An Attempt at Summarizing
A Great Week of Science & Clinical Research
in Molecular Imaging and Therapy

3th IPET Meeting, Vienna, October 2015

ORA ISRAEL
Department of Nuclear Medicine
Rambam Health Care Campus & Technion, Haifa, Israel
Overview of Lecture

• Who participated?
• What did we present and discuss?

• What do we have in common?
• What can we learn from each other?

• Where are our strengths?
• What can we improve?

• Where should we be in future?
We gathered from Every Corner of the globe!

372 Abstracts submitted by colleagues from 72 Countries

Invited lectures by more than 60 experts coming from 22 countries and the IAEA
We presented our Work on a Large Variety of Topics in Clinical & Basic Research

**Clinical topics: 73%**
- Oncology
- Cardiology
- Neurology
- Infection/inflammation
- Pediatrics
- Benign processes

**Basic & Related topics: 27%**
- New technology
- New tracers
- QC
- Radiation exposure
- Education & Ethics
- National regulations & needs

Myriad of subtopics
What is Molecular Imaging?
What are the Expectations?

Molecular Imaging:
- the temporo-spatial distribution, characterization & measurement of biological processes at (sub)cellular/molecular level with diagnostic and/or therapeutic applications

By tradition imaging
- examines gross anatomical & functional consequences of disease - late manifestations
- normalized morphology and function are late indicators of response to treatment

Molecular Imaging is expected to but is also being currently proven to
- allow early diagnosis, stratification of disease
- precede in detecting restorative cellular & molecular response
Imaging in Personalized Medicine

M. Hacker
Liver metastasis missed by CT

- Single procedure for diagnosis
- Precise localization & extent
- Treatment tailoring

CT: Fatty liver with sparing
PET/CT imaging for cancer evaluation
586 sites / 204 patients

PET/CT additional value
99 patients (49%)


Improved image interpretation
178 sites (30%) / 99 patients (49%)

Impact on patient management
28 patients (14%)

Characterization as benign - 60 sites (10%)
Characterization as malignant - 31 sites (5%)
Precise localization of malignant - 37 sites (6%)
Retrospective detection on PET - 7 sites (1%)
Retrospective detection on CT - 63 sites (11%)

Exclusion of cancer - 5 patients (2%)
Guidance invasive procedures - 7 patients (3%)
Referral & planning surgery - 5 patients (2%)
Referral & planning chemo - 5 patients (2%)
Referral & planning radiotherapy – 6 pts (3%)
PET/CT has changed the therapy in 38.5% from:
- no therapy to surgery or
from surgery to medical therapy (78%), or
- expansion of surgery (22%).

Sensitivity and specificity was about 92% and negative predictive value more than 94%.

PET/CT is very effective in the staging of MM, especially through the detection or exclusion of the lesions at distance.
RESULTS
In the group with FDG positivity at baseline, recurrence (intra- and extra-hepatic) was 84.6%. None of the patients with tumour to background ratio >3 or absolute SUV of >9 had tumor-free survival exceeding 8 months.
In the FDG negative subgroup, recurrence was only 18%, with overall, tumour free survival 80% at 4 years. There was a significant association between recurrence and FDG avidity (p = 0.0003).

CONCLUSIONS:
In the effort to offer curative liver transplant to maximum number of patients with HCC, merely considering tumor macromorphology appears insufficient. Instead, a multidisciplinary approach including factors providing reliable insight into tumor biology would be more appropriate.
In this regard, the metabolic information provided FDG PET could be the single most important factor in guiding the decision making process in advanced tumors.
PET/CT in Paediatric Oncology
Hybrid Imaging PET/CT & PET MRI

Robert Howman-Giles MD FRACP FAANMS DDU

- PET/CT- standard of diagnostic care
- PET/CT should be considered in most malignant paediatric solid tumours
- FDG PET/CT usually higher specificity than CI in response and end of Tx staging
Osteogenic sarcoma & Response to Chemotherapy

**Poor responder**

$\text{SUV}_{\text{max}}^{\text{10.6}} \rightarrow 6.1$

Surgery: 25% viable cells

Mx changes: more aggressive chemotherapy

**Very good response**

$\text{SUV}_{\text{max}}^{\text{17.8}} \rightarrow 2.1$

Surgical Resection: Histopath: no viable cells
The role of $^{68}$Ga-DOTATATE PET/CT imaging in treatment plan change in patients with Neuroendocrine Tumors

$^{68}$Ga-DOTATATE PET/CT imaging changed patient treatment plan in 40.9% of 728 pts, irrespectively of location of primary, most frequent in Medullary Thyroid Ca or lung NETs. In most instances the new treatment comprised chemotherapy or peptide receptor radionuclide treatment (PRRT)

Influence of $^{68}$Ga-DOTATATE PET/CT imaging in the decision of Peptide Receptor Radionuclide Therapy (PRRT) administration

1258 $^{68}$Ga-DOTATATE in patients with confirmed/suspected NET. In 13.4% cases radioisotope therapy, ($^{177}$Lu-DOTATATE, $^{90}$Y-DOTATOC, $^{131}$I-MIBG) was administered after $^{68}$Ga-DOTATATE PET/CT.

Skoura et al [modified]
Ga-68 DOTA compounds at the Western Cape Academic PET/CT Centre: Clinical experience

Doruyter A, Ellmann A, Rubow SM
Western Cape Academic PET/CT Centre and Stellenbosch University, Cape Town

- Ga-68 DOTA PET/CT (gold standard in well-differentiated GEP-NET imaging) successfully implemented at TBH
- Excellent results
- Some interpretative pitfalls
- Rapidly growing interest
- Radiolabelling of peptides for use in therapy (Lu-177 DOTATATE) also implemented recently
Potential use of 18F-NaF-PET/CT in the detection of extra-skeletal metastases of osteosarcoma. Comparison with 18FDG-PET/CT

Gabriel Bruno, Christian González, Carolina Tinetti, Sonia Traverso, Fernando Jaimez, Nicolás Bustos
Fundación Centro Diagnóstico Nuclear (FCDN), Buenos Aires, Argentina

CONCLUSION

The aim of our study is to demonstrate the potential use of 18F-NA PET/CT for the detection of extra-skeletal metastases in patients with osteosarcoma.

