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## Role of Nuclear Medicine in Infection Imaging

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### 1. Introduction

Inflammation is a complex tissue reaction to injury that may be caused by physical, chemical, or immunological agents or even by radiation. Acute inflammation is the early or an immediate response to injury that lasts for a short duration (8-10 days), whereas the condition characterized as chronic inflammation is of longer duration, lasting for several weeks to even years.

A variety of conventional imaging modalities such as radiography, computed tomography and magnetic resonance imaging are available for evaluation of osteomyelitis. The diagnosis of acute osteomyelitis is relatively straight forward. Conventional imaging modalities perform poorly when there is a previous insult (fracture, trauma and infection) to the bone. The limitations of the conventional imaging modalities necessitate utilization of functional modalities. Nuclear medicine techniques are ideally suited for these patients.

Several different nuclear medicine techniques are utilized for the evaluation of osteomyelitis. Bone scintigraphy with diphosphonates is an easily available technique in the initial evaluation of osteomyelitis. It has high sensitivity but suffers from low specificity. However, in patients with chronic osteomyelitis and those with previous insult to the bone, the diagnostic performance of bone scintigraphy alone is limited. To overcome the low specificity of bone scintigraphy alone, bone scintigraphy combined with <sup>67</sup>Gallium, leukocytes and bone marrow imaging could improve the specificity. An approach of labeled antibiotics imaging preferentially picks up active bacterial infection in both soft tissue as well as bone. <sup>18</sup>F Fluorodeoxyglucose-positron emission tomography (FDG-PET) has become an encouraging imaging modality in musculoskeletal infection. This application has an incremental value in the assessment of both acute and chronic infection and has shown to be more accurate in detecting chronic osteomyelitis than conventional radionuclide imaging.

Functional imaging modalities are especially useful in patients with orthopedic hardware and those with diabetic foot infection. The above mentioned conditions are dealt separately because of the peculiar difficulties posed by them. Nuclear medicine and PET techniques are cornerstone in the evaluation of infected orthopedic hardware.

## 2. Inflammation and infection

Inflammation is a complex tissue reaction to injury that may be caused by physical, chemical, or immunological agents or even by radiation. If the injury is caused by or involves living microbes, the injury leads to infection. In general, the inflammatory response is characterized by local hyperemia (rubor, calor), edema or swelling (tumor), pain (dolor). Inflammation may be classified broadly as acute or chronic depending on the duration of inflammatory reaction and also on other pathological and clinical features.

Acute inflammation is the early or an immediate response to injury that lasts for a short duration (8-10 days), whereas the condition characterized as chronic inflammation is of longer duration, lasting for several weeks to even years. Acute inflammation is associated with many regional and systemic changes, such as vasodilation, increased vascular permeability, and formation of exudate. These events are followed by local cellular events [1]. Neutrophils are the predominant cells in acute inflammation. If the inciting agent persists chronic inflammation follows. Chronic inflammatory stage is characterized by reduction in the number of neutrophils and an increased infiltration of macrophages, lymphocytes, plasma cells, and fibroblasts.

### 2.1 Osteomyelitis

Osteomyelitis is an infection involving the cortical bone as well as the myeloid (bone marrow). The infection may be limited to the periosteum (periosteitis) without involvement of cortex and marrow but when the cortex is involved, it is called osteitis and osteomyelitis. Osteomyelitis may be classified based on several factors such as route of infection (hematogenous or nonhematogenous), underlying etiology (diabetic foot), age of onset (infantile). *Staphylococcus aureus* is the most common gram-positive bacterium involved [2]. One of the consequences of osteomyelitis is reactive new bone formation resulting in increased blood flow. Chronic osteomyelitis is characterized by less marked infiltration of inflammatory cells than seen in the acute state and may exhibit variable amount of necrotic tissue. Osteomyelitis in the diabetic foot is a unique clinical and pathologic problem. It is a common complication of diabetes and generally occurs as a result of the spread of infection from adjacent foot ulcers. Patients undergoing hip or knee arthroplasties may experience discomfort due to loosening with or without infection. The extent of reactive bone formation, however, depends on the nature of prosthetic material; the cementless porous coated prosthesis induces more reactive bone formation than the cemented prosthesis. Finally, infectious or septic arthritis refers to the invasion of synovial space by microorganisms and represent medical emergency.

## 3. Imaging techniques of osteomyelitis

### 3.1 Radiological techniques

Standard radiography, magnetic resonance imaging (MRI), and computed tomography (CT) commonly are used to detect skeletal infections. Radiographs provide morphological data about the region of interest. MRI has been used widely because of its excellent soft-tissue contrast and its sensitivity to tissue edema and hyperemia. MRI is valuable in the visualization of septic arthritis, spinal infection, and diabetic foot infections. However, these modalities are of limited value to detect early infection when morphological changes are absent. Similarly in

patients with previous insult to the bones (previous infection, fracture, surgery replacement etc), morphological imaging methods have limited role. Artifacts caused by prosthetic joints or metallic implants in the spine or extremities can degrade images sufficiently to make diagnosis impossible in both CT and MRI. Therefore, nuclear medicine procedures are needed as a functional adjunct to complement morphologic imaging techniques [2].

### 3.2 Nuclear medicine techniques

A variety of radiopharmaceuticals are available for skeletal infection imaging [3] and several new tracer are being evaluated for use in imaging infection [4]. The characteristics of an ideal infection imaging agents are mentioned in Table 1. The physical characteristics, advantages and disadvantages of the commonly used radiopharmaceuticals are summarized in Table 2. The various Nuclear Medicine skeletal imaging techniques are as follows:

- a. **Static imaging:** Static imaging of a part of the body is the one of the most commonly used technique in nuclear medicine. The technique is similar to radiography. Images are obtained using gamma camera for a fixed amount of time or for fixed counts. Images can be obtained in any of the views, though anterior, posterior and oblique views are the ones that are commonly performed.
- b. **Dynamic imaging:** Dynamic imaging is rapid acquisition of several static images which can be later viewed in a cine format. It is especially useful in studying the changes in blood flow, uptake of the tracer in the bones etc. Dynamic imaging is frequently performed in the diagnosis of osteomyelitis. The significant increase in the bloodflow to the affected site can be easily identified using dynamic imaging.
- c. **Whole body imaging:** Whole body imaging is routinely used for the evaluation of bone disorders, especially in the case of metastatic bone disease. This technique images the whole body and displays the entire skeleton as a single image.
- d. **Three phase imaging:** Three phase imaging is a combination of dynamic imaging followed by static imaging at fixed time intervals. It involves an initial dynamic imaging of the site of interest immediately after the intravenous injection of the radiotracer. These images help in identification of the increase in bloodflow, if any, to the site of interest. This is followed by static images of the region during the soft tissue phase (immediately after completion of the dynamic phase) and bone phase (3 hours after injection). Fourth phase imaging (static image at 24 hours) can also be done and shows modest increase in specificity for identifying osteomyelitis)
- e. **Fusion imaging (Hybrid SPECT/CT):** The lack of anatomic detail in nuclear medicine images can be overcome by fusion imaging. Fusion imaging consists of a combined anatomic (usually CT scan) and a functional imaging (nuclear medicine imaging) in a single sitting in the same position. The two images are then fused together and used for interpretation. Addition of CT aids in anatomical localization, attenuation correction and also helps in increasing specificity by providing anatomical details. In the case of osteomyelitis, it is especially useful in differentiating soft tissue infection from bony infection.
- f. **Positron emission tomography (PET):** PET is a functional imaging technique which utilizes annihilation radiation (two 511 keV gamma rays) for imaging. It has advantage of high sensitivity and higher spatial resolution compared to the general nuclear medicine procedures.

