SPECT/CT and PET/CT of Bone disease

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Methods for evaluation of the skeleton

**XR:**
bone destruction (30-60% mineral bone loss)

**CT:**
structural bone changes (non RECIST),
lytic: 50-75% destroyed trabecular bone

**WB-MRI, DW-MRI:**
involvement of bone marrow, functional

**DXA:** bone mineral density

**US:** blood flow, soft tissue

**SPECT**
99mTc HDP/MDP (BS)
White blood cell scintigraphy (WBC)
Bone marrow scintigraphy

**PET:**
NaF
FDG
Choline/acetate etc
Radiopharmaceuticals

**Bone remodelling**
- NaF
- Biphosphonates

**Infection/inflammation**
- FDG
- WBC
- Ga-citrate
- Nannocolloids
- IgG/albumin

**Specific tumor markers**
123I, 123I mIBG,
111In SST, 64 Cu DOTA
Clinical application of PET/SPECT

• Bone pain
  – Metastatic tumour
  – Benign bone tumour
  – Trauma
  – Avascular necrosis
  – Infection
  – Osteomalacia, Paget’s disease
• Malignancy
  – Initial staging and recurrence
  – Discordant scan/X-ray findings
  – Assessment of extent of disease
  – Assessment of response to therapy
  – Hypertrophic pulmonary osteoarthropathy
  – Primary bone tumours
• Benigne bone disease
  – Orthopedic disorders
  – Sports/exercise related injuries
  – Metabolic bone disease – Paget’s disease, hyperparathyroidism
  – Infection
  – Benign bone tumors
  – Degenerative disease
• Miscellaneous
  – Vascular abnormalities
  – Abnormalities of the renal and urinary tract
  – Soft tissue accumulation of dihphsphonate

Methods

Bone Scan (BS):
Pharmacokinetics of bisphosphonates

Intravenous administration
20%-60% cleared to mineral phase of the skeleton (hydroxyapatite and amorphous calcium phosphate)

Remainder excreted through the kidneys

Plasma protein binding is often a significant factor
30% immediately after injection
50% by 4 hours
70% by 24 hours

Renal clearance is comparable with GFR and independent of urine flow rate

Uptake is affected by:
- Blood flow
- Extraction efficiency
- Vitamin D
- Parathyroid hormone
- Corticosteroids
- Intraosseoustissure pressure
- Capillary permeability
- Acid-base balance
- Sympathetic tone
Imaging

**Standard:**
- Delayed imaging: 4+ hrs
- Regional or WB SPECT

**3 phase imaging**
- Arterial phase: blood flow
- Blood pool phase: increased vascular permeability and flow
- Delayed imaging (3-4 hours): osteoblastic activity

SPECT improves sensitivity to detect vertebral lesions 20-50% compared to planar imaging
Clinical application of PET/SPECT

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Clinical application of PET/SPECT

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- Trauma
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- Infection

**Benigne bone disease**
- Orthopedic disorders
- Sports/exercise related injuries
- Metabolic bone disease – Paget’s disease, hyperparathyroidism
- Infection
- Degenerative disease
Clinical application of PET/SPECT

Bone pain
  - Trauma
  - Avascular necrosis
  - Infection

Benigne bone disease
  - Orthopedic disorders
  - Sports/exercise related injuries
  - Metabolic bone disease – Paget’s disease, hyperparathyroidism
  - Infection
  - Degenerative disease
65 y female with pain in left hemipelvis

4 month ago moped accident

Fractures with minimal displacement
Fracture of femoral neck

Garden I fracture: Incomplete and minimally displaced (impacted)
Bone pain
- Trauma
- Avascular necrosis
- Infection

Benigne bone disease
- Orthopaedic disorders
- Sports/exercise related injuries
- Metabolic bone disease – Paget’s disease, hyperparathyroidism
- Infection
- Degenerative disease
Avascular necrosis

Healing may be affected by disruption of the arterial blood supply to the fracture site and the femoral head.
There are many other causes for osteonecrosis (irradiation, hypercortisolism, renal transplant, alcholism etc).
Other vulnerable sites: humeral head, body of the thalus-scaphoid bone
A childhood hip disorder initiated by a disruption of blood flow to the femoral head. **Avascular necrosis** or osteonecrosis occur due to the lack of blood flow, the bone dies. The bone stops growing. Over time, healing occurs by new blood vessels infiltrating the dead bone and removing the necrotic bone which leads to a loss of bone mass and a weakening of the femoral head.

4 y old with Calvé-Legg-Perthes Disease

On the right side
Clinical application of PET/SPECT

Bone pain
- Trauma
- Avascular necrosis
- Infection (WBC, bone marrow, FDG)

Benigne bone disease
- Orthopedic disorders
- Sports/exercise related injuries
- Metabolic bone disease – Paget’s disease, hyperparathyroidism
- Infection
- Degenerative disease
Infection/inflammation

FDG
Accumulation in neutrophils, macrophages and activated leucocytes in relation to their metabolic rate and the number of glucose transporters.

