Nuclear medicine and Prosthetic Joint Infections

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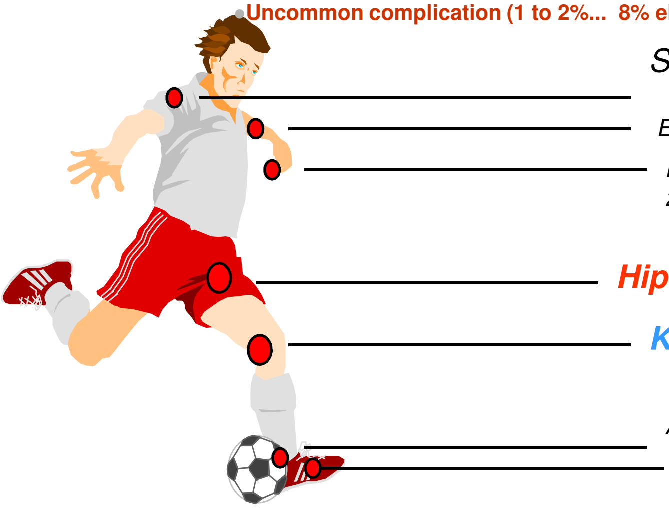
Orthopedic prostheses: world market 1996

Prosthetic joint infections:

Uncommon complication (1 to 2%... 8% elderly)!!!!!!!!



Overview

- **Prosthetic joint infections:**
  - **Pathogenesis and microbiology**
  - Risk factors
  - Clinical presentation
  - Diagnostic studies
  - Treatment (ABs and Surgery) and prevention
  - Conclusions

Pathogenesis

- Host defense
  - Glycoprotein layer
- Development of biofilm
  - Adherence of bacteria
  - Inhibition of antibiotics and leukocytes
- Contiguous spread (2/3)
  - Direct contamination
  - Trauma
- Hematogenous dissimination (1/3)

Microbiology

- Most common organisms:
  - Staphylococcus aureus (33%)
  - E. coli and Pseudomonas species (38% total)
  - Staphylococcus epidermidis (12%)
  - Enterococcus species (10%)

Microbiology

- Early Infections (<1 year postoperatively)
  - S. epidermidis
  - S. aureus
  - Streptococcus species
  - Gram negative bacilli (E. coli and Pseudomonas)

Microbiology

- Late Infection (>1 year postoperatively)
  - S. epidermidis
  - S. aureus
  - Gram-negative bacilli

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Risk Factors

- Host Factors:
  - Advanced age
  - Diabetes mellitus
  - Malignancy
  - Rheumatoid arthritis
  - Sickle Cell
  - Prior joint replacement

Risk Factors

- Intraoperative Factors:
  - Oversized components
  - Wound hematoma
  - Conflicting skin incisions

Risk Factors

- Postoperative Factors:
  - Hematogenous dissimination
  - Skin ulceration

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Clinical Presentation

- Painful joint with swelling (90%)
- Warmth
- Erythema
- Fever
- Drainage
- Hypotension
- Sepsis