- Should be easily available, cheap and easy to prepare
- Should have high sensitivity and high specificity to detect infection
- Should differentiate between acute and chronic infection
- Should differentiate between infection and sterile inflammation
- Should be non-immunogenic and non-toxic
- Minimum radiation burden to the patient

Table 1. Characteristics of an ideal skeletal infection imaging agent.

RP	Mechanism of localisation	Advantages	Disadvantages
<sup>99m</sup> Tc -MDP	Increased vascularity and permeability. Uptake in areas of new bone formation	Simple to perform Very high sensitivity	Low specificity
<sup>99m</sup> Tc - HMPAO labeled leukocytes	Migration of WBCs into areas of infection	High specificity Reasonable sensitivity	Handling blood products Low sensitivity in chronic infection
<sup>99m</sup> Tc- Ciprofloxacin	Increased vascular permeability ? Binding to bacteria	Simple preparation High sensitivity	Specificity not proven yet.
<sup>68</sup> Ga- citrate	Vascular permeability Binds to transferrin, lactoferrin and siderophores	More specific than diphosphonates	Long half life. Radiation burden
<sup>111</sup> In- Oxine labeled leukocytes	Migration of WBCs into areas of infection	High specificity	Long half life Prolonged imaging times Radiation burden is higher.
<sup>18</sup> F- FDG	Uptake by GLUT receptors. Localises in areas of increased glycolysis	Simple with high sensitivity	Higher cost. Specificity yet to be proven
<sup>18</sup> F- FDG labeled WBC	Migration of WBCs into areas of infection	High specificity	Handling blood products. Skilled person is necessary

Table 2. Radiopharmaceuticals for skeletal infection imaging

4. Radionuclide imaging of osteomyelitis

4.1 Acute osteomyelitis

Patients with acute osteomyelitis usually present with pain and swelling at the involved site with systemic features of infection. Among the radionuclide techniques, the three phase bone scan is the frequently used for evaluating acute osteomyelitis. The three phase bone scan reveals increased perfusion, soft tissue blood pooling and bony uptake in a typical case of acute osteomyelitis (Fig.1). In some patients, especially pediatric population, there may be a cold area (cold osteomyelitis) [5]. Spread of infection to the joint space can be detected, if

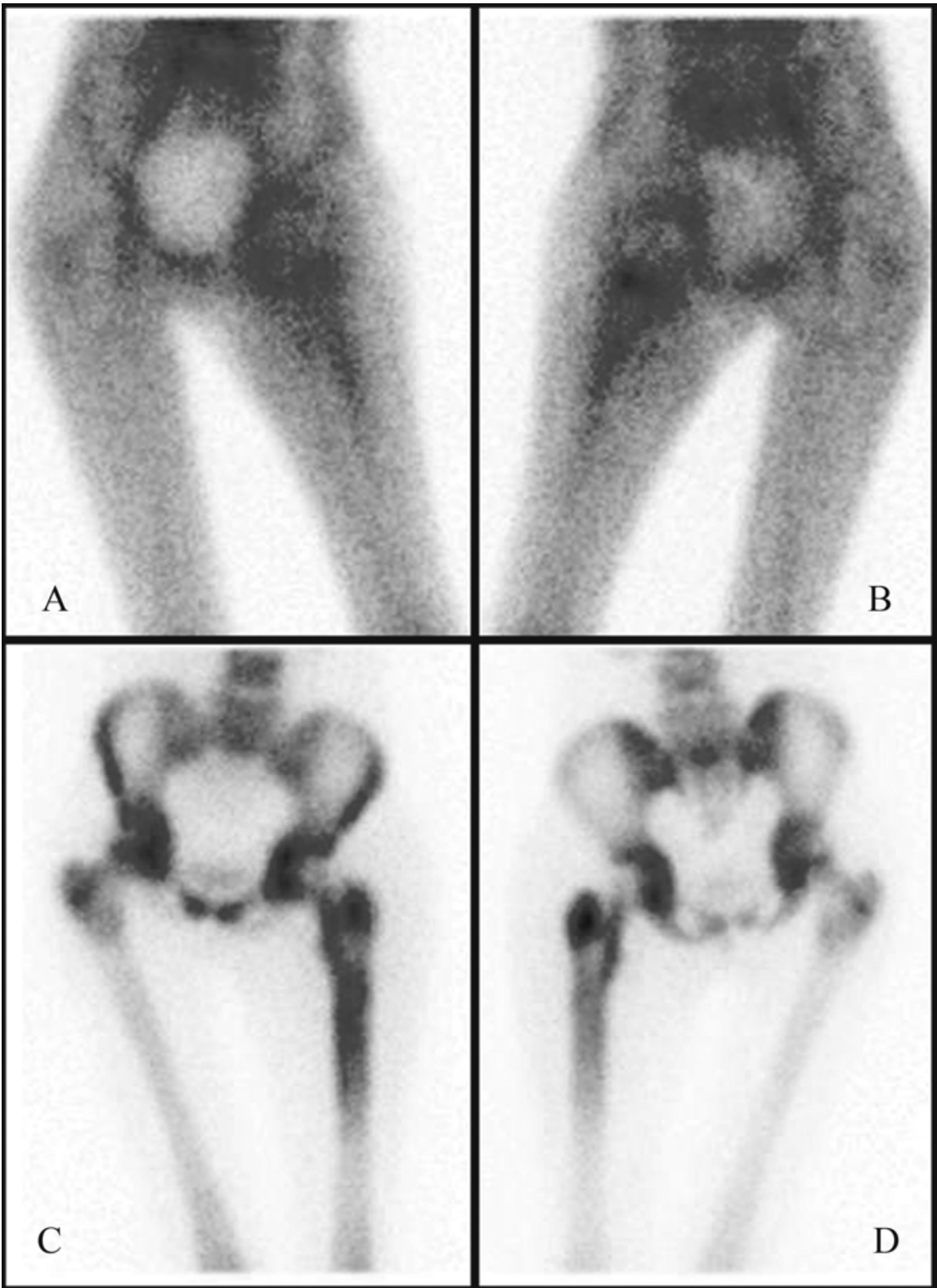


Fig. 1. Images of three phase bone scintigraphy of a patient with osteomyelitis of the left femur. Blood pool images in the anterior (A) and posterior (B) views show increased perfusion and soft tissue pooling of tracer around the proximal part of the left femur. Bone phase images in the anterior (C) and posterior (D) views also show increased tracer uptake in the proximal shaft of the left femur.