Autologous WBC
Specific migration to the site of inflammation

Ga-citrate, nannocolloids, IgG/albumin
Increased blood flow
Enhanced vascular permeability
**Osteomyelitis**

- Infection and inflammation of the bone or bone marrow.
- Classified on the basis of:
  - causative organism
  - the route
  - duration
  - anatomic location
  - acute/chronic
Bone scan
Very sensitive (>80%),
specificity (planar) is low (50%)
Specificity (SPECT/CT) is high (>80%)

A positive BS should lead to further investigation of the affected region.
WBC scan
Because of physiologic uptake into bone marrow, sensitivity and specificity may be impaired

Combined with Nannocolloid for bone marrow
Sensitivity and specificity > 90%

Combined with BS
Sensitivity and specificity > 90%
**WBC imaging:**

*low sensitivities (app 50%)*

Due to inability of leucocytes to migrate to the encapsulated infection

A **photopenic lesion** is not specific for infection and, together with the physiologic uptake of WBC into the bone marrow, hamper accurate detection of spinal infection
FDG PET
Sensitivity > 95%
Specificity > 85%

Surgery < 6 mo:
specificity = 75%

Osteosynthetic material present:
specificity = 65%
Case 14
Case 14

35 cm
Septic/aseptic loosening?

Extremely important because the treatment is very different.

Combined WBC and marrow imaging has an accuracy of 90% and is the method of choice.

There is little role for FDG.
Loosening

Post operative high uptake:

1. 12 months
2. 24 months
Infection? WBC
**Adults, hematopoietic marrow:**

the skull, vertebrae, ribs, sternum, pelvis and proximal portions of the humerus and femur.

Fatty marrow in other bones may contain islands of hematopoietic tissue.

Variations are frequent.

Acquired alterations: surgery, trauma, **infection** and other destructive processes.

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**Infection? Bone marrow scan**
Combined $^{111}$In-white blood cell (WBC)/$^{99m}$Tc-diphosphonate bone and/or $^{111}$In-WBC/$^{99m}$Tc-sulfur colloid marrow scans are preferred in difficult cases of osteomyelitis at sites with existing bone alteration and/or adjacent soft-tissue infection.
Infection?

Femoral osteotomy due to Calvé-Legg-Perthes.

Now young adult.
Removal of osteosynthesis material due to pain.

No pain relief.

Infection?
Infection? WBC and marrow
Infection? WBC scan

WBC SPECT/CT
For computerized diabetes patient

Extent of infection

WBC SPECT/CT: diabetic foot amputation. Soft tissue infection extending into bone.
69 y male severe kyfoscoliosis; osteotomies and fixation of vertebral spine to pelvis and sacrum in order to stabilise the vertebral spine

Initially good effect, however collapse after some months.

Severe pain, reduced pulmonary function and abdominal pain.

Hospitalised due to infection

Where?
Clinical application of PET/SPECT

Bone pain
- Trauma
- Avascular necrosis
- Infection (WBC, bone marrow)

Benigne bone disease
- Othopedic disorders
- **Sports/excercise related injuries**
- Metabolic bone disease – Paget’s disease, hyperparathyroidism
- Infection
- Degenerative disease
Osgood Slatter

Most frequent sports/exercise related injury in children.

A painful condition that affects the upper part of the shin bone. It most commonly occurs in teenagers who play sport. It causes pain and swelling just below the knee. It is not serious and usually goes away in time.

There is one suffering from Osgood Slatter at each football team.
Sports/exercise related injuries

- Calcaneus – jumping
- Tibia/fibula – running
- Patella – hurdles
- Pelvis – gymnastics, football
- Ribs – swimming, rowing, weight lifting,
- Vertebra – weight lifting
Sports/exercise related injuries
Medial tibial stress syndrome (MTSS), exertional shin pain, medial traction periostitis
Sports/excercise related injuries
Clinical application of PET/SPECT

**Bone pain**
- Trauma
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- Infection (WBC, bone marrow)

**Benigne bone disease**
- Orthopedic disorders
- Sports/exercise related injuries
- Metabolic bone disease – Paget’s disease, hyperparathyroidism
- Infection
- Non infectious inflammatory disease
Arthritis og arthrose

Reumatoid arthritis

Gouty Arthritis
Non infectious inflammatory disease

52 y female with pain in right shoulder

22 y female
With painful joints
The role of nuclear medicine imaging in the assessment of RA is currently unclear.

Paradigmatic changes have been taken place in the treatment of RA in the last 2 decades requiring highly sensitive imaging modalities that will also allow to repeated imaging.

