Nuclear Medicine Infection Imaging: A Musculoskeletal Focus

63rd Annual Meeting SWC-SNMMI
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UT Southwestern Medical Center
Disclosures

• None
Educational Objectives

• List the available radiopharmaceuticals for nuclear medicine infection imaging

• Identify sources of Appropriateness Criteria for Infection Imaging

• Explain the most appropriate exam for a musculoskeletal infection of a diabetic foot that is otherwise uncomplicated

• Interpret the exam findings expected with infection for a patient with a Charcot joint using a dual isotope exam
Outline

• 2017 ACR Appropriateness Criteria for MSK infections (except foot and spine)
• Radiopharmaceuticals for MSK infections with normal biodistribution and illustrative cases and interpretation criteria
• A radionuclide imaging approach in Charcot neuropathic osteoarthropathy (Charcot changes)
• Diabetic Foot Infections
• The road ahead- radiotracers in the pipeline
• SAM Questions
Background: MSK Infections

- **Imaging** plays a **central role in** characterizing ST and bone infections: **location, extent** of involvement and identifying **complications** such as abscesses or sinus tracts. ST infections domain of Anatomic imaging, Nuclear Medicine imaging for complications, e.g. infected fluid

- OM is common clinical problem, incidence as high as 20-50% in DM
  - Direct contiguous spread from ST infection
  - Inoculation after surgery or trauma
  - Hematogenous seeding during bacteremia

- Septic-arthritis/joint infection: Rapidly progressing, debilitating, significant morbidity and mortality, joint pain, swelling and diminished range of motion

- DFI*: Multiple pathogens are usually isolated, Staph aureus is common, amongst the Gr- E. coli is common, MDR is more

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ACR Appropriateness Criteria for Suspected OM, Septic Arthritis or Soft Tissue Infection-2017

- Literature reviewed - 1993-2014
- Search terms not provided
- **Criteria does not cover spine or diabetic foot**
- 42 references included
- Apply the RAND/UCLA Appropriateness Method and Grading of Recommendations Assessment, Development and Evaluation (GRADE)
- Radiopharmaceuticals — $^{67}$Ga not mentioned
- 9 variants of bone and soft-tissue conditions were considered
- RADIOGRAPH is First Exam in almost all circumstances

J Am Coll Radiol 2017; 14:S326-S337
# Rating Scale

<table>
<thead>
<tr>
<th>Rating</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 2, 3</td>
<td>Usually not appropriate</td>
</tr>
<tr>
<td>4, 5, 6</td>
<td>May be appropriate</td>
</tr>
<tr>
<td>7, 8, 9</td>
<td>Usually appropriate</td>
</tr>
</tbody>
</table>
## Variants

<table>
<thead>
<tr>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Suspected OM, SA, or STI*</td>
</tr>
<tr>
<td>2</td>
<td>ST/JA swelling. Suspected STI</td>
</tr>
<tr>
<td>3</td>
<td>ST/JA swelling + puncture wound. Suspected Foreign body; -Radiograph</td>
</tr>
<tr>
<td>4</td>
<td>ST/JA swelling + cellulitis AND skin lesion/injury ulcer etc. <strong>Suspected OM</strong></td>
</tr>
<tr>
<td>5</td>
<td>ST/JA swelling with Hx prior surgery; <strong>Suspected OM or SA</strong></td>
</tr>
<tr>
<td>6</td>
<td>Pain and swelling/cellulitis in site of previous non-arthroplasty hardware. <strong>Suspected OM or SA</strong></td>
</tr>
<tr>
<td>7</td>
<td>Draining sinus (not assoc’d with joint prosthesis); <strong>Suspected OM</strong></td>
</tr>
<tr>
<td>8</td>
<td>Clinical exam suggesting crepitus. <strong>Suspected ST gas.</strong> First Imaging Exam</td>
</tr>
<tr>
<td>9</td>
<td>Initial radiographs showing ST gas in absence of puncture wound</td>
</tr>
</tbody>
</table>

*OM = osteomyelitis; SA = septic arthritis; STI = soft tissue infection
JA = juxta-articular;
### Ratings for Variants involving Nuclear Medicine: Variant 4

**Variant 4. Soft-tissue or juxta-articular swelling with cellulitis and a skin lesion, injury, would, ulcer, or blister. Suspected osteomyelitis. Additional imaging following radiographs**

<table>
<thead>
<tr>
<th>Radiologic Procedure</th>
<th>Rating</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI area of interest without and with IV contrast</td>
<td>9</td>
<td>Radiographs and MRI are both indicated and complementary.</td>
</tr>
<tr>
<td>MRI area of interest without IV contrast</td>
<td>7</td>
<td>This procedure is an alternative to MRI without and with contrast if contrast is contraindicated. Contrast is preferred to aid in soft-tissue evaluation</td>
</tr>
<tr>
<td>CT area of interest with IV contrast</td>
<td>7</td>
<td>This procedure is an alternative if MRI is contraindicated</td>
</tr>
<tr>
<td>Labeled leukocyte scan (In-111 or Tc-99m) and Tc99m sulfur colloid marrow scan area of interest</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Tc-99m three-phase bone scan and labeled leukocyte scan (In-111 or Tc-99m) area of interest</td>
<td>6</td>
<td>SPECT improves sensitivity</td>
</tr>
<tr>
<td>CT area of interest without IV contrast</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Tc-99m three-phase bone scan area of interest</td>
<td>5</td>
<td>SPECT improves sensitivity</td>
</tr>
<tr>
<td>FDG-PET/CT area of interest</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>CT area of interest without and with IV contrast</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>US area of interest</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Labeled leukocyte scan (In-111 or Tc-99m) area of interest</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Tc-99m three-phase bone scan and labeled leukocyte scan (In-111 or Tc-99m) and Tc-99m sulfur colloid marrow scan area of interest</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
## Ratings for Variants involving Nuclear Medicine: Variant 5

**Variant 5.** Soft-tissue or juxta-articular swelling with a history of prior surgery. Suspected osteomyelitis or septic arthritis. Additional imaging following radiographs.