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Diagnosis

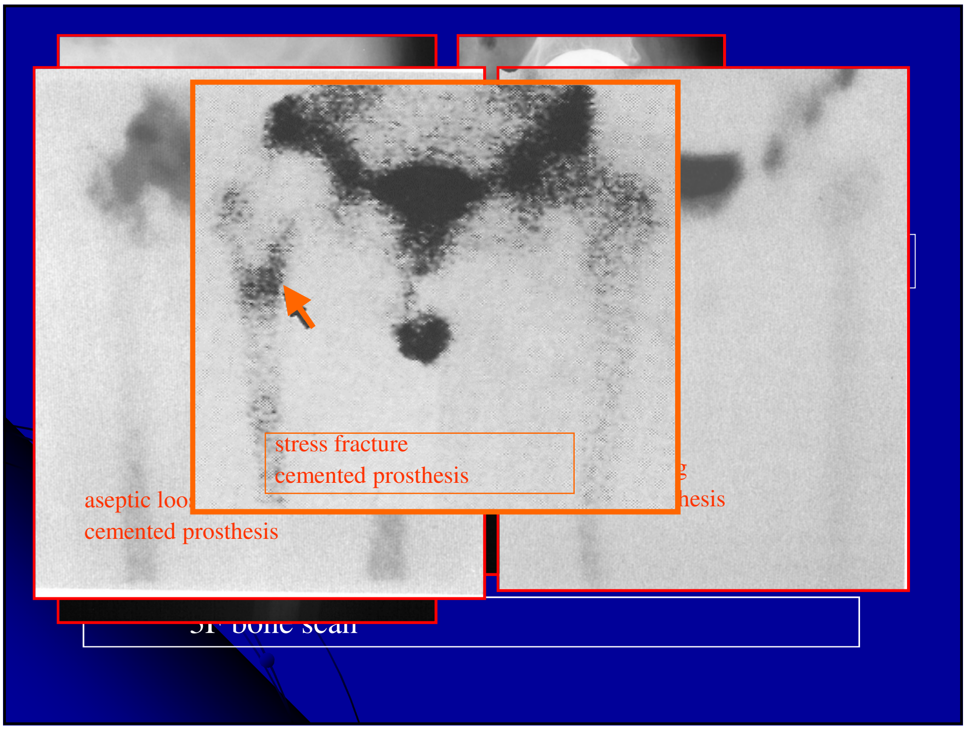
- **Gold Standard**: Joint aspiration or intraoperative specimen…
  - Aerobic and anaerobic cultures
  - Fungal and mycobacterium cultures

Diagnosis

- Laboratory Testing:
  - Elevated WBC
  - Elevated ESR (1/2 of all patients)
  - Elevated C-reactive protein

Diagnosis

- Imaging Studies:
  - X-rays
  - Bone scan (immediate, 15 min, 4 hr)
  - WBC scan
  - Colloid scan
  - FDG PET

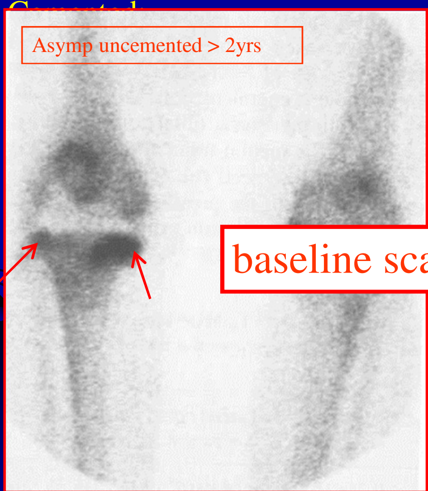


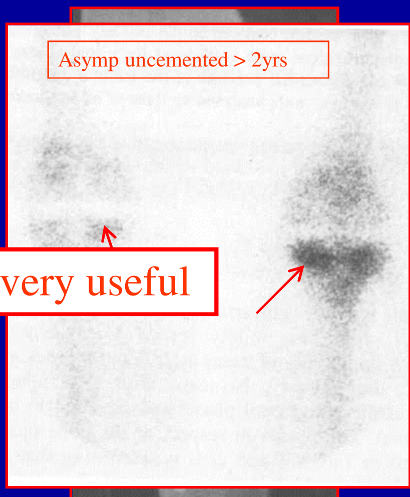
Hip: Cemented versus cementless

- Cemented prostheses
  - < 1 yr:
    - bone scan pattern variable
  - >1 yr:
    - 80-90% of asymptomatic pts turn normal
    - ± 10-20%: ↑ uptake at the tip and gr trochanter

- Cementless prostheses:
  - More distal stress transfer
  - maybe abnormal > 2 years after surgery
  - > 3 yrs:
    - Simultanuous ↑ uptake at tip **and** lesser trochanter
    - Diffuse periprosthetic uptake
    - Increased bloodpool

