Impact of FDG and PET-CT in Assessing Infection and Inflammation

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Biologic Basis for FDG Uptake in Infection and Inflammation

- Inflammatory cells utilize glucose as a source of energy when activated by a variety of stimuli as a consequence of either inflammatory or infectious processes.
• Inflammatory and infectious processes similar to malignant disorders can result in increased levels of glucose transporters on the membranes of the inflammatory cells.
A variety of cytokines and growth factors, whose levels are often elevated in such disorders, dramatically enhance glucose uptake by the inflammatory cells.
Effect of Glucose Levels on FDG Uptake by Malignant Cells

![Graph showing the effect of glucose levels on FDG uptake by malignant cells. The x-axis represents glucose concentration (mg/dL) ranging from 50 to 400, and the y-axis represents counts/minute ranging from 0 to 5000. The graph depicts a downward trend indicating a decrease in FDG uptake with increasing glucose concentration.]
Effect of Glucose on FDG Uptake by Inflammatory Cells

Counts/Minute

Glucose Concentration (mg/dL)
Chronic Osteomyelitis

FDG-PET is as—or possibly more—accurate than labeled WBC in detecting infection

WBC = white blood cell.
### Performance of FDG-PET in Chronic Osteomyelitis: Result of a Meta-analysis

<table>
<thead>
<tr>
<th>Modality</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDG-PET</td>
<td>96% (95% CI, 88%-99%)</td>
</tr>
<tr>
<td>WBC</td>
<td>61% (95% CI, 43%-76%)</td>
</tr>
<tr>
<td>WBC/BM</td>
<td>78% (95% CI, 72%-83%)</td>
</tr>
<tr>
<td>MRI</td>
<td>84% (95% CI, 69%-92%)</td>
</tr>
</tbody>
</table>

*Termatt et al. J Bone Joint Surg Am 2005; 87:2464-2471*
## Comparison of FDG-PET and Labeled WBC

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDG-PET</td>
<td>93% (13/14)</td>
<td>100% (14/14)</td>
</tr>
<tr>
<td>WBC/BM/B</td>
<td>86% (12/14)</td>
<td>93% (13/14)</td>
</tr>
</tbody>
</table>

WBC/BM/B = leukocyte/bone marrow/bone.
WBC/BM Suggest Soft-Tissue Infection

Tc-99m SC

In-111 Leukocytes

Tc = technetium; SC = sulfur colloid; In = indium.
In this case, FDG-PET showed osteomyelitis, which was confirmed by surgery, demonstrating that PET is more sensitive than WBC imaging in detecting infection.
Comparison of FDG-PET and WBC Imaging

WBC imaging suggested infection.

FDG-PET excluded infection; the pain subsequently diminished without surgery.

MDP = methylene diphosphonate.
Malignant Otitis

Gallium SPECT

FDG-PET
Chronic Osteomyelitis

Sinus Track Connecting Soft-Tissue Abscess With Bone

<table>
<thead>
<tr>
<th>Sagittal FDG-PET</th>
<th>Precontrast SPGR</th>
<th>Postcontrast SPGR</th>
</tr>
</thead>
</table>

SPGR = spoiled gradient.
Chronic Osteomyelitis of the Proximal Tibia

FDG coincidence imaging with a DHC imaging system (sagittal slices) 120 minutes after injection of FDG in a 35 year old patient with COM in the right proximal tibia (A, sagittal view; B, transversal view).
FDG-PET (dual-time protocol 30 minutes and 60 minutes after injection, sagittal slices) in a 63 year old patient with tarsal COM. The extent of the inflammatory uptake and the SUV decreased with time (A, 30 minutes after injection, maximum SUV = 4.22; B, 90 minutes after injection, maximum SUV = 3.58).
FDG-PET images of a patient with COM in the proximal left humerus 90 minutes after injection of FDG (coronal view).
Chronic Osteomyelitis of the Spine
Osteomyelitis of the Lumbo-Sacral Junction

FDG-PET images of a 48 year old patient with osteomyelitis of the ventral lumbosacral junction extending to the soft tissue. (A, sagittal view; B, coronal view).
FDG-PET images (coronal view) of a 62 year old patient with multi-focal osteomyelitis of the spine and soft tissue involvement of the adjacent areas.
FDG-PET in the Diagnosis of Chronic Osteomyelitis