<table>
<thead>
<tr>
<th>Radiologic Procedure</th>
<th>Rating</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspiration area of interest</td>
<td>9</td>
<td>This procedure is recommended if there is concern for septic arthritis.</td>
</tr>
<tr>
<td>MRI area of interest without and with IV contrast</td>
<td>9</td>
<td>This procedure is recommended for evaluation of osteomyelitis and extent of infection. It may be complementary to aspiration for evaluation of septic arthritis. Contrast is preferred if not contraindicated.</td>
</tr>
<tr>
<td>MRI area of interest without IV contrast</td>
<td>7</td>
<td>This procedure is recommended for evaluation of osteomyelitis and extent of infection. It may be complementary to aspiration for evaluation of septic arthritis. Contrast is preferred if not contraindicated.</td>
</tr>
<tr>
<td>CT area of interest with IV contrast</td>
<td>6</td>
<td>This procedure may be helpful if MRI is contraindicated or extensive MRI artifact from metal is present.</td>
</tr>
<tr>
<td>CT area of interest without IV contrast</td>
<td>5</td>
<td>This procedure may be helpful if MRI is contraindicated or extensive MRI artifact from metal is present.</td>
</tr>
<tr>
<td>Labeled leukocyte scan (In-111 or Tc-99m) and Tc-99m sulfur colloid marrow scan area of interest</td>
<td>5</td>
<td>This procedure may be appropriate but there was disagreement among panel members on the appropriateness rating as defined by the panel’s median rating.</td>
</tr>
<tr>
<td>Labeled leukocyte scan (In-111 or Tc-99m) area of interest</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Tc-99m three-phase bone scan and labeled leukocyte scan (In-111 or Tc-99m) area of interest</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>CT area of interest without and with IV contrast</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>US area of interest</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Tc-99m three-phase bone scan area of interest</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Tc-99m three-phase bone scan and labeled leukocyte scan (In-111 or Tc-99m) and Tc-99m sulfur colloid marrow scan area of interest</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>FDG-PET/CT area of interest</td>
<td>1</td>
<td>This is promising new technology but data are limited.</td>
</tr>
<tr>
<td>Radiologic Procedure</td>
<td>Rating</td>
<td>Comments</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------------------</td>
<td>--------</td>
<td>----------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Aspiration area of interest</td>
<td>9</td>
<td>This procedure is recommended if there is concern for septic arthritis.</td>
</tr>
<tr>
<td>MRI area of interest without and with IV contrast</td>
<td>9</td>
<td>This procedure is recommended for evaluation of osteomyelitis and extent of infection. It may be</td>
</tr>
<tr>
<td></td>
<td></td>
<td>complementary to aspiration for evaluation of septic arthritis.</td>
</tr>
<tr>
<td>MRI area of interest without IV contrast</td>
<td>8</td>
<td>This procedure is an alternative to MRI without and with contrast if contrast is contraindicated.</td>
</tr>
<tr>
<td>CT area of interest with IV contrast</td>
<td>7</td>
<td>This procedure is an alternative if MRI is contraindicated or extensive MRI artifact from metal is</td>
</tr>
<tr>
<td></td>
<td></td>
<td>present.</td>
</tr>
<tr>
<td>Labeled leukocyte scan (In-111 or Tc-99m) and Tc-99m sulfur colloid marrow scan area</td>
<td>7</td>
<td>This procedure is an alternative to CT and MRI if extensive hardware is present.</td>
</tr>
<tr>
<td>of interest</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT area of interest without IV contrast</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Labeled leukocyte scan (In-111 or Tc-99m) area of interest</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Tc-99m three-phase bone scan area of interest</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Tc-99m three-phase bone scan and labeled leukocyte scan (In-111 or Tc-99m) area of</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>interest</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FDG-PET/CT area of interest</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>CT area of interest without and with IV contrast</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>US area of interest</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Tc-99m three-phase bone scan and labeled leukocyte scan (In-111 or Tc-99m) and</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Tc-99m sulfur colloid marrow scan area of interest</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Radiopharmaceuticals

- $^{99m}\text{Tc}$ radiolabeled diphosphonates (MDP/HDP)
- Radiolabeled WBCs- $^{111}\text{In}$, $^{99m}\text{Tc}$
- $^{99m}\text{Tc}$ colloid
- $^{67}\text{Ga}$ citrate
- $^{18}\text{F}$-FDG
- Radiolabeled amino acid and sugar analogues
  - Future directions
99mTc radiolabeled Diphosphonates (MDP/HDP): Uptake

• Changes of bone scan with age
  – Decreasing epiphyseal plate activity

• Chemistry and structure
  – Structurally similar to phosphate containing compounds that bind Hydroxyapatite (HA)

• Bone Retention
  – Blood flow dependent, high first pass extraction
  – Binds to ACP and HA

• Best for osteoblastic activity, limited for osteolytic lesions

• High sensitivity without specificity

• Use in “uncomplicated” bone; fractures etc. lower specificity
### $^{99m}$Tc-MDP/HDP Cellulitis vs Osteomyelitis

<table>
<thead>
<tr>
<th>Phase</th>
<th>Cellulitis (soft tissue infection)</th>
<th>Osteomyelitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flow</td>
<td>Increased</td>
<td>Increased</td>
</tr>
<tr>
<td>Blood Pool/Tissue</td>
<td>Increased</td>
<td>Increased</td>
</tr>
<tr>
<td>Delay</td>
<td>Normal</td>
<td>Increased</td>
</tr>
</tbody>
</table>
73 y/o F with T2DM and right foot redness and swelling. No hx of Trauma: Cellulitis vs Osteomyelitis
3-Phase Bone Scan of the Feet: Cellulitis with OM in the First MTP region
Case: Patient with painful swelling of the foot. No history of trauma.
$^{67}$Ga Citrate: Uptake Mechanism

- Iron mimetic
- Binds to transferrin in circulation
  - Complex binds to transferrin receptors on WBCs
- Increased flow and vascular membrane permeability results in increased delivery of plasma proteins at inflammatory/infectious sites
- Binds to lactoferrin at the infection/inflammatory site
  - Complex is internalized into WBCs
- Bacterial uptake
  - Some uptake by nonspecific binding and facilitated diffusion
  - **Binds to siderophores**
    - Small molecule chelators produced by micro-organisms

