IAEA Regional Training Course on Hybrid Imaging

SPECT/CT Imaging of the Diabetic Foot

Giuliano Mariani
Regional Center of Nuclear Medicine, University of Pisa Medical School, Pisa, Italy

Vilnius, August 27 – 31, 2012
Clinical/Pathophysiologic Background

- 15%-20% of diabetic subjects develop a lower limb ulcer in their lifetime.
- 85% of lower limb amputations in diabetics are preceded by an ulcer.
- 40%-50% of the diabetic patients who have undergone an amputation go on to have amputations in the other limb within 5 years.
- Two or more risk factors generally concur to the development of a foot ulcer in diabetic patients:
  - 25%-30% of the ulcers are neuropathic;
  - 30%-35% of the ulcers are ischemic;
  - 35%-40 of the ulcers have mixed etiology.
- Vascular or ischemic foot is caused by peripheral artery disease (PAD), a major factor in the evolution of the ulcer.
- Neuropathic foot is caused by diabetic neuropathy with sensory and/or motor impairment.
- Other conditions causing atherosclerotic lesions: obesity, hyperlipidemia, hypertension, smoking, hereditary factors associated with diabetes.
Vascular, or Ischemic Foot

Normal

Diabetic risk

Blood vessel damage in the feet may cause tissue damage
Poor circulation in the foot causes sores, infections and cuts difficult to heal because of reduced blood supply carrying vital elements (e.g., oxygen) that the body tissues need for healing.

**Symptoms:**

- Claudication (a dull cramping pain in the calf muscle that comes on after walking a certain distance – it is relieved by rest).
- Numbness or tingling in the foot or toes.
- Discoloration of the skin, that can become pale, bluish, or reddish (depending on, e.g., body posture).
- Changes in skin temperature (the foot becomes cooler).
- Skin breaks, infections, and sores do not heal easily.
Vascular, or Ischemic Foot
Diabetic Foot Infection

**Acute diabetic foot infection**
- Cellulitis and abscess, wet gangrene (or infection with gas-forming microorganisms), and necrotizing fasciitis.
- Inflammatory infiltrate with neutrophils, and edema.
- Vascular congestion with thrombosis of small vessels.
- Within days bone necrosis can occur caused by ischemia due to infection of peripheral tissues.

**Chronic diabetic foot infection**
- Involvement of soft tissues only (cellulitis and phlegmon).
- Involvement of deeper tissues and bone (osteomyelitis).
- Cells of the chronic phase of inflammation.
- Reactive healing phase with osteoclasts’ activation, fibroblasts proliferation, formation of new bone, demarcation of the necrotic bone, fragmentation of reactive bone, and formation of fistulas reaching the skin surface.
- Bone sites most frequently affected: metatarsal heads and joint capsules.
Diagnosis of Diabetic Foot Infection

• Based on X-ray, MRI, radionuclide imaging, and bone biopsy with microbiologic culture (1-4).

• Radiolabeled leukocytes scintigraphy is the nuclear medicine technique of choice to diagnose infection and define involvement of soft tissues and/or osteomyelitis.

• $^{99m}$Tc-HMPAO-WBC scintigraphy in 42 patients with diabetes and a total of 56 foot ulcers showed 88.4% sensitivity and 96.6% specificity (5).

• Three-phase bone scintigraphy and $[^{18}F]$FDG PET/CT have lower diagnostic accuracy (6).

(1) Tan PL. Br J Radiology, 2007; 80: 939-948.
Diabetic Foot Infection

Ulcer

Normal skin

Ulceration
Diabetic Foot Infection
Diabetic Foot Infection
Planar $^{99m}$Tc-HMPAO-WBC scintigraphy in 42-yr old diabetic woman with suspected osteomyelitis of right toe: spot images at 30 min (upper panel) and at 6 hr p.i. (bottom panel). Focus of labeled leukocyte uptake increasing over time indicating infection (but no clear localization).
Planar and SPECT/CT $^{99m}$Tc-HMPAO-WBC imaging in 57-yr old diabetic woman with suspected osteomyelitis of right foot: focus of increased labeled leukocytes uptake in the hindfoot. SPECT/CT images (right panel) 20 hrs p.i. allow to localize the leukocytes accumulation in calcaneal region, consistent with bone infection.
Neuropathic foot (Charcot’s foot)

- Progressive degenerative condition affecting joints in the feet.
- It is associated with nerve damage (neuropathy) that decreases the ability to sense stimuli (including pain) and decreases muscle reflexes that control movement.
- Joints in the feet therefore undergo repeated trauma and injury causing progressive damage to ligaments, cartilage, and bones.
- Nerve damage causes muscle weakness (motor neuropathy) and slack ligaments, resulting in joint instability and subsequent subluxation and/or dislocation.
- Subluxation initiates the process of degenerative joint disease (arthropathy).
- Misaligned bones grind against each other and fragments of bone and cartilage enter the joint and often produce a coarse grating sound (audible crepitus) when moving the joint.
Charcot’s foot

