Diagnosis of osteo-articular infection in nuclear medicine

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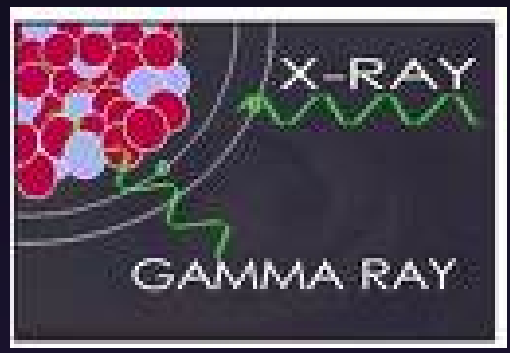
Some basic principles in Nuclear Medicine

Scintigraphy



- A tracer is injected (IV) which emits gamma-rays due to radioactive decay.
- Radioactivity comes from the inside of the patient, in contrast with X-ray or CT, in which radioactivity is emitted by a device and transmitted through the body.

Some basic principles in Nuclear Medicine

- Technetium-99m is the most often used tracer in nuclear medicine and is bound to a different ligand in function of the organ under study.
  - Technetium-labeled MDP (bone scan)
  - Technetium-labeled HMPAO (brain perfusion scan)
  - Technetium-labeled MAG3 (nephrogram)
  - Technetium-labeled MIBI (myocardial perfusion)

SPECT

- SPECT: Single Photon Emission Computed Tomography
- = tomoscintigraphie (Fr)
- SPECT images are tomographic acquisitions as in CT. The camera rotates around the patient and acquires data.

SPECT

- These data are reconstructed into slices in different planes (transversal, coronal and sagittal).
- SPECT increases sensitivity and specificity of the scintigraphy.
- No need for a new injection of radioactive tracer.

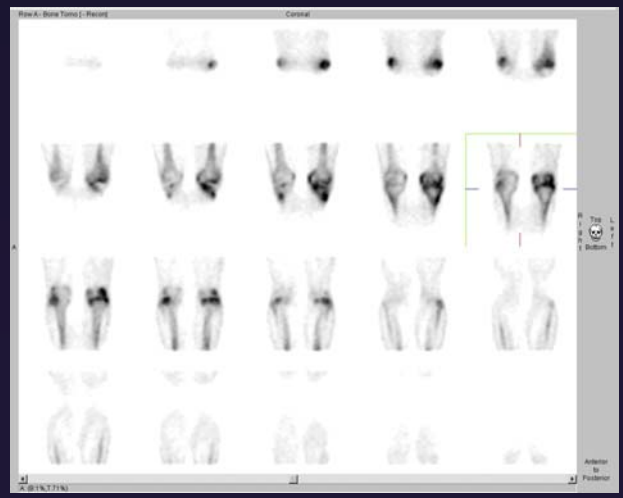
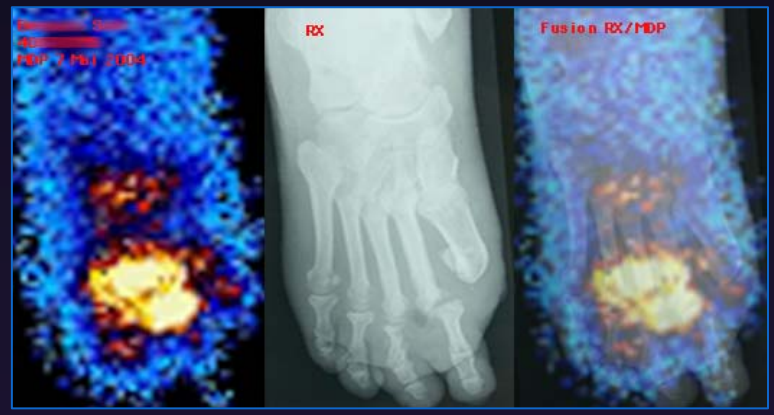


Image fusion

-> Can improve localization of scintigraphic lesions

Bone scan **X-ray** **Fusion**



Leucocyte scan **X-ray** **Fusion**

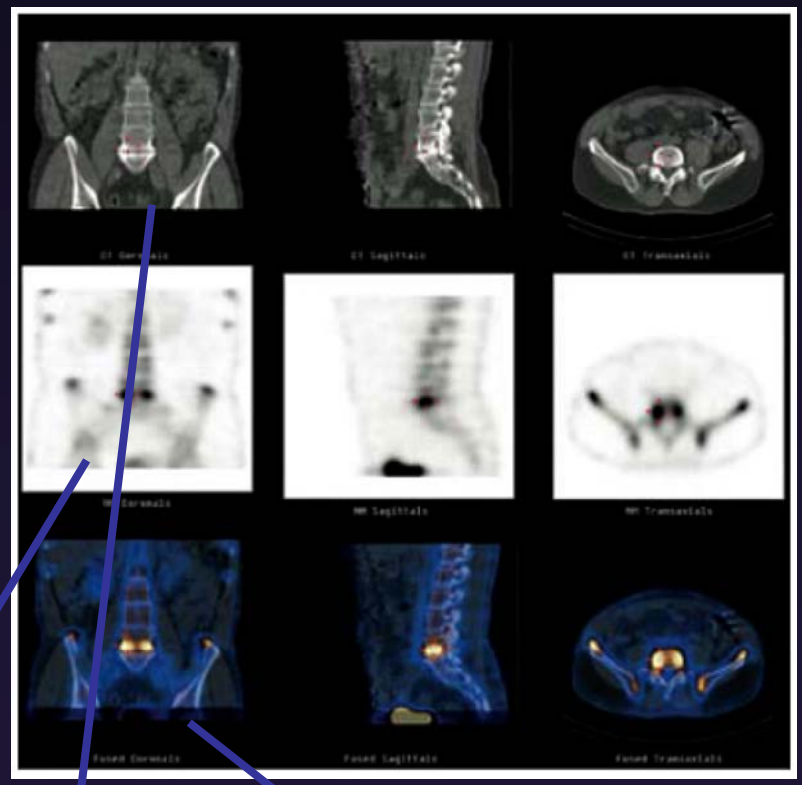
<u>Software fusion</u>

Scintigraphy is fused with an other imaging modality performed on a separate device with the help of a software program.

SPECT/CT

- SPECT/CT is a hybrid camera that couples a SPECT-camera with a CT-scan (hardware fusion).
- It resolves the problem of low resolution on scintigraphic imaging and allows to localize lesions more accurately.

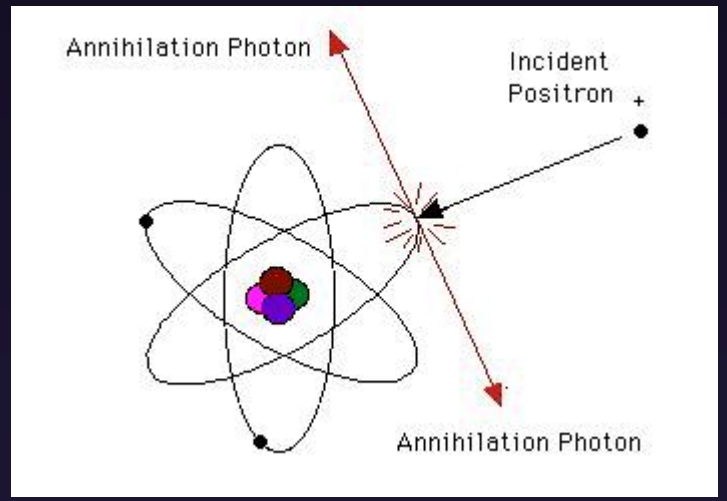
SPECT/CT



SPECT CT Fusion SPECT/CT

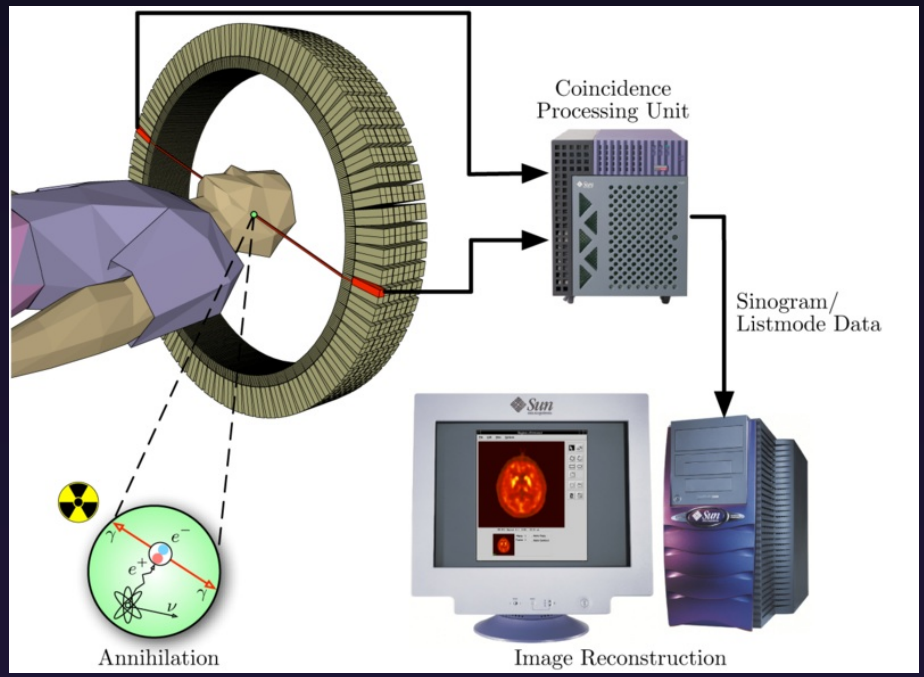
PET

- = Positron Emission Tomography
- A PET-tracer emits positrons.
- The positron annihilates with an electron, which produces a pair of annihilation photons moving in opposite directions.