67Ga Clinical Applications in Infection Imaging

- Used in infection imaging for four decades
- Largely limited now to spinal infections
- Sarcoidosis/suspected sarcoidosis
- Malignant otitis externa
- Skull base osteomyelitis
- Infection imaging in immunocompromised patients
- Fever of unknown origin
$^{67}$Ga Normal Biodistribution

56 year old female with history of discitis/osteomyelitis. A) Planar, B) Axial,C) Coronal, D) Sagittal Ga-67 with SPECT/CT demonstrating markedly abnormal increased gallium uptake at the L3-L4 disc space with continuous extension into the left psoas muscle consistent with worsening Discitis/Osteomyelitis with paravertebral/psoas abscess.

SPECT/CT allows accurate differentiation between disk space infection, psoas infection, or both, or false gallium uptake in healing bone would not be possible with out SPECT CT. Abnormal signal on MR usually cannot be well differentiated from normal healing infection and can take numerous months to resolve after therapy.

E) Sagittal STIR Lumbar Spine MR shows increased signal suggestive of Discitis/Osteomyelitis.
67Ga-Imaging in Spinal Osteomyelitis: Is a companion bone scan needed?

Interpretation of scans: A. Ga only scan: focal intense uptake centered on disc space but overlapping bone. + for osteomyelitis with disciitis. SPECT may negate need for Bone Scan

**Healing phase maybe problematic** B. Dual tracer approach with 99mTc-M/HDP: Compare spatial and intensity. Improves specificity
Summary Statistics for $^{67}$Ga based Infection Imaging

• Compared to Disphosphonates, $^{67}$Ga scan identifies soft tissue involvement

• With SPECT or SPECT/CT may not need to use bone scan to enhance specificity (J Nucl Med 2016;57:1406-1412)

• Applications in the spine maybe/are being replaced by FDG-PET/CT (Clin Radiol 2016; 71:632)
\textbf{\textsuperscript{111}In-WBCs Normal Biodistribution}

- \textsuperscript{111}In-WBCs-
  - Low photon flux limits image quality
  - Spleen, liver, bone marrow
    - Lack of bowel activity is a strength
  - Labeling method gets both granulocytes and lymphocytes
    - Contrast with 99mTc-WBC which focus mostly on granulocytes
    - Better chance of imaging chronic lymphocyte driven infections

- Temporal distribution 1-4h vs 24h
  - 1-4h: Lung trafficking
  - 24h: Spleen, liver, bone marrow
Case: 57y/o male with Suspected OM in Spine
$^{111}\text{In-WBC WB Scan in Patient with Suspected Graft Infection}$
Axial SPECT/CT
Sagittal and Coronal SPECT-CT
99mTc-WBC Normal Biodistribution

- 99mTc-WBCs-
  - Early Images
    - Lungs
    - Bone marrow, liver and spleen, bladder
  - Late images (24h)
    - Bowel
    - Bladder

- Comparison w 111In-WBC
  - Faster uptake of leukocytes in sites of infection, permitting earlier imaging
  - Can give higher activity
  - Lower absorbed dose
# State of the Art $^{99m}$Tc-WBC scan Imaging: Time Decay Corrected Acquisition

DOI 10.1007/s00259-013-2631-4

## Table 4 Diagnostic performance of qualitative (visual) analysis of $^{99m}$Tc-HMPAO-WBC scintigraphy images in relation to the final diagnosis

<table>
<thead>
<tr>
<th></th>
<th>Osteomyelitis</th>
<th>Hip prosthesis</th>
<th>Knee prosthesis</th>
<th>Soft tissue</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FT DTC</td>
<td>FT DTC</td>
<td>FT DTC</td>
<td>FT DTC</td>
<td>FT DTC</td>
</tr>
<tr>
<td>True positive (n)</td>
<td>23 11</td>
<td>7 14</td>
<td>15 14</td>
<td>7 9</td>
<td>55 48</td>
</tr>
<tr>
<td>True negative (n)</td>
<td>23 20</td>
<td>10 29</td>
<td>8 25</td>
<td>1 5</td>
<td>42 79</td>
</tr>
<tr>
<td>False positive (n)</td>
<td>2 0</td>
<td>1 0</td>
<td>2 0</td>
<td>0 0</td>
<td>5 0</td>
</tr>
<tr>
<td>False negative (n)</td>
<td>1 0</td>
<td>1 1</td>
<td>1 1</td>
<td>0 1</td>
<td>3 3</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>96 100</td>
<td>87 93</td>
<td>94 93</td>
<td>100 90</td>
<td>95 94</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>92 100</td>
<td>91 100</td>
<td>80 100*</td>
<td>100 100</td>
<td>89 100*</td>
</tr>
<tr>
<td>Accuracy (%)</td>
<td>94 100</td>
<td>89 98</td>
<td>88 98*</td>
<td>100 93</td>
<td>92 98*</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>92 100</td>
<td>87 100</td>
<td>88 100*</td>
<td>100 100</td>
<td>92 100*</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>96 100</td>
<td>90 93</td>
<td>89 93</td>
<td>100 83</td>
<td>93 96</td>
</tr>
</tbody>
</table>

*p < 0.05 versus FT  
^a Includes three patients with a shoulder prosthesis
State of the Art \(^{99m}\)Tc-WBC scan Imaging: Time Decay Corrected Acquisition

Original article

**Utility of 8 h and time decay-corrected acquisition scintigraphy with in-vitro labeled white blood cells for the diagnosis of osteoarticular infection**

Edel Noriega-Álvarez, Guillermo A. Martínez Pimienta, Ana M. Benítez Segura, María T. Bajén Lázaro, Alba Rodríguez-Gasén, Julio Rodríguez-Rubio Corona and Jaime Mora-Salvadó

Goal: Distinguish inflammation from Infection

Gold standard: The final diagnosis was confirmed by culture and/or biopsy in 47 patients and by clinical follow-up of at least 6 months in the remaining 47 patients.
## Summary Statistics

