Review article

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Emerging role of bone scintigraphy single-photon emission computed tomography/computed tomography in foot pain management

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Foot and ankle joints being weight-bearing joints are commonly subjected to wear and tear and are prone to traumatic and other pathologies. Most of these foot and ankle pathologies present with pain. The diagnosis of pathology and localization of pain generators is difficult owing to the complex anatomy of the foot and similar clinical presentation. This makes the management of foot pain clinically challenging. Conventional anatomical imaging modalities are commonly employed for evaluation of any anatomical defect; however, these modalities often fail to describe the functional significance of the anatomical lesions, especially in presence of multiple lesions which is common in ankle and foot; however, hybrid single-photon emission computed tomography/computed tomography (SPECT/CT) by virtue of its dual modalities, that is, highly sensitive functional imaging and highly specific anatomical imaging can serve as a problem-solving tool in patient management. This review attempts to describe the role of hybrid SPECT/CT in overcoming the limitation of conventional imaging and describes its potential application in the management of foot and ankle pain. *Nucl Med Commun* 44: 571–584

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Introduction

Human foot is a very strong structure, developed to bear the weight of the entire body and support the bipedal stance. This makes it prone to damage and injury, so foot pain is one of the common clinical problems. Structurally foot is very complex. It consists of 26 bones, 33 joints with 20 joints actively articulating, 3 arches, and more than 100 muscles, tendons, and ligaments compactly packed. This often makes it exceptionally difficult to accurately identify the true pain generator clinically [1–3].

The common causes of foot pain include posttraumatic injuries (acute bone fracture, tendon rupture, ligament sprain/tear, stress fracture, and osteochondral injury), arthropathy (primary and secondary degenerative and inflammatory), impingement syndrome, infective/inflammatory disorder (plantar fasciitis, Achilles tendonitis, osteomyelitis), and rarely tumors (e.g. enchondroma, osteochondroma, osteoid osteoma, bone cyst, etc) [4,5]. The identification of the foot pain generator is crucial in the clinical management of pain [6].

Conventionally anatomical imaging modalities including X-ray, CT, MRI, and ultrasonography have been used to identify the pathologies in the foot. But, due to the complex anatomy of ankle and foot joints and many times the coexistence of multiple pathologies, anatomical imaging failed to identify the true pain generator. Bone scintigraphy is a time-tested functional imaging modality that has very high sensitivity in the identification of very minimal osteoblastic activity; however, its use has been limited by low specificity due to a lack of anatomical correlates [7]. Recently, the increasing use of hybrid imaging like single-photon emission computed tomography/computed tomography (SPECT/CT) and PET/CT which harness the benefits of both anatomical and functional imaging has proved its utility in overcoming the challenges of the low specificity of functional Nuclear Medicine imaging. In bone scintigraphy, SPECT/CT, combining the functional information of bone scan with the anatomical information of CT, the exact nature of the pathologies can be identified. In the current review, we will particularly focus our discussion on the strengths and limitations of current imaging modalities used in the assessment of foot pain with a special emphasis on the emerging role of ^{99m}Tc-diphosphonate SPECT/CT and discuss its potential applications [8].

Conventional imaging

Plain radiograph

Plain X-ray remains the preferred initial imaging choice for the evaluation and management of bone pathologies including foot pain [9]. It can distinguish tissues of different densities based on differential absorption of X-rays beam [10]. Two radiographic projections at right angles usually delineate abnormalities that can potentially be obscured by superimposition [11]. The potential advantages of X-rays are their wide availability, easy accessibility, and cost-effectiveness. These make it especially useful in the management of acute trauma, however, in chronic injuries, its utility is limited as the complementary imaging technique to others [7].

CT scan

CT especially multidetector CT (MDCT) has a well established role in the management of foot pain. In MDCT, the focus of the X-ray tube follows a helical path around the bed with simultaneous constant movement of the bed in the horizontal axis. This enables the acquisition of high-resolution volumetric data, which can be reconstructed in any plane and provides spatial resolution as low as <0.5 mm [12]. It is especially adept to evaluate bone cortex and trabeculae; however, it has limited utility in the assessment of the tendon and other soft tissue pathologies when compared to ultrasonography and MRI [13]. Its 3-D representation and multiplanar reformatted images make it convenient to evaluate the complex anatomy of the foot and presurgical planning [14]. CT after injection contrast into the joint space can outperform magnetic resonance (MR) for the postoperative assessment of chondral repair owing to the MR image degradation secondary to postoperative changes and micrometallic artifacts; however gold standard imaging for soft tissue assessment remains to be MRI [4,15].

MRI

It is based on the principle of NMR. NMR refers to the fact that atoms with some net charge demonstrate the ability to absorb and reemit radiofrequency energy when placed in a magnetic field. Protons being the common element in the body with high magnetic dipole moment are used in the MRI. Hence, MRI involves imaging protons *in vivo* and multiplanar reconstruction similar to CT but without the use of ionizing radiation [15,16]. MRI has exceptional resolution, a high signal-to-noise ratio, and reproducible image acquisition. This makes MRI the preferred imaging modality for benign osseous lesions and soft tissue pathologies [17]. It is especially useful to evaluate menisci, articular cartilage, cruciate ligaments, tendons, synovium, and joint fluid particularly in small joints such as in hands and feet as well as tendon, fascial and neuronal pathologies, and impingement syndrome [18]. MRI can also be used in presurgical planning similar to CT. It has shown a good correlation with intraoperative findings. Distinct advantage of MRI is seen in the evaluation of osteomyelitis where it can detect marrow edema very early in course of the disease, avascular necrosis of bones, transient regional osteoporosis, and infiltrative and neoplastic pathologies [19]; however, MRI has certain disadvantages including claustrophobia, extremity coil design, especially for high strength magnets and its inability to be used in presence of metallic implant as well as image distortion caused by metallic and micrometallic artifacts [20].

Ultrasonography

It is based on the interaction of sound waves with living tissue to form dynamic, real-time images of the tissue that can provide quantitative, structural, and functional information from the target organ. Ultrasonography is highly proficient in the visualization of soft tissue [21,22]. In foot pain, it is especially useful in the evaluation of soft tissue disorders like inflammation, tear or injury to tendon, ligaments, cartilage and bursae, articular ganglions, peripheral nerve neuromas, soft tissue masses, and the presence of nonmetallic foreign bodies [23]. Ultrasonography is especially advantageous due to its ability to directly correlate clinical symptoms and imaging in real time, and acquire dynamic imaging of the foot in multiple planes and positions. It can additionally be used for guided targeted therapy (e.g. aspiration and targeted injections). It is widely available, portable, and like MRI does not uses ionizing radiations; however, it is highly operator dependent, limited to structures superficial to the bony cortex, and has limited acoustic windows for imaging, especially in small joints in the foot [24,25].

