Conventional Nuclear and PET Imaging of Suspected MSK infections

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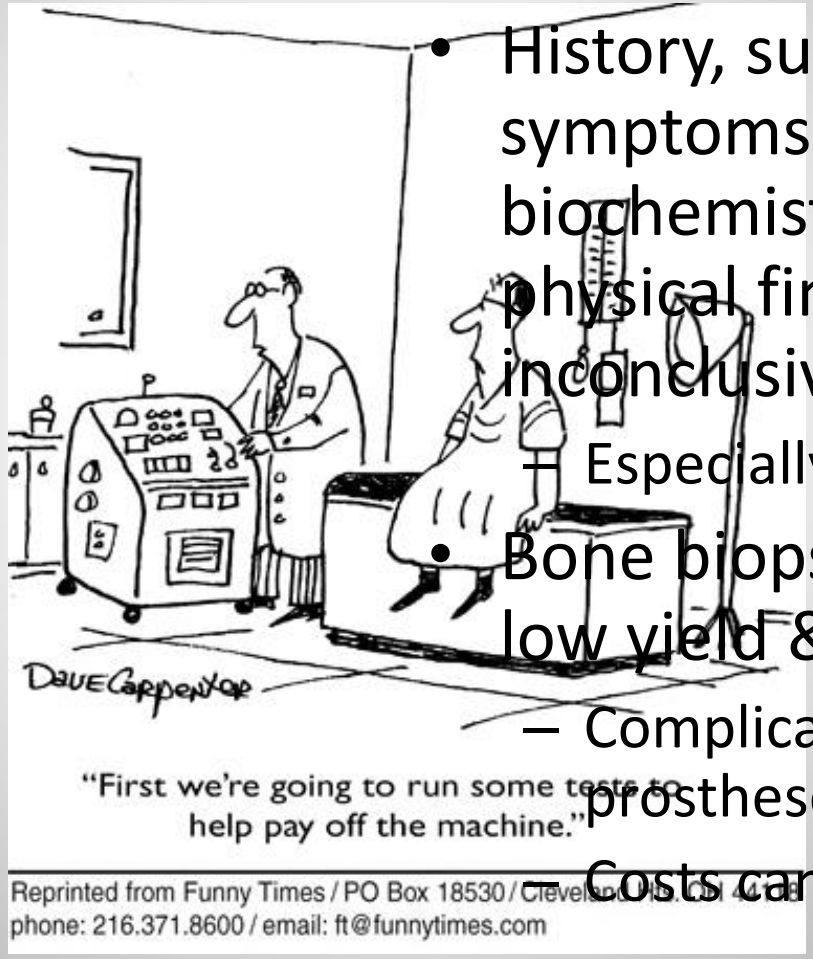
Why Image Suspected MSK Infection?



- History, subjective symptoms, biochemistry, and physical findings often inconclusive
  - Especially early disease
- Bone biopsy relatively low yield & invasive
  - Complications, especially prostheses
  - Costs can mount

MSK Infections

- Acute osteomyelitis
- Diabetic foot infection
- Spondylodiscitis
- Post-traumatic bone infection
- Inflected orthopedic prosthesis
- Chronic osteomyelitis

Anatomic Imaging of MSK Infections

- **Radiography** is **moderately Sn** for **early** OM
  - X-ray not Sn for OM until 10 to 21 days because to be radiographically visible bone density loss must reach 30-50%
- **CT & MRI** also **moderately Sp** for **OM** when complicated by **hardware**
  - Metallic implants cause artifacts on CT
  - Can't do MRI on traditional metal implants
  - *Conventional functional imaging* also *moderately Sn* because of increased non-specific accumulation due to implants

Comparing Modalities in MSK (OM)

Table 2 – Diagnostic Imaging Studies for Osteomyelitis

Imaging modality	*Sensitivity (%)*	*Specifcity (%)*	*Comments*
Computed tomography	67	50	Generally should not be used in osteomyelitis evaluation
Leukocyte scintigraphy	61 to 84	60 to 68	Combining with technetium-99 bone scintigraphy can increase specifcity
Magnetic resonance imaging	78 to 90	60 to 90	Useful to distinguish between soft tissue and bone infection, and to determine extent of infection; less useful in locations of surgical hardware because of image distortion
Plain radiography (anteroposterior, lateral, and oblique views)	14 to 54	68 to 70	Preferred imaging modality; useful to rule out other pathology
Positron emission tomography	96	91	Expensive; limited availability
Technetium-99 bone scintigraphy	82	25	Low specifcity, especially if patient has had recent trauma or surgery; useful to differentiate osteomyelitis from cellulitis, and in patients in whom magnetic resonance imaging is contraindicated

Hatzenbuehler J and Pulling TJ. Diagnosis and management of osteomyelitis. Am Fam Physician 2011; 84(9):1027-33.

Conventional Nuclear Imaging of MSK Infections

Tc-99m MDP Bone Scan

- Tc-99m labeled bisphosphonates (MDP and HDP) demonstrate **osteoblastic** activity
- In general, Sn of Tc-99m MDP for osteomyelitis is > 90% but Sp depends
  - If bony structure **not** complicated by fracture or hardware, **Sp is > 90%**
  - *If post-traumatic or post-surgical*, Sp is *~35%*

Tc-99m MDP Bone Scan

- 740 MBq (20 mCi) of Tc-99m MDP injected IV
- Imaging on LEHR collimator
  - Photopeak set at 140 keV
- Effective dose: 6.3 mSv
- **3 phases** to increase Sp
  - 1st phase: flow
  - 2nd phase: blood pool
  - 3rd phase: delayed (3-4 hours post injection)

Gallium Scan

- In general, Ga-67 has high Sn for acute and chronic infection and non-infectious inflammation
- But **Sp for infection is low**
- Other shortcomings
  - Need for delayed imaging beyond 24 hours
  - Can't administer high dose activity (*high effective dose*, 15 mSv, and *long half life* of Ga-67, 78 hrs)
  - Limited spatial resolution because low counts
  - Physiologic bowel and soft tissue uptake

Gallium Scan

- 150-220 MBq (4-6 mCi) of Ga-67 Citrate injected IV
  - Up to 330 MBq (9 mCi) for larger patients
- Imaging on MEGP collimator
  - Photopeaks set at 93 and **184** (and 296) keV
- Effective dose: 15 mSv
- Images acquired 24-72 hrs after injection
  - 4- or 96-hr images help abdomen interpretation

Sulfur Colloid Marrow Scan

- In general, Tc-99m sulfur colloid correlates with red bone marrow
- 300-370 MBq (8-10 mCi) of Tc-99m sulfur colloid injected IV
- Imaging on LEGP collimator
  - Photopeak set at 140 keV
- Effective dose: 2.1 mSv
- Images acquired 30 min after injection

Radiolabeled WBC Scan

- In the **proper clinical context**, Tc-99m and In-111 labeled WBC have **Sp > 90%**
  - Sn is excellent in peripheral skeleton (Sn > 95%)
- But Sn of radiolabeled WBC for infection in **central skeleton is poor**
- Other shortcomings
  - Laborious preparation, requiring specialized equipment & handling of possibly infected blood
  - Poor spatial resolution – can't always separate bone from soft tissue infection
  - Normal bone marrow can cause False Positives
  - Not useful in leukopenic patients (granulocytes < 2K/mL)

Radiolabeled WBC Scan

- 40 mL of patient's blood is drawn and labeled with In-111-Oxine (or *Tc-99m-HMPAO*)
- 18-24 MBq (0.5-0.6 mCi) In-111 WBC injected IV
  - 185-370 MBq (*5-10 mCi*) *Tc-99m HMPAO* IV
- MEGP with photopeaks at 174 and 247 keV
  - *LEGP* with *140 keV* photopeak for *Tc-99m HMPAO*
- Effective dose: 6.7 mSv for In-111 WBC
  - *8.1 mSv for Tc-99m HMPAO*
- Acquisition immediately if preferred, always 18-24 hours later

Radiolabeled WBC Scan

Radiolabeled WBC Scan

- Acquisition by 24 hours
- Great Sn and higher Sp for acute infections than Gallium Scan
  - Not as Sn as Gallium Scan for *chronic* infections
- Less variable physiologic uptake (especially In-111 WBC)
- Concurrent antibiotics & photopenic central skeleton lesions produce FP & FN

Gallium Scan

- Acquisition by 48 hours, sometimes longer
- Excellent Sn for infection, inflammation and neoplasm
- Lot of variability of physiologic uptake, which is usually in GI tract, GU tract and soft tissues

Radiolabeled WBC Scan

In-111 WBC

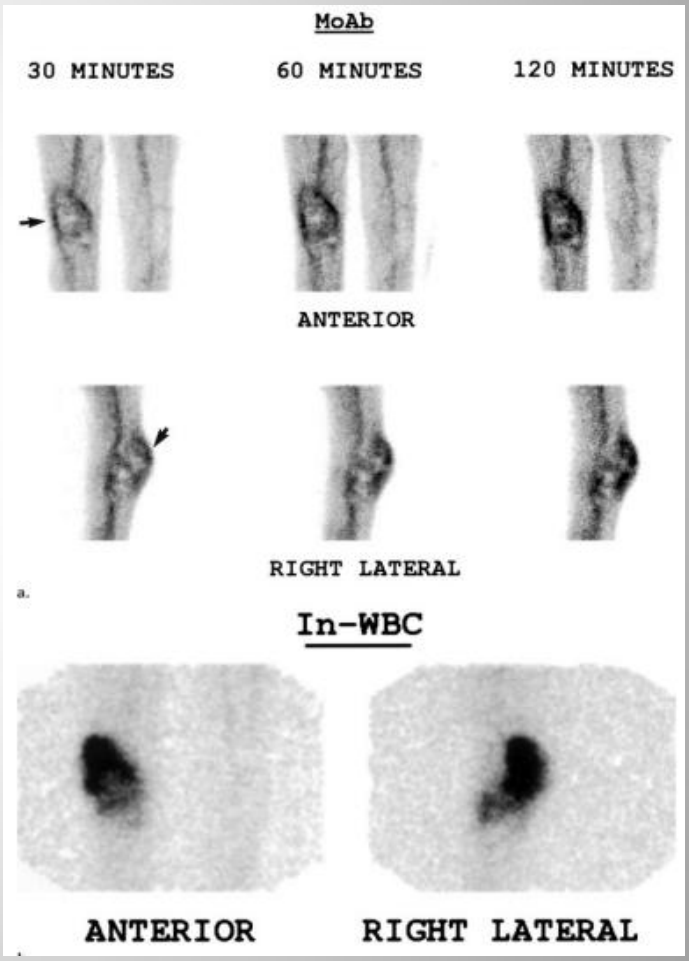
- Does **not** concentrate in GI tract, GU tract or GB, thus better for abdominopelvic infections
- Longer half-life of In-111 (67 hours) allows better delayed imaging than Tc-99m
- Obligates us to use lower administered dose, causing grainier images

Tc-99m-HMPAO WBC

- Labeling less stable than In-111 WBC
  - Tracer in GIT, GUT and GB
- 6 h H.L. of Tc-99m leads to higher dose, thus more counts and better quality images
- Faster uptake in infection sites, thus better earlier imaging
- Better visualization of small anatomy
- Low absorbed radiation doses make it more suitable than In-111 for infants & children

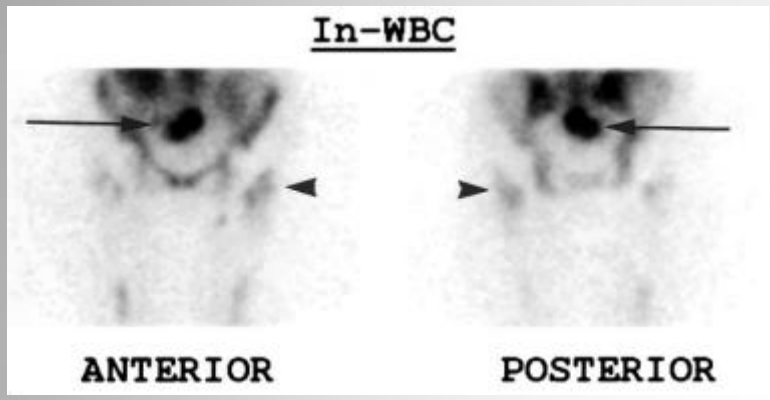
Bone + Radiolabeled WBC Scan

- Palestro's team at Long Island Jewish Medical Center studied 24 patients with a **variety of suspected OM** (prosthetic joint, long bone, and diabetic foot)
  - Also screened with antigranulocyte scan, In-111 WBC scan & bone scan



Palestro CJ et al. Osteomyelitis: Diagnosis with 99m Tc-labeled Antigranulocyte Antibodies Compared with Diagnosis with 111 In-labeled Leukocytes—Initial Experience . Radiology 2002; 223:758 –764

Bone + Radiolabeled WBC Scan



Example of false positive, as this was read as hip prosthesis infection

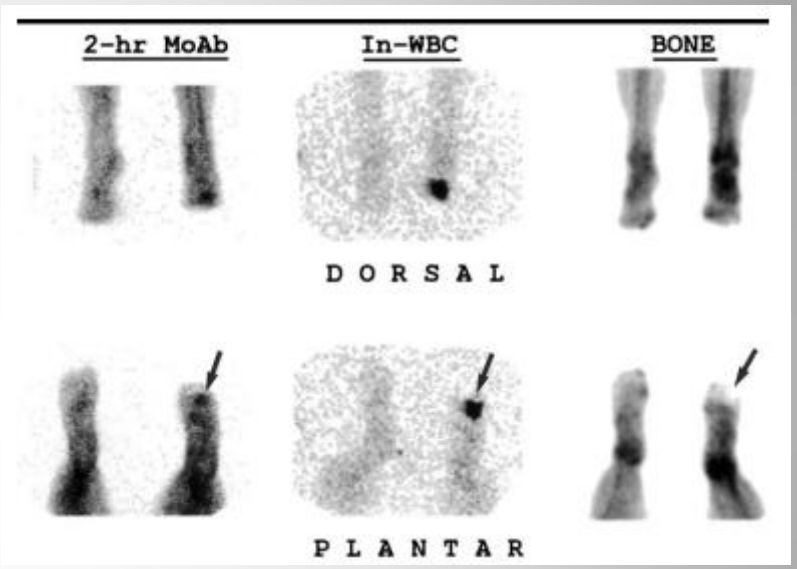
Other false positives included soft tissue infection and gangrene

- **11 cases** (5 DM foot OM and *6 infected joint prostheses*) proven by histopath
- Radiolabeled WBC scan was TP in 10 cases, but FP in 4 cases
  - *1 FP but 5 TP in knee prostheses*
- Thus, Sn was 91% but Sp 62%

Palestro CJ et al. Osteomyelitis: Diagnosis with 99m Tc-labeled Antigranulocyte Antibodies Compared with Diagnosis with 111 In-labeled Leukocytes—Initial Experience . Radiology 2002; 223:758 –764

Bone + Radiolabeled WBC Scan

- Bone scan was 100% Sn, thus excellent NPV
  - But Sp was 38%
- Adding bone scan to radiolabeled WBC scan **improved Sp to 77%**
  - Sn remained 100%



A case where bone scan prevented a false positive. The photopenic defect on bone scan proved to be gangrene.

Palestro CJ et al. Osteomyelitis: Diagnosis with 99m Tc-labeled Antigranulocyte Antibodies Compared with Diagnosis with 111 In-labeled Leukocytes—Initial Experience . Radiology 2002; 223:758 –764

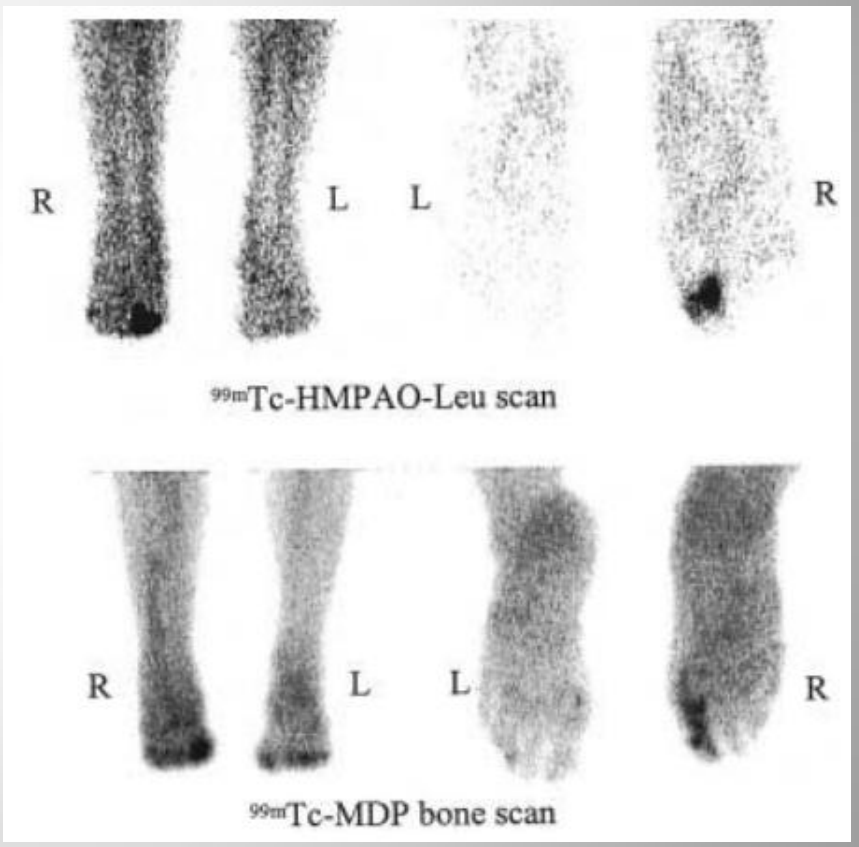
Bone + Radiolabeled WBC Scan

- In **diabetic foot**, seems best to combine bone scan with radiolabeled WBC scan
- Bone scan is 100% Sn, but Sp low largely because of **neuropathic joint disease**
- In French study, 75 diabetics with 83 foot ulcers were scanned for suspected OM

Poirier JY et al. Diagnosis of Osteomyelitis in the Diabetic Foot with a Tc-99m HMPAO Leucocyte Scintigraphy Combined with a Tc-99m Bone Scintigraphy. Diabetes Metab (Paris) 2002, 28, 485-490.

Bone + Radiolabeled WBC Scan

- 41 (of 83) **ulcers** diagnosed as **OM** by histopathology (15) or follow-up x-rays
- Concordant findings: positive for infection
- Discordant findings: negative
  - Focus on radiolabeled WBC scan but **correlation to bone** on bone scan



OM of the Right 1st toe

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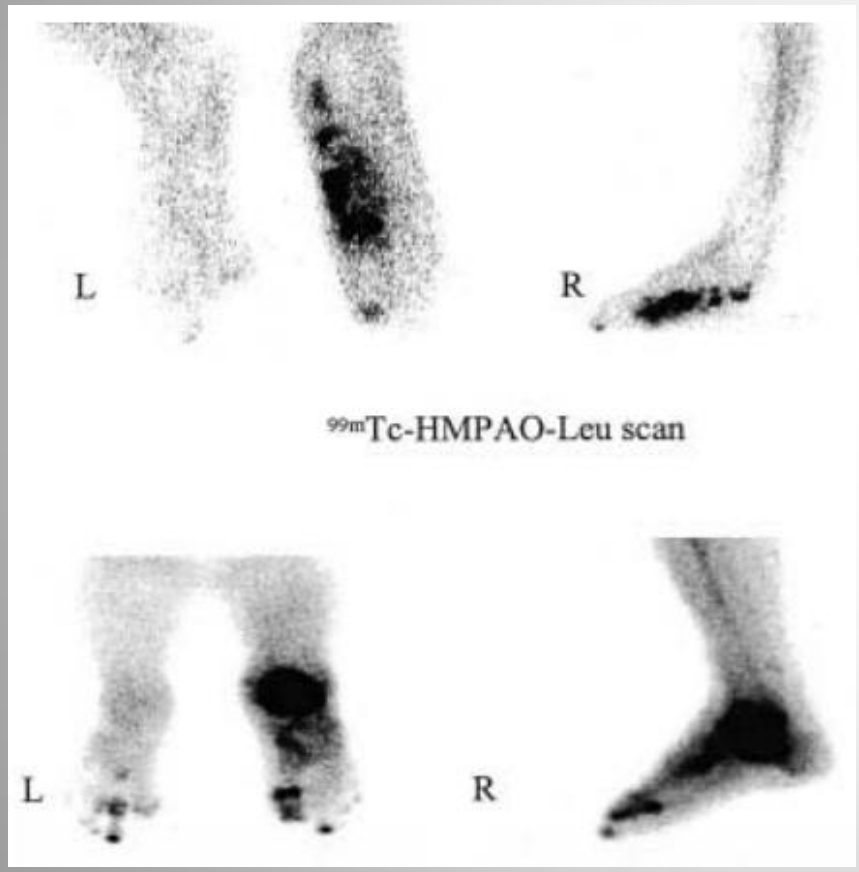
Bone + Radiolabeled WBC Scan



- Bone + radiolabeled WBC scintigraphy was TP in 38 cases → **Sn of 93%**
- Among 42 ulcers not associated with OM, combination scintigraphy had 41 TN → **Sp 98%**

Poirier JY et al. Diagnosis of Osteomyelitis in the Diabetic Foot with a Tc-99m HMPAO Leucocyte Scintigraphy Combined with a Tc-99m Bone Scintigraphy. Diabetes Metab (Paris) 2002, 28, 485-490.