there is any. In the absence of previous insult to the bone, the clinical and radionuclide imaging features are adequate for the diagnosis of acute osteomyelitis. Though labeled leukocytes are highly specific for the diagnosis, they are usually not indicated. Labelled leukocytes imaging, because of the limited spatial resolution cannot differentiate between soft tissue and bone infection in the peripheral skeleton. Addition of hybrid imaging techniques like SPECT/CT helps in precise anatomical localization. Among the various conventional nuclear medicine procedures,  $^{111}\text{In}$ -labeled leukocytes is one of the most specific imaging techniques and is useful in acute infection, in osteomyelitis of the diabetic foot, and in the neuropathic joint. Disadvantages in imaging with Indium labeled leukocytes include need for prolonged imaging, combining with bone marrow imaging, higher radiation burden, need for handling blood and limited availability.  $^{99\text{m}}\text{Tc}$ -labeled leukocytes are a better alternative. Images are acquired at 1, 4 & 24-h. However, interpretation without bone marrow imaging is difficult.

#### 4.2 Chronic osteomyelitis

Chronic and low grade infections are more difficult to diagnose with the routine imaging modalities. Bone / Gallium imaging is extremely useful in cases of vertebral osteomyelitis. FDG PET has a special role in the evaluation of chronic infection because the activated macrophages avidly take up FDG. A negative FDG PET can virtually rule out osteomyelitis [6]. FDG PET is also better than labeled leukocyte imaging for axial skeleton. FDG-PET and FDG-PET/CT have many advantages over conventional nuclear medicine imaging techniques: complete image acquisition within 1 hour, high sensitivity, high target-to-background contrast, and high-resolution tomographic images. PET/CT also provides exact anatomic localization of FDG uptake and increases the specificity compared with PET alone. The logistics of the PET technique make its use easier in chronic than in acute inflammation.

#### 4.3 Disc space infection

Diagnosis of disc space infection is a challenge. Radiography may be normal within the first 8 weeks. Contrast enhanced MRI shows high sensitivity in the early diagnosis of disc space infection. Degenerative lesions in the spine can potentially mimic infection on MRI. Three phase bone scintigraphy and labeled leukocytes have a limited role. Bone scintigraphy with  $^{67}\text{Ga}$  SPECT is the radionuclide imaging of choice. Recently, FDG-PET has been shown to have higher sensitivity and specificity than gallium SPECT. Paravertebral soft tissue involvement can also be detected by PET. FDG PET is also useful in excluding disc space infection when equivocal MRI findings are present. One study has shown FDG PET to be 100% sensitive and specific while MRI had sensitivity of only 50% [7].

#### 4.4 Prosthesis Infection

Nearly 700,000 hip and knee arthroplasties are performed annually in the United States [8]. Although, the clinical results of these procedures in the vast majority of cases are excellent, these implants do fail. Failures caused by heterotopic ossification, fracture, and dislocation are now relatively rare and usually can be diagnosed radiographically [9]. Failure caused by aseptic loosening, however, has continued to increase in frequency.

More than one-quarter of all prostheses eventually demonstrate evidence of loosening, often necessitating revision arthroplasty [10]. The most frequent cause of aseptic loosening is an inflammatory reaction to one or more of the prosthetic components. Particulate debris, produced by component fragmentation, presumably attracts and activates tissue phagocytes normally present around the prosthesis. The heightened inflammatory response leads to osteolysis, causing loss of supporting osseous tissues and, eventually, loosening of the prosthesis.

Infection, although uncommon, is perhaps the most serious complication of joint arthroplasty surgery, ranging in frequency from about 1% to 2% for primary implants, to about 3% to 5% for revision implants. Approximately, one-third of prosthetic joint infections develop within 3 months, another one-third within 1 year, and the remainder more than 1 year after surgery. Histopathologically, the inflammatory reaction that accompanies the infected prosthesis can be similar to that present in aseptic loosening, with one important difference: neutrophils, which usually are absent in aseptic loosening, are invariably present in large numbers in infection [10,11]. The treatment of infected hardware often requires multiple admissions. An excisional arthroplasty, or removal of the prosthesis, is performed, followed by a protracted course of antimicrobial therapy. A revision arthroplasty eventually is performed. Aseptic loosening, in contrast, usually is managed with a single-stage exchange arthroplasty requiring only 1 hospital admission and 1 surgical intervention [10, 12]. Because their treatments are so different, distinguishing infection from aseptic loosening of a prosthesis is extremely important.

Unfortunately, differentiating aseptic loosening from infection can be challenging. Clinical signs of infection often are absent. Increased peripheral blood leukocytes, erythrocyte sedimentation rate, and C-reactive protein levels are neither sensitive nor specific for infection. Joint aspiration with Gram stain and culture is considered the definitive diagnostic test; its sensitivity, however, is variable, ranging from 28% to 92%. Its specificity is more consistent, ranging from 92% to 100% [13]. Among the various imaging studies, plain radiographs are neither sensitive nor specific and cross-sectional imaging modalities, such as computed tomography and magnetic resonance imaging, can be limited by hardware induced artifacts. Radionuclide imaging is not affected by metallic hardware and is the current imaging modality of choice for evaluation of suspected joint replacement infection.

## **5. Scintigraphic techniques**

### **5.1 Bone scintigraphy**

Bone scintigraphy is an extremely sensitive investigation for detecting bone disorders. Its role in the evaluation of painful joint replacement has been extensively investigated. Magnuson and coworkers [14] reviewed 49 painful lower-extremity joint replacements and found that 3-phase bone scintigraphy was 100% sensitive, 18% specific, and 53% accurate for diagnosing infection.

Weiss and coworkers, [15] using focally increased uptake at the tip of the femoral component or in the region of the acetabular component as the criterion for an abnormal study, reported that bone scintigraphy was 100% sensitive and 77% specific for diagnosing infection or loosening of the total hip replacement.