Knee prostheses: bone scan





baseline scan very useful

- High negative predictive value

Nuclear medicine in the infected joint prosthesis

- Bone scan: broad screening for complication

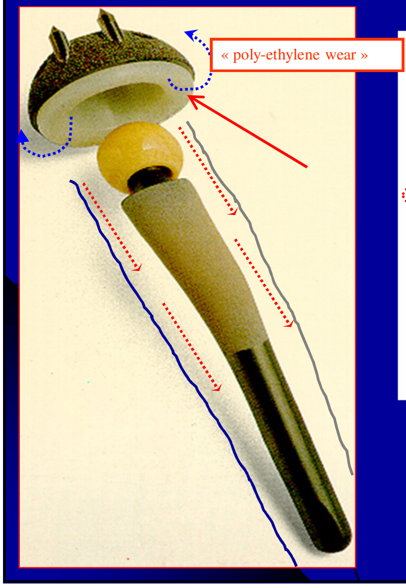
  ΔΔ septic versus aseptic loosening **not possible** even with bloodflow

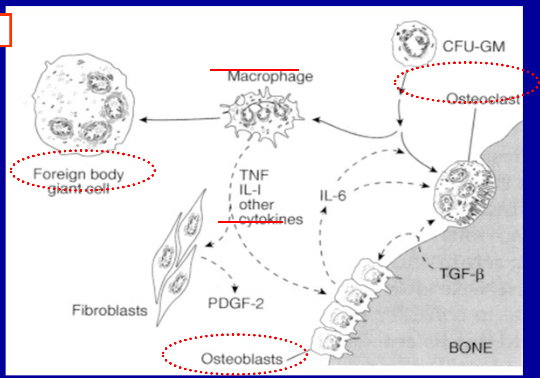
- Increasing specificity for infection
  - BONE + Gallium-67: accuracy 70-80%
    - Lacks specificity (< 70%) ⇔ incidence of infection
  - Labeled leukocytes (In-111; Tc-99m HMPAO)?

Diagnosis

- Imaging Studies:
  - X-rays
  - Bone scan (immediate, 15 min, 4 hr)
  - WBC scan
  - Colloid scan
  - FDG PET

Mechanisms of aseptic loosening in (un)cemented prostheses





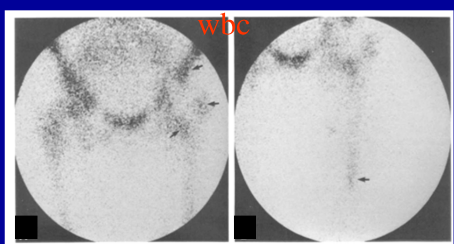
no polymorphonuclears!

ΔΔ infectious loosening

HIP: Bone/leukocyte imaging

- Interpretation
  in combination with bone scan
  improves accuracy (Palestro et al, 1997);

  « higher congruent uptake »
  « incongruency »



- Wukich et al, 1987;
  Johnson et al, 1988 (THP):
  sensitivity ↓ (100%=>70%-88%),
  specificity ↑ (35-50%=>80-95%)

Bone/leukocyte imaging

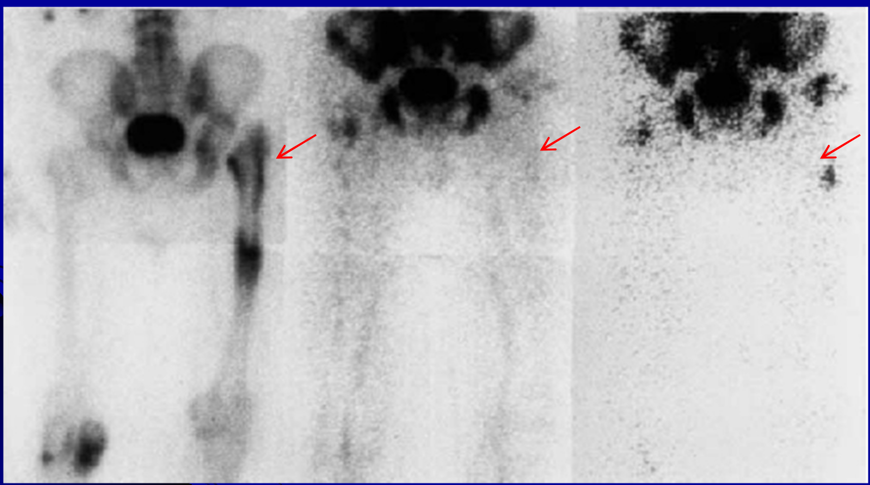
Bone/leukocyte scan: why not so accurate?

