal ion (Fe, Ni, Mn) impurities was <5 ng/mL. The suitability of 68Ga for biomedical applications was evaluated by labelling DOTA-TATE with the radionuclide. Only, 20 µg of DOTA-TATE (13.9 nmol) was sufficient for labelling ~296 MBq (8 mCi) of 68Ga with >99% complexation yield. Thus we have successfully demonstrated the feasibility of developing a Ge-68/Ga-68 generator which can directly be used for biomedical applications.
FIG. 1. Elution performance of the generator over a period of 1 year.
Validation of the nano-ceria-polyacrylonitrile composite based Ge-68/Ga-68 generator for the routine clinical preparation of Ga-68-DOTA-TATE

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Generator-produced Ga-68 based positron emission tomography (PET) tracers have gained much attention recently due to favourable imaging characteristics, accessibility and affordability. The half-life of 68Ga (68min) matches the pharmacokinetics of many peptides and other small molecules owing to rapid diffusion, localization at the target and fast blood clearance. The long half-life of the parent radionuclide 68Ge (T1/2=270.8 days) ensures the cost-effective availability of 68Ga within the PET facility for long periods of time. Somatostatin (SST) receptors are expressed in a variety of tumours, especially neuroendocrine tumours (NETs). DOTA conjugated analogues have been labelled with Ga-68 to image such tumour bearing SST receptors. We have succeeded in the development of a nano-ceria-polyacrylonitrile composite sorbent based Ge-68/Ge-68 generator (of 740 MBq) that enables elution of Ga-68 with a 0.1 M HCl solution. Its chemical form allows universal application in radiopharmaceutical preparations. Long-term sustainability of this generator for clinical purposes was evaluated by studying the quality aspects of 68Ga availed from this generator. The generator was regularly eluted with 0.1 N HCl solution at 24 hr intervals over a period of 1 year. The study of the elution profile of the generator revealed that even 2 ml of 0.1 N HCl solution were sufficient for elution of 68Ga with >75% yield. The radioactive concentration of the eluted Ga-68 solution (>500 MBq per ml) is adequate for radiolabeling. The level of competing metal ions in Ga-68 which may hinder the Ga-68 in its complexation chemistry, was estimated by ICP-AES analysis of the decayed Ga-68 samples. The presence of Ce ions in the 68Ga eluate, possibly due to bleeding of the column matrix was found to be as low as <0.1 µg/mL. The level of other metal ions of elements such as Cu, Pb, Co, Cr, Cd, Ni, Fe, Mn was determined to be <5 ng/mL. The presence of trace amounts organic residue from the polyacrylonitrile binding matrix in Ga-68 was assayed by UV-Visible spectrometry by monitoring the weak absorption at λmax of 278 nm, corresponding to the n→π* transition of nitrile-groups. It could be inferred from this study that PAN residue was not present in the 68Ga eluate as no absorption was observed at this wavelength. Finally, the suitability of 68Ga for biomedical applications could be demonstrated by labelling DOTA-TATE (in nano-molar concentrations) with 68Ga. It was observed that as low as 20 µg of DOTA-TATE (13.9 nmol) was sufficient for labelling ~370 MBq of 68Ga with >99% complexation yield. The performance of the generator remained consistently good over the period of 1 year. Thus, Ga-68 availed from this generator opens the door toward synthesis of Ga-68 DOTA-TATE in nuclear medicine departments for PET evaluations.
18F-labeled choline proves to be useful for diagnosis of prostate and brain cancer using positron emission tomography (PET). This paper describes a new module system for routine 18F-choline production for clinical application. 18F-bromofluoromethane is produced in a reactor then allowed to react with N,N-dimethylaminoethanol on tC18 cartridge. After purification on CM cartridge the 18F-choline is eluted by isotonic NaCl solution. This system shows a reliable 20% radiochemical yield and synthesis time of 30 minutes. The radiochemical purity was > 95%. The concentration of DMAE was < 100 ppm were the concentration of CH2Br2 was BDL.
RADIOPHARMACY NON-PET
The quality control of 99Tcm-MAG3 radiopharmaceutical

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The use of MAG3 as a radiopharmaceutical is well known. MAG3 is the gold standard of radiopharmaceuticals for renal scintilography. In this study we propose 3 methodologies based on Thin Layer Chromatography (TLC) using a new stationary phase (paper Hahnemuhle and Whatmann) and new mobile phase (MEK and Acetone) in different conditions. The results showed that all the 3 conditions were very close, and for this reason can be interchangeable. This result is of great importance, especially for developing countries where the use of more simple techniques are requested due difficulties in financial support.

Method: MAG3 was provided as a ready-for-labelling kit by EDQM. In the labelling procedure, each vial received 1100 MBq of a 99mTc-pertechnetate solution, measured in a Capintec CRC®-25R dose calibrator, obtained from a 99Mo/99mTc generator (IPEN-SP). The vial was submitted to heating for 10 minutes and then cooled to room temperature. Radiochemical purity (RcP) assays and paper chromatography conditions 5 μL of [99mTc]MAG3 was spotted 1 cm above the strip bottom. The strip was developed in the mobile phase until the eluent front had reached the upper mark, already made 1 cm below the strip top.

In this study, three different paper chromatography conditions were used for the 99mTc-MAG3 quality control, as described in Table 1.

TABLE 1: TLC condition

<table>
<thead>
<tr>
<th>Condition</th>
<th>Mobile Phase</th>
<th>Stationary Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>methylethylketone(MEK);</td>
<td>Hahnemuhle 2040B paper (10 cm x 2 cm)</td>
</tr>
<tr>
<td>2</td>
<td>methylethylketone(MEK);</td>
<td>Whatman nº1 paper (12 cm x 1 cm)</td>
</tr>
<tr>
<td>3</td>
<td>acetone</td>
<td>Whatman nº1 paper (12 cm x 1 cm)</td>
</tr>
</tbody>
</table>

After chromatography, the ratio between the [99mTc]MAG3 and total activity was used to calculate the RcP. Two methods were used: A 1 minute static image of the strips was made using a gamma camera, for qualitative evaluation; and count in a gamma-counter, for quantitative evaluation.
Results and Discussion: In order to prevent an influence of the RcP in the evaluation, all tested samples showed 80-95% labelling efficiency results. After imaging in gamma camera, the strip chromatographic paper was cut into four equal pieces and counted in the gamma-counter; the results are shown in Fig. 1.

**FIG. 1.** (1a) Chromatographic paper image. The RcP was calculated using the image processing software, RcP = 85%; (1b) RcP was calculated relating the activity in the lower strip piece (0-2, 5 cm) with the total activity in all four pieces, RcP = 83%.

Condition evaluation: In all three conditions tested, [99mTc]MAG3 remained at the starting point, as expected. The results showed that among all the three conditions the best one was obtained using Whatman nº 1/MEK. In this condition 99mTc-MAG3 showed Rf~ 0-0,1 while radioactive impurities Rf~0,5 in well defined resolution image obtained in gamma camera (Fig. 2).

**FIG. 2.** Chromatographic of the MAG3 using scintigraphy method

Conclusion: The 99mTc-MAG3 radiochemical purity in all cases was alike, proving that the results were condition independent. WH1/MEK better chromatographic resolution and the well-established use of WH1 as stationary phase on radiopharmaceuticals chromatography result in a better cost-benefit method of 99mTc-MAG3 control in hospital radiopharmacy.
Nanoradiopharmaceuticals are under intense research in many parts of the world. In the field of nanotechnology and biotechnology, nanoradiopharmaceuticals are the most promising compounds. However, they are the most complicated substance to obtain in nano scale, due to the radioisotope linked to the ligand part. The Laboratory of Nanoradiopharmaceuticals has been working in the research of novel methodologies in order to obtain nanoradiopharmaceuticals for nuclear medicine. In this work, we discuss the main methodologies used as the results achieved. The preliminary results are very exciting. We have already formed 2 nanoradiopharmaceuticals: the EDTMP-nano and the DMSA-nano.

Laboratory of Nanoradiopharmaceuticals Experience: The Nanoradiopharmaceutical Laboratory has been dedicating a great effort in the search for nanoradiopharmaceuticals formulas that allow the nanovectorization of existing radiopharmaceuticals and that enable the development of new radiopharmaceuticals based on nanotechnology, as described below:

Case 1 - 153Sm-EDTMP: Nanoparticles were produced by double emulsion methodology. Nanoparticles morphology and dimension were characterized using MFP-3D-BIOTM (Asylum Research). Topography were captured using Contact Mode with NPS probe (Fig. 1).
Case 2- Mesoporous Silica Model: The P123 block copolymer was used combined with TEOS (Tetraethyl orthosilicate). After 20 h the gel solution formed was heated at 100°C for 48 h. Then, the solid was calcinated under air flux at 500°C for 10 h. After all these steps a solution of 10% 99mTc-MDP was added to the silica and then agitated for 30 minutes. Figure 2 represents a Transmission Microscopy of the compound obtained.

![Mesoporous Silica filled up with 99mTc-MDP solution (10%) obtained by Transmission Microscopy.](image)

Conclusion: Although at an early stage, research in the field of nanotechnology applied to radiopharmaceuticals is under high development. The preliminary results are very promising and imply that the future of nuclear medicine may lie in the development of nanoradiopharmaceuticals. The nanoradiopharmaceuticals should, before use, be extensively studied in two directions:

1) Toxic effects: Many nanoformulations may use toxic components (i.e. PVA) or can even develop toxic effects due to a weak link with plasmatic proteins or other unknown mechanisms.

2) Effective targeting: Radiopharmaceuticals are already molecular targets of tumour. Nanoradiopharmaceuticals should be proved more efficient than the conventional radiopharmaceuticals in use.
Radiopharmaceuticals in numbers: Brazil

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Nuclear Medicine and consequently the production of radiopharmaceuticals, represent an increasingly important part of the global medical market. This market is estimated at over $3 billion per year and growing. In this study, we compare the current Brazilian radiopharmaceuticals production and consumption with that of the USA and Europe. The Brazilian market is increasing although the number of facilities are too small compared with other countries (4 : >30 : >100 facilities in Brazil, USA, and Europe, respectively). Current production capacity is inadequate to meet the growing demand, especially if the SUS (Health System of Brazil) approves the reimbursement of all Nuclear Medicine procedures. Rectifying Brazil’s national policies to permit international competition in the production of radiopharmaceuticals would allow an increase in the capacity and the sustainability of the Nuclear Medicine and the radiopharmaceutical industry in Brazil.

In terms of sales, Brazil is a major player in the radiopharmaceutical market despite considerable barriers to production and reimbursement. In 2009, Brazil sold almost 70 million (in Reais) of FDG. Converting this value to US dollars, sales of FDG in Brazil were approximately $35 million compared to US sales of $249 million in 2004. Despite having only two PET radiopharmaceuticals facilities Brazilian production was equal to 6.7% of the US production from more than 30 PET facilities. This is an impressive feat. However, it is not clear that these facilities can continue to expand production to meet the growing demand for imaging using radiopharmaceuticals. The reliance on just two high-volume facilities for the entire national production of PET Radiopharmaceuticals suggests an urgent need to increase the number of production facilities in Brazil. Not only will this increase production capacity, but it will potentially decrease costs with the possibility of exporting excess products regionally. This benefits not only Brazil, but improves the stability of the worldwide market for radiopharmaceuticals.
Quality control of labeled MDP-99mTc with different chromatographic systems

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This work is part of a standardization quality control of radiopharmaceuticals labelled with Tc-99m. The aim of this study is the development of a simple and cheap paper chromatographic control method for common use in routine applications of nuclear medicine clinics. We have used different chromatographic papers that are widely available in the market. We have found that for MDP (HMDP) different chromatographic papers such as stationary phase are convenient as well as different mobile phases. Chromatographic papers Whatman Chr1 and Whatman S&S2598C and all mobile phase tried except for 0.9%NaCl are shown to be the best media for quality control of MDP (HDP) labelled with Tc-99m.

Literature and routine practice of nuclear medicine departments underline the importance of radiochemical purity of radiopharmaceuticals. Different methods such as HPLC, ITLC, TLC, chromatography exclusion, electrophoresis, liquid-phase extraction method, solid-phase extraction cartridge method (e.g. Sep-Pak, etc.) are available to control radiochemical purity. Some of these methods give good results but they are expensive and time consuming. Paper chromatography combines rapid implementation, simplicity as well as reasonable expenses. Chromatographic papers are generally inexpensive and widely available in the market. In this context, for the first phase, it is necessary to compare different quality control methods to identify the radiochemical purity of both the technetium generator eluent and the Tc-99m-labelled MDP by means of paper chromatography using different stationary and mobile phases. Results concerning the control of the generator eluent are demonstrated in another paper. In this paper we present the results taken for Tc-99m-MDP.

Materials and Methods: HPLC and ITLC Sg were used as reference standard methods for quality control of the eluent and Tc-99m-MDP according to Pharmacopoeia recommendations. The MDP kit used belongs to Mallinckrodt Company. For HPLC, equipment from the KNUER company was used. The column used was Nucleosil C18 5\textmu m. The eluent used is a mixture of 0.01M acetate buffer in pH=5 and methanol in ratio 93% and 7%. The flux of liquid was 0, 2 ml/min, pressure 2-4 Mpa and 30 min were sufficient for this investigation. The eluent used for ITLC-Sg in this experiment was MEK, saline, acetone and others. The chromatographic papers Whatman S&S2598, Whatman No32ETChr, Whatman S&S2598C; Whatman4; Whatman Chr1 were used as stationary phase. Mobile phases under investigation were: Ethanol absolute, 0.9% NaCl, MEK (Methylethylketone), 13.6% Na-Acetate 50% acetonitrile; Ethylacetate-MEK 3:2 and acetone. Elumatic III from IBA Molecular Company served as generator.

Procedure: Chromatographic paper strips are generally used with dimensions of 1x9 cm. About 2-5\textmu l Tc-99m radiopharmaceutical complex are dropped at the starting position of the chromatographic paper. Chromatograms are developed immediately and then air-dried at
room temperature. Chromatographic strips are cut in pieces about 1 cm length and their radioactivity measured with NaI(Tl) detector. The picture of radioactivity distribution and evaluation of them is made manually. Also for evaluation was used in some cases scanning by a Berthold Automatic Linear Analyser Scanner.

Results and Discussion: Fig. No.1 and Fig. No.2 represent the HPLC elution profile of 99mTc generator elute and 99mTc-MDP complex respectively. On the other hand the purity study of the complex by ITLC-Sg methods with different elute shows some traces of free pertechnetate, (Fig. No 3; 4 and 5). It is clear that elute and complexes are radiochemically very pure and fulfill the criterion of pharmacopeia and do not contain any kind of radiochemical impurities so they can be used for our purposes in the studying of the different chromatographic systems.

FIG. 1. HPLC profile of 99mTc elute.  
FIG. 2. HPLC profile of 99mTc-MDP.

FIG. 3. ITLC.Sg profile of MDP, mobile phase acetone.  
FIG. 4. ITLC.Sg profile of MDP, mobile phase MEK.  
FIG. 5. ITLC.Sg profile of MDP mobile phase alcohol abs.
Quality control by different PC systems: Fig.No.6 until Fig.No.9 represents an example of the chromatographic profile of MDP complex with different chromatographic papers and same mobile phase (acetone). It is evident the very good and clear separation of the complex, that remains in the origin.

**FIG. 6. Whatman S&S 2589 C, mobile phase, acetone.**

**FIG. 7. PC W4, mobile phase, acetone.**

**FIG. 8. Whatman Chr 1, mobile phase, acetone.**

**FIG. 9. Whatman No 32 ET Chr.**

A summary of results of total study with different chromatographic papers and mobile phase are represented in the following table.

