18F-NaF PET/CT: Normal Variants and Pitfalls

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18F-NaF History

- FDA approved 18F-NaF (1972)
- Decreased use in 70’s:
  - Availability of 99mTC generators
  - Development of PYP, polyphosphates and finally kit-based bisphosphonates
  - Poor imaging of 511 KeV photons with rectilinear scanner and Anger camera
- Hoh (UCLA) – Early 1990’s used for WB PET
- Wide availability of PET/CT accelerated interest.
18F-NaF Resurgence

- More sensitivity than MDP
- NEW PET/CT Cameras
- Occasional shortage of $^{99m}$Tc Generators.
1. Osteoblastic osseous metastasis (localization + extent)
   - Diagnosis
   - Following therapy
   - Bony pain/aches

2. Lower Back pain
18F-NaF Clinical Indications

- **Other reported uses:** (Research or inefficient information to be in routine use)
  1. Back pain (Ovadia 2007, Lim 2007) and unexplained bone pain (Fischer 2010).
  3. Abnormal radiographs or laboratory findings.
  4. Osteomyelitis.
  5. Trauma.
  6. Inflammatory and degenerative arthritis.
  8. Osteonecrosis of the mandible (Raje 2008, Wilde 2009)
  10. Metabolic bone disease (Uchida 2009)
  11. Paget's disease (Installe 2005)
  15. Distribution of osteoblastic activity prior to administration of therapeutic radiopharmaceuticals for treating bone scans.
MECHANISM OF UPTAKE

• exchange of 18F-ions with hydroxyl ions (OH) on the surface of the hydroxyapatite to form fluoroapatite
Hydroxyapatite

$\text{F} \quad \text{Na}$

Hydroxyfluorapatite

$\text{F} \quad \text{Na}$

Fluorapatite
Incorporation of $^{18}$F from NaF into the hydroxyapatite crystals of the mineral bone matrix to form the radioactive fluorapatite crystals (illustration by Kelley Kage)
Nuclear Medicine Radiation Dose Tool

**Select Nuclear Medicine Exam:**
- --Common exams--
- F-18 FDG
- Tc-99m DMSA
- Tc-99m Pertechnetate
- Tc-99m MAA
- Tc-99m MDP
- Tc-99m MIBI (exercise)
- Tc-99m Tetrofosmin (exercise)
- --List of all exams--
- H-3 Glucose

**Recommended Adult Injected Activity:**
- Minimum: 20.0 mCi (740.00 MBq)
- Maximum: 30.0 mCi (1110.00 MBq)

**Reference for adult injected activity:**
Donohoe et al, 'Society of Nuclear Medicine Procedure Guideline for Bone Scintigraphy', 2003

**Input Injected Activity:**
- 25 mCi or 925 MBq

**Select patient model:**
- Adult Male
- Adult Female
- 15-yr-old
- 10-yr-old
- 5-yr-old
- 1-yr-old
- early pregnant woman

**Radiation Dose Estimate:**
According to models recommended in ICRP 106, a 925 MBq injection for a Tc-99m MDP study would impart to an Adult Male an approximate effective dose of **5.3 mSv (0.53 rem)**. The critical organ for this study is the Bone surfaces, which would receive **58.3 mGy (5.83 rad)**.

**VERSION:** 1.04; 16-May-2015
Nuclear Medicine Radiation Dose Tool

Select Nuclear Medicine Exam:
- H-3 Glucose
- C-14 Urea, Normal
- Co-57 Cyanocobalamin
- Cr-51 Sodium Chromate RBCs
- F-18 FDG
- F-18 Sodium Fluoride
- Ga-67
- I-123 Hippuran
- I-123 Ioflupane (Datscan)

Recommended Adult Injected Activity:
- Minimum: 5.0 mCi, 185.00 MBq
- Maximum: 10.0 mCi, 370.00 MBq

Input Injected Activity:
- 7.5 mCi, 278 MBq

Select patient model:
- 10-yr-old
- 5-yr-old
- 1-yr-old
- early pregnant woman
- 3 month pregnant woman
- 6 month pregnant woman
- 9 month pregnant woman

Radiation Dose Estimate:
According to models recommended in ICRP 106, a 278 MBq injection for a F-18 Sodium Fluoride study would impart to an Adult Male an approximate effective dose of 7.5 mSv (0.75 rem). The critical organ for this study is the Bladder wall, which would receive 61.2 mGy (6.12 rad).

