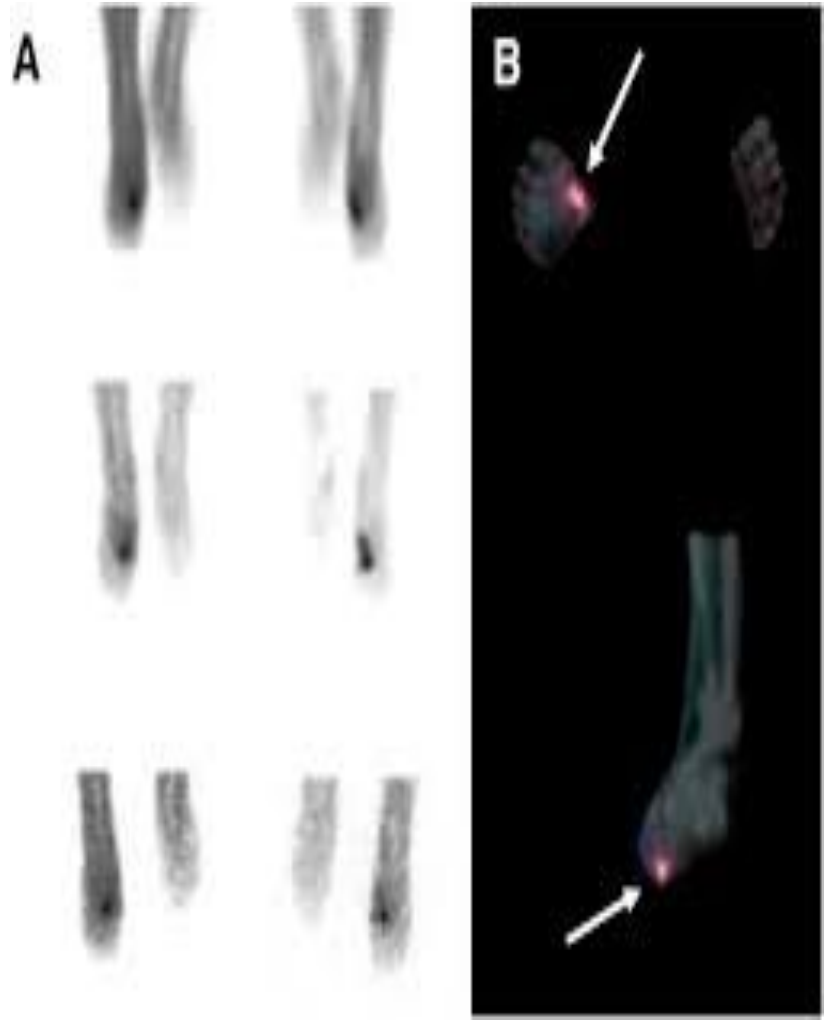
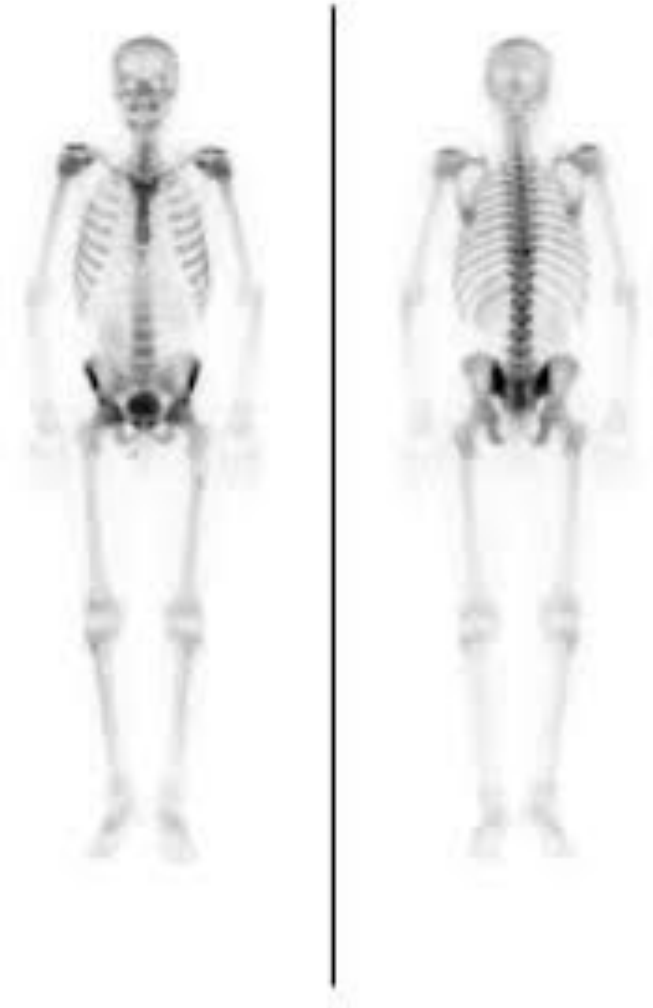


Nuclear medicine In Diabetic foot

Dr.Mohseni
Nuclear Medicine Physician

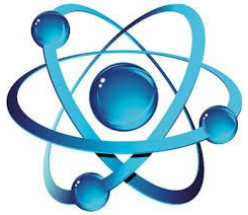
Nuclear medicine techniques to diagnose infections in diabetic foot include:

- Three-phase bone scintigraphy
- Scintigraphy with radiolabeled leukocytes
- PET/CT with [18F] FDG



Bone Scintigraphy

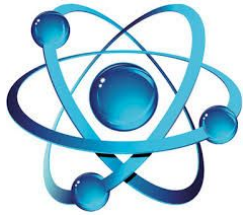
Why Bone Scan ???



Bone scintigraphy is a sensitive technique that can detect significant metabolic changes very early, often several weeks or even months before they become apparent on conventional radiological images. In addition, the technique provides an overview of the entire skeleton at a relatively modest radiation exposure.

While the diagnostic sensitivity of bone scintigraphy is very high, the low specificity often requires further investigation with other imaging modalities (e.g. plain radiography, CT or MRI) or nuclear medicine studies (e.g. FDG PET/CT). For this reason, anatomical imaging and bone scintigraphy should be considered as complementary methods.

