18F-FDG PET-CT IMAGING IN INFECTION AND INFLAMMATION

Professor Dr. Alex Maes

AZ Groeninge Kortrijk and KULeuven

Belgium

TOPICS

- FDG PET(-CT) IMAGING IN INFECTION
  - Skeletal infection
  - Fever of unknown origin
  - Graft infecton
  - HIV
  - Other
- FDG PET(-CT) IMAGING IN INFLAMMATION
  - Vasculitis/ polymyalgia reumatica
  - Sarcoidosis
  - Reumatoid arthritis
  - Inflammatory bowel disease

FDG PET(-CT) IMAGING IN INFECTION
SKELETAL

1. Osteomyelitis
2. Diabetic foot
3. Infected prothesis

Osteomyelitis

- Bacterial, fungal or mycobacterial
- Acute, subacute and chronic type
- MRI
  - shows good results in acute osteomyelitis
- CT
  - depict sequestered bone fragments and fistula tracts: signs of chronic osteomyelitis
- Three-phase bone scintigraphy
  - + Early diagnosis, high sensitivity
  - - non-specific in previous traumatized bone, prosthetic joint replacement and neuropathic joint
- White blood cell scintigraphy
  - high sensitivity and specificity
- MRI and CT image quality degrades in the presence of metallic implants
- PET ?

FDG PET(-CT) IMAGING IN ACUTE OSTEOMYELITIS

- Diagnosis of acute osteomyelitis based upon clinical history, clinical appearance, biochemical and conventional imaging is mostly straightforward

no need for complexe nuclear medicine techniques

FDG PET(-CT) IMAGING IN CHRONIC OSTEOMYELITIS

- First study
  - N= 22 pts
  - Suspected chronic osteomyelitis
  - FDG-PET
    - sens 100%, spec 87.5%, accuracy of 90.9%
  - 2 false positives: 1 tibial non-union, 1 osteotomy
  - Final diagnosis was made by surgical exploration or clinical follow-up during a 1-year period

- Second study:
  - FDG appears to normalize rapidly following traumatic or surgical fractures as fibroblast predominate in normally healing bone

Zhuang et al, Clin Nuc MEd 2000, Exclusion of chronic osteomyelitis with 18F-FDG PET imaging

Zhuang et al, EJNMI 2003, Rapid normalization of osseous FDG-uptake following traumatic or surgical fractures

FDG PET(-CT) IMAGING IN CHRONIC OSTEOMYELITIS

Fluorine-18 fluorodeoxyglucose-positron emission tomography: a highly accurate imaging modality for the diagnosis of chronic musculoskeletal infections

- Prospectively
- n = 60: 33 central skeleton, 27 peripheral skeleton; 35 pts had surgery in past 2 years
- histopathological studies or microbiological culture (18 patients) or on clinical findings after at least six months of follow-up (42 patients)
- **Results:**
  - 25 pts infection, correctly identified
  - 35 pts no infection
  - 4 false false-positive findings;
    - in 2: surgery < 6 months prior to the study

PET	Sensi	Speci	Accuracy
Whole group	100%	88%	93%
Central skeleton	100%	90%	94%
Peripheral skeleton	100%	86%	93%

- **Conclusions:**
  - 18F- FDG-PET is highly accurate as a single technique for the evaluation of chronic musculoskeletal infections.
  - Especially valuable in the evaluation of the central skeleton, where white blood-cell scans are less useful.
  - Simplicity and high degree of accuracy: the potential to become a standard technique for the diagnosis of chronic musculoskeletal infections.

De Winter et al, J Bone Joint Surg; 2001, 83-A: 651-660

FDG PET(-CT) IMAGING IN CHRONIC OSTEOMYELITIS

	Pooled sensi	CI	Pooled speci	CI
PET	96%	88-99	91%	81-95
Bone scintigraphy	82%	70-89	25%	16-36
Leuko scintigraphy	61% Perif 84%-axial 21%		77% Perif 80%-axial 60%	63-87
Bone and leukocyte scinti	78%	72-83	84%	75-90
MRI	84%	69-92	60%	

Conclusions:

1. FDG-PET has the highest diagnostic accuracy for confirming or excluding the diagnosis of chronic osteomyelitis.
2. Leukocyte scintigraphy has an appropriate diagnostic accuracy in the peripheral skeleton, but FDG-PET is superior for detecting chronic osteomyelitis in the axial skelet.

Termaat et al, Bone Joint Surg Am 2005;87:2464-71 The accuracy of diagnostic imaging for the assessment of chronic osteomyelitis: systematic review and meta-analysis

FDG PET(-CT) IMAGING IN CHRONIC OSTEOMYELITIS

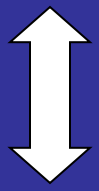
- Conclusions
  - High sensitivity and specificity values for chronic osteomyelitis with FDG-PET
  - Negative FDG-PET : excludes presence of the disorder

DIABETIC FOOT

- Early detection leads to treatment (antibiotics) and decreases amputation rate
- Bone marrow edema and contrast enhancement on MRI are
  - not specific for osteomyelitis
  - Occur in several other non-infectious diseases (stress fractures, necrosis and neuropathy)
- Bone biopsy: gold standard, risk of iatrogeneous infection!
- Radionuclide study of choice: labelled leucocyte imaging: accuracy 80%

FDG PET(-CT) IMAGING IN DIABETIC FOOT

- Keidar et al, The diabetic foot: intial experience with 18F-FDG PET/CT (J N Med 2005; 46:444-9)
  - FDG PET highly accurate in differentiation between osteomyelitis and soft-tissue infection
  - 1 out of 18 sites false positive due to osteoarthropathy misinterpreted as osteomyelitis
  - FDG PET/CT can be used for diagnosis of diabetes-related infection