<table>
<thead>
<tr>
<th>Reading Protocol</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy (%)</th>
<th>K-values Inter-observer Variat’n</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (30min, 4h images)</td>
<td>92</td>
<td>50</td>
<td>41</td>
<td>94</td>
<td>62</td>
<td>0.79</td>
</tr>
<tr>
<td>2 (30 min, 4h)</td>
<td>93</td>
<td></td>
<td>97</td>
<td></td>
<td>99</td>
<td>0.77</td>
</tr>
</tbody>
</table>

Conclusion: TDCA acquisition of WBCS at 8 h (1-day protocol) enables a faster diagnosis than 24 h acquisition. The use of TDCA with the same pixel intensity in all images enables an accurate diagnostic of osteoarticular infection, with a considerable interobserver agreement for all protocols.
$^{18}$F-Fludeoxyglucose (FDG) in MSK Infections

• Uptake mediated by glucose transporters
• Increased uptake in infection is presumably due to increased number and metabolic rates of neutrophils, macrophages and leukocytes in the inflammatory/infection region
• Increased affinity of the transporters for FDG in inflammation secondary to activation by cytokines
• FDG, as a small molecule, enters poorly perfused areas rapidly
• Uptake after trauma or surgery normalizes after 3-4 months
FDG in Infection Imaging

• Useful in OM (Sensitivities ~95%, specificities 75-99%)
• Very useful in spinal OM, considered to be an adjunct to MR (radionuclide exam of choice, Clin Radiol 71: 632, 2016)
• Role in DFO and prosthesis imaging remains unclear
  — “After nearly 10 years of investigation, the role of FDG-PET and PET/CT for this indication is yet to be established.” (Semin Nucl Med 43:367, 2013)
  — “Data on the accuracy of $^{18}$F-FDG for diagnosing diabetic pedal osteomyelitis and prosthetic joint infection are contradictory and its role for these indications remains to be determined” (Clin Radiol 71: 632, 2016)
• Reimbursement for FDG infection imaging is challenging to non-existent
FDG-PET/CT as an adjunct to MR in OM+Discitis Diagnosis

**Figure 6** Spinal osteomyelitis. There is decreased signal in the L4 vertebral endplate (arrow) on the T1 image. There is increased signal in this vertebra and in the intervertebral disc (arrows) on the T1 FSE image. Considerations included degenerative changes versus osteomyelitis. FDG PET/CT demonstrates increased activity in the L4 vertebra, which on the fused image can be seen extending into the intervertebral disc (arrow). Bone biopsy confirmed osteomyelitis/discitis. FDG-PET PET/CT is a useful adjunct to MRI for differentiating degenerative changes from infection in the spine.

Dual Isotope ($^{111}$In-WBC and $^{99m}$Tc-colloid) Applications

• Prosthetic joint infection imaging
  — “Best available imaging test for diagnosing prosthetic joint infection at the present time”
  — Overall Accuracy ~90% with most studies over 30 years showing high sensitivity as well (World J Radiol 2014; 6:446-58)

• Non-prosthetic joint orthopedic hardware infection
  — “Combined WBC/marrow imaging is the radionuclide imaging test of choice for diagnosing “complicating” osteomyelitis, including orthopedic hardware infection” (Clin Radiol 71: 632, 2016)
Dual Tracer Prosthetic Joint Imaging

Infected Femoral component

Congruence

In-WBC

Bone marrow

Aseptic Loosening

Incongruence

Infection Imaging in the Foot Complicated by Charcot Changes
Charcot Neuropathic Osteoarthropathy

- **Charcot arthropathy**, also known as Charcot foot and ankle, is a syndrome in patients who have neuropathy or loss of sensation for many reasons.
- Exact mechanism is unknown, but two theories of pathophysiology are neurotraumatic and neurovascular.
- It includes fractures and dislocations of bones and joints that occur with minimal or no known trauma.
- Diabetes is a common but not sole cause
  - Hindfoot, Midfoot, Hindfoot/Midfoot junction most common

http://www.aofas.org/footcare/md/conditions/diabetic-foot/Pages/Charcot-Arthropathy.aspx

Charcot Neuropathic Osteoarthropathy: Not infected on MR

Joint space loss; Lateral subluxation
Marrow Versus Infection in the Charcot Joint: Indium-111 Leukocyte and Technetium-99m Sulfur Colloid Scintigraphy

Christopher J. Palestro, Harendra H. Mehta, Mahendra Patel, Susan J. Freeman, William N. Harrington, Maria B. Tomas and Scott E. Marwin

*Long Island Jewish Medical Center, New Hyde Park; and Westchester County Medical Center, Valhalla, New York*
Study Design and Results

• N= 17 Patients
• $^{111}$In-WBC accumulation in Charcot changes seen on radiographs
• Subsequent $^{99m}$Tc-Sulfur Colloid scans or 3 phase bone scans
• Criteria:
  – Presence of labeled WBCs more intense than marrow or bone scan
  – Spatially incongruent distribution of the two tracers
• Results
  – Labeled WBCs did accumulate in areas of marrow expansion
  – Leukocyte/marrow studies + for OM in 4/20 Charcot joints
  – None of Charcot joints w/o WBC accumulation showed OM

Biopsy Tissue from WBC accumulation site

Hematopoietically active marrow

New bone

Osteoblasts

Osteoclasts

Congruent Uptake

Incongruent Uptake

Dual Isotope Dual Modality SPECT/CT imaging using $^{111}$In-WBCs and $^{99m}$Tc-Sulfur Colloid: Pathophysiology and Image Interpretation

• Leukocytes physiologically accumulate in bone marrow (axial skeleton, proximal humeri and femora).

• Areas of bone marrow hyperplasia and expansion (e.g. neuropathic joint) produce altered uptake of leukocytes. In these situations, bone marrow may be also be found in the soft tissues surrounding bone posing difficulties in image interpretation.

• $^{99m}$Tc bone marrow sulfur colloid imaging is useful to map the physiologic marrow activity and with the help of SPECT/CT localization, abnormal activity can help differentiate infection from marrow activity.

