18F Sodium Fluoride Bone PET

Is there a better bone scan in your future?
History of Bone Scintigraphy

Rectilinear Scanners (1960’s to 1970’s)
- $^{18}$F Sodium Fluoride, Ga-69, Sr-85

Anger Gamma Camera - planar (1970’s – present)
- Tc-99m MDP, Tc-99m HDP or Tc-99m pyrophosphate

SPECT (one, two or three head – (1980’s- present)
- circular and non-circular acquisitions

PET (full ring, partial ring, coincidence – (1990’s to present)
- $^{18}$F Sodium Fluoride

Hybrid Imaging – PETCT & SPECT CT (2000’s to present)
Indications for Bone Imaging

Trauma

- most sensitive for early identification of fractures
- at increased age, see decreased response
- blood pool helpful for soft tissue versus bone injury

Infection

- blood pool and delayed imaging required (3 and 24 hour)

Arthritis / degenerative joint disease

Orthopedic applications

- failed back or complications following spine surgery
- pain following joint surgeries
- unexplained pain
Indications for bone imaging - Oncology

The most prevalent cancers in the US are commonly associated with a high incidence of metastatic bone disease:

- 45-85% of breast cancer patients
- 33-85% of prostate cancer patients
- 33-50% of lung cancer patients
- 33-40% of renal cell carcinoma patients
- 28-60% of follicular thyroid cancer patients
Indications for bone imaging - Oncology

Staging / restaging evaluation of the presence and/or extent of metastatic bone disease

- Initial staging of patients at risk for bone metastases
  - exclusion of bone disease is required prior to initiation of potentially curative therapy

- Following patients with bone dominant metastases
  - evaluate effectiveness of systemic therapy
  - exclude new metastases at critical anatomic sites
Current tools

Standard diagnostic method since 1970’s:

- planar or SPECT bone scintigraphy using Tc99m-labeled polyphosphonates
  - advantages – widely available, relatively inexpensive
  - planar technique has variable sensitivity and low specificity
  - SPECT – to improve anatomic localization or to characterize indeterminate vertebral lesions seen on planar bone scans
Limitations of Nuclear Medicine Bone Scans

- less sensitive in detecting osteolytic lesions (marrow based)
  - associated with lung, thyroid, renal cell & breast CA
  - CT & MRI: > sensitive in detection of osteolytic lesions but are currently not practical as whole body techniques
- studies by Schirrmeister et al, evaluating the performance of planar bone imaging in oncology demonstrated:
  - 80-90% sensitivity for detection of peripheral skeletal metastases
  - only 20-40% sensitivity for detection of vertebral metastases
- recommended SPECT of the entire spinal column in patients at high risk for bone metastases, even in the setting of normal planar bone scan

JNM 40: 1623, 1999
NM Planar Bone Scan performed for increased pain, lumbar spine

Cause of uptake in L-spine, Rt SI joint: Metastases? Trauma? Old surgery?
NM SPECT Bone Scan L-Spine and Pelvis

Cause of uptake in L-spine, Rt SI joint: Metastases? Trauma? Old surgery?
NM SPECT-CT Bone Scanning with Symbia T6

Degenerative joint disease (DJD) in the lumbar spine, NOT metastases
NM SPECT-CT Bone Scanning with Symbia T6

CT correlation confirms degenerative joint disease (DJD) in Rt. SI joint
## Planar versus SPECT Bone Imaging

<table>
<thead>
<tr>
<th>Indication</th>
<th># of patients</th>
<th>Sensitivity (SPECT/Planar)</th>
<th>Specificity (SPECT/Planar)</th>
<th>PPV (SPECT/Planar)</th>
<th>NPV SPECT/Planar</th>
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<td>87 / 74</td>
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<td>Lung cancer</td>
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<td>71 / 39</td>
<td>85 / 79</td>
<td>73 / 52</td>
<td>83 / 64</td>
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</table>

Han EJNM 1998
Schirrmeister JNM 2001
Even-Sapir JNM 2006
Planar versus SPECT Bone Imaging

The major drawback of bone SPECT is acquisition time (25 to 30 min per FOV)
- whole body oncology SPECT (3 – 5 FOV) becomes impractical (require 1.5 – 2.5 hours /exam)
- at a busy facility, like MD Anderson, only 1/4 to 1/3 of their daily planar patient load could be completed per day

The major advantage of SPECT CT is that it allows direct correlation with anatomic changes, improves interpreter confidence and diagnostic accuracy.