Williamson and coworkers [16] found that focal periprosthetic uptake was associated with aseptic loosening, whereas diffuse uptake around the femoral and acetabular components was associated with infection.

Increased periprosthetic activity on bone images reflects increased bone mineral turnover, which can result from any of a number of conditions besides infection. This problem is further complicated by the numerous patterns of periprosthetic uptake associated with asymptomatic hip and knee replacements. Up to 10% of asymptomatic patients will have persistent periprosthetic uptake after 1 year of joint replacement. Assessment of the total knee replacement with bone scintigraphy also is problematic, with more than 60% of femoral components and nearly 90% of tibial components demonstrating persistent periprosthetic activity more than 12 months after implantation.

The overall accuracy of radionuclide bone imaging in the evaluation of the painful prosthetic joint is about 50-70%, too low to be clinically useful, except perhaps as a screening test, or in conjunction with other radionuclide studies like gallium or labeled leukocyte imaging.

5.2 Bone / gallium imaging

<sup>67</sup> Gallium Citrate has the propensity to accumulate in sites of infection and inflammation. When combined with a sensitive investigation like bone scan, the specificity of gallium study will help in better identification of infected prostheses. Reing and coworkers [17] evaluated 79 joint replacements with both bone and gallium scintigraphy. Bone scintigraphy had 100% sensitivity in identifying infected prostheses, but also was abnormal in 50 uninfected prostheses, rendering it very nonspecific (15%). In contrast, gallium had 95% sensitivity and 100% specificity in identifying infected prostheses. These results suggest that performing gallium imaging in addition to bone scintigraphy greatly enhances the accuracy of the radionuclide diagnosis of the infected joint replacement.

Gallium accumulates in both septic and aseptic inflammation, as well as in the bone marrow, and in areas of increased bone mineral turnover in the absence of infection. In an effort to improve the accuracy of both bone and gallium imaging, the two studies are often interpreted together, according to standardized criteria (Table 3).

Test result	Bone /Gallium Finidngs
Positive	a. Distribution of the 2 tracers is spatially incongruent b. Distribution is spatially incongruent with intensity of gallium uptake is greater than diphosphonate
Negative	a. Gallium images are normal b. Distribution of tracers is spatially incongruent with intensity of gallium uptake is lesser than diphosphonate
Equivocal	a. Distribution of the 2 radiotracers is congruent, both spatially and in terms of intensity

Table 3. Interpretation of combined bone / gallium imaging in the diagnosis of infection

However, many studies have reported less satisfactory results with combined bone gallium imaging. Overall, combined bone/gallium imaging, with an accuracy of about 65-80%, offers only a modest improvement over bone scintigraphy alone.

### 5.3 Labelled leukocyte imaging and leukocyte / bone imaging

Theoretically, labeled leukocyte imaging should be well suited for diagnosing the infected joint replacement because white cells usually do not accumulate at sites of increased bone mineral turnover in the absence of infection. However, its efficacy in infected prostheses has been disappointing. Poor sensitivity of labeled leukocyte imaging for diagnosing prosthetic joint infection has been attributed to the chronic nature of the process. Combining leukocyte imaging with bone imaging has been shown to increase the specificity of the study marginally (Fig.2).

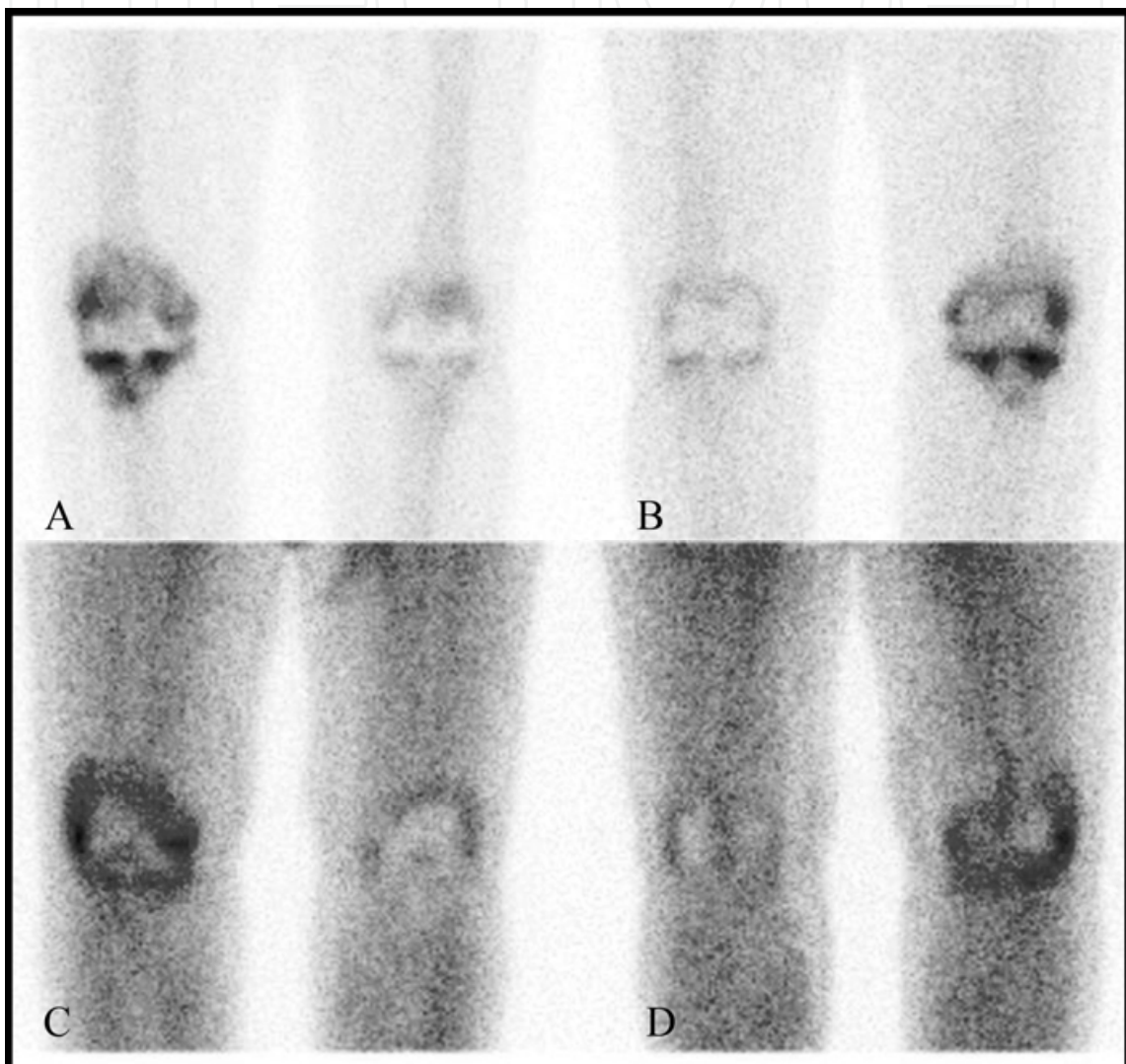


Fig. 2. Bone scintigraphic images of the knees in the anterior (A) and posterior (B) views showing increased tracer accumulation around the right knee joint. On labeled leukocyte imaging intense leukocyte accumulation around the right knee is noted in the anterior (C) and posterior (D) static images. Surgery confirmed infection around the knee prosthesis.