SPECT and FDG-PET may play a role in the early diagnosis of RA, patient exposure to radiation however hinders their use in repeated assessments.

US and MRI are likely to play the most important role.
Clinical application of PET/SPECT

**Bone pain**
- Trauma
- Avascular necrosis
- Infection (WBC, bone marrow)

**Benigne bone disease**
- Othopedic disorders
- Sports/excercise related injuries
- Metabolic bone disease – Paget disease, hyperparathyroidism, renal osteodystrophia
- Infection
- Degenerative disease
Paget disease (of the bone)

Excessive breakdown and formation of bone, followed by disorganized bone remodelling.

The bone weakens, resulting in misshapen bones, fractures, and arthritis in the joints near the affected bones. May have bone pain, headache, back pain, or nerve-related symptoms.

Often localized to only a few bones in the body. The pelvis, femur, and lower lumbar vertebrae are the most commonly affected bones.

Elevated levels of serum alkaline phosphatase may occur.
Paget disease
Metabolic bone disease

Renal osteodystrophy
(chronic kidney disease-mineral and bone disorder, CKD-MBD)

Osteomalacia
(vitamin D-deficiency)

Hyperparathyroidism

Disorders caused by abnormalities of minerals (calcium, phosphorus, magnesium) or vitamin D leading to dramatic clinical disorders that are commonly reversible once the underlying defect has been treated.
Metabolic bone disease

- "tie sternum"
- Beading of the costochondral junction
- Increased tracer uptake in axial skeleton
- Prominence of calvaria and mandible
- Reduced renal activity, faint or absent kidney images
- Increased tracer uptake in long bones
- Increased tracer uptake in periarticular areas


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  - Vascular abnormalities
  - Abnormalities of the renal and urinary tract
  - Soft tissue accumulation of dihydrophosphonate
A medical condition combining clubbing and periostitis of the small hand joints, especially the distal interphalangeal joints. Distal expansion of the long bones as well as painful, swollen joints and synovial villous proliferation are often seen.

May occur alone (primary), or secondary to diseases like non-small cell lung carcinoma, tuberculosis, emphysema, HD, cystic fibrosis, liver chirrose, IBD, Etc

BS shows symmetric periostitis; the tram line sign.
Clinical application of PET/SPECT

Bone pain
- Metastatic tumour
- Trauma
- Avascular necrosis
- Infection (WBC, bone marrow)

Malignancy
- Initial staging and recurrence

Benigne bone disease
- Orthopedic disorders
- Sports/exercise related injuries
- Metabolic bone disease
- Paget’s disease, hyperparathyroidism
- Infection
- Degenerative disease

Miscellaneous
- Vascular abnormalities
Osteogen sarcoma - examples
Differential diagnosis: Primary bone tumours

Giant cell containing or Histocytic lesions Locally aggressive?

Pooled sensitivity and specificity: 0.91 and 0.85
Malignant lymphoma
Clinical application of PET/SPECT

Bone pain
- Metastatic tumour
- Trauma
- Avascular necrosis
- Infection (WBC, bone marrow)

Malignancy
- Initial staging and recurrence

Benigne bone disease
- Othopedic disorders
- Sports/excercise related injuries
- Metabolic bone disease
- Paget’s disease
- hyperparathyroidism
- Infection
- Degenerative disease

Miscellaneous
- Vascular abnormalities
Purpose of bone imaging in metastatic disease

Identify *early* bone involvement and extent of disease

**Functional imaging**
- BS/SPECT
- NaF PET/CT
- FDG PET/CT

Determine the risk of fracture and cord compression

**Morphologic imaging**
- CT and MRI

Patients with bone metastasis only may survive for years.
Bone SPECT/CT

Sclerotic bone metastases from prostate cancer
NaF PET: Spinal cord compression
FDG PET: cord compression
# NaF PET: Indications

## Osseous metastases

Insufficient information exists to recommend the following indications in all patients (may be appropriate in certain individuals)

<table>
<thead>
<tr>
<th>Back pain/unexplained bone pain</th>
<th>Avascular necrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child abuse</td>
<td>Osteonecrosis of the mandible</td>
</tr>
<tr>
<td>Abnormal radiographic/laboratory findings</td>
<td>Metabolic bone disease</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>Paget’s disease</td>
</tr>
<tr>
<td>Trauma</td>
<td>Bone graft viability</td>
</tr>
<tr>
<td>Inflammatory/degenerative arthritis</td>
<td>Prosthetic joints</td>
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<td></td>
<td>Reflex sympathetic dystrophy</td>
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<td></td>
<td>Monitoring response to therapy</td>
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</tbody>
</table>
NaF PET: Indications (benigne)

Insufficient information

Child abuse  Osteomyelitis  Stress fracture  Paget  Increased PTH
NaF PET/CT
Stable fluoride is a natural trace element