• Both WBC’s and Sulfur Colloid accumulate in bone marrow but in the presence of osteomyelitis, only WBC’s accumulate/accumulate more in the site of active infection.

• Therefore, a discordant focus of increased $^{111}$In-WBCs with absence of $^{99m}$Tc labeled sulfur colloid is consistent with infection.

• SPECT/CT helps with localization, delineation of extent and severity of the discordant focus of infection and guides biopsy/therapy.
55 yo M with Charcot Neuropathy with left foot infection

A,B) 111In-WBC coronal and sagittal planar images demonstrate diffuse increased WBC accumulation in the left ankle. There is a small focus of increased WBC activity in the expected location of the left 1st toe.

C,D) 99mTc-Sulfur Colloid coronal and sagittal planar images shows concordant diffuse activity throughout the left ankle consistent with Charcot changes. These is no concordant activity in the left big toe.

SPECT/CT was performed for localization
55 yo M with Charcot Neuropathy with left foot infection

Dual Isotope 111In-WBC/99mTc Sulfur Colloid SPECT/CT imaging

A, B) Fused $^{111}$InWBC SPECT/CT demonstrates destructive changes throughout the left ankle with increased WBC activity. Focal WBC accumulation is localized to a small ulcer with increased WBC activity and erosion the terminal tuft.

C, D) $^{99m}$Tc Sulfur Colloid SPECT/CT shows concordant activity throughout the destructive Charcot changes in the left ankle. There is no marrow activity in the left toe.

Findings are consistent with Charcot changes in hindfoot and osteomyelitis of the distal left 1st phalange.
DIABETIC FOOT INFECTIONS
Background

- Global prevalence of DM >300 million by 2025
- Estimated 25% pts will develop foot ulcer and >50% ulcers are clinically infected at presentation; 20-50% involve bone
- Diabetic Foot Infection leading to osteomyelitis increases the risk of lower extremity amputation and is associated with high morbidity
- OM usually results from direct local spread of infection
- Poor healing of cut or other injury, often trivial, secondary microvascular and/or large vessel disease
- Neuropathy often contributes to patient being unaware of the injury
Background (cont’d)

• Osteomyelitis of the foot in diabetes is common and frequently undiagnosed.

• Diagnosis should be clinical and based on signs of infection, the size of the lesion, and the visibility of bone in the first instance but supported by the results of radiologic examination.

• The gold standard for diagnosis is histologic and microbiological examination of bone, which is not possible or necessary in all patients.
Risk for Amputation

- Persons with infections were 24.5x more likely to undergo amputation
  
  -(11.3 vs. 0.5%, p = 0.0001, RR = 24.5)

- Persons with osteomyelitis were 6.0x more likely to undergo amputation than were soft tissue infections
  
  -(32.3 vs. 5.4%, p = 0.0001, RR = 6.0)

IDSA Guidelines on OM Diagnosis

- Consider osteomyelitis potential for any infected, deep, or large foot ulcer especially if chronic or overlies a bony prominence (strong recommendation, moderate evidence)

- Most definitive way to diagnose DFO is by combined findings on bone culture and histology (strong, moderate)

- Consider using serial plain radiographs to diagnose or monitor suspected DFO (weak, low)

- MRI is recommended as diagnostic imaging test (strong, moderate). If MRI unavailable/contraindicated, consider a radiolabeled leukocyte or antigranulocyte scan, preferably combined with a bone scan

- Suggest Probe-to-Bone test for any DFI with open wound. When properly conducted and interpreted, it can help to diagnose (when the likelihood is high) or exclude (when the likelihood is low) DFO (strong, moderate)
Probe-to-Bone Assessment for Osteomyelitis

- Widely used
- Limb-threatening infections
- No inter-/intra-observer validity (κ)
- High versus low-prevalence population

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
<th>+PV</th>
<th>-PV</th>
<th>Osteo Preval</th>
</tr>
</thead>
<tbody>
<tr>
<td>66%</td>
<td>85%</td>
<td>89%</td>
<td>56%</td>
<td>66%</td>
</tr>
<tr>
<td>87%</td>
<td>91%</td>
<td>57%</td>
<td></td>
<td>98%</td>
</tr>
<tr>
<td>38%</td>
<td>91%</td>
<td>53%</td>
<td>85%</td>
<td>20%</td>
</tr>
</tbody>
</table>

*Grayson, JAMA 1995, Lavery Diabetes Care 2007, Shone Diabetes Care 2006*
### Diagnostics Summary - 2008 Meta-analysis

<table>
<thead>
<tr>
<th>Diagnostic modality</th>
<th>Total patients</th>
<th>Sensitivity</th>
<th>P value</th>
<th>Specificity</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probe-to-bone test or exposed bone</td>
<td>288</td>
<td>0.60 (0.46-0.73)</td>
<td>&lt;.001</td>
<td>0.91 (0.86-0.94)</td>
<td>.11</td>
</tr>
<tr>
<td>Radiography</td>
<td>170</td>
<td>0.64 (0.44-0.83)</td>
<td>&lt;.001</td>
<td>0.69 (0.53-0.80)</td>
<td>.01</td>
</tr>
<tr>
<td>MRI</td>
<td>135</td>
<td>0.90 (0.82-0.95)</td>
<td>&lt;.001</td>
<td>0.79 (0.62-0.91)</td>
<td>.41</td>
</tr>
<tr>
<td>Bone scan</td>
<td>185</td>
<td>0.81 (0.73-0.87)</td>
<td>&lt;.001</td>
<td>0.28 (0.17-0.42)</td>
<td>.01</td>
</tr>
<tr>
<td>Leukocyte scan</td>
<td>269</td>
<td>0.74 (0.67-0.80)</td>
<td>&lt;.001</td>
<td>0.68 (0.57-0.78)</td>
<td>.61</td>
</tr>
</tbody>
</table>

Paucity of SPECT/CT imaging data

Diabetic Foot Infection: Benefits of Hybrid Imaging

- High resolution “diagnostic-quality” CT with high-specificity SPECT of $^{99m}$Tc labeled white blood cells ($^{99m}$Tc WBC SPECT/CT), to allow for both precise localization and extent of DFI.