### 5.4 Leukocyte / bone marrow imaging

Labeled leukocyte and bone marrow images both reflect radiotracer accumulation in the reticuloendothelial cells, or fixed macrophages of the marrow. The distribution of bone

marrow activity is similar on leukocyte and bone marrow images in normal individuals as well as in those with underlying marrow abnormalities, i.e, the images are spatially congruent. However, in osteomyelitis there is spatially incongruent uptake i.e. accumulation of leukocytes with a cold spot in bone marrow imaging.

The quoted sensitivity, specificity, and accuracy of leukocyte/ marrow imaging were 96%, 87%, and 91%, respectively. The test was significantly more accurate than bone (50%), bone/gallium (66%), and leukocyte/bone imaging (70%) in their population. These results confirm the sensitivity and specificity of leukocyte/marrow imaging for diagnosing prosthetic joint infection as well as its superiority over other radionuclide tests (Fig.3). However, meticulous labeling of blood, handling of blood products, potential for spread of infection and prolonged imaging are the main disadvantages in this technique.

### 5.5 FDG PET imaging

Positron emission tomography has the inherent advantages of high sensitivity, high resolution and ability to acquire tomographic images. The procedure is simple, rapid and requires no handling of blood products. Zhuang and coworkers [18] evaluated FDG-PET in 74 joint prostheses, 21 of which were infected. Studies were considered positive for infection when an area of increased uptake was identified at the bone prosthesis interface. They reported a sensitivity, specificity, and accuracy of 90%, 89.3%, and 89.5%, respectively, for prosthetic hip infection, and sensitivity, specificity, and accuracy of 90.9%, 72%, and 77.8%, respectively, for prosthetic knee infection. Though, the FDG PET/CT patterns for infected elbow prostheses have not been reported, pattern of aseptic loosening has been described [19].

### 5.6 Labeled antibiotics

Ciprofloxacin, a broad spectrum antibiotic was labeled with <sup>99m</sup>- Technetium. It was hypothesized that this tracer will be concentrated only in the sites of infection and thus may be useful in differentiating sterile inflammation and infection (Fig.4). However, further studies have shown that localization is primarily due to tracer extravasation and stasis at the sites of increased vascular permeability. The tracer is rapidly cleared from circulation by the kidneys and shows no uptake in the bone marrow. Minimal localization is noted in the liver. Several studies have shown the ease of usage and good sensitivity of labeled ciprofloxacin in detection of osteomyelitis [20-23] . Recently, radiolabeled –third generation cephalosporin (Ceftriaxone) has been shown (Fig.5) to have improved sensitivity and specificity for the accurate diagnosis of active bacterial bony infections [24]. Labeled antibiotics can be used both in acute as well as chronic infections and it has also been tried in diabetic foot infections (Fig.6).

## 6. Imaging acute osteomyelitis

### 6.1 Imaging diabetic foot infections

Diabetic foot infections are one of the major causes of morbidity in diabetics. Imaging of diabetic foot infection poses several challenges. Infectious and non-infectious conditions affecting the foot of a diabetic often present clinically in a similar way. The conventional imaging techniques often are unable to ascertain the cause of the problem. Nuclear medicine techniques are of immense utility in differentiating and monitoring the different pathologies affecting the foot of a diabetic.