PET

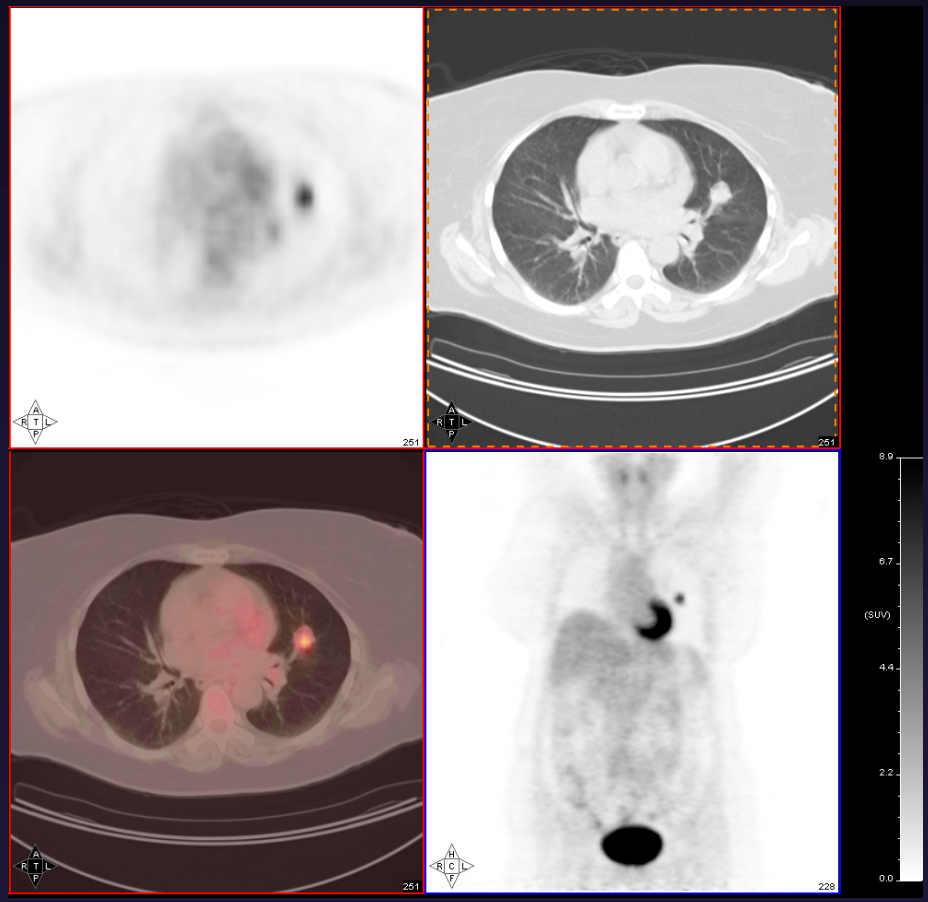
- These photons are registered when they reach simultaneously the detectors of the PET-scan. The PET technique depends on coincident detection of the pair of photons.



PET/CT

PET/CT

PET



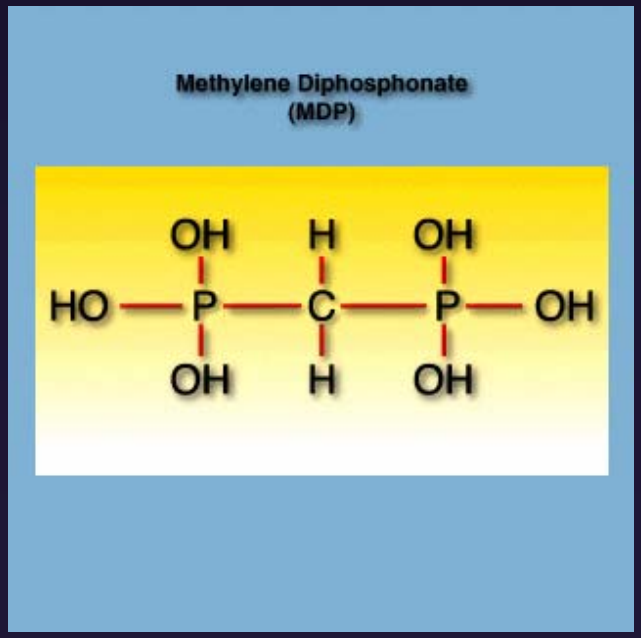
CT

Fusion
PET/CT

PET

Technetium-99m-MDP (Tc-MDP)

- The most often used scintigraphic tracer in imaging of OM is **MDP** (methylene diphosphonate), labeled with the radio-active isotope **Technetium-99m**



Tc99m-MDP : **bone scintigraphy**

- Technetium-99m emits gamma-rays and allows to trace the IV injected MDP.
- Uptake represents osteoblastic activity in the bone.
- Safe examination, no morbidity, suited for claustrophobia patients
- Easily accessible

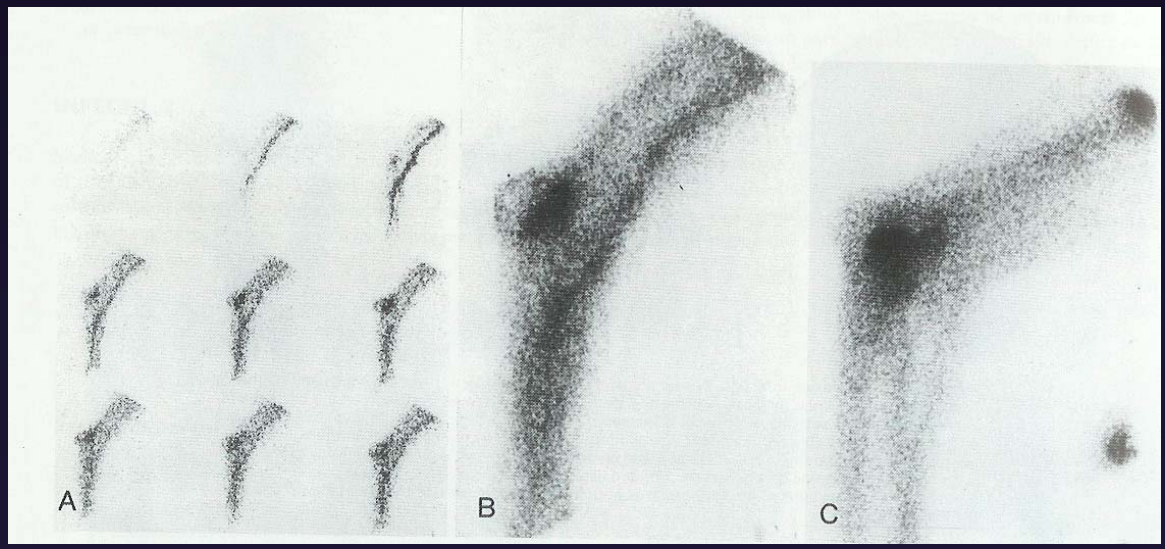
Bone scintigraphy

- Bone scintigraphy is highly sensitive for OM and is + within 48 h.
- A negative bone scan rules out OM in adults.
- In children, OM often presents as a photopenic defect
  - Vascular occlusion < subperiosteal edema and vasospasm

3 phase bone scan

- In most centers, standard approach to assess for OM with bone scintigraphy is with a **3-phase** bone scan to examine **perfusion**, soft-tissue **blood pool**, and delayed **bone** uptake
- At moment of injection: arterial + blood pool images (< 10 minutes).
- After 3-4h of bone uptake: the bone phase images
  - total body scan : 20 minutes
  - Static views: 2-4 minutes each
  - SPECT: 12 minutes

3 phase bone scan



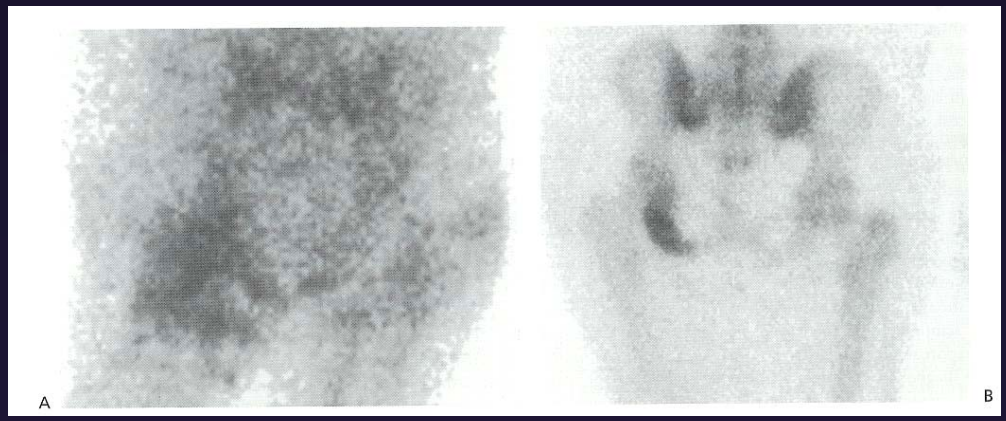
Perfusion Blood pool Bone phase

3 phase bone scan

- Main advantage of a study with early phases is its high negative predictive value:
  - normal perfusion excludes the presence of an acute inflammatory process.
  - In case of cellulitis w/o OM, increased tracer activity occurs only in the initial imaging phase
- OM manifests as an area of focally increased activity on delayed bone phase images