Reference for adult injected activity:
Segall et al, 'SNM Practice Guideline for Sodium 18F-Fluoride PET/CT Bone Scans 1.0', JNM 2010

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<table>
<thead>
<tr>
<th>Pharmaceutical</th>
<th>Effective dose/unit of administered activity for an adult patient</th>
<th>Activity</th>
<th>Total effective Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total-Body (mGy/MBq)</td>
<td>H (mSv/MBq)</td>
<td>E (mSv/MBq)</td>
</tr>
<tr>
<td>F^{18} NaF</td>
<td>2.64E-03</td>
<td>6.08E-03</td>
<td>4.75E-03</td>
</tr>
<tr>
<td>Tc^{99m} MDP</td>
<td>8.75E-03</td>
<td>2.70E-02</td>
<td>2.31E-02</td>
</tr>
<tr>
<td></td>
<td>MDP</td>
<td>NaF</td>
<td></td>
</tr>
<tr>
<td>--------------------------</td>
<td>---------------</td>
<td>----------------</td>
<td></td>
</tr>
<tr>
<td><strong>RBC Uptake</strong></td>
<td>Negligible</td>
<td>30 – 40 %</td>
<td></td>
</tr>
<tr>
<td><strong>Protein Binding</strong></td>
<td>25 – 70 %</td>
<td>Negligible</td>
<td></td>
</tr>
<tr>
<td><strong>First Pass Extraction</strong></td>
<td>40 – 60 %</td>
<td>70 – 100 %</td>
<td></td>
</tr>
<tr>
<td><strong>Renal Excretion</strong></td>
<td>GFR</td>
<td>GFR – Tub.Reabsp</td>
<td></td>
</tr>
</tbody>
</table>
RP DOSE AND ACQUISITION PROTOCOL (BED/MIN)
18F-NaF Imaging Protocol

• Dose
  ➢ **Adult:** activity is (5-10 mCi). A higher activity (10 mCi) may be used in obese patients.
  ➢ **[JACMI: 0.06 mCi/Kg]**
  ➢ **Pediatric:** activity should be weight-based (0.06 mCi/kg), Min-Max = [0.5 to 5 mCi].

• Acquisition
  ➢ **Axial:** 30-45 min post injection
  ➢ **WB/Extremities:** 90-120 min post injection
  ➢ **2 – 5 min/bed position**
  ➢ **[JACMI: BMI-based 2 - 3 min/bed = 40 or 50 min]**
  ➢ **3D acquisition mode recommended**
  ➢ **Diuretics or bladder cath. can be considered if needed.**
18F-NaF Imaging Protocol

- **Processing**
  - 128 x 128 (or 256 x 256) matrix
  - Same reconstruction iterations and subsets as with 18F-FDG
  - MIP
  - AC images
$^{99m}$Tc-MDP in case of Prostate cancer
$^{18}$F-NaF in the same case of Prostate cancer

<table>
<thead>
<tr>
<th>Metastases</th>
<th>18F PET</th>
<th>RNB</th>
<th>RNB/PET (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoblastic</td>
<td>67</td>
<td>33</td>
<td>49.3</td>
</tr>
<tr>
<td>Osteolytic</td>
<td>29</td>
<td>13</td>
<td>44.8</td>
</tr>
</tbody>
</table>

### Osseous Lesions Detected at Different Sites by Radionuclide Bone Scanning (RNB) Compared with $^{18}$F PET

<table>
<thead>
<tr>
<th>Region</th>
<th>$^{18}$F PET</th>
<th>RNB*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skull</td>
<td>5</td>
<td>4 (80.0)</td>
</tr>
<tr>
<td>Upper extremity</td>
<td>18</td>
<td>16 (88.9)</td>
</tr>
<tr>
<td>Ribs and sternum</td>
<td>24</td>
<td>19 (79.2)</td>
</tr>
<tr>
<td><strong>Spine</strong></td>
<td><strong>135</strong></td>
<td><strong>55 (39.6)</strong></td>
</tr>
<tr>
<td>Cervical</td>
<td>39</td>
<td>8 (20.5)</td>
</tr>
<tr>
<td>Thoracic</td>
<td>59</td>
<td>21 (33.6)</td>
</tr>
<tr>
<td>Lumbar</td>
<td>37</td>
<td>16 (43.2)</td>
</tr>
<tr>
<td>Pelvis</td>
<td>12</td>
<td>5 (41.7)</td>
</tr>
<tr>
<td>Lower extremity</td>
<td>11</td>
<td>9 (81.8)</td>
</tr>
</tbody>
</table>

*Values in parentheses indicate percentage of lesions detected by $^{18}$F PET.