Nuclear medicine

The most common nuclear medicine technique used for the evaluation of bone pathologies is bone scintigraphy. The commonly used radiopharmaceutical is ^{99m}Tc-labeled methylene diphosphonate. It localizes to sites of increased osteoblastic activity aided by increased vascularity and is then chemisorbed into the osteoid matrix [26,27]. Bone scintigraphy is a highly sensitive technique that has played an integral role in the diagnosis and management of benign and malignant skeletal pathology for more than 5 decades [28]; however, planar bone scintigraphy has poor specificity and resolution, so its utility in foot pain was limited until recently. Recently hybrid SPECT/CT systems can provide high-resolution MDCT images coregistered with SPECT, thus combining high sensitivity of functional imaging (SPECT) with high Specificity of anatomical imaging [29–31]. It has established its essential role in the detection of pathologies like osteomyelitis, avascular necrosis, Sudeck's atrophy, etc. It is being increasingly used in the identification of pain generators in ankle and foot pain. Existing literature on the utility of SPECT/CT in foot pain is limited, however, suggests bone scintigraphy SPECT/CT is helpful in identifying pain generators in the foot with high accuracy and can help in appropriate guided management. Mohan *et al.* in their review recommended SPECT/CT in patients with foot pain in postsurgical patients, patients with metal

Table 1 Comparison of imaging modalities in evaluation of foot pain

Modalities	Advantages	Disadvantages
Plain radiography	Fast acquisition Less expensive Wide availability	Limited soft tissue resolution Less sensitive in early disease stage Limited three-dimensional information Ionizing radiation (+)
Ultrasonography	Widely available Low cost Dynamic real-time imaging ultrasonography guided targeted treatment No ionizing radiation	Operator dependent Limited sensitivity for bony abnormalities Limited field of view Poor visualization of deep structures
Computed tomography	Fast acquisition High spatial resolution Better disease characterization Better resolution of the cortical bone Multiplanar reformatting	Ionizing radiation (++++) Limited soft tissue contrast
Planar bone scintigraphy	Low cost Easily standardized Whole-body imaging High sensitivity Detection of occult fractures	Ionizing radiation (++) Limited specificity Limited soft tissue information Not widely available
Bone scintigraphy with SPECT/CT	Improved spatial resolution Multiplanar reformatting Improved specificity Early disease detection	Ionizing radiation (+++) Limited soft tissue information Not widely available
MRI	Excellent soft tissue contrast Can define the anatomy of intra-articular components Multiplanar imaging No ionizing radiation	Time-consuming Expensive Difficult in claustrophobic patients and those with metallic implants due to metal artifacts Children may need anesthesia

CT, computed tomography; SPECT, single-photon emission computed tomography.

implants, and in patients with unidentified pain generators on MRI [32–34]. The advantages and disadvantages of different imaging modalities have been summarized in Table 1.

Agrawal K *et al*. compared the diagnostic utility of MRI and SPECT/CT in the localization of pain generators in foot and ankle pain in 37 patients. They found the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) 82%, 31%, 74%, and 42%, respectively for MRI and 84%, 60%, 84%, and 60% respectively for bone SPECT/CT. Further, on subgroup analysis, the authors found sensitivity, specificity, PPV, and NPV in soft tissue lesions (n = 16) to be 88%, 40%, 83%, and 50% respectively for MRI and 75%, 25%, 80%, 33% respectively for SPECT/CT. While in the case of bone pathologies sensitivity, specificity, PPV and NPV of MRI were 73%, 25%, 57%, and 40% respectively, and of bone, SPECT/CT was 91%, 75%, 83%, and 86% respectively. Bone SPECT/CT changed the management in 26% of patients over MRI [35]. Potential indications of SPECT/CT in foot pain include degenerative disease, osteochondral lesions (OCLs), stress fracture, postoperative evaluation of joint fusion of foot, tarsal coalition, and soft tissue pathologies such as Achilles tendonitis, and plantar fasciitis [36].

Bone pathologies

Osteoarthritis

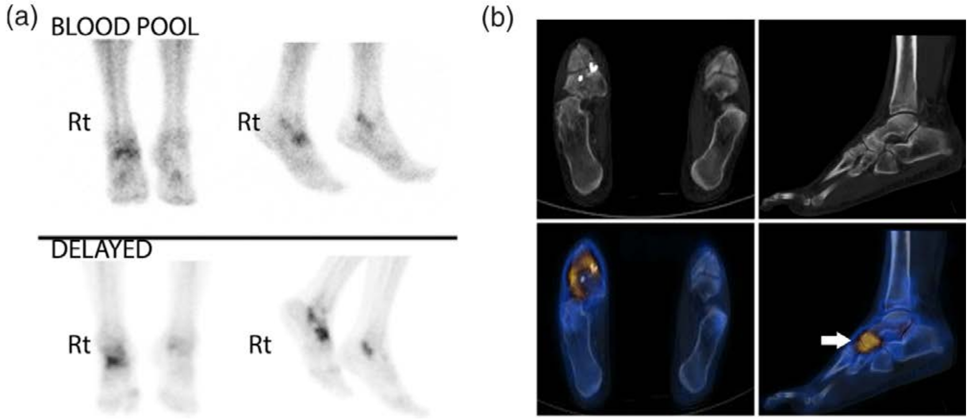
Osteoarthritis is characterized by progressive destruction and loss of articular cartilage, thickening of subchondral bone with the formation of osteophytes, and inflammation of the synovium [37]. Localization of the exact site is essential for appropriate patient management, especially for local steroid with or without anesthetic injection and surgical intervention [38]; however, in complex anatomical locations like the foot, identifying the exact site of pain generation becomes challenging. Anatomical imaging like CT and MRI can detect subchondral sclerosis, loss of joint space, subchondral cysts, and osteophytes associated with osteoarthritis but are limited by low specificity and detects disease late in its course [39,40]. Further, there may be multiple joint involvements in the anatomical imaging, however only one could be a pain generator. Planar bone scintigraphy, although sensitive, is limited by its lower resolution. Bone scintigraphy can detect changes in osteoblastic very early, way before the appearance of morphological changes, and can detect the most active osteoblastic site in patients with multifocal lesions [41]. SPECT/CT helps in the localization and characterization of the increased uptake lesion, enhancing its diagnostic accuracy compared to conventional imaging [32]. In a study of 50 patients with foot pain by Singh *et al*., SPECT/CT demonstrated high diagnostic accuracy of 94% with osteoarthritis being the most common diagnosis. SPECT/CT changed management in 78% (39/50) of patients [42]. Similar results were found by Parthipun A *et al*. in their prospective study involving 205 patients with foot and ankle joint degenerative change. The authors evaluated the role of SPECT/CT in the localization of pain generators and guiding steroid injection. They found that SPECT/CT offered a change in the site of steroid injection in 37% of patients compared to clinical assessment (Fig. 1a and b). The overall success rate for SPECT/CT-guided injections was 90% [43].

Osteochondral lesion

OCL is a common condition and is mostly related to sports injuries. The most common location of OCL is the ankle joint. It is commonly associated with a history of ankle sprains, fractures, or ligament injury/instability [4].

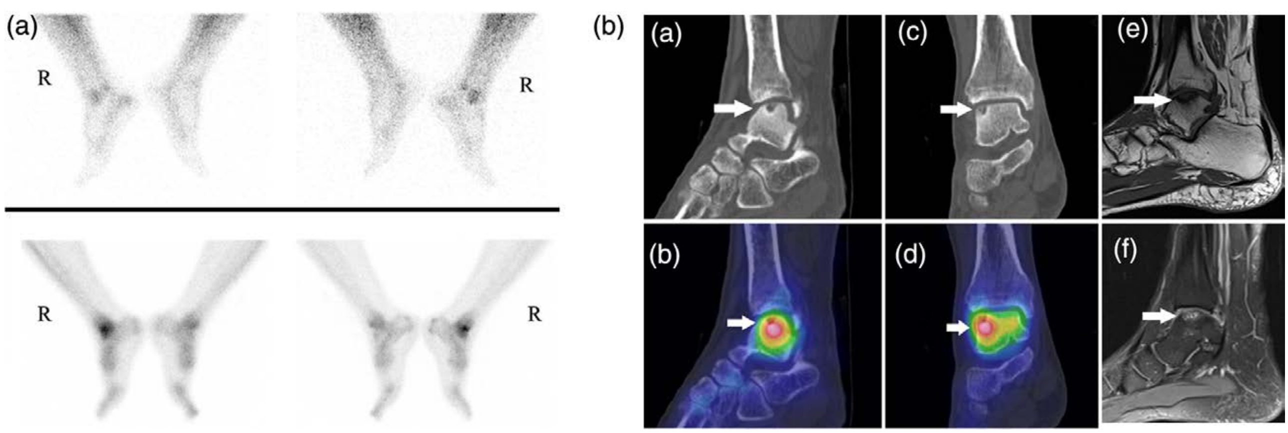
OCL is caused by repeated microtrauma to the subchondral area from repeated overload during vigorous physical activity or acute trauma. This disrupts the blood supply and leads to devitalization and separation of bone and cartilage fragments, which leads to pain in the affected area [44]. These are thus characterized by injuries to synovium and cartilage with variable involvement of the subchondral bone. Morphological imaging assessing the structural changes fails to delineate the exact site of origin of pain in presence of multiple nonspecific pathologies like in the foot [45]. Functional imaging identifies

