Diabetic Foot. Diagnostic and follow-up imaging techniques.

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Learning objectives

- To describe the findings, utility and limitations of the different imaging techniques, in the diagnosis and follow-up of the different pathologies associated with diabetic foot.

- To describe the role of Nuclear Imaging in the differential diagnosis between osteomyelitis and neuroarthropathy.
Background

Diabetes mellitus is a multi-systemic disease that is associated with significant complications affecting multiple organs being a very common cause of cardiovascular disease, end-stage renal disease, and lower extremity non-traumatic amputations. As the prevalence of diabetes increases, a number of important complications affecting the muscles, spine, and feet are being seen more frequently [1].

Vasculopathy, neuropathy and an altered immune response are the three major pathological processes that lead to the development of diabetes-related foot complications [2,3,14]. Costs arising from interventions to prevent and treat ulcers, from amputation, and from postoperative care are compounded by the economic effects of lost productivity, disability, and premature mortality [1].

Motor and sensory neuropathies combine to alter biomechanics and proprioception, with resultant skin breakdown. Skin ulceration provides an entry portal for soft-tissue and bone infections. Anhidrosis due to autonomic neuropathy produces dry skin that is vulnerable to callus formation and cracking, which contribute to skin ulceration [1]. Also, the distribution of peripheral atherosclerosis in patients with diabetes is often more distal than in patients without diabetes. Diabetic patients often show involvement of the arteries below the knee, especially the tibial and peroneal arteries. It is frequently more symmetric and multisegmental and stenoses can be seen even in the collateral vessels [4].

We will describe the main manifestations of the diabetic foot and the role of MRI in the diagnosis of its most important complications: osteomyelitis and neuroarthropathy.

We describe the use of Nuclear Imaging techniques in problematic cases regarding this pathology.
Imaging findings OR Procedure details

1. Skin and soft-tissues lesions:

Patients with diabetes are particularly susceptible to these type lesions and these can serve as point of entry for infections.

**Ulcers** tend to occur in the anatomic sites that are subjected to the highest contact pressures: at the plantar aspect of the first metatarsophalangeal joint and fifth metatarsal head and at the tip of the distal phalanx of the great toe. Hindfoot ulceration is less common than ulceration in the forefoot and predictably occurs at the heel. Midfoot ulcers are rare in the absence of neuropathic osteoarthropathy and occur beneath the cuboid bone [1, 5, 7]. Large (>2 cm) and deep (>3 mm) ulcers are more likely to be associated with infections of the underlying bone [1]. Ulcers typically appear as focal skin interruptions with elevated margins and associated soft tissue defects (Fig 1, 2). In MRI ulcers are detected as hyperintense areas on T2-weighted images, with intense peripheral enhancement on T1-weighted images, a finding indicative of granulation tissue at the base of the ulcer (Fig 3) [5, 14].

**Cellulitis** represents an acute infection of the dermis and subcutaneous tissues that results in pain, erythema, edema, and warmth. Focal or diffuse soft tissue swelling, which appears as increased opacity within the infected tissue, can be detected using conventional radiography (CR) (Fig 4) [2]. Computed Tomography (CT) demonstrates skin thickening, septation of the subcutaneous fat, and thickening of the underlying fascia [6], as well as homogeneous enhancement after the administration of contrast material.

At MR imaging, skin thickening and edema are seen in both soft-tissue edema and cellulitis, and reticulation of fat is more prominent, with intermediate signal intensity on T1-weighted images and high signal intensity on T2-weighted images. Contrast enhancement is a distinguishing feature of cellulitis and is not seen in diabetes related edema or neuropathic disease [5, 14] (Fig 5). Conventional radiography and CT are useful in gas detection, a finding that may be present in necrotizing infections or caused by gas producer germs (Fig 6).
Fig. 6: Soft tissue gas. Plain film demonstrating soft tissue bubbles of gas in the second toe (arrow), narrowing of the second, third and fourth metatarsophalangeal joints spaces and focal desmineralization of the third metatarsal head secondary to osteomyelitis.