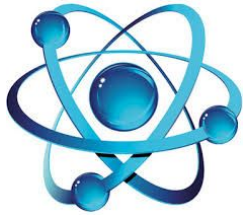
MRI



MRI can efficiently discriminate soft-tissue infection from bone involvement and can effectively detect the development of infection in anterior parts of the bone; however, efficacy is dramatically compromised at the midfoot and hindfoot.

Despite high sensitivity, the application of MRI for the recognition of osteomyelitis in the diabetic foot is compromised by lower specificity regarding Charcot neuropathic osteoarthropathy.

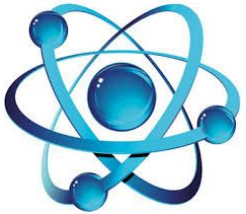
In addition, if there is an inflammatory hyperemia, the diagnostic accuracy is further decreased to 40%–50%



Phosphonates concentrate in the mineral part of bone, nearly two thirds in hydroxyapatite crystals and one third in calcium phosphate. Two major factors control the accumulation of phosphonates in bone, namely blood flow and extraction efficiency, which in turn depend on capillary permeability, acid– base balance, parathyroid hormone levels, etc.

Peak activity through the kidneys is reached after approximately 20 min.

99mTechnetium-MDP

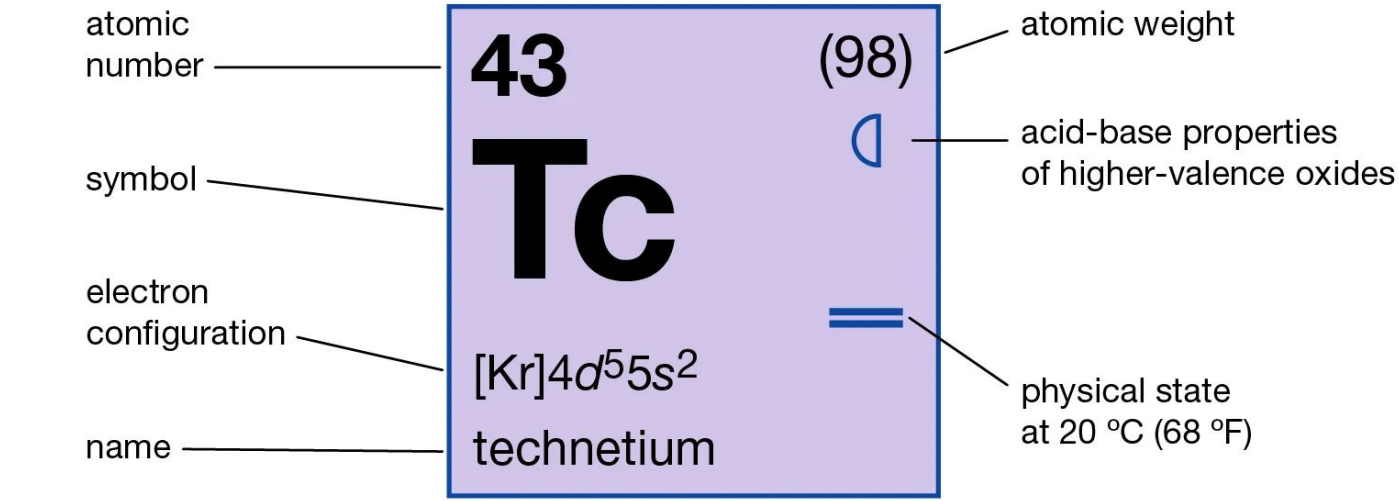


Technetium-99m is used as a radioactive tracer and can be detected in the body by medical equipment (gamma cameras). It is well suited to the role, because it emits readily detectable gamma rays with a photon energy of 140 keV (these 8.8 pm photons are about the same wavelength as emitted by conventional X-ray diagnostic equipment) and its half-life for gamma emission is 6.0058 hours (meaning 93.7% of it decays to ^{99}Tc in 24 hours).

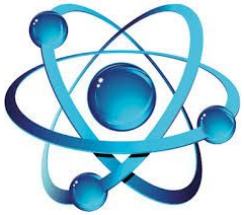
The relatively "short" physical half-life of the isotope and its biological half-life of 1 day (in terms of human activity and metabolism) allows for scanning.

The molecules most commonly used for performing bone scintigraphy are bisphosphonates: methylene diphosphonate (MDP), hydroxymethylene diphosphonate (HMDP) or hydroxyethylene diphosphonate (HDP), and 2,3dicarboxypropane-1,1-diphosphonate (DPD)

Technetium



( ) indicates the mass of the longest-lived isotope.



The first isotopes to be synthesized were ^{97}Tc and ^{99}Tc in 1936

have no stable isotopes

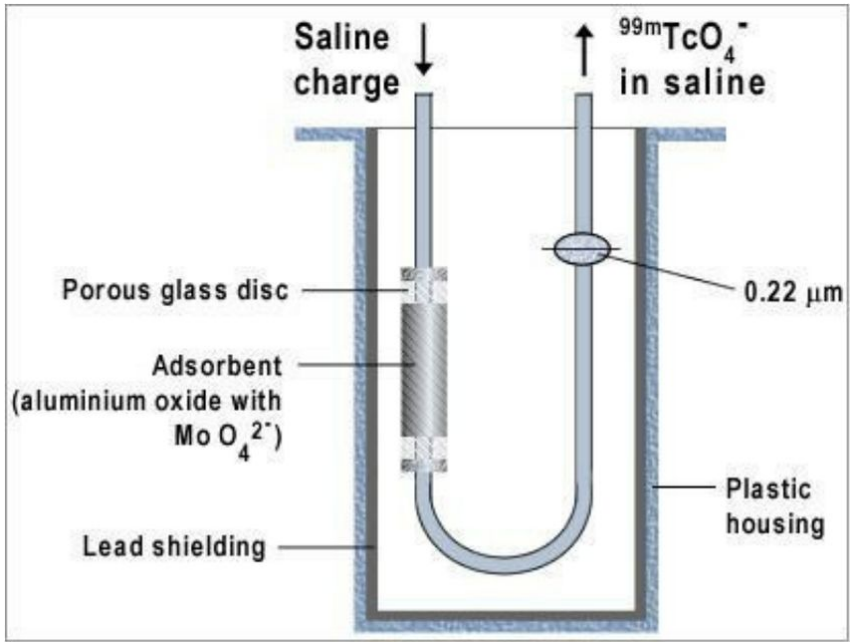
Thirty-three other radioisotopes have been characterized with atomic masses ranging from ^{85}Tc to ^{120}Tc