<table>
<thead>
<tr>
<th>Mobile/stationary phase</th>
<th>ITLC Sg</th>
<th>Whatman S&amp;S2598</th>
<th>Whatman 4</th>
<th>Whatman Chr1</th>
<th>WhatmanNo32ETChr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetone</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>0.9% NaCl</td>
<td>-</td>
<td>-</td>
<td>++</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>MEK</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Ethanol abs.</td>
<td>++</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Ethylacetate:MEK</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>50% acetonitrile</td>
<td>?</td>
<td>+++/+</td>
<td>+++</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>13.6% Na-acetate</td>
<td>?</td>
<td>--</td>
<td>+++</td>
<td>+++</td>
<td>-</td>
</tr>
</tbody>
</table>

Legend: +++ excellent separation; ++ very good separation; + good separation; - bad separation; -- very bad separation; + not clear separation

Conclusions: 1) Different chromatographic system and mobile phase are convenient to perform the quality control of the MDP technetium kit. 2) All mobile phases checked during this study are available to use with chromatographic paper Whatman 4. 3) The study must continue with other kits in order to get a universal method for all the common kits that are routinely used in the practice work of nuclear medicine clinics.
Comparative evaluation of chromatographic methods for radiochemical purity control of 99-Mo generator eluate

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The increasingly general use of a number of Tc-labeled compounds makes the need for an understanding of the capabilities of simple quality control procedures urgent. The present study, comprising part of an extended work, attempts to address the apparent need of quality control protocols for characterising radiopharmaceuticals applied in nuclear medicine. Quality control of radiopharmaceuticals is important, providing products of high standards. A number of 99m-Tc radiopharmaceuticals, which are already generally used, have been studied in various chromatographic procedures which might potentially provide adequate quality control. The comparative effectiveness of each of these chromatographic procedures for the accurate quality control of each radiopharmaceutical may be readily observed and an adequate procedure can be decided upon. The practical ease of each chromatographic system handling is discussed.

In this study, HPLC (High Pressure Liquid Chromatography) and ITLC (Instant Thin Layer Chromatography) are used as standard methods. They are the best tools for radiochemical quality control of radiopharmaceuticals, very accurate and sensitive methods, but meanwhile they are relatively expensive. The aim of this work is the comparison and evaluation of the results taken from these two chromatographic methods performed to control radiochemical purity of the eluate obtained from 99Mo-99mTc generator with the results from the other chromatographic methods. PC (Paper Chromatography) method in different systems is performed as an alternative method because of its cost and in our experience this technique is suitable for the quality control of short half-life radiopharmaceuticals. The 99-Tc eluate milked from Elumatic III (IBA Molecular Company) Generator is checked. HPLC equipment of KNUER Company and Nucleosil C18 5µm column are used to perform HPLC method. A mixture of 0.001M acetate puffer in pH 5.3 with methanol in 93% and 7% ratio is used as mobile phase. The flux of liquid was 0.2 ml/min and the pressure 2-4 Mpa. Gelman Silica Gel media (stationary phase) and Acetone, NaCl 0.9%, Acetonitrile 50%, MEK, Alcohol absolute, Ethyl acetate: MEK 3:2, Sodium acetate 13.6% as mobile phases are used in ITLC method. The same solvents are used to perform paper PC method in Whatmman S&S 2698C, Whatmman No. 4, Whatmman Chr.1, Whatmman S&S 2598a, Whatmman No. 31 ET Chr, as stationary phases. These chromatographic papers are cut in strips of 1x10cm and are placed in chromatographic tanks with the above mentioned solvents, so they did not touch the walls. After the chromatographic run, the strips are dried in air and cut in 1cm pieces. The activities are determined using detector NaI (Tl) or the chromatograms are scanned in Berthold Automatic Linear Analysator Scanner. So, a radioactivity curve for each of these systems (including specified stationary and mobile phases) is obtained. These systems, along with the results regarding the ability to separate the components, are presented shortly in the below table.
<table>
<thead>
<tr>
<th>Acetone</th>
<th>Whatman S&amp;S 2698C</th>
<th>Whatman No. 4</th>
<th>Chr.1</th>
<th>Whatman S&amp;S 2598a</th>
<th>Whatman No. 31 ET Chr</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaCl 0.9%</td>
<td>**</td>
<td>*</td>
<td>*</td>
<td>**</td>
<td>**</td>
</tr>
<tr>
<td>Acetonitrile 50%</td>
<td>***</td>
<td>***</td>
<td>**</td>
<td>***</td>
<td>***</td>
</tr>
<tr>
<td>MEK</td>
<td>***</td>
<td>*</td>
<td>*</td>
<td>***</td>
<td>**</td>
</tr>
<tr>
<td>Alcohol absolute</td>
<td>*</td>
<td>*</td>
<td>**</td>
<td>**</td>
<td>*</td>
</tr>
<tr>
<td>Ethyl acetate: MEK 3:2</td>
<td>*</td>
<td>**</td>
<td>***</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Sodium acetate 13.6%</td>
<td>***</td>
<td>***</td>
<td>***</td>
<td>***</td>
<td>***</td>
</tr>
</tbody>
</table>

- * very bad separation
- ** good separation
- *** very good separation

Conclusion: These results show that PC method is the simplest and cheapest one, which for some systems (indicated ***) can replace ITLC and HPLC methods (as expensive methods) to control radiochemical purity of pertechnetate. We have presented below the radiochromatograms (1-7) for ITLC method (as standard method) and chromatograms (8-14) of one of the PC systems (Chr. 1 / in different eluents) to clarify how all the systems in that table are compared and evaluated.
FIG. 7. Tc eluate, ITLC-SG / Na-Acetat 13.6%.

FIG. 8. Tc eluate Whatmman Chr 1/acetone.

FIG. 9. Tc eluate Whatmman Chr 1 / 0.9% NaCl.

FIG. 10. Tc eluate Whatmann Chr1/MEK.

FIG. 11. Tc eluate Whatmman Chr 1/alcohol absolute.

FIG. 12. Tc eluate Whatmman Chr 1/Na-Acetate 13.6%.

FIG. 13. Tc eluate Whatmman Chr 1/Ethyl acetate-MEK 3:2.

FIG. 14. Tc eluate Whatmman Chr1/acetonitrile 50%.
Good radiopharmacy practice in the preparation of radiopharmaceuticals: A practical implementation

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As the short physical half-life of technetium the final preparation of radiopharmaceuticals has to be done immediately before the administration to the patient. Reconstitution of the kits for labelling with 99mTc-pertechnetate solution requires that the current Good Manufacturing Practices (GMP) be employed prior to, during and after production. These include production of radiopharmaceuticals in designated clean areas, application of validated processes and analytical methods and a detailed documentation of the whole process. Moreover a comprehensive radiopharmaceutical Quality Control program (QC) should be developed and implemented to ensure that all the procedures used in the radiopharmacy result in a sterile and good quality product. The QC tests fall into two categories: physicochemical and biological tests. The physicochemical tests include pharmaceutical purity (to determine the pH and verify the absence of foreign particulate matter in the reconstituted kit) and radiochemical quality (to measure free radioisotope in the labelled compound). On the other hand biological tests include sterility of the final product and of the environment in which labelling operations are performed.

In this paper we present a practical implementation of QC program analysing areas of particular concern to prevent bacterial contamination; tests were conducted on two 99mTc-Technetium based radiopharmaceuticals (Tetrofosmin and DTPA). According to the European Pharmacopoeia, radiopharmaceuticals have been reconstituted in a laminar flow bench (class 100, grade A) with the recommended amount of radioisotope solution. Quality control analysis started immediately after completion of the kit preparation with a visual inspection of the vials for extraneous contamination or gross particulate. Then, after having sampled from the lot, analytical tests were performed to check the pH level and the radiochemical purity of the labelled products. The pH level of the solution is a critical parameter and any deviation from the manufacturing reference levels may indicate an alteration in the product performance and stability. Preliminary tests have been performed using paper colour indicators covering the range over which the pH value is expected; in case of deviation a qualified pH meter has been used. Radiochemical tests have been performed by paper chromatographic technique: radiopharmaceuticals were each spotted on the bottom line of two different Whatman 31-ET chromatography strips; then they were each placed in a vial containing acetone and developed until the solvent front had migrated to the top line. Each strip was then counted for activity using a phosphor imager for quantitative autoradiography. All the results of the previous inspections have been recorded and archived in the QC logbook. Regarding bacterial tests an aliquot of the final kit has been taken with a sterile, disposable needle and syringe, and inoculated into two different culture mediums (soybean casein digest medium TSB and sabouraud dextrose agar). Broths have been incubated for 10 days and then enumerated for microbial growth. Environmental tests have been conducted to detect microbial contamination of the atmosphere in the laminar flow bench. The testing involved exposure of two count agar plates in the working area during production of radiopharmaceuticals. We used blood agar plates designed for growing of staphylococcus and...
streptococcus microorganisms. After exposure, typically 3 hours continuatively, plates have been then placed in an incubator at 37°C for two days and monitored for any growth of colony-forming units (CFUs) for a week. A general summary of the obtained results is provided in the next table; values are arranged in horizontal groups in terms of the different performed tests.

<table>
<thead>
<tr>
<th>Test</th>
<th>Check performed</th>
<th>Positive results</th>
<th>Actions taken</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physicochemical</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visual inspection</td>
<td>120</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>120</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Radiochemical purity</td>
<td>120</td>
<td>2</td>
<td>stop the supply of the kit</td>
</tr>
<tr>
<td>Biological</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Environmental sterility</td>
<td>110</td>
<td>1</td>
<td>Clean and disinfect the work surface of the laminar flow bench using 70% ethanol</td>
</tr>
<tr>
<td>Sample sterility</td>
<td>120</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

**TABLE 1: Summary of quality control tests**

As summary during the 6-month period of measurements a total number of 120 finished kits were analysed. No variation of the pH level or presence of gross particulate and other defects had been recorded. On the other side when the chromatographic results are examined it becomes readily apparent that in some cases data exceed the reference levels. Data have been recorded in the QC logbook and a decision was taken to stop the supply of the kit and to recall the unused ones. Regarding sterility and bacterial tests results this study shows that the final product is free of viable bacterial and fungal contamination; the environmental monitoring results confirm that all kits have been reconstituted in a clean area. Of considerable interest is the analysis of the single outlier: it was consequently of the turning off of the laminar flow engine that a technician unintentionally performed after having heard some noises coming from the bench.

Conclusion: The on-site preparation of radiopharmaceuticals always requires that a comprehensive quality control program be developed and implemented. Even if it’s not possible to obtain the sterility tests results before releasing the product, however they should be performed as a monitor for the manufacturing process. First of all to ensure that the patient receives a good quality product free of viable bacteria and fungal contaminants; secondly to produce a scan without artefacts due to free and hydrolysed reduced Technetium-99m and finally to ensure the patient receive the correct radiation dose.
The use of medical radioisotopes is an important part of modern medical practices. Each year, over 40 million people from all around the world benefit from nuclear medicine processes. Medical radioisotopes are used in non-invasive nuclear diagnostic imaging techniques to help identify illnesses such as heart disease and cancer at an early stage. The main policy of Turkish Atomic Energy Authority (TAEK) is to provide necessary infrastructure for nuclear technology so as to make possible for Turkey to gain benefits from all products of the said technology. Being the first facility of its kind, TAEK Proton Accelerator Facility (TAEK-PAF) will serve as an important nuclear technological infrastructure in Turkey. End users of medical and research and the development sectors will benefit from this facility. Along with activities of private sector entities, TAEK is developing a national infrastructure with the capability of producing a sufficient supply of various radioisotopes to support clinical activities in Turkey. Such a capability would prevent shortages of isotopes and enhance the capabilities for domestic production of various radioisotopes and radiopharmaceuticals. The trend in demand of accelerator based radioisotopes in Turkey follows the trend in the world. There are more than 180 nuclear medicine centres in Turkey, which are equipped with 300 SPECT cameras and 60 PET scanners. There are 7 baby cyclotrons in Turkey; however these are not capable of supplying a variety of radioisotopes other than 18F. Hence Turkey is largely dependent on import cyclotron based radioisotopes, which needs higher cyclotron energies for production than those of existing baby cyclotrons. Objectives of establishment of TAEK-PAF are the production of primary radioisotopes of 123I, 111In, 67Ga, 201Tl and 18F and production of other radioisotopes on demand such as some PET radioisotopes like 15O, 11C, 13N and 124I. The planned production of radioisotopes and the production conditions are given in Table 1.

The facility is an integral type, which consists of the production of radiopharmaceuticals as well as quality control of these radiopharmaceuticals. Research and development activities on nuclear physics, material science, neutron activation analysis will also be undertaken in the Facility. The Facility will also serve for education and training in radiopharmacy and nuclear physics fields. With this invaluable infrastructure, TAEK will be a leading authority in Turkey for the utilization of accelerator technology in the fields of medical research. The technical features of TAEK-PAF are as follows: The proton accelerator in the Facility is CYCLONE-30 type (designed and manufactured by Ion Beam Applications), proton energy is 15 – 30 Mev (variable), maximum proton current on target is 1200 μA (variable), number of beam lines are four (three of them for radioisotope production, one of them for R&D). In this poster general overview of TAEK-PAF will be presented with emphasis on radiopharmaceutical production capabilities.
TABLE 1: The planned production of radioisotopes and the production conditions in TAEK-PAF

<table>
<thead>
<tr>
<th>Isotope &amp; Half life</th>
<th>Chemical Form</th>
<th>Target Reaction</th>
<th>Enriched Material</th>
<th>Energy of Proton Beam (MeV)</th>
<th>Current of Proton Beam (µA)</th>
<th>Irradiation Time (h)</th>
<th>Chemical Process Time (h)</th>
<th>Activity per Irradiation (Ci)</th>
</tr>
</thead>
<tbody>
<tr>
<td>111In (67 h)</td>
<td>InCl₃</td>
<td>112Cd(p,2n)¹¹¹In</td>
<td>¹¹²Cd</td>
<td>29</td>
<td>250</td>
<td>9.5</td>
<td>1.5</td>
<td>12</td>
</tr>
<tr>
<td>203Tl (73 h)</td>
<td>TICl</td>
<td>²⁰³Tl(p,3n)²⁰¹Pb → ²⁰¹Tl</td>
<td>²⁰¹Tl</td>
<td>29</td>
<td>200</td>
<td>9.5</td>
<td>1.5</td>
<td>3</td>
</tr>
<tr>
<td>⁶⁷Ga (78 h)</td>
<td>GaCl₃</td>
<td>⁶⁸Zn(p,2n)⁶⁷Ga → ⁶⁷Ga</td>
<td>⁶⁸Zn</td>
<td>29</td>
<td>250</td>
<td>9.5</td>
<td>1.5</td>
<td>12</td>
</tr>
<tr>
<td>¹²³I (13 h)</td>
<td>NaI</td>
<td>¹²⁴Xe(p,x)¹²³Cs → ¹²³Xe</td>
<td>¹²⁴Xe</td>
<td>29</td>
<td>70</td>
<td>10</td>
<td>1.5</td>
<td>4</td>
</tr>
</tbody>
</table>

PET Isotopes

<table>
<thead>
<tr>
<th>Isotope &amp; Half life</th>
<th>Chemical Form</th>
<th>Target Reaction</th>
<th>Target Material</th>
<th>Energy of Proton Beam</th>
<th>Current of Proton Beam</th>
<th>Irradiation Time (h)</th>
<th>Chemical Process Time (h)</th>
<th>Activity per Irradiation (Ci)</th>
</tr>
</thead>
<tbody>
<tr>
<td>¹⁸F (110 min)</td>
<td>F- (FDG)</td>
<td>¹⁸O(p,n)¹⁸F</td>
<td>H₂¹⁸O</td>
<td>18</td>
<td>40</td>
<td>1.2</td>
<td>0.3</td>
<td>5 (Volume of Target is 2 mL)</td>
</tr>
</tbody>
</table>
Design and building of the first hospital radiopharmacy with USP and GRPhP standard in Colombia

N. Delgado, A. De los Reyes, F. Arguelles, C. Villamil, J. Rada, O. Juan

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Objective: To design and build the first hospital radiopharmacy, meeting standards for radiation safety, clean rooms, controlled environment, and USP and GRPhP requirements for radiopharmaceutical preparation and compounding at the National Cancer Institute in Colombia.