Bone scan

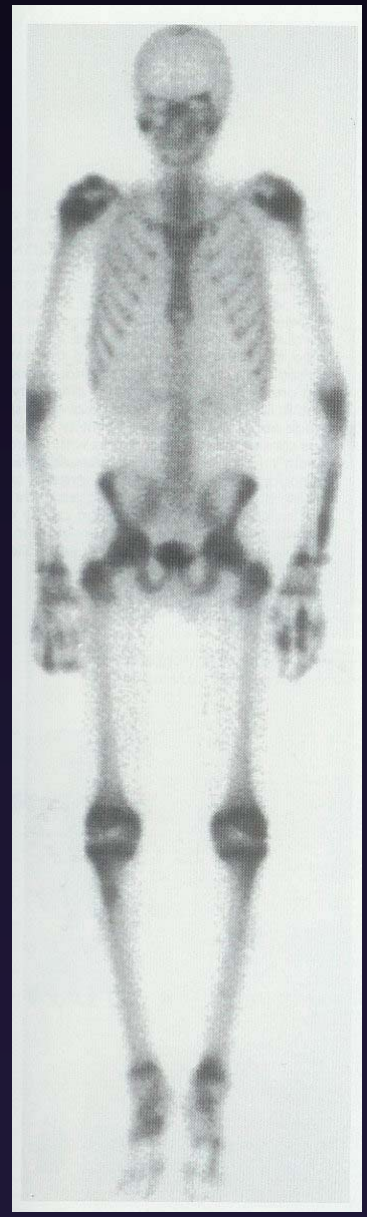
Bloodpool image Late (bone) image



Posterior view

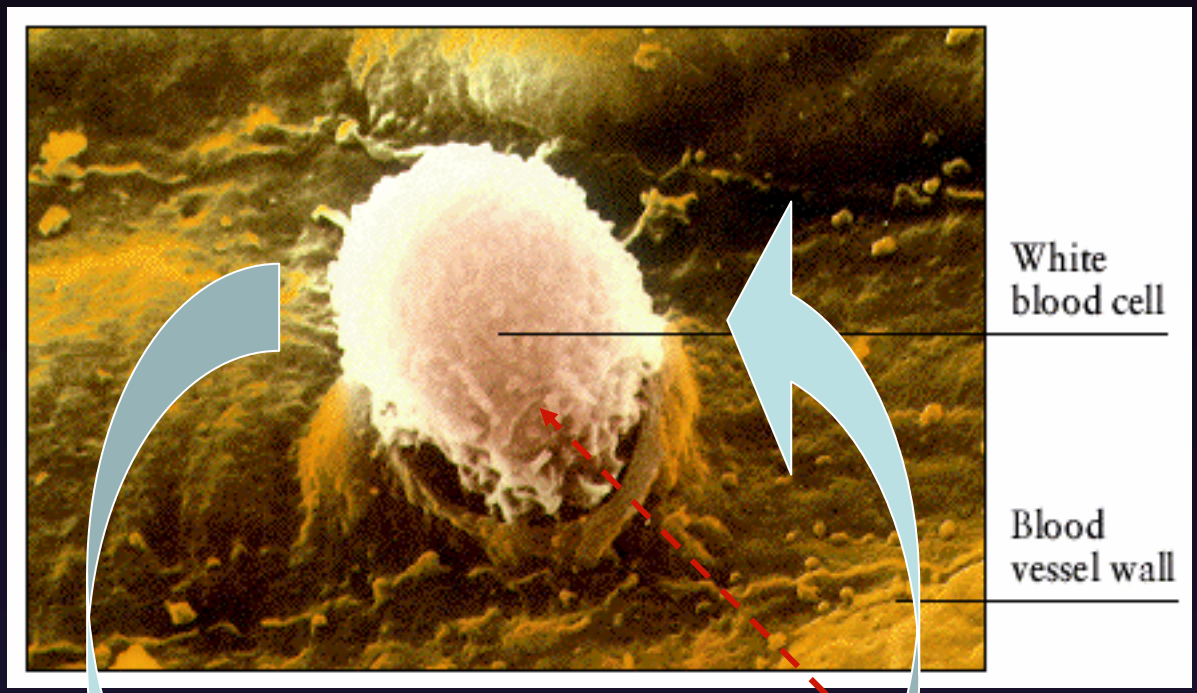
Bone scan

- An advantage of bone scintigraphy is the ability to image the entire skeleton, as in evaluation for multifocal OM.



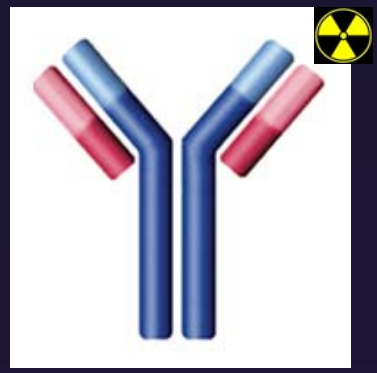
WBC scan

- Different kinds of labeled WBCs have been used to study bone infection.
- Important to perform images at 24 h PI, to increase specificity (chemotaxis).
- Several studies have indicated sensitivity and specificity of 80% or > for OM of the *appendicular skeleton.*



Ex vivo

In vivo



Indium-111

Tc-99m-HMPAO

IgG antibodies

WBC scan

- Ex vivo labeling of WBC with Indium or Tc-HMPAO has the limitation of requiring time consuming cell separation and labeling techniques.

WBC scan

WBC scan with Antigranulocyte-Ab

- These Ab are directed against non-specific cross-reacting antigen epitopes on the cell membrane of the granulocyte.
- The advantage of AGAB is the simplicity of the labeling process of Tc-99m with the antibodies and the in vivo labeling of granulocytes, not requiring any isolation of WBC.

WBC scan

WBC scan with Antigranulocyte-Ab

- Disadvantage of this direct labeling technique is the possible induction of human anti-mouse Ab (HAMA) in 3% of the patients.
- Until now, no severe side-effects have been reported.

WBC scan

Monitoring of efficacy of AB treatment:

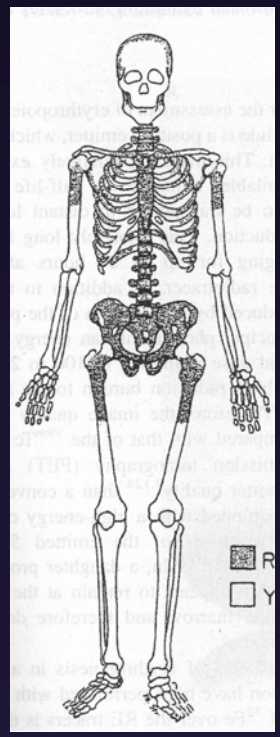
- Data lacking
- L Newman et al *:
  - FU of 35 diabetic patients with ulcers under AB treatment with WBC scan: in patients with OM, image normalized by 2 to 8 wks after initiation of AB, and preceded complete ulcer healing in most cases.
  - Conclusion: *" WBC scanning may be an accurate, noninvasive method of monitoring the efficacy of AB treatment."*

* JAMA, Sep 1991;266:1246-1251

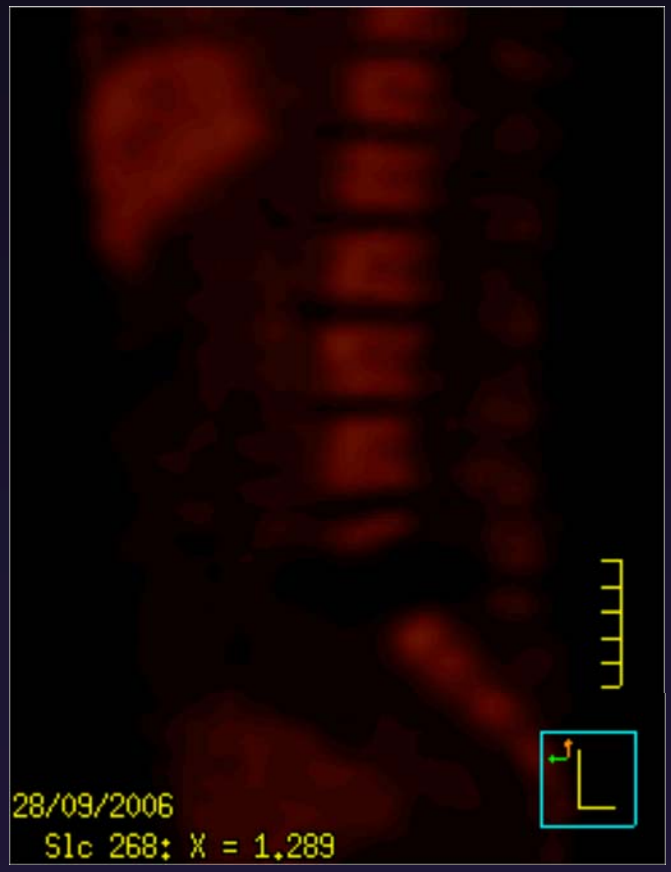
WBC scan

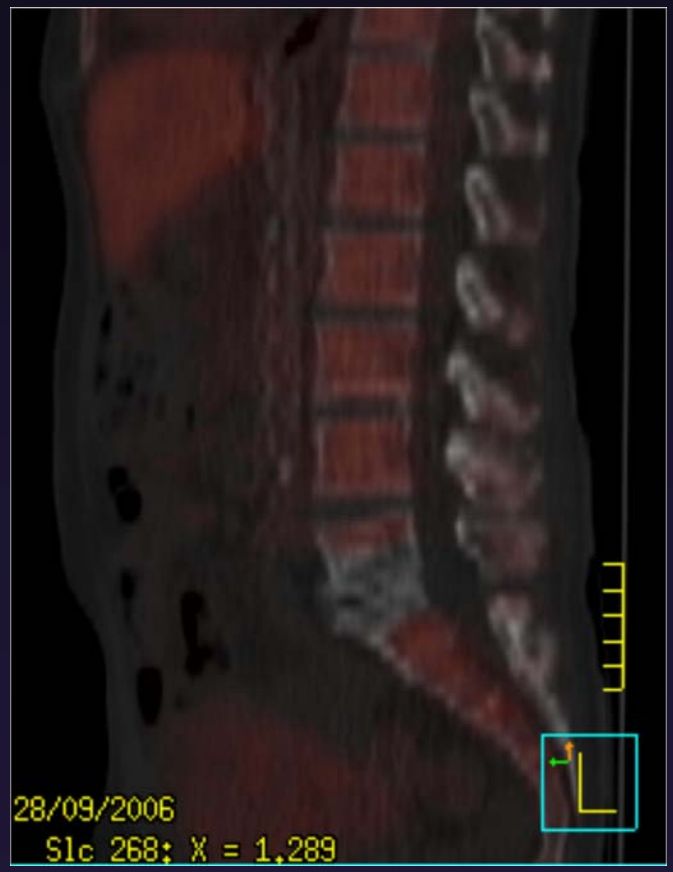
Spondylodiscitis

- The presence of active bone marrow reduces detection sensitivity of WBC-scintigraphy for OM in the central skeleton (40%)
- Infected areas may not take up more WBC than otherwise normal marrow sites -> normal appearance, or *cold* spots
- Cold spots have a long list of diff. diagnosis (post-surgical or anatomic deformities, hemangioma, radiation therapy, avascular necrosis, compression fractures, tumour, Paget ’s disease…)