- Schwegler et al, Unsuspected osteomyelitis is frequent in persistent diabetic foot ulcer and better diagnosed by MRI than by 18F-FDG PET or 99m Tc-MOAB (Int Med 2008;263:99-106)

  MRI (6/7) more sensitive than FDG-PET (2/7) for diagnosing diabetic pedal osteomyelitis
  - N = 20 pts, 7 had histopathological proof of osteomyelitis
  - MRI correct in all cases
  - Only if MRI is inconclusive, conventional radionuclide imaging or FDG-PET/CT might help in the diagnosis of osteomyelitis

FDG PET(-CT) IMAGING IN DIABETIC FOOT

Nuclear medicine and diabetic foot infections

- Bone scan as screening test or localization
- Labeled leukocyte imaging
  - Sensi range: 72%-100%
  - Speci range: 67%-98%
  - Accuracy 99mTc or 111 In: similar
- SPECT-CT: to be investigated, probably useful in mid and hind foot
- FDG-PET and PET/CT: limited results and inconclusive

Palestro and Love, Semin Nucl Med. 2009 Jan;39(1):52-65

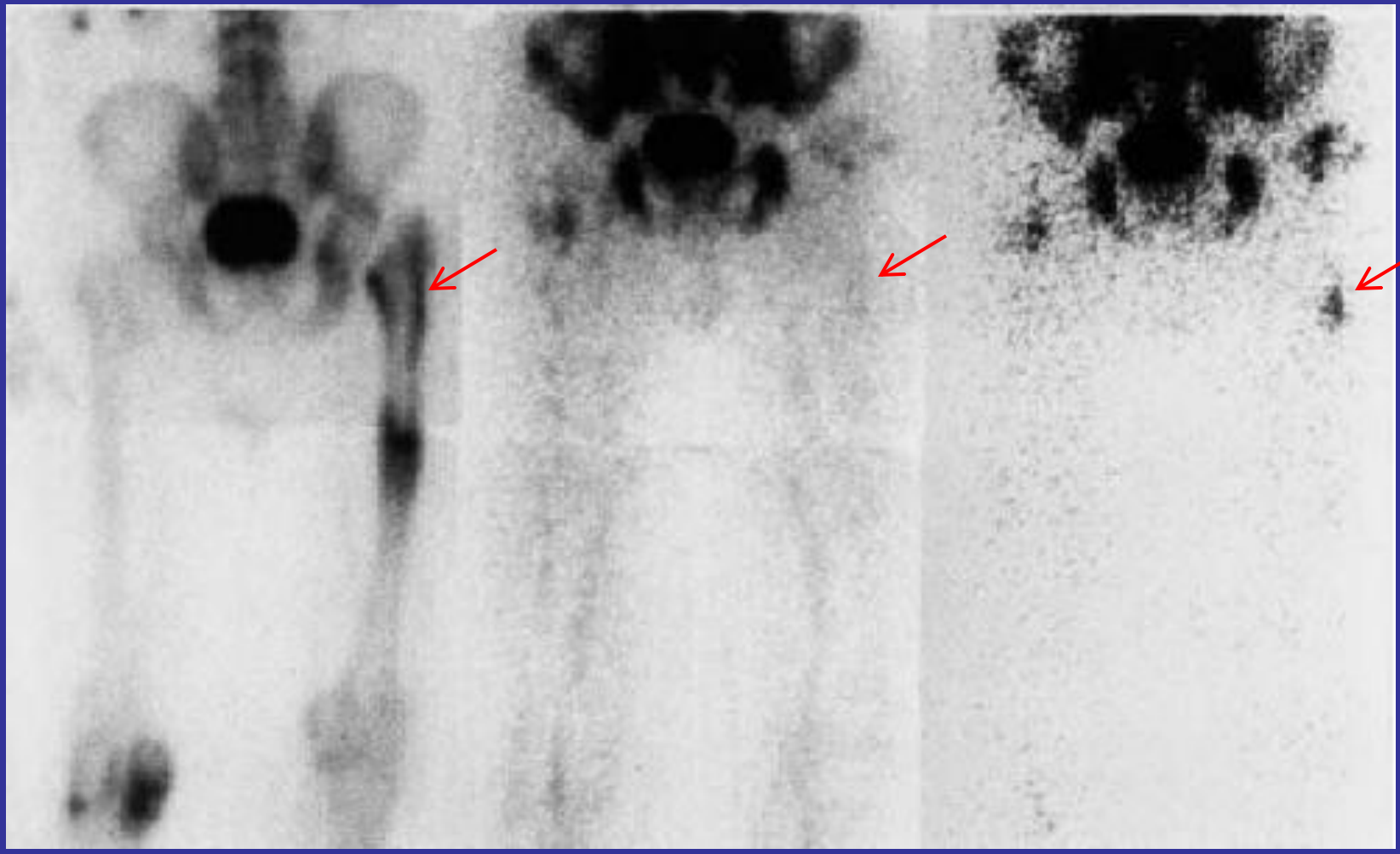
FDG PET(-CT) IMAGING IN INFECTED PROSTHESIS

- Risk of infection in 1-4% of first replacement
- 10% of lower limb arthroplasties need surgical revision, of which 70 % are due to loosening; risk of infection in up to 30% of pts

- 111 In oxin or 99m Tc HMPAO labeled leukocyte scanning in combination with Tc-sulfur colloid marrow imaging: accuracy > 95% in hip and knee