Both radiotracers are useful for evaluation of extraskeletal mets of osteosarcoma, detected all lesions equally. NaF had higher metabolic activity and may represent the tracer of choice due to its selective uptake in this osteogenic neoplasm.
PET/CT in TREATMENT Planning & Monitoring
BIOLOGICAL TARGET VOLUME DELINEATION WITH $^{18}$F-FDG PET/CT FOR RADIOTHERAPY PLANNING

1. Visual contouring of PET scan and definition of contours as judged by the experienced physician

2. Absolute Thresholds: Thresholding by a fixed percentage of the maximum SUV, mean SUV or maximum intensity

3. Adaptive Thresholding algorithms

4. Complex algorithms (Gradient-based, Statistical methods)
   - Robustness Studies
   - Validation studies

Dott. Marco Brambilla
Az. Ospedaliero Universitaria Maggiore della Carità, Novara, Italy
Inclusion of PET/CT Scanning and Respiratory Gating in the Radiotherapy Treatment Process of Thoracic Malignancies

J.A. Villalobos, A.C. Jiménez  
Costa Rica

Thoracic Malignancies Treated in 2014

- Breast: 86%
- Lung Cancer: 10%
- Mediastinum Cancer: 4%

<table>
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<th>Total patients</th>
<th>217</th>
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<td>Patients with Thoracic malignancies</td>
<td>81</td>
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Graph 1. Thoracic malignancies treated in 2014 at Clinica Radioterapia Siglo XXI.

Fig 1. Respiratory Gating System. Julianne Suhy, BS, CNMT, RT(N), Piotr J. Maniawski, MSc, Philips Healthcare – Nuclear Medicine, Cleveland.

Fig 2. Radiation therapy planning based on PET/CT. Reduction in target tumor volume compared with CT Planning. (Maldonado et al., 2007).
Biograph mCT Flow in Radiation Therapy Planning
Radiation dose escalation based on phase-matched PET and CT respiratory gating

CT-only RT Planning

Phase-matched PET/CT RT Planning

100% dose to tumor volume

130% dose to tumor volume

Courtesy B. Bendriem, Siemens
Sequential bed dimensions often force PET and CT to expose an area beyond what is needed.

Precise planning ensures only the targeted tissue is irradiated, eliminating over-scanning.

Courtesy B. Bendriem, Siemens
18F-FDG PET/CT IN THE FOLLOW UP OF PULMONARY CARCINOMA TREATED BY CYBERKNIFE

Chatti K ¹, Ouvrier MJ², Benisvy D², Zwarthoed C², Darcourt J²

¹ : Nuclear medicine department, CHU Sahloul, Sousse, Tunisia; ² : Nuclear medicine department, CAL, Nice, France

**AIM:** 18F-FDG PET/CT (18FDG) complete metabolic response is usually defined as the complete disappearance of 18F-FDG uptake within measurable target lesion but is that the rule after Cyberknife radio-surgery?

**Fig. 2** Example of Partial Metabolic Response
This case corresponded effectively to complete remission and distant progression.

**SUV 3 at 1st follow-up had a good predictive value**

**Fig. 3** Example of Partial Metabolic Response
This case corresponded to local complete remission and distant progression.
For a quantitative measurement of the degree of activity of the radiopharmaceutical in the lesions with pathological somatostatin expression an index of activity (IA) was introduced and calculated in 1-5 target lesions.
Molecular Imaging (we) Makes a Difference in Management of Prostate Cancer!
HORMONAL RECEPTORS

PSMA TRACERS

OTHER RECEPTORS

AMINOACIDS

FLUORIDE

Stefano Fanti, Bologna, Italy
Dual phase $^{11}$C-CHOLINE PET/CT was technically feasible
Useful for N&M evaluation of intermediate & high risk tumors, for selection & planning of Radiotherapy
Sensitivity for detection of recurrence was related to PSA levels
The impact of 18F-Choline PET/CT in the staging and restaging of prostate cancer. First single center experience in LEBANON.

**Staging group: 23 pts**
- Primary lesion within the prostate
  - 22/23 pts (96%)
- Locale metastatic lymph node
  - 3/23 pts (13%)
- Bone metastasis
  - 6/23 pts (26%)

Patients with localized recurrent disease
(prostate bed and pelvic lymph node metastasis)
- Treated by radiotherapy

Patients with metastatic bone deposit
- Treated by pelvic radiotherapy and hormonal therapy *rather than surgery*

**Restaging group: 63 pts**
- Local recurrence within the prostate bed
  - 22/63 pts (35%)
- Locale metastatic lymph node
  - 25/63 pts (39%)
- Bone metastasis
  - 19/63 pts (30%)

Patients with localized recurrent disease
(prostate bed and pelvic lymph node metastasis)
- Treated by pelvic radiotherapy and hormonal therapy *rather than surgery*

**Mohamad B. HAIDAR, MD**
American University of Beirut Medical Center
Prostate cancer radiation therapy response assessed with 11C-Acetate and mpMRI in the absence of a hybrid scanner.

**Andrzejewski et al, Vienna, Austria**

- 5 prostate cancer patients
- Prescribed dose: 78Gy to prostate and 50.4Gy to elective pelvic nodes (35 fractions, VMAT)
- mpMRI + PET/CT imaging @ 4 time points:
  1) at baseline, 2) after 20Gy, 3) after 40Gy, 4) at 3 moths after EBRT

<table>
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<th>mpMRI</th>
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<tr>
<td>T2w TSE</td>
<td>740MBq of [11C]Acetate</td>
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<td>DWI (4b values)</td>
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<tr>
<td>T1w DCE with 70 repetitions</td>
<td>MRSI</td>
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<tr>
<td>ADC, K_{trans}, iAUC and MRSI maps generated with Syngo®</td>
<td>imaging 20 minutes after injection</td>
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</table>

![T2w](image1)  ![ADC](image2)  ![K_{trans}](image3)  ![PET](image4)  ![MR/CT](image5)
Ga68-PSMA. Monitoring response.
Active bone metastasis show increased uptake (arrow) while non-active ones show no uptake (arrowhead)

68Ga-PSMA PET-CT in patients with prostate cancer. Initial experience at the Tel Aviv Medical center

Viktoria Kulikov MD, Natan Straus MSc, Einat Even-Sapir MD, PhD
PET/CT Beyond Oncology
Neurology & Cardiology
(10% Abstracts)
Dual radiotracer protocol that ruled out previous reputed vascular parkinsonism, ruling in degenerative parkinsonism.
18F-FDG, 11C-MET and 11C-CHO PET/CT in the Preoperative Evaluation of Suspected Adult Gliomas. Cai et al, Tainjin, China

FIGURE 1: A 48-year old woman with cerebral infarction.