Bone + Radiolabeled WBC Scan

- Bessette's group in Milwaukee reviewed 32 patients with suspected **sternal OM**
- Group composed of **12** patients with biopsy-proven sternal OM
- All scanned with CT and radiolabeled WBC + bone scans

- CT positive for sternal OM in **7** patients - 5 bony erosions & 2 severe demin (**Sn 58%**)
- Combination scintigraphy positive in **11** patients (**Sn 92%**)
  - 1 case of FP due to concurrent IV antibiotics which was not seen on radiolabeled WBC scan

Bessette PR et al. Evaluation of postoperative osteomyelitis of the sternum comparing CT and dual Tc-99m MDP bone and In-111 WBC SPECT. Clin Nucl Med. 1993 Mar;18(3):197-202.

Radiolabeled WBC & Vertebral OM

- Palesto's team in NY reviewed 71 patients where radiolabeled WBC scan performed for **possible vertebral OM**
  - 57 had bone scan too (31 were two-phase)
  - Final diagnosis based on variety of endpoints
- 28 patients identified with vertebral OM
  - 24 cases confirmed

- In many cases, radiolabeled WBC scans were photopenic in confirmed infection sites

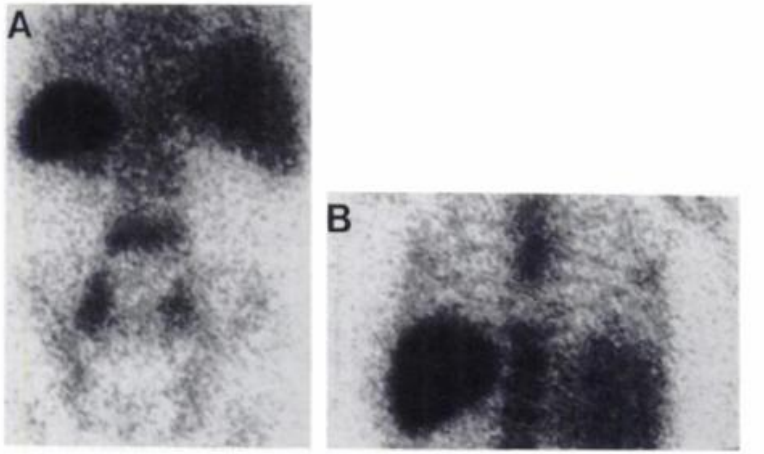
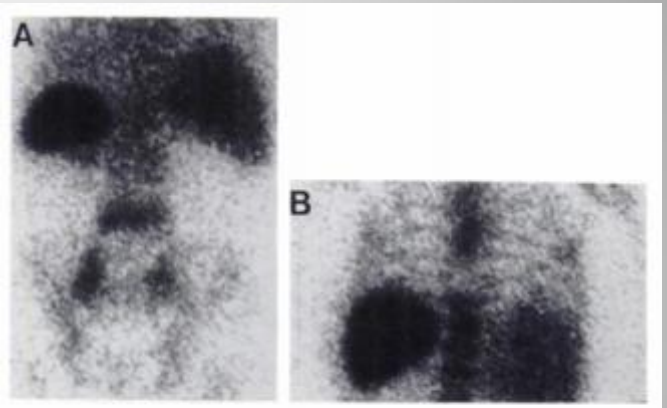


FIGURE 1. (A) Intensely increased leukocyte activity is present in L5 in an 81-yr-old male with vertebral osteomyelitis. The causative organism was *S. fecalis*. (B) A well-defined photopenic defect involving approximately T8 and T9 is present in a 31-yr-old female who had been symptomatic for 12 mo. The causative organism was M. tuberculosis.

Palestro CJ et al. Radionuclide diagnosis of vertebral osteomyelitis: indium-111-leukocyte and technetium-99m-methylene diphosphonate bone scintigraphy. J Nucl Med. 1991 Oct;32(10):1861-5.

Radiolabeled WBC & Vertebral OM

- 15 (of 28) cases of vertebral OM had absent or ↓ radiolabeled WBC activity
  - Sn 54% and Sp 52%
- Of 12 with ↑ vertebral activity, 11 had confirmed vertebral OM
  - Sp 98%, but **Sn 39%**
- 26 scans had "normal" vertebral uptake
  - 2 had confirmed OM



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Radiolabeled WBC & Vertebral OM

TABLE 3
Comparison of Leukocyte and Bone Scintigraphy for Diagnosis of Vertebral Osteomyelitis

Criterion	Sen	Spc	Acc	+PV	−PV
Leukocyte (I) (n = 76)	39%	98%	76%	92%	73%
Leukocyte (D) (n = 76)	54%	52%	53%	39%	66%
Leukocyte (I or D) (n = 76)	93%	50%	66%	52%	92%
Two-Phase bone (n = 31)	47%	71%	58%	67%	53%
Delayed bone (n = 57)	86%	49%	63%	51%	85%

Sen = sensitivity; Spc = specificity; Acc = accuracy; +PV = positive predictive value; −PV = negative predictive value; I = increased; and D = decreased.

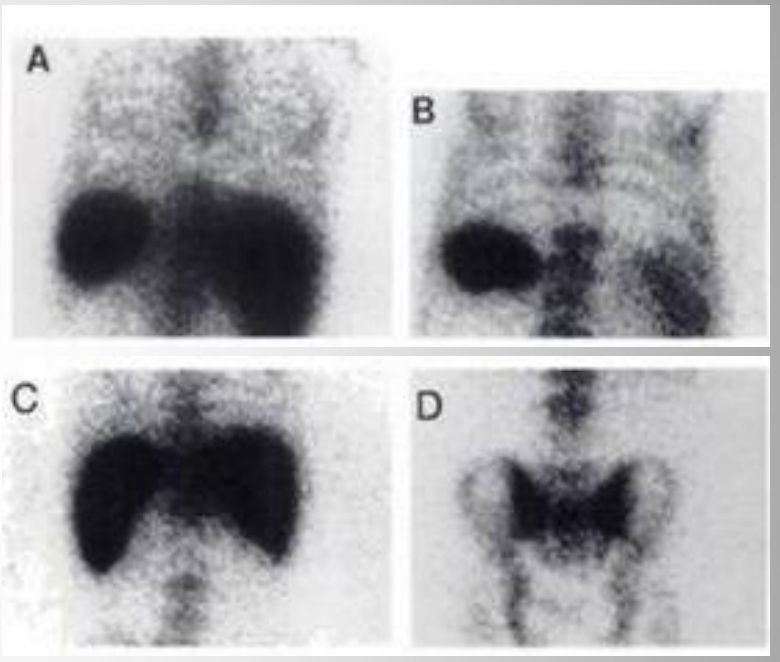


FIGURE 2. The principal limitation to labeled leukocyte imaging in vertebral osteomyelitis is the nonspecificity of skeletal photopenia, present in 54% of the cases of osteomyelitis in our series. We were unable to distinguish the skeletal photopenia seen in infection from other causes of skeletal photopenia. (A) Thoracic vertebral osteomyelitis in a 57-yr-old male symptomatic for 6 mo (purulence only was present in biopsy specimen—no organisms were cultured). (B) Prostate carcinoma metastases to the lower thoracic spine in a 73-yr-old male (photopenia involving a right lower posterior rib is also evident). (C) Lumbar spine compression fractures in a 66-yr-old female. (D) Paget's disease involving L5 in a 61-yr-old male.

Palestro CJ et al. Radionuclide diagnosis of vertebral osteomyelitis: indium-111-leukocyte and technetium-99m-methylene diphosphonate bone scintigraphy. J Nucl Med. 1991 Oct;32(10):1861-5.

Radiolabeled WBC & Skull OM

- In Seabold's study at the U. of Iowa, 26 patients with **suspected cranial OM** (16 were **post-operative**)
- Variety of studies including CT & MR with contrast and SPECT bone and radiolabeled WBC scan

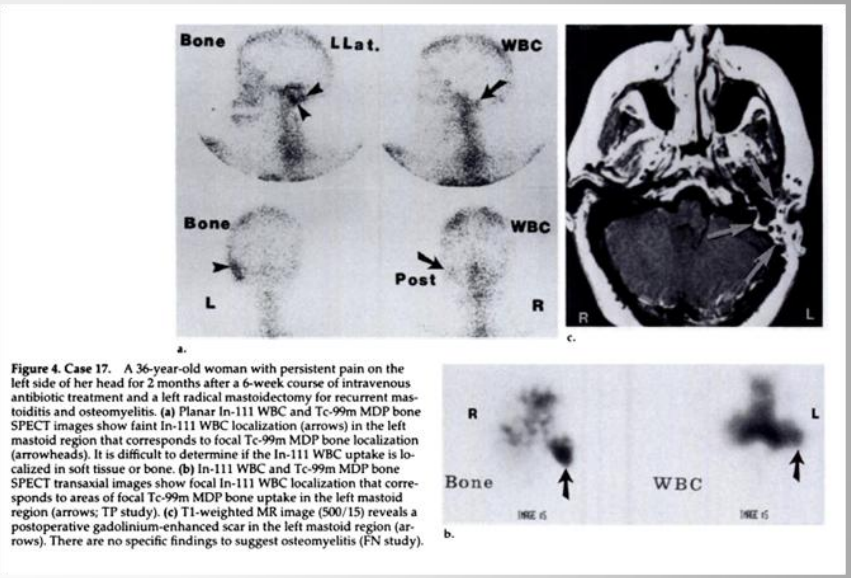
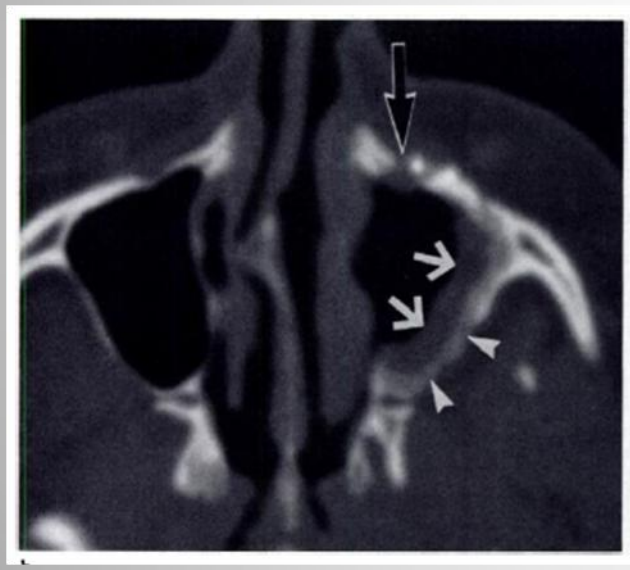
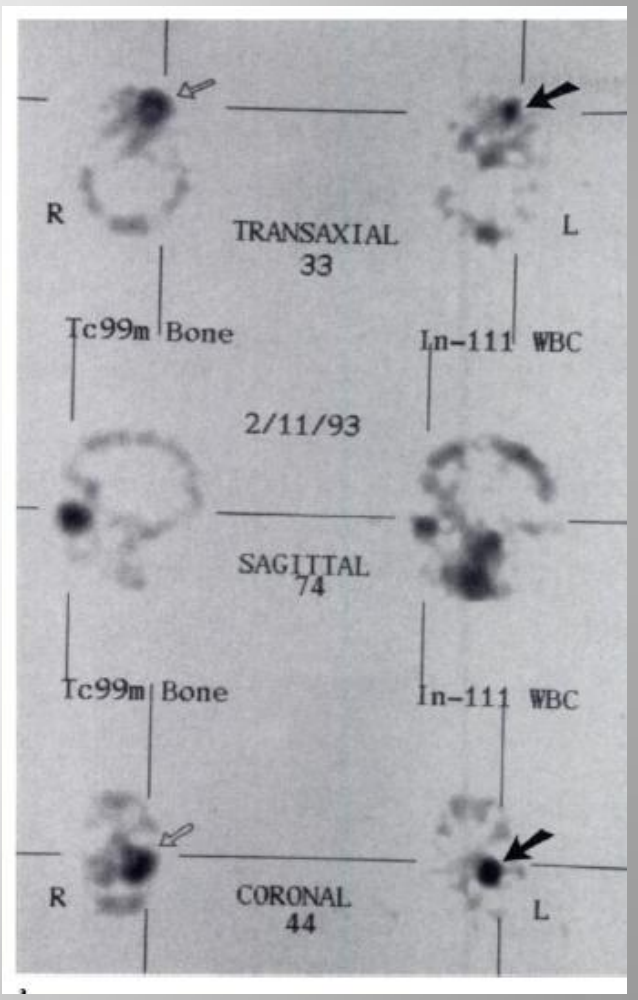


Figure 4. Case 17. A 36-year-old woman with persistent pain on the left side of her head for 2 months after a 6-week course of intravenous antibiotic treatment and a left radical mastoidectomy for recurrent mastoiditis and osteomyelitis. **(a)** Planar In-111 WBC and Tc-99m MDP bone SPECT images show faint In-111 WBC localization (arrows) in the left mastoid region that corresponds to focal Tc-99m MDP bone localization (arrowheads). It is difficult to determine if the In-111 WBC uptake is localized in soft tissue or bone. **(b)** In-111 WBC and Tc-99m MDP bone SPECT transaxial images show focal In-111 WBC localization that corresponds to areas of focal Tc-99m MDP bone uptake in the left mastoid region (arrows; TP study). **(c)** T1-weighted MR image (500/15) reveals a postoperative gadolinium-enhanced scar in the left mastoid region (arrows). There are no specific findings to suggest osteomyelitis (FN study).

Seabold JE et al. Cranial osteomyelitis: diagnosis and follow-up with In-111 white blood cell and Tc-99m methylene diphosphonate bone SPECT, CT, and MR imaging. Radiology. 1995 Sep;196(3):779-88.

Radiolabeled WBC & Skull OM





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Radiolabeled WBC & Skull OM

- If **no prior intervention in skull** (with minimal bone marrow), CT and bone scan most Sn for OM
- In **skull base** without prior intervention, MR and bone scan most Sn for OM
- MR is best imaging to assess extent of soft tissue involvement
- In **skull with pre-existing abnormality** (e.g., post-surgery), combined radiolabeled WBC & bone scans most Acc for OM
- Abnormal findings **revert back to normal** sooner with radiolabeled WBC scan vs MRI and CT in successfully treated patients

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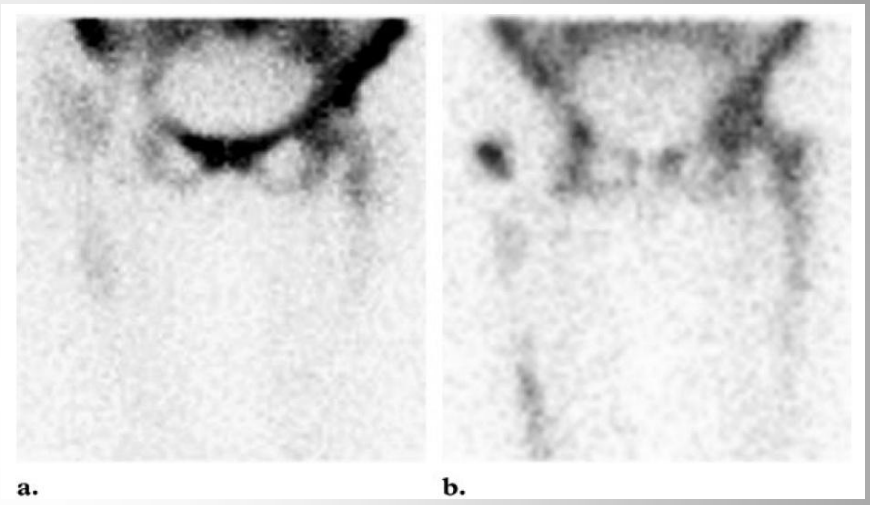
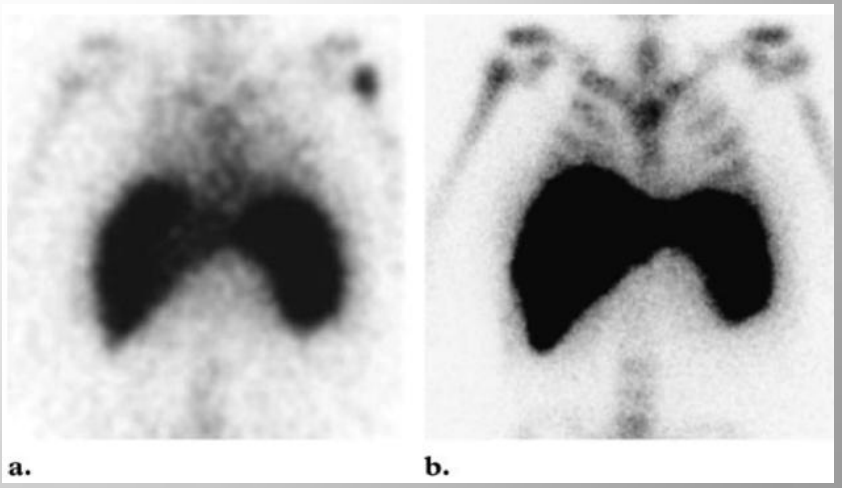
Radiolabeled WBC + Marrow Scan in Hardware Infections

