PET Bone Imaging with Sodium Fluoride F 18 Injection

Presented by:
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Sodium Fluoride F 18 Injection (\(^{18}\text{F} \text{NaF}\))
Imaging with PET/CT

Indication and Safety Information

Imaging Techniques

Why Consider \(^{18}\text{F} \text{NaF}\) imaging with PET/CT?

Case Examples

Are We Ready?
**Fludeoxyglucose F 18 Injection***
Indicated for PET imaging in the following settings

<table>
<thead>
<tr>
<th>Oncology</th>
<th>Cardiology</th>
<th>Neurology</th>
</tr>
</thead>
<tbody>
<tr>
<td>For the assessment of abnormal glucose metabolism to assist in the evaluation of malignancy in patients with known or suspected abnormalities found by other testing modalities, or in patients with an existing diagnosis of cancer.</td>
<td>For the identification of left ventricular myocardium with residual glucose metabolism and reversible loss of systolic function in patients with coronary artery disease and left ventricular dysfunction, when used together with myocardial perfusion imaging.</td>
<td>For the identification of regions of abnormal glucose metabolism associated with foci of epileptic seizures.</td>
</tr>
</tbody>
</table>

*Full prescribing information is available from the instructor*
Fludeoxyglucose F 18 Injection*
Important safety information

Radiation Risks
- Radiation-emitting products, including Fludeoxyglucose F 18 Injection, may increase the risk for cancer, especially in pediatric patients. Use the smallest dose necessary for imaging, ensure safe handling to protect the patient and health care worker.

Blood Glucose Abnormalities
- In the oncology and neurology setting, suboptimal imaging may occur in patients with inadequately regulated blood glucose levels. In these, consider medical therapy and laboratory testing to assure at least two days of normoglycemia prior to Fludeoxyglucose F 18 Injection administration.

Adverse Reactions
- Hypersensitivity reactions with pruritus, edema and rash have been reported; have emergency resuscitation equipment and personnel immediately available.

*Full prescribing information is available from the instructor
Sodium Fluoride F 18 Injection*
Indications and usage

Sodium fluoride F 18 injection is a radioactive diagnostic agent for positron emission tomography (PET) indicated for imaging of bone to define areas of altered osteogenic activity.

*Full prescribing information is available from the instructor
Sodium Fluoride F 18 Injection*
Important safety information

**Allergic Reactions**
- As with any injectable drug, allergic reactions and anaphylaxis may occur. Emergency resuscitation equipment and personnel should be immediately available.

**Cancer Risk**
- Sodium Fluoride F 18 Injection may increase the risk of cancer. Use the smallest dose necessary for imaging and ensure safe handling to protect the patient and health care worker.

**Adverse Reactions**
- No adverse reactions have been reported based on a review of the published literature, publicly available reference sources, and adverse drug reaction reporting systems. The completeness of the sources is not known.

**Pediatrics**
- Children are more sensitive to radiation and may be at higher risk of cancer from Sodium Fluoride F 18 Injection.
Applications for Bone Imaging

- Trauma
- Infection
- Arthritis
- Degenerative joint disease
- Orthopedic applications
- Oncologic applications
Applications for Bone Imaging
Oncology

The most prevalent cancers are associated with a high incidence of metastatic bone disease:

- 73% of breast cancer patients
- 68% of prostate cancer patients
- 42% of follicular thyroid cancer patients
- 36% of lung cancer patients
- 35% of renal cell carcinoma patients

Source: Galasko C. In Bone metastases. Weiss L, Gilbert A, editors. Boston
Applications for Bone Imaging
Metastatic bone disease

- Exclusion of bone disease before treatment
- Initial staging – extent of bone disease
- Monitoring response to therapy
- Follow-up after completion of treatment
Sodium Fluoride F 18 Injection (18F NaF)
Imaging with PET/CT

Indication and Safety Information

Imaging Techniques

Why Consider $^{18}$F NaF imaging with PET/CT?