* Slow uptake process … low grade infections
(lymphocytes, monocytes)
importance of late (24 hr) imaging (sensitivity!)

* Distribution of bone marrow post surgery highly variable

« ectopic hematopoietic marrow »

Importance of late imaging

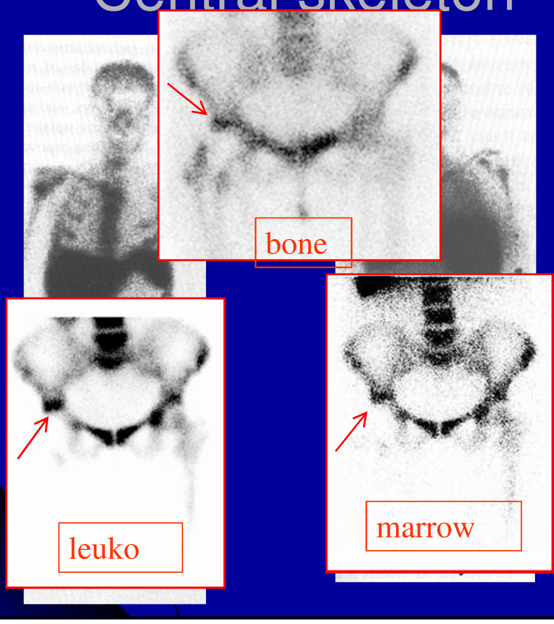


BONE WBC 4 hr WBC 24 hr

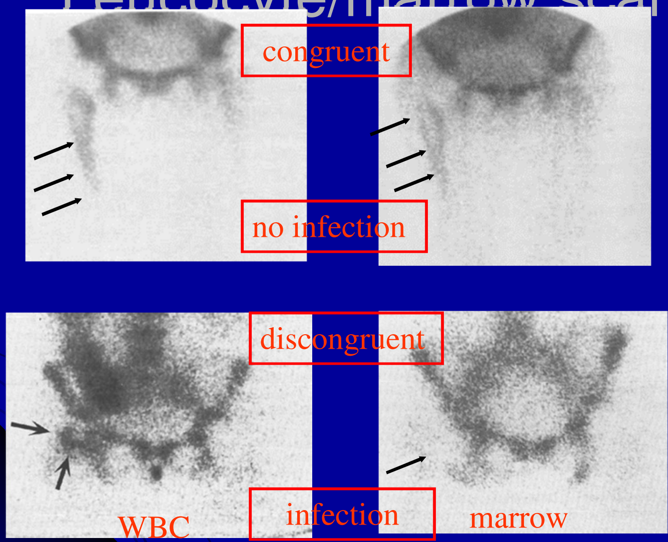
Diagnosis

- Imaging Studies:
  - X-rays
  - Bone scan (immediate, 15 min, 4 hr)
  - WBC scan
  - Colloid scan
  - FDG PET

Central skeleton



Leucocyte/marrow scan



accuracy ranging from 89% to 98%

Diagnosis

- Imaging Studies:
  - X-rays
  - Bone scan (immediate, 15 min, 4 hr)
  - WBC scan
  - Colloid scan
  - FDG PET

FDG PET(-CT) IMAGING IN INFECTED PROSTHESIS

- Why need for other techniques?:
  - Separating, labeling and re-injection of patient's white blood cells
  - Complex, time consuming
  - Delayed imaging after 24 h

FDG PET(-CT) IMAGING IN INFECTED PROSTHESIS

Use of 18F-FDG-PET in the diagnosis of endoprosthetic loosening of knee and hip implants

- N= 32, 74 components (44 knee, 30 hip endoprosthetic components)
- All underwent revision surgery at a later stage
- Endoprosthetic component was considered septic if the microbiological smear grew cultures