Methods: The Radiopharmacy will be an area where varying procedures must be performed such as compounding radiopharmaceuticals with 99mTc, 90Y, 111In, 177Lu, in-house production of 131I capsules and cold kits, including freeze-dried preparations, elutions of generators 188Re and 68Ga for research and production of PET tracers (18F, 11C and 15N). We are looking for quality standards as described in the “Draft Guidelines on Good Radiopharmacy Practices for Radiopharmaceuticals” (GRPhP) in Nuclear Medicine and PET, the USP <797>, USP <823>, “Operational guidance in hospital radiopharmacy IAEA”, and ‘Cyclotron produced radionuclides: guidelines for setting up facilities IAEA’, because these papers provide us quality standards and current scientific information for the preparation of radiopharmaceuticals including PET tracers. The complexity was evaluated, as well as the radiation risk levels and the patterns of work flows in each area. The Radiopharmacy then, should have clean rooms, environments controlled to minimize airborne contamination during radiopharmaceutical labelling; there must be well-shielded rooms because radiation exposures should be kept as low as reasonably achievable and to provide safe areas to operators.

Results: The Radiopharmacy is divided into two large areas. The radiopharmacy where radiopharmaceuticals used in diagnostic and therapeutic Nuclear Medicine are prepared and the Radiopharmacy PET. Our facilities can be classified as operational level 3, and cyclotron facility type II. The Nuclear Medicine radiopharmacy includes four clean rooms with Grade C environment (ISO Class 7, 20 air changes) with HEPA filtered air. Three of the clean rooms are equipped with class II vertical laminar air flow (LAF) safety cabinets and sterilized articles for use in the clean rooms enter via a passthrough hatch. The LAF cabinets are shielded and additionally they have a lead glass in the centre. The first clean room with two LAF and radionuclide calibrators are used for compounding radiopharmaceutical with 99mTc, 90Y, 111In, 177Lu and 188Re. The second clean room is used for producing in-house cold kits including freeze dried operation. The third clean room with LAF and shielded centrifuge is used for safe manipulation and radiolabelling of autologous blood cells. The fourth room has a hot cell shielded with a lead layer of 5cm with suitable filters and air flow and is used to produce NaI-131 capsule with activities from 3 to 300mCi. Radiopharmacy PET has 3 areas; cyclotron area with room pressure of -60 Pa, and 20 air changes per hour, synthesis area that is a clean room designed to produce 11C, 13N, and 18F based radiopharmaceuticals, equipped with two hot cells and three synthesis boxes in a Grade C environment (20 air changes) plus a dispensing laminar flow with manipulators, in a grade A environment. Quality control area with big space to accommodate the equipments, and accessories, -10 Pa room pressure and 10 air changes per hour. The hospital radiopharmacy has an independent in-let and out-let for
radioactive substances and a storage room for technical gases, smooth walls covered with impervious washable paint and the cables encased to facilitate cleaning and decontamination. Both Nuclear Medicine and PET radiopharmacies share a common space for pharmacy-grade refrigerators with temperature recorder, glassware washing and drying area, a changing room restrooms, waste storage area, and offices.

Conclusions: Our Hospital Radiopharmacy includes radiopharmacy for Nuclear Medicine and PET following the USP standards and GRPhP with some common areas, and safe facilities within a controlled environment and clean rooms.
INSTRUMENTATION AND QUALITY CONTROL
Use of a novel acquisition strategy to facilitate respiratory motion correction and evaluation of potential impact in lung SPECT

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Introduction: Respiratory motion (RM) is a degradation factor in nuclear imaging; however, such effect has not been extensively evaluated for quantitative SPECT. Our aim was to evaluate the potential impact of RM correction for lung perfusion SPECT and to describe a novel acquisition method to facilitate RM measurement.

Method: In order to correct for RM, we propose SPECT to be performed using dynamic acquisition at each projection angle (DP). DP SPECT acquisitions were performed in 3 patients referred for lung perfusion using 64 angles of 20 sec, each step containing 40 frames (0.5 sec each). Center of mass (CM) was calculated for each image and curves reflecting RM were generated. To assess potential impact of motion correction, a model of SPECT lung perfusion was produced using a virtual torso phantom and reconstruction using OSEM. Three situations were evaluated: a) with no RM; b) RM simulating diaphragmatic displacement of 2 cm; c) RM simulating 4 cm displacement. For b) and c), additional thorax expansion of 1.2 cm was included to better reproduce a respiratory pattern. Seven “cold lesions” were located in the phantom simulating pulmonary emboli (PE) in superior, middle and basal aspects of the lungs. Lesion contrast was measured on attenuation-corrected, reprojected images. For analysis, a total of 20 lesions were considered, with a separate analysis focused on 8 basal lesions.

Results: Characterisation of RM using CM and clinical dynamic SPECT yielded a sinusoid curve containing typically 4 respiratory cycles / projection, with slightly variable amplitude (Fig.1). By visual assessment, pixel displacement was more prominent at the base, whereas the vertex remained practically still. Lesion contrast values using the phantom were: for the total of 20 lesions (mean±SD), 0.22±0.08, 0.20±0.07 and 0.15±0.04 for no RM, with 2 cm and with 4 cm displacement respectively (p<0.05 between all values). Considering 8 basal lesions only, 0.26±0.06, 0.23±0.05 and 0.17±0.04 respectively (p<0.05 between all values and between total and basal lesions).

Discussion: SPECT imaging for diagnosis of PE and other respiratory conditions could be improved with RM correction. The influence of RM on perfusion defect contrast has not been previously investigated quantitatively; our results demonstrate the potential impact of RM correction since there is contrast deterioration proportional to the degree of RM, more evident for basal lesions. Detection of RM was achieved using CM, without external gating devices. Acquisition using DP SPECT permits “retrospetive gating”, allowing identification of end-expiration and end-inspiration frames; work is in progress to “stretch” images in order to achieve registration prior to summation.
Conclusions: Image contrast is affected by RM in SPECT. A method for characterisation of RM with DP SPECT has been developed, avoiding the need for external gating devices which involve varying complexity and cost; information can be used to support a practical RM correction algorithm.

FIG. 1. Displacement of the center of mass of the lungs in 4 consecutive respiratory cycles.
GE Discovery 690 performance reference tests

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During 2010, the first two GE Discovery 690, PET/CT systems with time of flight capability, were installed in the Cancer Institute of the State of São Paulo, ICESP, Brazil. The PET component consists of 24 rings containing LYSO block detectors, with nominal axial and trans-axial fields-of-view of respectively, 15.7cm and 70cm. The CT component is a 64 multi-slice GE LightSpeed VCT scanner, equipped with 64 parallel rows of solid state detectors. This hybrid system allows 3D and 4D, with respiratory gating, acquisition modes. In order to obtain a set of performance characteristics reference data, tests based on NEMA NU 2-2007 and IAEA Quality Assurance for PET and PET/CT Systems were carried out. The main results of both systems are shown in Table 1. TOF timing was not tested, as it needs special information from the manufacturer that was not available. In accordance to Brazilian specific requirements, the following additional tests were also performed for the CT component: Standard dose to patient – adult protocols for abdomen, lumbar column and head; Laser alignment; Slice thickness and increment; Spatial linearity and uniformity; Contrast of acrylic spheres; CT number linearity; High contrast spatial resolution; Low contrast resolution sub and super slice; Noise; CT number calibration and uniformity in air; and Integral Non-uniformity. The results showed good performance of both systems, except for the CT/PET alignment with load for system A, which needs slight adjustment, and the average residual lung error for both systems in non-TOF mode, which is not important in TOF mode. In conclusion, performance reference tests, as those carried out in this work, are recommended for a comprehensive knowledge of a complex imaging system such as Discovery 690.
### TABLE 1 - PET component tests results

<table>
<thead>
<tr>
<th></th>
<th>SYSTEM A</th>
<th>SYSTEM B</th>
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<tbody>
<tr>
<td><strong>SPATIAL RESOLUTION</strong></td>
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<tr>
<td><strong>POSITION</strong></td>
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<td>FWHM (mm)</td>
<td>TRANSVERSE</td>
<td>AXIAL</td>
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<td>10 cm</td>
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<td><strong>SENSITIVITY</strong></td>
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<tr>
<td>Position</td>
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<td>10 cm</td>
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<tr>
<td>Sensitivity [cts/s/kBq]</td>
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<tr>
<td></td>
<td>Mean</td>
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<tr>
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<td>TOF</td>
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<tr>
<td>Average Residual lung error %</td>
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<tr>
<td></td>
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<tr>
<td><strong>NEC RATE</strong></td>
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<td>Peak NEC [kcts/s]</td>
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<tr>
<td>Expected conc. [kBq/ml]</td>
<td>28.1</td>
<td>28.1</td>
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<tr>
<td>Scatter fraction (last frame) %</td>
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<td>35.7</td>
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<td><strong>CORRECTION ACCURACY</strong></td>
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<tr>
<td>Max error below peak NEC %</td>
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<td>2.64</td>
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<td><strong>SUV VALIDATION</strong></td>
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<td>SUV (mean)</td>
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<td>1.0 ± 0.1</td>
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<td><strong>CT/PET ALIGNMENT</strong></td>
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<tr>
<td>Method</td>
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<td>Without Load</td>
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<tr>
<td>Shift</td>
<td>0.8 mm</td>
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<tr>
<td></td>
<td>With Load</td>
<td>With Load</td>
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<tr>
<td></td>
<td>0.3 mm</td>
<td>2.7 mm</td>
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</table>
Implementation of quality assurance programme (QAP) in PET centre in Malaysia

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The government of Malaysia has recognized the continuous improvement quality in health care as a national priority in the country. Hence, the manual to implement Quality Assurance Programme (QAP) in the Nuclear Medicine Centre including those with Positron Emission Tomography (PET) facility is being introduced. The QAP is aimed to ensure that the optimum diagnostic information is obtained with the available resources yet minimizes the radiation dose to the patient as well as the workers, in order to comply with the Atomic Energy Licensing Act 1984 (Act 304) in the country. The manual is established by the RHSS, with a joint working group of 12 members, and consulted by the Radiological Advisory Committee (RAC) in the country with reference to the IAEA documents. There were three elements being identified and addressed in the manual, which are Quality Control (QC) of imaging modality and associated equipment, Continuous Professional Education (CPE) and the performance indicator of the nuclear medicine services. For QC tests, the standards/tolerance limits were adopted from the IAEA document and the draft of Medical Regulations under Act 304. All these were being harmonized and presented in the manual. Users will be required to submit a record of the mentioned element to national authority (RHSS) for evaluation. Meanwhile, regulatory inspections might be carried out for verification purposes. For the second element in QAP manual, all the involved medical professionals were required to attend CPE courses with a minimum of 6 cumulative hours per year. This element is very important to improve the competency in order to provide the optimum nuclear medicine services. Besides, the rate of repeat study had been identified as a performance indicator for a nuclear medicine centre. This study will consider those cases that require re-injection of the same radiopharmaceutical when and where the first injected radiopharmaceutical has not achieved its intended purposes as a result of any technical or non-technical causes. The standard for the rate of repeat study was agreed not to exceed 5%. The performance indicator will be monitored by the National Steering Committee for MOH QAP annually. In the early stage of the QAP implementation, it will focus on two public PET centres prior to others private centre. The implementation of QAP in nuclear medicine centres is the effort of the MOH to continuously upgrade and enhance the quality, safety and efficacy of nuclear medicine services in the country. This national project is on-going and constructive comments are always needed for improvement. The co-operations from regulator, users and clinical auditors will be of paramount importance to ensure the successful implementation of the manual in all nuclear medicine centres nationwide.
The importance of having a quality control program for a hybrid equipment SPECT-CT, considering the financial cost and the equipment downtime

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The implementation of a quality control program for medical imaging devices is usually complicated due to the common belief that it is expensive and causes excessive equipment downtime that affects the service to the patient. This perception is even worse for a Hybrid SPECT-CT, which requires additional investment on phantoms. This work tries to show that the establishment of a good quality control program is a long-term investment in fact saves time and money. We reviewed the basic quality control tests for each image generating system involved in the hybrid SPECT-CT equipment and implemented a basic quality control program. One of the tests included was the high-count intrinsic flood calibration, which allowed us to identify uniformity problems in both detectors from the gammacamera system. In order to determine the origin of these issues, an asymmetric energy window was used in the acquisition of a high-count intrinsic flood to check the detectors for possible hydration, confirming a problem in this area. The manufacturer agreed with the hydration diagnostic and both detectors were changed. Additionally, since the equipment had difficulties to pass its own laser lights alignment test, a quality control test with an accreditation phantom helped to identify a misalignment between the gantry and the patient’s bed in the axial direction of about 3mm, as well as some laser misalignment. Using the problems identified by the quality control program, we developed a comparative analysis between the resources (time and money) spent to fix such problems when they were found by the quality control test and the projected costs if the same issues were detected through imaging problems during the patient’s examination. The analysis showed significant maintenance cost savings when using the quality control test to identify problems in the hybrid SPECT-CT equipment. The quality control program allowed the identification of hydration problems in both gammacamera detectors in a new hybrid equipment SPECT-CT. The detectors were changed before the SPECT-CT’s guarantee ended, without any additional expenditure but the cost of the quality control phantoms, which was less than 1% of the price of the new detectors required if the problem had gone undetected by the quality control program. Furthermore, because of the early detection of hydration problems, there was no equipment downtime either because of imaging problems or because the replacement work for the detectors. Also, the misalignment was corrected when the detectors were changed, with no additional equipment downtime.
Development of low-cost phantom for Positron Emission Tomography-Computed Tomography (PET-CT) performance tests

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This project aims to develop the sphere performance test phantom (as shown in the figure below) for PET-CT system’s performance test evaluation. It also evaluates the possibility of using the fabricated phantom for some routine performance tests that are typically done with commercial phantoms, which can help to simplify the methods, that is used for a performance test on a routine basis in hospitals with limited resources. Six sizes of spherical cavity were developed using Borosilicate glass. The spheres were attached in a circular array at the acrylic holder which consisted of six universal holders, and the assembly was inserted inside a CT abdomen phantom. Routine image quality test for PET-CT was carried out in this study using the fabricated phantom. The PET-CT systems (GE Discovery™, USA) were used. The results of the uniformity, radioactivity concentration and spatial resolution were recorded. No artefact was found in the reconstructed PET slices. The phantom design was low cost and better in mimicking patient in clinical settings. The developed phantom was found to be suitable as an alternative phantom for PET-CT routine performance tests due to its cost-effectiveness, feasibility and reproducibility.

FIG. 1. Sphere Performance Test Phantom
An overview of the installation project of a SPECT/CT (BrightView XCT) in Malaysia

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Introduction: The ability to fuse the molecular and functional SPECT data and anatomical CT data has tremendously impacted the level of patient care, where without the use of SPECT/CT, some cases would have needed additional imaging diagnostic tests or quite possibly may have been overlooked. SPECT/CT has delivered better image quality that has improved the accuracy of some studies. Anatomic localization of lesions has also improved with the scintigraphic study. BrightView XCT is a SPECT/CT system designed to incorporate SPECT in a co-planar design with advanced Philips flat-detector X-ray CT technology. SPECT/CT installation and implementation are unique to each institution, and each practice will need to examine its facility, workflow, and processes to best adapt them for the new technology.

Methods: The projected duration of the project was 151 days. Installation of a SPECT/CT system require changes in infrastructure such as shielding, flooring that can support its weight and proper room space to ensure optimal installation performance. This study was initiated to evaluate shielding requirements and critical procedures involved in the overall installation process. A proper plan such as Gantt chart should be followed closely and frequently updated by the designated project engineer and UMMC’s medical physicists. Manoeuvrability within an existing room space should also be mapped out well in advance prior to equipment delivery (loading and unloading) and its installation. Furthermore, field or project engineers will require access to the modality's components, and their needs should be taken into consideration in order to minimize downtime of the installation.