- $^{99m}$Tc has good energy characteristics for gamma imaging and short 6 hour half life which allows for administration of higher activities and one day imaging.

- SPECT/CT shows delineates cortex of bone with higher spatial resolution (from CT) than MRI which aids in the diagnosis by identify cortical erosion seen in osteomyelitis.

- $^{99m}$Tc WBC SPECT/CT targets a more specific pathophysiology than MRI which shows only edema and hyperemia seen in many entities other than osteomyelitis.
62 yo M with Diabetes and ESRD on Hemodyalisis admitted with a left foot abscess. A,B) Indium 111 labeled WBC Planar images show discordant focus of increased activity in the left mid foot. C,D) 99mTc Sulfur Colloid show diffuse activity through out both mid and hind feet likely related to evolving Charcot changes E) Axial and Sagittal Indium WBC SPECT/CT localized activity to abscess in the plantar aspect of the Left mid foot. Osteomyelitis was excluded.
Indexing Severity of Diabetic Foot Infection With $^{99m}Tc$-WBC SPECT/CT Hybrid Imaging

RESEARCH DESIGN AND METHODS—Masked retrospective $^{99m}Tc$-white blood cell (WBC) single photon emission CT (SPECT)/CT image interpretation and independent chart review of 77 patients (101 feet) suspected of DF1-associated osteomyelitis at a large municipal hospital between January 2007 and July 2009. CSI scores were correlated with probability of favorable outcome (no subsequent amputation/readmission after therapeutic intervention) during median 342-day follow-up.

William A. Erdman, MD
Ji Buethe, MD
Rafia Bhore, PhD
Hans K. Ghayee, DO
Chiarra Thompson, MD

Param Maewal, MD
Jon Anderson, PhD
Steve Klemow, MD
Orhan K. Oz, MD, PhD

Diabetes Care 35:1826–1831, 2012
Composite Severity Index: A more comprehensive view of DFI

OUTCOMES:
CSI performance better than traditional binary read of osteomyelitis vs. no osteomyelitis
Prognostic Utility: CSI correlated with outcome (amputation or readmission as poor outcomes) and predict efficacy of duration of antibiotic therapy

Table 1 — CSI staging system for diabetic foot infection

<table>
<thead>
<tr>
<th>Intensity (WBC activity relative to blood vessels)</th>
<th>Stage (WBC focus proximity to cortex, cortical erosion, marrow involvement)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0, WBC activity below blood vessel activity</td>
<td>0, WBC epicenter in soft tissue only, does not extend to the cortex of the bone</td>
</tr>
<tr>
<td>1, focal WBC activity equal to blood vessel activity</td>
<td>I, epicenter extends to the cortex but does not cause cortical erosion on CT</td>
</tr>
<tr>
<td>2, moderate focal increase above blood vessel activity</td>
<td>II, epicenter extends to the cortex of the bone and causes cortical erosion on CT</td>
</tr>
<tr>
<td>3, intense focal increase above blood vessel activity</td>
<td>III, epicenter extends through the cortex of the bone and into the marrow space with erosion of cortical bone on CT</td>
</tr>
</tbody>
</table>

Number of lesions (if two or more, intensity and stage scores are summed)

CSI: overall severity of infection in a foot based on multiplicity of lesions, stage, and intensity
\textbf{99mTc-WBC SPECT/CT} can be used to follow up patients with osteomyelitis at clinical intervals to determine endpoint of therapy.

46 year old diabetic male with diabetic foot infection. (A) Initial 99mTc WBC SPECT/CT demonstrated osteomyelitis of the 2\textsuperscript{nd} metatarsal head with additional involvement of the 2\textsuperscript{nd} proximal phalanx. (B,C) Sequential SPECT/CT scans at 2 month clinical intervals showed improvement of osteomyelitis followed by resolution of infection after prolonged antibiotic therapy. This allowed physicians to determine when it was the proper time to stop antibiotic therapy.
$^{99m}$Tc-WBC SPECT/CT vs. MR
$^{99m}\text{Tc-WBC SPECT/CT vs MR: Introduction}$

- MRI is the recommended diagnostic imaging test for diabetic foot osteomyelitis (DFO).
- The recognized gold standard for diagnosing osteomyelitis in the clinical infectious diseases literature is the presence of abnormal bone culture or histopathology findings from bone biopsy studies.
- Bone biopsy is invasive and subject to sampling errors
- How does $^{99m}\text{Tc-WBC SPECT/CT}$ compare with MR in diagnosis for biopsy proven OM?
99mTc labeled WBC SPECT/CT is Not Inferior to MRI for Diagnosis of Biopsy Proven Diabetic Foot Osteomyelitis

K Bhavan, K Lam, FJ Lazaga, L Lavery, J LaFontaine, OK Oz, W Erdman
RSNA 12/2013 Chicago, IL

- **Purpose**: To assess the accuracy of hybrid image 99mTc-WBC SPECT/CT for diagnosis of DFO as determined by bone biopsy results in comparison to MRI.

- **Methods**: Retrospective chart review of 71 patients who underwent 99mTc-WBC SPECT/CT and bone biopsy between 2011 -2013 to confirm the diagnosis of DFO. 25/71 pts had MRI in addition to SPECT/CT. Pts whose scan(s) was not within a clinically relevant timeframe of biopsy (8 weeks) were excluded
## Results

<table>
<thead>
<tr>
<th></th>
<th>SPECT/CT</th>
<th>MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>43/71</td>
<td>15/25 (25/71 MR&amp;SPECT/CT)</td>
</tr>
<tr>
<td>Sens</td>
<td>0.91</td>
<td>0.67</td>
</tr>
<tr>
<td>Spec</td>
<td>0.25</td>
<td>0.67</td>
</tr>
<tr>
<td>PPV</td>
<td>0.84</td>
<td>0.89</td>
</tr>
<tr>
<td>NPV</td>
<td>0.4</td>
<td>0.33</td>
</tr>
<tr>
<td>Accuracy</td>
<td>0.79</td>
<td>0.67</td>
</tr>
</tbody>
</table>

9 Biopsied within 8wks, in 3/9 MR and SPECT discordant, 2/3 SPECT correct, 1/3 MR correct
Positive Case of Osteomyelitis on both MRI & WBC SPECT/CT Imaging

61-year-old diabetic male with right heel ulcer on MR (A) Proton Density Fat Saturation coronal and (B) STIR saggital images showing increased amount of sclerotic bone with nonspecific increased signal involving greater than 60% of the calcaneus and sparing the anterior structures. (C) Tc 99m WBC SPECT/CT imaging confirms the presence of osteomyelitis as noted by accumulation of radiolabelled WBCs in the right calcaneus along with bone destruction.