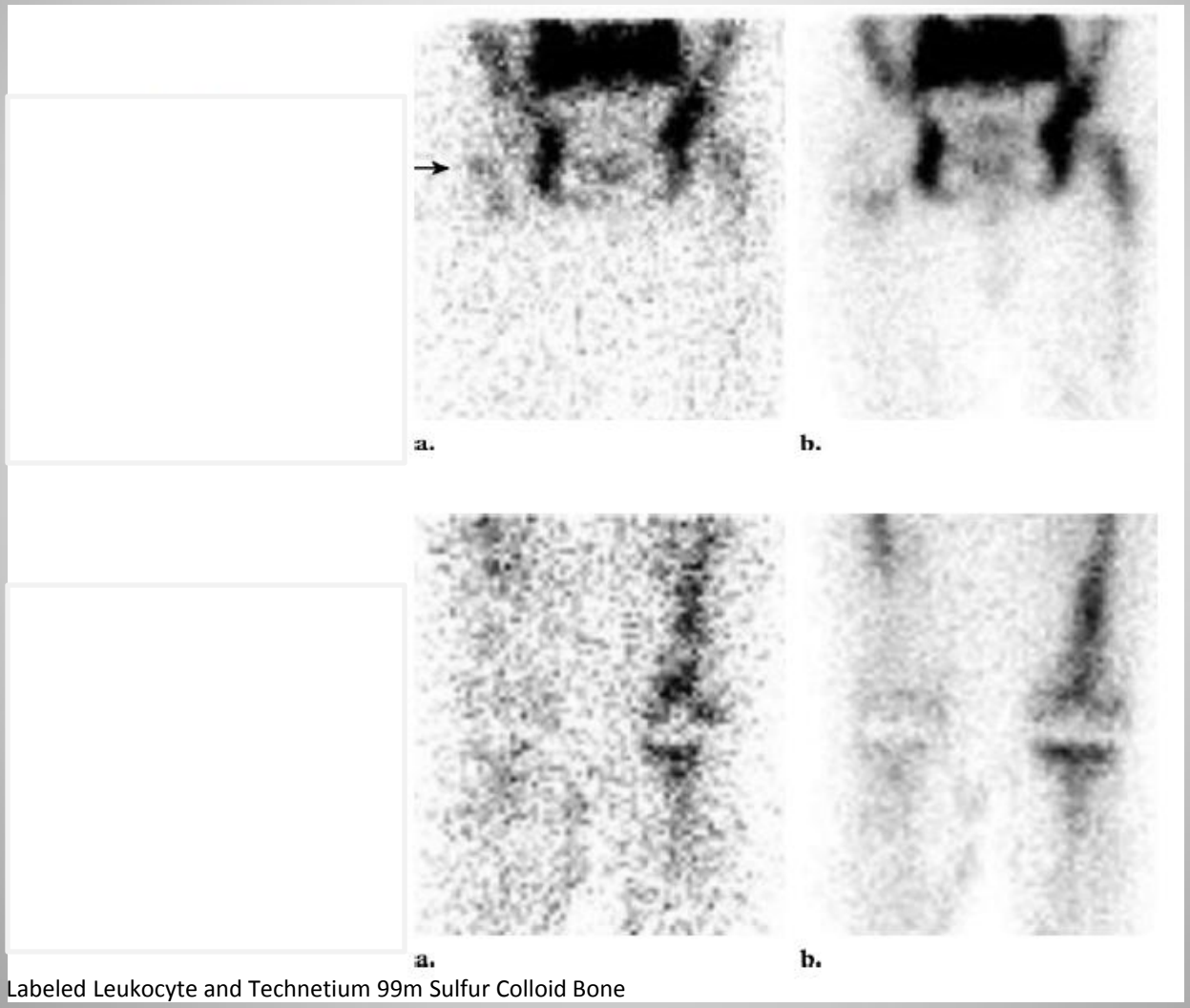
- In painful prostheses, radiolabeled WBC hard to interpret because poor Sp
  - WBC accumulate in normal marrow via phagocytosis
  - Bone scan also poor Sp
- Radiolabeled WBC + Tc-99m sulfur colloid (marrow) scans investigated since 1990
- Combination of WBC & marrow scans is **positive** for HW-associated infection when positive WBC scan finding has no corresponding activity on marrow scan (i.e., **incongruent**)





Palestro CJ et al. Combined Labeled Leukocyte and Technetium 99m Sulfur Colloid Bone Marrow Imaging for Diagnosing Musculoskeletal Infection. RadioGraphics 2006; 26:859–870.

Radiolabeled WBC + Marrow Scan in Hardware Infections



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Radiolabeled WBC + Marrow Scan in Hardware Infections

Neuropathic Arthropathy

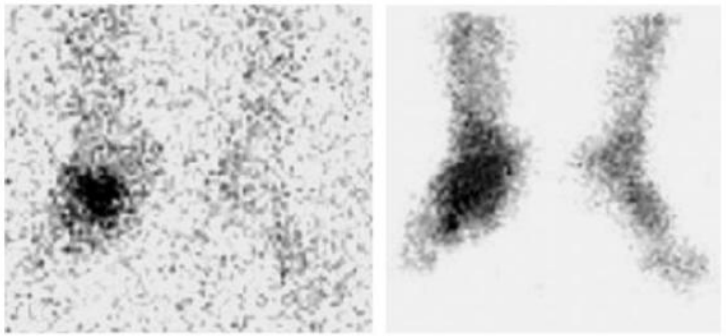
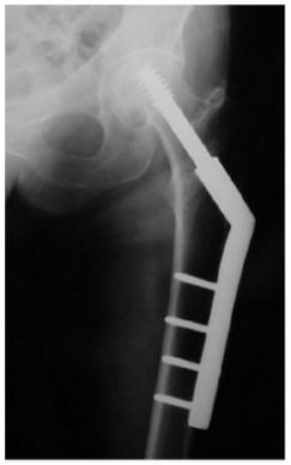


Figure 10. Uninfected neuropathic joint in a diabetic patient. WBC (**a**) and marrow (**b**) images show increased activity in the right midfoot.

Uninfected Hardware



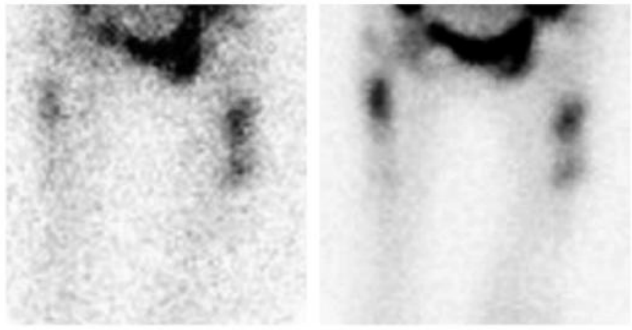


Figure 8. Uninfected orthopedic hardware. (**a**) Radiograph depicts a left hip dynamic screw. (**b, c**) WBC (**b**) and marrow (**c**) images show two foci of increased activity in the left femur and one focus in the proximal right femur.

a. b. c.

Palestro CJ et al. Combined Labeled Leukocyte and Technetium 99m Sulfur Colloid Bone Marrow Imaging for Diagnosing Musculoskeletal Infection. RadioGraphics 2006; 26:859–870.

Radiolabeled WBC + Marrow Scan in Hardware Infections

- Vexing issues with this combination
  - If no WBC activity (like central skeleton when photopenic defect corresponds to infection), marrow scan no help
  - Photopenic defect on marrow scan may **not** be present in **1st week after onset of OM**
  - Sulfur colloid degrades **2 hours after preparation**, causing erroneous conclusions

Palestro CJ et al. Combined Labeled Leukocyte and Technetium 99m Sulfur Colloid Bone Marrow Imaging for Diagnosing Musculoskeletal Infection. RadioGraphics 2006; 26:859–870.

Radiolabeled WBC + Marrow Scan in Hardware Infections

- 92 **hip arthroplasties** studied by Palesto's team at NY Mount Sinai Center
  - Arthroplasties considered infected if operative cultures grew organisms (n=19) or gross purulence at surgery (n=4)
- Among 42 with only In-111 WBC scan, Sn best in femoral head zone, 87%, and Sp 94%
- Among 50 with combined radiolabeled WBC/marrow scans, Sn was **100%** and Sp **97%** using criteria of **incongruence**

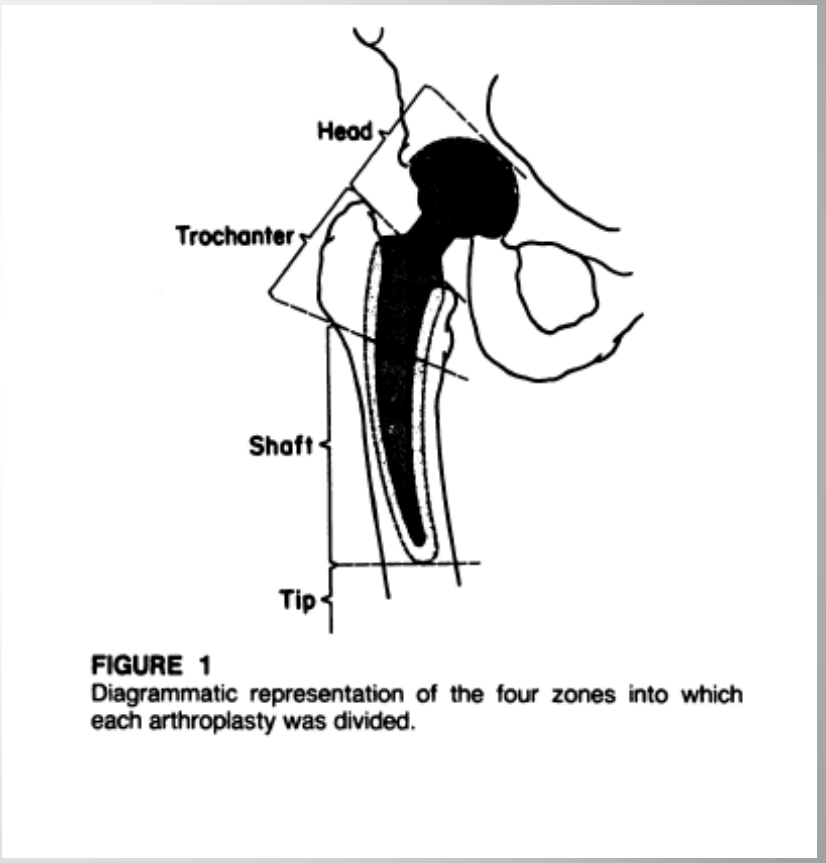


FIGURE 1
Diagrammatic representation of the four zones into which each arthroplasty was divided.

Palestro CJ et al. Total-hip arthroplasty: periprosthetic indium-111-labeled leukocyte activity and complementary technetium-99m-sulfur colloid imaging in suspected infection. J Nucl Med. 1990 Dec;31(12):1950-5.

Radiolabeled WBC + Marrow Scan in Hardware Infections

- Love's team in NY reviewed 59 patients with **painful prosthesis** who had FDG, marrow and radiolabeled WBC scans
  - Also had histopath and/or microbiology dx
  - Only non-AC FDG PET images reviewed

TABLE 1

^{18}F-FDG PET vs. WBC/Marrow Imaging in 59 Joint Replacements

Parameter	Sensitivity	Specificity	Accuracy	PPV	NPV
PPA	1.00 (25/25)	0.09 (3/34)	0.47 (28/59)	0.45 (25/56)	1.00 (3/3)
FDG/Ma	0.96 (24/25)	0.35 (12/34)	0.61 (36/59)	0.52 (24/46)	0.92 (12/13)
BPI	0.52 (13/25)	0.44 (15/34)	0.47 (28/59)	0.40 (13/32)	0.56 (15/27)
T/B ratio	0.36 (9/25)	0.97 (33/34)	0.71 (42/59)	0.90 (9/10)	0.67 (33/49)
WBC/Ma	1.00 (25/25)	0.91 (31/34)	0.95 (56/59)	0.89 (25/28)	1.00 (31/31)

PPV = positive predictive value; NPV = negative predictive value; PPA = any periprosthetic activity; FDG/Ma = FDG/marrow; BPI = BPI activity; T/B ratio = target-to-background ratio; WBC/Ma = labeled leukocyte/marrow.

TABLE 2

^{18}F-FDG PET vs. WBC/Marrow Imaging in 40 Hip Replacements

Parameter	Sensitivity	Specificity	Accuracy	PPV	NPV
PPA	1.00 (14/14)	0.12 (3/26)	0.43 (17/40)	0.38 (14/37)	1.00 (3/3)
FDG/Ma	0.93 (13/14)	0.46 (12/26)	0.63 (25/40)	0.48 (13/27)	0.92 (12/13)
BPI	0.57 (8/14)	0.46 (12/26)	0.50 (20/40)	0.36 (8/22)	0.67 (12/18)
T/B ratio	0.43 (6/14)	0.96 (25/26)	0.78 (31/40)	0.86 (6/7)	0.76 (25/33)
WBC/Ma	1.00 (14/14)	0.88 (23/26)	0.93 (37/40)	0.82 (14/17)	1.00 (23/23)

PPV = positive predictive value; NPV = negative predictive value; PPA = any periprosthetic activity; FDG/Ma = FDG/marrow; BPI = BPI activity; T/B ratio = target-to-background ratio; WBC/Ma = labeled leukocyte/marrow.

TABLE 3

^{18}F-FDG PET vs. WBC/Marrow Imaging in 19 Knee Replacements

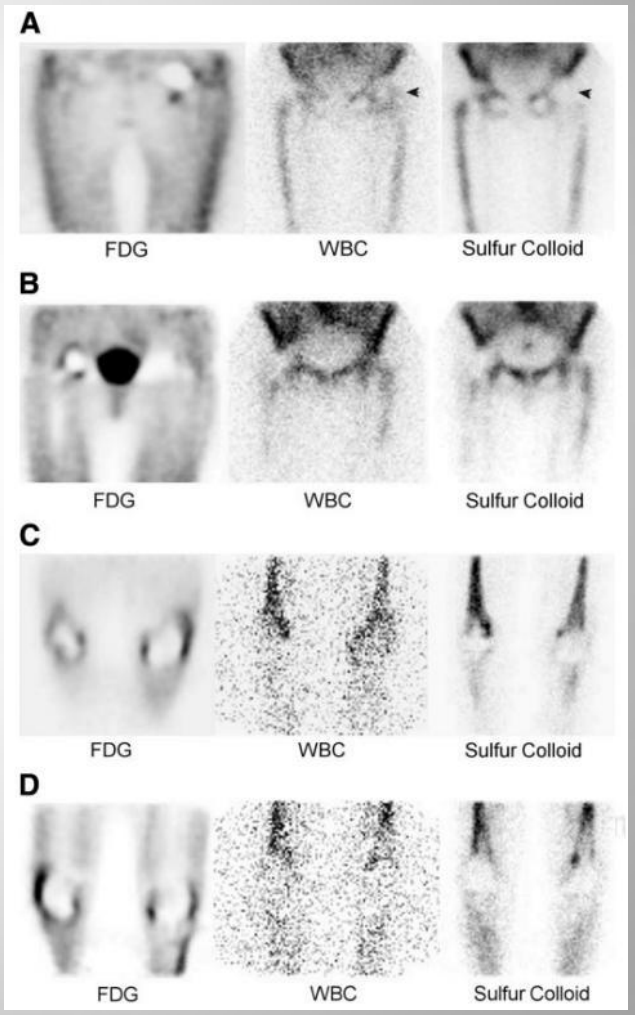
Parameter	Sensitivity	Specificity	Accuracy	PPV	NPV
PPA	1.00 (11/11)	0.00 (0/8)	0.58 (11/19)	0.58 (11/19)	0.00 (0/0)
FDG/Ma	1.00 (11/11)	0.00 (0/8)	0.58 (11/19)	0.58 (11/19)	0.00 (0/0)
BPI	0.45 (5/11)	0.38 (3/8)	0.42 (8/19)	0.50 (5/10)	0.33 (3/9)
T/B ratio	0.27 (3/11)	1.00 (8/8)	0.58 (11/19)	1.00 (3/3)	0.50 (8/16)
WBC/Ma	1.00 (11/11)	1.00 (8/8)	1.00 (19/19)	1.00 (11/11)	1.00 (8/8)

PPV = positive predictive value; NPV = negative predictive value; PPA = any periprosthetic activity; FDG/Ma = FDG/marrow; BPI = BPI activity; T/B ratio = target-to-background ratio; WBC/Ma = labeled leukocyte/marrow.

Love C et al. Diagnosing infection in the failed joint replacement: a comparison of coincidence detection 18F-FDG and 111In-labeled leukocyte/99mTc-sulfur colloid marrow imaging. J Nucl Med. 2004 Nov;45(11):1864-71.

Radiolabeled WBC + Marrow Scan in Hardware Infections

- Radiolabeled WBC + marrow scans very Sn (100%) and Sp (91%) for infected prosthetic joints
  - **Sn/Sp 100%** for painful **knee** prostheses (n=19)
- Acc 95% vs 61% for FDG PET
- Tracers are different
  - Neutrophils present in acute infection but absent in loosening, thus high Sp/Sn
  - FDG into activated inflamm cells, thus high FP



Love C et al. Diagnosing infection in the failed joint replacement: a comparison of coincidence detection 18F-FDG and 111In-labeled leukocyte/99mTc-sulfur colloid marrow imaging. J Nucl Med. 2004 Nov;45(11):1864-71.

Radiolabeled WBC + Marrow Scan in Hardware Infections

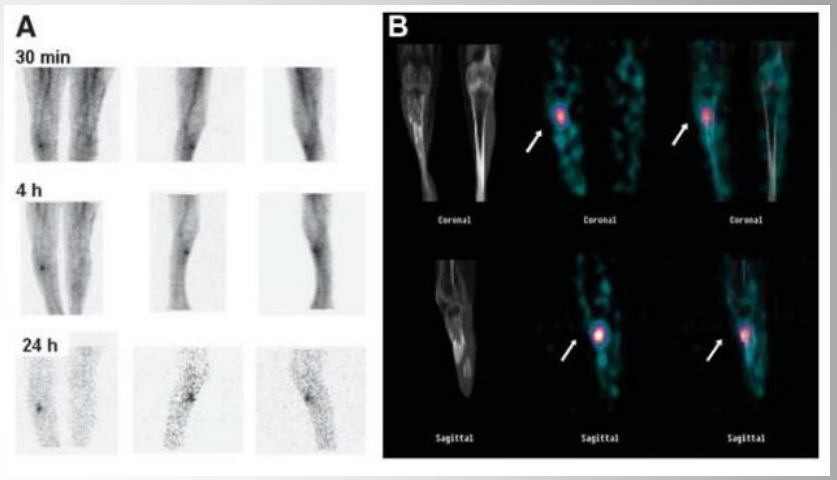
- Van Acker's team in Belgium prospectively studied 21 patients with 3-phase bone scan to exclude **TKA infection**
- Radiolabeled WBC scan with Tc-99m HMPAO; SPECT 4 hours & planar 24 hours post-injection
  - Used 0-4 grading scale for uptake, and **uptake at bone-prosthesis interface (BPI) considered positive**
- Compared to FDG PET

- Focal radiolabeled WBC activity alone was **53% Sp**
- **Sp** became **93%** when correlated with "hot spot" on bone scan
  - 4 FP (loosening) on WBC scan ↓ to 1 because of bone scan
  - Radiolabeled WBC 100% Sn
- Focal FDG uptake alone was **73% Sp**
- **Sp** became **80%** when correlated with "hot spot" on bone
  - FDG scan 100% Sn

Van Acker F et al. FDG-PET, 99mtc-HMPAO white blood cell SPET and bone scintigraphy in the evaluation of painful total knee arthroplasties. Eur J Nucl Med. 2001;28(10):1496-504.

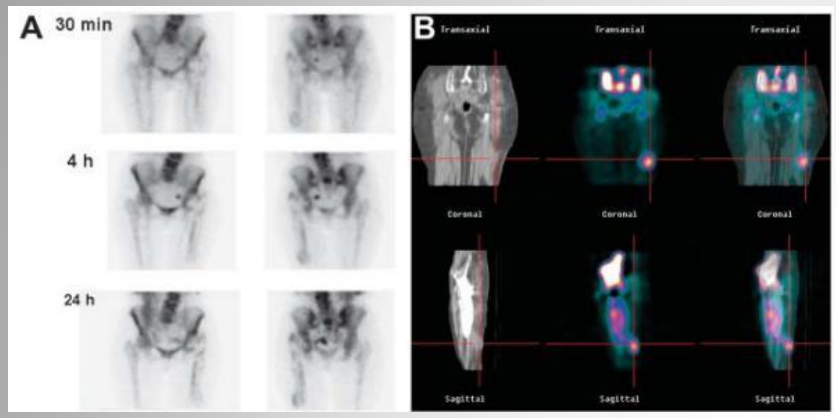
Radiolabeled WBC SPECT/CT

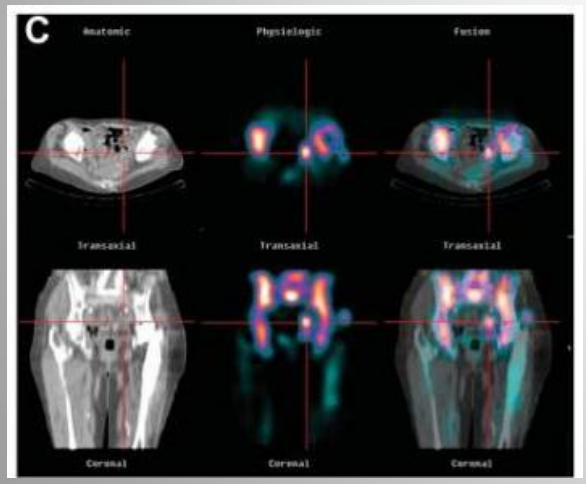
- Filippi's team in Rome studied 15 patients with **suspected OM** and 13 patients with **suspected HW infection**
- Planar 99m-Tc HMPAO images taken ½, 4 & 24 hr post injection
- 99m-Tc HMPAO ***SPECT/CT*** taken 6 hr post injection



Filippi L and Schillaci O. Usefulness of hybrid SPECT/CT in 99mTc-HMPAO-labeled leukocyte scintigraphy for bone and joint infections. J Nucl Med. 2006 Dec;47(12):1908-13.