WBC scan





(Sagittal slice)

Gallium-67

- Gallium has been used to study OM, especially in cases in which OM is under clinical suspicion and findings on routine bone scans are equivocal.
- Early imaging 24 h after injection may show increased uptake at the site of suspected involvement.
- It is important to perform imaging at 48 h post-injection, especially of the axial skeleton.

Gallium-67

- Gallium can show non-specific increased activity in areas of increased bone remodeling, such as fractures, surgical sites, neuropathic changes and pseudoarthrosis.

Gallium-67

- Proven method to increase specificity for the detection of OM:

  Compare gallium uptake in the suspect lesion with that on a bone scan.

  – The mismatch of greater increased Gallium uptake versus normal or less increased activity of MDP on bone scan indicates infectious involvement

FDG*-PET(/CT)

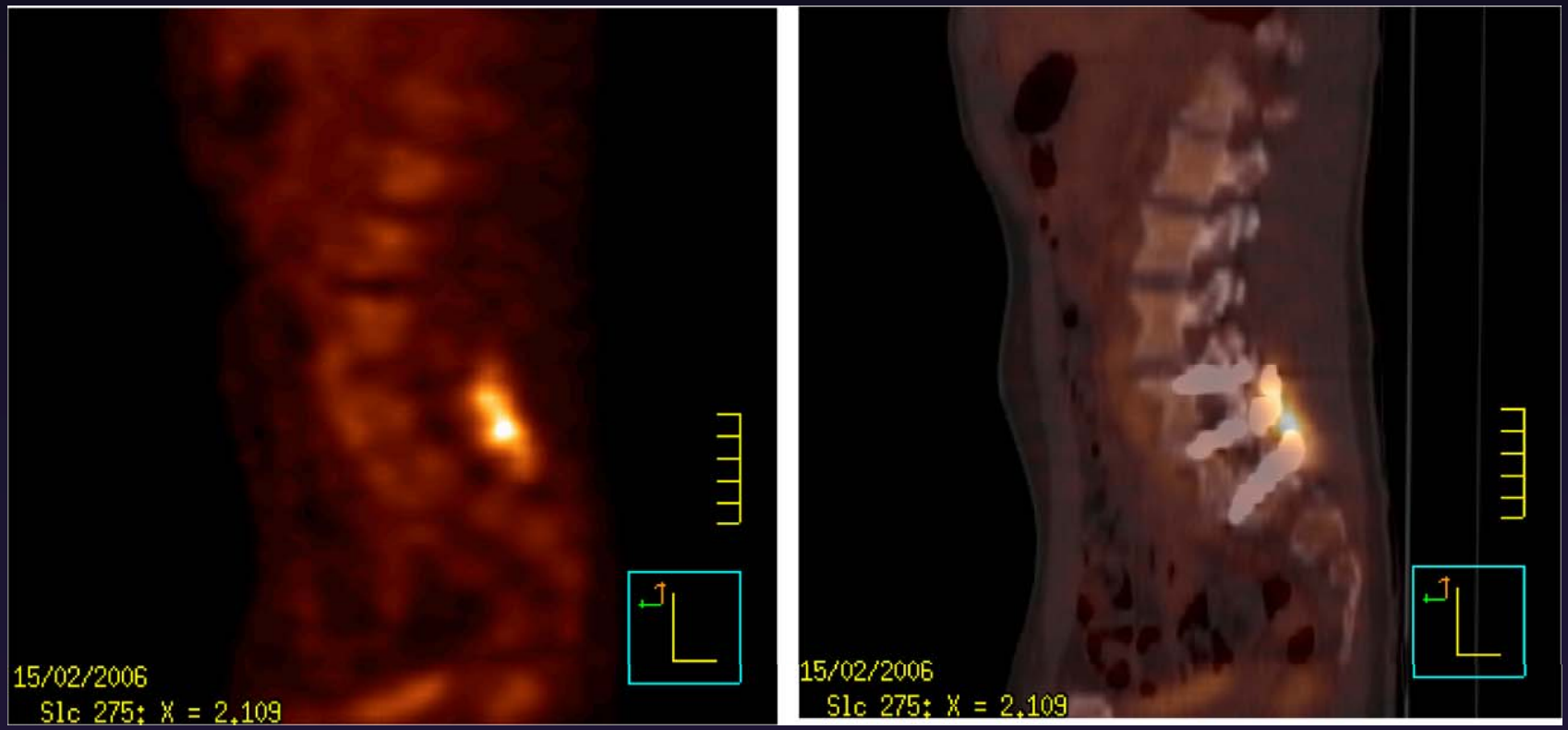
- Inflammatory cells such as neutrophils and activated macrophages present in areas of acute or chronic inflammation take up FDG avidly.
- Normal bone marrow shows only low glucose metabolism, making FDG-PET suitable for detection of OM in the axial skeleton.
- Indeed, within active bone marrow, FDG-PET has been found highly accurate in the diagnosis of chronic OM.

* 2-[18F]fluoro-2-deoxy-D-glucose

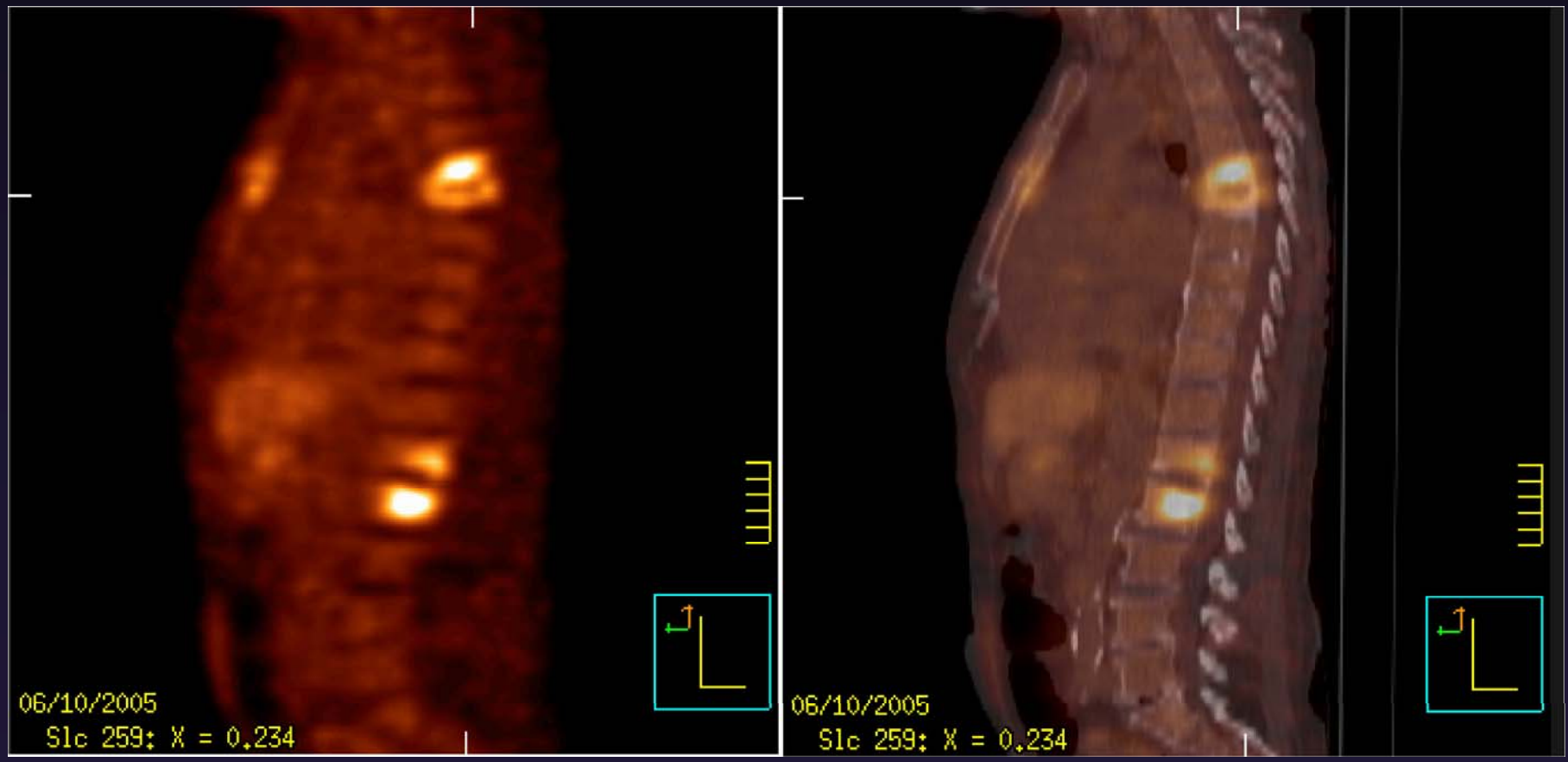
FDG-PET(/CT)

- In the early post-operative phase FDG-PET is of limited value owing to unspecific tracer uptake

FDG-PET(/CT)



FDG-PET(/CT)



OM in non-violated bone

- In non-violated bone, sensitivity and specificity of **bone scintigraphy** for detection of OM approaches 90%
- Plain X-ray is the initial procedure of choice in cases in which OM is suspected because of its low cost, availability, and lack of total body radiation dose.
- When X-ray findings are normal or equivocal in the face of significant clinical suspicion, you can proceed with a 3P bone scan.