Increased Marrow Signal on MRI cannot differentiate whether it represents acute or chronic versus healing infection in the short interval after therapy setting. Intense Focal WBC activity on SPECT/CT demonstrates an active physiologic neutrophilic response to active infection.
False Positive Case of Osteomyelitis on Radiographs and MRI confirmed by 99mTc WBC SPECT/CT Imaging and Subsequent Biopsy

73 year old female with uncontrolled diabetes complicated by neuropathy status post left 2\textsuperscript{nd} toe amputation 2 months prior with infection at the amputation site.

A) Radiograph of the left foot shows subtle cortical discontinuity at the 2\textsuperscript{nd} metatarsal amputation site likely related to osteomyelitis.  
B) Axial STIR MR of the left foot demonstrated subcutaneous edema with faint nonspecific increased signal at the 2\textsuperscript{nd} metatarsal amputation site suggestive of marrow edema from osteomyelitis.  
C) Axial 99mTc WBC SPECT/CT shows diffuse edema with no focal WBC activity at the amputation site excluding osteomyelitis which was confirmed on subsequent biopsy.

In this case, radiographs and MRI were read as positive for osteomyelitis. 99mTc SPECT/CT was more accurate. Non specific marrow edema and cortical bone changes were probably related to post-surgical changes and healing.
Summary: Preliminary Study of $^{99m}$Tc-WBC SPECT/CT vs MRI in DFO

• Our preliminary data suggests that SPECT/CT is not inferior to MRI in the diagnosis of diabetic foot osteomyelitis though sample size is small and it is retrospective study

• Furthermore $^{99m}$Tc-WBC SPECT/CT results correlated well with the bone biopsy results

• $^{99m}$Tc-WBC SPECT/CT maybe suitable substitute for guiding biopsy

• A potential advantage of $^{99m}$Tc-WBC SPECT-CT then is prognostic for severity and determination of endpoint of therapy for which MRI has limited value

• Head-to-head prospective clinical trial is on-going: $^{99m}$Tc-WBC SPECT/CT vs MR for diagnosis of DFO and as imaging biomarker for therapy response in patients with Bone Bx at the time of initial imaging and imaging after standard of care therapy
Detection of Osteomyelitis in the Diabetic Foot by Imaging Techniques: A Systematic Review and Meta-analysis Comparing MRI, White Blood Cell Scintigraphy, and FDG-PET

Medline and Embase searched for studies of diagnostic tests on patient known or suspected to have diabetes and a foot infection

6,649 articles found

Preferred reference standard was bone biopsy and subsequent pathological/microbiological exam

For the analysis reported in this study 29 studies included in the analysis
Summary of DFO Meta-analysis

<table>
<thead>
<tr>
<th>Test</th>
<th>Sens (%)</th>
<th>Spec (%)</th>
<th>DOR</th>
<th>+LR</th>
<th>-LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{18}$F-FDG-PET</td>
<td>89</td>
<td>92</td>
<td>95</td>
<td>11</td>
<td>0.11</td>
</tr>
<tr>
<td>$^{111}$In-WBC</td>
<td>92</td>
<td>75</td>
<td>34</td>
<td>3.6</td>
<td>0.1</td>
</tr>
<tr>
<td>$^{99}$mTc-WBC</td>
<td>91</td>
<td>92</td>
<td>118</td>
<td>12</td>
<td>0.1</td>
</tr>
<tr>
<td>MRI</td>
<td>93</td>
<td>75</td>
<td>37</td>
<td>3.66</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Author’s Conclusions: FDG-PET and $^{99}$mTc-WBC scintigraphy offer the highest specificity. Larger prospective studies with direct comparison among the different imaging techniques are required.
## Summary Radiopharmaceuticals and MSK Infection Imaging