Advances in scanner technology are facilitating “rapid acquisition” sequences (FLASH, Astonish) that may make whole body SPECT more practical. WIP*
Why should we consider PET or PETCT?

- 18F NaF is FDA approved (NDA 17-042 & FDAMA) and listed in USP DI for use in evaluation of altered osteogenic activity
- expanded PET infrastructure to support clinical use
  - increased number of clinical PET systems
  - widely available unit dose 18F NaF
- ability to offer an improved whole body tomographic technique for assessing the presence and extent of bone metastases
- potential to influence referring physician adoption by introducing the diagnostic utility of molecular imaging for a common clinical problem
Why PET?

superior image quality

- higher spatial resolution
- whole body tomographic images
- improved anatomic detail

superior quantitative accuracy

- measure regional skeletal kinetics
  - enables us to differentiate metastases from benign skeletal lesions
- evaluate response to therapy
Why PET?

improved sensitivity

• PET often demonstrates disseminated metastatic bone disease in patients with single lesion on NM bone scan

• higher accuracy in detecting both osteolytic & osteoblastic metastases

improved specificity

• greater ability to differentiate benign from malignant lesions

Image courtesy of Seattle Nuclear Medicine – Normal study SMp1726
Case Study Breast Cancer

Breast Cancer patient with lumbar back pain

Planar bone scan demonstrates abnormalities lumbar spine, pelvis, sacrum, lt acetabulum, sternum suspicious for metastatic disease

25 mCi Tc99m MDP
Boulder Community Hospital
Case Study Breast Cancer

10.2 mCi Na\textsuperscript{18}F PET Bone

25 mCi Tc\textsubscript{99}m MDP
Boulder Community Hospital
Tracer Dynamics $^{18}$F FDG vs $^{18}$F Sodium Fluoride

$^{18}$F FDG accumulates in all cells relative to increased glucose metabolism

- marker of neoplasia, direct imaging of tumor metabolism
- uptake not limited to tumor involving the skeleton
- demonstrates soft tissue & bony metastatic sites
- prior to PETCT, precise anatomic localization of lesions was difficult
Tracer Dynamics $^{18}$F FDG vs $^{18}$F Sodium Fluoride

$^{18}$F Sodium Fluoride

• preferentially deposited at sites of high bone turnover & remodeling

• bone metastases are seen indirectly, uptake depends on skeletal reaction to tumor

• tracer kinetics depend both on regional blood flow & osteoblastic activity – similar to other NM bone agents

• bone uptake is two times higher & blood clearance is faster than Tc$^{99m}$-polyphosphonates
  ▪ superior bone to background ratios
  ▪ high contrast images as early as 60 minutes after injection
Breast Cancer Case Study

Patient w/ 2wk history of back pain after a fall. Bone scan results: abnormal activity L2 vertebral body, mets versus post-traumatic fracture. Minimal focal activity Lt 7th rib, suspicious for metastasis versus injury related to trauma.

30 mCi Tc$^{99m}$ MDP
3 hour delay
Planar whole body with spot views of spine & pelvis.

MRI Lumbar spine: suspicious for possible bone marrow metastases
Breast Cancer Case Study

FDG PET scan ordered for restaging prior to treatment planning.

Scan results: No abnormalities seen. Since $^{18}$F FDG PET can be negative in sclerotic or osteoblastic lesions, further evaluation with $^{18}$F Sodium Fluoride was recommended.
Breast Cancer Case Study

$^{18}$F Sodium Fluoride Bone PET results: disseminated metastatic bone disease.
Breast Cancer Case Study

Patient received appropriate systemic therapy after accurate identification of the presence and extent of bone disease with $^{18}\text{F} \text{ Sodium Fluoride}$ PET Bone imaging.