OM in non-violated bone

- In infectious bone disease, X-ray tends to depict bone abnormalities late in the course of the disease.
- Abnormal findings on bone scans occur **early** in the process and allow early institution of treatment.

Spondylodiscitis in non-violated bone

- Early diagnosis of spondylodiscitis leads to early treatment and consequently to the prevention of severe and sometimes life-threatening complications.
- Classic scintigraphic criteria on bone scan:
  - increased uptake in the vertebral bodies on either sides of the affected disk space
  - increased blood-pool activity.

Violated bone*

Peripheral skeleton:

- Bone scan + WBC scan: very good results for the detection of OM (accuracy 80-100%).
- Better than Bone scan + Gallium scan (acc 70-80%)

Axial skeleton:

- (Bone scan +) Gallium scan

* Orthopedic surgery, amputation, fracture, prosthesis, Charcot joint, etc.

Violated bone

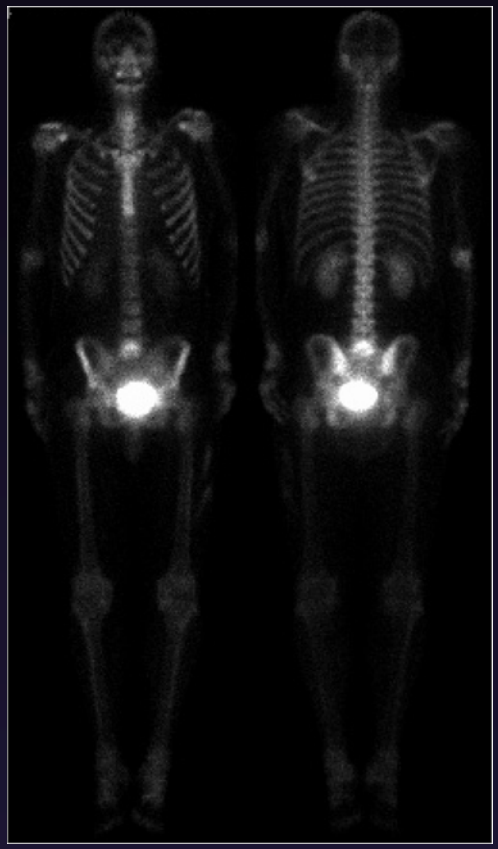
- In the early postoperative phase (< 1 month) however, the Gallium accumulation does not necessarily mean presence of infection.

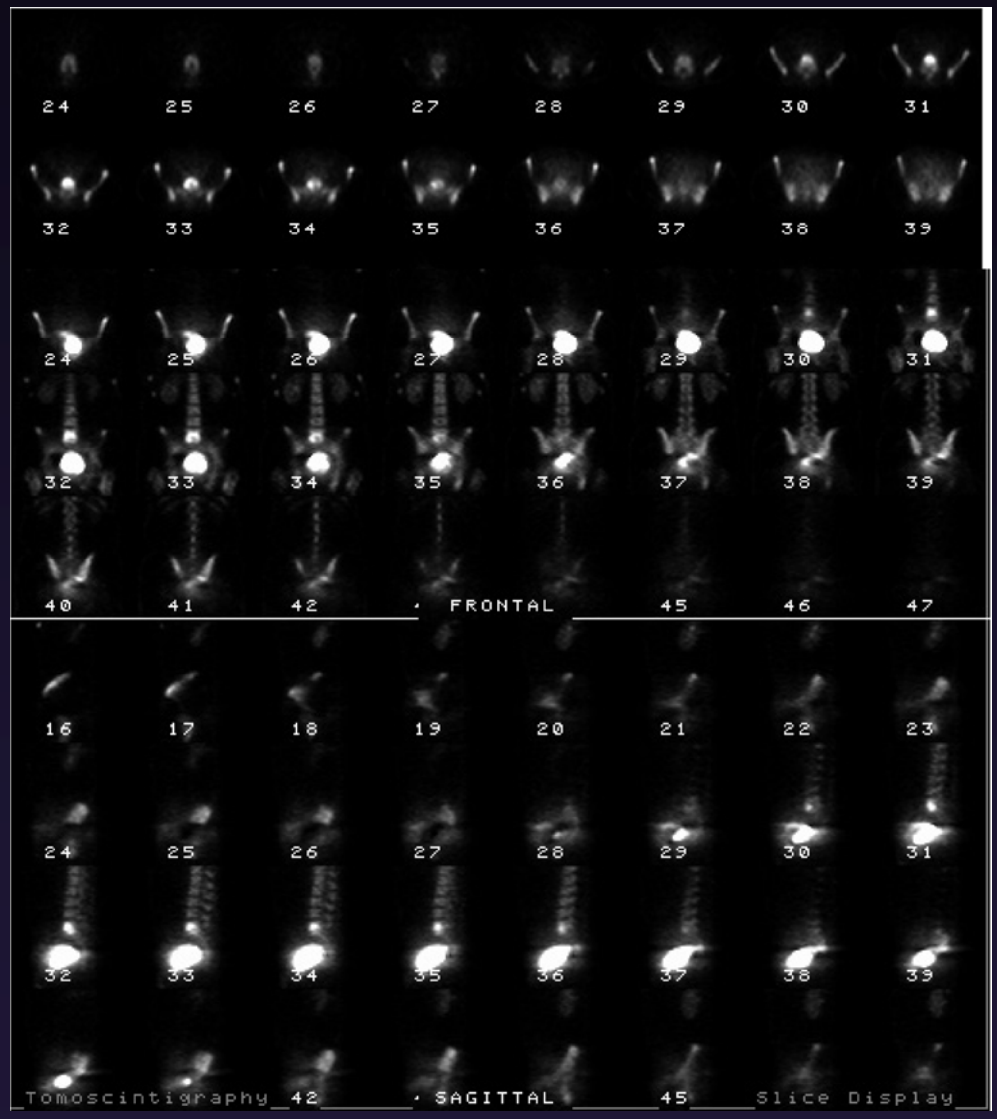
Violated bone

Post-operative spondylodiscitis

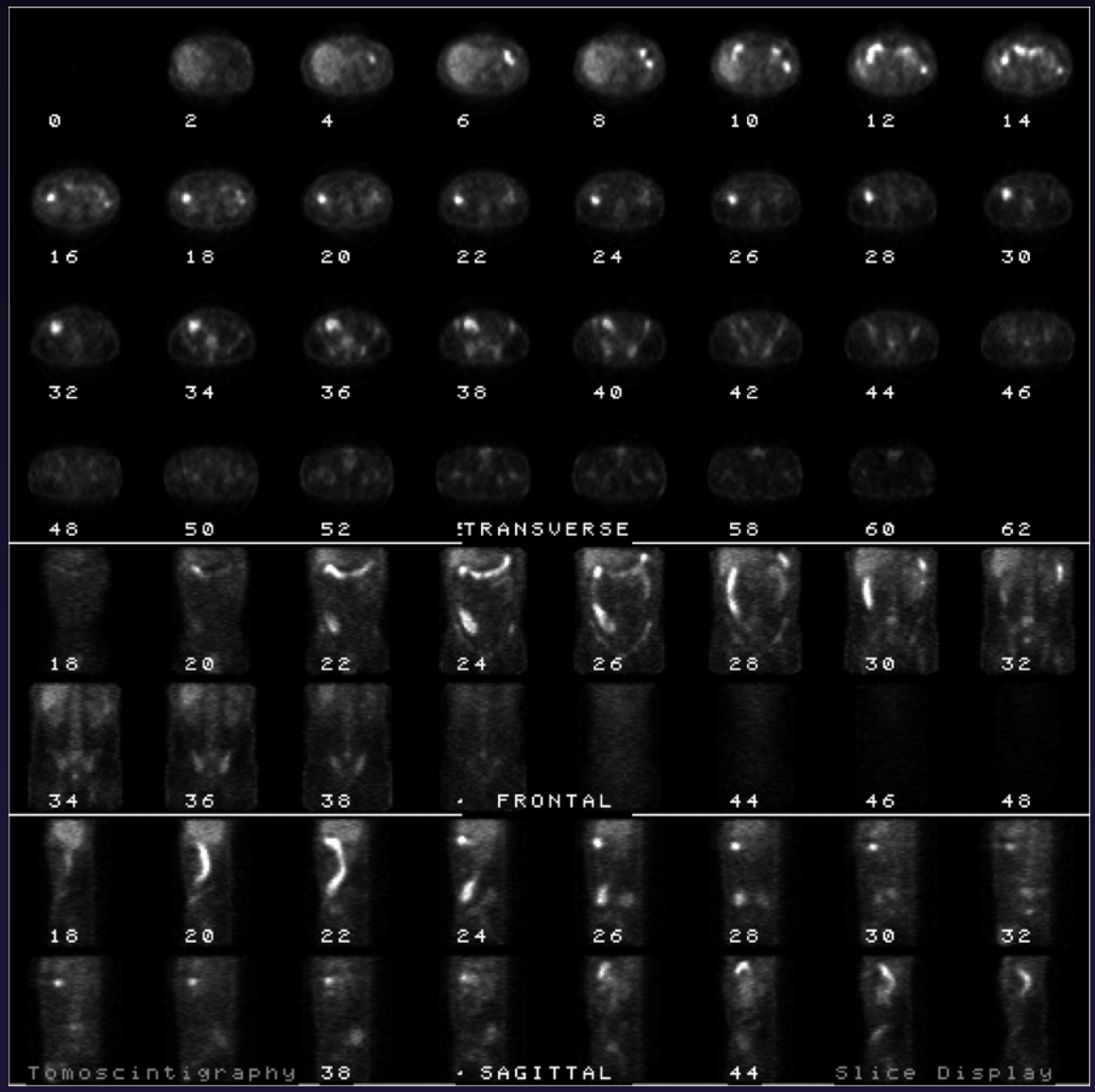
- The advantages of Gallium are:
  - not affected by artifacts from metallic implants;
  - its utility in therapy response monitoring.