Radiolabeled WBC SPECT/CT



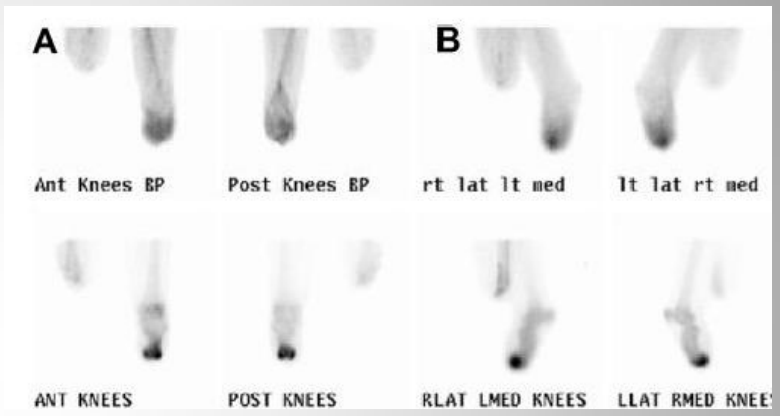


- **100% Sp** of SPECT + planar alone (no CT)
- But **Sn poor:** 7 FNs & 3 false extent of disease (soft tissue & bone)
- SPECT/CT **improved localization** of focal radiolabeled WBC activity in **35% of 28 cases**
- **Sn** and **Sp** of **SPECT/CT** for diagnosing infection was **100%**

Filippi L and Schillaci O. Usefulness of hybrid SPECT/CT in 99mTc-HMPAO-labeled leukocyte scintigraphy for bone and joint infections. J Nucl Med. 2006 Dec;47(12):1908-13.

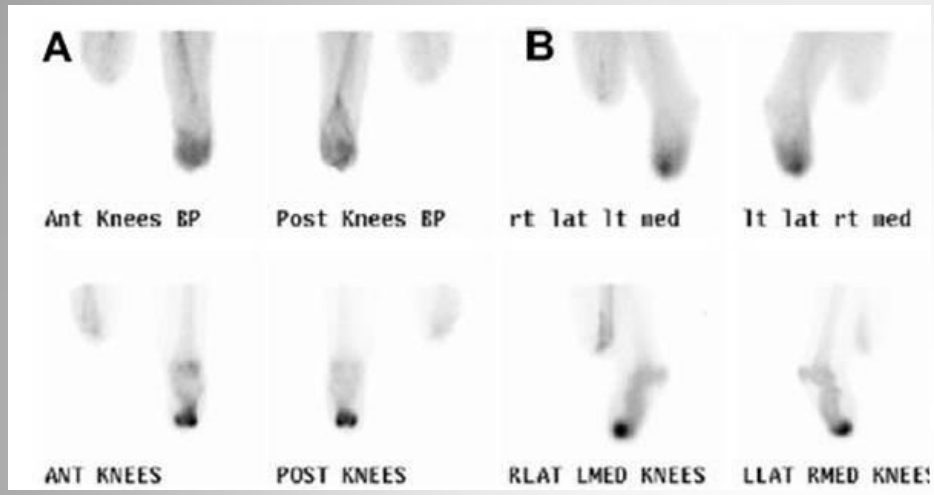
Tc-99m MDP Bone SPECT/CT Case

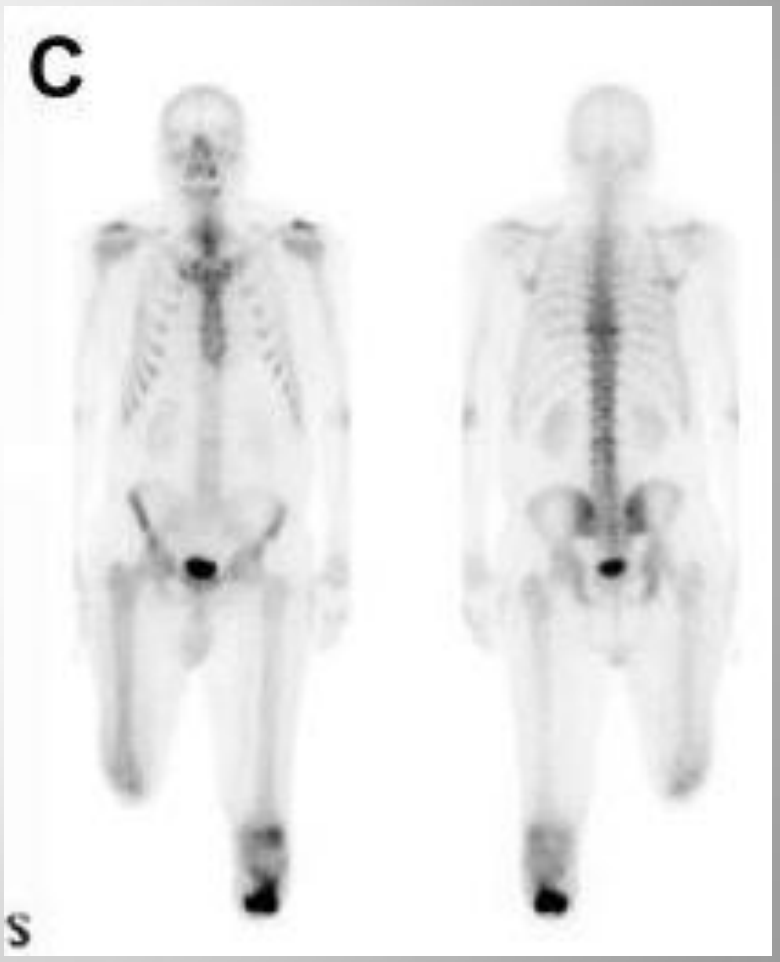
- 46-year-old man with history of bilateral amputations presents with long-standing chronic non-healing wound at the left below knee amputation (BKA), sustained after a crush injury
- Referred for bone scan to exclude osteomyelitis of left stump



Hassan FU et al. Heterotrophic Ossification in a Patient Suspected of Having Osteomyelitis: Additional Value of SPECT/CT. Clin Nuc Med. 2012;37: 170–171.

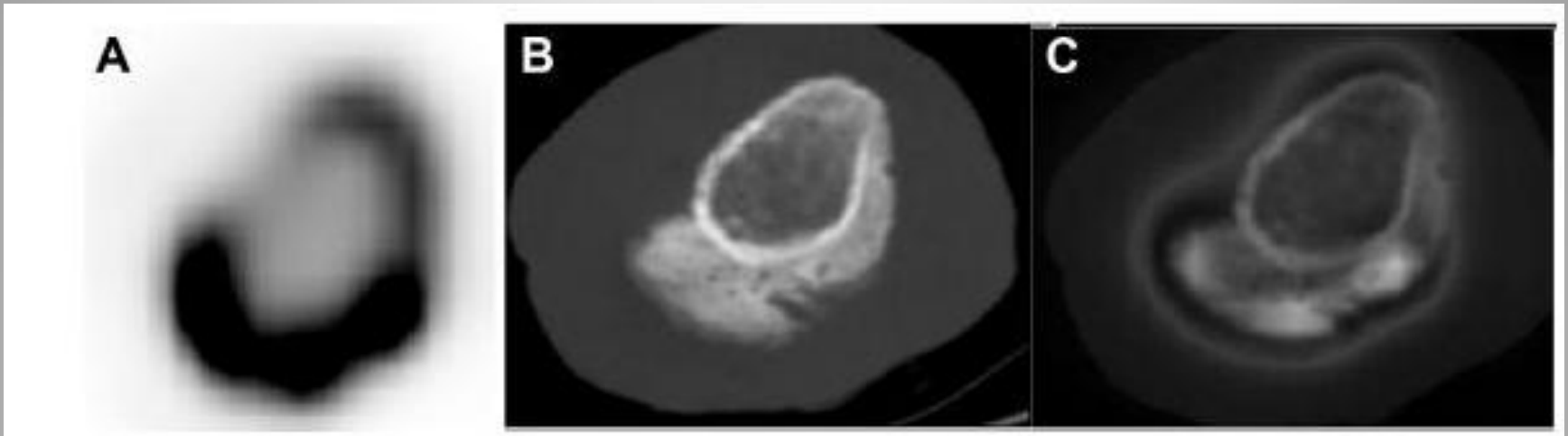
Tc-99m MDP Bone SPECT/CT Case





Hassan FU et al. Heterotrophic Ossification in a Patient Suspected of Having Osteomyelitis: Additional Value of SPECT/CT. Clin Nuc Med. 2012;37: 170–171.

Tc-99m MDP Bone SPECT/CT Case



- On Tc-99m MDP bone SPECT/CT, increased tracer accumulation corresponds to heterotopic ossification on CT, not to bone, thus excluding OM with high degree of Sn

Hassan FU et al. Heterotrophic Ossification in a Patient Suspected of Having Osteomyelitis: Additional Value of SPECT/CT. Clin Nuc Med. 2012;37: 170–171.

Adding CT to SPECT

- Disadvantages
  - **Lower count rate** versus planar imaging (as it is reconstructed and not truly tomographic imaging)
  - **Lower spatial resolution** than planar imaging
  - Takes **longer to acquire** good-quality images
- Advantages
  - **Localizes "**hot spot," thus showing whether it is at site of interest or outside of it
  - Regardless of tracer or disease entity, scintigraphy's **Sp goes up** when CT added
  - Improves **inter-reader agreement** & **management of patients**

Horger M, Eschmann SM, Pfannenberg C, et al: The value of SPET/CT in chronic osteomyelitis. Eur J Nucl Med Mol Imaging 2003; 30:1665-1673.

Horger M, Eschmann SM, Pfannenberg C, et al: Added value of SPECT/CT in patients suspected of having bone infection: preliminary results. Arch Orthop Trauma Surg . 2007; 127:211-221.

Summary of Gamma Imaging of Suspected MSK Infections

- Bone Scan has excellent Sn but poor Sp
- Radiolabeled WBC Scan has good Sp & Sn in peripheral skeleton
  - Poor Sn in central skeleton
- Bone + Radiolabeled WBC scans improve Sp (and thus accuracy)
  - But in diabetic foot ulcer/OM, neuropathic joint disease is problem
  - Good Acc in infected knee & hip prostheses

Summary of Gamma Imaging of Suspected MSK Infections

- Radiolabeled WBC + Marrow scans improve accuracy
  - Better in diabetic foot OM/ulcer
  - Perhaps better Acc in infected knee prostheses
- Impact of SPECT and SPECT/CT
  - Improves accuracy and localization

F-18 FDG PET Imaging of MSK Infections

F-18 FDG

- FDG enters cells via **glucose transporters**
  - Active transport mediated by GLUT 1-10, but primarily by **GLUT 1 & 3**
  - Active transport by Na^+-glucose transporter (primary mechanism for kidney epithelial & intestinal cells)
  - Passive diffusion is minor compared to active
- FDG gets **phosphorylated** and **not further metabolized**
  - 2'-FDG-6 phosphate **not substrate** for glycolytic pathway or pentose-phosphate shunt
  - Low initial concentrations of FDG in normal fasting heart & brain, but uptake increases over time

FDG & WBC

- Accumulates much more in **activated** (versus inactive) lymphocytes and especially **neutrophils & macrophages**
  - 24 hours after activation of WBC, increased de novo synthesis of GLUT-1 & 3
  - **Blood glucose < 250 mg/dL**, FDG uptake into inflammatory cells **not** impaired
- Radiolabeled WBCs are different, going wherever WBC are, activated or not
  - FDG relatively **low accumulation in normal marrow**

Zhuang HM et al. Do high glucose levels have differential effect on FDG uptake in inflammatory and malignant disorders? Nuc Med Comm. 2001; 22(10): 1123-8.

Forstrom LA et al. 18F-FDG labelling of human leukocytes. Nuc Med Comm. 2000; 21(7): 691-4.

Patient History & FDG PET

- Positive PET findings have to be interpreted **in context of patient history**
  - FDG PET is a **non-specific** tracer
  - Active inflammation present for **months to year after** orthopedic surgery
  - Inflammation related to **bone remodeling** after fracture or surgical intervention

F-18 FDG PET/CT Scan

- 370-740 MBq (10-20 mCi) of F-18 FDG by IV
- Imaging on PET/CT scanner
  - Low-dose CT for anatomic localization & attenuation correction
- Effective dose: 14.1 mSv
- **Partial body** PET/CT to reduce radiation dose
- Image acquisition starts about 45 min after injection and lasts 35 minutes (3-5 min for CT)

FDG PET & Chronic OM

- In **acute OM**, FDG PET adds no value over CT, MRI and combination scintigraphy
  - *Conventional Imaging has > 90% accuracy*
- **FDG PET** useful in **chronic OM (COM)**, where these modalities are limited
  - **COM**: **> 6 weeks** of ongoing bone infection whether or not signs & symptoms are present
  - Anatomic imaging: low Sp of X-ray, CT & MR (most Sn?) for various reasons
  - Functional imaging: low Sp (bone & gallium scans) or low Sn (radiolabeled WBC scan), also potential for suboptimal preparation, lots of time and costs

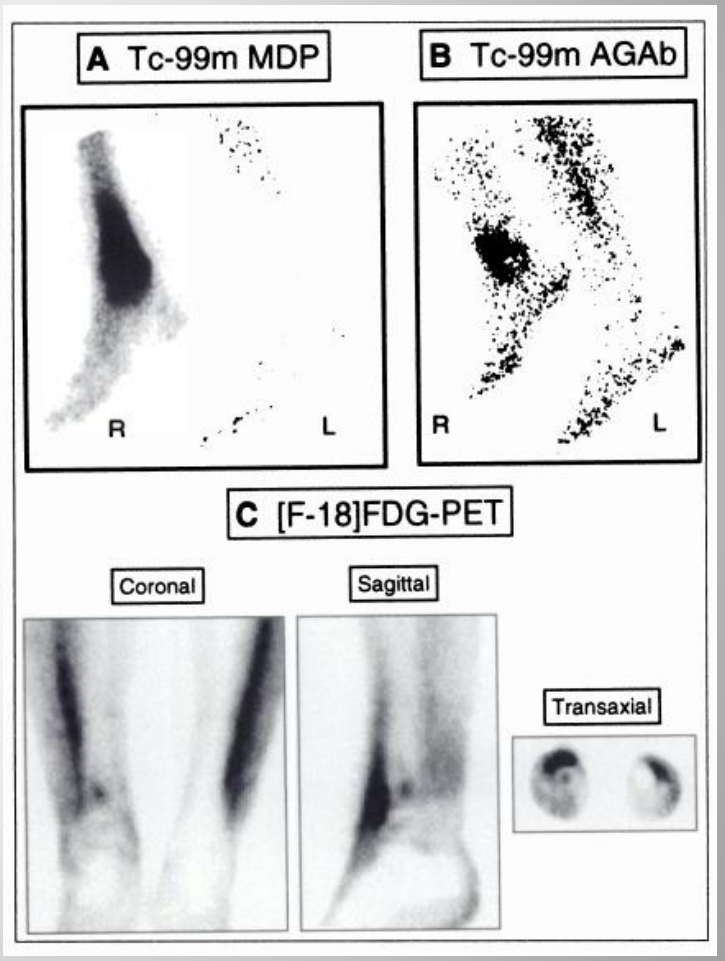
FDG PET & Chronic OM

- Zhuang's team studied 22 patients at Penn
  - 6 diagnosed with **COM** *but no criteria* defined (except 1 year follow-up)
- All 6 COM cases diagnosed by 3 readers using **FDG PET** (no CT), thus **Sn 100**%
  - 2 patients had False Positive diagnosis by PET (both osteotomy-related inflammation), thus **Sp not good**

Zhuang H. Exclusion of Chronic Osteomyelitis With F-18 Fluorodeoxyglucose Positron Emission Tomographic Imaging. Clin Nucl Med. 2000; 25(4):281-4.

FDG PET & Chronic OM

- Guhlmann's team prospectively studied 51 patients, 28 **proven COM**
  - Recurrent or OM sx > 6 wks
- **FDG PET** detected COM in 27 of 28 → **Sn of 96%**
- Excluded COM in 22 of 23 patients → **Sp 96%**
- AGAb scan (+ bone scan) had Sn/Sp 82%/88%

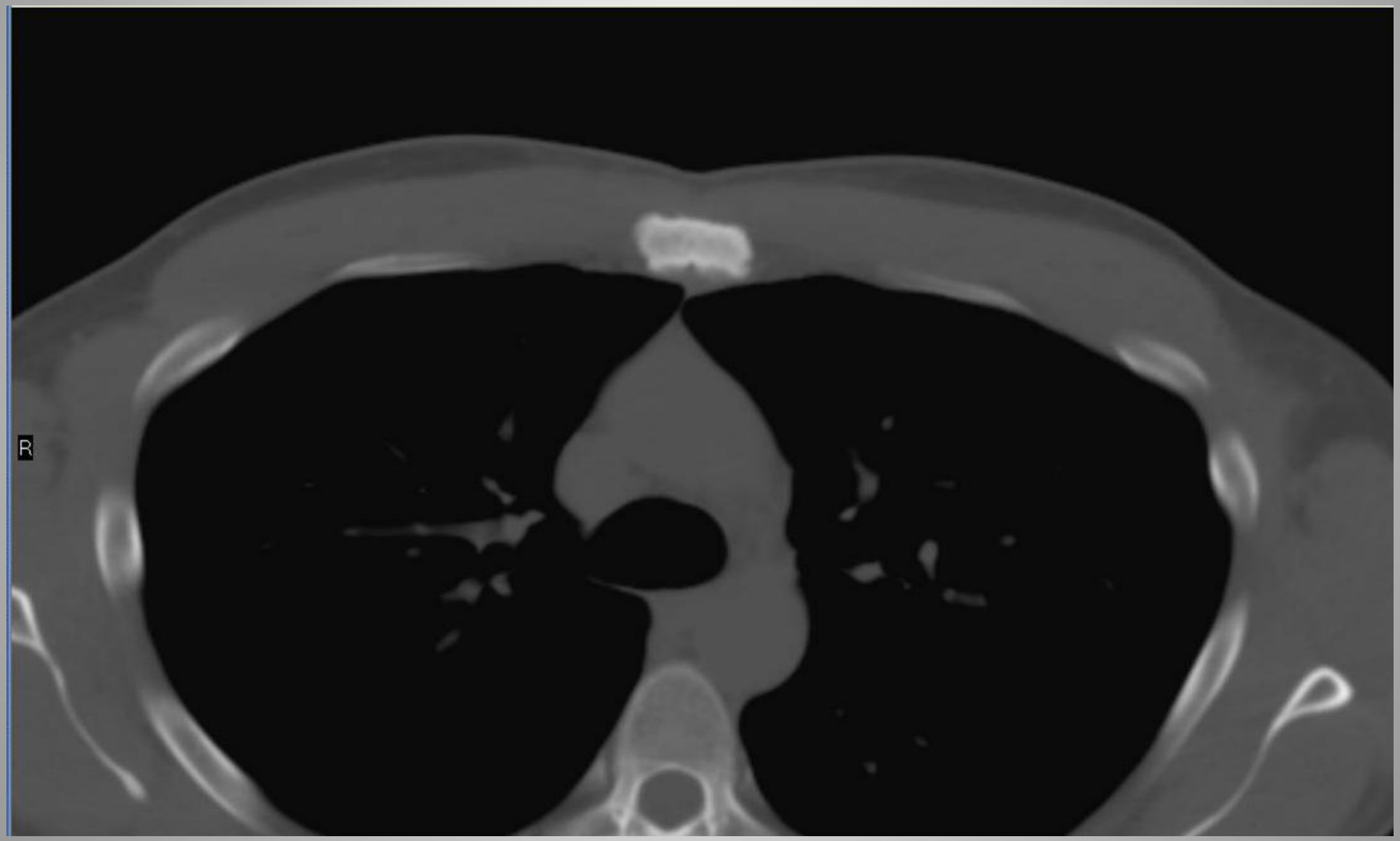


Guhlmann A et al. Fluorine-18-FDG PET and Technetium-99m Antigranulocyte Antibody Scintigraphy in Chronic Osteomyelitis. J Nuc Med 1998; 39:2145-2152.