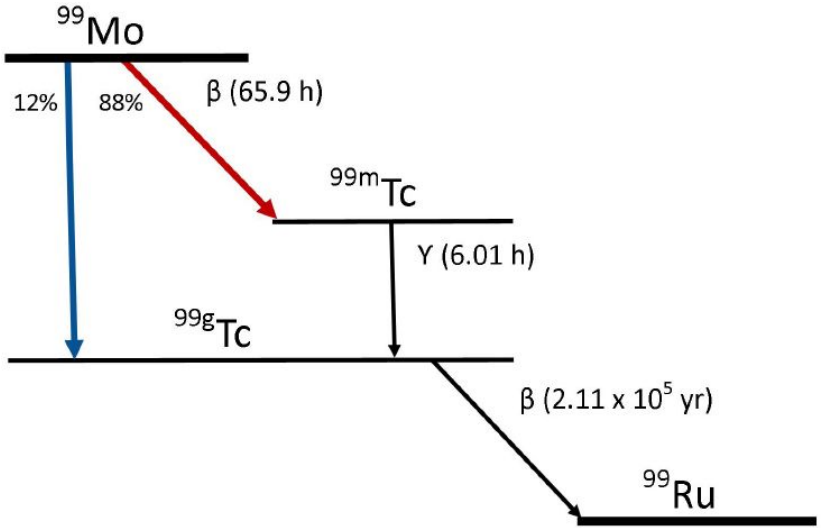
Technetium-99 is the most common and most readily available isotope, as it is a major fission product from fission of actinides like uranium and plutonium

Isotopes of technetium ($_{43}$Tc)

Main isotopes[1]			Decay	
	abun-dance	half-life ($t_{1/2}$)	mode	pro-duct
^{95m}Tc	synth	61.96 d	β^+	^{95}Mo
			IT	^{95}Tc
^{96}Tc	synth	4.28 d	ε	^{96}Mo
			γ	–
^{97}Tc	synth	4.21×10^6 y	ε	^{97}Mo
^{97m}Tc	synth	91.1 d	IT	^{97}Tc
			ε	...
^{98}Tc	synth	4.2×10^6 y	β^-	^{98}Ru
			β^+	–
^{99}Tc	trace	211.1×10^3 y	β^-	^{99}Ru
^{99m}Tc	synth	6.01 h	IT	^{99}Tc
			β^-	–


PARS ISOTOPE company
PARSTEC® II


Saline charge
$^{99m}TcO_4^-$ in saline
Porous glass disc
0.22 μm
Adsorbent (aluminium oxide with MoO_4^{2-})
Plastic housing
Lead shielding


^{99}Mo
12%
88%
β (65.9 h)
^{99m}Tc
Y (6.01 h)
^{99g}Tc
β (2.11 x 10^5 yr)
^{99}Ru

MDP cold kit

• MDP (methylene diphosphonic acid)	5.0 mg
• Stannous chloride dihydrate	0.80 mg
• Ascorbic acid	0.50 mg

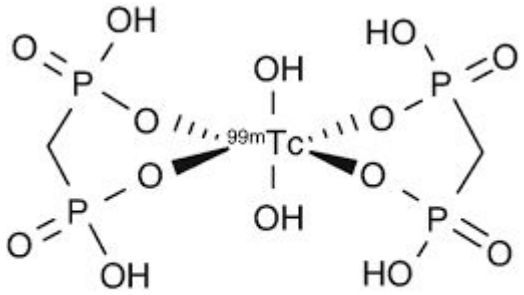
After adding a sterile and pyrogen free solution of pertechnetate $^{99m}TcO_4^-$, one obtains an injectable solution of ^{99m}Tc -MDP with the following characteristics:

• Volume	2 - 5 mL
• Max. Activity	300 mCi
• Radiochemical purity	> 90.0 %
• pH	5 - 6
• Stability of ^{99m}Tc - MDP	6 hrs

These kits can be used until the expiry date of the batch (1to2 years after the date of manufacture).

Radiotracer preparation

- Injection sterile ^{99m}Tc(up to 300 mCi) aseptically into the vial in a volume of 2-5 mL.
- Dissolve the lyophilized material by shaking the vial for 10 seconds and wait for 15 minutes.
- Examine the radiochemical purity (RCP).
- Labelled preparation is to be used within 6 hrs. Within this period the total RCP of ^{99m}Tc-MDP should be more than 95.0%



[^{99m}Tc]Tc-MDP

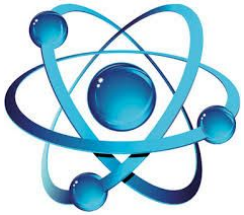
- Store the kit 2 – 8 °C and protect from light
- Store the reconstituted kit 15 – 25 °C

Pharmacokinetics

The injected radiolabelled bisphosphonates adsorb to the surface of hydroxyapatite crystals in proportion to local bone vascularization and osteoblastic activity.

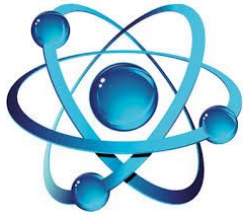
Tracer elimination through the gastrointestinal tract is insignificant. Maximum bone accumulation is reached 1 h after tracer injection and remains practically constant up to 72 h.

Patient preparation



- They may eat and drink (no fasting)
- Report a pregnancy or active breastfeeding
- In patients with severe pain, an appropriate analgesic strategy should be implemented in consultation with the treating/referring physician
- Be well hydrated, drink one or more litres of water during the time between injection and imaging and during the 24 h after scan
- Void their bladder frequently during the time between injection and delayed imaging as well as immediately prior to the scan

Possible drug interactions



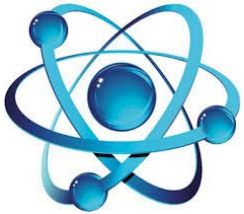
1. Aluminium: reduced skeletal tracer uptake, diffuse hepatic tracer uptake, increased renal tracer uptake

2. Androgen deprivation therapy for prostate cancer (bicalutamide, oestrogens): increased mammary tracer uptake in case of gynecomastia

3. Bone-modifying agents (including bisphosphonates and denosumab) or agents interfering with osteoblast function (e.g. cabozantinib): reduced skeletal tracer uptake

4. Corticosteroids: reduced skeletal tracer uptake, reduced tracer uptake at fracture site

Possible drug interactions



5. Haematopoietic growth factors: increased spinal tracer uptake, possible increased tracer uptake in the appendicular skeleton