Fig. 1



(a and b) A patient underwent two-phase ^{99m}Tc-MDP bone scan and SPECT-CT of feet and ankles for evaluation of pain in the right mid-foot. (a) Increased tracer uptake is seen in both ankles and right foot in the blood pool and delayed images. (b) SPECT-CT feet and ankles shows right-side talonavicular fusion. Increased tracer uptake in the right foot localizes to medial cuneiform and navicular bones showing subarticular cyst formation (arrow), suggestive of mid-foot degenerative changes. CT, computed tomography; SPECT, single-photon emission computed tomography.

Fig. 2

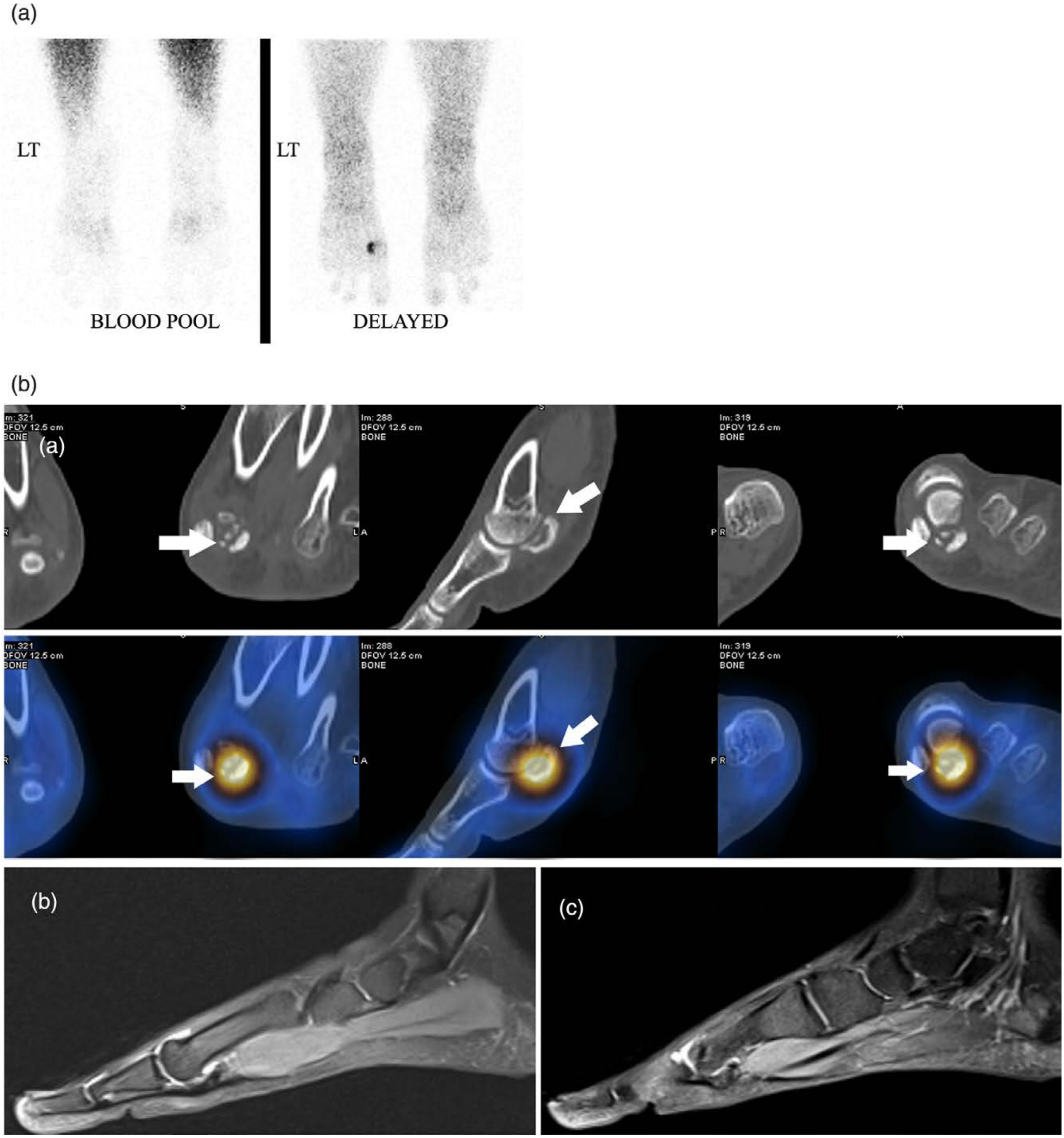


(2a and 2b) A 33-year-old male presented with pain in right ankle for the past 8 months, after a twisting injury. (2a) Blood pool and delayed images of three phase bone scan shows increased tracer accumulation in the right ankle region. (a–d in 2b) SPECT-CT of the ankle localizes the increased osteoblastic activity to an osteochondral defect at the superolateral aspect of the right talus bone (arrow). (e in 2b) Sagittal T1 weighted and fat-suppressed fast spin-echo proton density-weighted sequences, (f in 2b) PDFS MRI of the foot shows marrow edema in talar dome with subchondral PDFS hyperintense lesion in superior aspect of talus (arrows) which was reported as avascular necrosis; however, diagnosis of osteochondral defect was confirmed on arthroscopy. CT, computed tomography; PDFS, proton density fat suppressed; SPECT, single-photon emission computed tomography.

the site with an enhanced osteoblastic response, central to the pathogenesis of OCL, and maybe the cause of pain [46,47]. Three-phase bone scintigraphy is usually performed and typically shows focal uptake in the talar dome in all three phases with sensitivity and specificity for the diagnosis of OCL approaching 94 and 76% respectively [48].

Various studies have shown the superiority of SPECT/CT over morphological imaging (Fig. 2a and 2b). Leumann *et al*. compared the added value of SPECT/CT over MRI and found that SPECT/CT alone and in combination with MRI changed the management in 48 and 52% of patients respectively. They thus concluded SPECT/CT is complementary to standard MRI imaging for a thorough evaluation of foot pain patients, especially in patients with a risk of involvement of subchondral bone plate and subchondral bone due to the superiority of the latter for visualization of bone [49]. Similarly, Meftah *et al*. in their study involving 22 patients with OCL of talus evaluated the role of SPECT/CT over MRI. The patients were managed surgically ($n = 12$) or conservatively