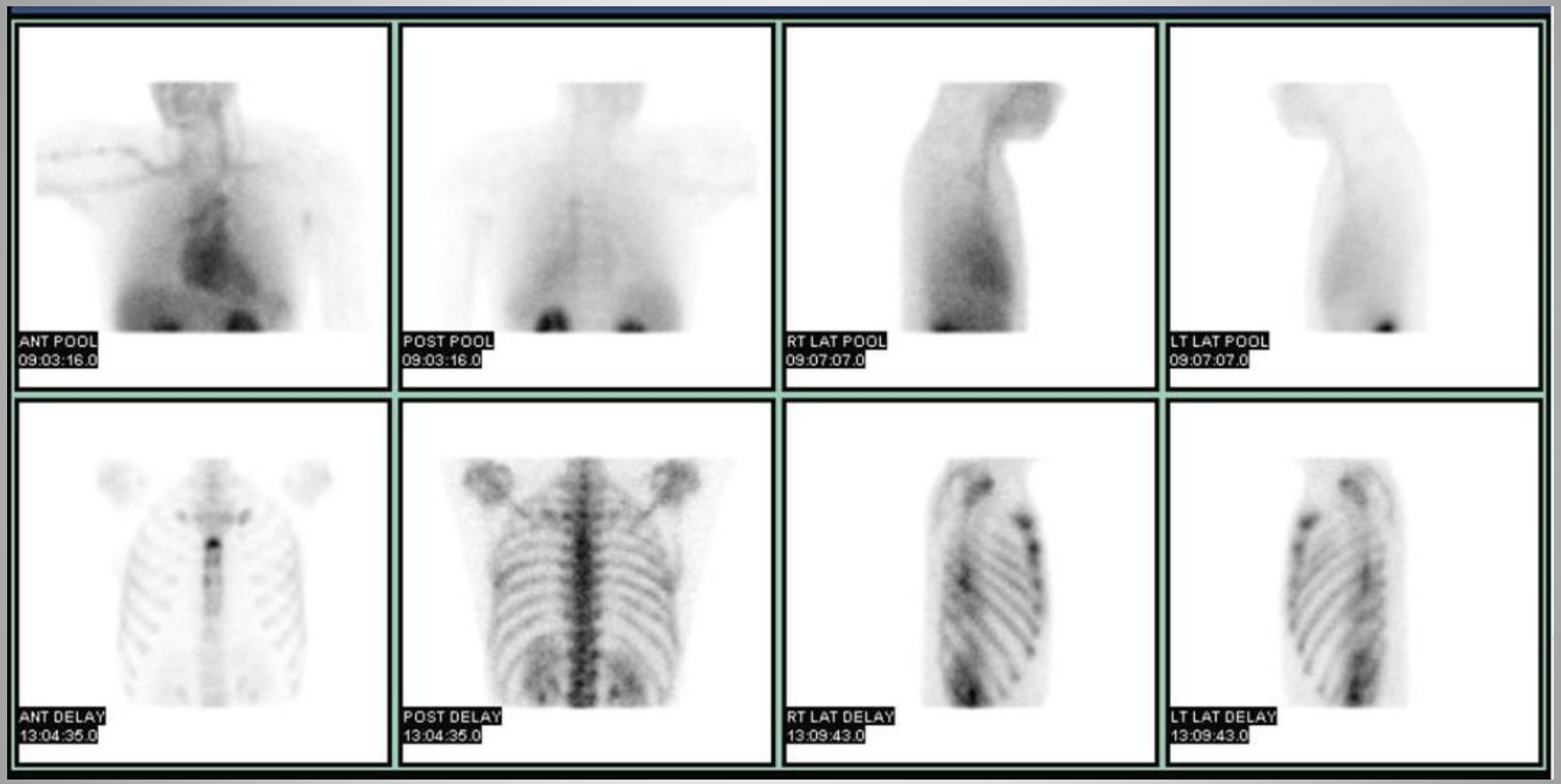
Case 1

- Man in his 50s complains of long standing central chest pain (“for years”)
  - PCP localizes it to sternum, which is TTP and worse with exertion
  - Remote history of trauma to sternum, but no surgical intervetion
  - Labs were relatively normal
- Seen at VA in 2009 from OSH, then again in 2011

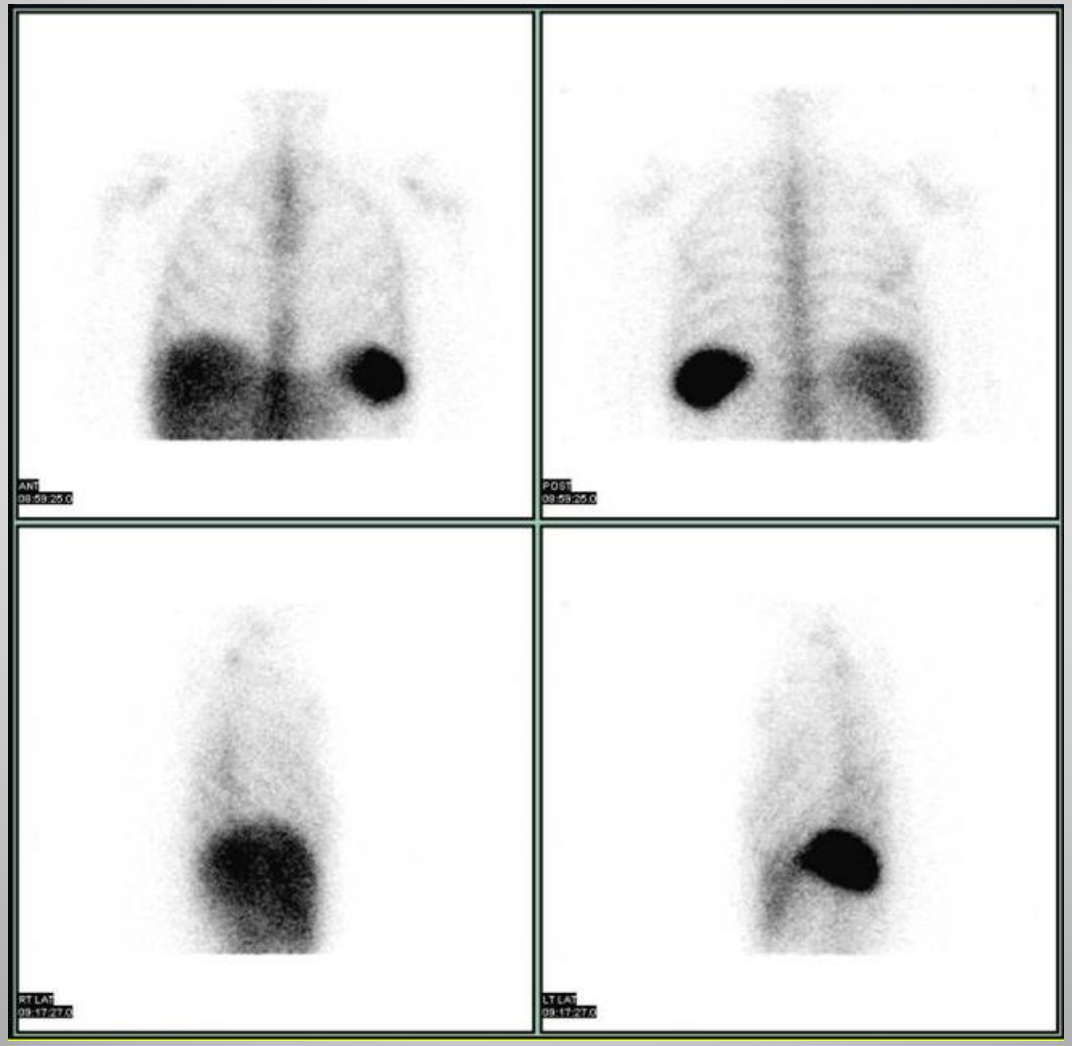
CT Chest 7/2009



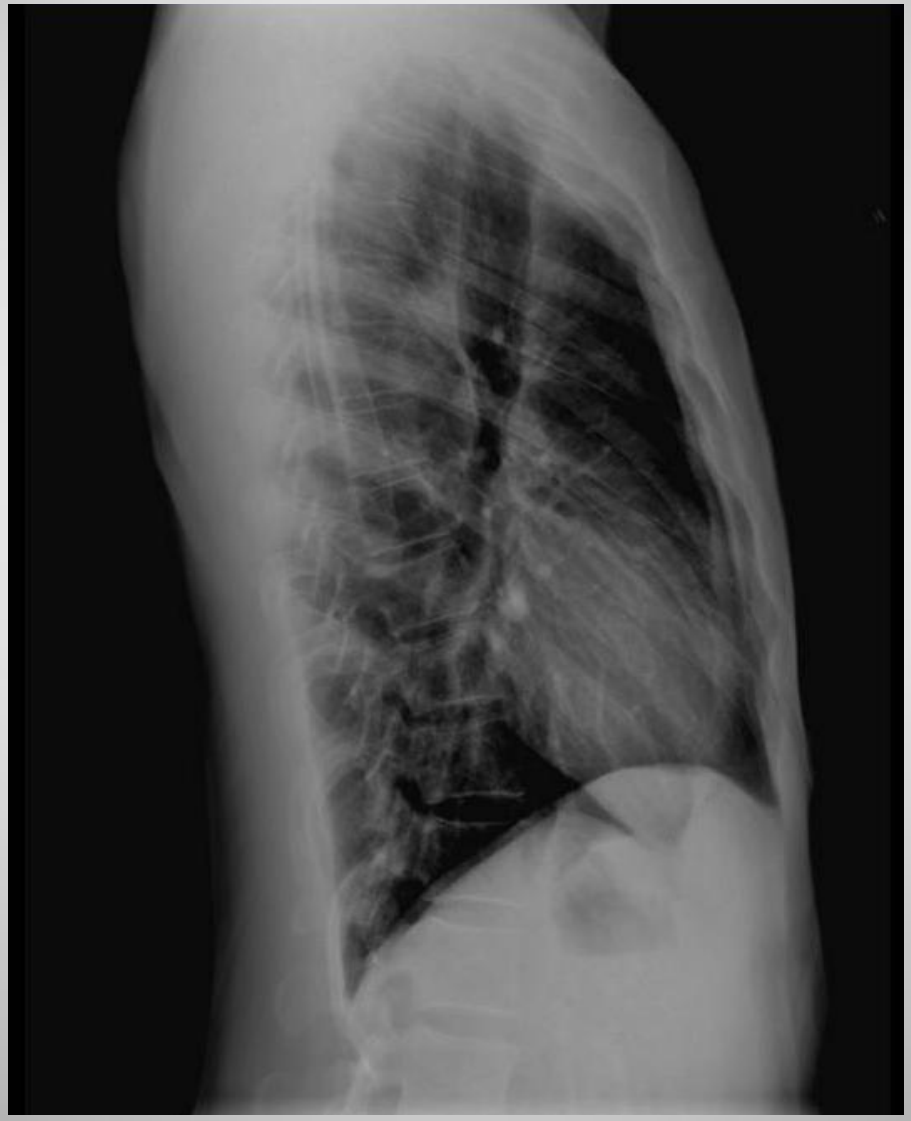
Bone Scan 7/2009



Radiolabeled WBC Scan 9/2009



Chest X-ray 9/2011



Case 1

- PCP relied on negative WBC study
  - Recall that this has poor to moderate Sn for **chronic** infections
- CT-guided aspiration biopsy was negative
  - Sensitivity of procedure is **moderate** (73-87%), on lower end if on antibiotics
- New PCP reviewed reports and wants bone scan because patient's sternal complains slightly worsening

Sutton PR et al. Diagnosing Osteomyelitis with Percutaneous Bone Biopsy in Patients with Diabetes and Bone Ulcerations. J of Gen Int Med 2008; 15(s2):6.

Howard CB et al. Fine-Needle Bone Biopsy to Diagnose Osteonyelitis. J Bone Joint Surg 1994; 76-B:311-4.

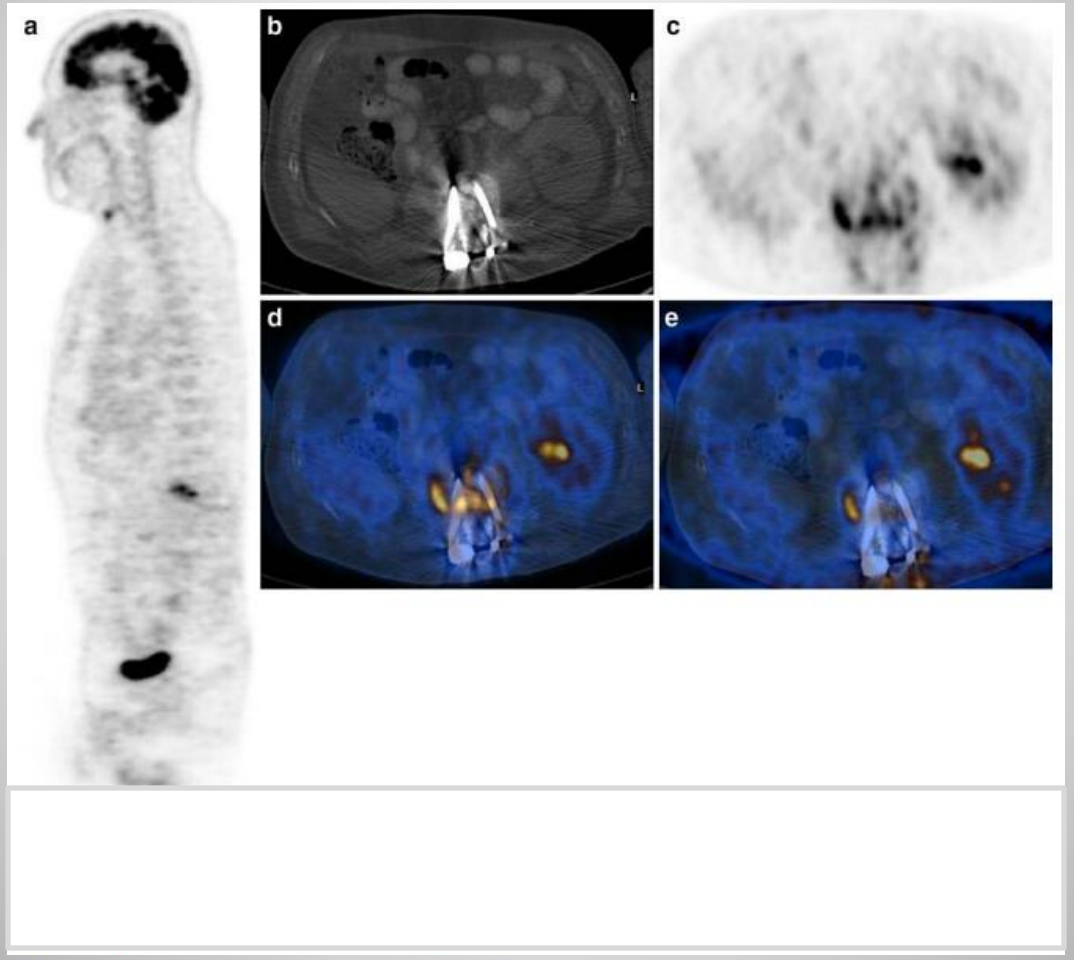
FDG PET & Post-traumatic OM

- Hartmann's team in Switzerland reviewed 33 partial body **FDG PET/CT** in **post-trauma** patients **suspected to have COM**
- 18 had metallic implants
- Histopathology or culture was standard reference

- Radiolabeled WBC/Marrow scans study of choice for **post-traumatic** infection imaging
  - MRI & CT susceptible to safety issue & beam-hardening artifact
  - Bone scan susceptible to post-traumatic bone remodeling

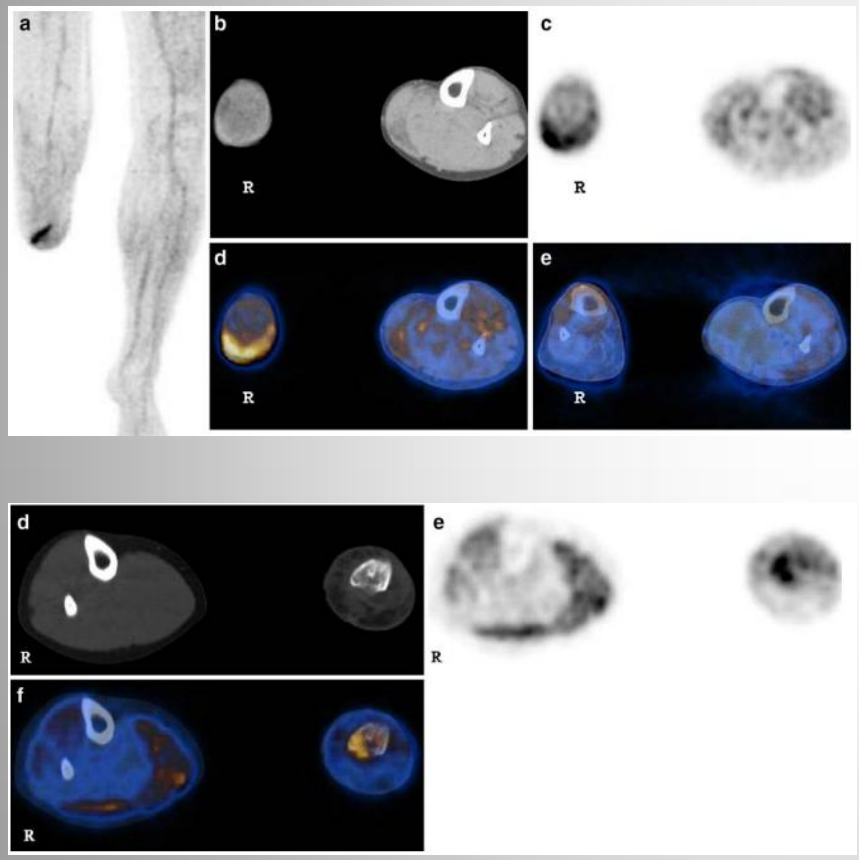
Hartmann A et al. Diagnostic value of 18 F-FDG PET/CT in trauma patients with suspected chronic osteomyelitis.eEur J Nucl Med Mol Imaging 2007; 34:704–71.

FDG PET & Post-traumatic OM



Hartmann A et al. Diagnostic value of 18 F-FDG PET/CT in trauma patients with suspected chronic osteomyelitis.eEur J Nucl Med Mol Imaging 2007; 34:704–71.