FIGURE 2: A 56-year old men with astrocytoma (WHO grade II).

FIGURE 3: A 49-year old men with oligodendroglioma (WHO grade II).

FIGURE 4: A 63-year old men with anaplastic astrocytoma (WHO grade III).
Vereos PET/CT System
Digital Photon Counting

Analog * Time of Flight

Digital Time of Flight

Brain imaging of neurological disorders using a digital PET prototype: Initial clinical experience and comparison with analog PET

Patient data courtesy of University Hospitals, Cleveland
"Results from case studies are not predictive of results in other cases. Results in other cases may vary."

* Analog (GEMINI TF) to digital comparison

Courtesy of

PHILIPS
Assessment of Myocardial Contractile Reserve Added to Perfusion/Metabolism (SPECT-CT/PET-CT) Viability Study

Štalc M¹, Simonič B¹, Gužič Salobir B¹, Vrtovec B², Ležaič L¹. University Medical Centre, Ljubljana, Slovenia

Aim: to determine the technical feasibility of evaluation of myocardial contractile reserve concurrently with perfusion/metabolism viability study

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<tr>
<td>ESV (mL)</td>
<td>4.8 ± 21</td>
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<tr>
<td>EDV (mL)</td>
<td>0.4 ± 18.4</td>
</tr>
<tr>
<td>Mot</td>
<td>-1.9 ± 5.1</td>
</tr>
<tr>
<td>Thk</td>
<td>-1.1 ± 5.1</td>
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Conclusions
✓ Assessment of myocardial contractile reserve added to perfusion/metabolism (SPECT-CT/PET-CT) viability study is technically feasible.
✓ ...potential added predictive value of this method for segmental and global functional improvement after revascularization ...............
Case 1: Woman, 56 years old with Ca poorly differentiated squamous of Lung 2012 and pleura metastases. Cardiovascular factors smoking, HTA.

Case 2: Man 70 years old with colon carcinoma, in monitoring tumor marker elevation. PET/CT evidenced metastasis to liver, lung, mediastinum, peritoneal implants and hypermetabolism in left of abdominal aorta wall, associated with aneurysmal dilatation. SUV max 6 g/ml
Molecular Imaging in the Management of Infection & Inflammation
Infectious diseases - current status:

- major cause of illness in spite of the development of potent and safe antimicrobial agents
- new diseases have emerged, known diseases once in decline have reappeared
- 2\textsuperscript{nd} cause of death worldwide
  > 25\%, 15/57 million directly caused by infectious diseases, and more due to secondary effects

High priority in research for better diagnosis \& treatment
TUBERCULOSIS MIMICKING METASTASIS CANCER
Pr N. BEN RAIS, RABAT MOROCCO

- F, 23, Weight loss, tiredness; Lacunar bone lesion, moderate CA125
- PET-CT: OVARIAN CANCER WITH METASTASES « SUV : 4 to 12 »

MIP IMAGE FDG avid lesions diagnosed firstly as metastasis with moderate raised tumor marker “Ca 125”

FDG avid Right ovarian lesion peritoneal carcinomatosis

Metastatic bone lesions with Lytic vertebral and pelvic avid FDG lesions
Case -1: F, 58, fever of upto 101 degrees. FDG PET CT revealed mildly FDG avid consolidative lesion in the right hilar region, FDG avid multiple osteolytic and sclerotic skeletal lesions with mildly FDG avid leptomeningeal enhancement in the brain.

Bronchoscopic biopsy from the right middle lobe lesion was taken which was positive for adenocarcinoma lung.
In patients with tuberculosis, malignant incidental findings using $^{18}$F-FDG PET/CT were detected in a small but not negligible percentage of patients (5.7%).

Co-existent malignancy was found in patients of advanced age (> 60 years).

$^{18}$F-FDG PET/CT scans alone cannot sufficiently discriminate between inflammatory and malignant lesions. The diagnostic CT in PET/CT scans component plays an important role in enhancing the diagnostic efficacy in thoracic findings.

Quantitative analysis has shown no clinical usefulness.
PET-CT for mediastinal lymph node staging of NSCLC in a tuberculosis-endemic area

JA Shaw¹, EM Irusen¹, F Von Groote-Bidlingmaier¹, JM Warwick², B Jeremic³, R Du Toit¹, CFN Koegelenberg¹Divisions of 1. Pulmonology, 2. Nuclear Medicine, and 3. Radiation Oncology, Stellenbosch University and Tygerberg Academic Hospital, Cape Town, South Africa

- TBH data
  - low threshold gives good sensitivity
  - NPV good, even with enlarged nodes
  - there will always be false negative results with microscopic disease

- PET/CT is not a diagnostic test, but a complimentary technique to guide node sampling
PET/CT in assessment of treatment response of TB

Paradigm shift in our understanding of lesion progression

- Heterogeneity of TB lesions
- Caseous necrotic lesions: Neutrophil-dominated (↑ Mortality)
- Early detection of non-responders
- Prognosis and detection of residual disease in extrapulmonary TB
- Duration of treatment and prediction of relapse

Ehlers S et al, Front. Immunol 2013
The avid uptake of 68Ga-DOTA-UBI at Staph-A infection lesion in rat within 30min post-injection, which increased dramatically at 60min post-injection, and very fast kinetics of clearance from the blood pool and soft-tissues suggested a very high clinical potential for this agent.
Developing New Biomarkers
A Major Step Forward
Radiopharmaceuticals in Molecular Imaging