**References:** Radiology, Hospital Clinico San Carlos - Madrid/ES

**Abscesses** often present as a well-demarcated fluid collection with a peripheral pseudocapsule showing rim enhancement on CT [6]. On MRI, contrast enhancement along the wall of the fluid collection and a higher T2 signal intensity are highly suggestive of an abscess (Fig 7). If a sinus tract is present, an ulcer may extend to the level of the adjacent osseous prominence. On contrast-enhanced images, sinus tracts display a "tram-track" pattern of enhancement (Fig 8) [5, 14].

Foreign bodies may be seen in diabetic patients with sensory neuropathy or after surgery. On MRI usually has low signal intensity on both T1- and T2-weighted MR images, and blooming artifact may be seen on gradient-echo images [5]. Conventional radiography and CT are also useful in their identification.

**Septic tenosynovitis** commonly occurs in the peroneal tendons from a lateral malleolus ulcer and in the Achilles tendon from a calcaneal ulcer. In the forefoot, nearly two-
Thirds of all tendon infections involve the flexor tendons and are a result of plantar forefoot ulceration [5]. Tendon thickening, hyperintensity on T2-weighted images, and enhancement may indicate infection, but these findings are nonspecific; they also may be seen with other inflammatory, neoplastic or posttraumatic conditions (Fig 9) [5].

**Fig. 9:** Spectrum of tendon involvement in three different diabetic patients. (A) Sagittal T2-weighted fat suppresed image showing fluid in the tendon sheath of the flexor of the great toe (arrow). (B) Sagittal T1-weighted image showing tendon thickening (arrow). (C) Axial postcontrast T1-weighted image showing peripheral enhancement of the flexor tendons and rim-enhancing abscesses (arrow).

**References:** Radiology, Hospital Clinico San Carlos - Madrid/ES

**2. Bone lesions:**

The early and accurate differentiation of osteomyelitis from neuroarthropathy in the diabetic foot has the potential to help reduce the incidence of infection-related morbidities, the need and duration of hospitalization and the incidence of major limb amputation [7]. In addition, it is very important to determine infected from noninfected acute neuroarthropathy because the therapeutic approach will vary. Although bone biopsy is
still considered the gold standard, MRI is currently considered the modality of choice in the evaluation of bone marrow changes in the diabetic foot when osteomyelitis is suspected.

**Osteomyelitis** develops, almost exclusively, by the contiguous spread of infection from skin ulceration at predictable sites, whereas neuroarthropathy is primarily articular [5]. The most common locations are the heads of the metatarsals, phalanges and calcaneus, although any bone can be affected [14] (Fig 10).

The MRI-based diagnosis of osteomyelitis hinges on the identification of abnormal bone marrow signal, typified by hypointensity on T1-weighted images and hyperintensity on fluid-sensitive images (T2-weighted, STIR). Although T2-weighted images are considered the most sensitive, it is the abnormal T1-weighted signal that is more indicative of osteomyelitis because the loss of fatty marrow signal represents infiltration of the bone by the infectious process. The associated appearance of hypointense periosteum separated by a hyperintense layer (representing fluid or pus) from the underlying bone is also strongly supportive of osteomyelitis. Gadolinium-enhanced T1-weighted images demonstrate enhancement of the abnormal bone marrow (Fig 10, 11, 12) [7, 14].
**Fig. 12**: Calcaneous osteomyelitis in MRI. Sagittal postcontrast T1-weighted fat suppressed image showing bone marrow enhancement of the calcaneous with intraosseous abscess (arrow) in a patient with osteomyelitis.

**References**: Radiology, Hospital Clinico San Carlos - Madrid/ES

Signs supporting the diagnosis of osteomyelitis are the presence of ulcers, fistulas and abscesses next to the affected bone [14]. The isolated T2 signal abnormality even in the presence of marrow enhancement, suggests reactive bone marrow edema secondary of infection and noninfective entities (as postsurgical changes and artrophathy) [5, 7].