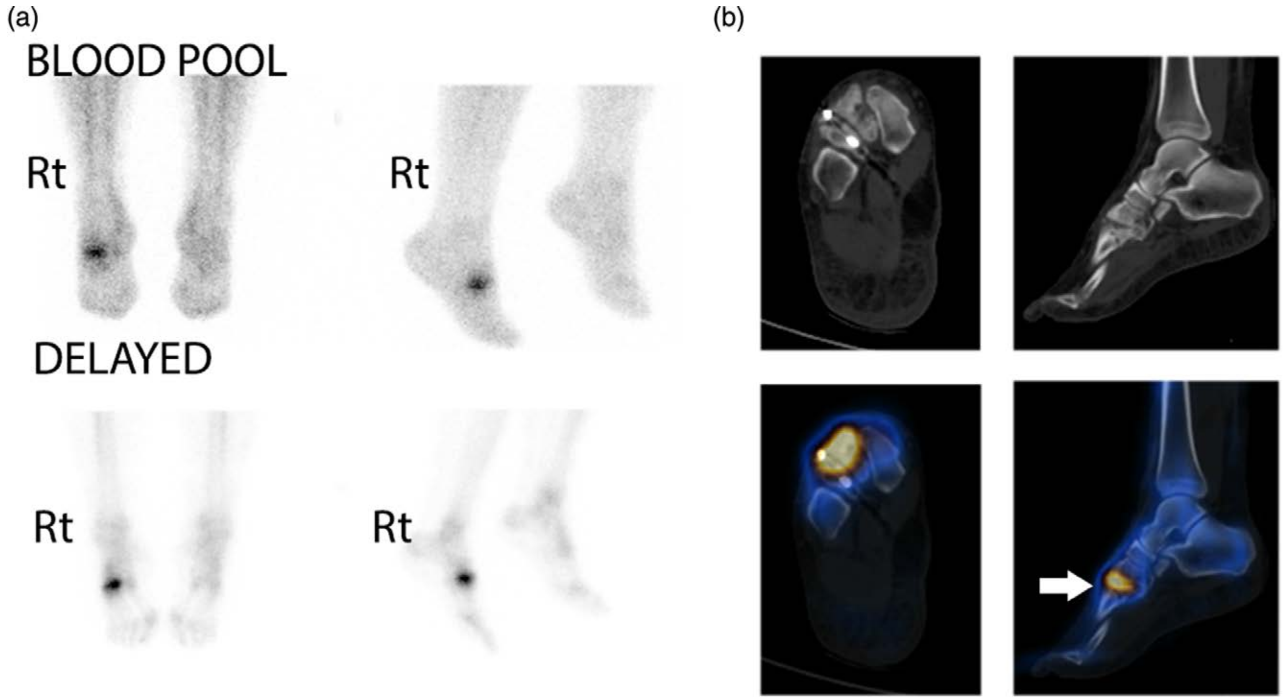
Fig. 3



(3a and 3b) A 22-year-old female with left foot pain near first metatarsophalangeal joint for 2 years after history of sprain. (3a) Initial blood pool image does not show any abnormal increased tracer accumulation in the left foot. Delayed images show increased osteoblastic activity in the first metatarsal bone region distally. (3b) upper and middle panel: SPECT-CT of the left foot localizes the uptake to a fragmented sesamoid bone below the head of first metatarsal bone (arrows) suggestive of sesamoiditis. (3b) lower panel: Sagittal PDFS MRI of left foot reported synovial effusion at first MTP joint of left foot. Pain was managed with footwear modification compatible with diagnosis of sesamoiditis. CT, computed tomography; MTP, metatarsophalangeal; PDFS, proton density fat suppressed; SPECT, single-photon emission computed tomography.

(n = 10) and American Orthopedic Foot and Ankle Society (AOFAS) score was calculated at follow-up. The authors used SPECT/CT to allocate patients to a surgical and conservative group. On follow-up at 6 months, the authors found that the mean AOFAS scores were 83.6 and 78.8 (normal range 40–100) for the surgical group and conservative group, respectively. Also, in the surgical group, seven patients had chronic foot pain with recent

Fig. 4



(a) Two-phase ^{99m}Tc-MDP bone scan of a patient referred for pain in the right foot shows increased vascularity and tracer uptake in the right midfoot. (b) SPECT-CT of the right foot localizes the tracer uptake to the base of the right second metatarsal and middle cuneiform region. This finding is highly suggestive of stress fracture of metatarsal bones. CT, computed tomography; SPECT, single-photon emission computed tomography.

trauma, SPECT/CT demonstrated acute activity in the lesion and accurately imaged the depth of the lesion, thus helping in allocating the patients to the surgical group as well as in preoperative planning, especially in cases with multiple lesions [50].

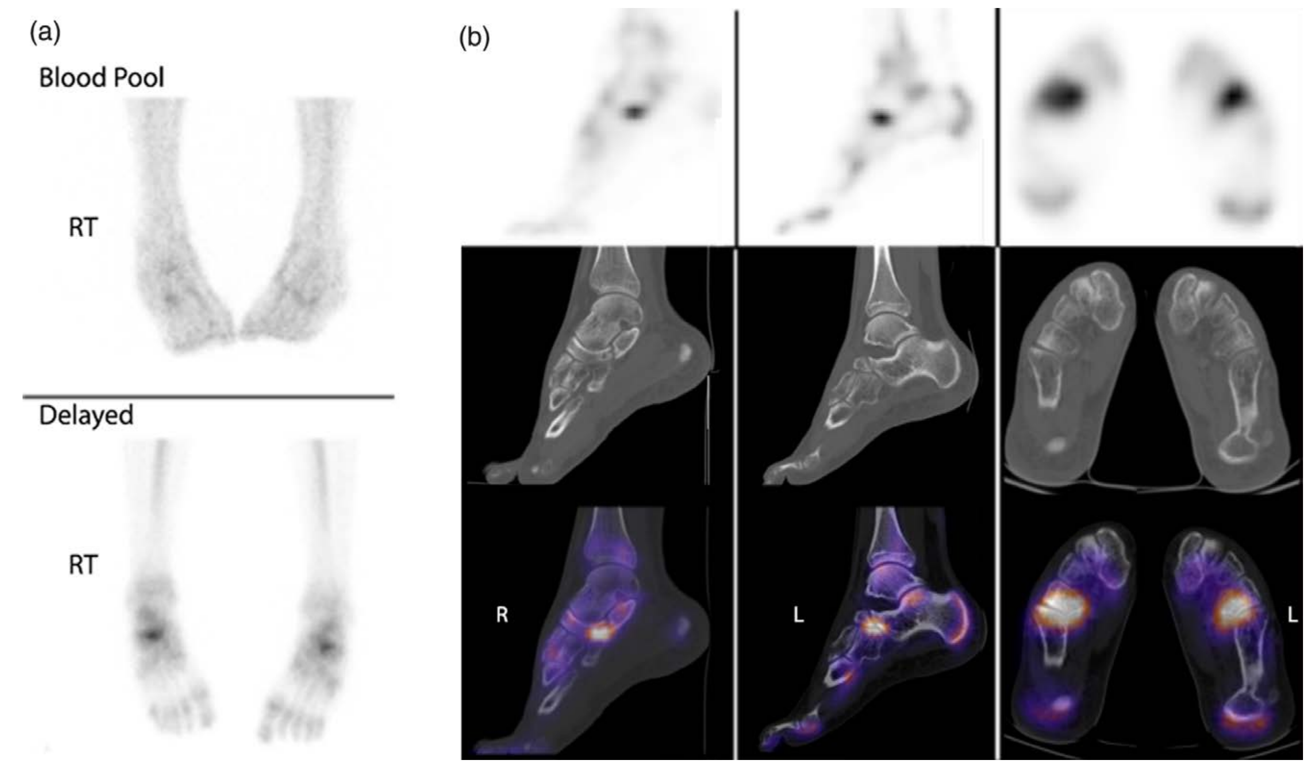
Painful accessory bones

Accessory bones are well corticated bony structures formed when the secondary ossification center fails to fuse with the rest of the bone. These are common in the foot with accessory navicular bones (ANBs) and Os trigonum being the most common accessory bones. These are considered normal variants in the foot as found in 18–36% of the population [51]. These are generally asymptomatic and symptoms appear only secondary to degenerative changes, trauma, or soft tissue edema in surrounding tissue. Bone scintigraphy and MRI are commonly used in the evaluation. Bone scintigraphy shows increased tracer uptake while MRI shows marrow edema. SPECT/CT is an excellent technique for the evaluation of painful accessory bones (Fig. 3a and 3b). SPECT demonstrates altered metabolic activity with high sensitivity while CT localizes and characterizes the abnormalities associated with it [52,53]. Sungwoo *et al.* in their study correlated the maximum standardized uptake value (SUVmax) using Tc-99 m HDP (SUVmax) in patients with symptomatic ANB. They found a strong association between SUVmax and symptoms, surgical treatment outcomes, and high-risk ANBs. Thus, the author advocated bone scintigraphy with SPECT/CT for risk stratification of ANB for surgical treatment [54].