*Philip Elsinga, UMC Groningen, The Netherlands*

- The applications of PET radiopharmaceuticals are virtually unlimited
- Combination of PET-tracers with other imaging modalities starts to be explored
- The chemistry tools available for the preparation of PET tracers are still limited but toolbox for preparation gets bigger
- Legislation for clinical preparation (GMP) shows tendency to become more risk-based
- Multi-center trials are required to achieve breakthrough in clinical application of more new PET-tracers
PET Radiopharmaceutical beyond FDG
Lewis J, Memorial Sloan Kettering Cancer Center, NY, USA

Targeted Imaging – Frontiers of Diagnosis

99Tc – Bone Scan

18F-FDG PET/CT Glycolysis

18F-FDHT PET/CT Androgen Receptor
Zirconium 89 and associated radiopharmaceuticals

Lewis J, Memorial Sloan Kettering Cancer Center, NY, USA

$^{89}$Zr-Trastuzumab: A Tool for Monitoring Treatment of Gastric Cancer
Zhu Z, et al. Peking Union Medical College Hospital, Beijing, China

Clinical translation of $^{68}$Ga-PRGD2 PET/CT for integrin imaging

- Grading of glioma (n = 12)
- Diagnosis of lung cancer (n = 64)
- Evaluation of myocardial infarction (n=23)
- Imaging rheumatic arthritis (n = 20)
- Evaluation of Stroke (n=16)
“\(^{11}\text{C-SAM}: \text{A NEW POTENTIAL AGENT FOR PROSTATE CANCER DIAGNOSIS}”

Zoppolo F\(^{1}\); Buccino P\(^{1}\); Porcal W\(^{1,2}\); Oliver P\(^{1}\); Savio E\(^{1,2}\); Engler H\(^{1}\).

text

florencia.zoppolo@cudim.org

\(^{1}\)Centro Uruguayo de Imagenología Molecular, Montevideo, Uruguay

\(^{2}\)Facultad de Química, Udelar, Montevideo, Uruguay
Development of Rituximab Radioimmunoconjugates as PET-Radiopharmaceuticals

Gjorgieva Ackova Darinka, Smilkov Katarina, Makreski Petre, Stafilov Trojče, Janevik-Ivanovska Emilija, DIP, Macedonia

Proposed approach: In order to obtain $^{68}$Ga anti-CD20-radioimmunoconjugates for use in PET studies, different bifunctional chelating agents-anti-CD20 conjugates (BFCA-rituximab) were assessed.

Key Results: After lyophilisation, diluted rituximab-immunoconjugates remain stable, no modification of its physico-chemical characteristics, no aggregation, and retention of antibody secondary structure were observed, supporting the possibility of developing a “ready-to-label” formulations for PET screening of the therapeutic outcomes of radiopharmaceuticals.
Biomarker Quantitation

- **Aim of quantitation** - objective measures closely related to biologic characteristics and less prone to individual reading interpretations
- **Approach**: single or dynamic sequence imaging
- **Potential benefit**:
  - Defining the biologic behavior of malignant vs. benign tissues
  - Delivering better criteria for optimized medical care (individualized treatment strategies) by better patient selection and stratification
  - Demonstrating the presence and degree of a potential therapeutic effect

**Need for standardization**
Why Quantitation?

“If you cannot express it in numbers your knowledge is meager and insufficient.”

Lord Kelvin
Image-derived PET metrics in monitoring response to treatment

Habib Zaidi¹,²,³

Image-derived PET metrics

The information derived from $^{18}$F-FDG-PET allowed the development of a wide range of PET quantitative analysis techniques ranging from simple semi-quantitative methods (e.g. standardized uptake value - SUV) to “high order metrics” that require a segmentation step and additional image processing.
**PET quantification as a function of the total acquisition time in PET/CT**

**Figure 1.** Transversal views of one of the reconstructed $^{18}$F-FET brain scans, with 10 (left), 3 (center) and 1 (right) min frame times.

**Figure 2.** Mean deviations, for frame times below 10 min, of the SUV$_{\text{max}}$ and SUV$_{\text{mean}}$ values measured in OSEM and PSF reconstructions of the $^{18}$F-FET brain scans (6 patients scanned and 7 lesions analyzed). The images reconstructed with all the events (10 min listmode acquisitions) are used as reference.

We observed significant deviations of the SUV values when using frame times below 2 min (SUV values 20% higher in PSF reconstructions and $\sim$10% higher in OSEM reconstructions).
Association of biological and technical factors with extreme values of SUV in F-18 NaF PET/CT studies.

Moreira, R; Duarte, PS; Coura GBF; Carvalho G; Sapienza, MT; Buchpiguel, CA Instituto Do Câncer Do Estado de São Paulo, University of São Paulo

- Some technical and biological factors are associated with higher SUVs on F-18 NaF PET/CT studies.
- SUVs can vary depending on the patient’s weight and gender and the injection-image interval.
- These associations should be considered when SUV is used.
Molecular Medicine

Treatment Using Unsealed Radioactive Sources

A MAJOR COMPONENT OF OUR PROFESSION

CAESAREA
"Give the right target-radionuclide combination as part of the right “multi-step” treatment strategy to the right patient by the right “provider team” at the right time to achieve the right outcome at the right price"
In CRPC patients with symptomatic bone metastases, Radium-223 dichloride vs. placebo:

- significantly prolonged OS compared with BSC alone by 3.6 months (HR=0.7; \( P=0.001 \)) \( \Rightarrow \) 30.5% reduction in risk of death
- significantly prolonged median time to first SRE compared with BSC alone by 5.8 months (HR=0.66, \( P<0.001 \))
- had relatively similar frequency of grade 3/4 AEs (bone pain, anemia) of 57% compared to 63% from BSC alone
- Common adverse events
  - Non-hematologic: bone pain, nausea, diarrhea, vomiting
  - Hematologic: anemia, thrombocytopenia (no 2\textsuperscript{nd} CA yet)
- Clinical trials of retreatment with Ra-223 or in combination with either docetaxel, enzalutamide, or abiraterone

Ra-223 provides a new standard of care for the treatment of CRPC with bone metastases; incorporated into updated NCCN Guidelines v3.2013