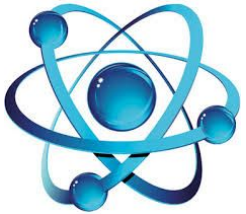
6. Iron:increased renal tracer uptake,increased tracer uptake at site of intramuscular injection, diffuse hepatic tracer uptake

7. Methotrexate: diffuse hepatic tracer uptake

8. Nephrotoxic chemotherapy: increased renal tracer uptake and reduced skeletal tracer uptake

9. Nifedipine: reduced skeletal tracer uptake

Precautions



- In patients on renal replacement therapy, haemodialysis performed from 15 min to 5 h after injection of the radiopharmaceutical can successfully decrease blood pool and soft tissue activity to nearly normal level.
- In a patient who is known or suspected to be pregnant, a clinical decision is necessary to consider the benefits against the possible harm of carrying out any procedure.
- While interruption in breastfeeding is not essential according to the ICRP, this is on the basis that there is no free pertechnetate in the radiopharmaceutical. Therefore, an interruption of at least 4 h during which one meal is discarded is advised.

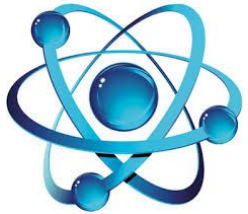
Administered activity

In adults,the average activity administered by a single intravenous injection should be 500 MBq (300–740 MBq, 8–20 mCi)

8 and 10 MBq/kg

obese adult patients: 11–13 MBq/kg

Imaging Protocol



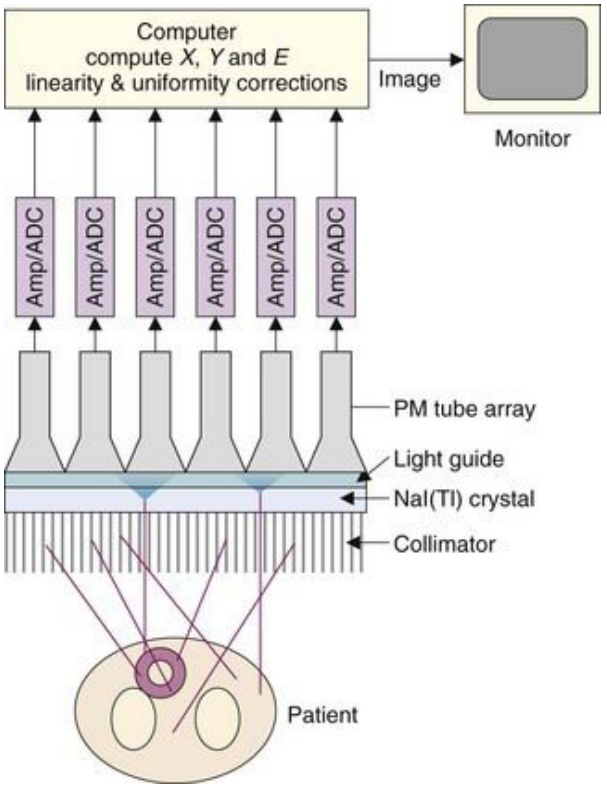
by a double-head SPECT scintillation camera with a low-energy all-purpose collimator using a matrix of 128 × 128 on a 20% window at a 140-keV peak.

Multiphase bone scan

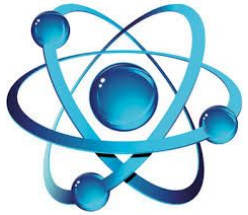
The flow phase is acquired during intravenous injection, for 60 s, followed by a blood-pool image,the soft tissue distribution of the radiopharmaceutical in the region of interest, is performed within the first 5–10 min after injection. Finally, delayed whole-body, using the same projections for at least 500,000 counts., focal views, and/or tomographic images are usually acquired between 2 and 4 h after injection.

In some patients, it may be useful to acquire late-phase images up to 24 h.

Gama camera

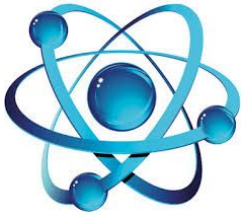

Computer
compute X, Y and E
linearity & uniformity corrections
Image
Monitor
Amp/ADC
Amp/ADC
Amp/ADC
Amp/ADC
Amp/ADC
Amp/ADC
PM tube array
Light guide
NaI(Tl) crystal
Collimator
Patient

24 hr imaging indications:



- increase the time between tracer injectin and image acquisition(6–24 h) in order to optimize the bone-to background ratio
- If the skeleton is poorly visualized (e.g. renal insufficiency)
- for the imaging of specific anatomical regions (e.g. the pelvis patients with urinary retention
- the distal extremities in patients with peripheral circulatory disorders
- in older patients with impaired bone metabolism (osteoporosis, osteomalacia)