Stress fracture

Stress fractures are caused by repeated mechanical stress that overweighs the remodeling capacity of bone. These are common in weight-bearing areas like the lower extremities. The shaft of the tibia is the most common site of stress fracture. Other common sites include the metatarsal, distal fibula, calcaneus, talus, sesamoid, and navicular bones [55–57]. Radiographs have a low sensitivity for the detection of stress fractures, especially in the early stages. CT has high specificity for diagnosis ranging from 88–98%, however, its low sensitivity (32–38%) limits its utility [58]. Bone scintigraphy and MRI show high sensitivity for detection of stress fracture even for early disease, that is, not apparent on radiograph. MRI demonstrates bone marrow edema associated with osseous stress reactions [59]. MRI has very good sensitivity and variable specificity in the range of 68–99% and 4–97% respectively [8]. Bone scan is highly sensitive for the detection of stress fracture (sensitivity 50–97%). It shows focal area of increased tracer uptake at the site of mechanical stress; however, the use of hybrid SPECT/CT provides high specificity (33–98%) to highly sensitive

Fig. 5



(a and b) History of old fracture of the left fifth metatarsal. Bone scan was performed to evaluate the cause of ongoing pain in bilateral feet. Increased tracer uptake with no significant increased vascularity is noted in (a) bilateral mid feet. (b) SPECT-CT of feet localizes the uptake in the mid feet to bilateral fibrous calcaneo-navicular coalition, more prominent on the right side. Normal tracer uptake was seen at the site of the previous fracture in the left fifth metatarsal bone (not shown). CT, computed tomography; SPECT, single-photon emission computed tomography.

bone scintigraphy, thus increasing the accuracy for diagnosis [8,60,61] (Fig. 4).

Talocalcaneal coalition

Tarsal coalition refers to the fusion of two or more tarsal bones by the formation of bridges across the intertarsal joint. Bridging can be fibrous, cartilaginous, or osseous. It leads to motion restriction of the affected joint and at times is associated with pain [62]. The most commonly involved tarsal joints are calcaneo-navicular and talocalcaneal joints. Prevalence of tarsal coalition in the general population was initially considered to be <1%, however recent data shows a higher prevalence, as high as 6% with half of the cases having bilateral disease [63]. Tarsal coalition may be congenital (most common form) or acquired secondary to trauma, inflammatory arthropathies, joint degeneration, or infection [64].

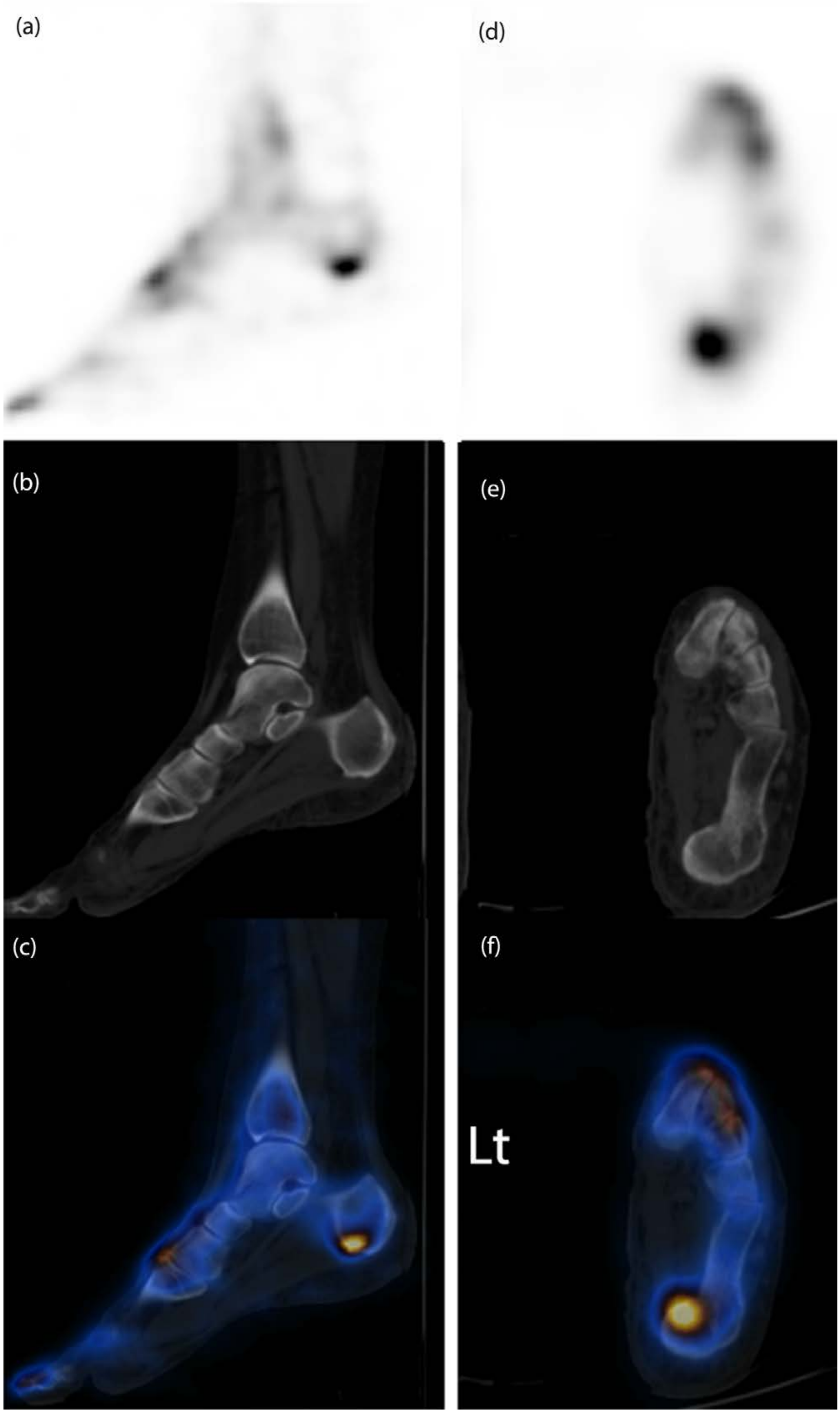
Radiographs are the initial imaging of choice but are less sensitive in the detection of tarsal coalition. CT and MRIs are highly potent imaging modalities for diagnosing tarsal coalition but are unable to differentiate symptomatic and asymptomatic lesions [65]. SPECT/CT however can effectively demonstrate abnormally increased activity due to shearing forces at the site of pain generation. Thus, can identify the exact culprit site and can guide intra-articular injections. SPECT/CT using a combination of functional and structural information, can also detect additional potential pain generators missed by other modalities [45].

Mohan *et al.* in their review found SPECT/CT is superior to CT in the localization of the site of pain in the foot, mainly due to the addition of functional information. There are increased stress forces on the abnormal connection between the bones than normal articulation, leading to increased bone turnover and thus increased tracer uptake (Fig. 5a and b). Thus, the author recommended SPECT/CT over CT alone for decision-making and guiding intra-articular injections [15].