Results: Several factors that created incremental costs as a result of SPECT/CT installation in UMMC such as room and all mechanical, electrical and civil work modifications resulting in renovation costs, separate processing and control area for the operators resulting in renovation costs, radiation protection compliance resulting in additional room shielding costs, workflow and scheduling modifications resulting in renovation time costs, built-in furniture for new spaces resulting in renovation costs and the need of powerful environmental control system to be installed to keep the room and equipment cool also resulting in renovation costs.

Conclusions: Duration of project has to be extended and additional cost incurred due to several factors such as changes in room layout in order to comply with regulatory requirement, difficulty in procurement process of radioactive sources for acceptance testing.
and system’s calibration purposes and date of machine delivery has to be extended due to changes in shipment schedule.
Measurement methods and realization of PET/CT image fusion accuracy

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Objective: To measure the same plane PET and CT image fusion accuracy.

Methods: Using spatial resolution phantom, respectively in the PET image and CT image, to measure the corresponding point source center distance.

Results: The distance of the center source (0cm, 1cm) is 0.8732mm, respectively, the radial distance of 10cm is 2.3993mm and 1.0822mm.

Conclusion and Discussion: Measurement results were confirmed by eFilm software displaying the same image. Image fusion accuracy can also be affected by bed deformation and needs further experimental verification.
Positron Emission Tomography combined with Computed Tomography (PET/CT) is an important part of molecular imaging technology which is widely used in cancer diagnosis and treatment in China. According to the national survey, China currently has 153 sets of PET/CT operating in about 120 hospitals and more than 300,000 cases were accumulated. However, the standard and accuracy of diagnosis are still under-evaluated. One of the problems in clinical practice is artefact recognition and correction. This paper will summarize some key points of artefact of 18F-FDG PET image and provide some methods to correct or avoid artefacts in PET/CT image.

First we should recognize the normal uptake image of 18F-FDG in brain, heart, liver, gastric-intestinal and muscle and then recognize the patterns of 18F-FDG PET images: (1) true positive image, (2) false positive image, (3) true negative image, (4) false negative image and (5) artefact image. Among them only true positive image and true negative image are accurate images. The factors of artefacts include radiotracer related, instrument related and patient related reasons. The artefacts of 18F-FDG image will influence image quality and contrast resolution, cause false bone metastasis, degrade lesion detectability and miss smaller lesions, as well as decrease the value of SUV. Good quality of the 18F-FDG tracer and good QC of PET/CT instrument will reduce the artefacts and improve diagnostic accuracy. Comparison between the early image and the delayed image will reduce the artefact from gastric-intestinal ducts, and comparison between the images with and without CT attenuation correction will avoid or reduce the artefacts caused by metal and dense contrast materials.
EDUCATION AND TRAINING
Planning and education of a multidisciplinary team to implement PET/CT in Peru

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A project begun in Peru in 2003, experts from Chile, Colombia and Germany lectured in a Nuclear Medicine course. Meetings in universities and societies were held, with the goal of encouraging PET technology. In 2006, a private enterprise began to work and perform financial arrangements, up till 2009, to have the first cyclotron and PET/CT equipment installed in Lima. A public social security facility and IPEN worked from 2009, to install a cyclotron and purchase PET/CT. In 2010, a cyclotron and two PET/CT devices were acquired. IPEN, through PER 6/016, developed strategies, for planning and educating a multidisciplinary team to implement PET/CT in Peru. First, a SWOT analysis of skills, of professionals from different specialities, was performed. In this analysis main strength was multidisciplinary work and professionals interested in being trained in PET/CT. Weaknesses were lack of knowledge of basic engineering for PET/CT facilities and dependence in skills given by manufacturers, as well as lack of training in physicians, physicists and technologists. Strategies included meetings with professionals and leaders of institutions where PET/CT would be installed. Agendas were distributed, to discuss training needs, having agreements between experts and trainees. Hard study and benchmarking with other countries were helpful for solving challenges. Physicians attended a PET/CT in early 2010, having experts in hospitals, lecturing for oncologists, radiologists and other specialists. Training for technologists was included, in addition to Distance Assisted Training modules, with PET/CT subjects. There was a course for engineers, who received workshops to prepare their facilities for PET/CT. Managers and personnel of PET/CT facility were trained in PET/CT Quality Management aspects. PET/CT was added to Nuclear Medicine training courses. Lack of appropriate education in universities was overcome through courses in curricula since 2004. Peruvian medical societies had meetings including PET/CT. Physicists are scarce for Nuclear Medicine and just three have PET/CT knowledge. Master program for Medical Physicists had two courses, in 2008 and 2010, for training in PET/CT. Students from several universities attended this course. As a second aspect, infrastructure and regulatory issues were studied and faced in time. Strategies were insufficient initially and unpredictable situations occurred. Regulatory items were worked together with solutions performed with the first PET/CT installed, using international standards, which were gradually adapted to local reality, but without compromising quality management, and during the course professionals eagerly sought help for regulatory issues and expertise, for new buildings that were being constructed. Since PET/CT devices were not yet installed in public facilities, participants requested new workshops, to be locally performed in dates close to installing procedures or at least online advisory. In these years challenges rose in different aspects: Choosing correct places for installing PET/CT equipment, economical and political issues. A third strategy was performed for public concerns, mainly radiation fears and understanding of procedures. It can be concluded that there is a multidisciplinary team with initial training achieved in PET/CT in Peru, people working and studying, to have good standards in PET/CT implementation and with possibilities to maintain technology.
Biomedical imaging in the era of molecular medicine: PET-CT versus alternate clinical modalities

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Technology and research in biology are accelerating progress in the emerging field of molecular medicine. Innovative imaging provides the means to examine individual organ systems for molecular errors of disease. Radiology, Nuclear Medicine, biology, the pharmaceutical and the bioengineering sciences are joining to optimize imaging of biological functions. These disciplines will accelerate and improve the discovery, clinical application and monitoring of new molecular therapies. We review current strengths and limitations of clinically established imaging modalities in this endeavour.

PET versus SPECT: Positron emission tomography (PET) records high-energy-rays emitted from within the subject. The main difference between SPECT and PET measurements is the necessity of lead collimators for the definition of the angle of incidence in SPECT, compared with electronic collimation in PET. The sensitivity of PET is relatively high in the range of $10^{-11} - 10^{-12}$ mole/L, and is independent of the location depth of the reporter probe of interest. Naturally occurring atoms can usually be substituted readily by positron emitting isotopes, and therefore PET is a more robust technique than SPECT for imaging most molecular events.

PET-CT: A new class of imaging technology that fuses 2 technologies is now being established. It allows the merging of anatomically and biologically based information into a single device, procedure, and image. CT findings are combined with PET to meet several objectives: first, acquisition of CT-based diagnostic information, second, identification and definition of biological abnormalities by PET with display of the surrounding anatomy by CT for improved localization, third, improvement of PET image quality through fast, accurate, and low-noise attenuation correction by CT. PET/CT is excellent for planning of surgery, radiation therapy, better definition of local separation of diseased tissue, and evaluation of therapy outcome. However, combining anatomic and biological information comes here with significant radiation exposure.

MRI: MRI has particular advantages over techniques that involve the use of radionuclides: Higher spatial resolution (micrometres versus several millimetres) and the fact that physiological/molecular and anatomical information can be extracted simultaneously without radiation exposure. However, MRI is several magnitudes less sensitive than radionuclide techniques. Variations on standard MRI techniques for greater functional analysis include diffusion-weighted MRI to obtain information on the microscopic behaviour of tissues; and perfusion-weighted MRI for monitoring the hemodynamic status. The combination of both techniques is extremely promising for early detection and assessment of stroke, tumour characterization, and for the evaluation of neurodegenerative diseases.

Ultrasound: Ultrasonography excels with low cost, availability, and safety. Contrast in the images obtained depends on the imaging algorithm used, backscatter, attenuation of the
sound, and sound speed. Targeted ultrasonic contrast agents for molecular imaging of specific cell-surface receptors hold great promise for the future, although ultrasound requires experienced investigators.

Conclusion: Biomedical imaging provides powerful tools for validation and monitoring of molecular medicine. PET/CT, MRI and ultrasound will be key clinical players in this endeavour. Careful selection of the best suited modality with consideration of strengths and weaknesses of each technique will be essential for optimal results.
A tool to facilitate collaboration and training in nuclear medicine for Latin America

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During the period 2009 -2011, RLA039/ARCALCXX Project has been carried out with the main objective of creating knowledge net about subjects related to radiopharmacy, radiochemistry and nuclear medicine in order to improve and promote knowledge productivity, quality and development in the mentioned areas. By providing one of the products of the mentioned Regional Project, CNEA (Argentina) has contributed to the development, implementation and administration of a Website to facilitate collaboration and Knowledge transfer in NM (Nuclear Medicine). The portal, available since 2010, has been developed in Spanish by using methodologies and tools of KM (knowledge management) in an open source software. As it is a Web2.0 portal, the Web Pages are dynamic and allow the integration of different multimedia resources, such as video and sounds. The main feature of this kind of portal is the interaction between users. People can participate by uploading documents, by making comments or by initiating discussions. As a consequence, the users can feel as if they are part of the Web site. This NM Portal includes some components whose characteristics, in short, are presented as follows:

- **Document Management Module**: It includes the typical operations which take place with the electronic documents, such as: uploading, the search engine indexing and the assigning users’ permissions for resource management. The system assigns permissions not only for individuals but also for “user groups”.

- **Search Engine with in-built assistant**: It facilitates the access to the available information which may consist of database records, images, documents and other types of files. It provides a listing of best-matching results. In the case of using Advanced Search, the assistant retrieves documents from their metadata or Knowledge Map domain.

- **Forum**: It allows the capturing of virtual discussions.

- **RSS (Really Simple Syndication) reader**: It feeds headlines news from OIEA, WNN or other Websites that allows subscription process. Pieces of news can be sorted and filtered with one or more keywords regarding the user’s interest.

- **Calendar Event**: A tool to manage the schedule and notification of upcoming events, such as local, regional or international workshops, seminars and conferences in Radiopharmacy, Nuclear Medicine and related topics.

- **Yellow Pages of NM experts and academic resources**.

- **An interesting feature is the possibility of establishing an instant on-line communication with all the users connected at the same time as a chat tool.**
• Through the Knowledge Map, it is possible to surf the Net accessing to the training material provided in Local and Regional Workshops downloaded to the Nuclear Medicine net.

• Additionally, this site is linked to Latin America NM websites and IAEA Campus site in Medical Health.

This Website greatest strength is language, because communication and training are facilitated when and Portuguese (publications, recommended bibliography, presentations, training material), it may also contain documents in other languages, mainly in English. Basically, this NM portal has been created to promote collaboration and cooperation in Latin America. A selection of possible ways of achieving these goals is mentioned here:

• Encourage formal and informal interchanges among specialists in NM either domestically or regionally. By using the interactive tools available in the Website (forum and chat), it may be possible for two or more professionals located in different countries to hold a live meeting to discuss different subjects. Almost all time zones in Latin America have a maximum time difference of 3 hours.

• Allow the users to find the suitable expert.

• Allow the users to find colleges and courses of study related to the different NM specialities.

• Provide a platform where it is possible to implement training programmes.

• Allows the creation of regional or local platforms. The fact of managing groups of users with different profiles allows the creation of private specific net inside the Website which can be available only for specific users of a particular country, a particular speciality or subject using all Web components as if since they were they were private (documents, events, forums).

• The users can share equipment failures and corresponding solutions, helping others in diagnosis and gravity assessment. Nuclear Medicine practices, patient diagnosis are other possible collaborative fields where this tool can be used.

This site, designed to facilitate online interaction and the availability of useful information for the specialists working in the field, is intended to work as an environment whereby good practices can be shared, along with operative experiences, useful information and training material between all participants, as a kind of CoP (Community of Practice) in NM applications, providing elements for a more efficient and effective development of the activity. However, the success of this NM Portal will only be possible thanks to specialists’ use and feedback as well as the reliable contents created to ensure the Website usefulness.
Nuclear Medicine Latin American Portal
Setting-up and implementing a nuclear medicine specialty training programme in a service hospital and university set-up: Experience from Malaysia

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The Nuclear Medicine Service in Malaysia has its humble beginning in Kuala Lumpur, the capital city of Malaysia, in 1964. The expansion of nuclear medicine has been relatively slow from 1964 until 1990. It was in the 1990s onward that the expansion of nuclear medicine grew with the addition of 12 centres and in 2010 Malaysia had a total of 16 operational nuclear medicine centres operating with different capabilities. From the inception of the first nuclear medicine center in the 1960s until 2007, there was no structured local training programme for nuclear medicine specialists. In May 2002, the Ministry of Health Malaysia (MOH), spearheaded a national conference “Way Forward Plan For the Nuclear Medicine Services” to further chart the development of nuclear medicine for the country. One of the resolutions from this conference was to develop the structured nuclear medicine training for all categories of staff; the programme was implemented in 2008 and at present, the first batch of trainees are in their final year of a 4 year training programme. Some of the issues that had to be addressed to ensure smooth implementation of the programme are: 1) Before starting the programme: justification for starting the programme, turf challenges with other specialty, appropriate design and standard setting of programme, choosing of candidates. 2) During implementation: unavailability of equal modalities in training the centers, limited trainers, infrastructure and staffing constraints, meeting trainee’s practical issues. 3) Upon completion of the programme: placement of candidates, sustainability issues, recognition of postgraduate status, career pathway of graduates, brain drain issues. Various personnel and agencies both in the private, governmental and universities were involved to address these issues/challenges and in ensuring the success of the programme. This presentation will give an insight of the triumphs and tribulations of planning, implementing and sustaining the structured training programme for nuclear medicine specialists in Malaysia.
PLANNING/ESTABLISHING/EXPERIENCES PET CENTRES
The EC Medical Exposure Directive (MED) requires member states to ensure that appropriate quality assurance (QA) programmes, including quality control measures are implemented by the holder of the radiological installation. Detailed requirements on QA in nuclear medicine (NM) in Finland have been given in the guide ST 6.3, Use of Radiation in Nuclear Medicine (2003) and on diagnostic x-ray devices in the guide ST 3.3, X-ray Examinations in Health Care (2006) to establish a good practice in Finland and to harmonise the routine QA at NM departments. Radiation and Nuclear Safety Authority (STUK) collaboratively developed and published guidance on quality control (QC) of SPECT-CT and PET-CT cameras “Advice from STUK 1/2010, Quality control guidance for nuclear medicine equipment” with experts in medical physics, nuclear medicine and radiography.

The number of hybrid imaging devices in Finland is now three times higher than in 2006. The number of PET examinations has increased 44 % from 2006 to 2009. In diagnostic radiology the population dose from CT examinations per inhabitant has risen from 0, 21 mGy in 2005 to 0, 26 mGy in 2008 which is 19 %. The optimization of CT procedures in hybrid imaging was surveyed for the first time in 2011.

The implementation of the guidance, education and training of staff and estimated patient doses from the most commonly used hybrid imaging procedures were surveyed in 2011. A questionnaire was sent to all 19 hospitals and clinics where SPECT-CTs or PET-CTs are used. The response rate was 100 %.