**ALSYMPCA: Summary**

3 x PRLT cycles: 16.3 GBq of Lu-177 PSMA

Overall survival: median not reached

Progression-free survival: median 14 months
Radionuclide Therapy with 153Sm-EDTMP in painful bone metastasis

S. Rahabi*MD, SE Bouyoucef *MD, PHD, Prof
*Department of nuclear medicine, CHU Bab El Oued, 16000 Algiers, Algeria

- Clinical improvement was observed in 85% of patients including decrease of the dose of morphine or drugs
- The drugs and morphine were totally stopped in 13% after 3 months of radionuclide therapy with few major side effects (myelosuppression only in one patient at 6 months)
- The response to treatment was much better when the number of lesions is limited and widespread and when it is prostate cancer rather than breast cancer
IMPROVING & RENEWING THE IMAGING TECHNOLOGY
Advances of detector technology in nuclear medicine

S Somanesan
Senior Principal radiation Physicist, Department of Nuclear Medicine & PET
SGH & Singhealth Radiation Safety Officer
Consultant physicist, NHCS, TTSH, NHCS, KTPH, JH
14 August 2015
INTRODUCING Q.CLEAR

FULL CONVERGENCE PET RECONSTRUCTION
UP TO 2x IMPROVEMENT IN IMAGE QUALITY (SNR) & QUANTITATION ACCURACY (SUV_{mean})

BMI: 52.5 | ROI: 15mm | OSEM

Courtesy Le Bich, GE Healthcare
Future of PET imaging

**PET**
Research - era of discovery
The “basement” era

**PET/CT**
Era of image quality, and integration with CT
Era of lesion detection and localization
Image “Beautification”

**PET/CT**
Era of quantitative accuracy and integration with MRI

**Personalized Diagnosis & Treatment**
Era of targeted therapy and imaging
Individual patient management

*Courtesy Piotr Maniawski, PHILIPS*
Complementary information in PET and MR

Male, 70 kg, 180 cm
Lung Cancer

FDG Dose: 209 MBq (5.7 mCi)
Uptake time: 90 min
Detection of lung & liver mets
4 mm in diameter

Courtesy E. Almos, GE Healthcare & University Hospital Zurich, Switzerland
PET/CT or PET/MR? Who should PET partner with?  

**Thomas Beyer, Vienna, Austria**

**PET/CT**
- High-resolution anatomy
- Best possible, intrinsic co-registration
- Accurate attenuation correction
- Fast whole-body imaging

**PET/MR**
- High soft tissue contrast through MR
- Oblique image planes ("no-dose tilt")
- Quasi-simultaneous imaging
- Less ionizing radiation (MR=0)

**pro**
- MR-compatible PET detector
- MR-based attenuation correction
- Clinical and research applications
- Limited sensitivity for pulmonary lesions

**con**
- Patient exposure from CT
- Motion-induced misalignment
- Only hardware upgrades
Key applications of PET/MR

T. Beyer, Vienna, Austria

Key application (Definition)
Producing an image or result that provides new or substantially more information and clarity than anything else can provide today.

International expert panel: „The real work has just started.“
Breast cancer evaluation: role of image fusion between FDG PET/CT in prone position and MR

D. Grigolato¹, G. Pollini², F. Pellini², M. Cucca¹, M. Zuffante¹, M. Barillari, E. Zivelonghi³, R Pozzi Mucelli, C. Cavedon³, M. Ferdeghini¹

¹Nuclear Medicine Unit, ²Dept of Surgery, ³Dept of Physics, Dept of Radiology. AOUI Verona, ITALY.

Integrated information between PET and MR images increased the sensitivity, specificity and accuracy in diagnostic work-up of breast cancer.

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PET-CT-MRI triple fusion and its application in head & neck oncology: an alternative to integrated PET-MRI in developing countries.

*Partha Choudhury et al, Rajiv Gandhi Cancer Inst & Research Center, Delhi, India*

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<th>MRI * HP / FUP</th>
<th>PET-MRI * HP / FUP</th>
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<td><strong>95% CI</strong></td>
<td><strong>Sensitivity</strong></td>
<td><strong>Sensitivity</strong></td>
</tr>
<tr>
<td></td>
<td>76.09%</td>
<td>89.13%</td>
</tr>
<tr>
<td></td>
<td>61.23% to 87.41%</td>
<td>76.43% to 96.38%</td>
</tr>
<tr>
<td></td>
<td>94.12%</td>
<td>47.06%</td>
</tr>
<tr>
<td></td>
<td>71.31% to 99.85%</td>
<td>22.98% to 72.19%</td>
</tr>
<tr>
<td>Disease prevalence</td>
<td>73.02%</td>
<td>60.35% to 83.43%</td>
</tr>
<tr>
<td>Positive Predictive Value</td>
<td>97.06%</td>
<td>84.67% to 99.93%</td>
</tr>
<tr>
<td>Negative Predictive Value</td>
<td>55.17%</td>
<td>35.69% to 73.55%</td>
</tr>
<tr>
<td>AUC</td>
<td>0.83</td>
<td>0.68</td>
</tr>
</tbody>
</table>

Partha Choudhury et al, Rajiv Gandhi Cancer Inst & Research Center, Delhi, India
Treated case of Ca Vocal Cord: Post RT. Now with suspected recurrence

PET CT: MA lesion anterior commissure

PET MR: Small area of restricted diffusion with mild tracer uptake in anterior commissure
PET/MRI fusion is an effective alternative that brings together the benefits of both imaging methods. Preliminary results observed in our case series match recently published preliminary results that guide towards greater benefit in tumors of central nervous system, head and neck, lung, pelvic and soft tissues.
PET/RM
18F FDG
CERVICAL UTERINE CANCER
MRI-guided attenuation correction in PET/MRI

Attenuation correction (AC) strategies in PET/MRI

- Segmentation-based (3, 4 or 5 classes)
- Atlas-based registration and machine learning
- Emission-based (Maximum Likelihood for Activity and Attenuation reconstruction)

Mehranian, Arabi and Zaidi Med Phys (2015) under revision
PET/MR – Expectations for assessment of cancer and beyond