• Highly accurate in both axial and peripheral skeleton
• Excellent bone/soft-tissue differentiation
• Tomographic images allow comparison with modern anatomic methods
Infection of Hip and Knee Arthroplasty
Hip Arthroplasty and Infection

• Infection rate of hip arthroplasty
  - 1%–4% following first-time arthroplasty
  - Approximately 25% after revision arthroplasty

• Detection of infection associated with hip arthroplasty is challenging
  - Establishing accurate diagnosis is unsuccessful in most settings
Hip Arthroplasty and Infection

Non-specific

Infection

Uncomplicated Hip Prosthesis

- 53 year old male
- *Asymptomatic*
- 9 months post arthroplasty
Nonspecific Uptake Is Not Correlated With the Time Interval Postsurgery (Short Term)
Nonspecific Uptake Is Not Correlated With the Time Interval Postsurgery (Short Term)

- 77 years old
- Right hip arthroplasty, summer 1977
- “Feel great.” “Never had pain.”
- FDG-PET: 2001—14 years later!
- SUV = 2.5

SUV = standardized uptake value.
Infection Associated With Hip Prosthesis

Coronal
Aseptic Hip Prosthesis

71 year old patient with left hip prosthesis and left lateral thigh abscess.

Mild FDG uptake in the proximal part of the left hip prosthesis secondary to inflammation.

Increased uptake in the left lateral thigh slightly thickened into the patient's history of abscess in the thigh.
Infection Associated With Hip Prosthesis: WBC/BM Inconclusive
Infection Associated With Hip Prosthesis: FDG-PET

Pathological examination proved periprosthetic infection.
Infection Associated With Hip Prosthesis

62 year old female

Pathological examination proved periprosthetic infection.
Infection Associated With Hip Prosthesis

- 73 year old female
- Status-post right hip arthroplasty, 14 years

Coronal
Skin Fistula

294-298  298-302  302-306  306-310
# PET vs WBC in Painful Hip Prosthesis Arthroplasty: Latest PENN Data

<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>FDG- PET</strong></td>
<td>84.8</td>
<td>92.6</td>
<td>80.0</td>
<td>94.6</td>
<td>90.6</td>
</tr>
<tr>
<td><strong>WBC/BM</strong></td>
<td>35.7</td>
<td>94.3</td>
<td>81.3</td>
<td>97.0</td>
<td>77.6</td>
</tr>
</tbody>
</table>

PPV = positive predictive value; NPV = negative predictive value.

Kwee et al. (2008) meta-analyzed published data on PET for detecting hip and knee prosthesis infection (total 694 prostheses).

Pooled sensitivity and specificity of FDG-PET for the detection of prosthetic hip or knee joint infection were 84.6% (95% CI, 71.0-92.5%) and 84.0% (95% CI, 68.0-92.8%), respectively.
<table>
<thead>
<tr>
<th>Study and Year</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Value</td>
<td>95% CI</td>
</tr>
<tr>
<td>Chryssikos et al. 2008</td>
<td>84.9</td>
<td>69.1-93.4</td>
</tr>
<tr>
<td>Garcia-Barrecheguren et al. 2007</td>
<td>63.6</td>
<td>35.4-84.8</td>
</tr>
<tr>
<td>Pill et al. 2006</td>
<td>95.2</td>
<td>77.3-99.2</td>
</tr>
<tr>
<td>Delank et al. 2006</td>
<td>40.0</td>
<td>11.8-76.9</td>
</tr>
<tr>
<td>Reinartz et al. 2005</td>
<td>93.9</td>
<td>80.4-98.3</td>
</tr>
<tr>
<td>Love et al. 2004</td>
<td>100</td>
<td>86.7-100</td>
</tr>
<tr>
<td></td>
<td>52.0</td>
<td>33.5-70.0</td>
</tr>
<tr>
<td>Stumpe et al. 2004</td>
<td>33.3</td>
<td>12.1-64.6</td>
</tr>
<tr>
<td></td>
<td>22.2</td>
<td>6.3-54.7</td>
</tr>
<tr>
<td>Chacko et al. 2003</td>
<td>91.7</td>
<td>74.2-97.7</td>
</tr>
<tr>
<td>Vanquickenborne et al. 2003</td>
<td>87.5</td>
<td>52.9-97.8</td>
</tr>
<tr>
<td>Manthey et al. 2002</td>
<td>100</td>
<td>51.0-100</td>
</tr>
<tr>
<td>Van Acker et al. 2001</td>
<td>100</td>
<td>61.0-100</td>
</tr>
<tr>
<td>Zhuang et al. 2001</td>
<td>90.5</td>
<td>71.1-97.4</td>
</tr>
<tr>
<td><strong>Pooled estimate</strong></td>
<td><strong>84.6</strong></td>
<td><strong>71.0-92.5</strong></td>
</tr>
</tbody>
</table>
Aseptic Knee Prosthesis

52 year old male

Increased FDG uptake in the anterior compartment of the knee on both femoral and tibial side.