Case Examples

Are We Ready?
Imaging Techniques for Bone Imaging
Comparisons of standard methods

Rectilinear Scanners
- 1960’s and 1970’s
- $^{18}$F NaF, $^{69}$Ga, $^{85}$Sr

Anger Gamma Camera
- 1970’s
- $^{99m}$Tc MDP, $^{99m}$Tc HDP or $^{99m}$Tc pyrophosphate

SPECT/CT
- Present
- $^{99m}$Tc MDP

PET/CT
- Present
- $^{18}$F NaF
Imaging Techniques
Comparisons of standard methods

- Planar or SPECT bone scintigraphy have been the standard diagnostic methods using $^{99m}$Tc-labeled compounds
- Planar technique has variable sensitivity and low specificity
- SPECT/CT can improve anatomic localization and characterize indeterminate vertebral lesions seen on planar bone scans
Imaging Techniques
Comparisons of standard methods

- Advantages of SPECT/CT
  - Allows direct correlation with anatomic changes, improves interpreter confidence and diagnostic accuracy

- Drawbacks of SPECT/CT
  - Acquisition time is 25 to 30 min per field of view (FOV)
  - Whole body oncology with 3 to 5 FOV is impractical
  - Requires 1.5 to 2.5 hours per exam
  - At a busy facility, only 1/4 to 1/3 of their daily planar patient load could be completed per day

- Advances in scanner technology are facilitating “rapid acquisition” sequences that in the future may make whole-body SPECT more practical
<table>
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<th>Imaging Techniques</th>
<th>Comparisons of standard methods</th>
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<td><strong>Planar</strong></td>
<td><strong>SPECT/CT</strong></td>
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<tr>
<td>- Less sensitive than PET in detecting osteolytic lesions&lt;sup&gt;1&lt;/sup&gt;</td>
<td>- Correlation with anatomic changes</td>
</tr>
<tr>
<td>- Less sensitive than SPECT</td>
<td>- Improves interpreter confidence</td>
</tr>
<tr>
<td><strong>CT</strong></td>
<td><strong>MRI</strong></td>
</tr>
<tr>
<td>- Sensitive for osteolytic metastases&lt;sup&gt;2&lt;/sup&gt;</td>
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</tr>
<tr>
<td>- Detailed bone morphology&lt;sup&gt;3&lt;/sup&gt;</td>
<td>- Identifies early involvement of bone marrow&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>- Not practical for whole-body&lt;sup&gt;2&lt;/sup&gt;</td>
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Imaging Techniques
Comparisons of standard methods

- Integrated PET/CT scanners
- CT component allows morphologic characterization
- Five-minute whole-body scans
- More comfortable patient exams
- Exceptional image quality
- Low patient doses
- Intelligent software
- Accurate quantification
18F NaF was one of the first series of agents used for bone imaging originally approved for use in 1972.

18F NaF was used for skeletal scintigraphy in the early 1960s.

Replaced by 99mTc diphosphonates as the principal radiopharmaceutical for bone imaging.
Imaging Techniques
Radiopharmaceuticals

- $^{18}$F NaF reaffirmed for PET use in 2000
- National Oncologic PET Registry (NOPR) reimbursement commenced February 2011
- Expanded Medicare reimbursement
- Expanded commercial availability

Image courtesy of Architect of the Capitol public domain and licensed for reuse under the Wikipedia Commons License
Nuclear medicine planar bone scan was performed for increased pain in lumbar spine

Cause of uptake in lumbar spine and right sacroiliac joint:

- Metastases?
- Trauma?
- Old surgery?
Planar vs. SPECT Imaging
Case example Cont’d

SPECT/CT bone scan aided the physician in diagnosing degenerative joint disease in the lumbar spine, rather than metastases

Courtesy of University of Texas, MD Anderson Cancer Center, Houston, Texas, USA
CT correlation provided data to confirm degenerative joint disease in right sacroiliac joint.
Sodium Fluoride F 18 Injection (18F NaF) Imaging with PET/CT

Indication and Safety Information

Imaging Techniques

Why Consider $^{18}$F NaF imaging with PET/CT?

Case Examples

Are We Ready?
Why Consider $^{18}$F NaF Imaging with PET/CT?

**Availability**

- Widespread availability of clinical PET/CT systems
- Expanded infrastructure and wide availability of unit dose $^{18}$F NaF
Why Consider PET/CT?

**Comparison to $^{99m}$Tc Bone Scans**

- Increased sensitivity
- Increased specificity
- Increased spatial and contrast resolution
- Faster completion of whole-body scanning
- Fusion with anatomic information – CT or MRI
- 3-axis and whole-body viewing

Characteristics of $^{18}$F FDG

Fludeoxyglucose F 18 Injection ($^{18}$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 & some bony metastatic sites


Courtesy of University of Tennessee Medical Center, Knoxville, Tennessee, USA
Characteristics of $^{18}$F NaF

$^{18}$F NaF is preferentially deposited at sites of high bone turnover and remodeling.