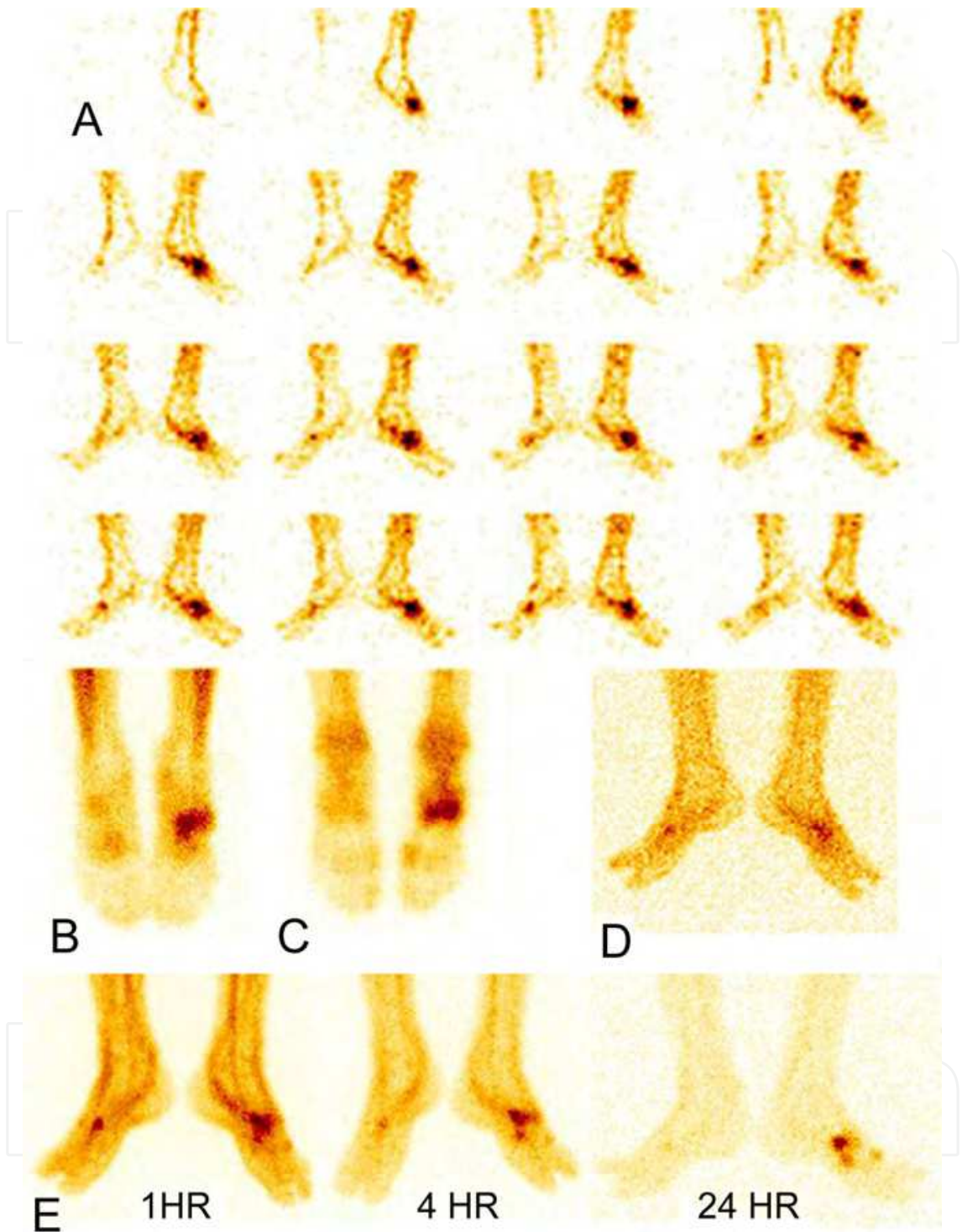


Fig. 3. Three phase bone scintigraphy of the feet with  $^{99m}\text{Tc}$ -MDP showing increased flow (A) and soft tissue concentration (B) of tracer in the mid part of the left foot. The delayed images (C) at 3h shows focally increased bony uptake of tracer in the mid-tarsal region, indicating active bony infection.  $^{99m}\text{Tc}$ -HMPAO labeled leukocyte images (E) at 1, 4, 24-h show focal tracer concentration in the mid-tarsal region of the left foot indicative of active infection. Bone marrow scan (D) performed 1-h after injection of 4.0 mCi of filtered  $^{99m}\text{Tc}$ -Sulfo-colloid shows mild uptake in the mid-tarsal region less than  $^{99m}\text{Tc}$ -MDP and labeled leukocyte uptake.

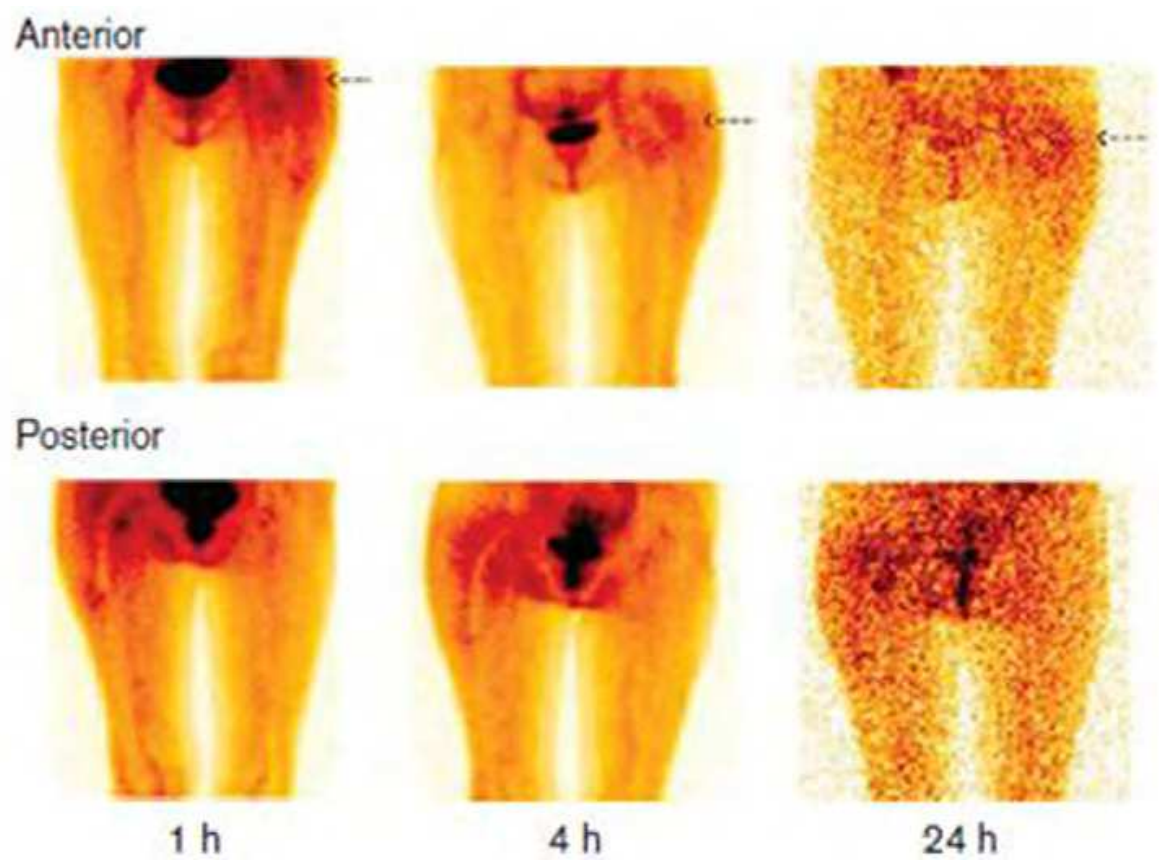


Fig. 4. 99mTc-Ciprofloxacin (Diagnobact™) scan (static anterior and posterior images) acquired at 1, 4 & 24h indicating increased radiotracer concentration in the region of left hip joint prosthetic (arrows)