> 99% of whole-body fluoride is present in the skeleton as fluoroapatite

18F is a diagnostic molecular imaging agent used for identification of new bone formation
Pharmacokinetics of NaF

Intravenous administration

Taken up by red blood cells; erythrocyte concentration 50% of plasma concentration

Negligible protein binding

Single passage extraction of whole blood by bone is close to 100%; less than 10% in the blood after 1 h

Clearance (tubular reabsorption): dependent on urine flow rate
  60-90% of GFR at high flow
  5% at low urine flow

63-y-old man with prostate cancer. Visibility of lesions increases with time. Acquisition time: 12, 30, 57, and 119 min p.i of 121MBq 18F-NaF

Average time–activity curves for blood pool and normal bone in patients with prostate cancer
Uptake reflects blood flow and bone remodeling:

18F is substituted for hydroxyl groups in hydroxyapatite, and covalently binds to the surface of new bone.

**Uptake is higher in new bone (osteoid) due to higher availability of binding sites.**

Processes that result in minimal osteoblastic activity, or primarily osteolytic activity, may not be detected

**Pharmacokinetics of NaF**

Inorganic matrix (65%)
osteoblasts, hydroxyapatite etc.
Uptake is higher in new bone (osteoid) due to higher availability of binding sites.

Processes that result in minimal osteoblastic activity, or primarily osteolytic activity, may not be detected.

NaF PET may be more sensitive than BS to detect the minimal osteoblastic activity associated with lytic bone metastases.

Kawaguchi M et al. 18F-fluoride uptake in bone metastasis: morphologic and metabolic analysis on integrated PET/CT.
Lytic or sclerotic

Lytic (osteoclastic)
- All cancer types
- Bladder, kidney, thyroid, multiple myeloma

Sclerotic (osteoblastic)
- Prostate, breast
- Occasionally: lung, stomach, pancreas, cervix
- Infrequently: CRC

Mixed

Skeletal involvement is seen in 20-70% of all cancer patients
Lytic (osteoclastic) metastases

A lytic metastasis is hypodense (dark)

Lytic metastases from leiomyosarcoma
Lytic (osteoclastic) metastases

Lytic metastases from RCC
Deposition of NaF

Greater deposition in the axial skeleton than in the appendicular skeleton and in the bones around joints than in the shafts of long bones. Changes over time.
Deposition of NaF

Image acquisition

Normal bone

Metastasis

10 min                                           30 min                                           90 min

SUVmax

Deposition of NaF
*Uglenholdt H Sammenligning af tiden pr bed-position ved 18F-NaF PET-knogleundersøgelser.
Bachelorprojekt, bioanalytikeruddannelsen København, professionshøjskolen Metropol, København 2011
Deposition of NaF
18F NaF is injected intravenously (direct or catheter).

**Adult activity:**
185-370 MBq. Higher activity may be used in obesity

**Pediatric activity:**
Weight-based (2.22 MBq/kg; min 18.5 MBq - max 185 MBq)

Patients should be well hydrated to promote rapid excretion (decrease radiation dose and improve image quality)

No fast, all medications can be taken

No recommendation about interruption of breastfeeding,
But limited contact with baby
Image quality and sensitivity of PET is 2-3 orders of magnitude compared to planar/SPECT.

The gamma camera (collimator system) acquire ~0.01% of emitted photons.
The PET scanner (coincidence detection) acquire ~1% of emitted photons.

Fluoride PET has higher spatial resolution than bone scan.
The favorable kinetic characteristics of sodium fluoride provide better bone–soft tissue contrast ratio than that of HDP imaging.
## Effective radiation dose

### Table 1
Comparison between PET and conventional bone scintigraphy.

<table>
<thead>
<tr>
<th></th>
<th>Skeletal PET</th>
<th>Conventional bone scintigraphy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiopharmaceutical</td>
<td>F-18 sodium fluoride</td>
<td>Tc-99m MDP</td>
</tr>
<tr>
<td>Physical half life</td>
<td>110 min</td>
<td>6 h</td>
</tr>
<tr>
<td>Emissions</td>
<td>511 keV photons from positron annihilation</td>
<td>140 keV photons</td>
</tr>
<tr>
<td>Spatial resolution</td>
<td>3–6 mm</td>
<td>4–15 mm</td>
</tr>
<tr>
<td>Binding to serum protein</td>
<td>Minimal</td>
<td>30% initially, 70% at 24 h</td>
</tr>
<tr>
<td>Clearance</td>
<td>Rapid</td>
<td>Relatively slow</td>
</tr>
<tr>
<td>Total uptake by bone</td>
<td>~50%</td>
<td>~30%</td>
</tr>
<tr>
<td>Organ receiving highest radiation</td>
<td>Bladder</td>
<td>Bone surface</td>
</tr>
<tr>
<td>Time to imaging after injection</td>
<td>30–60 min</td>
<td>3–6 h</td>
</tr>
<tr>
<td>Effective radiation dose (mSv/MBq)</td>
<td>$200 \times 0.0024 = 4.8$</td>
<td>$740 \times 0.0057 = 4.2$</td>
</tr>
</tbody>
</table>
Comparison with BS