Post-op evaluation of arthrodesis

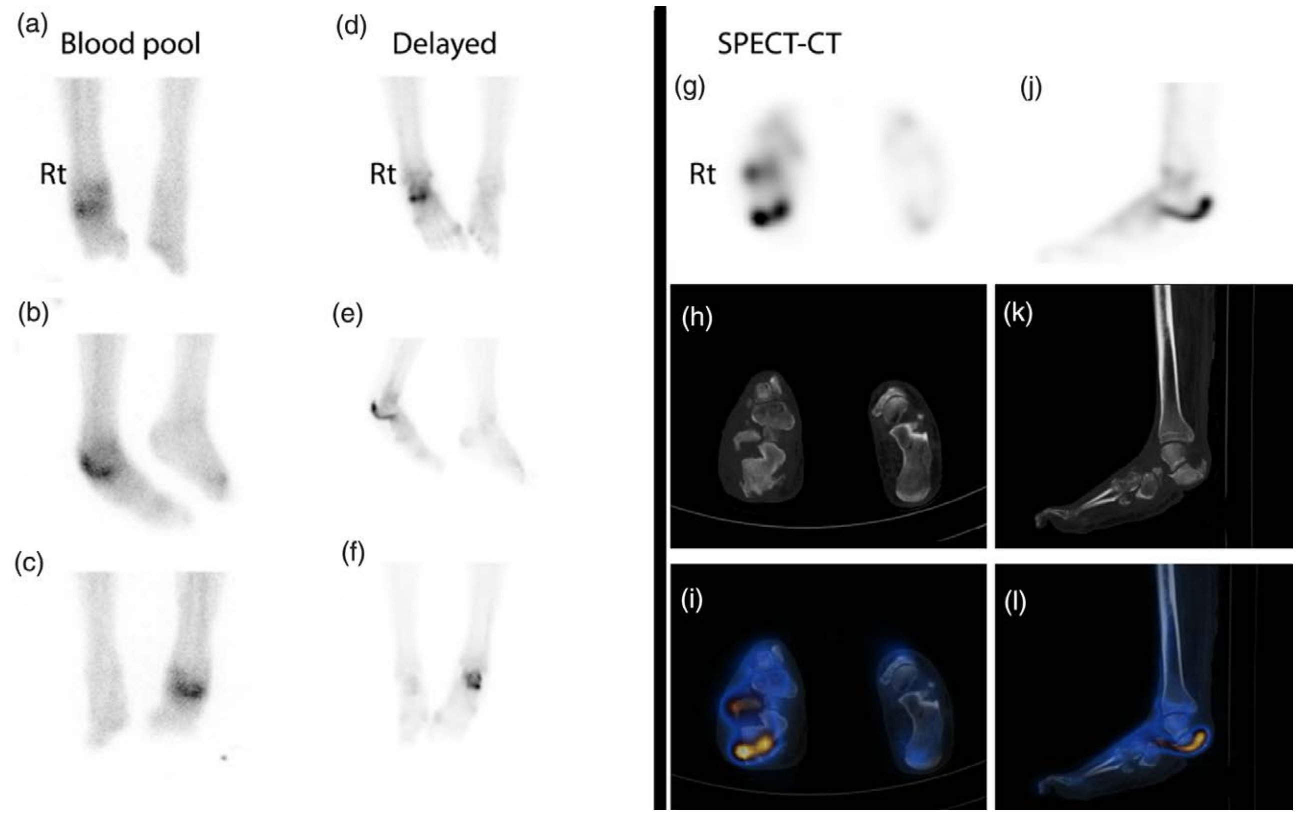
Arthrodesis (fusion) of joints is used as a treatment option for various foot pain pathologies like severe osteoarthritis, postinflammatory joint destruction from (rheumatoid) arthritis, fractures or posttraumatic malalignment after complex trauma, and Charcot osteoarthropathy in diabetic foot syndrome. Though the time for osseous union varies based on different joints, it is usually completed in 6 months. When the joint union is completed in

Fig. 6



A patient with vague pain in the left hindfoot underwent two-phase ^{99m}Tc-MDP bone scan and SPECT-CT of the left foot to determine the pain etiology. Increased vascularity and tracer uptake was seen in the left calcaneum on two-phase bone scan (not shown), which on (a–f) SPECT-CT localizes to the inferior aspect of left calcaneum at the site of attachment of planar fascia with adjacent plantar fascia thickening. This is suggestive of left planar fasciitis, which is likely the cause of pain. CT, computed tomography; SPECT, single-photon emission computed tomography.

Fig. 7



A patient with diabetic heel ulcer on the right side with past history of right heel osteomyelitis underwent two-phase ^{99m}Tc-MDP bone scan and SPECT-CT to confirm recurrence and extent of osteomyelitis. (a–c) Blood pool images show intense hyperemia in the region of the right heel with (d–f) delayed images demonstrating increased tracer activity in the region of the right calcaneum. (g–l) SPECT-CT localizes the abnormal tracer uptake to the right calcaneum having an irregular margin likely due to osteomyelitis. Additionally, small bony fragments are seen adjacent to the calcaneum along with soft tissue thickening in the right foot. CT, computed tomography; SPECT, single-photon emission computed tomography.

9 months, it is called a delayed union [66–68]. Remerand *et al.* reported that 21 and 43% of patients develop moderate-to-severe pain one year after surgery, at rest, and during walking respectively [69]. The cause of pain in such cases can be nonunion, severe mechanical overload, subsequent osteoarthritis, and infection. The management differs in these cases, thus there is a need to delineate the pain generator in postoperative cases. Morphological imaging including radiograph and CT are used routinely in cases of postoperative pain but is ineffective in many cases. MRI is unable to localize pain generators due to metallic artifacts; however, bone SPECT/CT has proven useful in cases of postoperative pain [70]. Nathan *et al.*, in their study, have reported that bone SPECT/CT could accurately localize the site of the pain generator in 98% of cases and had led to a change in patient management in 75% of cases [4]. Thus, SPECT/CT has tremendous potential to aid in the detection of the cause of foot pain and to strategize patient management. SPECT/CT should be considered when the diagnosis remains occult even on CT with or without MRI. Many studies have found the important role of SPECT/CT in the evaluation of foot pain. Ha seunggyn *et al.* compared SPECT/CT and MRI in the diagnosis of foot pain and found the sensitivity, specificity, PPV, and NPV to be 100%, 8%, 27%, and 100% for MRI and 71%, 73%, 48%, and 88% respectively for SPECT/CT [71]. Pagenstert *et al.* in their study found that the mean intraobserver reliability for SPECT/CT to be higher for SPECT/CT than for CT and bone scanning together, thus reinforcing the role of SPECT/CT in localizing the site of foot pain [72]. Claassen *et al.* also compared SPECT/CT and MRI and found higher interrater and intra-rater reliability for SPECT/CT for diagnosing complex foot and ankle pathologies [33]. Singh *et al.* studied the diagnostic value of bone scintigraphy in foot and ankle pain and found accuracy, sensitivity, specificity, positive predictive, and NPV of 94%, 95.45%, 83.3%, 97.6%, and 71.43% respectively. In the same series, SPECT/CT modified treatment in 78% of patients [42].