Mansi et al, EJ NMMI 2012

**To do better than PET/CT because of:**
- Absence of ionizing radiation – specific clinical indications (pediatrics, non-oncology)
- Ability to evaluate soft tissues and complex territories or pathologies (H&N, pelvis; recurrences)

**To do as well as PET/CT**
- Validation of attenuation correction with MRI
- Shorten time of study

An impressive technological advancement seeks opportunities of clinical benefit to justify incremental costs

**To do what cannot be done by PET/CT!**
More Advancements in Devices & Technology
• 36-year-old woman with an axillary tail hamartoma in her left breast.
• Two lesions in the left breast, adjacent to the pectoral muscle.
• Two in right breast located in the upper quadrant and in the inferointernal quadrant.
• Low tracer uptake in the left axillary tail (hamartoma) visible on mammography.
• Dx. Bilateral infiltrating lobular carcinoma.
US provides good visualization of the prostate capsule, CT provides good visualization of implanted seed, F-18 Choline PET provides physiologic information of the prostate. MATLAB algorithm was used to fuse US and PET/CT of prostate phantom.

Fused US-PET-CT could improve diagnostic and/or therapeutic outcomes for prostate cancer. Accuracy of US-PET-CT registration was estimated to be 1.3 mm.
Ultrasound image acquisition

PET-CT image acquisition

Developed MATLAB program for image fusion in study
Molecular Imaging – an Important Tool for Precise Tissue Diagnosis & Treatment

Guided tissue sampling of metabolically active lesions using the precise localization provided by the anatomic component
Fundamental Forces Driving the Growth of Radioguided Surgery

- Oncologic surgery becoming as less invasive/mutilating as possible.
- The emerging concept of the **sentinel lymph node** in oncologic surgery for staging parameter “N”.
- Growing applications of **non-sentinel lymph node radioguided surgery** with different approaches to tumor targeting (interstitial or systemic routes).
- Growing applications of **robotic surgery**.
- Growing collaboration of surgeons with other specialists (crucial).
3/14 patients: SN mets in superficial inguinal region

SN localisation is feasible in vulvar cancer, using a combined technique with $^{99m}$Tc Dextran and patent blue dye
Initial Experience with PET-CT guided biopsy/FNA using automated robotic arm.

Dr Rakesh Kumar, Nuclear Medicine, AIIMS, Delhi, India
Who Believes in SPECT/CT?

SPECT/CT?

PET is not enough...
History of SPECT/CT (1999-2015)
Why was it only slow to be accepted?

- We thought we know it all (general NM)
- We were busy understanding PET/CT (“new toy in town”)
- SPECT/CT was considered [by some]: 2nd class hybrid imaging
- Temporary Tc^{99m} shortage
- New tracers?

18% of abstracts in 3rd IPET are related to single photon emitting tracers & SPECT or SPECT/CT technology
Place of Sentinel Node in Uterine Cancers:

Preliminary joint Study between Nuclear Medicine Departments of the Hospital St. Antoine of Paris and General Hospital of Grand Yoff of Dakar

Dr Diop OUSSEYNOU
DAKAR - SENEGAL
IPET 383: Cadmium Zinc Telluride (CZT) GAMMA CAMERA MULTI-PINHOLE AND THYROID IMAGING. PRELIMINARY EXPERIENCE

Mora-Ramírez, E¹,²,³; Berrocal-Gamboa, I¹
¹Hospital San Juan de Dios, Servicio de Medicina Nuclear, Caja Costarricense del Seguro Social
²Universidad de Costa Rica, Escuela de Tecnologías en Salud
³Universidad de Costa Rica, Escuela de Física

emorara@ccss.sa.cr / erick.mora@ucr.ac.cr
Aim: The goal of this study is create images of thyroid using a CZT gamma camera.

Table 1. Volunteers characteristics

<table>
<thead>
<tr>
<th>Voluntary</th>
<th>Age</th>
<th>BMI</th>
<th>Thyroid hormones results</th>
<th>Thyroid hormones references</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>38</td>
<td>32</td>
<td>T₃L = 4.2 pg/ml</td>
<td>T₃L = 1.8 – 4.71 pg/ml</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T₄L = 1.12 uIU/m</td>
<td>T₄L = 0.742 – 1.76 uIU/m</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TSH = 2.46 ng/dl</td>
<td>TSH = 0.4 – 4 ng/dl</td>
</tr>
<tr>
<td>Female</td>
<td>36</td>
<td>24</td>
<td>T₃L = 2.93 pg/ml</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T₄L = 1.09 uIU/m</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TSH = 1.56 ng/dl</td>
<td></td>
</tr>
</tbody>
</table>

Results: the acquisition and pre-processing software was able to recognize acquisition lower of 180 degrees and generate image reconstruction of the gland. It is capable of generating volumetric images of a thyroid.

Conclusion: This method is not used regularly in our patients; however, imaging in small structures such as thyroid seems well delineated. We encourage manufacture to produce an acquisition and processing software for creating images of small organs especially of thyroid gland in order to be used in daily practice.
Impact of SPECT/CT 99mTc-EDDA/ HYNIC-TOC in the diagnosis and the extension of neuroendocrine tumors

SE Bouyoucef*MD, PHD, Prof, M. Habbache*MD, S. Rahabi*MD, Department of nuclear medicine, CHU Bab El Oued, 16000, Algiers, Algeria

Conclusion: Despite the lack of Gallium peptide PET, SPECT/CT with 99mTc-EDDA/ HYNIC-TOC has a great clinical impact in the management of NETs
Case 1, Diagnostic role: Diagnosis (confirmed by pathology) of Neuro endocrine pancreatic tumor mass of 6mm seen in CT scan with positive $^{99m}$Tc-octreotide.

Case 2, Diagnostic and extension roles: Zollinger Ellison with uptakes of $^{99m}$Tc-octreotide by gastric mucosa and retro peritoneal nodule.

Case 3, Follow up role: Multiple uptakes of $^{99m}$Tc-octreotide by metastatic relapses of malignant pheochromocytomas located in left latero-cervical, higher part of mediastinum and vascular renal hilum.