SPECT/CT



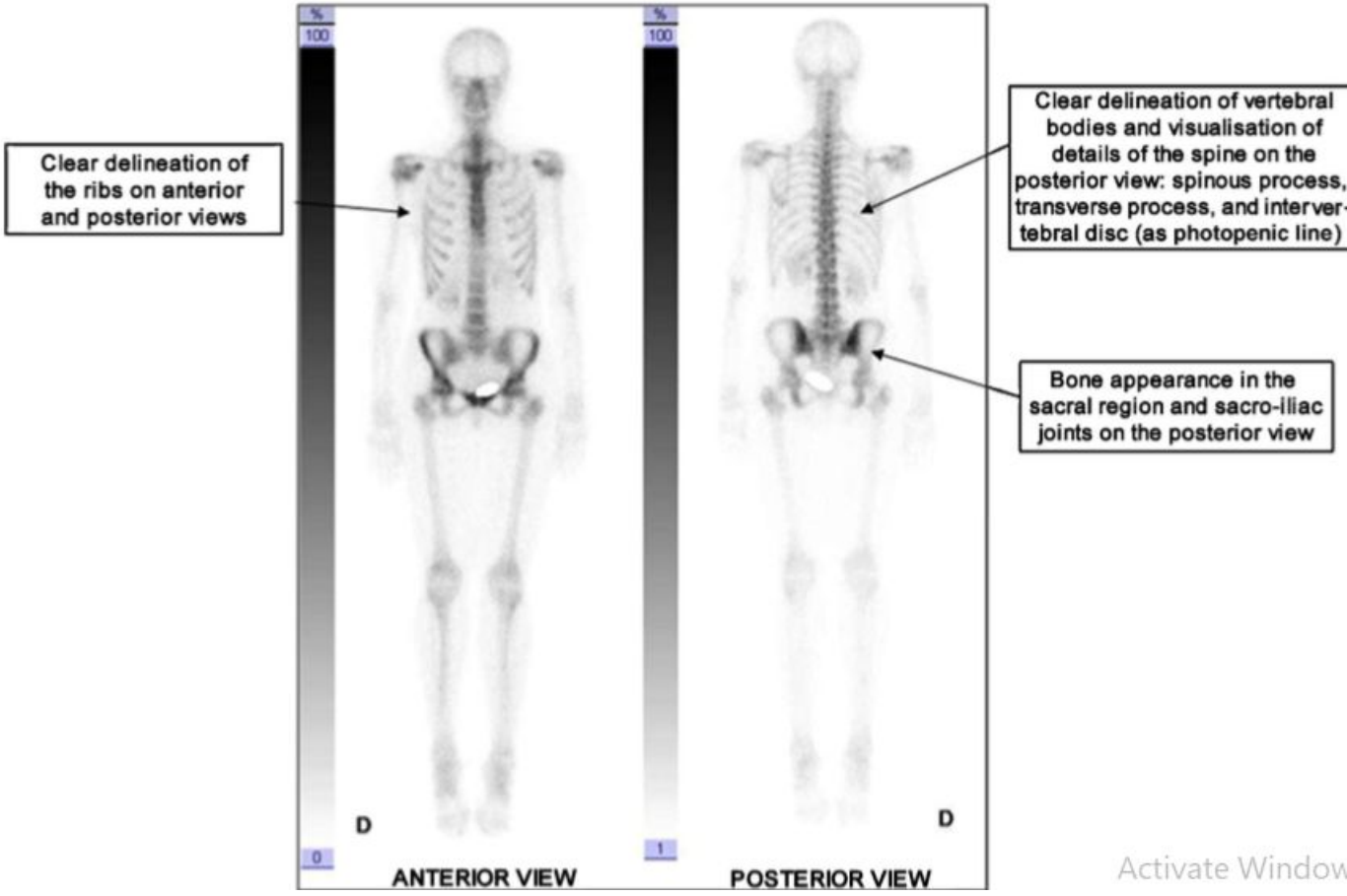
Diagnostic sensitivity and specificity of bone scanning can be significantly increased by using SPECT or, if available, SPECT/CT.

allows the visualization of the three dimensional distribution of the radiopharmaceutical in the skeleton, assist in localizing anomalies seen on the whole-body images and to improve lesion contrast

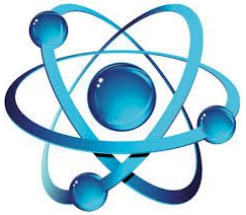
The detector heads oriented in a 180° geometry, a total of 60 or 64 frames per detector head, each with duration of 10 to 30 s are acquired over 360° into a 128×128 matrix (pixel size 4.6×4.6 mm)

Normal distribution

Particular attention should be paid to the symmetry and homogeneity of tracer uptake. Image quality should be assessed before starting to report scan findings

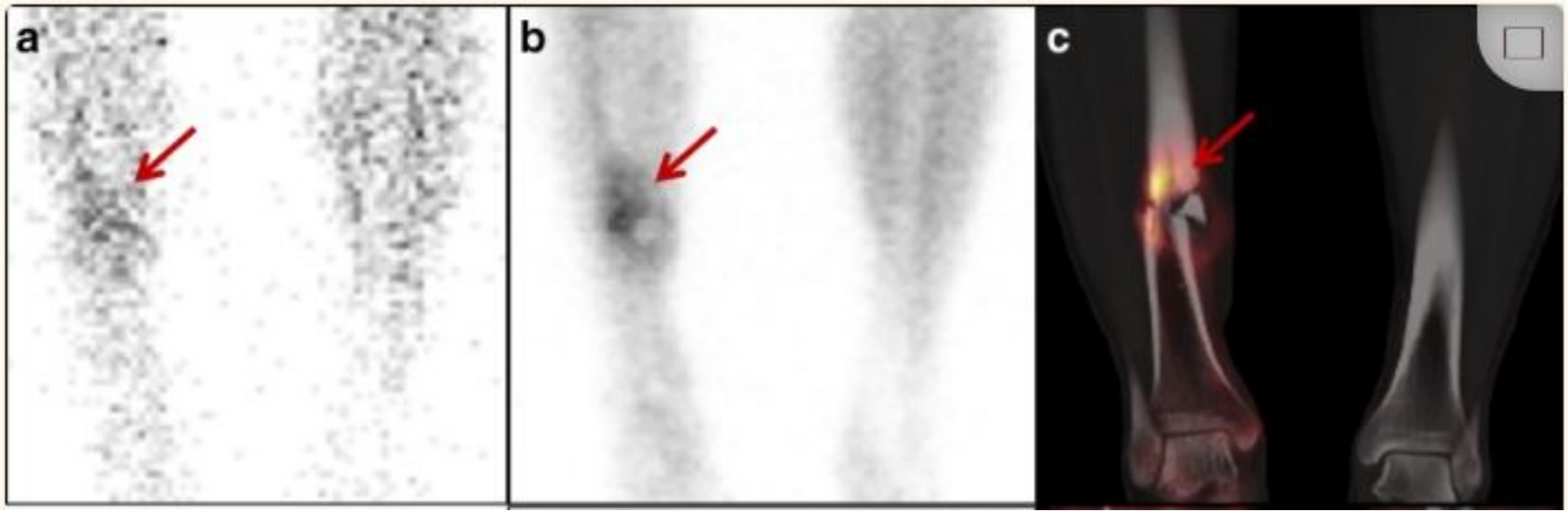


Soft tissues findings



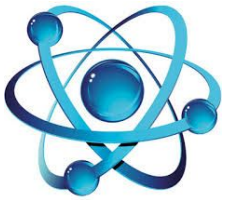
A diffusely increased soft tissue uptake can be caused by drug interference, failed 99mTc labelling, severe osteoporosis,renal failure,dehydration,or an insufficiently long interval between tracer injection and image acquisition.