**Neuropathic osteoarthropathy** usually presents in patients who have had diabetes more than 10 years and have developed symmetric distal neuropathy [7]. Is an aggressive, deforming arthritis results from a combination of repetitive microtrauma and macrotrauma to the articular surfaces, peripheral neuropathy and ischemia with poor healing leads to joint instability, dislocation and resultant deformity [15]. The most often affected joint is the tarsometatarsal or Lisfranc joint [14, 15]. Other joints may be involved including the talonavicular, subtalar and intertarsal joints [8].

The MRI findings in the acute or active stage of neuroarthropathy (AOA) are the most confounding for osteomyelitis. These include soft tissue edema, joint effusions, fluid collections, and periarticular soft tissue enhancement [5, 7, 14].

In the early phase of the acute stage, conventional radiology appears normal, but the MRI shows subchondral bone marrow edema with or without microfracture. The more advanced stage of the acute hyperemic Charcot neuroarthropathy is characterized by edema and swelling of soft tissues and muscles, and edema of bone marrow, without definite bone destruction [8]. The bone marrow edema typically is not restricted to one or two bones, yet is seen in the entire area of pathology, thus the entire midfoot. Bone marrow edema and its enhancement are typically centered in the subchondral bone, suggesting the relation to joint disease (Fig 13) [8, 14].

The chronic or inactive stage is typified by a deformed foot and little bone marrow edema, with the classic constellation of destruction, debris, disorganization, dislocation and sclerosis (Fig 14, 15, 16).
Fig. 14: Charcot’s neuroarthropathy. Osteoporosis, erosions and bone destruction on midfoot and second and third metatarsal heads and periostal reaction in the first metatarsal bone.

References: Radiology, Hospital Clinico San Carlos - Madrid/ES

In an uncomplicated neuropathic joint at chronic stage, the bone marrow is typically hypointense on all sequences, compatible with sclerosis, and any abnormal hyperintensity in the bone marrow or cortex should raise suspicion for superimposed infection or recent fractures related to the neuropathy (Fig 17) [7]. Acute neuropathic arthropathy may be superimposed on the chronic form of disease reflecting more recent injury or possibly more acute instability [15].

Due to the clinical importance of differentiating infected arthropathy of the uninfected, several signs have been described in MRI. The presences of fistulas, abnormal subcutaneous fat and thick wall enhancement joint, indicate superimposed infection. However, the preservation of subcutaneous fat, the presence of subchondral cysts and intraarticular bodies indicate arthropathy without infection [5, 8, 14].

3. Role of Nuclear Medicine:
Three-phase bone scintigraphy with delayed 24-hours imaging is a very sensitive test but is not specific for osteomyelitis of the foot; however, improvement in diagnostic accuracy was obtained when it was supplemented with leukocyte-labeled scintigraphy. These modalities used conventional planar imaging, which posed a limitation in identifying the precise site of osteomyelitis or even determining whether or not an infection is within bone or soft tissues, owing to their relatively low spatial resolution and lack of anatomic specificity.

The SPECT/CT imaging protocol of the foot is a non-invasive and effective technique that combines various important pathophysiologic SPECT data derived from bone scintigraphic, leukocyte-labeled scintigraphy and bone marrow scintigraphy, with CT to accurately diagnose foot infection in addition to exact registration of these functional images with distinct anatomic landmarks [9]. SPECT/CT represent a potential tool for differentiating between bone and soft-tissue involvement and by more precisely defining the extent of the disease, especially in osseous structures of the mid and hindfoot (Fig 18, 19, 20) [10, 11]. Their limitations lie in the availability and the accuracy for the evaluation of small anatomical structures such as forefoot bones.
Fig. 19: Osteomyelitis of third and fourth left metatarsal bases. Planar image showing focally increased activity in left tarsal bones. On the axial, coronal and sagittal SPECT/TC images the labeled leukocyte activity clearly extends into the bone.