Case 4, Diagnostic, extension and therapy management: Uptake of $^{99m}$Tc-octreotide by a neuro endocrine tumor (confirmed by pathology) of the pancreatic head with multiples liver metastasis.
The role of SUV SPECT perfusion defect quantification of the lung as a predictor of severe cardiovascular events in a cohort of patients with congestive heart failure

Zhai et al, Huadong Hospital, China

Objectives

- The aim of this study was to investigate the use of SUV SPECT to quantify lung perfusion defects in both non-CHF and CHF patients and to explore its correlation index as an outcome predictor for CHF patients.

Methods

- 30 patients were enrolled in the study. 17 CHF patients were followed for 16±5 mo (mean±SD) and 13 patients were a non-CHF control group. All patients underwent a lung perfusion scan, an independent diagnostic CT plus echocardiography. The lung perfusion scan was reconstructed using the software to convert the recorded counts per voxel into activity per unit volume to allow for SUV calculations. The diagnostic CT was co-registered with the SPECT perfusion scan in order to relate the perfusion function to anatomy. Using the software 'Hybrid 3D Lung Lobe Finder'. The lungs where further split semi-automatically into individual lobes by placing 10 to 15 points along each fissure. Using the computed anatomical volumes it was possible to record the total SUV and volume of each lung and lobe. The SUV difference between the CHF group and the control group were compared. Cardiac death, acute MI, unstable angina, and late revascularization (>3 mo) experienced by the patients during follow-up were defined as cardiac events. Multivariate Cox regression analysis was applied for cardiovascular events patients and different SUV index.

Figure

Conclusions

- SUV SPECT perfusion defect quantification of the lung is a promising method for assessing pathology, physiology state and the rate of severe cardiovascular events in CHF patients.

Results

- Preliminary results showed that there were no significant differences between the total lung SUV of the two groups. There were 10 patients (33.3%) who had cardiac events, including 2 acute MI, 3 late coronary artery bypass grafting, and 5 unstable angina pectoris during the follow-up. Upon completion of the study, a differential SUV analysis between the CHF group and the control group will be presented.
“We must approach imaging with ... humility”

Only with a strong evidence base (large body of data coming from well-powered randomized trials clearly showing net benefit) we should feel comfortable recommending [tests] in spite of the fact that they come with their own elements of danger.
SPECT/CT for Personalized Radionuclide Treatment & Quantitation for Dosimetry

Activity & Residence time
Calculation of radiation dose to normal organs & sites of disease

Courtesy Avi Bar-Shalev, GE Healthcare
Dose Assessment in Molecular Radiotherapy: Need for Standardization and Harmonization of Nuclear Imaging Procedures

Marco D'Arienzo\textsuperscript{1,2}, Marco Capogni\textsuperscript{1}, Vere Smyth\textsuperscript{3}, Maurice Cox\textsuperscript{3}, Lena Johansson\textsuperscript{3}, Andrew Fenwick\textsuperscript{3}, Jaroslav Solc\textsuperscript{4}, Christophe Bobin\textsuperscript{5}, Hans Rabus\textsuperscript{6}, Leila Joulaeizadeh\textsuperscript{7}

\textsuperscript{1}National Institute of Ionizing Radiation Metrology, ENEA-INMRI, Department of Human Anatomy, Histology, Forensic Medicine and Orthopedics, Sapienza University of Rome, Rome, Italy, \textsuperscript{3}National Physical Laboratory NPL, Middlesex, UK, \textsuperscript{4}Czech Metrology Institute (CMI), Inspectorate for Ionising Radiation, Prague, Czech Republic, \textsuperscript{5}Commissariat a l’Energie Atomique (CEA) Gif-sur-Yvette Cedex, France, \textsuperscript{6}Physikalisch-Technische Bundesanstalt (PTB), Braunschweig, Germany, \textsuperscript{7}VSL, Dutch Metrology Institute, Delft, Netherlands

An EURAMET Joint Research Project was undertaken from 2012 to 2015 (MetroMRT, Metrology for Metrology for Molecular Radiotherapy) with the purpose of providing a standardized methodology for calculation of internal dose quantities and associated uncertainties. This project has now been completed. The final results will be available shortly with the final reports and recommendations on the project website:

**Conclusions:** An agreed dosimetry protocol for MRT dosimetry is needed to bring MRT treatments up to an acceptable standard. Standardization and harmonization of nuclear imaging procedures for quantitative imaging is the first step towards the development a dosimetry protocol for MRT.

It is expected that by treating dosimetry as a formal traceable measurement with an associated uncertainty, the culture of treating patients with a nominal activity radiopharmaceutical will change to individualised patient treatments based on absorbed dose.

The research leading to these results has received funding from the European Commission (EC), Grant Agreement N° 217257 between the EC and EURAMET under the Seventh Framework Programme.
MCID: A Software Tool To Provide Monte Carlo Driven Dosimetric Calculations Using Multimodality NM Images

Vergara et al, Cuba & Italy

- MCID can read output files and convert them to a dose study.
- Converts Energy deposited to Absorbed Dose (optional).
- Dose study is reported as Absorbed Dose (mGy) or Dose per Disintegration (µGy/MBq).
- Dose study is exported as medical format.
- MCID produces a preliminary report with the Cumulative Dose-Volume chart (DVH).
- It can be seen graphically the registration between CT and Dose images.

Output processing and some clinical results

<table>
<thead>
<tr>
<th>Gate Ranges (Gy)</th>
<th>Gate Interpolation (Gy)</th>
<th>MCNP5 (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.056</td>
<td>0.744</td>
<td>0.75</td>
</tr>
<tr>
<td>1.501</td>
<td>1.083</td>
<td>1.19</td>
</tr>
<tr>
<td>1.613</td>
<td>1.159</td>
<td>1.40</td>
</tr>
<tr>
<td>1.444</td>
<td>1.066</td>
<td>1.46</td>
</tr>
<tr>
<td>1.051</td>
<td>0.824</td>
<td>1.46</td>
</tr>
</tbody>
</table>
RESULTS: The delivered doses were: mean 2146.5 MBq (range 1016-5506; SD 1239; Moda 1105; Median 1846). Comparing the ¹²⁴I PET/CT and post-therapeutic ¹³¹I scan, we found a complete agreement in 91.3% of cases for number, site and extension of remnants and other pathological foci. Complete ablation was obtained in 90% of the cases (62/69).