Soft tissue pathologies

Plantar fasciitis

Plantar fasciitis is defined as the inflammation of the thick, pearly-white plantar fascia of the foot. It is one of the most

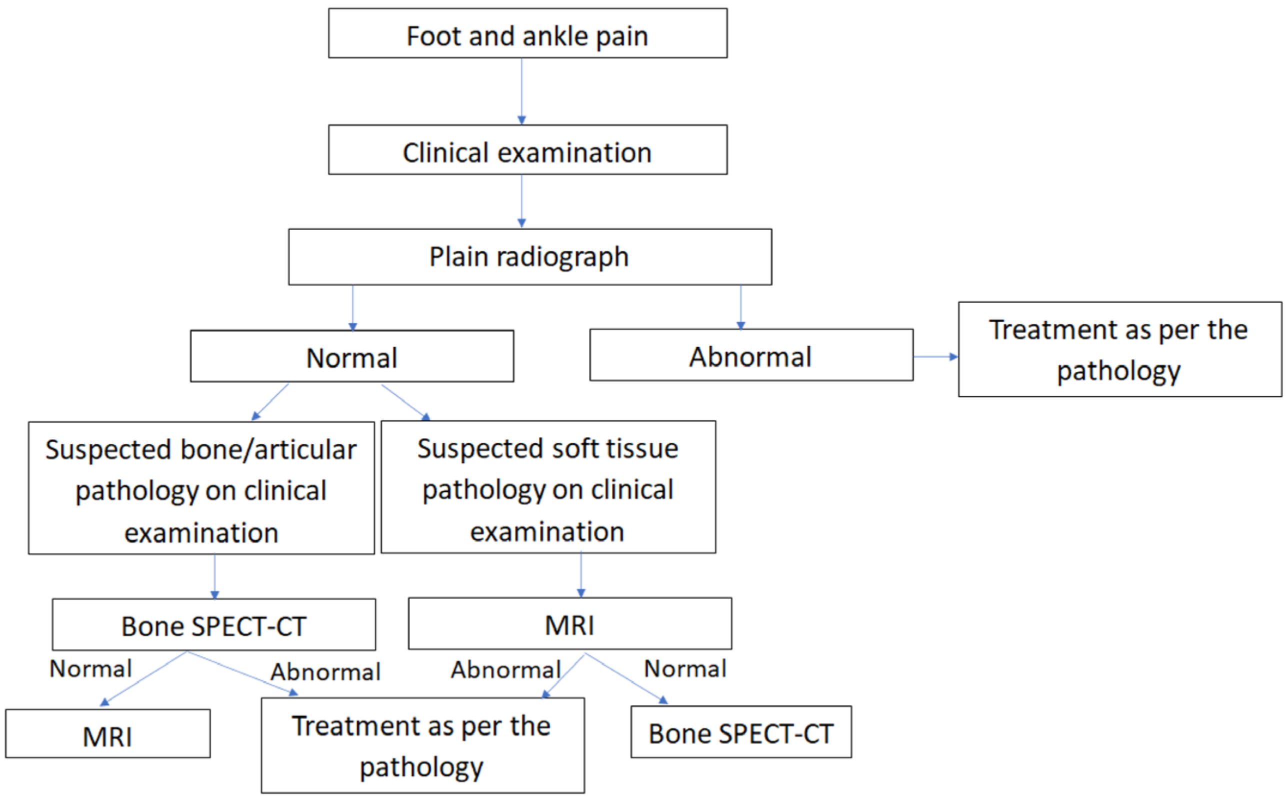
Table 2 Summary of the literature review: utility of single-photon emission computed tomography/computed tomography in evaluation of foot pain

Study	Design	Results	Level of evidence
Linke R. *et al*. (2010) [104]	Retrospective study Diagnostic value of SPECT versus hybrid SPECT/CT 71 patients with pain in the extremities	Hybrid SPECT/CT lead to change in diagnosis in 32.4% (23/71) of patients compared to SPECT alone	IV
Leumann *et al*. (2011) [49].	Retrospective study Impact of SPECT/CT in decision–making compared to MRI 25 patients of OCLs of talus	Compared to MRI, SPECT/CT alone influenced decision–making in 48% of cases and in combination with MRI in 52% of cases SPECT/CT provided additional information and improved the outcome	IV
Wiewioski *et al*. (2011) [46].	Prospective study Pain from OCL of ankle joint and assess the improvement in visual analogue score to ≤50% score in response to guided local anesthetic injection in 15 patients	Highly significant correlation between SPECT/CT findings and pain VAS improved from 4.6 to 0.8 with SPECT/CT-guided local anesthetic injection	IV
Claassen *et al*. (2014) [33]	Retrospective study Impact of SPECT-CT on decision-making in ankle, subtalar, Chopart, and Lisfranc joint pathologies of foot and ankle.	Hybrid SPECT/CT changed the diagnosis in 64.5% of patients in ankle joint pathologies, 65.2% of patients in subtalar joint pathologies, and 75% in both Chopart and Lisfranc joint pathologies The overall sensitivity, specificity, PPV, and NPV were 94%, 57%, 87%, and 75% respectively.	IV
Ha S. (2015) [71]	Retrospective study Diagnostic performance of SPECT/CT versus MRI in diagnosis of symptomatic lesion of foot and ankle	Sensitivity, PPV, and NPV for SPECT/CT were 93%, 56%, and 91 while for MRI were 98%, 48%, and 95% respectively Specificity of SPECT/CT was higher than MRI for bone and ligament/ tendon lesions	IV
Parthipun (2015) [43]	Prospective analysis of detection efficiency for pain generators in foot pain in 203 patients. Evaluation of response to SPECT/CT guided anesthetic injection.	Final analysis including 52 patients treated with SPECT/CT guided anesthetic injection revealed SPECT/CT changed the site of pain generators in 37% (19/52) patients. The response to anesthetic injection was seen in 88% (43/52) of patients. The response rate in patients' whole management was altered by SPECT/CT was 95% (18/19).	IV
Claassen *et al*. (2019) [40]	Retrospective comparison of interrater and intrarater reliability of diagnostic performance of SPECT/CT versus MRI. Comparison of diagnostic performance of SPECT/CT vs MRI and their impact on management.	The kappa Cohen's for interrater agreement was: SPECT/CT: 0.68 MRI: 0.38 SPECT/CT+MRI: 0.71 And for intrarater agreement was: SPECT/CT: 0.67 MRI: 0.35 SPECT/CT+MRI: 0.75 The sensitivity, specificity, PPV, and NPV for SPECT/CT and MRI for localizing pain generators were: 92%, 60%, 90% & 67% vs 57%, 7%, 31%, and 18% respectively.	IV
Pountos *et al*. (2019) [105]	Retrospective analysis of role of SPECT/CT in influencing decision–making in 272 patients with foot and ankle pathologies.	SPECT/CT changes initial diagnosis in 55% of the cases and added confidence to clinical diagnosis in 89% of the cases. SPECT/CT also reduced the need for further work-up in 93% of cases.	IV
Yeats *et al*. (2020) [106]	Retrospective evaluation of diagnostic yield of SPECT/CT compared to radiographs and CT/MR in 33 pediatric patients	SPECT/CT provided decisive clinical value in 84.8% (28/33) patients compared to radiographs and CT/MR. Compared to MRI alone, SPECT/CT added further clinical information in 72% (13/18) of patients.	IV
Eelsing *et al*. (2021) [34]	Systemic review of the diagnostic value of SPECT/CT in foot and ankle pathology.	Analysis of eight studies revealed SPECT/CT improved diagnosis in 40–79% of patients and changed the management in 40–79% of patients with an overall symptomatic improvement of 92% in patients with SPECT/CT guided management.	V
Agrawal K. *et al*. (2021) [35]	Retrospective study Diagnostic performance of SPECT/CT versus MRI to detect pain generators in 37 patients with ankle and foot pain	Sensitivity, specificity, PPV, and NPV for SPECT/CT were 84, 60, 84 and 60%, while for MRI were 82, 31, 74 and 42%, respectively SPECT/CT led to treatment change in 26% of patients over MRI	IV

CT, computed tomography; MR, magnetic resonance; NPV, negative predictive value; OCL, osteochondral lesion; PPV, positive predictive value; SPECT, single-photon emission computed tomography ; VAS, visual analogue scale.