M, 36 y: discectomy L5-S1; relapse sciatica postoperatively,



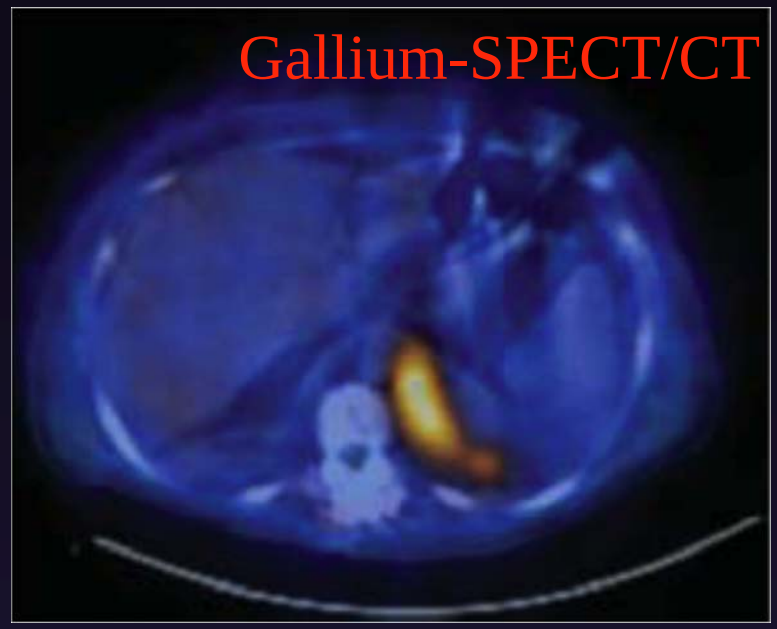


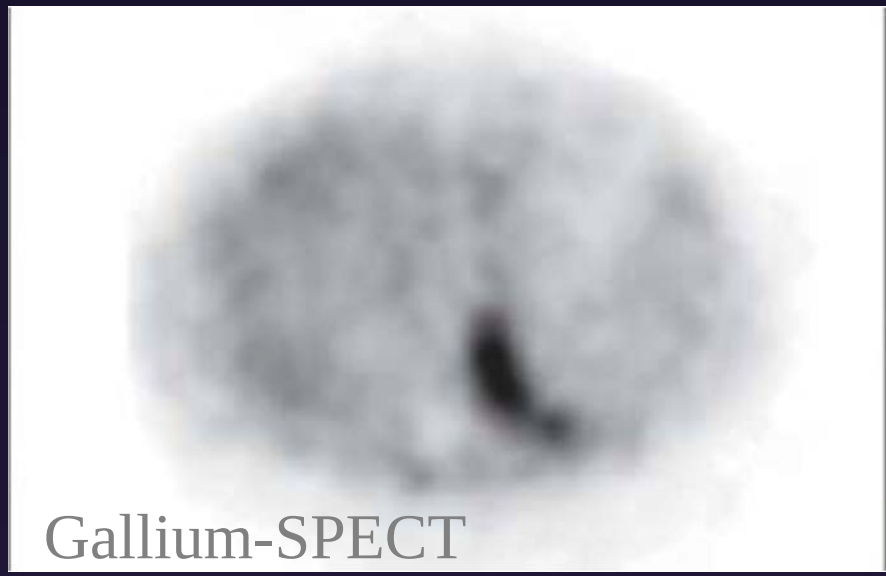
Bone SPECT 3 weeks after surgery

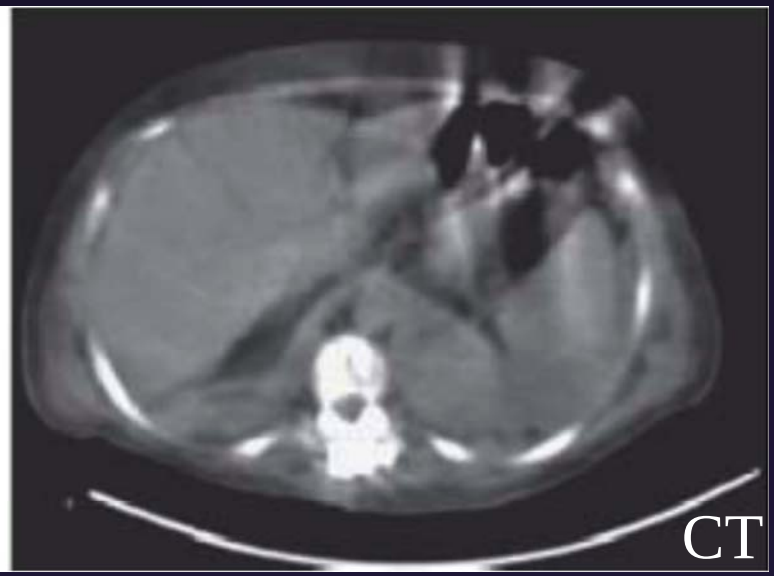


Gallium SPECT 3 weeks after surgery

56 y old W, fever, low back pain, infected scar 1 mo after spinal surgery







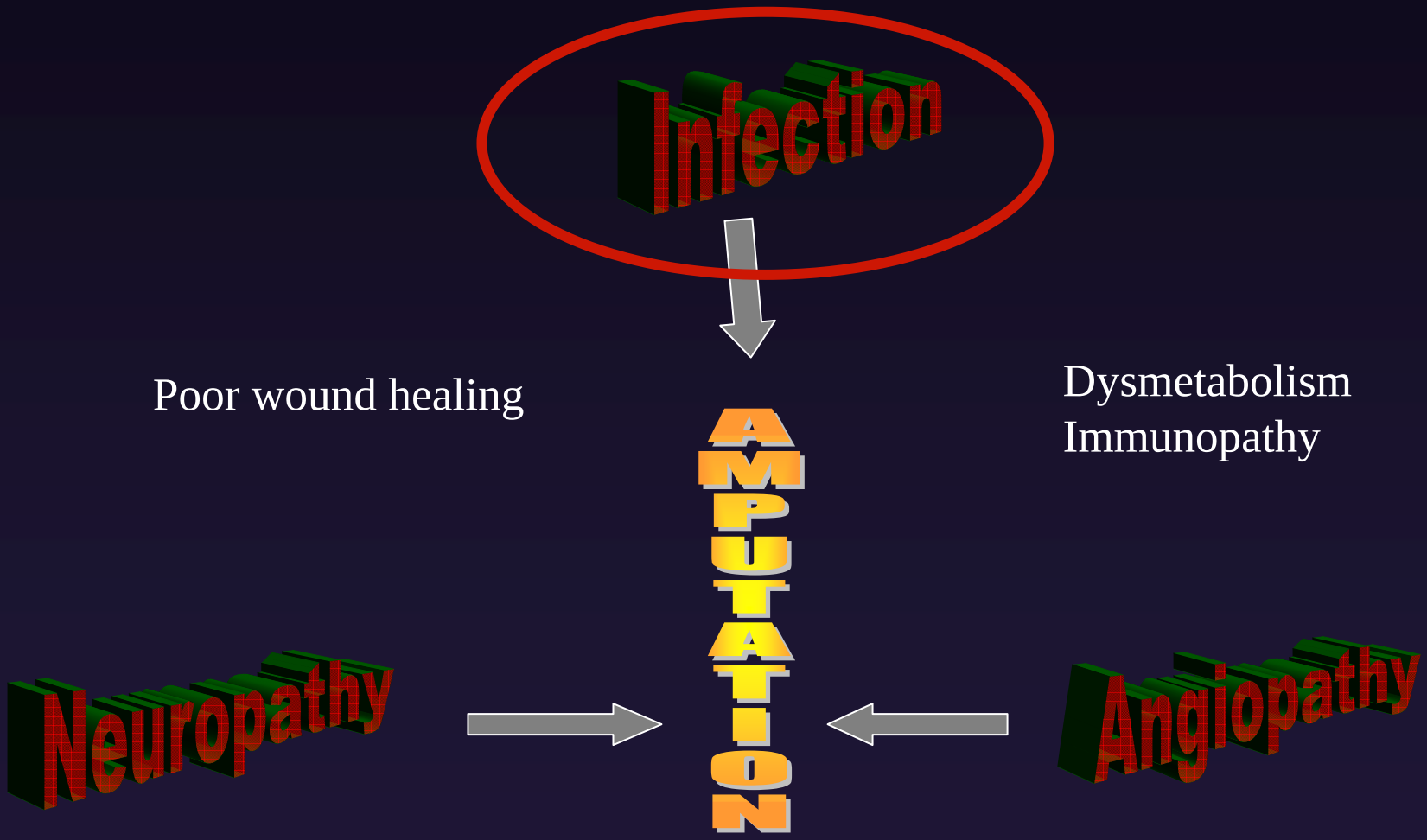
* Bar-Shalom et al, JNM 2006;47:587-594

Peri-prosthetic infection

- When infection of an orthopedic prosthesis is suspected, first a bone scan should be performed.
- In case of a /-/ bone scan, periprosthetic infection is ruled out.
- In case of + bone scan, complete with WBC scan for diff. diagnosis aseptic/septic loosening.
- In the monitoring of infection following hip prosthesis, the combination of bone and gallium scan has been shown to be useful to determine time for prosthetic reimplantation.