FDG PET & Post-traumatic OM



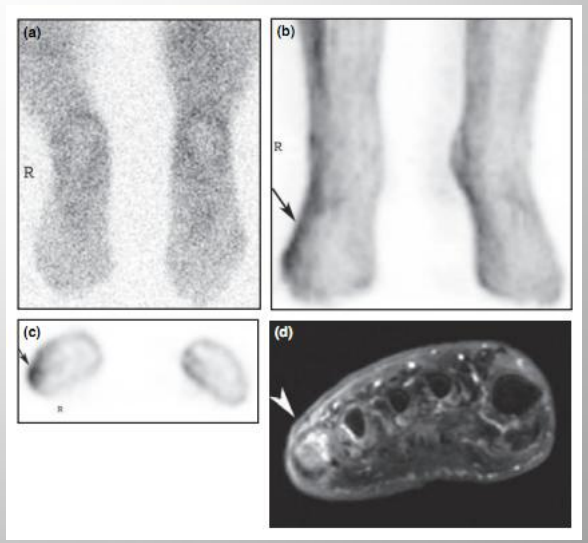
- Of 33 partial **PET/CT**, 17 were TP (and 2 FP) → **Sn 94%**
- 13 were TN (and 1 FN) → **Sp 87%**
- **Axial** (or **central**) skeleton: 88% Sn and **100% Sp**
- **Appendicular** skeleton: **Sn 100%** and Sp 85%

Hartmann A et al. Diagnostic value of 18 F-FDG PET/CT in trauma patients with suspected chronic osteomyelitis.eEur J Nucl Med Mol Imaging 2007; 34:704–71.

FDG PET & OM of Diabetic Foot

- Schwegler's Swiss team prospectively studied 20 **DM** patients with **chronic foot ulcer** (> 8 weeks) *but* no signs of OM
- **7 biospy-proven OM** in ***un***suspected foot

- MRI: TP in 6 patients
- **FDG PET** (*no CT*): TP in 2 patients
- Both TN in 12 of 13 patients



Schwegler B et al. Unsuspected osteomyelitis is frequent in persistent diabetic foot ulcer and better diagnosed by MRI than by 18 F-FDG PET or 99m Tc-MOAB . J of Int Med 2007; 263; 99–10.

FDG PET & OM of Diabetic Foot

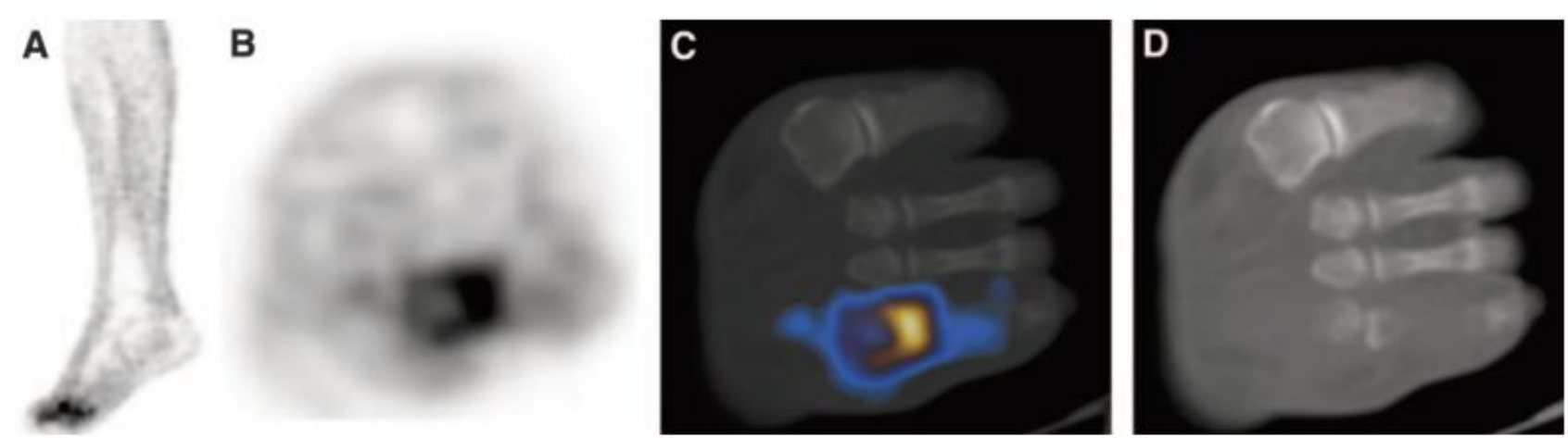


FIGURE 1. PET/CT-based diagnosis of osteomyelitis complicating diabetic foot in 50-y-old man with nonhealing wound in right forefoot. (A and B) ^{18}F-FDG PET coronal (A) and transaxial (B) images show area of increased ^{18}F-FDG uptake in lateral aspect of forefoot. (C) PET/CT localizes abnormal ^{18}F-FDG uptake to head of fourth metatarsus. (D) CT shows normal bone structure in corresponding area. Osteomyelitis was further confirmed by histopathologic examination of tissue samples obtained at surgery.

- Keidar's Israeli team prospectively studied 18 **pedal sites** in 14 **diabetic** patients
- **PET** found 14 foci
- **PET/CT** localized 8 foci to bone (4 patients)
  - 1 case characterized findings as neuropathic arthropathy

Keidar Z et al. The Diabetic Foot: Initial Experience with 18 F-FDG PET/CT. J Nucl Med 2005; 46:444-449.

FDG PET & OM of Diabetic Foot

- PET/CT read by NM docs & skeletal radiologist
- Of **8 OM** findings on **PET/CT** (**4 pts**), 5 in metatarsal bones
  - CT characterized 5 'likely OM' (of which 3 normal)
- All 4 patients PET/CT positive patients **confirmed** to have **OM** (3 histopath, 1 clinical + x-rays hx)

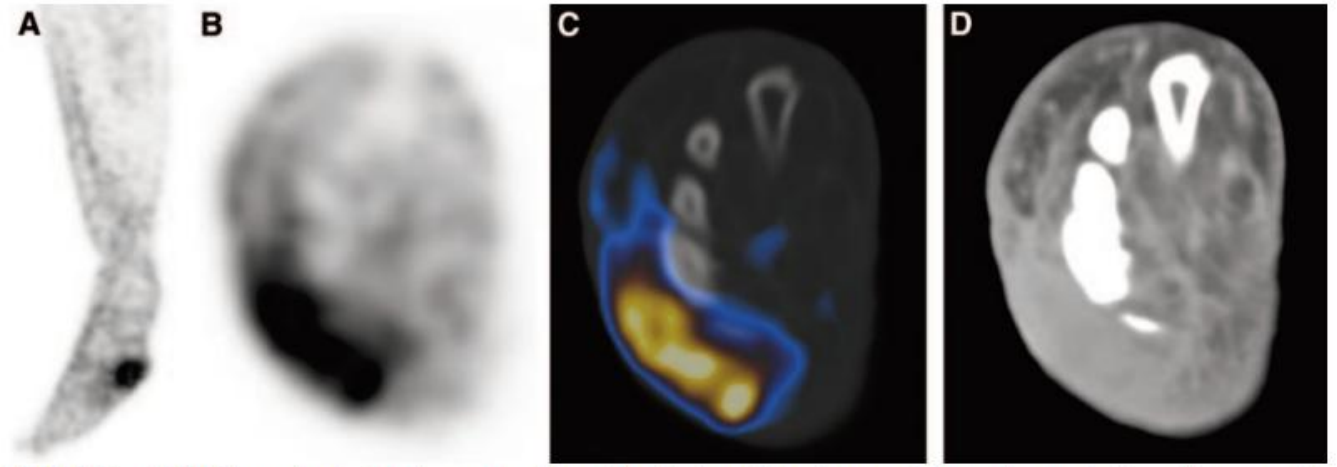
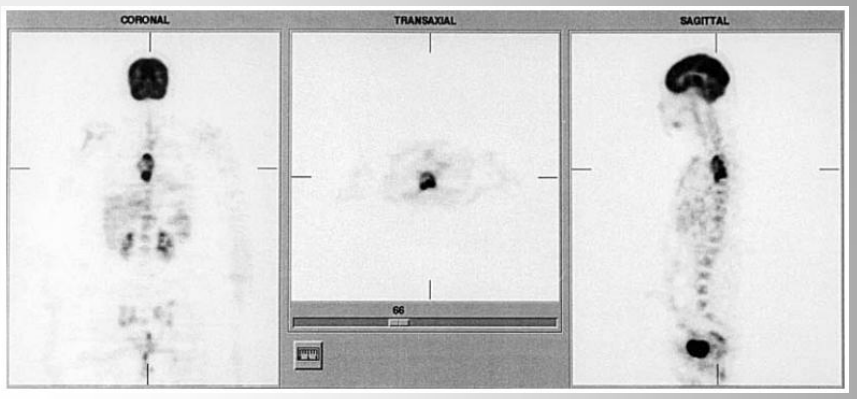


FIGURE 2. PET/CT-based exclusion of osteomyelitis and localization of infection to soft-tissue abscess in 43-y-old woman with nonhealing ulcer and cellulitis in lateral aspect of right foot. (A and B) ^{18}F-FDG PET coronal (A) and transaxial (B) images show area of increased ^{18}F-FDG uptake in lateral aspect of mid foot. (C) PET/CT localizes abnormal ^{18}F-FDG uptake to soft tissues. (D) CT shows soft-tissue swelling in same area. Patient underwent local drainage and short course of antimicrobial therapy with good clinical response. No evidence of osteomyelitis was found during a clinical and imaging follow-up of 12 mo.

Keidar Z et al. The Diabetic Foot: Initial Experience with 18 F-FDG PET/CT. J Nucl Med 2005; 46:444-449.

FDG PET & Spondylitis (Vertebral OM)

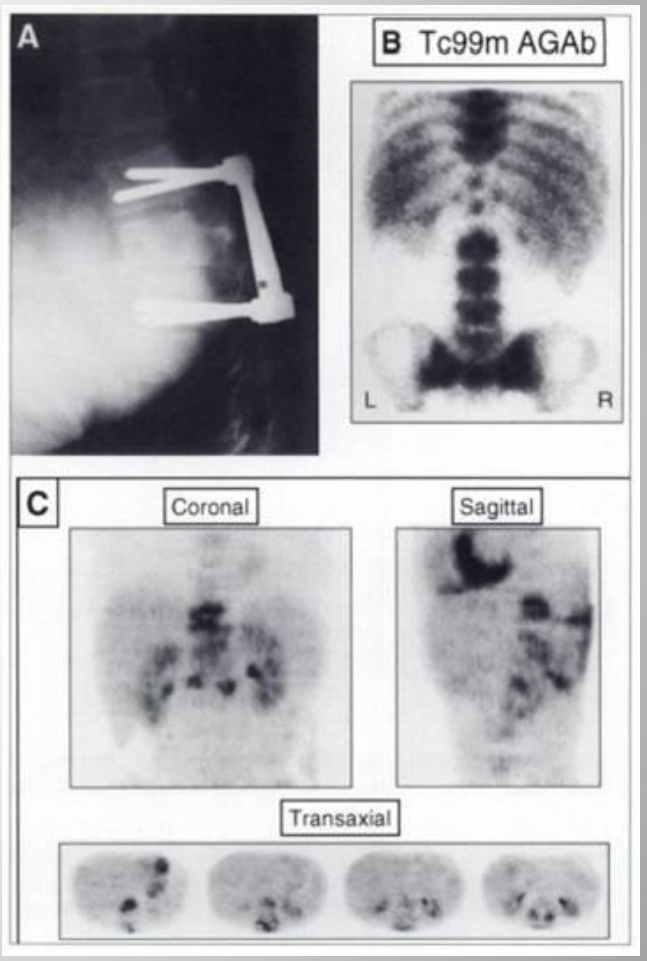
- In Schmitz' Germany study, PET scans in 16 patients with **suspected spondylodiscitis**
  - All had **surgery**
- 12 (of 16) had histopath confirmed SDitis
- **FDG PET**: **all 12 TP**
- **FDG PET**: **3** of 4 **TN**



Schmitz A et al. Fluorine-18 fluorodeoxyglucose positron emission tomography findings in spondylodiscitis: preliminary result. Eur Spine J 2001; 10 534–539.

FDG PET & Spondylitis (Vertebral OM)

- Of 15 patients with **suspected central skeleton COM**, **Sn** of FDG PET (*no CT*) was **95%** and **Sp 100%**
- **FDG PET** is **96% accurate** diagnosing **COM** of **central skeleton** (eg, chronic spondylitis)



Guhlmann A et al. Fluorine-18-FDG PET and Technetium-99m Antigranulocyte Antibody Scintigraphy in Chronic Osteomyelitis. J Nuc Med 1998; 39:2145-2152.

FDG PET & Spondylitis (Vertebral OM)

- De Winter's study used FDG PET in 33 patients with **suspected central skeleton OM**:
  - **Sn 100%** and **Sp 90%**
- Vertebral column: **10 TN** & **2 TP**
  - **No** false findings
- 5 lesions complicated by **HW**
  - **4 TN** & **1 TP** (**No** False findings)

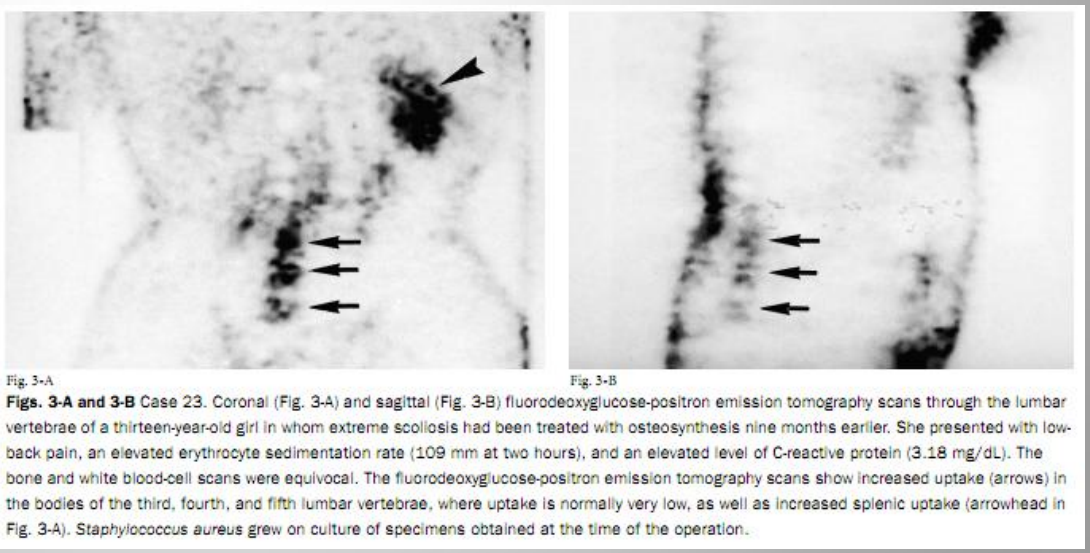


Fig. 3-A

Fig. 3-B

Figs. 3-A and 3-B Case 23. Coronal (Fig. 3-A) and sagittal (Fig. 3-B) fluorodeoxyglucose-positron emission tomography scans through the lumbar vertebrae of a thirteen-year-old girl in whom extreme scoliosis had been treated with osteosynthesis nine months earlier. She presented with low-back pain, an elevated erythrocyte sedimentation rate (109 mm at two hours), and an elevated level of C-reactive protein (3.18 mg/dL). The bone and white blood-cell scans were equivocal. The fluorodeoxyglucose-positron emission tomography scans show increased uptake (arrows) in the bodies of the third, fourth, and fifth lumbar vertebrae, where uptake is normally very low, as well as increased splenic uptake (arrowhead in Fig. 3-A). *Staphylococcus aureus* grew on culture of specimens obtained at the time of the operation.

De Winter F et al. Fluorine-18 fluorodeoxyglucose-position emission tomography: a highly accurate imaging modality for the diagnosis of chronic musculoskeletal infections. J Bone Joint Surg Am. 2001;83-A(5):651-60.

FDG PET & Spondylitis (Vertebral OM)

TABLE III Advantages and Disadvantages of Fluorine-18 Fluorodeoxyglucose-Positron Emission Tomography for the Diagnosis of Musculoskeletal Infections[18,20,21,33,34,38,41,43]

Advantages	Disadvantages
Early (1-hr) imaging	[redacted]
High target-to-background ratio	Possible lower sensitivity in diabetic patients
High resolution (±5 mm)	Patient must be sober for at least 4 hrs
High-count tomographic images	[redacted]
Low bone and bone-marrow uptake	Differentiation between tumor and infection is not possible
Highly accurate in central skeleton	
Not hindered by metal implants	
No additional scans necessary, all-in-one technique	
High interobserver agreement	
Theoretically sensitive in low-grade infections	
Use may be feasible in neutropenic patients	

De Winter F et al. Fluorine-18 fluorodeoxyglucose-position emission tomography: a highly accurate imaging modality for the diagnosis of chronic musculoskeletal infections. J Bone Joint Surg Am. 2001;83-A(5):651-60.

FDG PET & Infected Hip Prostheses

- In U. Penn study of 53 **hip prosthesis**, **FDG PET** had 11 TP of 12 **pathology-proven** infections (**Sn 92%**)
- Of 41 **non-infected hip cases**, PET was TN in 40 cases (**Sp 98%**)

- **Criteria** to call FDG-avid finding an infection:
  - **Location**, not intensity, determining factor
  - FDG uptake at **Bone-Prosthesis Interface** considered positive
  - Other publications showed BPI FDG uptake increases Sp
  - FDG uptake in *soft tissue* was *non-specific*

Chacko TK et al. Applications of fluorodeoxyglucose positron emission tomography in the diagnosis of infection. Nuc Med Comm 2003; 24: 615-24.

FDG PET & Infected Hip Prostheses

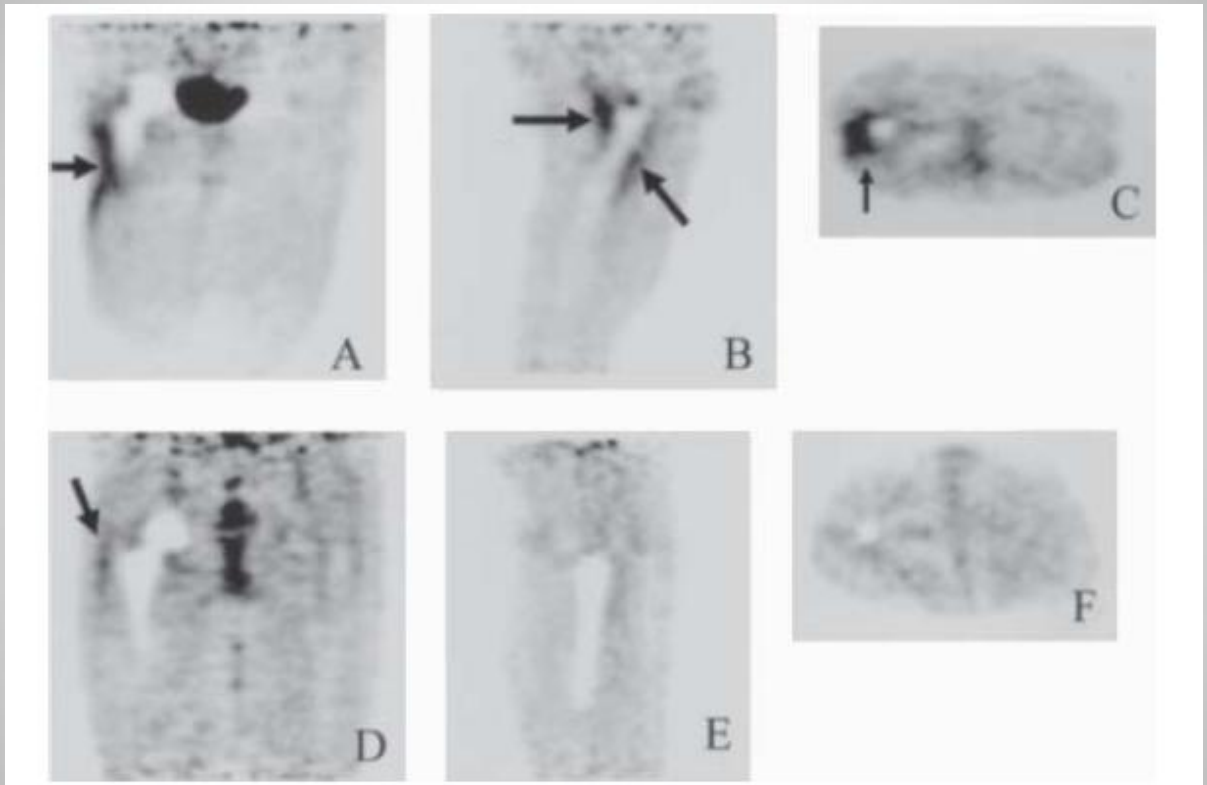


Fig. 1. Coronal (A), sagittal (B), and axial (C) FDG PET images from a 44-year-old female who presented with painful right hip prosthesis. Arrows indicate increased activity in direct contact with the prosthesis in the region of the femoral component, corresponding to the bone–prosthesis interface. Histopathological examination of tissues obtained during revision arthroplasty was consistent with infection. Similar views (D, E and F) from a 53-year-old, asymptomatic male with a history of total hip arthroplasty 9 months prior to FDG PET imaging. In D, arrows indicate increased activity in the region of the femoral neck and greater trochanter, which is a non-specific finding and does not indicate infection.