A low or absent tracer uptake in the soft tissues may be caused by an excessive avidity for the tracer of osteoblasts populating the axial skeleton, resulting in a super bone scan appearance or an excessively long interval between tracer injection and imaging



Increased blood flow (*arrow*) and blood pool activity (*arrow*) was detected on the perfusion (a) and blood pool (b) phase of the 3-phase bone scan and matched increased bone uptake (*arrow*) was seen at the fracture site on the bone SPECT/CT image (c, coronal view)

Cellulitis



diffuse increased uptake occurs in the first two phases, but uptake is normal

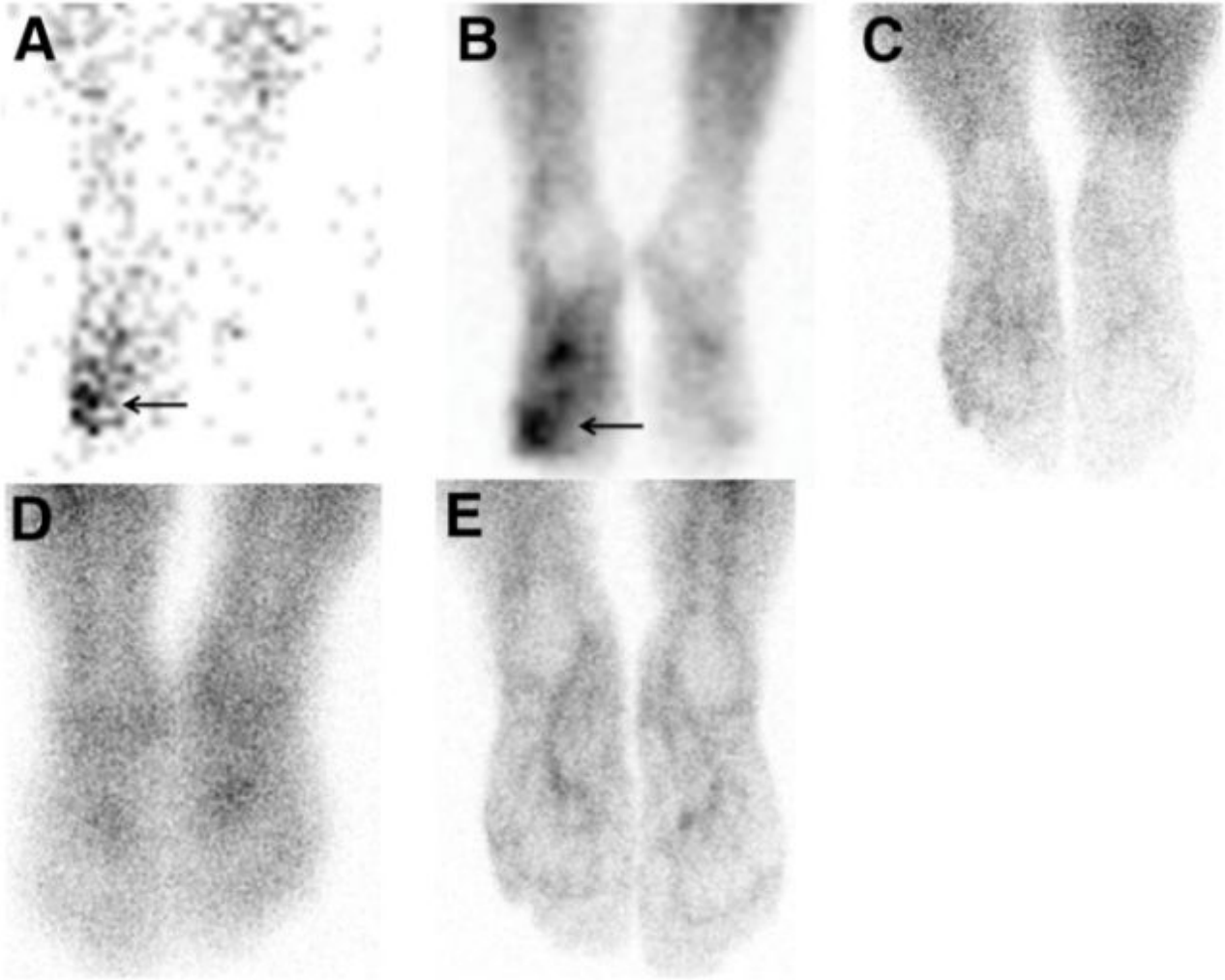
or diffusely increased in the third phase. If present, diffuse increased uptake in the third phase is probably due to regional hyperemia caused by the cellulitis