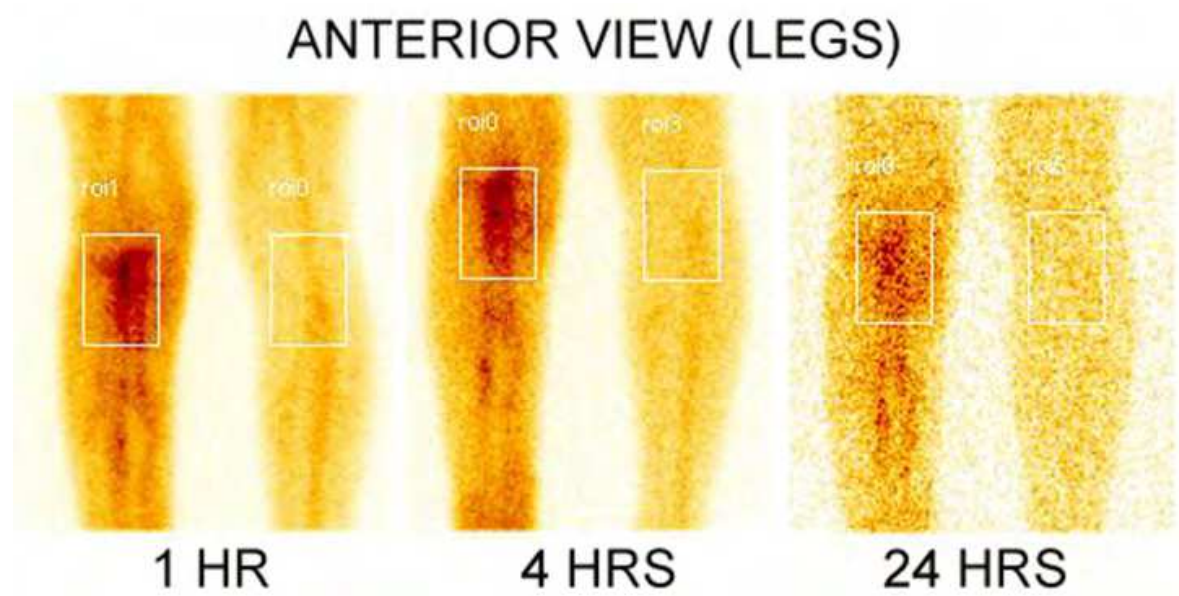


Fig. 5. 99mTc-Ceftriaxone (Scintibact) images of the legs showing focally increased concentration of the radiotracer in the proximal part of the right tibia. The radiotracer concentration remained consistent till 24-h of imaging time indicating active tibial infection



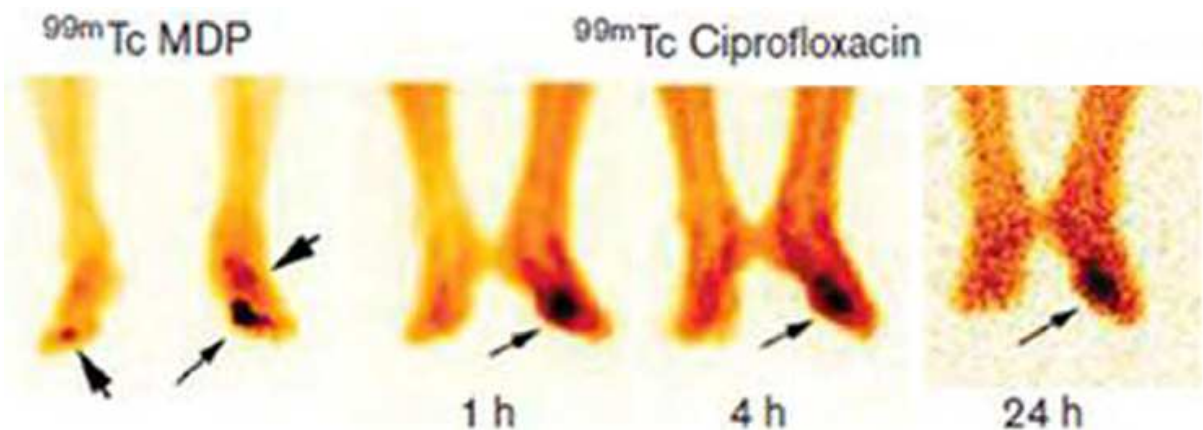


Fig. 6.  $^{99m}\text{Tc}$ -MDP bone scan in the diabetic foot showing two foci of abnormal tracer uptake in the left foot and one focus in the right foot with  $^{99m}\text{Tc}$ -ciprofloxacin scan indicating only one focus of increased tracer concentration in the left foot (arrow) at 1, 4 & 24h.

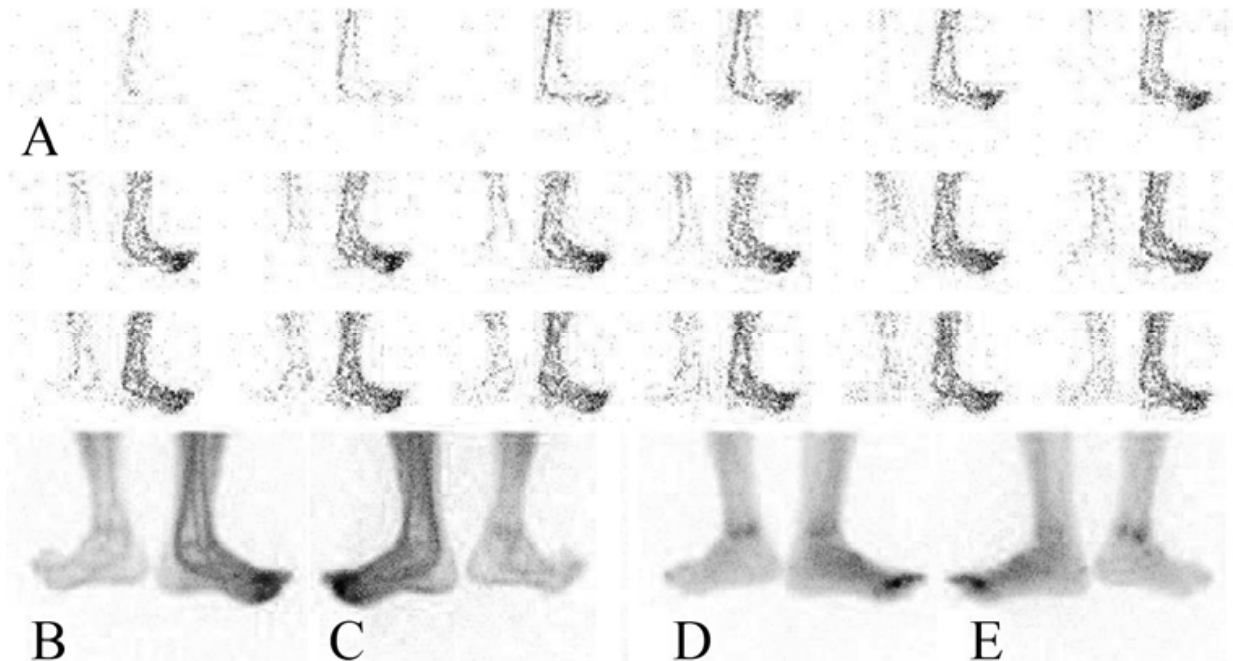


Fig. 7. Three phase bone scintigraphy in a diabetic patient with an ulcer in the left foot showing increased flow of tracer in the perfusion phase (A) images. Blood pool images in the medial (B) and lateral (C) and bone phase images in the medial (D) and lateral (E) views also show increased soft tissue pooling and increased tracer uptake in the fore foot region indicating active infection. SPECT CT (not shown here) localized the tracer uptake in the head of 2nd metatarsal.