Tracer kinetics depend both on regional blood flow and osteoblastic activity.

Bone uptake is two times higher and blood clearance faster than $^{99m}$Tc MDP.

Superior bone to background ratios than $^{99m}$Tc MDP.

High contrast images as early as 60 minutes after injection.

Little residual retention in soft tissues and the renal parenchyma.


Courtesy of University of Tennessee Medical Center, Knoxville, TN, USA
Why Consider $^{18}$F NaF Imaging with PET/CT?

$^{18}$F NaF PET/CT

- Improved sensitivity over planar bone scan
- PET often demonstrates disseminated metastatic bone disease in patients with single lesion on planar bone scan
  - Higher accuracy in detecting osteolytic and osteoblastic metastases
- Improved specificity over planar bone scan
  - Greater ability to differentiate benign from malignant lesions

Staging
Second case example

Breast cancer patient scanned the same week with both planar $^{99m}$Tc MDP and $^{18}$F NaF PET

$^{18}$F NaF clearly identifies numerous lesions with greater confidence due to increased sensitivity and spatial resolution

Courtesy of Seattle Nuclear Medicine, Seattle, Washington, USA
Staging
Third case example

Increased $^{18}$F NaF uptake in the condyle of the left mandible
A patient with history of breast cancer presented with increasing back pain two weeks after a fall.

The planar bone scan revealed abnormal activity in the L2 vertebral body and minimal focal activity in the left 7th rib which was suspicious for metastatic disease.

A subsequent MRI of the lumbar spine was suspicious for possible bone marrow metastases.

An $^{18}$F FDG PET scan was ordered for restaging prior to treatment planning.
Staging
Fourth case example

$^{18}$F FDG PET scan was ordered for restaging prior to treatment planning. There were no abnormalities seen. Since $^{18}$F FDG PET can be negative in sclerotic or osteoblastic lesions, further evaluation with $^{18}$F NaF was recommended.
Staging
Fourth case example

$^{18}$F NaF PET bone results:
disseminated metastatic
bone disease

Courtesy of Seattle Nuclear Medicine, Seattle, Washington, USA
Patient was scheduled for appropriate systemic therapy after accurate identification of the presence and extent of bone disease with $^{18}$F NaF bone imaging with PET.

30 mCi $^{99}$mTc MDP

10 mCi $^{18}$F FDG

10 mCi $^{18}$F NaF
\textbf{\textsuperscript{99m}Tc MDP vs. \textsuperscript{18}F NaF PET Bone Imaging}

Clinical study 1 – primary cancers

- 44 patients with known lung, prostate, thyroid cancers
- PET bone imaging with \textsuperscript{18}F NaF detected 96 metastases
  - 67 osteoblastic metastases in prostate cancer
  - 29 osteolytic metastases in lung and thyroid cancer
  - Twice as many benign and malignant skeletal lesions as MDP bone scans
- MDP bone imaging detected 46 metastases (33 prostate and 13 lung and thyroid)
  - Sensitivity was highly dependant on anatomic localization

\textsuperscript{18}F NaF PET is more sensitive than MDP bone imaging in detecting osseous lesions, with higher detection rates and more accurate differentiation between benign and malignant lesions.

99mTc MDP vs. 18F NaF PET Bone Imaging
Clinical study 2 – breast cancer

- 34 breast cancer patients with known or suspected bone metastases
- 18F NaF PET identified 64 bone metastases in 17 patients
- 99mTc MDP bone scan identified 29 metastases in 11 patients
- In 11 of the 17 patients the extent of metastatic disease was underestimated by 99mTc MDP bone scan
- Patients with normal 99mTc MDP bone scans had metastatic disease confirmed by 18F NaF PET
- 18F NaF PET results influenced clinical management in ~12% of patients

Source: Schirrmeister, et al. JCO 1999; 17:2381-2389
Comparison of Planar Bone Scan, SPECT and PET
Clinical study 3 – lung cancer

- 53 patients with lung cancer (osteolytic bone metastases)
- 12 patients had metastatic bone disease
- Planar bone scan false negatives – 6
  - 2 patients with degenerative disease were falsely read as metastases
- SPECT false negatives – 1
  - Significantly improved sensitivity
  - Longer SPECT acquisitions were required
  - Changed clinical management in 5 patients
- $^{18}$F NaF PET false negatives – 0
  - 52 out of 53 (98%) patients were correctly classified
  - Changed clinical management in 6 patients