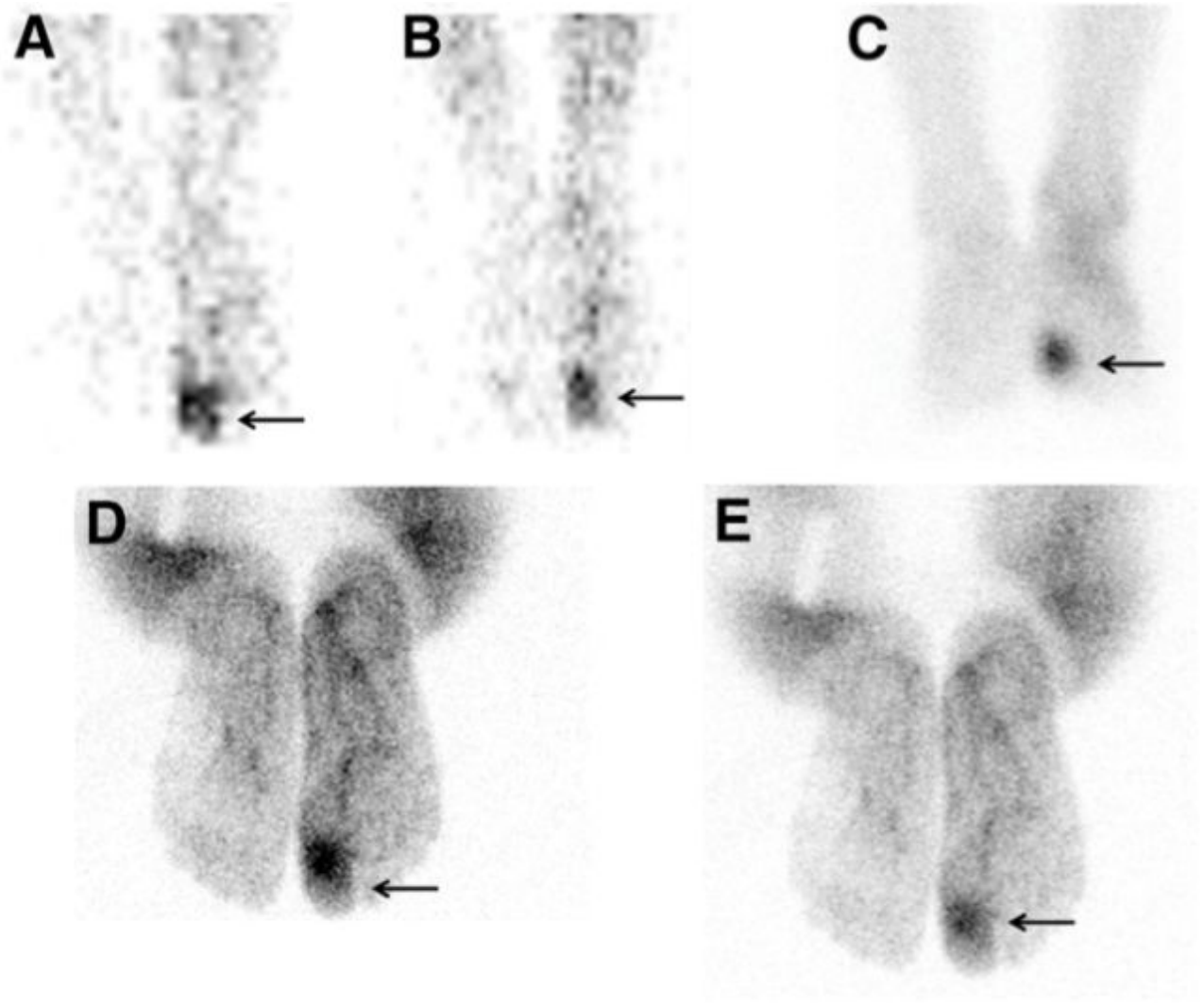
adding a 24-hr image to the three-phase bone scan to create the four-phase bone scan. The amount of radionuclide in the lesion vs the amount in normal bone should continue to increase during the fourth phase, if the lesion is osteomyelitis

Uptake of 99mTc-methylene diphosphonate stops at about 4 hr in lamellar bone (normal skeleton) but continues for about 24 hr in woven bone (abnormal bone around osteomyelitis and bone tumors)

False-positive results have been reported for degenerative diseases and metastases

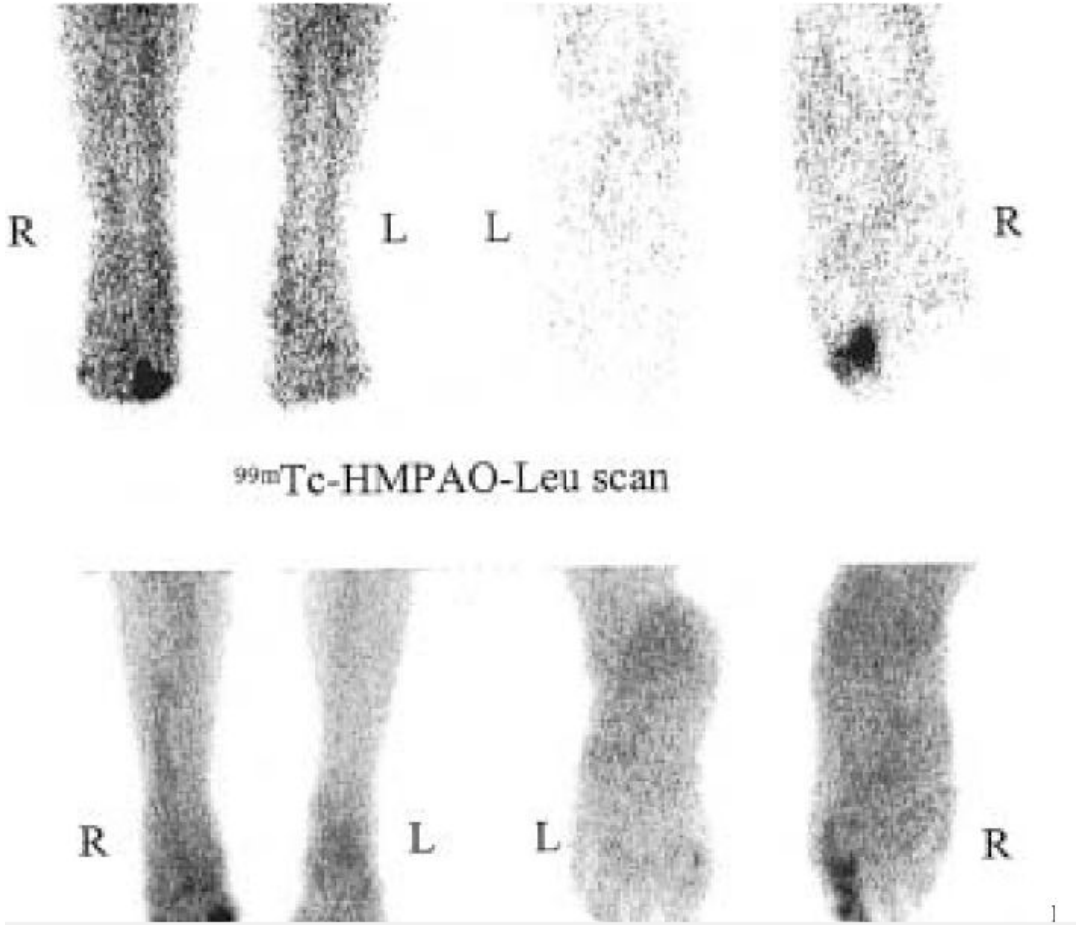
Significant uptake of 99mTc-MDP is seen in left fifth metatarsi in flow and blood-pool phases of skeletal scintigraphy, but activity is normal in delayed phase(celulitis)