- Interpretation cirteria according to other autors
  - Hip: unspecific: head and neck uptake, end of femoral stem
    pathologic: acetabular, bone-prosthesis interface of the stem
  - Knee:
    - unspecific: proximal prosthesis-bone interface, medial or lateral prosthesis-bone interface of tibial plateau
    - pathologic: distal prosthesis-bone interface of femoral shield, prosthesis-bone interface of stem of tibial prosthesis

Mayer-Wagner et al, Arch Orthop Trauma Surg, november 2009

FDG PET(-CT) IMAGING IN INFECTED PROSTHESIS

- Use of 18F-FDG-PET in the diagnosis of endoprosthetic loosening of knee and hip implants

PET in loosening	Sensi	Speci	PPV	NPV
Hip aseptic	80%	87%	86%	81%
Hip septic	75%	71%	75%	71%
Knee aseptic	56%	82%	64%	77%
Knee septic	14%	89%	50%	57%

Mayer-Wagner et al, Arch Orthop Trauma Surg, november 2009

FDG PET(-CT) IMAGING IN INFECTED KNEE AND HIP PROSTHESES

TABLE IV.—*Diagnostic efficiency of positron emission tomography with [18F]fluorodeoxyglucose in patients with symptomatic prostheses.*

Authors	Year	Type	DC	N.	Sensitivity	Specificity	Accuracy
Chryssikos *et al.*[68]	2008	Hip	Qualitative	127	85	93	91
Pill *et al.*[50]	2006	Hip	Qualitative	92	95	93	94
Reinartz *et al.*[32]	2005	Hip	Qualitative	92	94	95	95
Mumme *et al.*[40]	2005	Hip	Qualitative	70	91	92	91
Stumpe *et al.*[41]	2004	Hip	Qualitative	35	33	81	69
Vanquickenborne *et al.*[69]	2003	Hip	Qualitative	17	88	78	82
Manthey *et al.*[28]	2002	Hip	Qualitative	14	100	100	100
Zhuang *et al.*[26]	2001	Hip	Qualitative	38	90	89	90
Hip prostheses total				**Σ 485**	**85**	**90**	**89**
Sterner *et al.*[70]	2007	Knee	Qualitative	14	100	56	71
Manthey *et al.*[28]	2002	Knee	Qualitative	14	100	100	100
Van Acker *et al.*[23]	2001	Knee	Qualitative	21	100	73	81
Zhuang *et al.*[26]	2001	Knee	Qualitative	36	91	72	78
Knee prostheses total				**Σ 85**	**98**	**75**	**83**
Love *et al.*[54]	2004	Hip/knee	Quantitative	59	36	97	71

DC: diagnostic criteria.

Reinartz, Q J Nucl Med Mol Imaging 2009; 53:41-50 FDG-PET in patients with painful hip and knee arthroplasty: technical breakthrough or just more of the same

FDG PET(-CT) IMAGING IN INFECTED PROSTHESIS

Accuracy	HIP	KNEE
BONE scintigraphy	80%	81%
WBC	91%	84%
FDG-PET	89%	83%

- Results of SUV values to discern septic from aseptic loosening are discouraging
- Use of CT in combination with FDG-PET in metallic implants?
- Advantages of PET: 1 injection, diagnosis within 4 hours, no blood manipulation, slightly lower accuracy than WBC, SENSITIVITY NOT INFLUENCED BY ANTIBIOTICS

Reinartz, Q J Nucl Med Mol Imaging 2009; 53:41-50 FDG-PET in patients with painful hip and knee arthroplasty: technical breakthrough or just more of the same

FDG-PET for diagnosing prosthetic joint infection: systematic review and meta-analysis