• Some people with neuropathy have no symptoms at all.
• In other patients, numbness, tingling, or pain in the feet is often the first symptom.
• Both pain and numbness are often experienced.
• Symptoms are often minor at first; since most nerve damage occurs over several years, mild cases may go unnoticed for a long time.
• Complications of Charcot’s foot include calluses and ulcers, which occur when bony protrusions (high pressure areas) rub inside the shoes and may become infected.
• Differential diagnosis between neuro-arthropatry and acute osteomyelitis is extremely important in a Charcot’s foot.
Charcot’s foot)
Diagnosis of Charcot’s foot

• Based on X-ray, MRI (repeated every 2-3 weeks to monitor the disease), bone scintigraphy, radiolabeled leukocyte scan (to exclude osteomyelitis), and bone biopsy (1).

• Radiolabeled leukocytes do not accumulate in uninfected neuropathic joints, but hemopoietically active bone marrow can be present in some cases.

• Dual tracer scintigraphy (WBC/colloids) can distinguish WBC accumulation due to active bone marrow from infection (2-3).

• A combination of MRI, labeled leukocyte scintigraphy (with SPECT/CT), $^{18}$F]FDG PET/CT and PET/MRI seem to be the best noninvasive approach to diagnosis.

Charcot’s foot)
Charcot’s foot)

STIR image showing neuropathic change of the midfoot with misalignment of the talar-navicular joint and marked bone marrow edema secondary to neuropathic disease.

Destruction of the cuneiform bones, the metatarsal bases, and parts of the cuboid and talus, with excessive scar formation and edema.
Planar $^{99m}$Tc-MDP bone scan, showing increased uptake in the right talar neck and distal tibia.
Charcot’s foot)

SPECT/CT with $^{99m}$Tc-MDP shows markedly increased extremely uptake at the right talus, navicular and talo-navicular joint.
58-yr old diabetic woman with prior amputations in left foot (3rd and 4th metatarsal bones); non-healing ulcer in left foot. Charcot’s foot and/or osteomyelitis? MRI cannot be performed because of an implanted spinal cord stimulator.

X-ray: signs of prior bone amputations.

Three-phase $^{99m}$Tc-MDP scan: increased blood pool activity (A) and increased bone turnover in late scan (B). Nonspecific signs of inflammation: infection or non-infection?
$^{99m}$Tc-HMPAO-leukocyte SPECT/CT (at 20 hr): mild labeled WBC accumulation in soft tissues without bone involvement, consistent with inflammation without bone infection.
55-yr old diabetic man with prior several amputations in both feet; non-healing ulcer in left foot, positive for *Pseudomonas aeruginosa*. Infection limited to soft tissues only or osteomyelitis?

Planar $^{99m}$Tc-HMPAO-leukocyte scan: accumulation of labeled leukocytes in left foot increasing with time until 20 hr post-injection, consistent with infection (as in osteomyelitis). In left groin, we can see another spot of leukocytes accumulation in 20h scan (C), which may be reactive lymph nodes.
$^{99m}$Tc-HMPAO-leukocyte SPECT/CT: focal accumulation involving both the soft tissues and the 2$^{rd}$ metatarsal bone (soft tissue infection and concomitant osteomyelitis).
$^{99m}$Tc-HMPAO-leukocyte SPECT/CT with 3D fusion Volume Rendering
Diabetic Foot Infection

$^{99m}$Tc-HMPAO-Leukocyte scan concordant with $[^{18}$F]$FDG$ PET/CT in patient with osteomyelitis.

Discordant $^{99m}$Tc-HMPAO-WBC scan and $[^{18}$F$]FDG$ PET/CT in patient with osteomyelitis.

Diabetic Foot Infection

99mTc-HMPAO-Leukocyte scan concordant with [18F]FDG PET/CT in patient with unconfirmed osteomyelitis.
• [^{18}F]FDG PET/CT had low diagnostic accuracy in patients with suspected diabetic foot infection.
• No useful SUV_{max} differentiating soft-tissue infection from osteomyelitis could be defined.
• Combining visual assessment of PET and CT images was more useful.
• Dual-time acquisition was not helpful for the diagnosis.
• Labeled leukocyte scintigraphy currently remains the gold standard imaging technique in patients with suspected diabetic foot infection.


“The data on the role of PET and PET/CT in the evaluation of diabetic foot infections are limited. What is the verdict for [^{18}F]FDG and diabetic foot infections? The jury is still out.”

(Palestro CJ. J Nucl Med 2011; 52:1009-1011)
Indexing Severity of Diabetic Foot Infection With $^{99m}$Tc-White Blood Cell Single Photon Emission Computed Tomography/Computed Tomography Hybrid Imaging

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 Ahead of Print, published online June 20, 2012