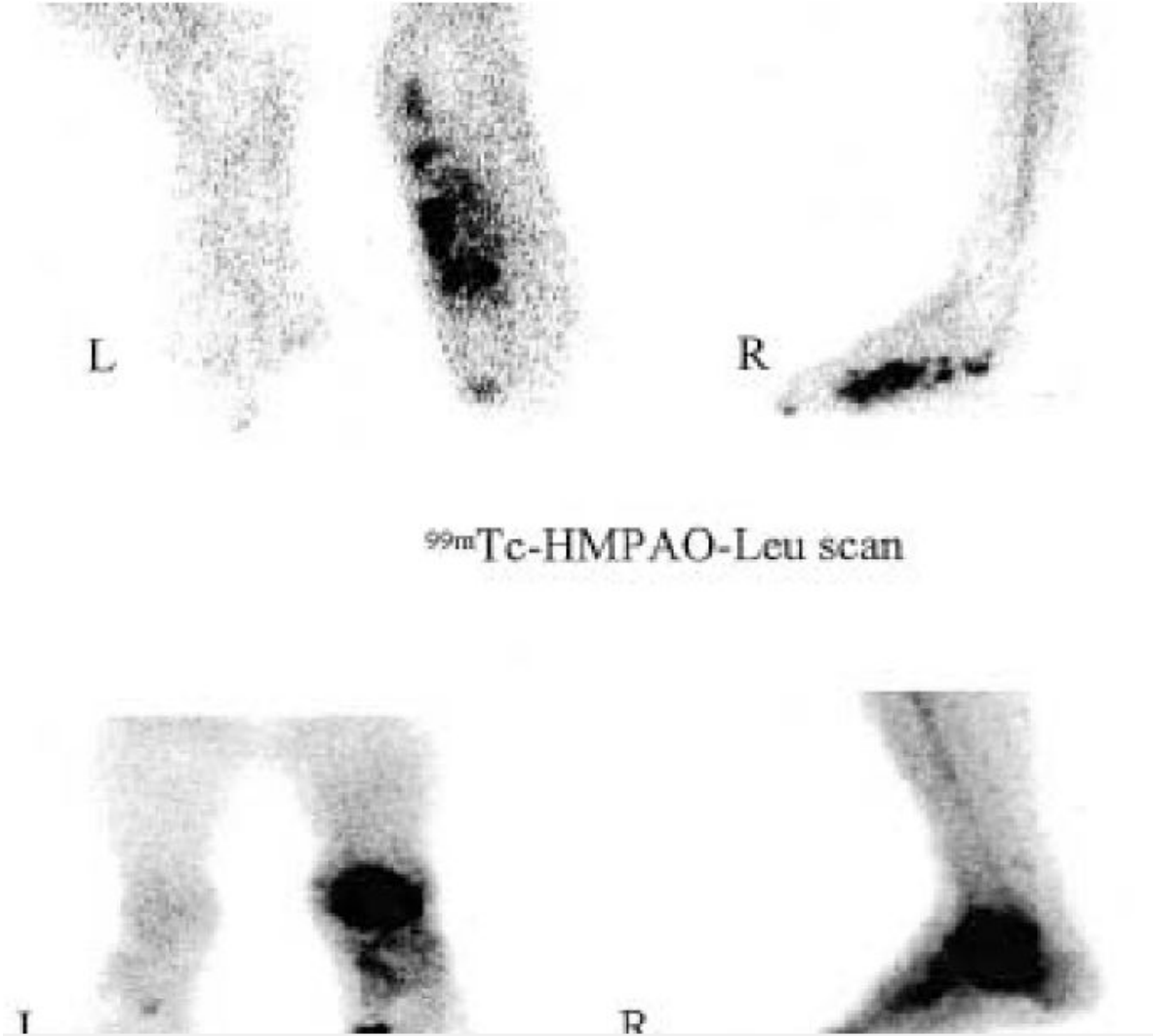


Significant uptake of 99mTc-MDP is seen in right first toe in all 3 phases of skeletal scintigraphy

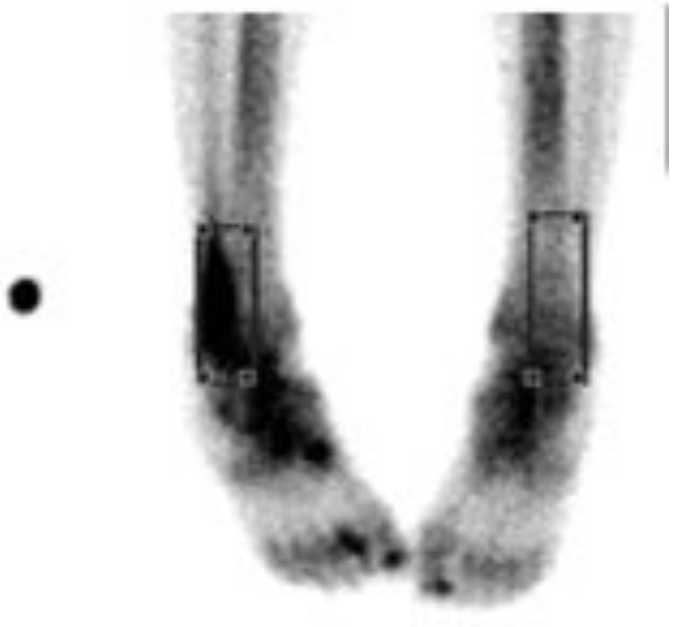
Ulcer of the right first toe. Focal MDP uptake on bone scintigraphy (bottom) concordant with HMPAO accumulation on leucocyte scintigraphy (top): Osteomyelitis of the right first toe.



Two ulcers (heel and midfoot) of the right foot with neuroarthropathy. Intense HMPAO uptake at the midfoot (top) without concordant MDP uptake (bottom): Soft-tissue infection of the midfoot.

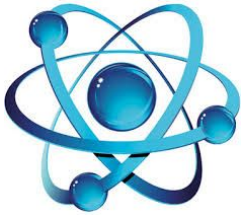


Quantitative Uptake of ^{99m}Tc-MDP



A/N ratio in patients with no evidence of osteomyelitis was 2.1 ± 1.2(A;abnormal)

Radiation dosimetry



- The organ that receives the largest dose of radiation is bone.
- 50 % of the injected activity is absorbed by the skeleton with an uptake half-life of 15 min, 15 % of the injected activity is retained in the skeleton with a clearance half-life of 2h,and the remaining 35% of the injected activity shows a clearance half-life of 3 days.
- The effective dose for an adult is in the order of 3–4 mSv and in children 2.5 mSv
- The much lower milliampere-second values used for localization or attenuation correction CT scans result in maximum effective doses of 3 mSv
- For hospitalized patients all solid waste is collected for 3 days and kept in storage for 4 days to allow sufficient decay


THANK YOU!