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

BONE and WHITE BLOOD CELL SCINTIGRAPHY IN INFECTED HIP PROSTHESIS



BONE scintigraphy white blood cell after 4h white blood cell after 24h

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

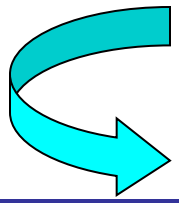
Study and year	Country	No. of patients	Mean age in years (range)	Sex (M/F)	No. of prostheses	Age of prostheses
Chryssikos et al. [12], 2008	USA	113	59 (31–87)	54:59	127 (H)	12, 18, and 24 months
Garcia-Barrecheguren et al. [13], 2007	Spain	24	68 (37–81)	12:12	24 (H)	>6 months
Pill et al. [15], 2006	USA	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 periprosthetic 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

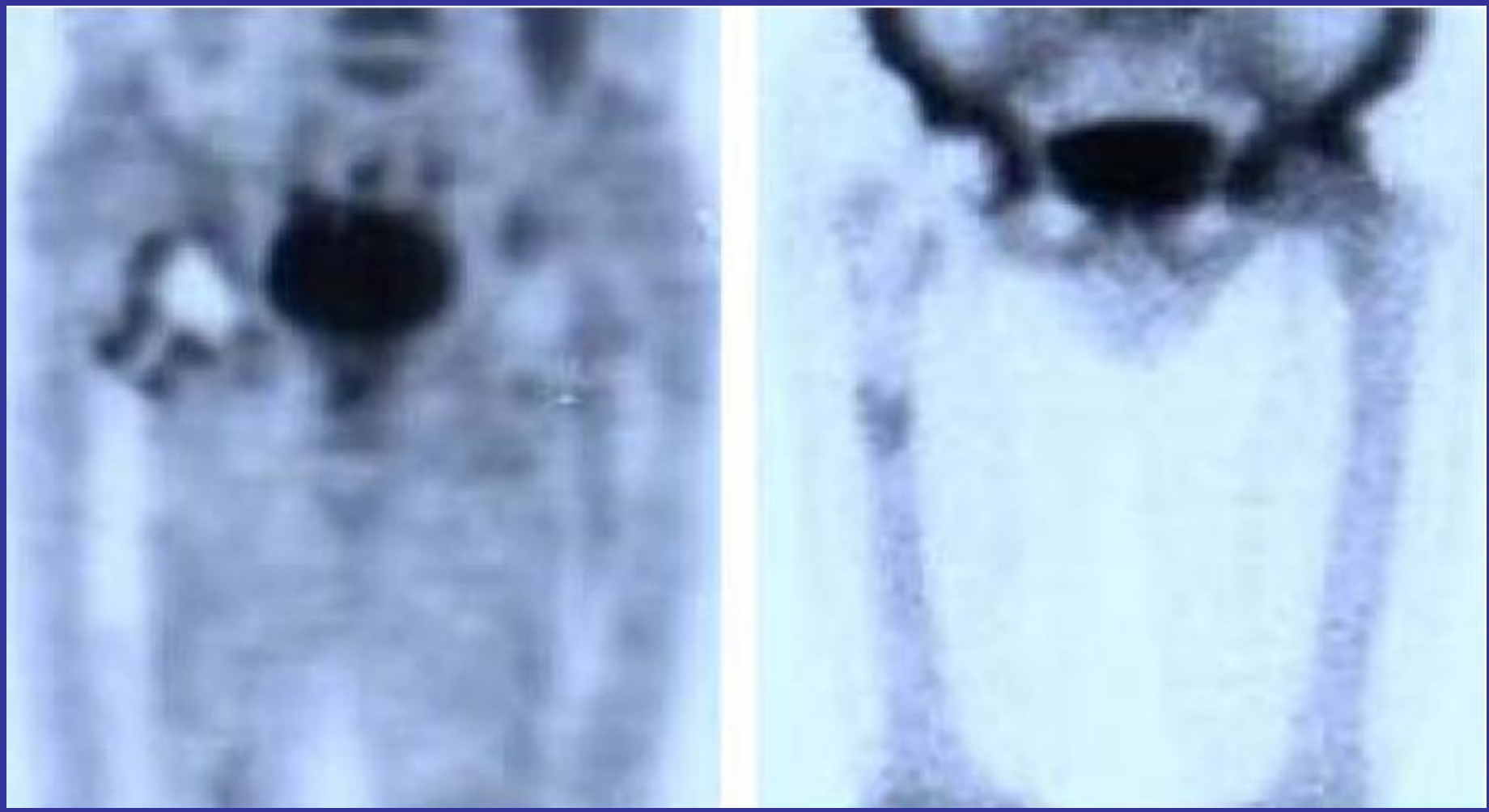
Patterns I, II, and III are not associated with loosening, pattern IV should be associated with aseptic loosening, and in pattern V there should be infection.