OM in the diabetic foot

Major predisposing factors leading to foot disorders in diabetic patients

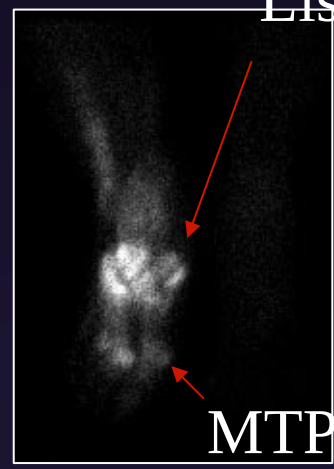


OM in the diabetic foot

- Clinical presentation and X-ray changes in a Charcot joint can make diagnosis of OM a real challenge
- Bone infection occurs most often in the forefoot, in particular in the toes and the metatarsal heads.

OM in the diabetic foot

Lisfranc



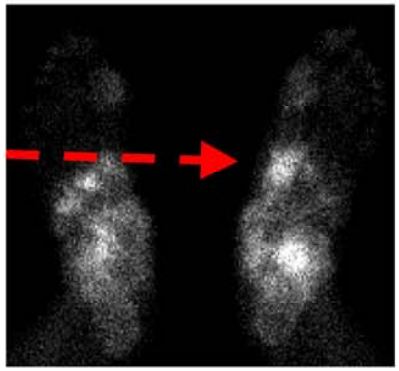
MTP joints

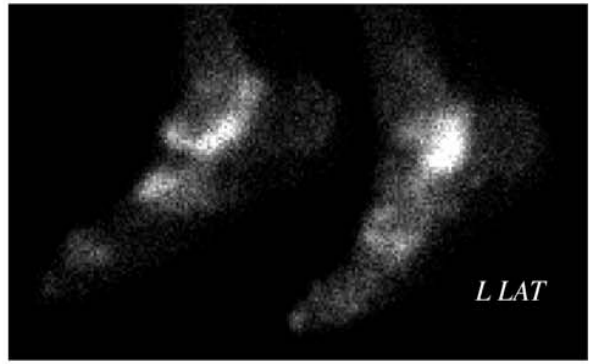
Bone scan (Tc - MDP)

- The considerable new bone formation in Charcot joint limits the use of the sensitive, but non-specific bone scan.
- A negative bone scan rules out the presence of OM.
- Bone scan helpful for anatomical landmarks, lacking on WBC scan and Gallium-scan.
- If bone scan is +, complete with WBC scan.


R


G

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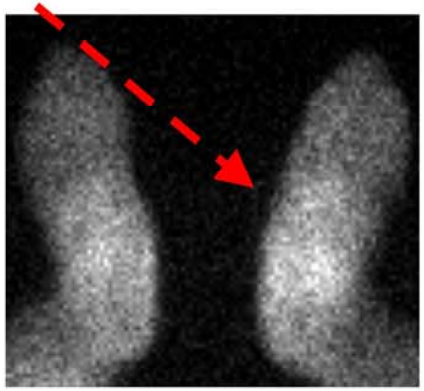

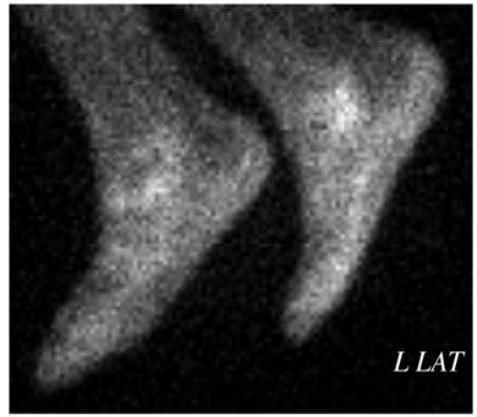
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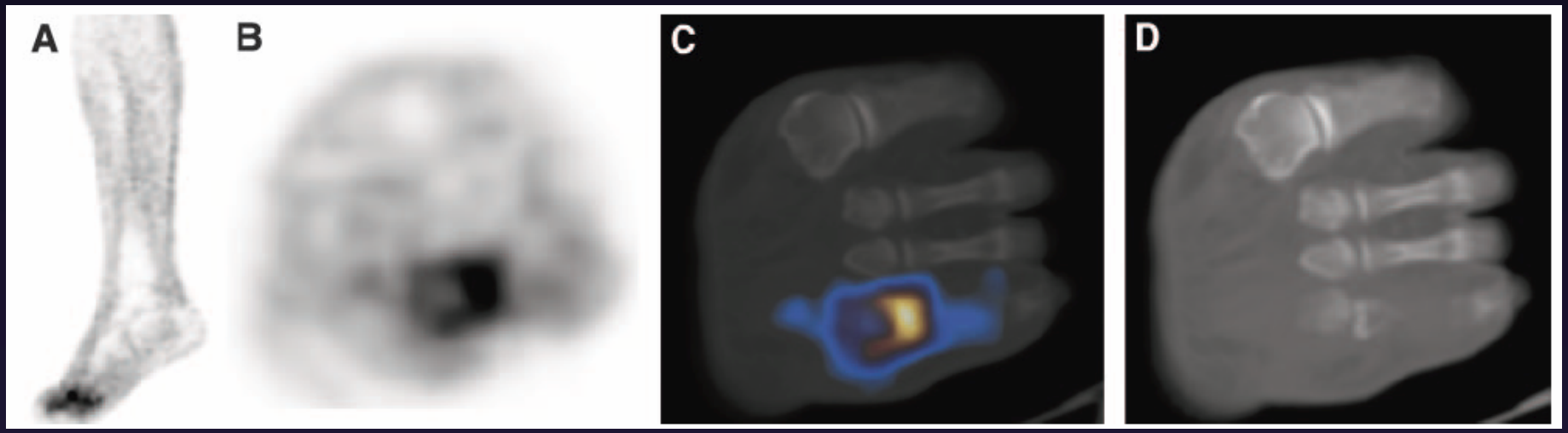
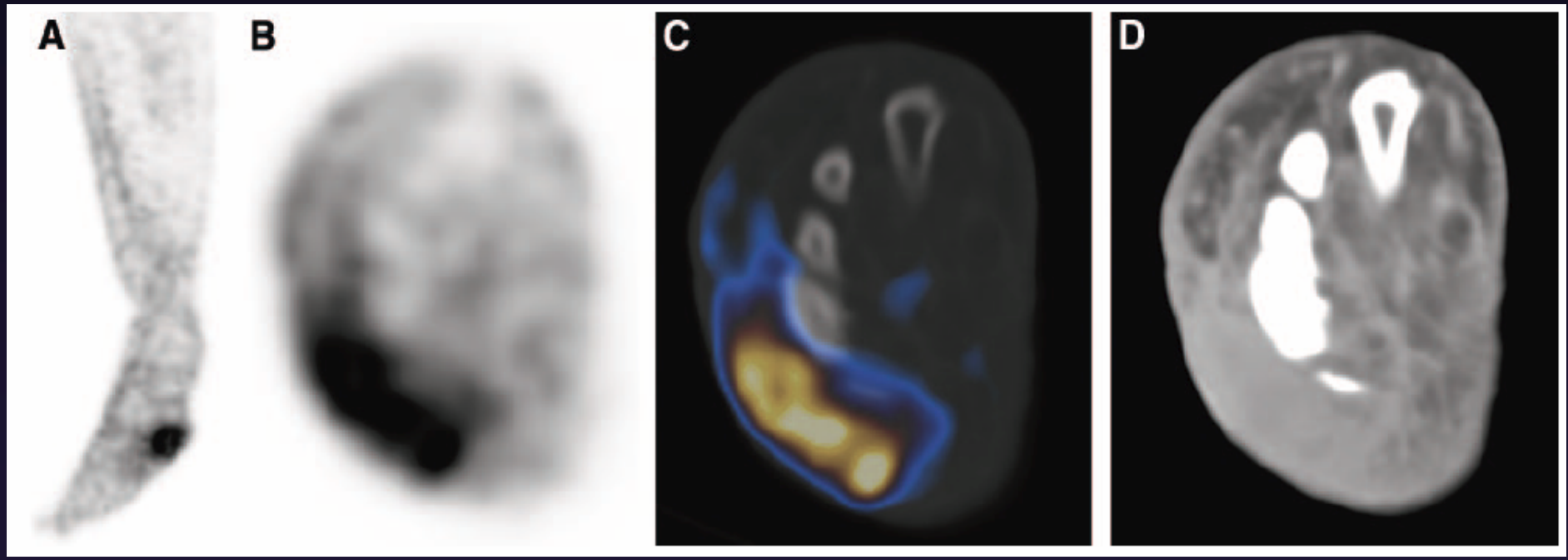
Diabetic Foot and FDG PET/CT *