Long term clinical follow up confirms the absence of infection.
Increased FDG uptake in the soft tissue lateral to the left knee prosthesis and at the bone-prosthesis interface.

Intra-operative findings and histopathology confirm the presence of infection.
### Accuracy of FDG Imaging Painful Knee Prostheses Using Full-Ring, Dedicated PET Scanner

<table>
<thead>
<tr>
<th>Author et al</th>
<th>Year</th>
<th>Prostheses (N)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van Acker F</td>
<td>2001</td>
<td>21</td>
<td>100% (6/6)</td>
<td>73.3% (11/15)</td>
<td>81% (17/21)</td>
</tr>
<tr>
<td>Zhuang H</td>
<td>2001</td>
<td>36</td>
<td>90.9% (10/11)</td>
<td>72.0% (18/25)</td>
<td>77.8% (28/36)</td>
</tr>
<tr>
<td>Manthey N</td>
<td>2002</td>
<td>14</td>
<td>100% (1/1)</td>
<td>100% (13/13)</td>
<td>100% (14/14)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>71</strong></td>
<td><strong>94.4% (17/18)</strong></td>
<td><strong>79.2% (42/53)</strong></td>
<td><strong>83.1% (59/71)</strong></td>
</tr>
</tbody>
</table>

**PET in Painful Knee Prosthesis Arthroplasty: Latest PENN Data**

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity (%)</th>
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<th>NPV (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDG- PET</td>
<td>85.7</td>
<td>100.0</td>
<td>100.0</td>
<td>96.7</td>
<td>97.2</td>
</tr>
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</table>

PPV = positive predictive value; NPV = negative predictive value.
FDG-PET/CT Scans: Potential Problem
Diabetic Foot
Increased signal on T2 images in keeping with osteomyelitis.

Interval development of lucency of first digit concerning for osteomyelitis.

70 year old Female. Non-healing ulcer of right great toe. PET, MRI, X-Ray suggest osteomyelitis, which was confirmed by pathology.
Pathology report confirms gangrenous toe with chronic osteomyelitis, abscess formation, inflammatory reaction at the margins of the bone and soft tissue.
Loss of signal on T2 images. No abscess or subjacent osteomyelitis. Diffuse subcutaneous edema in keeping with venous stasis as opposed to cellulitis.

Mild periostitis around proximal phalanx of the third digit: suggestive of osteomyelitis (False Positive).

74 year old diabetic male with an ulcer on the plantar surface of midfoot. Clinical follow-up confirms the absence of osteomyelitis.
PET images consistent with cellulitis of the sole of the right foot.

Clinical Follow-Up: Within one month of scan, ulcer is clean, cellulitis improved on oral antibiotic treatment.
## Comparison of Imaging Modalities in the Diagnosis of Osteomyelitis in the Diabetic Foot: Most Recent PENN Data

<table>
<thead>
<tr>
<th>Modality</th>
<th>n</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDG-PET</td>
<td>98</td>
<td>78%</td>
<td>93%</td>
<td>90%</td>
<td>78%</td>
<td>94%</td>
</tr>
<tr>
<td>MRI</td>
<td>88</td>
<td>95%</td>
<td>78%</td>
<td>82%</td>
<td>56%</td>
<td>98%</td>
</tr>
<tr>
<td>X-Ray</td>
<td>82</td>
<td>57%</td>
<td>85%</td>
<td>78%</td>
<td>57%</td>
<td>85%</td>
</tr>
</tbody>
</table>
60 year old diabetic male

Plantar left 5th metatarsal head region ulcer. Initial clinical impression: osteomyelitis vs. Charcot.