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

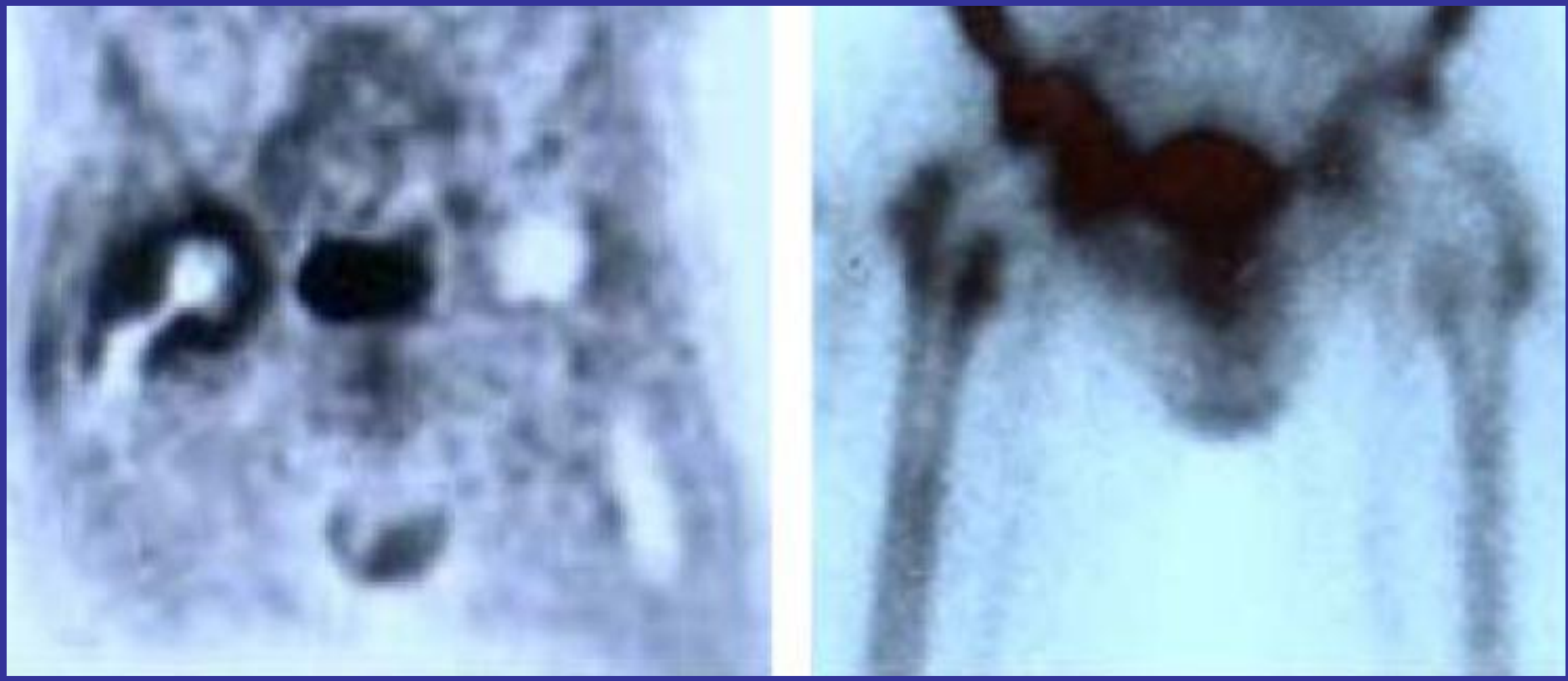
FDG PET VS BONE SCINTIGRAPH PATTERN I



FDG PET

TPBS

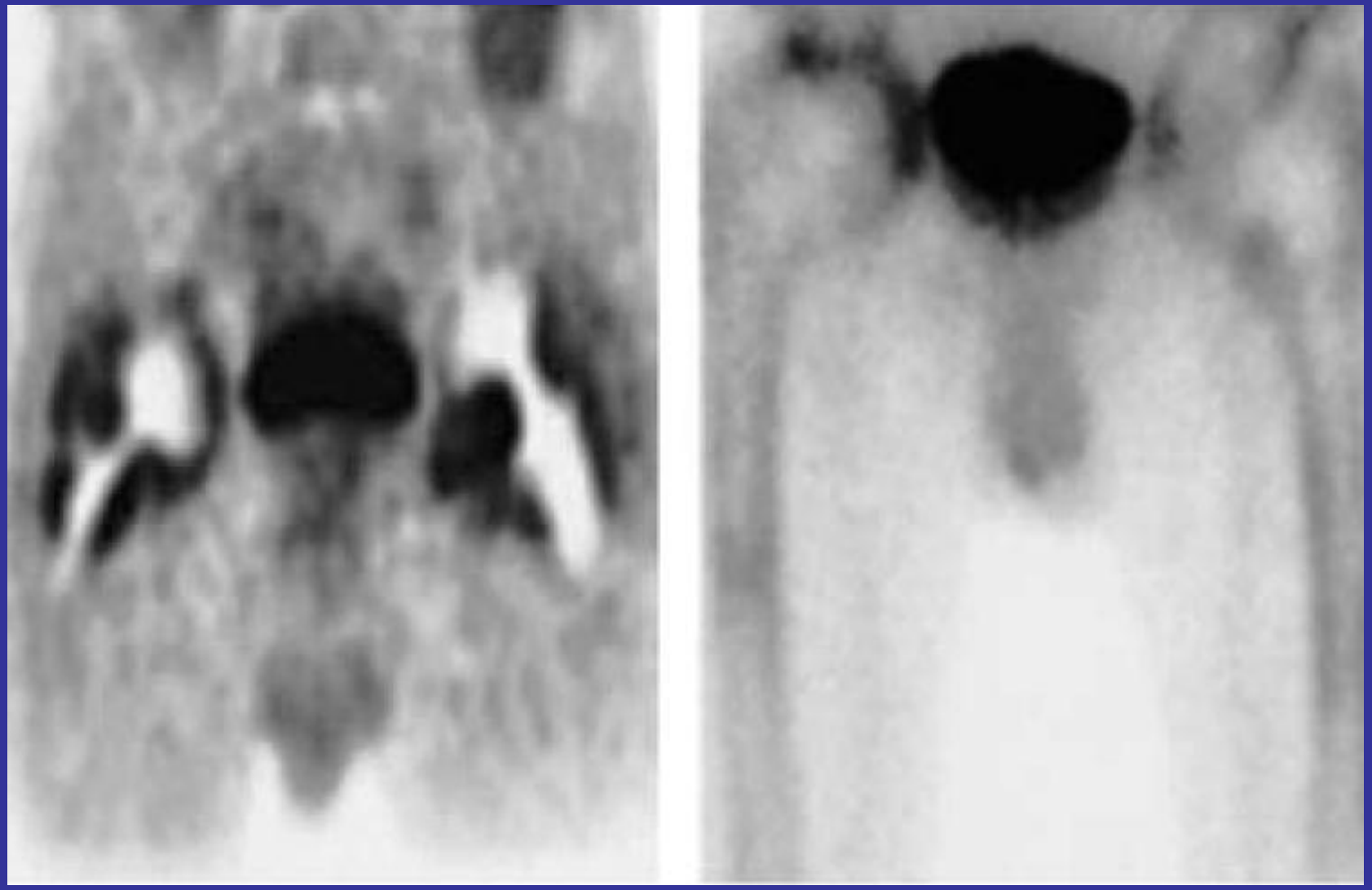
FDG PET VS BONE SCINTIGRAPH PATTERN II



FDG PET

TPBS

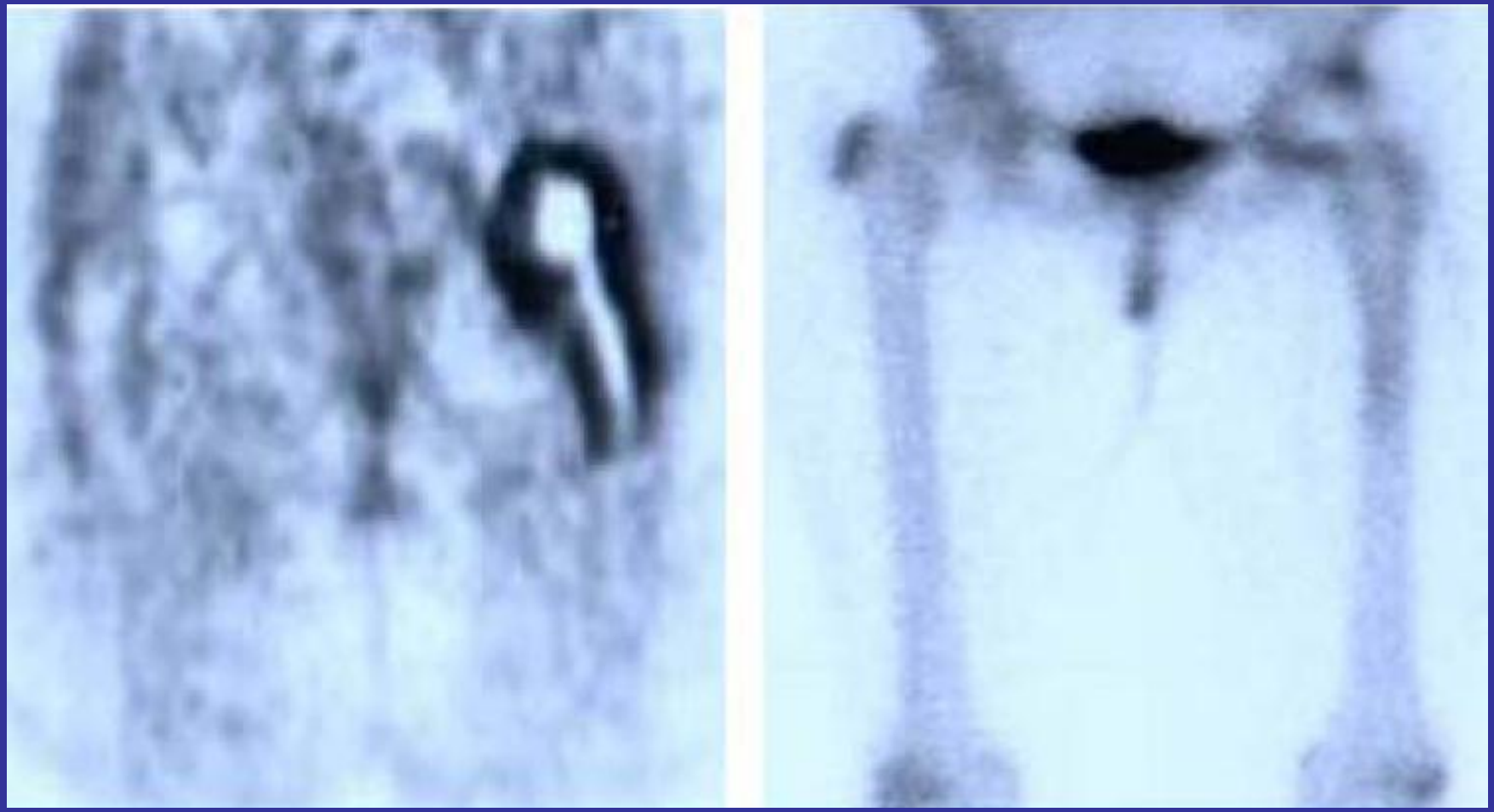
FDG PET VS BONE SCINTIGRAPH
PATTERN III



FDG PET

TPBS

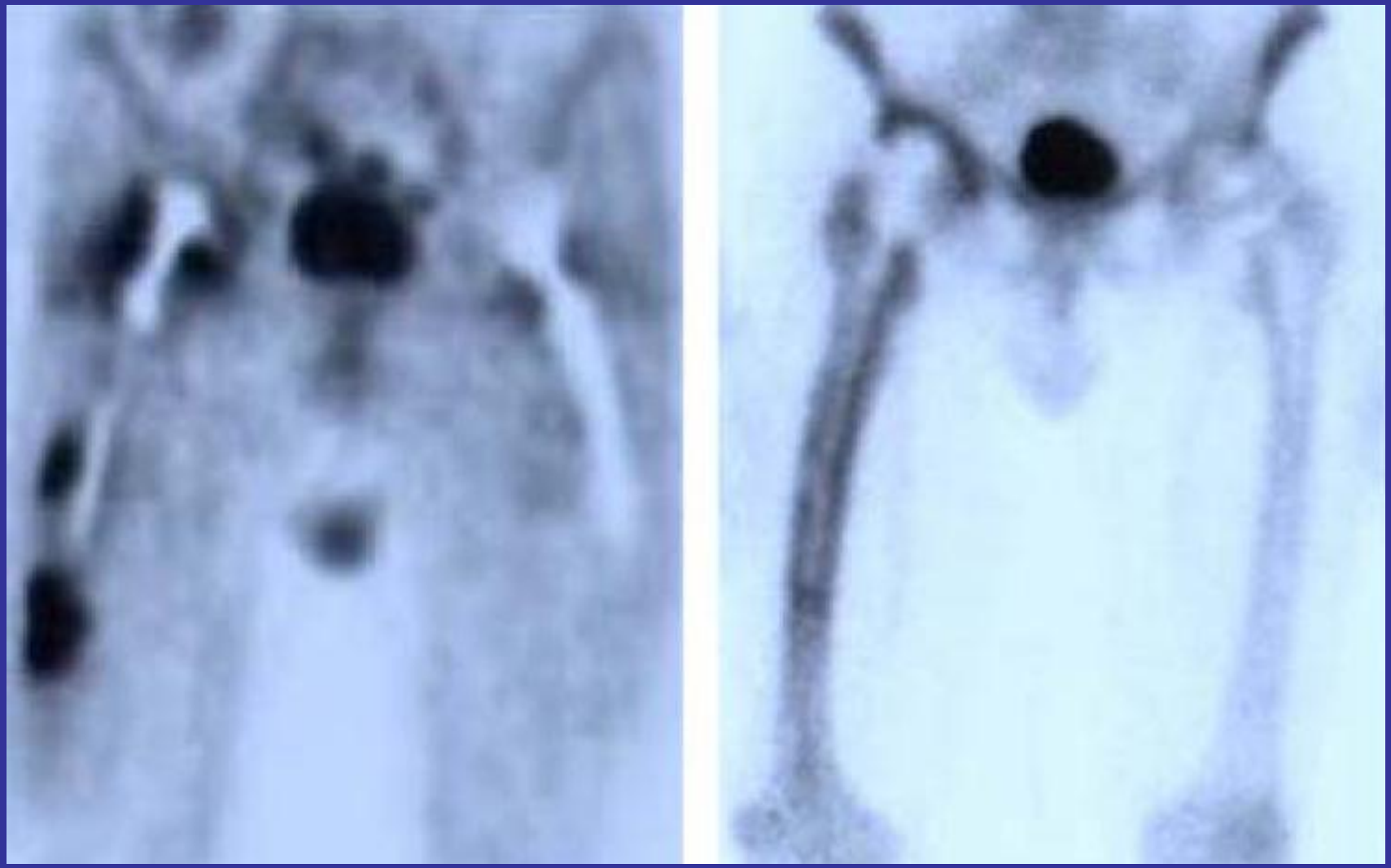
FDG PET VS BONE SCINTIGRAPH PATTERN IV



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

Fever of unknown origin

Definition of fever of unknown origin

- 1962: Petersdorf:
  - Fever of higher than 38.3 °C
  - Documented on several occasions
  - Duration of at least 3 weeks
  - Uncertain source after 1 week of comprehensive investigation with conventional techniques as an inpatient in the hospital setting