Table 3 Patient characteristics of included studies

Study and year	Country	No. of patients	Mean age in years (range)	Sex (M/F)	No. of prostheses	Age of prostheses
Chryssikos et al. [12], 2008	USA	113	59 (31–87)	54:59	127 (H)	12, 18, and 24 months
Garcia-Barrecheguren et al. [13], 2007	Spain	24	68 (37–81)	12:12	24 (H)	>6 months
Pill et al. [15], 2006	USA	89	NR (29–85)	NR	92 (H)	NR
Delank et al. [17], 2006	Germany	27	NR (45–82)	NR	36 (H+K)	0.8–19.4 years (*n*=27); NR (*n*=9)
Reinartz et al. [19], 2005	Germany	63	68 (43–88)	32:31	92 (H)	1–31 years
Stumpe et al. [20], 2004	Switzerland	35	69 (46–89)	23:12	35 (H)	12–260 months
Chacko et al. [23], 2003	USA	NR	NR	NR	53 (H)+36 (K)	NR
Vanquickenborne et al. [24], 2003	Belgium	17	NR (42–77)	8:9	17 (H)	2–163 months
Manthey et al. [27], 2002	Germany	23	70 (35–83)	9:14	14 (H)+14(K)	NR
Van Acker et al. [28], 2001	Belgium	21	66 (33–78)	8:13	21 (K)	7 months–9 years
Zhuang et al. [30], 2001	USA	62	NR (27–81)	NR	38 (H)+36 (K)	3 months–8 years

H hip prostheses, *K* knee prostheses, *NR* not reported

Kwee et al, EJNMI 2008;35:2122-2132

FDG-PET for diagnosing prosthetic joint infection: systematic review and metaanalysis

Study and year	Sensitivity (%)		Specificity (%)	
	Value	95%CI	Value	95%CI
Chryssikos et al. [12], 2008	84.9	69.1–93.4	92.6	85.4–96.4
Garcia-Barrecheguren et al. [13], 2007	63.6	35.4–84.8	61.5	35.5–82.3
Pill et al. [15], 2006	95.2	77.3–99.2	93.0	84.6–97.0
Delank et al. [17], 2006	40.0	11.8–76.9	100	89.0–100
Reinartz et al. [19], 2005	93.9	80.4–98.3	94.9	86.1–98.3
Stumpe et al. [20], 2004	33.3[a]	12.1–64.6[a]	80.8[a]	62.1–91.5[a]
	22.2[b]	6.3–54.7[b]	84.6[b]	66.5–93.9[b]
Chacko et al. [23], 2003	91.7	74.2–97.7	89.2	79.4–94.7
Vanquickenborne et al. [24], 2003	87.5	52.9–97.8	77.8	45.3–93.7
Manthey et al. [27], 2002	100	51.0–100	100	86.7–100
Van Acker et al. [28], 2001	100	61.0–100	73.3	48.1–89.1
Zhuang et al. [30], 2001	90.5	71.1–97.4	81.1	68.6–89.4
Pooled estimate	84.6	71.0–92.5	84.0	68.0–92.8

Kwee et al, EJNMI 2008;35:2122-2132

FDG-uptake patterns and clinical correlates in (hip) arthroplasty

Pattern I: No uptake in interface bone-prosthesis
Pattern II: Uptake surrounding femoral neck
Pattern III: Uptake localised in the area surrounding the femoral neck and in a part of the bone–acetabular cup and/or I and VII Gruen's zones
Pattern IVa: Uptake in the area surrounding the femoral neck and in the totality of the bone–femoral cup interface, without compromising peri-prosthetic soft tissue
Pattern IVb: Uptake localised in the neck area and in most of the bone–stem interface without compromising periprosthetic soft tissue
Pattern IVc: IVa plus IVb
Pattern V: Uptake in bone–prosthesis interface and in periprosthetic soft tissue