The quality and quantity of training of staff will be discussed in the presentation in two components: radiation protection training compared to the national guidance and introductory briefing for using hybrid imaging devices. The performed quality control measurements for the hybrid imaging devices will be compared to the recommendations by STUK. Attention will be paid to the image fusion accuracy tests and the optimization of CT imaging. Doses to the patients from the most common hybrid procedures separately from NM procedures and CT procedures will be presented and they will be compared to the diagnostic reference levels given by STUK. As results of the survey the possible deficiencies in the quality assurance, training of the staff and in the safe use of the devices will be discussed. The results of the survey will be used to improve the supervision of SPECT-CT and PET-CT devices.
Improving diagnostic accuracy in molecular nuclear medicine in Ghana

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The choice of radionuclides and imaging instruments in molecular nuclear medicine has undergone phases of transformations over the years in a quest to improve on diagnostic accuracy. Accurate interpretation of SPECT and PET images require the adoption of quantitative analytical tools for in-depth review of image reconstruction, correction, and modelling of internal radionuclide dosimetric purposes, to address limitations inherent in the qualitative method. The application of SPECT, PET and PET/CT systems have demonstrated improvements in diagnostic sensitivity and specificity by enhancing contrast resolution in images. Adequate quality control and assurance checks on nuclear medicine imaging systems give users the needed confidence to believe in the output of the equipment. With diagnostic accuracy being a target in nuclear medicine imaging, performance evaluation tests of the Siemens e.cam\textsuperscript{®} SPECT system at the Korle-Bu Teaching Hospital in Ghana has been performed according to NEMA protocols, for compliance with manufacturer’s specifications and users’ requirements, after successful installation of the equipment. Extrinsic uniformity, system energy resolution, system spatial resolution (without scattering), detector shield leakage, and system planar sensitivity were evaluated. The performance evaluation confirmed that the system met requirements for clinical nuclear medicine imaging. On the basis of satisfactory testing results, the Siemens SPECT system has been applied in a number of studies including oncology, cardiology, neurology, and nephrology. SPECT is especially notable for its superiority in detecting bone metastasis. Since the installation of the SPECT system, bone imaging has accounted for \sim{} 83\% of all scintigraphic studies at the Korle-Bu Hospital. Female reported cases have dominated over male reported cases, with peak age at bone tumour detection between 51 and 60 years. Diagnosed bone tumours with their origin in the cells of the bone itself have been found to be less prevalent compared to tumours that metastasize from other parts of the body, notably the prostate. Diagnosed metastatic bone tumours due to spread from prostate cancers have contributed to 19\% of bone tumour cases reported at Korle-Bu. With PET’s ability to provide images of better resolution and sensitivity than SPECT, the study has been extended to focus on improvement of diagnostic accuracy through the development of improved codes for the fusion of prostatic images from PET, CT and transrectal ultrasound (TRUS), based on the principle of mutual information. CT provides better visualization of denser materials e.g. implanted brachytherapy seeds and ultrasound provides better visualization of prostate capsule, compared with SPECT. Codes in MATLAB are being developed to improve on noise reduction, contrast enhancement, and sharpness in images. Image segmentation, construction and reconstruction algorithms will also be written in the MATLAB program for image enhancement and analysis, and the images from the PET/CT and US systems co-registered using rigid-body transformation. The on-going research on the fusion of PET, CT and US images would not only be for diagnostic purposes but help in the better assessment of doses and tumour volumes for improved dose calculation algorithms for treatment planning.
How to make PET-CT feasible in countries with limited economic resources: Estonian experience

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Introduction: PET-CT is a non-invasive and sensitive imaging method for detecting metabolic changes in oncological, neurological, cardiovascular and other diseases which seems to be more expensive than some other diagnostic methods. Estonia is a country with limited economic resources, where the health care expenditures are much lower than in neighbouring developed countries. Estonian health care system, having a predominantly reimbursement-based financing system, sets a significant managerial and financial challenge to any attempt to introduce new innovative and expensive technologies. However, first and regular PET-scans were launched in Estonia already in 2002 and regular PET-CT scans are now performed in three centres.

Aim of the current study was to analyse the crucial managerial and financial key factors that have assured the regular use of PET-CT in clinical practice at North Estonia Medical Centre. Key factors making PET-CT feasible were according to our observation the following: 1) Interdisciplinary collaboration of nuclear medicine and radiology staff; 2) Education of referring doctors; 3) Thorough observation of cost-effectiveness issues; 4) Exploiting the PET-CT scanner as a regular CT unit during the time when it was not used for PET scans.

Description of key factors:

1) Training, partly provided in the framework of collaboration with IAEA, formed a solid basis for collaboration of nuclear medicine and radiology staff. Another important factor was the establishment of close interdisciplinary collaboration - first thousand PET-CT scans were interpreted together by radiologists and nuclear medicine physicians. These two factors have assured optimal use of the available work force.

2) For the education of referring doctors simultaneously with seminars and other training events, system of individual supervision was introduced, providing justification in every individual clinical case, and assistance in clinical implementation of PET-CT scans.

3) Clinical use of PET-CT has been demonstrated to be cost-effective in many clinical conditions, e.g. for staging of non–small cell lung cancer, differential diagnosis of solitary pulmonary nodules, restaging of Hodgkin disease and non-Hodgkin lymphoma, and restaging of colorectal carcinoma. Savings in the order of $91–$2,200 per patient have been shown. In our case we have been able to demonstrate that in well justified cases change in intended management of the patient may result in savings exceeding the double amount of PET-CT costs.

4) At our centre, PET-CT scanning is performed on 2-3 days of the week. During the remaining working hours our scanner is used as a regular CT scanner, which allows radiology to partially take over the responsibility of a part of investment costs.
Conclusion: In countries with limited economic resources PET-CT scanning can be made feasible by the means of a number of managerial and financial measures.
FDG-PET/CT and mediastinoscopy in mediastinal staging of lung cancer: Case report

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Introduction: 58 year old male patient was submitted to 18FDG-PET/CT for the staging of the central cancer of the right lung. Patient presented with cough, chest pain and dyspnoea. Bronchoscopy revealed malignant central tumour of the right upper lobe, squamous cell carcinoma was diagnosed on pathology.

Methods: Whole body 18FDG-PET/CT was performed on GE Discovery STE scanner. PET study was performed one hour after injection of 170 MBq FDG with low-dose CT.

Results: PET/CT scan showed 16 x 13 mm soft tissue mass in the hilum of the right lung with intense FDG uptake (SUVmax 11, 2). Additionally, there was increased FDG uptake (SUVmax 5, 2) in mediastinal and bilateral hilar (group 2R, 4R, 4L, 5, 7, 10R, 10L, 11R) lymph nodes. On CT, lymph nodes were clearly seen with short axis diameter up to 1 cm. No pathological FDG uptake elsewhere in the body was found. PET/CT confirmed the presence of metabolically active tumour in the hilum of the right lung. Mediastinoscopy was performed to assess mediastinal lymph nodes, no malignancy was found in paratracheal and subcarinal (groups 2, 4R, 4L and 7) lymph nodes. Surgery was planned according to results of PET/CT and mediastinoscopy. Right upper lobectomy was performed with removal of paratracheal, subaortic, para-aortic, subcarinal, left and right hilar and interlobar lymph nodes. Consecutive pathologic evaluation revealed metastases in 3 out of 5 right hilar lymph nodes, in mediastinal and left hilar lymph nodes inflammatory changes were found.

Discussion: In this case many of the mediastinal and hilar lymph nodes were metabolically active, which in the presence of malignant lung tumour always raises the suspicion of metastases in the lymph nodes. However, it is well known that inflammatory lymph nodes can show increased FDG uptake. Probability of inflammatory changes is especially high with symmetric involvement like in our case. Therefore pathologic verification of FDG-positive mediastinal lymph nodes is highly recommended. In present case only 3 lymph nodes in right hilar region were metastatic, but the other lymph nodes that showed similar FDG uptake were inflammatory. Our case underlines the fact that metabolically active lymph nodes should not be considered metastatic in treatment planning before pathologic verification. The results of 18FDG-PET/CT and mediastinoscopy were complementary and allowed accurate treatment planning.

Conclusion: Inflammatory changes are common in mediastinal lymph nodes; therefore pathologic verification of FDG-positive lymph nodes is essential for correct staging of lung cancer.
Implementing a hospital radiopharmacy in the Uruguayan centre of Molecular Imaging

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The Uruguayan Centre of Molecular Imaging (CUDIM) is a venture of the country to meet the care needs in the area of molecular imaging, enabling this technology since its creation. In addition to the diagnostic purpose, research and development of new clinical protocols and PET tracers, as well as the training of specialized human resources are the objectives of the centre. The existence of a facility that has clinical and pre-clinical areas can synergize healthcare services, research and development as strategic lines. To achieve these goals, equipment is required that enables the synthesis of a variety of radiopharmaceuticals, allowing their characterization and monitoring of physical, chemical and biological quality controls. The production of radionuclides and radiopharmaceuticals for use in patients implies a range of services: electricity, air, gas and water system of high purity. From the point of view of patient care quality standards, the radiopharmaceutical production area should fulfil the radiation protection and pharmaceutical quality requirements. The Radiopharmacy area has a PET Trace Cyclotron (General Electric-GE), a 220m2 GMP area segregated in laboratories for the production of different radiopharmaceuticals: 18FDG (18-fluordeoxiglucose) laboratory with a module Fastlab-GE, 11C-radiopharmaceuticals laboratory with a Tracerlab-GE module, a 68Ga radiopharmaceuticals laboratory with a Gallea module (GE) and a development laboratory, which contains a module for 11C-radiopharmaceuticals and a module for nucleophilic 18F-radiopharmaceuticals synthesis, placed in hot cells and shielded laminar flows. The Radiopharmacy also has a physicochemical quality control laboratory and sterility/pyrogens control laboratory. Moreover, there are chemical development, animal facilities, cell culture and animal surgery laboratories. A trimodal camera PET / SPECT / CT (Triumph, GE) for small animals complements these facilities. The major handicaps in the Centre building phase have been the development of services (air and gases) and clean areas. The previous training of the staff members in reference centres has played a key role, giving Uppsala University very import support. The Centre is actually producing on a regular basis 68Ga-DOTATATE and 18FDG, planning several 11C-radiopharmaceuticals production before July 2011 (methionine, choline and PIB). From the aforementioned, the design, implementation, commissioning and development of a Radiopharmacy area, with healthcare, research and development purposes requires a multidisciplinary staff with strong background in chemistry, pharmacy, biology and expertise in radiochemistry/radiopharmacy.
Challenges in establishing PET/CT-cyclotron facility in a developing country-
Bangladesh experience

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Over the past decade PET/CT technology has emerged as a powerful and very sensitive
diagnostic tool especially in the management of cancer patients. In the developed world it is
accepted as an integral part in quality management of oncology patients, particularly after
introduction of fused PET/CT. Yet in the developing world the setting up of PET/CT
programme has been considerably slower, and in some regions no such facilities are available
yet. In Bangladesh cancer poses a serious health problem and is a leading cause of mortality,
and the establishment of a PET/CT facility has been well-justified. Attempts and efforts to
justify and convince the government ministries including Planning Commission regarding its
essentiality were successful. The project for establishment of PET/CT was proposed in 2006,
but it took a few years for clarifications and settling other issues. The main application of
PET/CT is in oncology, and the ideal location for this equipment should be a tertiary level
institution dealing with cancer patients. It is critical for the cyclotron to be set up assuring
availability of positron-emitters of shorter half-lives beyond F-18. We faced difficulties in
selecting the appropriate site for cyclotron because of different authorities’ desire to have the
cyclotron established in their control. The government has now decided to establish a
cyclotron in the hospital campus. Selection of the type of cyclotron to bet set-up is also
crucial. Initially we were planning to establish a high energy 30MeV cyclotron to produce not
only positron-emitters but also the SPECT isotopes, but when we faced the reality regarding
the expenditure and time for such establishment from vendors and also the IAEA, the decision
was revised finally to have a cyclotron of around 10MeV. This delay occurred due to
inexperience on our part, as well as local agents of vendors. For PET/CT, the specifications
should be prepared by experienced persons; vendor’s help is also extremely important. Lack
of reimbursement for PET/CT studies is a serious limitation to sustain any business plan.
Human Resource Development (HRD) for this advanced technology is a major issue for all
developing countries. Assistance from international agencies like IAEA is very much required
in providing technical support for HRD where PET technology is still unavailable. The factors
affecting the implementation of PET/CT-Cyclotron programme in a country like Bangladesh
are multifarious and even minor discrepancies may cause unforeseen impediments. Few of
these come as a result of ignorance on the part of anyone involved even in the evaluating
process, not to mention about the decision makers, while personal observations, if not
objective and realistic, may cause unexpected delays and deviations, this results in a waste of
time and efforts and also frustrate the initiative. These problems are encountered in a
government set-up but not in a private/corporate set-up, where the decisions come fast and
implementation completed exceedingly smoothly due to automatic elimination of the
bottlenecks. Facilities have been created in the private sector within a short time span.
Belarus has roughly 9.49 million inhabitants. At present radiotherapy in the Republic Belarus is realised in 13 cancer institutions (N.N. Alexandrov National Cancer Centre (ANCC) of Belarus and 12 regional oncological clinics).

Due to multiple factors Belarus cancer centres have been slow to implement and utilize a number of techniques that are considered components of routine radiation oncology practice. These include PET scanning for cancer staging and RT planning, IMRT, 3D and 4D treatment planning, modern HDR brachytherapy and stereotactic treatments. Till now there are 36 units for external beam therapy in the country: 28 – 60Co-units and 8 – linear accelerators. X-Ray therapy is realised on 18 devices. For undertaking brachytherapy in Republic Belarus there are 16 devices. There is also IBU in ANCC. There are 23 planning systems in Belarus, including SWIFT planning system for image-guided prostate brachytherapy in ANCC.

The barriers for the implementation of new technologies in radiation oncology are multifactorial and include the following points: An extensive refurbishment program in the frame of the National Cancer Program of Belarus is underway and most of the treatment units are modern or due to replacement. There is moderate health expenditure in Belarus compared with many other developed countries and funding of the national cancer program is relatively limited. This fact explains the absence of PET technology in the country at the present time (installation is programmed for the next years). Also despite the presence of motivated and well trained professionals in Belarus there is a distinct lack of radiotherapy technologists within pre-treatment imaging areas (including PET, SPECT MRI) for both external beam radiation treatment/brachytherapy, and there is no system of education for radiotherapy technologists and no formal training program for medical physics specialists.

As possible solutions to resolve these barriers for implementation of new technologies in radiation oncology, the following steps will be of importance: 1) to provide the national cancer program with enough financial support for the adequate provision of the necessities of the country in radiation oncology units in relation to the population number and in accordance with recommendations and guidelines of IAEA and others professional societies; 2) to organize the national system of education for radiotherapy technologists and for medical physics specialists including formal training programs.
Current status and perspectives of clinical PET in Korea

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The first medical cyclotron MC50 was installed in Korea in 1984 at the Korea Cancer Centre Hospital (KCCH), which was used mainly for research and radioisotope production such as Ga-67, Tl-201 rather than positron emission tomography (PET) tracers. So it was not followed by installation of PET for 10 years. The first PET was installed in other hospitals in 1994: one in Seoul National University Hospital (SNUH) and another in Samsung Medical Centre (SMC) with their own medical cyclotrons. KCCH installed PET in 1995. Installation of PET in Korea was accelerated by commercial cyclotrons in 2000. Several companies competed in installing commercial cyclotrons. The first PET/CT was installed in 2003 which was followed by rapid growing numbers of PET/CT facilities. Coverage of medical insurance for staging and restaging of cancer, determination of myocardial viability as well as detection of seizure focus by PET accelerated installation of PET/CT in Korea. By the end of 2009 the number of PET/CT and PET was 129 and 14 in 78 institutions. Production of home-made medical cyclotron by the Korea Institute of Radiological and Medical Sciences (KIRAMS) accelerated installation of cyclotron centres. By the end of 2009 the number of cyclotrons was 34 which included 7 home-made cyclotrons. The number of PET tracer distribution centres operated by private-public partnership (PPP) was 14. PPP was one of reasons of successful growth of PET/CT and cyclotron services in Korea. PPP services were imported by university hospitals first, and then expanded to private clinics. Mostly using PET application is F-18 FDG PET for oncology which occupies more than 95% of all PET examinations, and 25% of all nuclear medicine imaging tests. Other PET applications include brain and cardiac studies. Recently two new PET tracers, F-18 FP-CIT and F-18 fluoromisonidazol, were approved by the authorities for commercial use, and clinical trials for new PET tracers are gradually becoming more active. The first PET/MRI was installed in 2008, which is being used for neurologic research purposes, which was followed by the installation of whole body PET/MRI, again for research purposes. They were composed of two separate PET/CT and MRI systems. First clinical PET/MRI is installed in 2011, which is expected to be followed by many clinical PET/MRI facilities in the near future.
Over one decade of experience in PET imaging at KFSH&RC-Riyadh, Saudi Arabia

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Over the past decade PET/CT imaging has become a standard of care in cancer management worldwide. In Saudi Arabia, PET was introduced at the KFSH&RC in 1995. One of the major challenges of its implementation was the availability of 18FDG. So, the institution installed its own production facility, initially with one in 1982 and currently operating three cyclotrons. The last two were installed in 2005 and 2010, respectively. Presently the production facility supplies more than 7 PET/CT centres nationally; in addition to meeting the institutional needs. Our centre receives about one Curie average of (639) mCi of 18FDG daily, which is used to scan about 18-patient-daily-work load using two PET/CT scanners with the prospect of increasing our patients load to 25-30 a day in the coming year 2011. The section of nuclear medicine performed a total of 2449, 2638, and 2315 in 2010, 2009, and 2008, respectively. In this presentation, an overview of the KFSH&RC’s 15 years of experience with PET/CT imaging and 18FDG production will be presented with a discussion on our vision for the future. The discussion will also present examples of the major types of cancer and service provided by our centre.
Nuclear Cardiology in Tajikistan

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Aim: This first survey of the working scientists in the Department of Nuclear Medicine of the Institute of Gastroenterology in cooperation with the working group at the Cardiology Centre in Tajikistan and other hospitals, was to deliver information on the procedures and in particular on the development of myocardial perfusion scintigraphy (MPS) from 2009 to 2010.