- Last Petersdorf criterion: no diagnosis after appropriate inpatient or outpatient evaluation
- 3 major categories: infections, malignancies and noninfectious inflammatory diseases

Fever of unknown origin

- Main part is due to infectious disease
  - Focal
  - Chronic osteomyelits
- 15-20% due to non-infectious inflammatory diseases (Vanderschueren et al, 2003)
  - Vasculitis
  - Sarcoidosis
  - Still's disease
  - Crohn disease
- Till 12 % due to malignancy, nowadays decreasing due to better detection of tumours
- Drug fever

FDG PET(-CT) IMAGING IN FUO

TABLE I.—*Studies with FDG-PET in patients with classical FUO.*

Author	Design	Patients (n=292)						PET helpful (%)
		N.	IF (%)	ID (%)	NP (%)	MISC (%)	ND (%)	
Meller *et al.*[52]	p	20	40	25 (15)	10	15	10	55 (PPV: 92; NPV: 75)
Blockmans *et al.*[54]	p	58	18	29 (14)	10	9	34	41 (PPV: —; NPV: —)
Lorenzen *et al.*[53]	r	16	19	50 (18)	6	6	19	69 (PPV: 92; NPV: 100)
Bleeker-Rovers *et al.*[55]	r	35	17	11 (3)	17	9	46	37 (PPV: 87; NPV: 95)
Kjaer *et al.*[56]	p	19	26	16 (5)	6	16	36	16 (PPV: 30; NPV: 67)
Buysschaert *et al.*[57]	r	74	9	5 (4)	16	19	51	26 (PPV: —; NPV: —)
Bleeker-Rovers *et al.*[58]	p	70	17	23 (4)	7	3	50	33 (PPV: 70; NPV: 92)

FDG: 2-[^{18}F]fluoro-2-deoxy-D-glucose; PET: positron emission tomography; FUO: fever of unknown origin; n.: percentage of patients with medium- and large sized vasculitis in a study; IF: infection; ID: inflammatory non-infectious disease; NP: neoplasia; MISC: miscellaneous disorders; ND: non-diagnostic scans; p: prospective, r: retrospective; PPV: positive prospective value; NPV: negative prospective value.