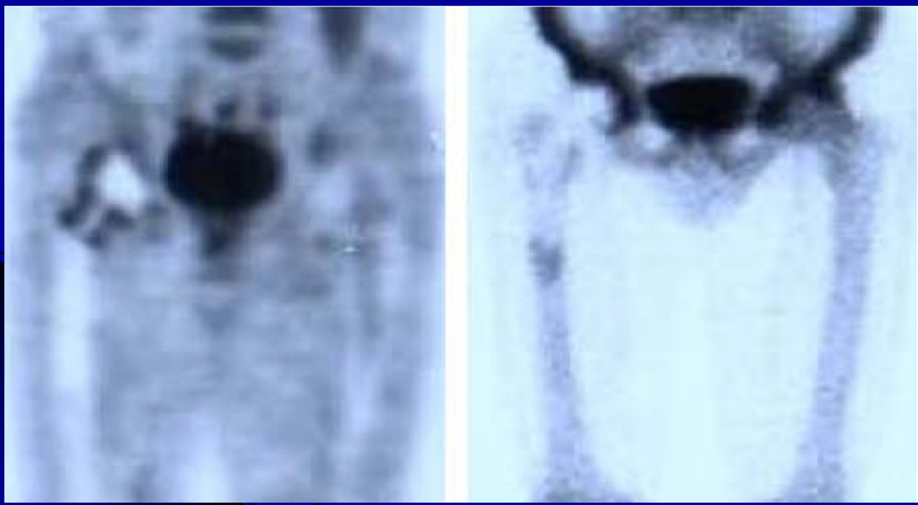
Patterns I, II, and III are not associated with loosening, pattern IV should be associated with aseptic loosening, and in pattern V there should be infection.

by Mumme

Description	Clinical correlate
No increased FDG uptake in the prosthesis-tissue interface	No loosening
Increased FDG uptake in the femoral neck area	No loosening
Increased FDG uptake in the femoral neck area and in parts of the prosthesis-bone interface of the acetabular cup without covering the whole cup	No loosening
Increased FDG uptake in the femoral neck area and in parts of the prosthesis-bone interface of the proximal stem	No loosening
Pattern 3a + 3b	No loosening
Increased FDG uptake in the femoral neck area and in the whole prosthesis-bone interface of the acetabular cup	Loosening
Increased FDG uptake in the femoral neck area and in wide parts of the prosthesis-bone interface of the stem	Loosening
Pattern 4a + 4b	Loosening