Method: A questionnaire was produced to evaluate MPS for the years 2009-2010.

Results: 106 completed questionnaires were returned (13 private practices, 93 hospitals). MPS of 106 patients were reported with 85 stress and 106 rest studies. All patients (106) was performed with (99m)Tc-MIBI. The types of stress were exercise (treadmill) in 94.3%, vasodilation with adenosine in 5.6%. 106 patients of all MPS were SPECT studies. 8.4% of all MPS were requested by ambulatory care cardiologists, 12.4% by internists, 2.8% by primary care physicians, 66% by hospital departments and 4.7% by others.

Conclusion: In Tajikistan, MPS is predominantly performed with (99m)Tc-perfusion agents. The common type of stress is the treadmill. SPECT and attenuation correction do not yet represent standards of MPS practice in Tajikistan, which indicates some potential of optimization.
In the State Reform and Development Program of Health of the Republic of Kazakhstan for 2005-2010 oncology diseases were defined as socially significant. One of the most important methods of reducing mortality and disability in the population of socially significant diseases is the introduction of innovative diagnostic technologies that can detect the disease and its complications at an early stage. In this regard, the Ministry of Health decided to create Kazakhstan's first PET-Center based of JSC "Republican Diagnostic Center." It should be noted that the development projects and commissioning works were carried out with the direct participation of the Institute of Nuclear Physics, National Nuclear Center of Kazakhstan (INP NNC RK), in close cooperation with system integrator for the supply of equipment - the company «Inter-Medico Gmbh», Germany. Through this, we managed to avoid many pitfalls in the design and timely adjust the project to construction stage. The whole course of work on launching the Centre justifies the choice of diagnostic and production equipment from companies leading in their respective fields. Cyclotron and equipment for the synthesis of the radiopharmaceutical (RFP) were supplied by IBA, Belgium; protective equipment - the company COMECER, Italy, equipment for quality control laboratory - the company RAYTEST, Germany. Thus, we managed to improve on the criteria of reliability and performance of the processing chain for the production of the RFP.

The main problems we faced and continue to face in establishing the first PET Centre in Kazakhstan are: the lack of legal framework, lack of trained personnel and there are also persist to be problems in the maintenance of the equipment which remain to be resolved since the warranty terms had expired.
Tumour markers investigation in every-day practice of reproductive health clinic in Kazakhstan

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According to “Interfax-Kazakhstan” information agency there are more than 30 000 new registered cases of cancer in Kazakhstan every year, and half of these patients – 15 000 – die every year, including 1 500 Almaty citizens. Almaty specialized oncology clinic (dispensary) investigations showed that the prevalent tumour type among the male population in the republic is lung cancer, followed by alimentary canal oncology diseases, and prostate cancer. The female population frequently suffers from breast cancer, followed by cancer in the uterus and malignant tumours in the ovaries. 30% of the patients referring to the oncologists are already in the 3-4th cancer stage. That is why the tumour markers screening is the actual problem in Kazakhstan. The screening programme for oncological diseases in the Republic was initialized in 2001-2002 by the IAEA Technical cooperation project RAW 6007 and was prolonged in the TC project KAZ 6005 in 2003-2004. The investigations were started from PSA total, PSA free, CA-15-3 on the basis of Republican Research Centre for Mother and Child Health Care (now Scientific Centre of Obstetrics, Gynaecology and Perinatology) endocrinology laboratory with the «Immunotech» Beckman Coulter IRMA kits. Later raw parameters were added with the CEA, hCG and AFP. At the present time the Scientific Centre of Obstetrics, Gynaecology and Perinatology (SCOGP) is the specialized clinic for reproductive health. The laboratory department have the opportunity to check the basic scale as CA-125, CA-15-3, CA-19-9, CEA, hCG, free β hCG, AFP, PSA total, PSA free by IRMA or ELISA methods.

The main occupation of the Centre is the maternity hospital and gynaecology. So the most employed tests are tumour markers for breast, ovaries and uterus cancer elicitation in patient’s blood with neoplasm growth. In this cases CA-125, CA-15-3, CEA, free β hCG, hCG and AFP help to differentiate malignant from noncancerous tumours. PSA tests are used in male patients in the reproductive technologies department. In case of “positive result” (double cut off result) the investigated patient is guided to Almaty Oncology Centre for special management according to the investigations and treatment protocols. But some patients prefer to spend the tumour markers monitoring after (or during) treatment in SCOGP laboratory.

Due to IAEA TC projects, which began the tumour screening in Kazakhstan, more than 7000 patients were investigated in SCOGP up to that time. The cut off results were found in 4, 6%. Diagnosis of cancerous tumour was confirmed in 1, 1% of all investigated patients. The quantity of tested patients and quality of cancer management is not perfect yet, but screening for tumour markers is a very important direction for clinical laboratory diagnostic in Kazakhstan. This programme needs to be further developed in order to achieve the best results and improve people’s health and quality of life.
The Nuclear Medicine Department at Inkosi Albert Luthuli Hospital was commissioned in January 2003. As this was a new hospital, planning started at grass roots level. The initial proposal indicated that there could be a PET scanner with an on-site cyclotron installed, and thereafter, lobbying for a PET-CT scanner began. In 2006, the Provincial Department of Health of KwaZulu-Natal announced that the delivery of a PET-CT scanner was imminent. Geographic location for such a scanner was an important consideration for ease of management as radiographers were a scarce resource. Also the new scanner would have to be fairly close to the existing Nuclear Medicine Department so as to access the existing hot-lab facilities. After much discussion and letters of motivation, the 'Isolation Ward' which was to be used for patients that needed to be isolated from other patients, was agreed on as a possible site. This area was directly adjacent to the existing department. The Isolation Ward was cleared out and plans to convert this ward to house the PET-CT scanner and patient rest area commenced. In May 2007, the PET-CT department officially opened and the first patient was imaged. This was a novelty in the country as the PET-CT scanner was the only PET facility in a public sector hospital not only in the KwaZulu-Natal province but also in the country of South Africa. The presentation will reflect on our early challenges and how most of these were bridged during the first few months; and we continue to explain the current situation.
Challenges of licensing on clinical PET and molecular Nuclear Medicine in Indonesia

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Indonesia as a developing country has started a new era in Nuclear Medicine. Indonesia has operated two PET-CTs in hospitals. FDG is used in supporting the operation of PET-CT and is produced by a cyclotron. The installation and operation of a cyclotron or PET-CT are controlled by the Nuclear Energy Regulatory Agency (NERA). Indonesia has three Cyclotrons. (1) Cyclotron operated by Government for research purposes (2) Baby Cyclotron operated by the private hospital to produce fluorodeoxyglucose (FDG) (3) the Cyclotron is under commissioning. The basic principles of nuclear energy regulation practice in Indonesia set out in the law provide that control of any nuclear energy application is aimed to:

a) Assure the safety and the health of workers and public, and the environmental protection.

b) Maintain the legal order in implementing the use of nuclear energy.

c) Increase the legal awareness of nuclear energy user to develop a safety culture in nuclear field.

d) Prevent the diversion of the purpose of the nuclear material utilization.

e) Assure for maintaining and increasing the worker discipline on the implementation of nuclear energy utilization.

Challenge and Strategy: License granting and license revocation is not a simple task for the Regulatory Body. Issuance of license should have serious study of those who issue licenses. Licensing requirement must have clear criteria. Users who operate PET-CT must have license from the NERA. To obtain license the use of PET-CT, license applicants must meet requirement of administrative; technical; and/or special requirements. Based on Government Regulation, the special requirement in the construction and operation phases of Cyclotron and PET-CT is: site selection; construction; commissioning; operations; and/or closure.

As a newcomer in the use of PET-CT, NERA is a challenge in determining the requirements to obtain operating licenses PET-CT, namely in determining the acceptance criteria: Operating Procedures; Standard of Technical Specifications Cyclotron and PET CT; Radiation Protection Equipment; Radiation Safety and Protection Program; Safety Verification (protocol to function test) and qualified personnel needs. NERA strategies done to overcome these challenges are: Inviting experts from manufacturing cyclotron for presentation and discussion of technical specifications; Inviting experts from manufacturing PET for presentation and discussion of technical specifications; Inviting personnel who had Clinical PET and Molecular Nuclear Medicine courses for presentation and discussion; Discussions with nuclear medicine specialists. Employees of NERA downloaded documents
related to Clinical PET and Molecular Nuclear Medicine, and discussed with other employees; requesting IAEA assistance.
The impact of the establishment of the first nuclear medicine centre in Yemen in 2008: The challenges and its effect on medical management, treatment and outcomes

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The establishment of the first nuclear medicine center in Yemen in mid-2008 was achieved after years of cooperative efforts coordinated between the IAEA and the local authorities represented by NATEC (national atomic energy commission) and Al-Thawara General hospital in Yemen.

The diagnostic and therapeutic services presented by the center to almost all the hospitals and health centers in the capital city of Yemen, later extended to other cities, gradually developed tremendous effects on the management and treatments strategies, mainly including management of coronary artery disease, obstructive renal disease, pre-and post-operative evaluation of potential nephrectomy cases, primary or secondary bone tumors and infectious bone diseases, joints prosthesis evaluation, benign thyroid tumors, evaluation and treatment plans for lymphomas, biliary atresia in newborns etc., playing decisive role over its medical or surgical management, in addition to the major role of the center in the management of post-operative cases of the differentiated thyroid cancer by the iodine 131. Over the last three years the medical staff in Yemen has greatly acquainted to the benefits of nuclear scans, its role among other imaging modalities, radioiodine therapy of the differentiated thyroid cancer, resulted in gradual increased numbers of referred cases to the center, introducing new protocols and nuclear tests. Among the major challenges faced by the center’s administration:

- Limited numbers of vendors (sources) of the radiopharmaceuticals - one vendor.
- Limited number of international curriers for radiopharmaceuticals- one currier.
- Restricted legislations concerning the radioactive materials in Yemen, from the security agencies in particular.
- Lack of awareness from other medical professionals about nuclear medicine applications.
- Public radiation phobia.

So in the last three years, the center’s administration has conducted many measures to overcome many of these challenges:

- Conducted many sessions, meetings, workshops with security agencies for the purpose of education, highlighted many aspects of radiopharmaceuticals, its international regulations and legislations. These sessions have been conducted in coordination with local atomic energy committee (NATEC) and international experts. Those activities are documented.
• Held indoors and outdoors academic and general activities with medical professionals from all departments and centers in all major cities (documented).

• Publishing brochures, booklets of nuclear medicine applications.

• Conducted multiple interviews in public media (documented) (TV satellite channels, local newspapers).

• Contacting other international radiopharmaceutical companies, signing preliminary importing agreements.

• Many consultations have been given to the private sectors intended to establish its own nuclear medicine departments, one sector just recently finished establishing its own center under direct consultation and supervising from our center.

• Documented regular (weekly, monthly, yearly) statistical data for all academic and clinical services at the center (will be presented if required).
Medical cyclotron project at the National Cancer Institute in Bogotá Colombia: A successful partnership with the IAEA

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Background: In modern medical science, nuclear imaging has become an important diagnostic tool in functional and metabolic imaging that provides clinically relevant information not obtainable with conventional imaging modalities. At present, there is only a baby-cyclotron in Colombia for a hospital's self-production of F-18 FDG. The National Cancer Institute (INC) is a public entity responsible for cancer prevention, care, teaching and research. A National Project was conceived at the INC and supported by the IAEA to establish a medical cyclotron at the INC to cover, at least partly, country-wide necessities.

Objective: 1) To establish a medical cyclotron facility, first of its kind in the country, at the National Cancer Institute (INC) in Bogotá, 2) To promote the use of PET CT for cancer management throughout the country by producing and marketing PET radioisotopes for diagnostic imaging and research at the INC.

Methods: Project implementation required interaction, input and approval by several government instances: [NC, the Ministry of Social Welfare, the Ministry of Energy and the National Planning Department. The National Project included (i) development of a project with IAEA support (COL 601 L 2004); (ii) submission of the project to the above-mentioned government entities for their appraisal and approval (2006); (iii) procurement of technology and equipment (2007); (iv) design of a facility following local and national building and licensing regulations (2008); (v) design a project for installation and implementation to ensure that the staff had the required skills and that all the specific additional technology was procured. Steps 2 through 5 were accomplished through the technical backstopping provided by the IAEA and the Ministry of Energy (2008-2009); (vi) design of a project to establish a centre of excellence and of a high quality production unit (2009-2011); vii) design and implementation of a teaching program including new lines of PET clinical research, medical training, training in radiopharmacy, radioprotection, medical engineering, PET centre management.

Expected Results: i) Trained human resources; ii) Nuclear medicine knowledge will be transferred through teaching programs; iii) New lines of research will be developed through clinical research protocols; iv) Teaching agreements will be signed with universities across the nation and abroad; v) National evidence-based guidelines will be developed; vi) International technical cooperation to strengthen the use of PET CT in cancer will be sought; vi) Standard operating procedures will be developed; vii) Patients will be confidently diagnosed and managed using PET CT. Currently, the construction of the new building that will house the cyclotron, radiopharmacy and PET CT is nearing completion. The new facility meets architectural design, radiation safety and GMP requirements and standards.

Conclusions: i) the Colombians that live under the most vulnerable conditions will have full access to personalized cancer management: this should have an impact on quality of life and...
equity indexes; ii) The Colombian nuclear medicine will be able to provide the "standard of care" diagnostic procedure in the field; iii) Effective transfer of knowledge and competence will provide us with the necessary means to manage the project and to design new ones; iv) The INC will strengthen its role as a national and regional training centre.
Nuclear medicine is a fast growing and dynamic specialization. In recent years with the advent and wide-spread use of PET, PET-CT, SPECT-CT and newer applications in radionuclide therapy, there has been a need for continuous appraisal and updating of nuclear medicine professionals on various aspects of the changing trends in this field. Although nuclear medicine is being practiced in most countries of the world, due to heterogeneous growth of this specialization there has been significant difference in the quality of practice between countries.