### Infection Imaging Radiopharmaceuticals

<table>
<thead>
<tr>
<th>Radiopharmaceutical and Administered Activity</th>
<th>Time of Imaging</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Common Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>111In white blood cells</strong>&lt;br&gt;300-500 µCi (10-18.5 MBq)<strong>&lt;sup&gt;1&lt;/sup&gt;</strong>&lt;br&gt;We use higher activity**</td>
<td>12-24 hr</td>
<td>No interfering bowel/renal activity&lt;br&gt;Delayed imaging possible&lt;br&gt;Simultaneous 99mTc-sulfur colloid or 99mTc-disphosphonate bone imaging possible</td>
<td>Less sensitivity for nonbacterial and non-pyogenic infections&lt;br&gt;111In label not ideal for imaging&lt;br&gt;Complex preparation</td>
<td>Bacterial infections&lt;br&gt;Indolent inflammatory conditions: e.g., prosthetic joint infections&lt;br&gt;Abdominal infections&lt;br&gt;Prosthetic vascular graft infections&lt;br&gt;Complicated osteomyelitis&lt;br&gt;Extremity infections: e.g., diabetic foot&lt;br&gt;Renal infections&lt;br&gt;FUO: acute phase</td>
</tr>
<tr>
<td><strong>99mTc-white blood cells</strong>&lt;br&gt;5-10 mCi (185-370 MBq)<strong>&lt;sup&gt;2&lt;/sup&gt;</strong>&lt;br&gt;We use higher activity**</td>
<td>0.5-4.0 hr&lt;br&gt;24 hr</td>
<td>Early imaging&lt;br&gt;Excellent early sensitivity&lt;br&gt;99mTc label ideal for imaging</td>
<td>Less sensitivity for nonbacterial and non-pyogenic infections&lt;br&gt;Delayed imaging not ideal&lt;br&gt;Early renal and bladder activity&lt;br&gt;Bowel activity after 1-2 hr&lt;br&gt;Complex preparation</td>
<td>Bacterial infections&lt;br&gt;Acute inflammatory conditions: e.g., inflammatory bowel disease&lt;br&gt;Complicated osteomyelitis&lt;br&gt;Extremity infections: diabetic foot&lt;br&gt;Osteomyelitis&lt;br&gt;Prosthetic vascular graft infections</td>
</tr>
<tr>
<td><strong>67Ga-citrate</strong>&lt;br&gt;5-10 mCi (185-370 MBq)<strong>&lt;sup&gt;3&lt;/sup&gt;</strong>&lt;br&gt;We use higher activity**</td>
<td>24-28 hr</td>
<td>A variety of infections detected, including opportunistic</td>
<td>Interfering bowel and renal activity&lt;br&gt;Delayed imaging necessary&lt;br&gt;67Ga not ideal for imaging</td>
<td>Immunocompromised patients&lt;br&gt;Uncomplicated osteomyelitis&lt;br&gt;Chronic infections&lt;br&gt;Diskitis/spinal osteomyelitis&lt;br&gt;FUO: chronic phase</td>
</tr>
<tr>
<td><strong>18F-FDG PET/CT</strong>&lt;br&gt;10 mCi (370 MBq)<strong>&lt;sup&gt;4&lt;/sup&gt;</strong>&lt;br&gt;We use higher activity**</td>
<td>1-2 hr</td>
<td>Excellent spatial localization&lt;br&gt;Very sensitive</td>
<td>Not currently FDA approved for infections; Not reimbursed&lt;br&gt;Nonspecific; also localizes in tumors&lt;br&gt;None but evolving evidence for “Suspected Spine Infection and FUO”</td>
<td></td>
</tr>
</tbody>
</table>

---

<sup>1</sup> After Mettler 6th edition Table 12-1
The Road Ahead: Pathogen Specific Bacterial Nuclear Medicine Imaging

- Bacterial specific metabolism
  - Amino acids- C-11 labeled D-AAs
  - Unique sugars: Sorbitol, Maltotriose
  - Enzymes: $^{124}$I-FIAU substrate for bacterial specific thymidine kinase
- $^{111}$In-biotin (Clin Nuc Med 2010; 35:12-17)
- $^{68}$Ga-citrate PET (J Nucl Med 2010; 51:1932-6)
- Radiolabeled antibiotics (been around for awhile but yet to pan out)
$^{124}\text{I}-\text{FIAU}$ Imaging of Infection

Figure 1 $^{124}\text{I}-\text{FIAU}$ signal in established infections as imaged by PET/CT. Fused PET and CT images, taken at 2 hours after radiotracer administration, are shown for the following cases: (A) septic arthritis (right knee), (B) septic arthritis (right knee), (C) osteomyelitis (left distal tibia), (D) cellulitis (left lower extremity), (E) necrotizing septic arthritis (left knee). Reprinted with permission by the Public Library of Science from Diaz et al.26

\( ^{18}\text{F}-\text{FDG} \) in Gram- Myositis vs Sterile Inflammation in Preclinical Model

Note that FDG accumulates in both aseptic inflammation and Gr- myositis

Semin Nucl Med 2017; 48:182–194
\textsuperscript{11}C-D-Met for Identifying Live Bacteria

- Note that C-11-D-Met accumulates in only live bacterial sites
- Note that %ID/cc is low

\textbf{Figure 4} In vivo studies using \textsuperscript{11}C-D-Met in a murine myositis model. Representative images show marked uptake in areas corresponding to live bacterial injection (left deltoid), in contrast to sterile inflammation (right deltoid) and normal muscle. The site of live bacterial inoculation is denoted by a red arrow, whereas the site of \textsuperscript{10}X heat-killed bacterial inoculation is denoted by a white arrow. Reprinted with permission by Springer Nature from Neumann et al.\textsuperscript{53}

\textbf{Semin Nucl Med 2017; 48:182–194}
Acknowlegements

- William Erdman, MD
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- Nuclear Medicine Technologists, Parkland Memorial Hospital
- Department of Radiology CTO
- ADA and Pak Foundation for funding
- Sania Khan (this presentation)
Question #1

1. Regarding the microbiome of diabetic foot infections?

A. *Staphylococcus aureus* is commonly found
B. Infections are most commonly mono-microbial
C. Among the Gram negative micro-organisms *Pseudomonas aeruginosa* is the most common
D. There are fewer multi-drug resistant organisms than in other soft tissue infections

Question #2

2. Charcot neuropathy may affect many joints and can be caused a variety of neurological insults. In patients with diabetes the region most commonly involved is?

A. the wrist
B. the knee
C. Calcaneus
D. Hindfoot/Midfoot
Question #3

3. Ga-67 uptake in infection

A. is facilitated by ferric ions
B. is facilitated by binding to circulating transferrin
C. is facilitated by binding to metal chelators, produced by WBCs, known as siderophores
D. is facilitated by potassium
Question #4

4. In the detection of osteomyelitis by imaging techniques applied to the diabetic foot,

A. Sensitivity varies by more than 10% between MRI, FDG-PET, and WBCs labeled with In-111 oxine and Tc-99m HMPAO
B. Specificity is greatest for MRI
C. FDG-PET and Tc-99m WBC seem to have similar specificity
D. Specificity in In-111 WBC scans is greater than specificity in Tc-99m WBC scans
Question #5

5. Which of the following is best for distinguishing marrow from infection in the Charcot joint?

A. Three phase bone scan  
B. Dual tracer imaging with radiolabeled WBCs and bone scan  
C. Dual tracer imaging with radiolabeled WBCs and Ga-67  
D. Dual tracer imaging with radiolabeled WBCs and Tc-99m sulfur colloid marrow scintigraphy