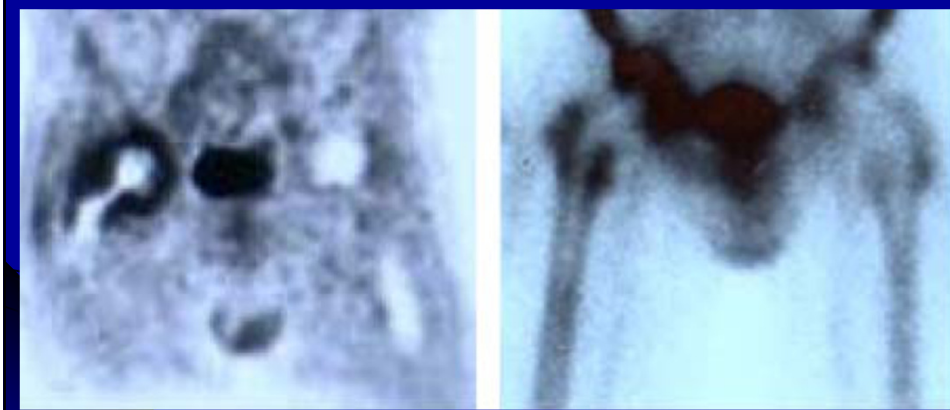
by Reinartz

FDG PET VS BONE SCINTIGRAPH PATTERN I



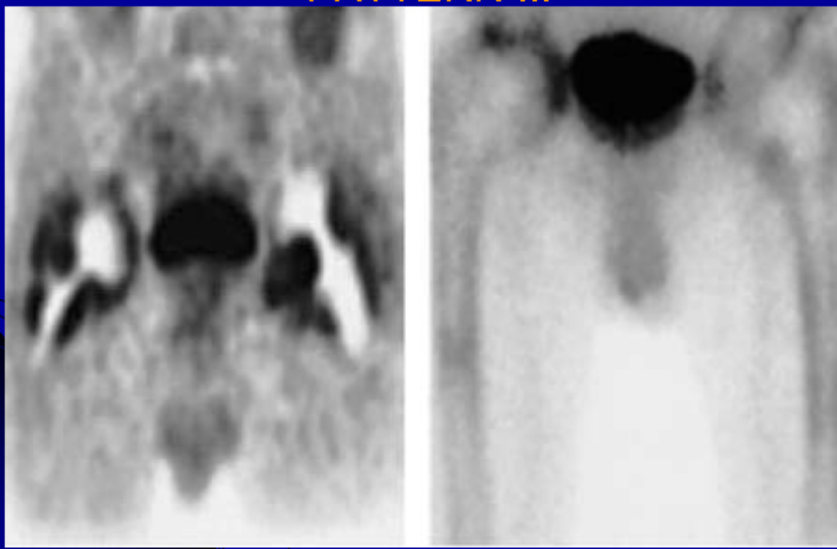
FDG PET TPBS

FDG PET VS BONE SCINTIGRAPH PATTERN II



FDG PET TPBS

FDG PET VS BONE SCINTIGRAPH PATTERN III

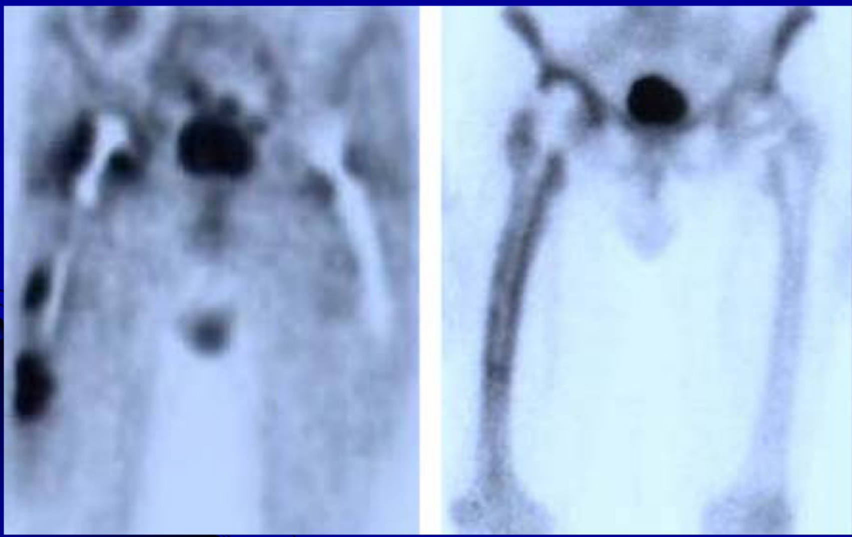


FDG PET TPBS

FDG PET VS BONE SCINTIGRAPH PATTERN IV

FDG PET TPBS

FDG PET VS BONE SCINTIGRAPH PATTERN V



FDG PET TPBS

FDG PET(-CT) IMAGING IN INFECTED PROSTHESIS

- No final conclusion in literature to diagnose septic from aseptic loosening in THR
- Pooled average sensitivity 84%, pooled specificity 84%
- Lower specificity than bone scintigraphy combined with leukocyte scintigraphy
- More accurate in hip than knee prostheses
- Difficult to differentiate between metal-wear induced chronic inflammatory and infectious processes seen around prostheses
- FDG uptake patterns need to be defined

FDG PET for prosthetic infections

false positive result: aseptic loosening of left total knee prosthesis on FDG PET (surgically proven); normal prosthesis at right side

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Treatment

- I&D with systemic antibiotics (prosthetic salvage)
- Systemic antibiotics with removal of hardware and reimplantation
  - Immediate replacement (84% cure rate)
  - Delayed replacement (90%)
- Antibiotics plus permanent removal of hardware
- Joint arthrodesis after removal of components
- Amputation
- Antibiotic therapy

Prevention

- Preoperative
  - Host factor optimization
  - Surgical antibiotic prophylaxis
- Perioperative
  - Wound hemostasis
  - Decreased operative time
  - Proper prosthetic size
  - Incision placement
- Postoperative
  - Wound care
  - Prevention of bacteremia

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Conclusions

Nuclear Medicine strategy dependent on clinical question:

Question: COMPLICATION?

3F bone scan reasonable strategy

Question: INFECTION?

Leukocyte scan (24 hrs!)

if any periprosthetic uptake proceed with

Marrow scan (sulfur colloid)