References: Radiology, Hospital Clinico San Carlos - Madrid/ES

18F-FDG, a nonspecific indicator of increased intracellular glucose metabolism, accumulates in sites of active malignancy as well as in infectious and inflammatory processes. The PET component identified FDG-avid foci in sites of acute infection which were precisely localized on fused PET/CT images allowing correct differentiation between osteomyelitis and soft-tissue infection [12]. Quantification of radiotracer activity using maximum SUV may potentially help to differentiate areas of infection from those of inflammation. The SUV max in the Charcot's lesions is lower than of osteomyelitis supporting the role of FDG-PET in the setting of Charcot neuroarthropathy where this mechanism is superior to other modalities in making such distinction [13]. However, given the fact that the reproducibility of SUV measurements between different institutions is suboptimal and the patient population varies from each institution, a single SUV alone is not sufficient for diagnosis.

4. Diagnostic algorithm: (Fig 21)

The initial screening modality is a radiograph of the foot in three directions (dorsoplantar, lateral and oblique). Both feet should be studied, to detect and compare metabolic disturbances and subtle changes [8]. The development of classic radiographic features of osteomyelitis, may lag behind the clinical manifestations by 10-20 days, and radiography is relatively insensitive to small amounts of bone destruction [1]. Although patients may present early in the acute active phase with normal radiograph, in Charcot neuroosteoarthropathy an advanced early stage can be diagnosed on a radiograph [8].

We considerer that the radiographs provide important anatomical information and It can be used as a control exam for further follow-up given its wide availability and low-cost realization.

The second step in analyzing the diabetic foot is MRI. A minimum of two planes should be acquired. For the forefoot and metatarsal, coronal images should be included. For flexed or deformed toes, sagittal images are very useful. Axial images provide excellent visualization of the bones of the midfoot. Sagittal images are optimal for evaluation of deformities of the plantar arch [15]. The first consideration should be the geographic distribution of pathology. A midfoot, subchondral and periarticular distribution of findings in the absence of a contiguous focus of skin disruption, most commonly at the Lisfranc or Chopart joints, would strongly support neuroarthropathy. But a forefoot focus of abnormal bone marrow away from the subchondral surface and adjacent to a skin ulcer, abscess or sinus tract would be indicative of osteomyelitis [7]. In cases of chronic osteoneuroarthropathy the parameters of bone marrow abnormality have been correlated with acute onset of infection include diffuse bone marrow abnormality, progressive
subarticular enhancement, loss of subchondral cysts and the presence of the MRI "ghost sign." [7]

The benefit of MRI in diabetic foot lies in its ability to detect early changes in the bone marrow signal, delineating the precise extension of pathology with higher sensitivity and specificity than the remaining diagnostic modalities [7].

SPECT/TC is indicated in cases with doubtful findings of bone involvement in MRI or problematic cases of infection superimposed to neuroarthropathy or degenerative changes.
Fig. 1: Skin ulcer. Lateral radiograph showing a subcutaneous ulcer on the hindfoot (arrow).

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Fig. 2: Skin ulcer. Lateral radiograph showing a focal skin interruption and a soft tissues defect secondary to an ulcer on the heel (arrow).

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**Fig. 3:** Heel ulcer and calcaneal osteomyelitis. MRI from the same patient as Fig 1. (A) Sagittal T1-weighted image and (B) T2-weighted fat-suppressed image showing bone marrow edema underlying a skin ulcer. (C) T1-weighted image with fat suppression showing enhancement of bone marrow, findings indicative of osteomyelitis. Hyperintense area on (B) with intense enhancement on (C) at the base of the ulcer indicate the presence of granulation tissue (arrow).

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**Fig. 4:** Cellulitis. Plain film (dorsoplantar view) demonstrating increase opacity and diffuse soft tissue swelling in a patient with cellulitis. Forefoot amputation.