Meller et al, Q J Nucl Med Mol Imaging 2009; 53:51-63

Difficult comparison between studies

- Definition of FUO differs
- Patient recruitment: classic FUO or postoperative sepsis
- FDG-PET technique
- No standardized diagnostic protocol
- No final diagnosis in all patients

FDG PET(-CT) IMAGING IN FUO

A prospective multi-centre study of the value of FDG-PET as part of a structured diagnostic protocol in patients with fever of unknown origin

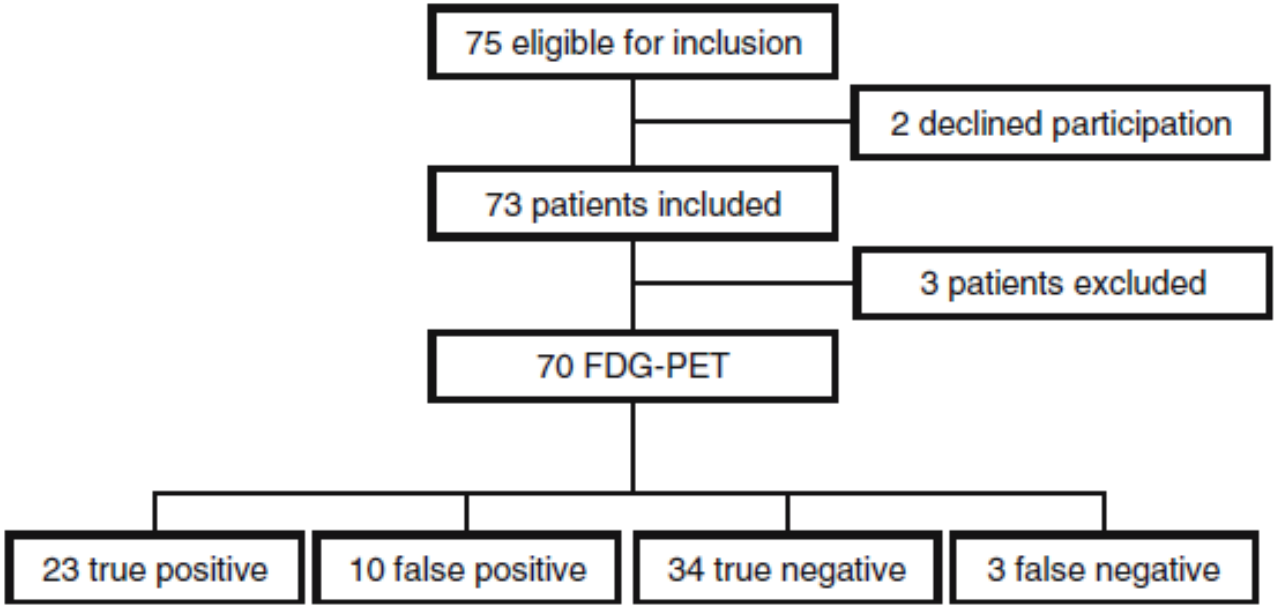


Fig. 2 Three patients had to be excluded: all symptoms resolved before FDG-PET was performed in one patient; in another patient, it proved impossible to obtain a reliable FDG-PET scan owing to severe contractures of the extremities; and one patient died before FDG-PET was performed

Bleeker-Rovers, EJNMI 2007; 34:694-703

FDG PET(-CT) IMAGING IN FUO

- Sensi 88%, speci 77%, PPV 70%, NPV 92%
- 70% of abnormal FDG-PET scans were clinically helpful
- FDG-PET contributed to the ultimate diagnosis in 33% of all patients
- FDG-PET contributed significantly more often to the final diagnosis in patients with continuous fever vs periodic fever(45% vs 12%, $p<0.005$)
- FDG-PET did not contribute in patients with normal CRP
- False positive PET results were responsible for less than 1 % of all diagnostic studies performed in these pts

Bleeker-Rovers, EJNMI 2007; 34:694-703

FDG PET(-CT) IMAGING IN FUO

- Advantages of FDG-PET
  - High resolution
  - Sensitivity in chronic low-grade infections
  - High accuracy in the central skeleton
  - Detection of vasculitis

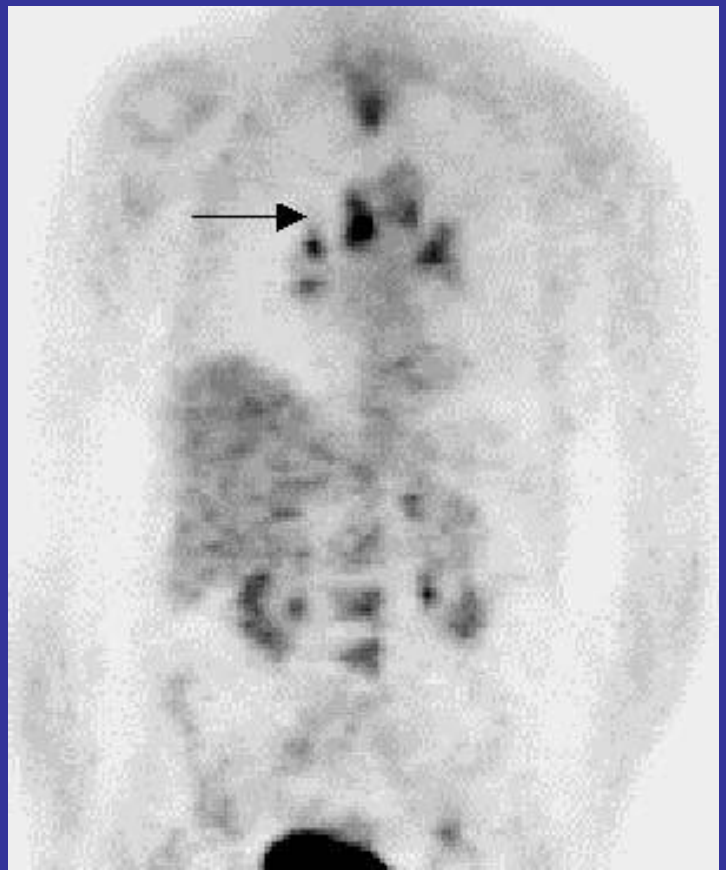
- Theoretical disadvantage impossibility of differentiating between malignancy and infectious diseases or inflammation
- Disadvantages of FDG-PET
  - Relatively high cost
  - Limited availability