In Morocco, hybrid imaging can improve management of cancer in different fields, SPECT-CT is the first step to optimize theragnosis in daily routine such as management of thyroid carcinoma and bone lesion in patients with cancer: In patients with differentiated thyroid carcinoma, SPECT/CT improves the diagnostic accuracy of the 131 I scan in differentiated thyroid cancer, by better distinguishing cervical lymph node metastases from residual thyroid tissue, lung from mediastinal metastases or bone from soft tissue metastases. Thus, SPECT/CT allows precise localization of equivocal lesions and their characterization as malignant or benign. SPECT/CT allows for the first time a reliable diagnosis of lymph node involvement as early as at the time of radioablation of the thyroid remnant, thus opening a new avenue to more accurate staging of patients with differentiated thyroid carcinoma. Moreover, the possibility of combining true attenuation corrected information on tissue distribution of radioactivity within the body with anatomical definition of tumour lesions allows better estimates for treatment planning to be derived in terms of both target size and radioiodine avidity. SPECT/CT offers the unique opportunity to correlate the scintigraphic findings with anatomical images for better classification of indeterminate, non-diagnostic bone lesions detected at 99mTc-MDP scintigraphy in patients with extra-skeletal cancers. Besides the improved diagnostic accuracy obtained by correlating functional with morphological images, SPECT/CT also provides better diagnostic confidence than side-by-side viewing of separate sets of images.

The strong commitment of Lalla Salma foundation fighting against cancer, established the first register in Casablanca in 2004, and the second one in Rabat in 2005; which indicates 35000 new cases in Morocco every year, of which only 12000 are taken in charge. In Casablanca, the incidence of 101, 7 new cases/year of 100.000 versus 120, 5 in Rabat city. Breast cancer is in the first position, followed by lung cancer, gynaecological neck cancer, prostate and bladder cancer. Cancer is considered nowadays one major cause of death in Morocco and constitutes one of the major problems of public health. However, hybrid imaging is actually the best relevant exam in the management of cancers. Morocco has under its disposal five public centres of oncology in: Rabat 2, Casablanca, Agadir, Oujda; 6 private centres 3 in Casablanca, 2 in Rabat and 1 in Fes. The number of nuclear medicine centres increased in both public and private centres: In all we have five university public centres, military hospital centre, two semi-private centres and six private centres.
Hybrid imaging begun to be implanted in Morocco since 2010 in university and private centres:

Hybrid imaging in University teaching centres:

- Rabat: IBN SINA teaching centre is the first department of nuclear medicine in Morocco: Planar camera, One SPECT, SPECT-CT “in progress”, project of PET-CT
  - Military hospital since 2003: SPECT-CT in 2010, PET-CT in progress
  - Sheikh Zayed hospital since 2005: SPECT, PET-CT in progress

Casablanca: IBN ROCHD teaching centre in since 2003: Planar camera, SPECT, PET-CT in 2011

Fes: In progress; One SPECT-CT in 2010, not yet operational

Marrakech: In progress; One SPECT-CT in 2010, not yet operational

Oujda: Not yet

Hybrid imaging in private centres:

- Rabat: Al Azhar Oncology centre: First PET-CT in Morocco: 26/11/2010
- Casablanca: Anoual Centre in Marsh 2011

Cyclotrons:

For PET centres, Morocco has two cyclotrons:

- RIM “Radio Isotop Mediterrannee” located at Bouznika city between Rabat “35 km” and Casablanca; this centre produce FDG
- Bouskoura centre; located at 100 km from RIM: in progress to produce FDG

Hybrid imaging is actually the best exam in nuclear medicine in the management of cancer and it will play a relevant role in the diagnosis, therapy, and theragnosis.
Modern technologies of logistics network creation for short-lived isotopes

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An overview of cyclotron based pharmaceutical production centres all over the world and the actual way of distribution will be given. The approach of producing radiopharmaceuticals for Positron Emission Tomography (PETpharms.) is very different when comparing continents, countries, the private and the public sector. Whereas marketing authorisations or authorised clinical tenders are an obligation when using PET pharmaceuticals in humans (e.g. France, USA), there are special soft regulations to authorise the use of these products under special conditions (e.g. Italy, eastern European countries, a.o.). Based on the paradigm that production of PETpharms labelled with ultra short-lived Nuclides is a necessity for running a state-of-the-art PET-CT, rather, a high density of cyclotrons - up to one installation per million inhabitants - are installed in some regions (e.g. Belgium, Milan-Lombardia). The authors show that a huge panel of PETpharms can be produced based on labelling with Fluorine-18 (shelf life 119 minutes). There is no more need for the production of PETpharms with Carbon-11 (shelf life 20 minutes). The clinical routine may easily be covered by the PETpharms shown by the authors covering a wide range of indications like oncology, cardiology, neurology and others. The national and international rules governing the production of PETpharms are requesting more and more accurate site planning for new cyclotron based pharmaceutical production. To comply with the guidelines on the good manufacturing practice, special concepts on work flow, HVAC-system, radiation protection, and clean rooms are needed. Therefore a higher investment in dedicated pharmaceutical production centres for PETpharms is needed instead of installing a high number of cyclotrons without a well prepared pharmaceutical infrastructure. Even the production yields of standard sites using 16-18 MeV cyclotrons have been increased by using better synthesis procedures or new materials (e.g. Niobium targets). Today, a professional organized PETpharms facility may supply 30,000 patients a year in a range of 4-5 hours logistic, thus supplying 15 PET/CT centres, each of them running 2,000 patients a year. This includes a number of even 5-10 products being supplied outside of Fludeoxyglucose (FDG), the most common PETpharm. The number of different PETpharms being delivered to the PET/CT users is increased based on Multi-Tracer concepts in the production. In case of supplying costumers not being reached by car within 5-6 hours, a distribution by aeroplane is suitable.

Conclusion: Modern Technologies, used in newly installed cyclotron based pharmaceutical production centres, are the basis for a wide range of PETpharms being available for a rising number of PET/CT users and patients. The higher production yields allow the distribution of PETpharms on a higher distance or logistic radius including planes. Due to a professional management of fluorine-18 labelled PETpharms for all requested indications, in-house production becomes a tool only needed when dedicated to (mostly animal) research. Adapting to regulatory needs, less but more dedicated PETpharm production sites should be installed.
DOSIMETRY AND RADIATION SAFETY
Internal dosimetry hyperthyroid patients by quantification in live: Method of images conjugated

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In nuclear medicine the quantification of organs is done through a procedure called Planar Image technique, however we face difficulties due to different factors which affect the quantification precision of radioactivity: such as the degrading of spatial resolution, the structures or organs that contain radioactivity, which in many cases can be over or beneath the organ of interest. To do this, we are going to use the method of images conjugated to determine the activity and after the doses calculus in patients with hyperthyroidism.

Methods: First we performed a description of the operation and the characteristics of Siemens Gamma camera model E-Cam, as an important base of the quantitative process of measurements. We carried out the different quality control procedures to the Gamma camera, such as: uniformity, sensibility and resolution (Table 1), and discussed the factors that affect the image quantification as Bio-kinetic of physical factors, and the corrections to achieve a better estimation of the activity.

### Table 1: Values of Uniformity

<table>
<thead>
<tr>
<th>DETECTOR 1</th>
<th>DETECTOR 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FOV Central</td>
</tr>
<tr>
<td>Integral (%)</td>
<td>1.72</td>
</tr>
<tr>
<td>Differential (%)</td>
<td>1.19</td>
</tr>
</tbody>
</table>

We not only made a calculus of corrections for scattered photons using the Triple Energy Window (TEW) for the lodo-131 with the Neck Phantom Thyroid, but also a correction calculus by attenuation of the source region and source thickness, considering the over-placing of the source regions when taking the images; it was given by following expression:

\[
A_{ROI} = \sqrt{\frac{I_{A \text{ IP}}}{{e^{-\mu t} f_j}} C}
\] (Ec. 1)

Where A is the activity on injure in MBq, IA and IP are the counts of anterior and posterior to 0° and 180° acquisitions respectively, C is the effectiveness of Gamma camera, (cps/MBq), t is the total thickness of the patient, ue is the coefficient of lineal attenuation of thickness t and fj is the factor of correction by thickness. Furthermore, we made the acquisitions of anterior and posterior images to determine the transmission factor (Rate of counts with the Phantom and on air) and calibration factor C of the Siemens E-cam Gamma camera using the model Thomas, Rate of counts per unit of activity (Ec. 2, Table II).
\[ C(\text{cps/MBq}) = \frac{\sqrt{cps_A \times cps_P}}{e^{-0.1 \times x \times t}} \]  
(Ec. 2)

**Table II: Calibration Factor of Gamma camera, C**

<table>
<thead>
<tr>
<th>Polietileno (cm)</th>
<th>Detector 1 (cps) Average</th>
<th>Detector 2 (cps) Average</th>
<th>Total Average</th>
<th>C (cps/MBq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>For 0, 1, 2, 3, 4, 5, 6, 7, 8 cm of thickness t</td>
<td>1850</td>
<td>1900</td>
<td>1875</td>
<td>50.67</td>
</tr>
</tbody>
</table>

Afterwards we made 2 acquisitions (Uptake) with a source in the tumour (T) and another with a source over Neck Phantom Thyroid (RC), we defined 2 ROIs in the anterior Tumour, and also 2 in the posterior; using the same procedure with the source on RC (Table III).

**Table III. Anterior and posterior image counts per seconds.**

<table>
<thead>
<tr>
<th>Source</th>
<th>Image</th>
<th>cps A</th>
<th>cps P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uptake 1</td>
<td>RC Only T</td>
<td>2982</td>
<td>8961</td>
</tr>
<tr>
<td>T Only T</td>
<td>48358</td>
<td>72444</td>
<td></td>
</tr>
<tr>
<td>Uptake 2</td>
<td>RC T + RC</td>
<td>51150</td>
<td>13992</td>
</tr>
<tr>
<td>T T + RC</td>
<td>57286</td>
<td>74190</td>
<td></td>
</tr>
</tbody>
</table>

Then we carried out an absolute quantification of 2D distribution with the I-131 (Gamma graphic Images), due to images degrading in nuclear medicine by attenuation factors, dispersion, losing of counting and sensibility of the system, being these restrictive to the quantitative capacity of Radioisotopes. We did the calculus of correction factor by background (Ec. 2), considering a definite source surrounded by the background of the activity of latter regions.

**Table IV: Background Subtraction method.**

<table>
<thead>
<tr>
<th>Background Source of Reference (RC)</th>
<th>Background Tumour (T)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. From the position of RC in image of Tumour only.</td>
<td>1. From the position of RC in image of Tumour only.</td>
</tr>
<tr>
<td>2. From the position of RC in image of Tumour only.</td>
<td>2. Area of ROI of surrounding on image of tumour only.</td>
</tr>
<tr>
<td>3. Surrounding area of RC in RC + image of Tumour.</td>
<td>3. Area of ROI of surrounding on image of tumour only.</td>
</tr>
</tbody>
</table>

\[ \frac{A_T}{A_{RC}} = \frac{C_T}{C_{RC}} \]  
(Ec. 2)

Where \( C_T \) geometry media of tumour counts and \( C_{RC} \) geometry media of tumour counts as source of reference.
Later on we carried out an analysis of the images obtained to get information about the areas and/or quantities of radioactivity in specific regions of interest. (Table VI)

**Table VI: Activity (MBq)**

<table>
<thead>
<tr>
<th>Source</th>
<th>Image</th>
<th>RC</th>
<th>T</th>
</tr>
</thead>
<tbody>
<tr>
<td>Net cps A</td>
<td>80.28</td>
<td>86.08</td>
<td></td>
</tr>
<tr>
<td>Net cps P</td>
<td>8.385</td>
<td>106.69</td>
<td></td>
</tr>
<tr>
<td>t (cm)</td>
<td>20</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>50.67</td>
<td>50.67</td>
<td></td>
</tr>
<tr>
<td>A (MBq)</td>
<td>1.39</td>
<td>5.14</td>
<td></td>
</tr>
<tr>
<td>Real A (MBq)</td>
<td>1.11</td>
<td>4.44</td>
<td></td>
</tr>
</tbody>
</table>

Results: We estimated the doses of radiation absorbed by the patient’s gland in the tumour and in the bone marrow, previous calculus of absolute quantification of radioisotope activity deposited in specific region of interest.

**Table VII: Counts per second of: anterior and posterior images of patients.**

<table>
<thead>
<tr>
<th>Source</th>
<th>Image</th>
<th>cps A</th>
<th>cps P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uptake 1</td>
<td>RC Only T</td>
<td>2472</td>
<td>1089</td>
</tr>
<tr>
<td></td>
<td>T Only T</td>
<td>2923</td>
<td>980</td>
</tr>
<tr>
<td>Uptake 2</td>
<td>RC T + RC</td>
<td>32594</td>
<td>8134</td>
</tr>
<tr>
<td></td>
<td>T T + RC</td>
<td>30817</td>
<td>7179</td>
</tr>
</tbody>
</table>

**Table VIII: Correction by Background**

<table>
<thead>
<tr>
<th>Uptake 1,2</th>
<th>Gross cps A</th>
<th>Backgr 1 A</th>
<th>Net cps A</th>
<th>Gross cps P</th>
<th>Backgr 1 P</th>
<th>Net cps P</th>
</tr>
</thead>
<tbody>
<tr>
<td>RC</td>
<td>32594</td>
<td>2472</td>
<td>30122</td>
<td>8134</td>
<td>1089</td>
<td>7045</td>
</tr>
<tr>
<td>T</td>
<td>30817</td>
<td>2618</td>
<td>28199</td>
<td>7179</td>
<td>806</td>
<td>6373</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Uptake 1,2</th>
<th>Geometric Media</th>
<th>Activity (MBq)</th>
<th>Tumor Dose (Gy) x mT(gr)</th>
<th>Bone Marrow Dose (mGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RC</td>
<td>14567</td>
<td>100</td>
<td>146</td>
<td>174</td>
</tr>
<tr>
<td>T</td>
<td>13405</td>
<td>92</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: Treatment efficiency with I-131 is not necessarily directly related with the dose of radiation absorbed. Due to factors like the lack of homogeneous distribution of radioactive material and the exact amount of the mass size of tumour remains. The information that came out from these studies is being implemented on nuclear medicine service at the Hospital National Edgardo Rebagliati - Lima.
In India, the use of radioisotopes in nuclear medicine has steadily increased in the last thirty years. According to the national regulatory requirement, the annual effective dose to radiation workers should not exceed 20 mSv in a year, whereas the annual equivalent dose limit to the extremities is 500 mSv. Monitoring of whole body radiation dose for occupational workers is being carried out routinely. Presently, there is no regulation for monitoring of extremity dose of these radiation workers in India. It has been shown (Anderson et al. 1973; Henson 1973; Schurnbrand et al. 1982; Thind 1987; Mebhah et al. 1993; McCormick and Miklos 1993; Jansen et al. 1994; Dhanse et al. 2000; Linemann et al. 2000 and Jankowski et al. 2003.) that large dose gradients may exist across the length of the hand while handling gamma emitting isotopes. Therefore, systematic monitoring of radiation exposure to the fingers of occupational workers handling radioactive sources becomes necessary so as to ensure the dose within the prescribed limit. For this purpose, the dose to the hands is taken as the dose to the most exposed part which, especially in nuclear medicine applications, will be fingers. In India, on average, a nuclear medicine department handles about 11.1 – 18.5 GBq of 18F-FDG radioisotope per day. In order to estimate the doses received in various types of work procedures, finger dose monitoring using thermoluminescent dosemeter (TLD) finger rings was carried out.

For the measurement of finger doses to these workers, plastic finger rings containing CaSO4:Dy dosemeter (6 mm diameter and 0.8 mm thick) as shown in figure 1 were used. These TLDs were embedded in the plastic rings and calibrated by using known activity of the 18F to obtain the calibration factor. Each worker of the nuclear medicine centre involved in handling 18FDG was given four TLD finger rings to be worn on index and ring finger of both right and left hands, where dosemeters were on the dorsal side of the palm. These dosemeters were intended to be used for a period of 1 month. The TL measurements for the dosemeters were carried out in a semi-automatic type TL reader by taking all the TL output values on the basis of area of the dosimetry peak.