30 mCi Tc$^{99m}$ MDP

10 mCi MetaTrace$^{\text{TM}}$FDG

10 mCi $^{18}\text{F} \text{ Sodium Flouride}$
Role for $^{18}$F Sodium Fluoride PET Bone Imaging

$^{99m}$Tc-MDP vs $^{18}$F Sodium Fluoride PET in 44 patients with a mixture of primary cancers (lung, prostate, thyroid)

PET Bone imaging

- identification of 100% of known metastases
  - detected all osteoblastic metastases in prostate cancer
  - detected all osteolytic metastases in lung & thyroid cancer
- detected twice as many benign & malignant skeletal lesions as MDP bone scans
- superior spatial resolution enabled 97% lesions to be correctly classified as benign or malignant versus 80.5% for MDP bone scans
- as sensitive as MRI in detecting both osteoblastic and osteolytic metastases

Role for $^{18}$F Sodium Fluoride PET Bone Imaging

$^{99m}$Tc-MDP vs Na$^{18}$F PET in 34 breast cancer patients with known or suspected bone mets. Results confirmed by a panel of reference methods (MRI, CT, radiographs). PET Results:

- $^{18}$F Sodium Fluoride PET identified 64 bone metastases in 17 patients
- 11/17 patients the extent of metastatic disease was underestimated by TcMDP bone scan
- 3 patients with normal TcMDP bone scans had metastatic disease confirmed by $^{18}$F Sodium Flouride PET
- 1 patient with known mets – $^{18}$F Sodium Fluoride PET identified an osteolytic metastasis missed on TcMDP scan – risk of fracture resulted in surgical stabilization
- Bone PET results influenced clinical management in ~18% of patients

Role for $^{18}$F Sodium Fluoride PET Bone Imaging

Tc$^{99m}$MDP Planar & SPECT vs $^{18}$F Sodium Fluoride PET in 53 patients with newly diagnosed lung cancer – prospective study. Results - 12 patients with metastatic bone disease planar bone imaging only identified 5/12 = 42%

- 6 patients falsely interpreted as negative
- 5 patients read as equivocal, 2 with confirmed bone mets
- 2 patients with degenerative disease were falsely read as mets

SPECT – significantly improved sensitivity

- identification of vertebral mets in 5/6 false negative planar scans
- two or three SPECT acquisitions were required to assess the entire vertebral column and pelvis

$^{18}$F Sodium Fluoride PET

- 52/53 patients were correctly classified = 98%
- one patient with isolated rib lesion was equivocal by all three techniques

Role for $^{18}$F Sodium Fluoride PET Bone Imaging

$^{99m}$Tc$\text{MDP Planar}$ & $\text{SPECT vs }^{18}$F Sodium Fluoride PET in 53 patients with newly diagnosed lung cancer – prospective study

Conclusions:

- $^{18}$F Sodium Fluoride PET Bone imaging is the most accurate whole-body modality for screening for bone mets

- Routinely performed SPECT imaging is practical, cost effective and improves accuracy, however
  - Two or three SPECT acquisitions were required to approach the sensitivity of PET
  - Patient compliance was poor & image degradation due to patient motion was an issue during extended imaging session

Case Study - Spindle cell CA, ? renal origin

56 yr old male with extensive miliary metastases on chest CT – spindle cell CA, possible renal origin

increasing pain Rt iliac crest, left leg

CT bone windows – several lucent bony lesions suspicious for lytic mets

L1 vertebral body, left of midline
L1 right transverse process
L3 left pedicle
sacrum, midline
subtle lucency mid anterior aspect of right ileum
Case Study - Spindle cell CA, ? renal origin

PET results: abnormalities consistent w/ metastatic disease to the bone, from renal primary

Photopenia with rims of activity seen:
- right iliac wing over crest
- L3, left pedicle
- sacrum, centered at S2
- L1, superior end plate

Suspicious for mets:
- L1, right transverse process
- right 5th rib, lateral aspect