BS planar
posterior

multi FOV SPECT
anterior

NaF PET

Even-Sapir E JNM 2006
**Similar to bone scan:**

- Kidneys, ureters, bladder normally seen
- Symmetric uniform uptake in adults
- Increased uptake in metaphyses in children/adolescents
- Visualization of diffuse/focal increased bone uptake
- Local hyperemia may cause soft tissue uptake
- Osteolytic processes may not be detected
- Degree of uptake does not differentiate between benign and malignant lesion
- The pattern of uptake may be helpful
- CT correlation is often helpful
### Assessment of Malignant Skeletal Disease: Initial Experience with \(^{18}\text{F}\)-Fluoride PET/CT and Comparison Between \(^{18}\text{F}\)-Fluoride PET and \(^{18}\text{F}\)-Fluoride PET/CT

Even-Sapir E et al JNM 2004;45:272-8

<table>
<thead>
<tr>
<th>18F NaF</th>
<th>Lesion-to-Lesion</th>
<th>Patient-to-patient</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sensitivity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PET</td>
<td>72</td>
<td>88</td>
</tr>
<tr>
<td>PET/CT</td>
<td>85</td>
<td>100</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td></td>
<td></td>
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<tr>
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<td>97</td>
<td>100</td>
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</table>

NaF PET/CT > NaF PET > MDP/HDP SPECT > MDP/HDP planar
A meta-analysis of $^{18}$F-Fluoride positron emission tomography for assessment of metastatic bone tumor

Ukihide Tateishi · Satoshi Morita · Masataka Taguri · Kazuya Shizukuishi · Ryogo Minamimoto · Masashi Kawaguchi · Takeshi Murano · Takashi Terauchi · Tomio Inoue · E. Edmund Kim

Received: 28 March 2010 / Accepted: 17 May 2010 / Published online: 18 June 2010 © The Japanese Society of Nuclear Medicine 2010

Abstract

Purpose The aim of this study was to assess the diagnostic performance of $^{18}$F-Fluoride positron emission tomography (PET) or positron emission tomography/computed tomography (PET/CT) compared with bone scintigraphy (BS) planar or BS planar and single photon emission computed tomography (SPECT) in evaluating patients with metastatic bone tumor.

Materials and methods We performed a meta-analysis of all available studies addressing the diagnostic accuracy of $^{18}$F-Fluoride PET, $^{18}$F-Fluoride PET/CT, BS planar, and BS planar and SPECT for detecting the metastatic bone tumor. We determined sensitivities and specificities across studies, calculated positive and negative likelihood ratios, and drew summary receiver operating characteristic curves using hierarchical regression models. We also compared the effective dose and cost-effectiveness estimated by data from the enrolled studies between $^{18}$F-Fluoride PET or

Results When comparing all studies with data on $^{18}$F-Fluoride PET or PET/CT, sensitivity and specificity were 96.2% [95% confidence interval (CI) 93.5–98.9%] and 98.5% (95% CI 97.0–100%), respectively, on a patient basis and 96.9% (95% CI 95.9–98.0%) and 98.0% (95% CI 97.1–98.9%), respectively, on a lesion basis. The Az values of $^{18}$F-Fluoride PET or PET/CT were 0.986 for the patient basis and 0.905 for the lesion basis, whereas those of BS or BS and SPECT were 0.866 for the patient basis and 0.854 for the lesion basis. However, the estimated effective dose and average cost-effective ratio were poorer for $^{18}$F-Fluoride PET or PET/CT than those of BS planar or BS planar and SPECT.

Conclusion $^{18}$F-Fluoride PET or PET/CT has excellent diagnostic performance for the detection of metastatic bone tumor, but the estimated effective dose and average cost-effective ratio are at a disadvantage compared with BS planar or BS planar and SPECT.
Sensitivity and specificity of NaF PET/CT

- On a patient basis: 96.2% and 98.5%
- On a lesion basis and 96.9% and 98.0%
- The diagnostic accuracy of PET or PET/CT was significantly higher than that of the planar and SPECT bone scintigraphy.
In osteolytic metastases, FDG uptake is higher compared to sclerotic lesions because of the presence of a larger amount of tumor cells with high glycolytic rate.