The maximum doses received during dispensing, injection and scintigraphy with 18F-FDG were 0.097, 0.324 and 0.054 mSvGBq-1, respectively. The various precautions such as avoiding delays while holding radionuclide loaded syringe, use of a “locator” syringe in patients with difficult veins, uses of tuberculin type long, narrow syringe for injecting radiopharmaceuticals are very effective in preventing high exposures. Use of syringe shields, now available commercially, should be considered as a regular protective device. Syringe shield made of tungsten reduce the dose by a factor 27 to 178, if the thickness of tungsten chosen in the range of 1.9 to 3.05 mm. If the above mentioned protective measures are not taken during the operations, the radiation exposure to fingers of the occupational workers may exceed the permissible limits.
From the above study, it can be concluded that the finger doses to nuclear medicine staff of certain institutions were significant, not mainly because of handling large radioactivity in the institution but also due to the poor work practices and availability of limited handling facilities in the institutions. It is therefore recommended that personnel should follow good work practices and monitoring of extremity doses using finger dosemeter routinely for all such nuclear medicine procedures. Though, these doses are well within the limits, monitoring of these doses periodically will help in optimization of doses during these procedures and adoption of better work practices.

*FIG. 1. Plastic finger rings containing CaSO4:Dy dosemeter (6 mm diameter and 0.8 mm thick)*
Practical radiation safety issues for ensuring safe working environment in a high volume PET Center in India

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We report here various practical radiation safety measures based on measured exposure rates in our high volume PET centre in India performing > 3000 studies a year. This is an observational study. We performed a routine radiation survey of PET CT facility at various times and distances from the radioactivity sources (bulk doses and the injected patient) and identified the high and low exposure areas in the department. The FDG doses for the patients were titrated as per body weight and sensitivity of the PET CT scanner. The time per bed position was also recorded and compared with the scan quality. The chest TLD doses before the commissioning of PET CT were compared with the combined exposure rates of conventional Nuclear Medicine and PET CT procedures. The exposure received was recorded over a period of 3 months and a radiation safety programme was developed and recommendations for safe work practices were made. We recorded radiation exposures from patients injected with 18F-FDG from different distances at various time intervals. Average exposure rate at 1 meter, 30 mins post injection was 27μSv/hr which falls by one third at a distance of 2 meters. The exposure rate subsequently falls exponentially with time and distance. Average exposure rate from the patient during the time of scan was 4-5μSv/hr at 2 meters. This is therefore the optimum distance to be maintained during guiding patients for the procedure. Whole body exposure recorded by pocket dosimeter for various activities like dose dispensing, injection of FDG with or without syringe shielding, patient positioning for the scan and removing the IV cannula post procedure after 3 hours was between 0.1-0.5μSv. Maximum dose of 2μSv was recorded while injecting FDG without syringe shielding. Annual whole body doses in mSv increased marginally from the pre PET time to post PET time for the technologist (average 1.45-1.55mSv respectively). There was however significant increase in whole body dose rate for the Physician (from 0.75-2.7mSv respectively). These results show the various exposure rates while performing various day to day tasks in a high volume PET-CT facility. Our adequate staffing, rotational duty roster and proper patient preparation, based on these observations have helped to keep the exposure rate in the acceptable range. Knowledge based on these findings, have helped in reducing the exposure rate for the patient comforters as well. Contrary to the fear among radiation workers, the difference in exposure rates with only conventional Nuclear Medicine procedures and after adding PET CT facility can be kept within acceptable limits based on our findings.
A Nuclear Medicine building project (diagnostic and therapy) was proposed at the “Hospital Regional de Alta Especialidad de Oaxaca” in México. The role of the Medical Physicist is project design, building supervision and commissioning stages for clinical use and continuing service of SPECT-CT equipment and therapy. First step, the medical physicist participates in several discussions about radiation safety and regulatory requirements according to National Regulatory Agency (called CNSNS in Mexico), and thereafter propose solutions for medical necessities and medical equipment installation, in order to fulfil technical and medical requirements. In the second step, the medical physicists ensure quality building materials and structural specifications according to shielding analytical calculus. In the meantime, regulatory documentation will be sent to CNSNS. Those documents include information about medical equipment, radioactivity facility, radiation workers and nuclear material data, with the purpose to obtain the nuclear medicine license. Third and final step, when all equipment has been installed, then the commissioning stage and quality control tests will be realized. Finally, the last responsibilities according to IAEA Human Health Reports No. 1 (2010) are shown to fulfil quality assurance program in a Nuclear Medicine facility. Therefore, in conclusion, the medical physicists’ role is imperative in fulfilling Mexican regulatory and International requirements in Nuclear Medicine facilities.
Nuclear medicine (NM) is associated to all uses of unsealed radioactive sources for diagnosis or therapy purposes. In NM, radiation protection of workers is a main concern. In this field, high radionuclide activities are needed, from few tens to several thousand MBq. Moreover, the procedures require the handling of radiopharmaceuticals at contact and/or very close to the extremities (hands, fingers) and often pure beta-emitters and mixed photon/beta-emitters are used. Workers are often not aware of which part of the hand receives the highest dose, even though it is recommended to measure the skin dose at the location with presumably the highest exposure to comply with the dose limit for extremities of 500 mSv per year. Work package 4 of the European project ORAMED (optimization of radiation protection of medical staff) aimed at enlarging the knowledge of hand doses delivered to NM staff when handling most frequently used radiopharmaceuticals, i.e. those labelled with Tc-99m and F-18 for diagnostic procedures, and those labelled with Y-90 for therapy procedures. The objectives were to evaluate maximum hand doses and dose distributions across the hands, to study the influence of protective devices (syringe and vial shields) and practice.

A unified protocol was defined and applied to measure the personal dose equivalent to the skin, Hp (0.07), at 11 points on each hand of NM workers. For the measurements thermoluminescent dosimeters (TLD) were taped on gloves worn by operators. The phases of preparation and administration the radiopharmaceuticals were separated. Additional information was recorded: identification of the hospital and operator, manipulated activities, radiation protection shield(s) and tool(s) used, and any difficulty that could occur during the operations, e.g. a contamination event. For most of the operators the measurement was repeated 5 times. Data was collected in 7 European countries, 34 hospitals and for 124 workers. Furthermore, in order to better understand the observed intra- and inter-operator variability of the doses, a sensitivity study was carried out thanks to Monte Carlo simulations. Six scenarios, based on realistic voxelized hand geometries, were defined, four for preparation and two for administration. The influence on doses of different parameters, such as the type of
radionuclide, the position of the manipulated radioactive vial or syringe and its orientation with respect to the hands, its volume and the shield used, could be analysed independently.

The analysis revealed that when the maximum dose is considered the annual limit can be exceeded for a large fraction of workers, larger than 20% for diagnostic procedures, particularly those associated with bad radiation protection practices. Based on this study, recommendations were proposed to reduce hand doses to an acceptable level. They concern the routine extremity dosimetry (position of the dosimeter and correction factor to account for the maximum dose), shielding (type, thickness of vial and syringe shields), training and practice. In addition, training materials were developed and a tool to estimate “levels of indicative reference doses” was made available.
Measuring through the noise: Using Mean Raw Pixel counts to characterize the SUV’s bias on differing count statistics encountered in gating scenarios

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Introduction: In PET imaging, respiratory or cardiac gating is an approach that can be used to try to limit degradation of information caused by patient motion during scanning. As gating is becoming more ubiquitous, it remains unclear how best to quantify benefits/drawbacks of gated data relative to its ungated analogue - both in research and in the clinic. At present the standardized uptake value (SUV) is often used as a (relatively) quantitative measure in gating literature. It is well recognized that many uncertainties can be associated with SUV measurements. However, with respect to the use of the SUVs in gating studies, it can be demonstrated that they will have a bias, possibly a large one, based simply on differing count statistics. In this work we try to highlight this problem relative to gating, and introduce a way one can characterize the expected loss of accuracy.

Methods: Software simulations were developed to model a spherical lesion with high activity over a warm background for comparison of measurements from ungated and gated scenarios (gated having 1/8th the statistics). Poisson noise was added to all data before measurements were derived for volume, true counts, and SUV for a volume defined with a region growing algorithm using a 70% max threshold. No motion or blurring was used in this simulation as our aim was to isolate the effects of noise on SUV measurements. Simulations were repeated 10^6 times to model the measurements using combinations of several different setup parameters: count statistics (2*10^1 -2*10^6), lesion diameter (9mm-32mm), and tumour to background ratio (2-10).

Results: We found many SUV measurements varied simply because of differing statistics between gated and ungated data sets. On closer inspection, we saw an asymmetric loss in accuracy can be related to the mean raw pixel counts in a 70% max threshold defined volume, as shown in the accompanying figure. According to our data, to achieve a 95% confidence window within an accuracy of 10% one would need ~ 900 measured raw counts/pixel.

Discussion: Dealing with noise is a large issue in PET, and especially in gated PET. We identified and confirmed that the SUV measurement of gated data can differ, sometimes significantly, simply because of changes in count statistics. We also found quite remarkably that irrespective of lesion size or tumour to background ratio, one can use the mean pixel counts (the raw data) derived from a threshold defined volume and predict the limitations of SUV measurement accuracy between gated and ungated data. This study was conducted to show that simply measuring an SUV from data with differing counts adds a new known bias to the commonly used SUV measurement. This work suggests that scan statistics should be taken into account when using threshold SUVs to compare gated and non-gated PET scenarios.
Inclusion of the effective radiation dose in the report of a diagnostic nuclear medicine procedure is a standard of good practice and the first step in order to attain the dosimetric history of patients undergoing ionizing radiation examinations throughout a lifetime. On the basis of an existing spreadsheet workbook for estimation of radiation doses in nuclear medicine developed at the University Hospital of Zaragoza, Spain, we included conversion factors for paediatric patients and for new radiopharmaceuticals, especially PET radiopharmaceuticals (labelled with 11C, 13N, 15O, 18F, and 82Rb). In addition we developed an algorithm for estimation of effective radiation dose from the CT portion of SPECT/CT and PET/CT studies (to be added to the emission dose) for attenuation correction, anatomic localization or both. We used Microsoft® Excel® 2003 for the workbook. The organ equivalent dose/administered activity, and effective dose/administered activity conversion factors were obtained from ICRP (International Commission on Radiological Protection) reports 53, 80 and 106. For radiopharmaceuticals not included in these reports an extensive bibliographical search was performed. The effective dose received from CT was calculated from the DLP dose length product provided by the SPECT/CT scanner and multiplied by the effective dose/DLP conversion factor corresponding to the anatomic region under study and the voltage (kVp) applied to the CT X-ray tube. The sheet for the calculation of the organ dose and effective dose per nuclear medicine procedure requires entry of patient and procedure data: name, date of birth, administered radionuclide and radiopharmaceutical, in addition to total activity. The sheet calculates and shows the dose to organs expressed in mGy contributing to the effective dose, the effective dose expressed in mSv, and the factors references. The date of birth entry assigns patients to one of the following age groups: One-Year-Old, Five-Year-Old, Ten-Year-Old, Fifteen-Year-Old and Adult, for application of corresponding published factors when available. A second sheet calculates the effective dose estimation from CT showing the dose received by the patient. A third sheet permits a second CT estimation in case the patient has undergone two CT acquisitions (i.e. some cases of 123I-MIBG, 67Ga-citrate, 111In-pentetrotide or 18FDG-PET whole body imaging). For all effective dose estimates, the equivalent time in months/days of exposure to natural radiation is calculated and shown, for better comprehension of the referring physician and patient of the magnitude of the reported dose.

The safety and quality of care are being addressed increasingly by patients, authorities, and scientific societies; and standards of good practice are defined and required for accreditation of Nuclear Medicine Units by national or international agencies. Inclusion of the effective dose in mSv in the report of a nuclear medicine procedure is an achievement in the context of safety and quality.
Evaluation of patient radiation dose during Nuclear Medicine investigations at Dr.M.Djamil Hospital- Padang- Indonesia

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Background: Radiation exposure for medical purposes is justified only when it is of benefit to the patient. Radiation dose for medical diagnostics should be low, reasonable and achievable; however, with provision for an adequate and optimum clinical diagnostics. The aim of this study is to determine the radioactivity levels and equivalent radiation dose during nuclear medicine investigations that is within the standardized safe limits at Dr. M. Djamil hospital Padang Indonesia.

Material and Methods: Subjects were selected randomly from the patients who were referred to our department for thyroid imaging, bone imaging and renography during the year 2009. They were divided into three groups, based on investigation types and radiopharmaceutical administration:

1) Group one: Thyroid imaging, Technetium 99m(99mTc)

2) Group two: Bone imaging, Technetium 99m-methylene-diphosphonate (99mTc-MDP).

3) Group three: Renography, Technetium 99m-diethylenetriaminepentaacetic acid (99mTc-DTPA).

Dose calibrator (Medisystem-202) and Thermoluminescence dosimetry -100 (TLD -100) were used to measure radioactivity level and equivalent radiation dose respectively. All subjects who were involved in this study had given an informal consent.

Results: Thirty four subjects were included in this study with age ranging from 29-65 years of age. 12 subjects participated in group one, 12 in group two and 10 in group three. Group one, two and three received average levels of radioactivity- per test were 4.08 mCi (151 MBq), 14.3 mCi (529 MBq) and 4.46 mCi (165 MBq) respectively. The average of equivalent radiation dose per test for group one, two and three were 0.31\(\pm\)0.11mSv, 0.7\(\pm\)0.31mSv, 0.33\(\pm\)0.88mSv respectively.

Conclusion: For patient safety, radioactivity levels and equivalent radiation dose during nuclear medicine investigations at our hospital within international and national guideline of radiation protection, working under standards of radiation protection is mandatory.
Presentation of a practical tool for shielding calculation in PET/CT facilities

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This paper presents the design of a practice spreadsheet for the development of shielding calculations for PET/CT facilities. This tool is shown applied to the design of the facility at the Instituto Nacional de Cancerología E.S.E Bogotá, Colombia. The tool is designed to work on separate spreadsheets with respect to properties accepted for the source and target distances used for floor, ceiling, and wall barrier calculations. So the program includes spreadsheets for the source points and the calculation of the workload, as well as control points (target). The program also creates arrays of distances between the source and control points and unshielded exposure calculations, which are weighed up with the number of patients scanned per week and the occupancy factor. Additionally, the program computes attenuation factors and the thickness required to shield the walls, the matrix of effective thickness between each control point and the point source, and finally a matrix display with a shielded exposure, including total contribution of all the source points to each control point, and its respective comparison with the dose constraint proposal. The thickness of the shielding of the walls has been calculated using attenuation data from Task Group 108 of The American Association of Physicists in Medicine and Report 147 of the National Council on Radiation Protection & Measurements. The validation of the program is verified with analytical calculations for some specific cases. The results obtained and their application to the design of the facility represent one of the goals of the institution to ensure the radiation protection for patients, members of the public and workers, through optimizing the value of dose limits.
The patients treated with I-131 represent a radiological risk to relatives, occupational exposure workers and the general public. The K0910241 (2010) document issued by the International Atomic Energy Agency (IAEA) recommends that the discharge of patients treated with radiopharmaceuticals must be based on the particular status of each patient, unlike the current criteria applied in Mexico based on the exposure rate at 1m of distance. At the National Cancer Institute in Mexico City, we measured the equivalent dose received by 40 family caregivers of patients with differentiated thyroid cancer who received therapeutic doses of I-131 for postoperative ablation of residual functioning thyroid tissue or the presence of metastasis. The caregivers were provided with thermoluminescent (TLD) dosimeters for a period of 15 days after the discharge of the patient treated with I-131 and were classified into two groups: 1 relative of a patient who received outpatient therapy and 2 relatives of patients who received hospital treatment, each group included 20 people. The average equivalent dose received by family members of the outpatients group was 0.92 mSv and that received by caregivers of inpatients group 0.52 mSv. In addition 70% of group 1 (outpatients) and 90% of group 2 (inpatients), received a dose lower than 1 mSv. Based on the data we obtained in this study, we will consider possible recommendations and amendments towards a change in the current policies of administration of I-131 in Mexico. We thank PAPIIT IN102610-UNAM, CONACYT scholarship 336089/235800.