Facet arthropathy in C-spine
- C2-3 activity, left side – extends inferiorly & involves lamina, suspicious for mets
- Uptake left greater trochanter, bursitis
- Uptake right acromion & humeral head related to rotator cuff surgery

10.7 mCi Na^{18}F PET Bone

Seattle Nuclear Medicine CCP8109
Sensitivity of FDG PET compared to NM bone imaging in the identification of skeletal metastases:

Bury, et al\textsuperscript{1} studied 110 patients with NCSL cancer
  - FDG PET had similar sensitivity and improved specificity over planar bone scans in detecting bone metastases

Chung, et al\textsuperscript{2} studied 145 patients with variety of cancers
  - FDG PET demonstrated higher sensitivity & specificity on a lesion-by-lesion basis

\textsuperscript{1} EJNM 25:1244, 1998 \textsuperscript{2} JNM 40:96P, 1999
Role for $^{18}$F FDG PET

Sensitivity of FDG PET compared to NM bone imaging in the identification of skeletal metastases.

Moog, et al$^{3}$ evaluated the use of FDG PET in lymphoma – skeletal metastases in lymphoma are more marrow-based rather than purely osseous.

- demonstrated increased sensitivity for disease detection with FDG PET
- concluded that staging with FDG might be able to replace bone marrow biopsy since PET offers the advantage of a whole body survey & is not limited to the iliac crest.

3 JNM 40:1407, 1999
Role for $^{18}$F FDG PET

These results were thought to be due in part to:

- improved sensitivity of the tomographic technique over planar imaging

- tracer dynamics - $^{18}$F FDG uptake is more specific to malignant tissue and is not hampered by nonspecific uptake in coincidental benign skeletal disease

- lesions were identified at an earlier stage when only the marrow is involved, prior to bone reaction occurring

Case study – Lung Cancer, ? bony mets

Tc MDP Bone Scan – blastic mets
abnormal uptake sternum,
isolated rib lesion

\(^{18}\)FFDG – lytic mets
multiple foci of marrow based
mets

Images: I. Davey, MD Intermountain Medical Imaging
Practice Profile Seattle Nuclear Medicine

Initiated $^{18}$F Sodium Fluoride PET Bone imaging in response to diagnostic challenge posed by their breast oncologists for higher accuracy in detection of bone metastases and for an improved ability to monitor patients with bone dominant disease.

Creation of a Breast Cancer Protocol combining two whole body PET scans, performed on separate days

- FDG PET for detection of soft tissue recurrences and lytic bone metastases missed on standard bone scans
- Sodium Fluoride PET to visualize blastic bone metastases with higher sensitivity and improved resolution over conventional nuclear medicine bone imaging
Breast Cancer – $^{18}$F FDG PET

Patient s/p Rt mastectomy, radiation, ongoing chemotherapy.

CT findings:
• hypodense liver lesions consistent with metastases
• review of bone windows shows multiple sclerotic lesions in clavicle, thoracic & lumbar spine & pelvis

$^{18}$F FDG PET findings:
• multiple hypermetabolic foci within liver, consistent with metastatic disease
• sclerotic bone lesions, not seen
Breast Cancer – $^{18}$F Sodium Fluoride Bone PET

$^{18}$F Sodium Fluoride PET findings

- abnormal foci identified C4, T8, L4 vertebral bodies consistent with metastatic disease

Image courtesy of Seattle Nuclear Medicine – CEp1729
Case Study – Breast Cancer

Patient DQ with history of Lt breast cancer, s/p lumpectomy, axillary node dissection, radiation therapy & Tamoxifen, presents with:

- multiple sclerotic bone lesions on CT
- pancreatic mass
- Lt adrenal mass
- elevated tumor markers for breast and abdominal malignancies

Breast PET protocol for restaging
Breast Cancer – $^{18}$F FDG PET

$^{18}$F FDG PET findings:

- hypermetabolic pancreatic lesion & associated activity around gallbladder most consistent w/ carcinoma
- extensive abnormalities correlating to bony metastases in cervical & thoracic spine, bilateral scapula & humerus, sacrum