MR images consistent with osteomyelitis of 5th metatarsal head and proximal phalanx. No Charcot. Mild intramuscular edema of midfoot in keeping with diabetic changes.
• PET images consistent with soft tissue infection.
• Oral antibiotics for 10 days during the evaluation period. Wound healed and clean. No cellulitis. (15 days post imaging procedures).

Clinical diagnosis: Charcot.
58 year old female: Charcot
<table>
<thead>
<tr>
<th></th>
<th>SUVmax Range (Mean)</th>
</tr>
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<tbody>
<tr>
<td>Charcot Joint</td>
<td>0.7 – 2.4 (1.3 +/- 0.4)</td>
</tr>
<tr>
<td>Midfoot (Non-Diabetic Subjects)</td>
<td>0.2 – 0.7 (0.42 +/- 0.12)</td>
</tr>
<tr>
<td>Midfoot (Uncomplicated Diabetic Subjects)</td>
<td>0.2 – 0.8 (0.5 +/- 0.16)</td>
</tr>
<tr>
<td>Charcot Joint w/ Osteomyelitis Lesion</td>
<td>6.5 (1 Subject)</td>
</tr>
<tr>
<td>Osteomyelitis Lesion</td>
<td>2.9 – 6.2 (4.38 +/- 1.39)</td>
</tr>
</tbody>
</table>
Differentiating Charcot Osteoarthropathy from Osteomyelitis

Unifactorial ANOVA test yielded a statistical significance in the SUVmax between the four groups (P<0.01).

In the setting of concomitant foot ulcer FDG-PET accurately ruled out osteomyelitis.

Overall sensitivity and accuracy of FDG-PET in the diagnosis of Charcot was 100 and 93.8%, respectively.*

FDG-PET/CT-Based Diagnosis of Osteomyelitis in a Diabetic Foot

- 50-year-old male with nonhealing wound in right forefoot
- ↑ FDG uptake in lateral aspect of forefoot (A&B)
- ↑ FDG uptake to 4th metatarsus (C)
- Normal bone structure (D)

Diagnosis of osteomyelitis confirmed by histopathologic examination of tissue samples obtained at surgery.
FDG-PET/CT in Diabetic Foot

FDG-PET/CT in Diabetic Foot
MRI Positive, PET Negative

Surgical pathology result: no infection.

Other Infections
FDG-PET in Fever of Unknown Origin

• The non specificity of FDG is of great value in evaluating patients with FUO because it accumulates in infections, malignancies and inflammatory diseases, which are the three major causes of FUO.

• Being a “catch-all” tracer, it has the potential to replace 67Ga and labeled leukocyte imaging in this setting.
Fever of Unknown Origin

<table>
<thead>
<tr>
<th>Coronal</th>
<th>Sagittal</th>
<th>Transverse</th>
<th>Chest X-ray Following FDG-PET</th>
</tr>
</thead>
</table>

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Fever of Unknown Origin
Fever of Unknown Origin
Fever of Unknown Origin
### Performance of FDG-PET in Fever of Unknown Origin

<table>
<thead>
<tr>
<th>Study</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meller et al.*</td>
<td>81%</td>
<td>86%</td>
</tr>
<tr>
<td>Bleeker-Rovers et al.</td>
<td>87%</td>
<td>95%</td>
</tr>
<tr>
<td>Stumpe et al.</td>
<td>98%</td>
<td>75%</td>
</tr>
</tbody>
</table>

*Meller et al. reported in this study a sensitivity and specificity of 67% and 78%, respectively, for gallium scanning.*
Infected Vascular Graft
Fungal Infection of Liver and Spleen

10 year old with a history of T cell lymphoblastic lymphoma.

Abnormal PET study demonstrating hypermetabolic liver and spleen foci consistent with the patient's known fungal infection.
MAI Infection

Projected Images

Pretreatment  Posttreatment  Normal

MAI = Mycobacterium avium-intracellulare.
Sarcoidosis

Anterior  Posterior  Right Lateral  Left Lateral

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Degenerative Disease of the Spine
Conclusions

• FDG-PET imaging is highly accurate for evaluation of patients with suspected infection

• FDG-PET is a simple and accurate technique for assessing and managing patients with suspected infection and inflammation in any organ/structure and in any setting

• The cost of performing FDG-PET imaging is substantially less than that of current radiological/nuclear techniques

• Considering these advantages, FDG-PET may completely replace other modalities in these settings
THANK YOU