common causes of heel pain. It is estimated to account for 11–15% of cases of foot complaints requiring professional care [9]. Commonly the initial investigation is radiography, which helps primarily to rule out other causes of foot pain. CT study is not of much use in Plantar fasciitis. The preferred investigation modality is MRI due to better soft tissue contrast [73]. Ultrasonography foot can also detect plantar fasciitis with high sensitivity as shown by Radwan A *et al*. in their systematic review, in which they found sensitivity and specificity of ultrasonography to be 80 and 88.5% respectively as compared to MRI as the gold standard [74,75]. MRI features associated with Plantar fasciitis include thickening and inflammation in the plantar aponeurosis, adjacent soft-tissue edema, reactive calcaneal marrow edema, and any evidence of rupture of the fascia if present. MRI has been given a score of 9 on the American College of Radiology appropriateness criteria [76,77]. Although, highly sensitive, MRI has limited specificity for the detection of the exact pain generator in the foot, especially in cases where multiple pathologies

Fig. 8



Adapted from Agrawal K, Swaroop S, Patro PSS, Tripathy SK, Naik S, Velagada S. Comparison of bone SPECT/CT and MRI in the detection of pain generator in ankle and foot pain: a retrospective diagnostic study. Nucl Med Commun. 2021 Oct 1;42(10):1085–1096.

coexist. Planar bone scintigraphy shows increased tracer uptake at the site of inflammation with high sensitivity but limited specificity. Hybrid SPECT/CT combining functional and morphological information can exactly localizes the tracer uptake to the site of plantar fascia insertion leading to the exact site of pain generation with high specificity and sensitivity [78]. Thus, it can guide steroid with or without anesthetic injections and improve patient outcomes (Fig. 6) [79–81]. It is especially useful in cases where MRI fails to localize the culprit pain generator and in presence of implants [15].

Tendinitis

Tendons in the foot maintain its shape against the weight of the whole body, and thus are at risk for tendinopathy, mainly due to overuse. Most involved tendons include the posterior tibial tendon, the peroneal tendon, the flexor hallucis longus tendon, and the anterior tibial tendon while in athletes Achilles para-tendinopathy and insertional Achilles tendinopathy are commonly seen. Repeated microtrauma due to overuse may lead to inflammatory changes and sometimes the formation of ectopic bone in the tendon [82–84]. The diagnosis is mainly clinical with imaging studies being performed mainly to validate the diagnosis. Achilles tendinopathy radiograph and CT show Haglund's deformity, that is, enlargement of the posterosuperior prominence of the calcaneus [85]; however, like other pathologies of the foot, this is not a specific finding as demonstrated in the study by Kang *et al*. The authors found no significant difference between Achilles tendinitis and Haglund deformity without tendinitis. MRI shows an increased T2-weighted signal or an increased tendon diameter, however, correlation with symptomatology remains poor [86]. Khan KM *et al.* in their prospective study found sensitivity, specificity, PPV, and NPV of MRI for diagnosing tendinopathy to be 95%, 50%, 56%, and 94% respectively [87].

SPECT/CT is emerging as an important investigation in foot pain of soft tissue origin, though less effective than in bony pathologies. In tendonitis, SPECT/CT bone scintigraphy localizes the tracer uptake to the site of insertion of the tendon indicating the exact site of the pain generator. In soft tissue, its role is mainly as an adjuvant to MRI and not to replace MRI as the investigation of choice as demonstrated in many studies [88,89]. Agrawal K *et al.* compared the utility of SPECT/CT and MRI in the detection of pain generators in the foot and found that the sensitivity, specificity, PPV, and NPV of MRI for soft tissue lesion was 88%, 40%, 83%, 50% while for SPECT/CT it was 75%, 25%, 80%, and 20% respectively [35].

Infection and inflammation

Infection of the foot and ankle can either involve soft tissue like cellulitis or bone. It is important to differentiate soft tissue infection from osteomyelitis as the management differs for both pathologies.

Soft tissue infection

Clinical and laboratory tests can only predict the presence or absence of infection but cannot define the site and extent of infection. To identify the site and extent, various imaging modalities are used. Plain radiographs have a limited role in soft tissue infection detection as they have low contrast resolution and thus low sensitivity and specificity. Ultrasound and CT have nonspecific findings in cases of cellulitis without complicating features [90–92]; however, in severe cases, ultrasound can localize the site of infection and abscess but is operator dependent and sometimes cannot be used for planning surgical intervention. Thus, CT and MRI are used for the localization of infection, especially in severe cases in which surgical management is needed.

Three phase bone scan is very useful in differentiating cellulitis from osteomyelitis [90]. In three phase bone scan, cellulitis shows increased tracer flow in the arterial phase and may have increased tracer pooling in the blood pool phase but normal uptake in the delayed phase, while increased uptake of tracer is seen in all three phases in osteomyelitis. SPECT/CT accurately localizes the uptake in the soft tissue and bone, therefore, furthermore accurately differentiates cellulitis and osteomyelitis. Nuclear medicine modalities for infection imaging like 67Ga or 111In WBC imaging have high sensitivity even in early cases. These make use of the specific diapedesis of radionuclide labeled white blood cells (WBC) to the site of infection and inflammation for localization of the site of infection and delineate its extent [93–95].

Osteomyelitis

Osteomyelitis is an infection of the bone. Bacterial infection is the leading cause of osteomyelitis and is most commonly caused by Staphylococcus aureus [90]. Bacteria can reach bone either by hematogenous route or by direct invasion like in open wounds. Imaging plays a crucial role in the management of osteomyelitis. It helps in initial diagnosis, especially in neonates and chronic diseases where inflammatory markers can be normal, delineate the extent, guided abscess drainage, guided biopsy, and follow-up during therapy to ensure complete resolution of disease. Plain radiographs are usually the initial imaging, but they lack sensitivity to detect osteomyelitis, especially in the first 2 weeks [90,96]. CT can detect osteomyelitis only when bone destruction has taken place.

MRI is considered the imaging modality of choice to detect osteomyelitis in a previously normal bone [96–98]. It shows a low-signal abscess cavity and a halo of bone edema separated by a high signal rim on T1 weighted sequence commonly known as penumbra sign [99,100]. This can also differentiate osteomyelitis from tumor. But MRI may not be diagnostic in cases with previous operative intervention due to the presence of metal artifacts. In such cases, a bone scan is indicated owing to its high sensitivity to detect osteomyelitis. Bone scans can detect osteomyelitis as early as 2–3 days [101]. Also, with the advent of hybrid SPECT/CT images, the detection efficiency is considered at par if not better than MRI (Fig. 7). Termaat M F *et al.* in their systematic review and meta-analysis found the pooled sensitivity of MRI to be 84%, while for bone scintigraphy it is 82% and most accurate investigation for osteomyelitis was found to be 18-F FDG PET/CT with sensitivity and specificity of 96 and 91% respectively [102,103]. Further, being a whole-body modality, bone scintigraphy is useful to screen the entire skeleton, particularly in multifocal osteomyelitis.

Conclusion

To conclude, SPECT/CT by combining both the functional and morphological information helps to detect the cause of foot pain with high sensitivity and specificity and thus, helps to provide appropriate management. Bone SPECT/CT is especially useful in bony pathologies where it can replace MRI as the first-line imaging modality while in soft tissue pathologies, it can be used as an adjuvant to MRI, especially in cases where the culprit lesion remains undetected even on MRI. The available literature is summarized in Table 2 along with the quality of evidence it provides based on guidance from the Oxford Centre for Evidence-Based Medicine [107]. On the basis of our previous study on foot pain, we propose the following algorithm for use of bone SPECT/CT in foot pain Fig. 8.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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