Image courtesy of Seattle Nuclear Medicine – DQP1723
Breast Cancer – $^{18}$F Sodium Fluoride Bone PET

$^{18}$F Sodium Fluoride PET findings:

- innumerable abnormalities consistent with metastatic disease to bone
- significant thoracic spine abnormalities worrisome for risk of cord compression or pathologic fracture

Image courtesy of Seattle Nuclear Medicine – DQp1723
Practice Profile Alaska Open Imaging Center

Availability of Na$^{18}$F from Seattle led this outpatient radiology group to add PET Bone imaging to their service offerings. Practice consisted of MRI, CT, US and PET results:

- created incremental revenue to offset fixed overhead costs
- supported growing procedure volumes
- increased awareness of practice among referring physicians
Sclerotic lesion, distal Lt femur

- hypermetabolic focus in area of sclerosis on plain film

- prime consideration is ostoid osteoma, although periosteal osteosarcoma or Brodie’s abscess cannot be excluded

- slight uptake in Lt ankle and bilateral lateral malleoli is typical of degenerative change
18F Sodium Fluoride Bone PET - Orthopedic

Fused Bone PET and CT images precisely localize activity to facet confirming diagnosis of facet arthropathy.

Images courtesy of R. Bridges, MD, Alaska Open Imaging Center
Role for $^{18}$F Sodium Fluoride PET Bone Imaging - PETCT

Assessment of Malignant Skeletal Disease: Initial Experience with $^{18}$F Sodium Fluoride Bone PETCT

44 oncology patients were studied to evaluate diagnostic accuracy in assessing malignant bone involvement and in differentiating malignant from benign lesions:

- 94/111 (85%) of metastases presented as sites of increased uptake with corresponding lytic or sclerotic changes on CT
- 16/17 of the remaining metastases appeared normal on CT bone-windows (confirmed w/MRI and/or FDG)
- 1 metastasis misclassified as benign lesion (isolated rib lesion)

Even-Sapir, MD, PhD, et al, JNM Vol 45 No 2, 2004 p272-278
Role for $^{18}$F Sodium Fluoride PET Bone Imaging - PETCT

Sensitivity of 99% for tumor detection (lesion basis) and in a patient based analysis the sensitivity = 100%

Specificity of 97%

- PETCT identified benign abnormalities at the location corresponding to the increased tracer uptake for 96% (85/89) of benign lesions
- Bone lesions with PETCT pattern of increased $^{18}$F Sodium Fluoride uptake but normal CT findings demonstrated high malignancy rate – 89%

Even-Sapir, MD, PhD, et al, JNM Vol 45 No 2, 2004 p272-278
Technical Protocol

Remember, it’s a bone scan!

No patient prep

Inject 5-12 mCi Sodium Fluoride

Encourage patient to drink fluids

Wait 30 – 60 minutes – patient can leave the department

Image whole body or partial FOV, dependent on clinical indication

Time per bed position ~ 1/3 – 1/2 of time used for FDG
Is it better medicine?

Sodium Fluoride PET Bone imaging offers:

- superior image quality
  - higher spatial resolution
  - whole body tomographic images
  - improved anatomic detail

- superior quantitative accuracy
  - measure regional skeletal kinetics
    - improved ability to differentiate metastases from benign skeletal lesions
Is it better medicine?

Sodium Fluoride PET Bone imaging offers:

improved sensitivity

- PET often demonstrates disseminated metastatic bone disease in patients with single lesion on NM bone scan
- higher accuracy in detecting both osteolytic & osteoblastic (sclerotic) metastases
- identifies early osteoblastic abnormalities prior to radiographic changes, question remains whether this changes patient management and/or outcomes – purpose of the AMI Clinical Trial

improved specificity

- greater ability to differentiate benign from malignant lesions
Delivering quality radiopharmaceuticals

Expanding the value of PET

Advancing a new paradigm for molecular imaging

Delivering, Expanding, Advancing the Science of Molecular Imaging

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