Sclerotic metastases contain smaller amounts of viable tumor cells and exhibit therefore less FDG uptake.
Comparison of NaF and FDG


Research Article

Prospective Evaluation of $^{99m}$Tc MDP Scintigraphy, $^{18}$F NaF PET/CT, and $^{18}$F FDG PET/CT for Detection of Skeletal Metastases

Andrei Iagaru, Erik Mittra, David W. Dick and Sanjiv Sam Gambhir

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(2) Department of Radiology, Molecular Imaging Program at Stanford (MIPS), Stanford, CA, USA
(3) Department of Bioengineering, Stanford, CA, USA
(4) Department of Materials Science & Engineering, Stanford, CA, USA
Comparison of NaF and FDG

Methods
• Prospective study
• N = 52 patients
• Gold standard
  – histological 46%
  – clinical follow-up
  – other imaging studies

Results patient basis:
• 24/52 NaF
  – Sens/spec = 95.8/92.9
  – NPV/PPV = 92.0/96.3
• 16/52 FDG
  – Sens/spec = 66.7/96.4
  – NPV/PPV = 77.1/94.0
  – 28/52 FDG extraskeletal metastases

Superior image quality and evaluation of skeletal disease extent with NaF over FDG. **FDG detects extraskeletal disease that can change disease management.**

*Sarcoma = 19, Prostate cancer = 18, Breast cancer = 6, Colon cancer = 2, Bladder cancer = 1, Lung cancer = 1, Malignant paraganglioma = 1, Lymphoma = 1, GIST=1, RCC=1, Salivary gland cancer = 1*
Comparison of NaF and FDG

Japanese Journal of Radiology
April 2013, Volume 31, Issue 4, pp 262-269

The role of F-fluoride PET-CT in the detection of bone metastases in patients with breast, lung and prostate carcinoma: a comparison with FDG PET/CT and 99mTc-MDP bone scan

Nishikant Avinash Damle, Chandrasekhar Bal, G. P. Bandopadhyaya, Lalit Kumar, Praveen Kumar, Arun Malhotra, Sneh Lata
Comparison of NaF and FDG

Methods
Prospective
N = 115
  breast 72
  prostate 49
  NSCLC 30

Gold standard:
MRI
CT
Histology when feasible

Results
Whole group:
Sensitivity = 100%
NPV = 100%

Conclusion:
To rule out bone metastases in cases where there is a high index of suspicion NaF is the most reliable investigation.
Several researchers concluded that 99mTc MDP SPECT is superior to 18F FDG PET in detecting bone metastases in breast cancer and that the sensitivity for osteoblastic lesions is limited with 18F FDG PET/CT.

Surveillance of metastatic spread to the skeleton in breast cancer patients based on FDG PET alone is not possible.

(Igaru et al 2012, Damle et al 2013)
Prostate cancer

(N=49, metastases confirmed in 32)

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>18F-FDG PET/CT</strong></td>
<td>71.9 % (CI = 53–85.6 %)</td>
<td>100 % (CI = 77.1–100 %)</td>
<td>100 % (CI = 82.2–100 %)</td>
<td>65.4 % (CI = 44.4–82.1 %)</td>
<td>81.6 % (CI = 70.7–92.5 %)</td>
</tr>
<tr>
<td><strong>18F-fluoride PET/CT</strong></td>
<td>100 % (CI = 86.7–100 %)</td>
<td>70.6 % (CI = 44–88.6 %)</td>
<td>86.5 % (CI = 70.4–94.9 %)</td>
<td>100 % (CI = 69.9–100 %)</td>
<td>89.8 % (CI = 80.3–97.7 %)</td>
</tr>
<tr>
<td><strong>99mTc-MDP bone scan</strong></td>
<td>96.9 % (CI = 82–99.8 %)</td>
<td>41.2 % (CI = 19.4–66.5 %)</td>
<td>75.6 % (CI = 59.4–87.1 %)</td>
<td>87.5 % (CI = 46.7–99.3 %)</td>
<td>77.5 % (CI = 65.8–89.2 %)</td>
</tr>
</tbody>
</table>

**Table 3 Prostate cancer**

<table>
<thead>
<tr>
<th></th>
<th><strong>18F-FDG PET/CT</strong></th>
<th><strong>18F-fluoride PET/CT</strong></th>
<th><strong>99mTc-MDP bone scan</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Table 5 Total number of lesions</strong></td>
<td>Total number of positive patients</td>
<td>15/30</td>
<td>23/30</td>
</tr>
<tr>
<td></td>
<td>Total number of lesions</td>
<td>124</td>
<td>188</td>
</tr>
<tr>
<td>Sclerotic</td>
<td>90</td>
<td>163</td>
<td>83</td>
</tr>
<tr>
<td>Lytic</td>
<td>17</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>Mixed</td>
<td>17</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>Total number of true positives</td>
<td>15/30</td>
<td>19/30</td>
<td>19/30</td>
</tr>
<tr>
<td>Total number of lesions in true positives</td>
<td>124</td>
<td>177</td>
<td>89</td>
</tr>
<tr>
<td>Sclerotic</td>
<td>90</td>
<td>153</td>
<td>70</td>
</tr>
<tr>
<td>Lytic</td>
<td>17</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>Mixed</td>
<td>17</td>
<td>12</td>
<td>11</td>
</tr>
</tbody>
</table>
Prostate cancer