A. BS Planar
B. BS SPECT/CT
C. 18F-NaF PET/CT

<table>
<thead>
<tr>
<th>Lesion to lesion analysis</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Planar Bone Scan</td>
<td>70</td>
<td>57</td>
</tr>
<tr>
<td>WB SPECT</td>
<td>92</td>
<td>82</td>
</tr>
<tr>
<td>$^{18}$F-NaF PET only</td>
<td>100</td>
<td>62</td>
</tr>
<tr>
<td>$^{18}$F-NaF PET/CT</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>
Skeletal PET with 18F-Flouride: Applying new technology to an old tracer.
18F-NaF PET/CT enables performance of whole-body imaging in a single examination but is costly and not readily available. A practicable and cost-effective strategy that had a significant effect on patient management in our study was the combination of planar BS with SPECT, complemented by MRI in unclear lesions.

Conclusion: Our prospective pilot-phase trial demonstrates superior image quality and evaluation of skeletal disease extent with 18F NaF PET/CT over 99mTc MDP scintigraphy and 18F FDG PET/CT.
CONCLUSION:

We believe 18F-NaF PET/CT is a sensitive modality for detection of bone metastases caused by prostate cancer. Whole-body DWI shows a higher specificity but lower sensitivity than 18F-NaF PET/CT. Future studies with a larger patient cohort along with analyses of costs and clinical availability are needed before implementation of these methods can be considered.

Whole-Body Diffusion-Weighted MRI Compared With 18F-NaF PET/CT for Detection of Bone Metastases in Patients With High-Risk Prostate Carcinoma

[AJR11-2012]
BONE METASTASES

18F-FDG
>90%

Lytic lesion

Blastic lesions

18F-NaF
>90%
F-18 Sodium Fluoride vs FDG

A. Osteoblastic

B. Osteolytic

NaF  FDG  NaF  FDG
F-18 Sodium Fluoride vs. FDG
WB Bone Scintigraphy

WB PET/CT
OBESITY AND SOFT TISSUE ATTENUATION
DIFFERENCE BETWEEN TWO CAMERA SYSTEMS
99Tc-MDP Bone Scan

-AVN Hip Right side
- 18F-NaF PET/CT
  - in the same case of AVN Right side
NORMAL BIODISTRIBUTION PATTERNS
Super scan
-no bladder

No extremities uptake

Axial uptake
Pitfalls:

- Patient Motion
- Truncation
- Urinary Catheter
- Dose Infiltration
- Contamination
- Metal Artifact
PITFALLS:
MOTION
PITFALLS:
TRUNCATION
When imaging extends beyond the CT FOV
PITFALLS:
URINARY CATHETER
PITFALLS: DOSE INFILTRATION
PITFALLS: CONTAMINATION
PITFALLS: BLADDER
Urinary Bladder Diverticulum
ileal conduit
cystectomy
PITFALLS: Metal Effect
Metallic implants such as dental fillings, hip prosthetics, or chemotherapy ports result in high CT numbers and generate streaking artifacts on CT images.
(A) High-density metallic implants generate streaking artifacts and high CT numbers (arrow) on CT image.

(B) High CT numbers will then be mapped to high PET attenuation coefficients, leading to overestimation of activity concentration.

(C) PET images without attenuation correction help to rule out metal-induced artifacts.
References:

- Sodium Fluoride PET/CT in Clinical Use. Kalevi Kairemo, Homer A. Macapinlac.


- Stanford University Sodium Fluoride PET/CT Bone Imaging: Theory and Practice, George Segall.

- PET/CT Imaging Artifacts. Waheeda Sureshbabu and Osama Mawlawi.

Thank you