* From Keidar et al, JNM 2005

Diabetic Foot and FDG PET/CT *



* From Keidar et al, JNM 2005

Combination of *HIGH ACCURACY* of WBC SCAN with *HIGH RESOLUTION* of PET/CT

WBC PET/CT

WBC PET/CT

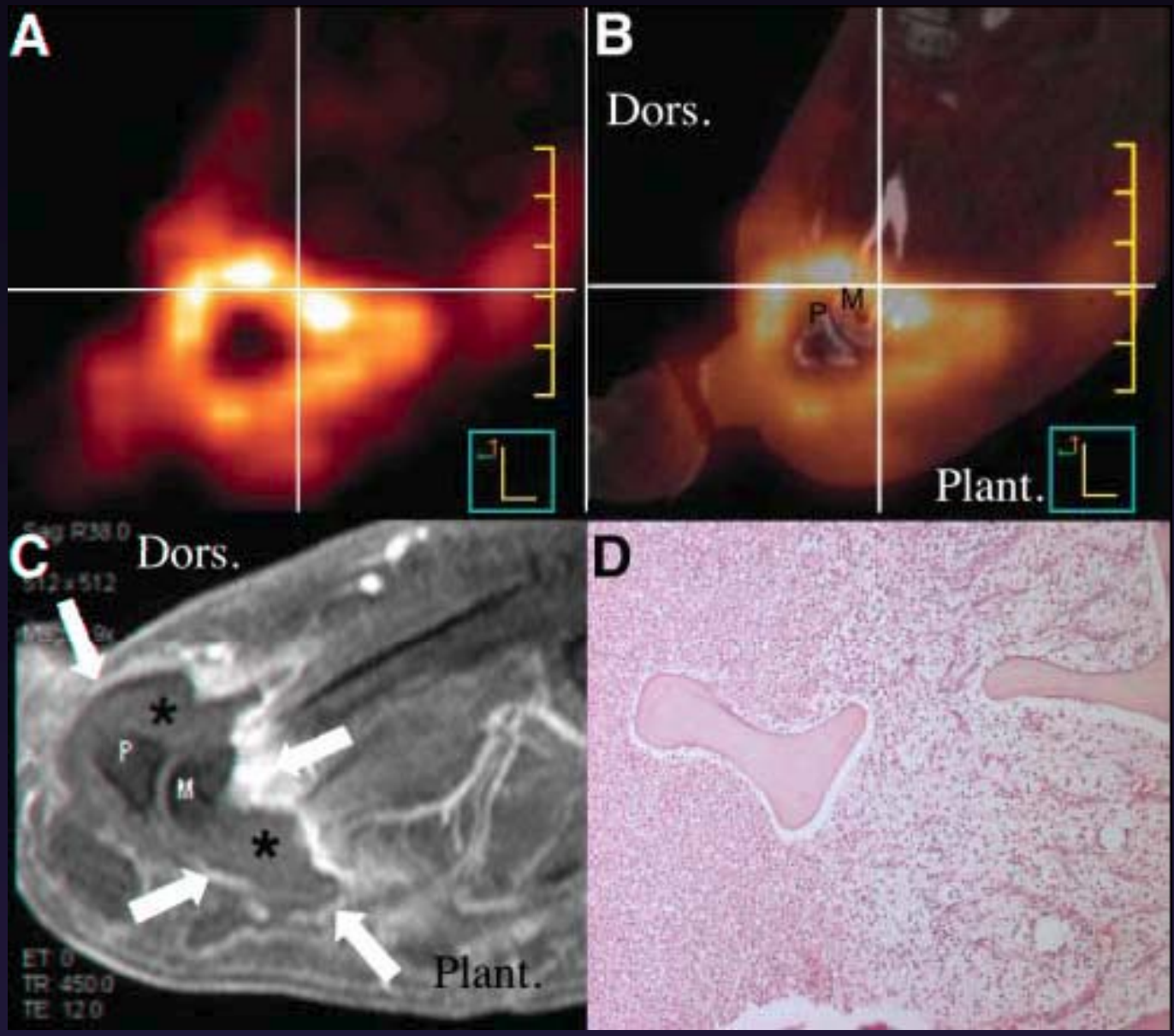
- Ongoing study in which we evaluate accuracy of PET/CT with FDG-labeled WBCs in diagnosis of infection
- Preliminary analysis on the first 21 patients*: WBC PET/CT excluded correctly OM or septic joint in 8/11 patients suspected of having this diagnosis and correctly diagnosed OM or septic joint in the other 3 patients of this group.

* Imaging Infection with ^{18}F-FDG–Labeled Leukocyte PET/CT: Initial Experience in 21 Patients

Nicolas Dumarey, MD[1]; Dominique Egrise, PhD[1]; Didier Blocklet, MD[1]; Bernard Stallenberg, MD[2]; Myriam Remmelink, MD, PhD[3]; Véronique del Marmol, MD, PhD[4]; Gaëtan Van Simaeys, PhD[1]; Frédérique Jacobs, MD[5]; and Serge Goldman, MD, PhD[1]

J Nucl Med 2006; 47:625–632

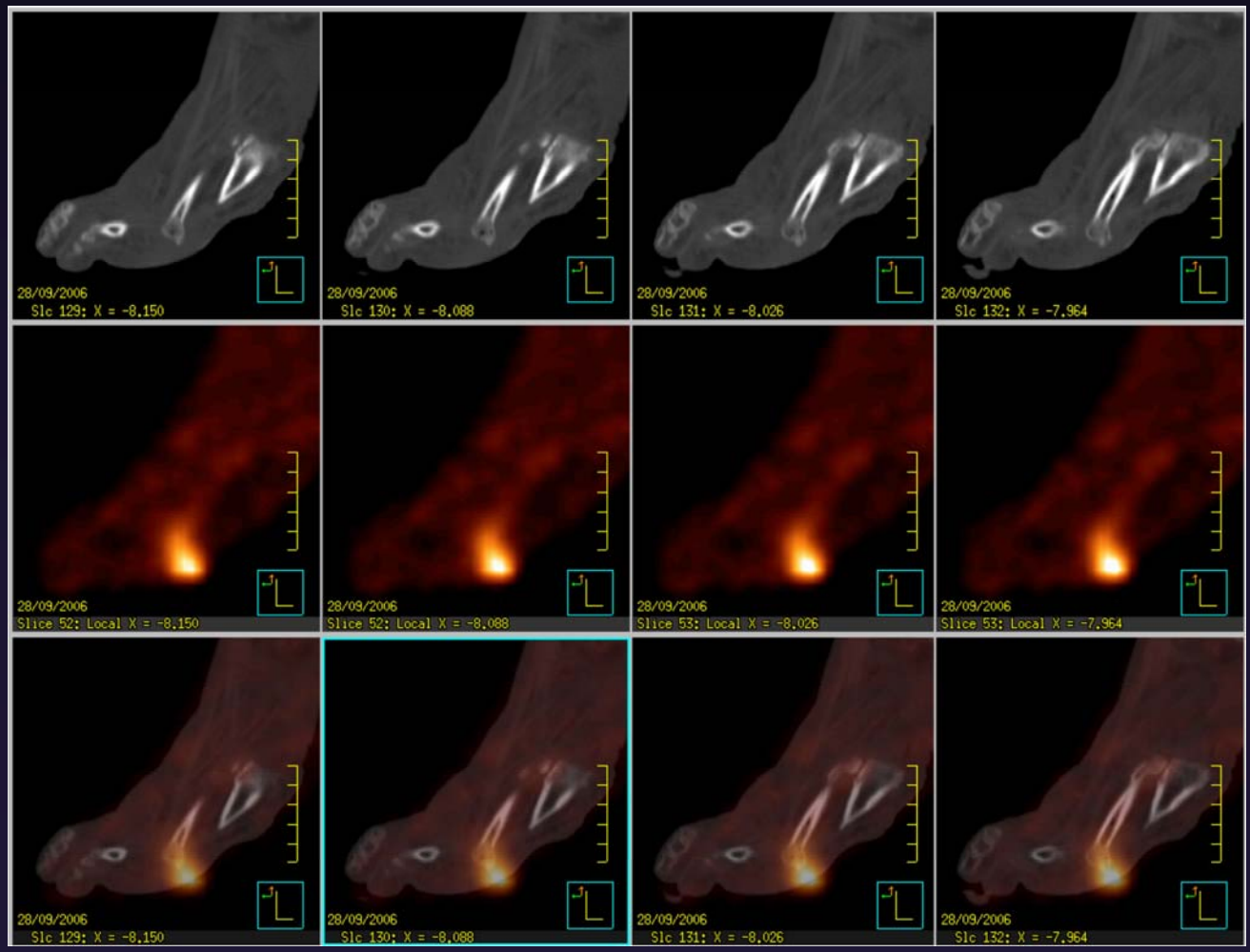
WBC PET/CT



P: phalanx

M: metatarsal bone

WBC PET/CT



CT

WBC-PET

WBC
PET/CT

Conclusions

- Depending on the location of infection and underlying bone conditions, the choice of imaging modalities must be tailored to each patient.
- Clinical history and the results of prior tests are therefore essential.

Conclusions

- Plain X-rays are performed first and may be sufficient. When they are not, nuclear medicine offers several radiopharmaceuticals for the imaging of OM.
- These include three-phase bone scans, WBC-scan, FDG-PET or -PET/CT, and Gallium-67.

Conclusions

- The three-phase bone scan is the NM test of choice in evaluating OM, but its specificity drops in bone altering conditions (surgery, trauma, Charcot joint etc.)
- In suspected OM in a context of violated bone, the combination of bone- and WBC-scintigraphy is the procedure of choice when it concerns the *appendicular skeleton.*

Conclusions

- For *vertebral* infection, MRI should be the first choice if readily available.
- If MRI not readily available, bone scan + gallium scan is a good alternative.
- In the presence of metallic implants, in post-operative settings and for follow-up, Gallium-scan can be indicated.

Conclusions

- Promising results have been published on FDG-PET in patients with suspected OM. Its resolution permits a better differentiation between soft tissue infection and OM.
- Especially in the assessment of inflammation of *spinal lesions*, FDG-PET, if available, represents an effective alternative to Gallium.
- FDG-PET(/CT) is of limited value however in early post-operative phase (< 6 months).

Conclusions

- False-positive findings on FDG-PET have been described in non-infected loosened prostheses.
- The hybrid PET/CT and SPECT/CT systems will further improve resolution and differentiation between soft tissue and bone infection.