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Fig. 5: Cellulitis in MRI. (A) Axial T1-weighted image showing skin thickening and fat reticulation in the dorsal midfoot and (B) Axial contrast enhanced T1-weighted fat suppressed image showing the characteristic enhancement of cellulitis (long arrows). Skin ulcer (solid arrows) is closely related with fifth metatarsal bone.

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Fig. 7: Soft tissue abscess in MRI. (A) Coronal T2-weighted image showing increased signal intensity (arrow) representing a localized fluid collection. (B) Coronal T1-weighted and (C) contrast enhanced T1-weighted fat suppressed images demonstrating enhancement of the abscess wall. (B) Low signal intensity in adjacent bone marrow of the cuboid (red star) and base of the fourth metatarsal with increased signal intensity on (A) and enhancement on (C) consistent with osteomyelitis.

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**Fig. 8:** Sinus track in MRI. Axial contrast enhanced T1-weighted fat suppressed image showing "tram-track" pattern (arrow).

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Fig. 10: Osteomyelitis as result of directly spreading cutaneous infection from the same patient as in Fig 8. (A) Axial T1-weighted image showing loss of normal T1 signal of the bone marrow on first metatarsal head with corresponding signal hyperintensity in the T2-weighted fat suppresed image (B) and enhancement in postcontrast T1-weighted fat suppresed image (C). Abscess closely related with the first metatarsal (red star). (B) and (C) images demonstrating diffuse high signal intensity in soft tissues and enhancement consistent with cellulitis.

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Fig. 11: Osteomyelitis in the midfoot in MRI. (A) Coronal T1-weighted image, (B) T2-weighted fat suppressed image and (C) postcontrast T1-weighted image. Concordant T1 hypointensity and T2 hyperintensity of the cuboid and the base of fourth metatarsal with corresponding enhancement (arrows) consistent with osteomyelitis.

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Fig. 13: Neuropathic osteoarthropathy. (A) Coronal T1-weighted image and (B) postcontrast T1-weighted image showing loss of the normal bone marrow signal and enhancement of the subchondral bone, fragmentation and subluxation of the entire midfoot and metatarsals heads.

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Fig. 15: Chronic neuroarthropathy in two different patients. (A) Space narrowing and disorganization of intertarsal and tarsometatarsal joints of left foot. (B) Plain radiography demonstrating joint space narrowing, osteophyte formation and sclerosis of the third metatarsophalangeal joint (arrow). Surgical changes of the fourth and fifth metatarsal.

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**Fig. 16:** Chronic diabetic neuroarthropathy in MRI in two different patients. (A) Sagittal T1-weighted image showing subluxation of metatarsophalangeal joint (arrow). (B) Coronal T1-weighted image from the same patient as on fig 15B with joint space narrowing and osteophyte (arrow) on the third metatarsophalangeal joint.

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**Fig. 17:** Neuroarthropathy with superimposed osteomyelitis in MRI. (A) Sagittal T1-weighted image demonstrating joint space narrowing at the tibiotalar joint, subchondral bone resorption at calcaneous and bone fragmentation. (B) Sagittal STIR image and (C) fat suppressed postcontrast T1 image showing bone marrow edema with enhancement, and rim-enhancing abscesses throughout the soft tissues of the ankle (arrow), probably related with superimposed infection.

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Fig. 18: Soft tissues infection. Planar image showing focally increased activity in right forefoot. On the axial, coronal and sagittal SPECT/TC images show labeled leukocyte activity on plantar soft tissues and unclear activity into fourth metatarsal head.

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**Fig. 20:** Osteomyelitis of metatarsal heads. Planar image showing focally increased activity in left forefoot. On axial, coronal and sagittal SPECT/TC images the labeled leukocyte activity clearly extends into the bone.

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Fig. 21: Diagnostic algorithm

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Conclusion

MRI is an useful imaging technique for evaluating infection and neuroarthropathy. SPECT-CT and PET/CT could be an useful complementary test to rule out superimposed infection.

Suspicion of diabetic foot complications requires the completion of imaging protocols for early diagnosis and avoiding complications and unnecessary cost.
References


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