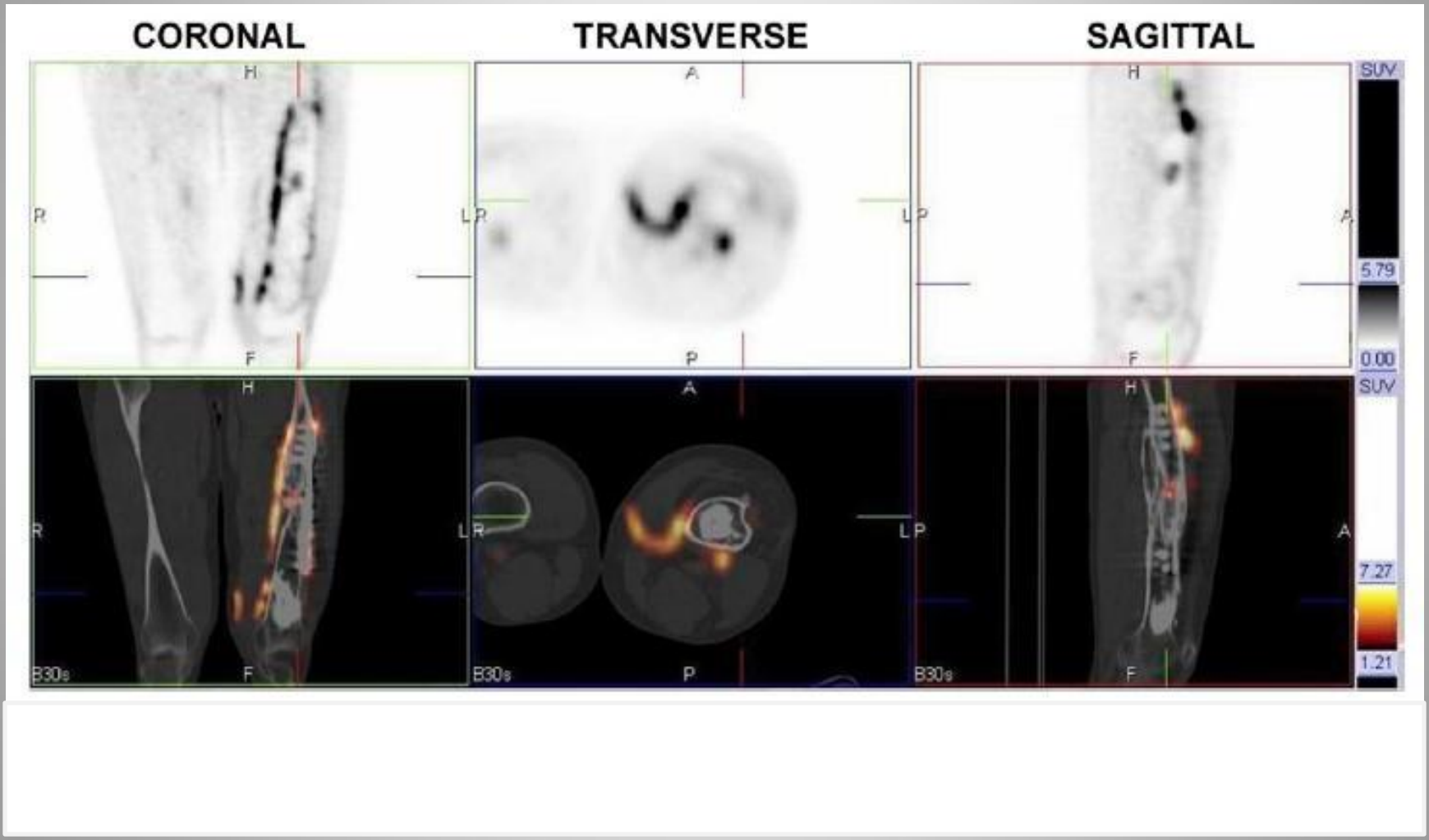
Chacko TK et al. Applications of fluorodeoxyglucose positron emission tomography in the diagnosis of infection. Nuc Med Comm 2003; 24: 615-24.

FDG PET & Infected Hip Prostheses

- Of 12 **pathology-proven knee prostheses** infections, **FDG PET** was TP in 11 cases (**Sn 92%**)
- Of 24 **non-infected knee prostheses**, **PET** was TN in 18 cases (**Sn 75%**)
- *In 15 patients with **HW other than the knees**, **PET** was TN in 11 cases and TP in 4 cases and zero False findings (**100% accuracy**)*

Chacko TK et al. Applications of fluorodeoxyglucose positron emission tomography in the diagnosis of infection. Nuc Med Comm 2003; 24: 615-24.

FDG PET & Infected Hip Prostheses



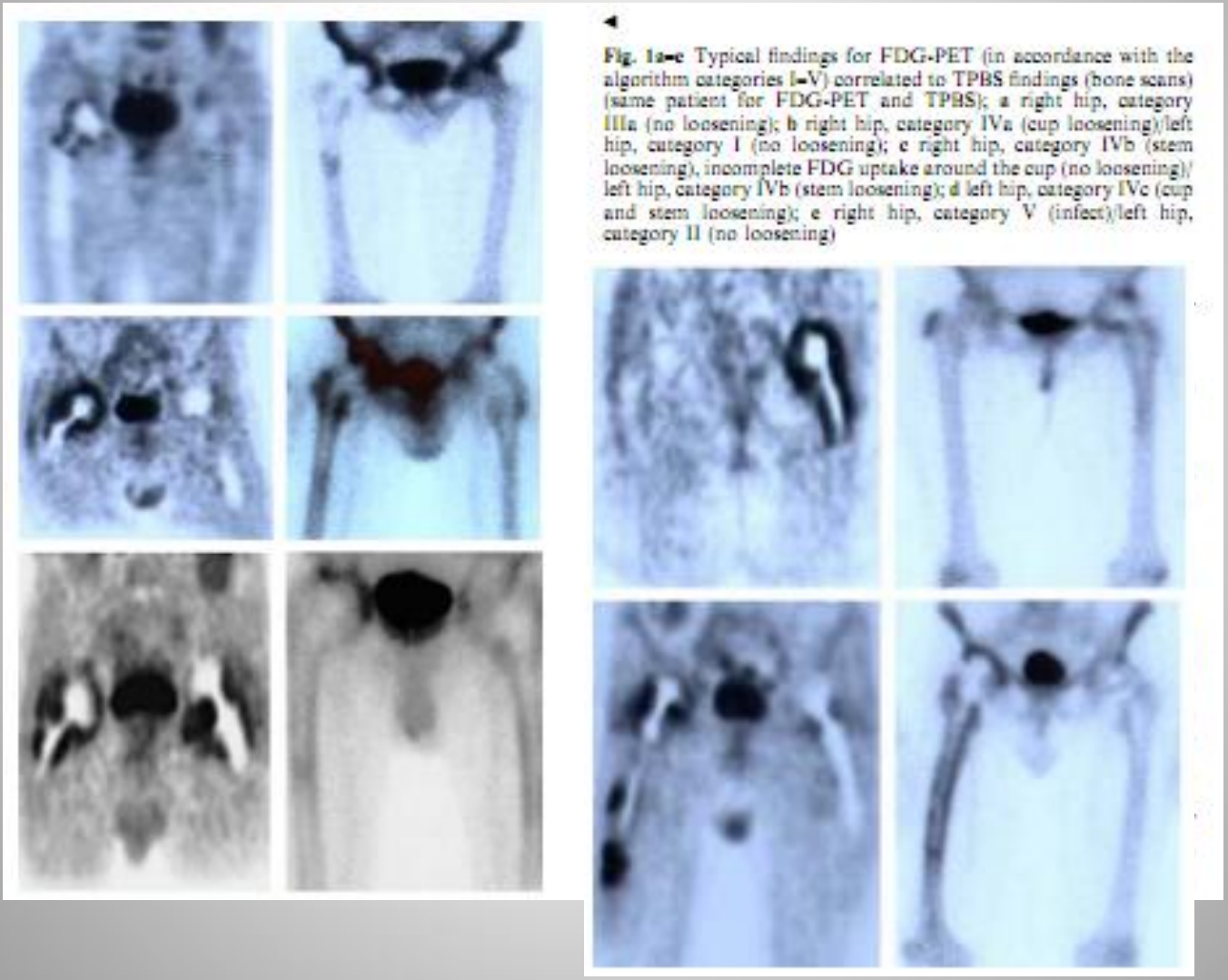
van der Bruggen W et al. PET and SPECT in Osteomyelitis and Prosthetic Bone and Joint Infections: A Systematic Review. Semin Nucl Med 2010; 40:3-15.

FDG PET & Septic Hip Loosening

- In Aachen, Germany, Mumme's team studied **70 hip prostheses with suspected loosening** in 50 patients
  - **50 hip prostheses had micro & histopath evaluation**; 20 prostheses did not
- 3-phase bone scan done to differentiate septic from aseptic loosening: **78%** Sn & **70%** Sp
- **FDG PET** (*no CT*): **91% Sn** & **92% Sp**
  - FDG uptake in B-P Interface & surrounding soft tissue is "inflammation" beyond loosening (category 5)
- Like Chacko's study, **SUV did not correlate** well with infected versus non-infected prosthesis

Mumme T et al. Diagnostic values of positron emission tomography versus triple-phase bone scan in hip arthroplasty loosening. Arch Orthop Trauma Surg 2005; 125: 322–329.

FDG PET & Septic Hip Loosening



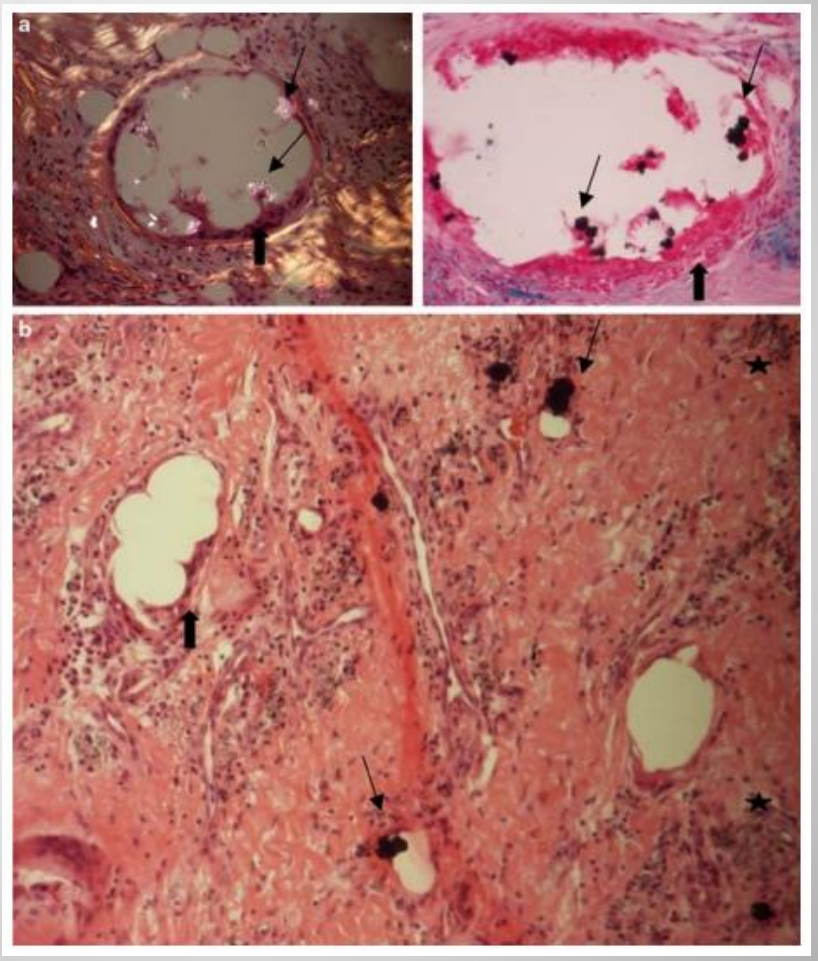
◀

Fig. 1a–e Typical findings for FDG-PET (in accordance with the algorithm categories I–V) correlated to TPBS findings (bone scans) (same patient for FDG-PET and TPBS); **a** right hip, category IIIa (no loosening); **b** right hip, category IVa (cup loosening)/left hip, category I (no loosening); **c** right hip, category IVb (stem loosening), incomplete FDG uptake around the cup (no loosening)/ left hip, category IVb (stem loosening); **d** left hip, category IVc (cup and stem loosening); **e** right hip, category V (infect)/left hip, category II (no loosening)

Mumme T et al. Diagnostic values of positron emission tomography versus triple-phase bone scan in hip arthroplasty loosening. Arch Orthop Trauma Surg 2005; 125: 322–329.

FDG PET & Septic Hip Loosening

Fig. 3a,b Histopathological findings from aseptic and septic arthroplasty loosening. **a** Polyethylene wear particles (*small arrows*) surrounded by macrophages and multinuclear giant cells (*big arrows*) (aseptic loosening); **b** polyethylene wear particles (*small arrows*) surrounded by leucocytes and parenchymal cell debris (*stars*) (septic loosening) as well as macrophages and multinuclear giant cells (*big arrows*) (polarization microscopy, ×100; H&E staining, iron reaction, ×100)



Mumme T et al. Diagnostic values of positron emission tomography versus triple-phase bone scan in hip arthroplasty loosening. Arch Orthop Trauma Surg 2005; 125: 322–329.

FDG PET & Infected Knee Prosthesis

- FDG PET **not as accurate** in **knee** prostheses
  - Unlike *hip prosthesis* where Sn & Sp are ~90%
- In Van Acker's study of 21 patients with **painful knee prostheses**, **PET** was **100% Sn** (using **non-AC** images), but **73% Sp**
  - When abnormal FDG activity on PET corresponded to "hot spot" on delayed bone scan, **Sp** improved to **80%**
  - 2 False Positives (even with bone scan) were due to aseptic loosening
- Non-specific focal FDG uptake seen *36 months after surgery* in asymptomatic TKA

Van Acker F et al. FDG-PET, 99mTc-HMPAO white blood cell SPET and bone scintigraphy in the evaluation of painful total knee arthroplasties. Eur J Nucl Med 2001; 28:1496–150.

FDG PET & Infected Knee Prosthesis

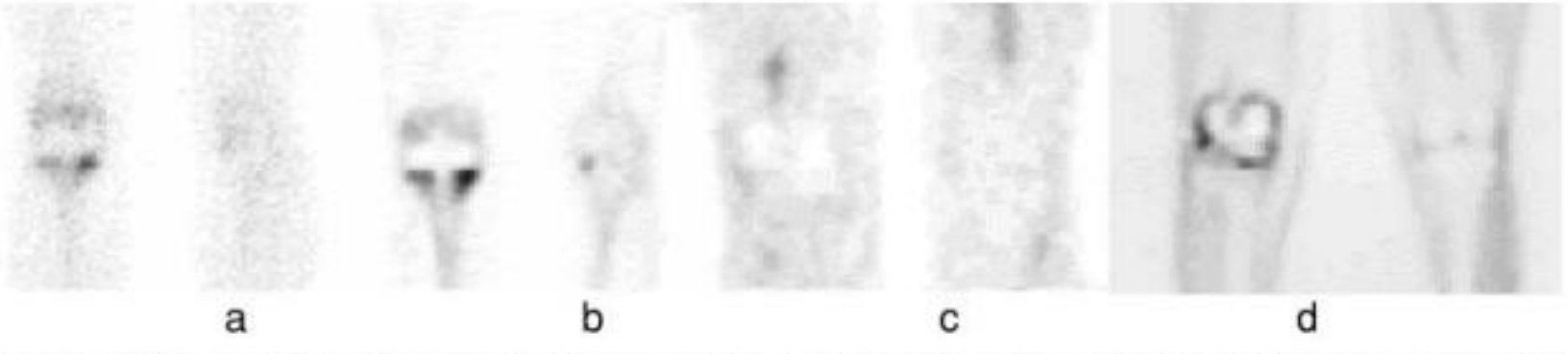


Fig. 6a–d. Loosening of a TKA. **a** Focal MDP uptake of grade 4 around the tibial neck of the prosthesis; **b** congruent focal lesion on MDP SPET; **c** no focal uptake on WBC SPET; **d** false-positive congruent lesion on PET (grade 4, SUV 3.2)

Van Acker F et al. FDG-PET, 99mTc-HMPAO white blood cell SPET and bone scintigraphy in the evaluation of painful total knee arthroplasties. Eur J Nucl Med 2001; 28:1496–150.

FDG PET & Infected Knee Prosthesis

- Zhuang U. Penn team published that **FDG PET better at diagnosing hip** versus knee **prosthesis** infections
  - **Knee**: 10 TP of 11 knee prosthesis infections, but 7 FP among 25 non-infected knees (**Sn 91%** & **Sp 72%**)
  - **Hip**: 9 TP of 10 hip prosthesis infections, and 3 FP among 28 non-infected hips (**Sn 90%** & **Sp 89%**)
- In all **10 False Positive** cases, **surgery > 1 year** before PET scan performed
- Study confirmed presence, not intensity, of FDG uptake at BPI is what best correlates to infection

Zhuang H et al. The Promising Role of 18 F-FDG PET in Detecting Infected Lower Limb Prosthesis Implants. J Nucl Med 2001; 42:44 – 4.