The Detection of Bone Metastases in Patients with High-Risk Prostate Cancer: $^{99m}$Tc-MDP Planar Bone Scintigraphy, Single- and Multi-Field-of-View SPECT, $^{18}$F-Fluoride PET, and $^{18}$F-Fluoride PET/CT

Einat Even-Sapir, MD, PhD \(^1\) \(^2\); Ur Metser, MD \(^1\) \(^2\); Eyal Mishani, PhD \(^3\); Gennady Lievshitz, MD \(^1\); Hedva Lerman, MD \(^1\) and Ilan Leibovitch, MD \(^2\) \(^4\)

**Methods:** Prospective study

N = 44 BS + NaF PET/CT

- 24 patients + multi-FOV SPECT
- 20 patients + single FOV SPECT

JNM 2006
Equivocal and malignant interpretation were categorized as suggestive for malignancy.
Detection of bone metastases in patients with lung cancer: $^{99m}$Tc-MDP planar bone scintigraphy, $^{18}$F-fluoride PET or $^{18}$F-FDG PET/CT

Stefan Krüger, Andreas K. Buck, Felix M. Mottaghy, Ellen Hasenkamp, Sandra Pauls, Christian Schumann, Thomas Wibmer, Tobias Merk, Vinzenz Hombach, Sven N. Reske
NSCLC is not curable in patients with bone / distant metastases.

N = 30 Bone mets confirmed: 19 patients
25 by other imaging modalities/5 by histopathology

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>18F-FDG PET/CT</td>
<td>78.9%</td>
<td>100%</td>
<td>100%</td>
<td>73.3%</td>
<td>86.7%</td>
</tr>
<tr>
<td></td>
<td>(CI = 53.9–93%)</td>
<td>(CI = 67.9–100%)</td>
<td>(CI = 74.7–100%)</td>
<td>(CI = 44.8–91.1%)</td>
<td>(CI = 76.9–96.4%)</td>
</tr>
<tr>
<td>18F-fluoride PET/CT</td>
<td>100%</td>
<td>63.6%</td>
<td>83.6%</td>
<td>100%</td>
<td>86.7%</td>
</tr>
<tr>
<td></td>
<td>(CI = 79.1–100%)</td>
<td>(CI = 31.6–81.6%)</td>
<td>(CI = 60.5–94.3%)</td>
<td>(CI = 56.1–100%)</td>
<td>(CI = 76.9–93.4%)</td>
</tr>
<tr>
<td>99mTc-MDP bone scan</td>
<td>100%</td>
<td>54%</td>
<td>79.2%</td>
<td>100%</td>
<td>83.3%</td>
</tr>
<tr>
<td></td>
<td>(CI = 79.1–100%)</td>
<td>(CI = 24.6–81.9%)</td>
<td>(CI = 57.3–92.1%)</td>
<td>(CI = 51.7–100%)</td>
<td>(CI = 72.8–93.8%)</td>
</tr>
</tbody>
</table>
Sensitivity

WIN

Specificity

LOSE
Combined $^{18}$F-Fluoride and $^{18}$F-FDG PET/CT Scanning for Evaluation of Malignancy: Results of an International Multicenter Trial

Andrei Iagaru¹, Erik Mittra¹, Camila Mosci¹, David W. Dick¹, Mike Sathekge², Vineet Prakash³, Victor Iyer³, Paula Lapa⁴, Jorge Isidoro⁴, Joao M. de Lima⁴, and Sanjiv Sam Gambhir⁵

¹Stanford University Medical Center, Stanford, California; ²Pretoria University Hospital, Pretoria, South Africa; ³Aalborg University Hospital, Aalborg, Denmark; ⁴Serviço de Medicina Nuclear, Hospitais da Universidade de Coimbra, Coimbra, Portugal; and ⁵Departments of Radiology, Bioengineering, Materials Science, and Engineering, Molecular Imaging Program at Stanford (MIPS), Stanford University School of Medicine, Stanford, California

N = 62 patients
Design: prospective, FDG PET/CT and combined FDG/NaF PET/CT.
NaF FDG cocktail approach