Up to 25% of diabetic patients are at risk of developing pedal ulcers. Diagnosis of osteomyelitis is often overlooked in diabetic patients because of the lack of pain and systemic inflammatory response. Bone scintigraphy has low specificity in diabetic patients. The sensitivity may reach up to 100%. Low specificity is due to conditions that mimic osteomyelitis i.e. trauma, fracture and neuropathic joints (Fig.7). An attempt to increase the specificity of bone scintigraphy is the fourth phase bone scan. This is based on the fact that tracer accumulation in woven or immature bone continues for several hours leading to an



increase in the lesion to background ratio in the fourth phase than the third phase bone scan. However, woven bone is also present in fractures and degenerative changes apart from osteomyelitis. Labeled leukocyte imaging is one of the most sensitive and specific investigation for diabetic foot infections [25-27]. The results are read in conjunction with the findings of the bone scintigraphy findings. One of the main disadvantages of labeled leukocytes imaging in diabetic patients is the co-existence of neuropathic joints. Labeled leukocytes accumulate both in infected and uninfected neuropathic joints. This is due to the presence of hematopoietically active bone marrow in neuropathic joints. Combining with bone marrow imaging helps in distinguishing infected from non-infected neuropathic joints. Addition of SPECT/CT helps in differentiating soft tissue from bone infection, though the lower resolution of SPECT images makes this difficult in the foot. FDG PET/CT is also being tried in diabetic foot. Some studies have shown the ability of PET to differentiate between infected and neuropathic joints using SUV values.

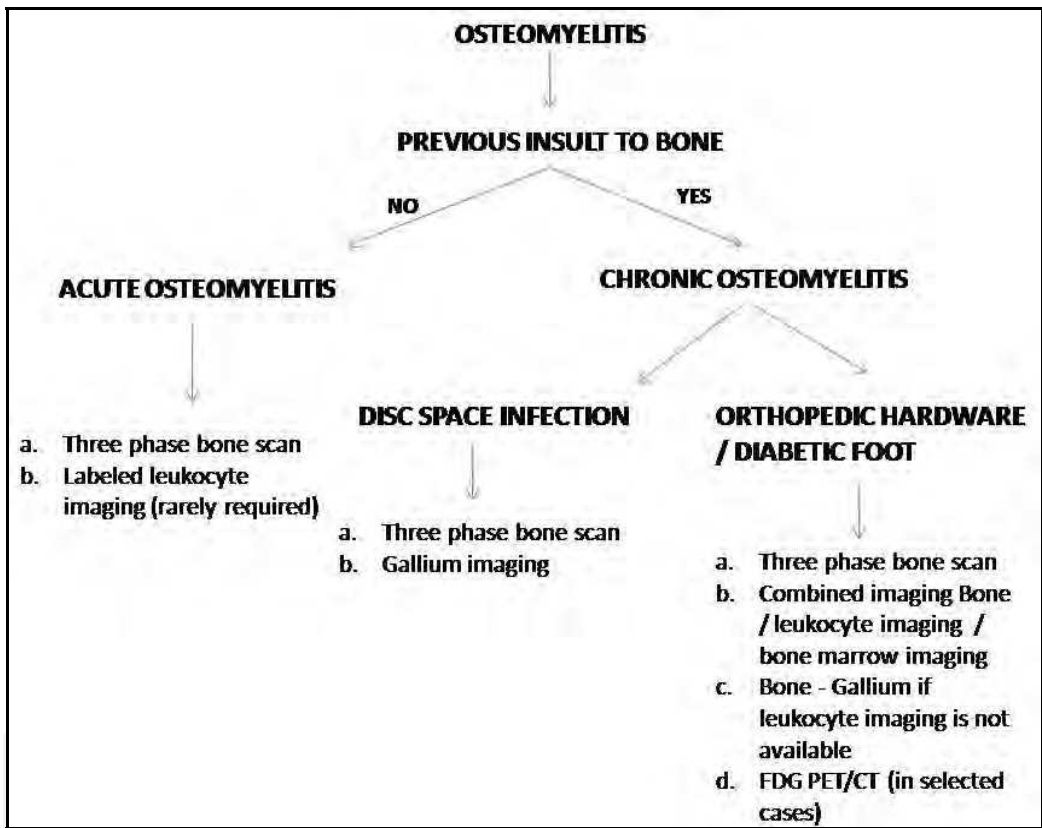


Table 4.

7. Conclusion

Diagnosis of osteomyelitis can be made clinical in a majority of patients without previous insult to the bone. However, with history of previous insult like fracture, surgery or previous infection, the diagnosis becomes more and more difficult. Conventional imaging modalities often fail in these patients. Nuclear medicine techniques owing to the functional information provided, is ideally suited for these patients. A variety of nuclear medicine and PET techniques are available for evaluation of these patients. Each of the nuclear medicine modalities has their own strengths and weaknesses. The decision to subject the patient to a

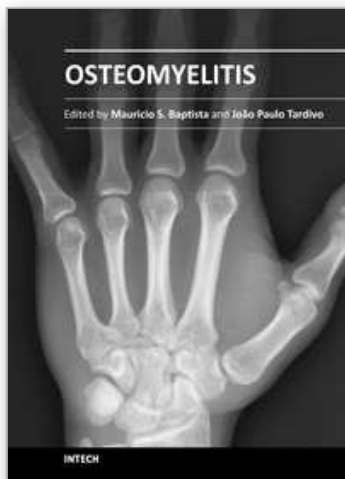
particular nuclear medicine technique is to be taken on a case by case basis and is illustrated as a Flow chart (table 4).

Nuclear medicine techniques add a new dimension to the diagnosis of osteomyelitis. They are also extremely effective monitoring tools. With the advent of fusion imaging such as SPECT/CT and PET/CT, the combined morphologic and functional information available has made significant impact in the effectiveness of nuclear medicine investigations.

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## **Osteomyelitis**

Edited by Prof. Mauricio S. Baptista

ISBN 978-953-51-0399-8

Hard cover, 180 pages

**Publisher** InTech

**Published online** 23, March, 2012

**Published in print edition** March, 2012

If you want to learn more about osteomyelitis you should not miss this book. The editors are professionals and scientists working in health sciences and the chapters have been prepared by experts in the field, covering subjects related with the fundamentals of osteomyelitis and new diagnosis and treatment tools. You will have the opportunity to review concepts as well as to learn state-of-the-art alternatives for diagnosis and treatments.

### **How to reference**

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Baljinder Singh, Sarika C.N.B. Harisankar, B.R. Mittal and Bhattacharya Anish (2012). Role of Nuclear Medicine in Infection Imaging, Osteomyelitis, Prof. Mauricio S. Baptista (Ed.), ISBN: 978-953-51-0399-8, InTech, Available from: <http://www.intechopen.com/books/osteomyelitis/role-of-nuclear-medicine-in-infection-imaging>

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