Conclusions: ¹²⁴I PET/CT allows excellent pre-therapy evaluation for an individualized dose, by a fast simple method, without stunning the therapeutic effectiveness, with a good rate of success of radioablation. It is a good compromise for the lesion’s kinetic evaluation and could be very useful in planning ¹³¹I radiomethabolic therapy.
Never Compromise on Quality!
What is Required for US Production of PET Drugs for Clinical and Research Uses?

International Atomic Energy Association
IPET 2015
Vienna, Austria
October 6, 2015

Sally W. Schwarz, MS, BCNP
Professor of Radiology
Co-Director Cyclotron Facility
Washington University School of Medicine
St. Louis, MO
ISO 7 PET drug production facility. Classified room allows routine production and commercial collaborative production.
PET-CT image uniformity is measured to assess response of PET-CT system to homogeneous activity distribution.

The image uniformity was assessed by:
1. Filling of uniform cylindrical phantom with different activity concentrations.
2. Acquisition of axial PET-CT images of cylindrical phantom.
3. Drawing of $10 \times 10$ mm$^2$ ROIs over axial images.
4. Estimation of Percentage Non-Uniformity and Coefficient of Uniformity Variation for the different activity concentrations.

**Fig. 3:** Variation of image uniformity with activity concentration
We Are a Global Community
We Have to Understand Everybody’s Needs
to Work Together & Learn from Each Other
Almost three quarters of NCD deaths occur in low- and middle-income countries.

The five main causes of death in the world (WHO)
• Early diagnosis and secondary prevention are important to fight against NCD, which can be effectively done by hybrid imaging (PET/CT).
• Actions promoting PET/CT use in developing countries are needed.
PET-CT scanners in Romania

Mititelu R, Bucharest, Romania

• The installation of a cyclotron and a unit of 18F-FDG production private facility were followed by an increase in PET-CT projects
• 5 PET/CT scanners installed in the private sector
• 2 PET/CT scanners in public hospitals 3 more projects where PET-CT scanners are expected to be installed this year

• At present only oncologic indications are approved.
• None of the centers performs studies such as cardiology or neurology.
• However there are several projects which include installation of PET-CT scanners in some university-related hospitals where new procedures including cardiology, neurology and inflammation will be introduced.

Increased use and widening of PET-CT applications in Romania will require a larger number of nuclear medicine specialists to increase their skills by accessing dedicated courses/trainings. Efforts should be made in this respect, to ensure high quality investigations and improve diagnostic management.
Asian School of Nuclear Medicine – An Emerging Platform of Nuclear Medicine Education

Mizanul Hasan, Bangladesh

- Asian School of Nuclear Medicine (ASNM) was founded in February 2003 in Dhaka, Bangladesh.

- ASNM has now three permanent campuses in Osaka, Shanghai and Seoul.

- The first Asian Nuclear Medicine Board (ANMB) examination was held in November 2014 in Osaka, Japan.

- In less than 10 years’ time ASNM has emerged as a very vibrant organization with Prof. Gang Huang from China as its 4th Dean.
PET research in Brazil: how are we so far?

*Wiefels et al*

- 17,960 J Clin Oncol
- 5,800 Eur J Surg Oncol

Low impact factors (ISI Web of Knowledge)

Importance of international cooperation!!!
Nuclear Medicine Global Initiative

Leadership initiatives in nuclear medicine practice

• Leaders from 13 nuclear medicine organizations around the world discussed the current challenges, promises and the future of nuclear medicine (EANM Annual Meeting, Milan 2013).

• Dose optimization & harmonization has been adopted as the first project.

Modified from
Akram Al-Ibraheem, MD
King Hussein Cancer Center, Amman, Jordan

We have come a Long Way in Detecting & Mapping Biological Errors

... ויש念佛מסתיח"ויראustria"ויראustria"

“... and ye shall bring forth the old from the new…”
It is risky to make predictions, especially about the future. Without vision there is no future.

In Jewish tradition, since the destruction of the 2nd Temple the gift of prophecy is given only to fools and young children.
What We Have Learned [Again] at This Meeting

Imaging the key biomolecules and molecular-based events which are fundamental to the state of disease has entered the clinical arena and will only gain in importance in coming years.

- Future developments in MI will continue to expand its almost unlimited capabilities with the ultimate goal of having an impact on patient management.
- Therapy selection should/is based on the non-invasively defined molecular characteristics of disease in partnership with new treatment strategies.
- MI should/plays a significant role in basic research and in clinical trials aiming at the development of new generations of targeted therapy.
Imaging in Personalized Medicine

Summary

- PET has high potential to link target identification with treatment and, thus, to personalize treatment
- High potential for in-vivo Tissue Characterization to improve Biopsy guiding, Response prediction and therapy monitoring

Work to do

- Increase Imaging Read-out
- Improve Quantification
- Increase availability of radiopharmaceuticals

Not only with PET!
Over the past [16] years, [molecular & hybrid] imaging, more than any other single development has steadily advanced [patient] care and has paved the road to personalized medicine.

Imaging now influences every step in [patient] care... and provides essential road maps for treatment planning

From “one size fits all” to 4P medicine predictive, preventive, personalized & participatory

Modified from H. Hricak
Presidential Address, RSNA 2010
Molecular Imaging

- Can save healthcare cost if it has a higher diagnostic accuracy
- Most expensive aspect of disease management is treatment
- More accurate diagnosis results in more appropriate and less expensive treatment

Our role as MI professionals:
- Maximize the effect & minimize toxicity
- Make the medical community aware of our unique capabilities
- Continue doing good clinical work and high quality research!
- Work together!!!
Thanks to Many Friends & Colleagues!

• All experts who have reviewed and shared with us their knowledge and experience
• All investigators and clinical researchers who have contributed to the success of this meeting [78% response rate to requests for slides]

IAEA – for organizing this meeting and for supporting and promoting high quality MI throughout the world and for encouraging professional collaborations and friendships with no boundaries!
The Meeting Was Great!

She did the best she could!
Thank You