62 patients

15 non malignant

47 malignant

16 comb. > FDG
29 comb. = FDG

2 soft tissue

Table 2
Demographics, malignancy, and imaging indication information in the 18 patients who had discordant findings between the PET/CT and combined PET/CT.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Gender</th>
<th>Cancer type</th>
<th>Imaging indication</th>
<th>Lesions detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>47</td>
<td>F</td>
<td>Breast</td>
<td>Subsequent treatment strategy</td>
<td>Combined: 18-FDG alone</td>
</tr>
<tr>
<td>48</td>
<td>F</td>
<td>Breast</td>
<td>Subsequent treatment strategy</td>
<td>Combined: 18-FDG alone</td>
</tr>
<tr>
<td>52</td>
<td>F</td>
<td>Breast</td>
<td>Subsequent treatment strategy</td>
<td>Combined: 18-FDG alone</td>
</tr>
<tr>
<td>59</td>
<td>F</td>
<td>Breast</td>
<td>Subsequent treatment strategy</td>
<td>Combined: 18-FDG alone</td>
</tr>
<tr>
<td>63</td>
<td>F</td>
<td>Breast</td>
<td>Subsequent treatment strategy</td>
<td>Combined: 18-FDG alone</td>
</tr>
<tr>
<td>69</td>
<td>F</td>
<td>Breast</td>
<td>Subsequent treatment strategy</td>
<td>Combined: 18-FDG alone</td>
</tr>
<tr>
<td>43</td>
<td>F</td>
<td>Breast</td>
<td>Initial treatment strategy</td>
<td>Combined: 18-FDG alone</td>
</tr>
<tr>
<td>57</td>
<td>F</td>
<td>Breast</td>
<td>Subsequent treatment strategy</td>
<td>Combined: 18-FDG alone</td>
</tr>
<tr>
<td>27</td>
<td>F</td>
<td>Breast</td>
<td>Subsequent treatment strategy</td>
<td>Combined: 18-FDG alone</td>
</tr>
<tr>
<td>74</td>
<td>M</td>
<td>Prostate</td>
<td>Subsequent treatment strategy</td>
<td>Combined: 18-FDG alone</td>
</tr>
<tr>
<td>65</td>
<td>M</td>
<td>Prostate</td>
<td>Subsequent treatment strategy</td>
<td>Combined: 18-FDG alone</td>
</tr>
<tr>
<td>50</td>
<td>M</td>
<td>Rectal</td>
<td>Subsequent treatment strategy</td>
<td>Combined: 18-FDG alone</td>
</tr>
<tr>
<td>59</td>
<td>M</td>
<td>Rectal</td>
<td>Subsequent treatment strategy</td>
<td>Combined: 18-FDG alone</td>
</tr>
<tr>
<td>57</td>
<td>M</td>
<td>Unknown primary</td>
<td>Initial treatment strategy</td>
<td>Combined: 18-FDG alone</td>
</tr>
<tr>
<td>70</td>
<td>M</td>
<td>Prostate</td>
<td>Subsequent treatment strategy</td>
<td>Combined: 18-FDG alone</td>
</tr>
</tbody>
</table>
“Combined 18F NaF/18F FDG PET/CT shows promising results when compared with separate 18F NaF PET/CT and 18F FDG PET/CT for evaluation of cancer patients”

Ignaru et al 2012
Prospective comparison of combined $^{18}$F-FDG and $^{18}$F-NaF PET/CT vs. $^{18}$F-FDG PET/CT imaging for detection of malignancy

Frank I. Lin · Jyotsna E. Rao · Erik S. Mittra · Kavitha Nallapareddy · Alka Chengapa · David W. Diek · Sanjiv Sam Gambhir · Andrei Iagaru
NaF FDG cocktail approach

115 patients
- 41 prostate
- 39 breast
- 22 sarcoma
- 13 others*

Procedure
NaF PET/CT
FDG PET/CT
combined NaF+FDG PET/CT (simultaneous injections)

Three scans performed sequentially within 4 weeks of each other

*lung, bladder, CRC, cervix, kidney, NHL, larynx, paraganglioma
**NaF FDG cocktail approach**

**NaF PET/CT:**
67/115 osseous metastases

**FDG PET/CT:**
38/115 osseous metastases
48 extraosseous lesions on FDG

**Combined NaF+FDG PET/CT**
19 osseous metastases more extensive on combined scan than on FDG
29 osseous metastases seen on NaF and combined but not on FDG
• Combined NaF and FDG PET scans increases sensitivity in detection of osseous lesions compared with FDG PET/CT alone
  Simultaneous injection or subsequent injection on same day with similar results

• Limitations
  No histologic confirmation for all detected lesions
  Additional lesions detected on the combined scans may not all represent metastases

Lin et al 2012
Methods for evaluation of the skeleton

XR:
bone destruction (30-60% mineral bone loss)

CT:
structural bone changes (non RECIST),
lytic:50-75% destroyed trabecular bone

WB-MRI, DW-MRI:
involvement of bone marrow

SPECT
99mTc HDP/MDP (BS)
White blood cell scintigraphy (WBC)
Bone marrow scintigraphy
123I, 123I mIBG, 111In somatostatin
Others…

PET:
NaF
FDG
Choline/acetate
Others….DOTA etc
Treasure your Bones!