FDG PET & Infected Knee Prosthesis

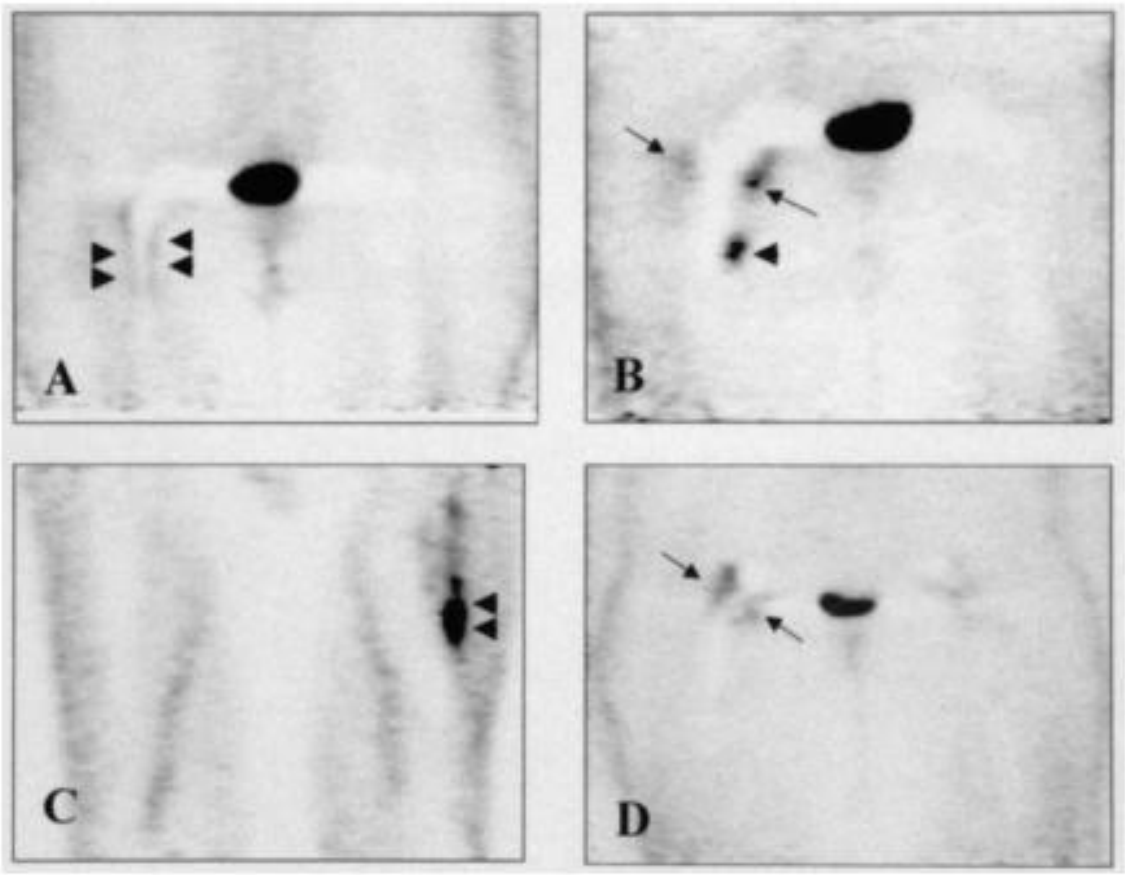


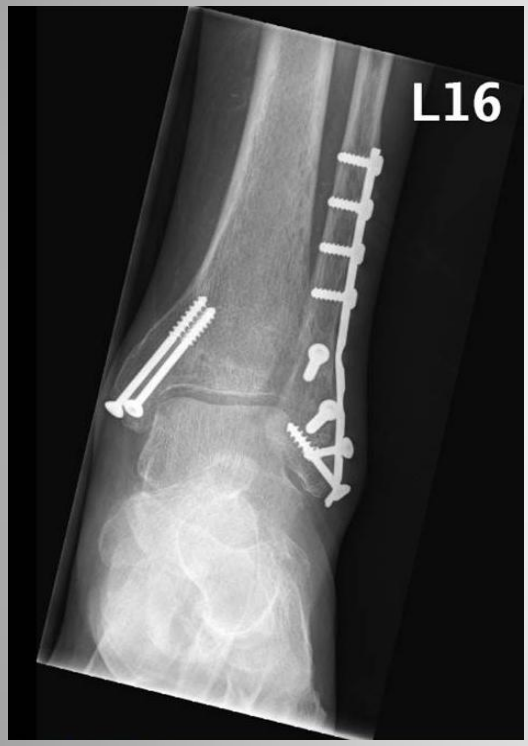
FIGURE 2. (A) Coronal image of 72-y-old woman with hip prosthesis. Periprosthetic infection on right side was identified (arrowheads). (B) Coronal image of 76-y-old woman with bilateral hip prostheses. Both infection (arrowhead) and loosening (arrows) were shown. (C) Coronal image of 78-y-old man with painful left hip prosthesis. Arrowheads indicate periprosthetic infection and osteomyelitis. (D) Coronal image of 76-y-old woman with bilateral hip prostheses. FDG uptake is noted only around neck of prosthesis (arrows). FDG PET diagnosis of loosening was confirmed after revision arthroplasty.

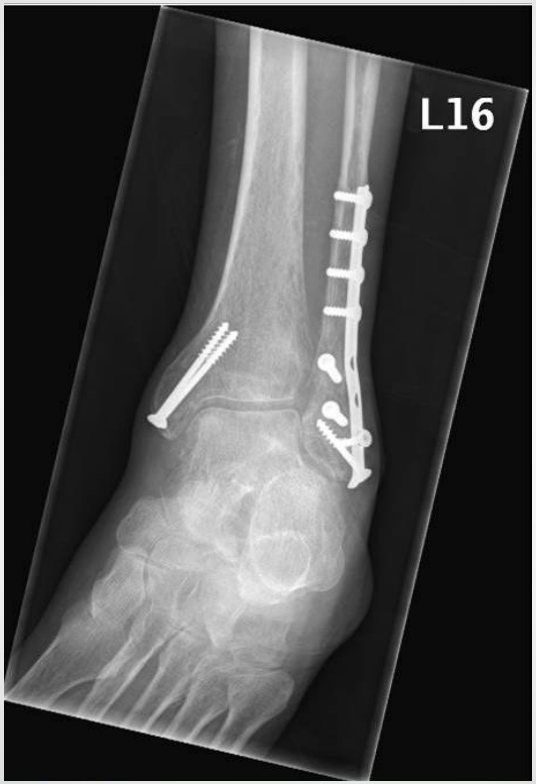
Zhuang H et al. The Promising Role of 18 F-FDG PET in Detecting Infected Lower Limb Prosthesis Implants. J Nucl Med 2001; 42:44 – 4.

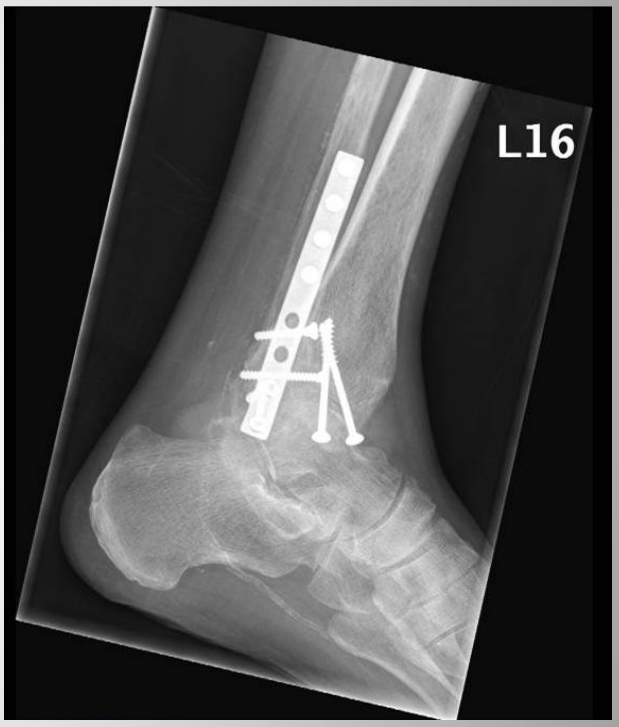
Case 2

- Man in his 60s complains of severe pain in L ankle
  - Recent of minor blunt trauma
  - Remote history of L ankle fracture s/p ORIF (“years ago,” at construction site)
- Seen at VA in late 2011 for ankle pain
  - WBC (especially neutrophils) & ESR high

X-ray 12/2011







Case 2

- Orthopedic team diagnosed patient with infected HW in L ankle
  - Plan to debride tissue and do HW Replacement

FDG PET False Positives & Prostheses

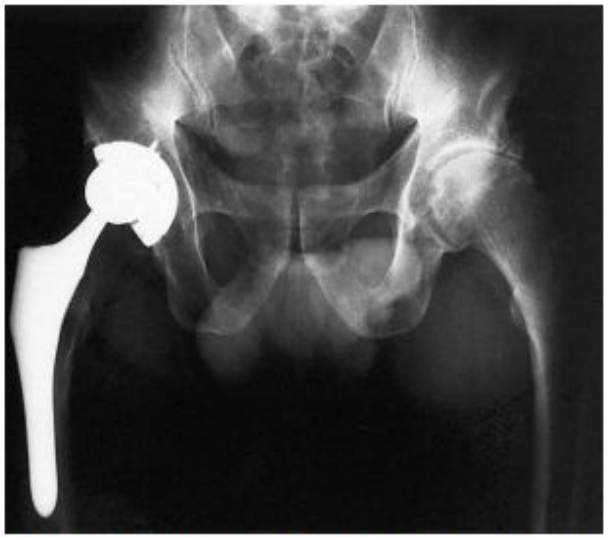
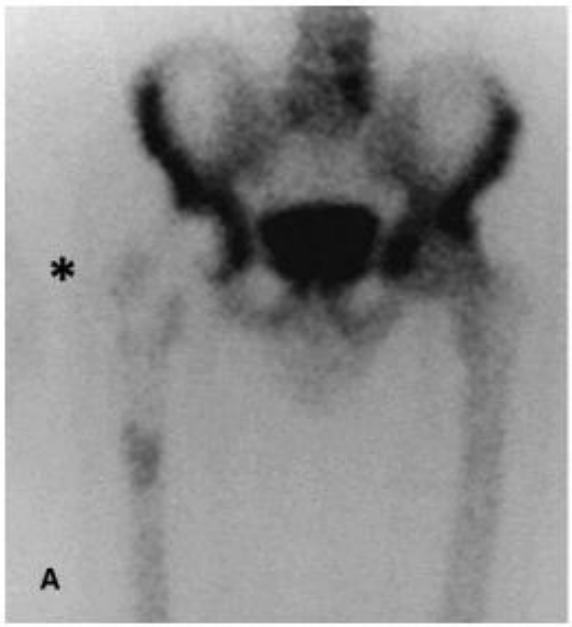
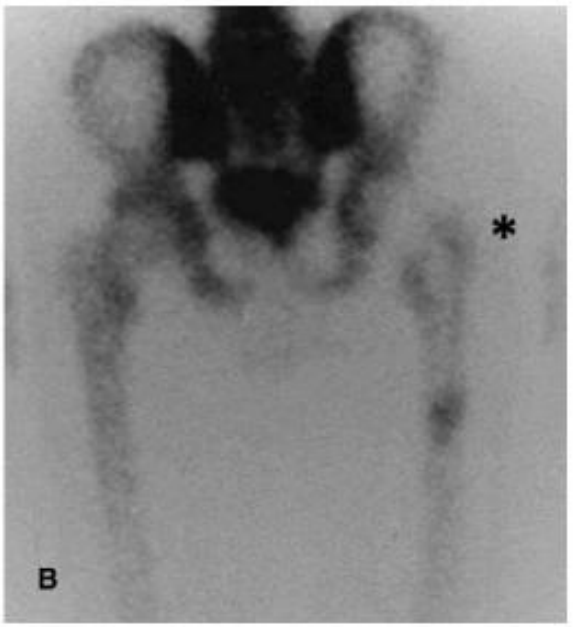


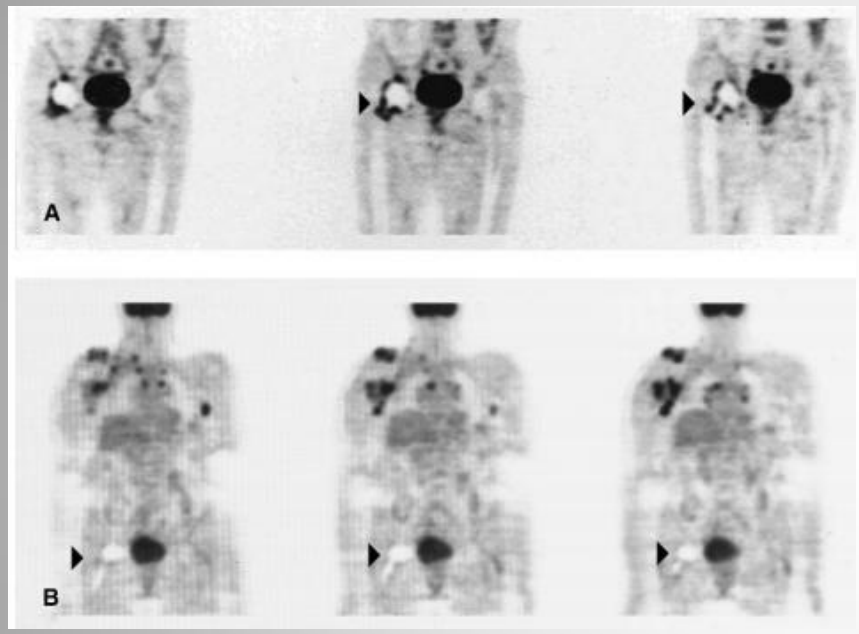
Fig. 1. Hip arthroplasty of the right side without any signs of loosening on the radiography. Note the prosthesis head localized eccentrically in the cup.





Kisielinski K et al. Fluordeoxyglucose Positron Emission Tomography Detection of Inflammatory Reactions Due to Polyethylene Wear in Total Hip Arthroplasty. J Arthroplasty 2003; 18(4): 528-32.

FDG PET False Positives & Prostheses



- **Positive FDG PET** at painful hip, but no infection on x-ray or bone scan
  - False Positive FDG PET
- Biopsy: macrophages & MNGCs around **polyethylene particles**

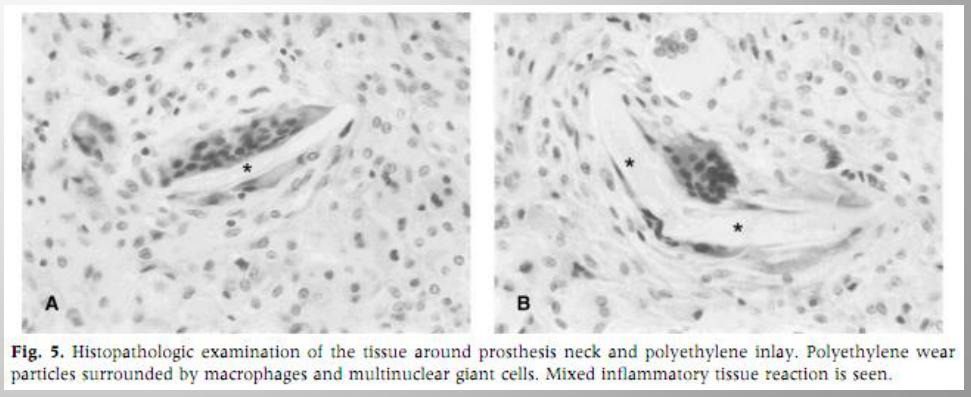


Fig. 5. Histopathologic examination of the tissue around prosthesis neck and polyethylene inlay. Polyethylene wear particles surrounded by macrophages and multinuclear giant cells. Mixed inflammatory tissue reaction is seen.

Kisielinski K et al. Fluordeoxyglucose Positron Emission Tomography Detection of Inflammatory Reactions Due to Polyethylene Wear in Total Hip Arthroplasty. J Arthroplasty 2003; 18(4): 528-32.

FDG PET False Positives & Other Cases

- **Uncomplicated** traumatic bone injury have abnormal FDG uptake up to **3 months post-trauma**
  - **Fracture healing** involves **bone remodeling**
- **Post-surgical bone** could have abnormal FDG uptake (but low) **greater than 1 year**
- Higher **FDG activity** (**SUV_{max} > 3**) **raised likelihood** of **infection**
  - In 21 patients **suspected with OM**, PET "showed high uptake of FDG within the infected tissue, with SUVs up to a maximum of 16.1. However, in fractures and pseudarthroses only very low FDG uptake, with **SUVs of 0.2–1.1**, was observed"
- **CT** (as in PET/CT) **improves Sp** (ie, reduces False Positives)

Kälicke T et al. Fluorine-18 fluorodeoxyglucose PET in infectious bone diseases: results of histologically confirmed cases. Eur J Nucl Med. 2000 May;27(5):524-8.

Summary of FDG PET of Suspected MSK Infections

- **FDG PET/CT** has the **best Sn and Sp** (ie, accuracy) in diagnosing **Chronic OM**
  - Any site, including **COM of vertebral bodies**
- No clear role for PET/CT in acute OM in ***un***complicated bone sites
  - Dedicated MRI, bone + radiolabeled WBC scans or radiolabeled WBC + marrow scans are **> 90% accurate**
  - **But PET/CT** has **improved Sp** over MR and gamma modalities in **suspsected acute OM** of **complicated bone**

Summary of FDG PET of Suspected MSK Infections

- **PET** has excellent negative predictive value (NPV) in **suspected diabetic foot infections**
  - Neuropathic arthropathy is still vexing issue (Radiolabeled WBC + Marrow scan may be better)
  - In patients with **high** clinical suspicion of diabetic foot OM, **FDG PET as Sn and Sp as MRI** (high)
  - When ***low*** suspicion, ***MRI much better Sn***

Summary of FDG PET of Suspected MSK Infections

- In **painful *hip* prostheses**, **FDG PET** appears **most accurate** of all modalities
  - **Best corresponding criterion** for infected prosthesis is focal FDG at **Bone-Prosthesis Interface** (BPI)
  - Focal FDG uptake has good correlation, *SUV has none*
  - Debate still on whether focal FDG at *head & tip* also *highly Sp for infection*
- **PET's Sn** is **excellent** for ***knee*** **prosthesis infection**, but **Sp is moderate**
  - May *need 2nd modality to reduce PET's false positives* in suspected knee prosthesis infection

Summary of FDG PET of Suspected MSK Infections

- To ↓ False Positive in prostheses, 6 months isn't always sufficient between date of prosthesis implantation & date of PET, especially in *knee* prostheses
- Adding **CT** to PET data (as with SPECT) marginally improves Sn but **significantly imrpoves Sp** (ie, significantly ↓ **False Positives**)

Best Nuclear Imaging for Suspected MSK Infections

- Suspected **acute OM** of the **diabetic foot**: Radiolabeled WBC + Marrow scans
  - Use Tc-99m HMPAO WBC (rather than In-111 WBC)
  - Ideally SPECT/CT
  - Consider MRI, Bone + Radiolabeled WBC scans

- Suspected **acute OM** of **peripheral bones**: Bone + Radiolabeled WBC scans
  - If complicated by HW or surgery, consider FDG PET/CT
  - Consider MRI if uncomplicated by prosthesis
  - Small bones: Tc-99m HMPAO WBC, not In-111 WBC

Best Nuclear Imaging for Suspected MSK Infections

- Suspected **acute OM** of **vertebral bodies** (spondylitis/spondlyodiscitis): FDG PET/CT
  - Consider MRI especially if not complicated by prosthesis or surgery

- Suspected **acute OM** of **skull**: Depends
  - No prior intervention in skull, CT or bone scan
  - Skull base without prior intervention, MR or bone scan
  - If prior intervention, combined radiolabeled WBC & bone scans
  - Role of FDG PET/CT unclear

Best Nuclear Imaging for Suspected MSK Infections

- Suspected **OM** in **post-fracture long bones**: Unclear
  - Consider any: MRI, CT, bone + radiolabeled WBC scans, or radiolabeled WBC + marrow scans and FDG PET/CT
  - Ideally SPECT/CT
  - If complicated by HW, consider FDG PET/CT

- Suspected **chronic OM**: FDG PET/CT
  - Especially central (skull and vertebral bodies)
  - Cases tend to be complicated by prostheses or sequestrum

Best Nuclear Imaging for Suspected MSK Infections

- Suspected **infected knee prosthesis**: radiolabeled WBC SPECT/CT + marrow scan
  - Consider MRI or bone + radiolabeled WBC scans
  - FDG PET/CT has excellent NPV but poor Sp in knee

- Suspected **infected hip prosthesis**: FDG PET/CT
  - Radiolabeled WBC SPECT/CT + marrow scan also highly accurate
  - Consider MRI or bone + radiolabeled WBC scans

Extended Bibliography & Thanks

- *For summary of studies*: van der Bruggen W et al. PET and SPECT in Osteomyelitis and Prosthetic Bone and Joint Infections: A Systematic Review. Sem. Nuc. Med. 2010; 40:3-15.
- *For effective radiation doses*: Mettler FA et al. Effective Doses in Radiology and Diagnostic Nuclear Medicine: A Catalog. Radiology 2008; 248(1): 254-63.
- *For protocols*: Society of Nuclear Medicine Procedure Guidelines Catalog, and Mettler FA and Guiberteau M. Essentials of Nuclear Medicine. Philadelphia: Saunders Elsevier, 2006.

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The End