Comparison of Planar, SPECT and PET
Conclusion of clinical study 3 – lung cancer

- $^{18}$F NaF PET bone imaging is the most accurate whole-body modality for screening bone metastases
- SPECT imaging is practical, cost effective and improves accuracy
- However with SPECT:
  - Two or three SPECT acquisitions were required to approach the sensitivity of PET
  - Patient compliance was poor and patient motion occurred
  - Image degradation occurred during extended imaging session

Evaluating diagnostic accuracy and differentiation of malignant from benign lesions

44 oncology patients were studied with PET and PET/CT

Uptake detected at 212 sites with 111 malignant lesions
- 94 lesions abnormal on CT – PET/CT identified all
- 16 lesions normal on CT – PET/CT showed increased uptake
- 1 metastasis misclassified as benign lesion (isolated rib lesion) by both modalities

PET/CT is both sensitive and specific for detection of lytic and sclerotic malignant lesions
- Differentiated malignant and benign lesions

Source: Even-Sapir, MD, PhD, et al, JNM Vol 45 No 2, 2004 p272-278
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Why Consider $^{18}$F NaF imaging with PET/CT?

Case Examples

Are We Ready?
Restaging Breast Cancer
Fifth case example

18F FDG PET revealed multiple hypermetabolic foci within liver

18F NaF PET identified additional abnormal foci in the C4, T8 and L4 vertebral bodies consistent with metastatic disease
Restaging Prostate Cancer
Sixth case example

In a planar bone scan a small focus of abnormal accumulation was seen, which was interpreted as possible traction spurring.

3 years later there is a large hypermetabolic focus in the same region.
Restaging Breast Cancer
Seventh case example

$^{18}$F FDG PET scan revealed hypermetabolic activity around the gallbladder and pancreas, as well spine, sacrum and humerus.

$^{18}$F NaF PET revealed innumerable abnormalities consistent with metastatic bone disease.

Courtesy of Seattle Nuclear Medicine, Seattle, Washington, USA
Sodium Fluoride F 18 Injection (18F NaF)
Imaging with PET/CT

Indication and Safety Information

Imaging Techniques

Why Consider $^{18}$F NaF imaging with PET/CT?

Case Examples

Are We Ready?
Imaging Protocols*

- Remember it is a bone scan!
- No patient preparation, no dietary restrictions, no activity restrictions
- Inject 8 to 12 mCi $^{18}$F NaF
- Encourage patient to drink fluids
- Wait 30 – 60 minutes
- Encourage patient to void
- Image whole body or selected body areas, dependent on clinical indication
- Time per bed position is approximately 1/3 to 1/2 of time used for $^{18}$F FDG imaging

* Any of the protocols presented herein are for informational purposes and are not meant to substitute for clinician judgment in how best to use any medical devices. It is the clinician that makes all diagnostic determinations based upon education, learning and experience.
February 26, 2010 Centers for Medicare and Medicaid Services (CMS) announced
- Coverage with Evidence Development (CED) through the NOPR
- $^{18}$F NaF PET and PET/CT imaging to identify bone metastasis of cancer
- June 22, 2010 NOPR announced data registry for $^{18}$F NaF PET
- February 7, 2011 first patients registered
- www.cancerpetregistry.org
Medicare Reimbursement
NOPR Cont’d

- On Sept 16, 2015 CMS posted decision memo in response to a written request by the NOPR to end the CED.
- NaF PET scan is not reasonable and necessary to diagnose or treat an illness or injury or to improve the functioning of a malformed body member and, therefore, is not covered.
- CMS will continue the NOPR until Dec 15, 2017
  - Does the additional of NaF PET imaging lead to:
    - Change in patient management to more appropriate palliative care
    - Change in patient management to more appropriate curative care
    - Improved quality of life or improved survival.
January 27, 2016 – Denial of claims since conversion to ICD-10

- Recent ICD-10 conversions
- Email registry directly pet_registry@phila.acr.org
  - ICN#, date of service, MAC that processed the claim.
  - No patient specific information is included in the email
Medicare Coverage
Limitations and requirements

- Coverage for $^{18}$F NaF Bone PET and PET/CT is limited to:
  - Patients enrolled in an approved CED clinical trial
    - Assist in initial antitumor treatment planning (ITS)
    - Guide subsequent treatment strategy (STS)
    - Aid in the identification, location and quantification of bone metastases
  - When bone metastases are strongly suspected based on
    - Clinical symptoms
    - Results of other diagnostic studies
Medicare Coverage
Clinical indications - oncology

- Initial staging of oncology patients at risk for bone metastasis
- Exclusion of bone disease prior to initiation of potentially curative therapy
- Base line evaluation and monitoring of patients with bone dominant metastases
  - Evaluate the effectiveness of systemic therapy
  - Exclude new metastases at critical anatomic sites
  - Assist in initial antitumor treatment planning
Medicare Billing Codes
Technical component or global billing

- Effective February 26, 2010
- $^{18}$F NaF PET oncologic claims billed with modifier TC or globally
- MUST include ALL of the following on the claim
  - CPT code (78811, 78812, 78813, 78814, 78815, 78816)
  - PI modifier (for ITS) or PS modifier (for STS)
  - ICD-10 cancer diagnosis code
  - Q0 modifier – investigational clinical service provided in a clinical research study
  - $^{18}$F NaF radiotracer code A9580
  - Institutional claims should also include V70.7 in the second diagnosis position and condition code 30

Source: CMS Transmittal 2096 and Change Request 7125
Medicare Billing Codes
Professional component

- Effective February 26, 2010
- $^{18}$F NaF PET claims billed with modifier 26 and modifier KX
- MUST include ALL of the following on the claim
  - PI modifier (for ITS) or PS modifier (for STS)
  - CPT code (78811, 78812, 78813, 78814, 78815, 78816)
  - ICD-10 cancer diagnosis code
  - Q0 modifier – investigational clinical service provided in a clinical research study
  - Do not include radiotracer code
    - Claims billed with modifiers 26 and KX should not include $^{18}$F NaF radiotracer code A9580

Source: CMS Transmittal 2096 and Change Request 7125
Private Insurers
Coverage

- No broad coverage for $^{18}$F NaF bone PET/CT
- No standard coverage policies
- Coverage is determined
  - Payer by payer
  - Varies regionally
- Pre-authorization may be required
- Notify payer of addition of $^{18}$F NaF bone imaging to scope of service
Private Insurers
Coding

- Confirm with payer
  - Coverage, coding and exam descriptions
  - Contracted payment rates
  - Frequency limitations to avoid future denials for oncology patient scheduled for both $^{18}$F FDG and $^{18}$F NaF PET/CT scans
- For billing private insurers use:
  - PET or PET/CT CPT code (78811, 78812, 78813, 78814, 78815, 78816) and
  - ICD-9 diagnosis code and
  - $^{18}$F NaF radiotracer code, HCPCS A9580
Practice Profile
Seattle Nuclear Medicine

- Initiated $^{18}$F NaF bone imaging for
  - Higher accuracy
  - Improved patient monitoring
- Created breast cancer protocol
  - Two whole-body PET scans
  - $^{18}$F FDG PET imaging
    - Soft tissue recurrences
    - Lytic bone metastases
  - $^{18}$F NaF PET bone imaging
    - Blastic bone metastases
    - Higher sensitivity and resolution
**Practice Profile**
Alaska Open Imaging

- Practice consisted of MRI, CT, US and PET imaging
- Added PET bone imaging to their service offerings
- Results
  - Supported growing procedure volumes
  - Increased awareness of practice among referring physicians


**18F NaF Bone Imaging with PET/CT**

Comparison summary

<table>
<thead>
<tr>
<th>PET/CT vs. Planar</th>
<th>18F NaF vs. 99mTc MDP</th>
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<tbody>
<tr>
<td>Increased spatial and contrast resolution&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Preferentially deposited at sites of high bone turnover&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Whole-body tomographic images&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Measures regional skeletal kinetics&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Fusion with CT or MRI for improved anatomic detail&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Superior bone to background ratios&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Faster scanning for patient convenience&lt;sup&gt;1&lt;/sup&gt;</td>
<td>High contrast images as early as 60 minutes after injection&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

### Improved sensitivity

- $^{18}$F NaF PET/CT often demonstrates disseminated metastatic bone disease in patients with single lesion on nuclear medicine bone scan
- Higher accuracy in detecting both osteolytic and osteoblastic (sclerotic) metastases
- Identifies early osteoblastic abnormalities prior to radiographic changes

### Improved specificity

- More specific than planar and SPECT bone scans
- Greater ability to differentiate benign from malignant lesions

Thank you!

Questions?