- Conclusion:
- FDG-PET is a valuable imaging technique as part of a structured diagnostic protocol in patients with FUO and raised CRP
- Very high negative predictive value

Bleeker-Rovers, EJNMI 2007; 34:694-703

FDG PET(-CT) IMAGING IN FUO

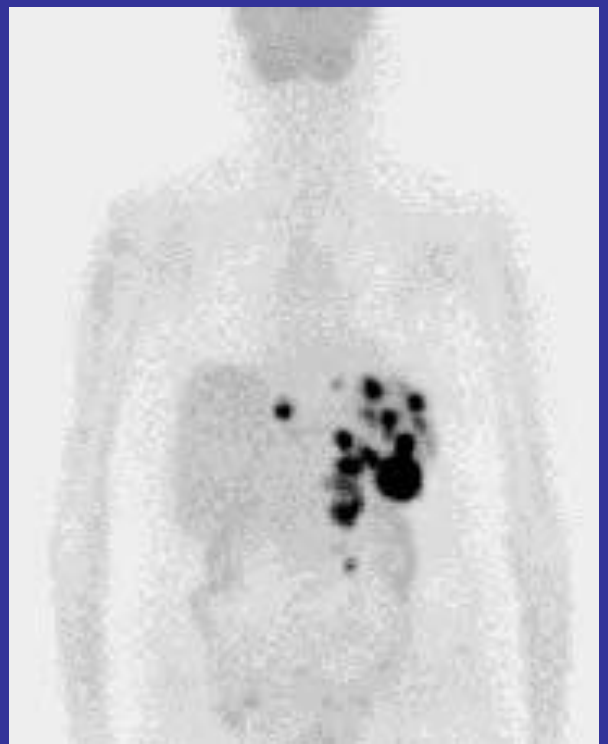
- 70-year-old female
- fever, fatigue and weight loss of 3 weeks' duration.
- A lymph node biopsy obtained by mediastinoscopy demonstrated granulomatous inflammation confirming a diagnosis of sarcoidosis.
- Symptoms resolved upon treatment with corticosteroids



Bleeker-Rovers, EJNMI 2007; 34:694-703

FDG PET(-CT) IMAGING IN FUO

- 76-year-old female
- Fever and weight loss
- Blood,urine, broncho-alveolar lavage fluid and bone marrow cultures
- were negative. Chest X-ray, abdominal and thoracic CT scans,
- MRI of the spine, bone scan, lung perfusion scintigraphy, 111In-
- WBC scan, gastroscopy, colonoscopy and bronchoscopy were all
- normal. Duodenum, liver, bone and temporal artery biopsies were
- normal.



Bleeker-Rovers, EJNMI 2007; 34:694-703

FDG PET(-CT) IMAGING IN ENDOVASCULAR GRAFT INFECTION

- Rare (0,5-5%), but severe complication.
- Generally within months after surgery.
- Delay in treatment can cause sepsis, hemorrhage, limb amputation .
- Death occurs in 50% of pts.
- Abcedation: detected by CT or NMR

FDG PET(-CT) IMAGING IN ENDOVASCULAR GRAFT INFECTION

Detection of aortic graft infection by FDG PET: comparison with computed tomographic findings

- N = 33 pts, clinical suspected arterial prosthetic graft infection
- Gold standard: surgical, microbiological and clinical FU findings

	Sensitivity	**Specificity**
CT	64%	86%
PET	91%	64% If only focal uptake was considered, up to 95% !

Fukuchi et al, J Vasc Surg 2005;42:919-925

FDG PET(-CT) IMAGING IN ENDOVASCULAR GRAFT INFECTION

Prosthetic vascular graft infection: the role of 18F-FDG PET/CT

- N = 39 pts, prospectively, unenhanced CT
- Total of 69 grafts (femoropop, aortobifem, other) of which 40 were clinical suspected for infection of prosthetic vascular graft
- FDG PET uptake criteria:
  - no or only linear uptake of low to moderate intensity along the graft region: considered negative
- Correlation with histopathology or clinical follow-up

Keidar et al, J Nucl Med Aug 2007;48:1230-1236

FDG PET(-CT) IMAGING IN ENDOVASCULAR GRAFT INFECTION

Prosthetic vascular graft infection: the role of 18F-FDG PET/CT: results :

	Sensi	Specif	PPV	NPV
PET/CT	93%	91%	88%	96%

- No uptake in any of the 29 not clinically suspected graft
- Co-registration with CT helps to determine location of the focus: graft or surrounding tissue

Keidar et al, J Nucl Med Aug 2007;48:1230-1236

FDG PET(-CT) IMAGING IN ENDOVASCULAR GRAFT INFECTION

High 18F-FDG uptake in synthetic aortic vascular graft on PET/CT in symptomatic and asymptomatic patients

- N = 16 pts, retrospectively
- Only 1 confirmed graft infection at time of examination

- Conclusion: Chronic aseptic inflammation in synthetic graft material can cause FDG uptake

Wasselius et al, J Nucl Med 2008;49:1601-1605

FDG PET(-CT) IMAGING IN ENDOVASCULAR GRAFT INFECTION

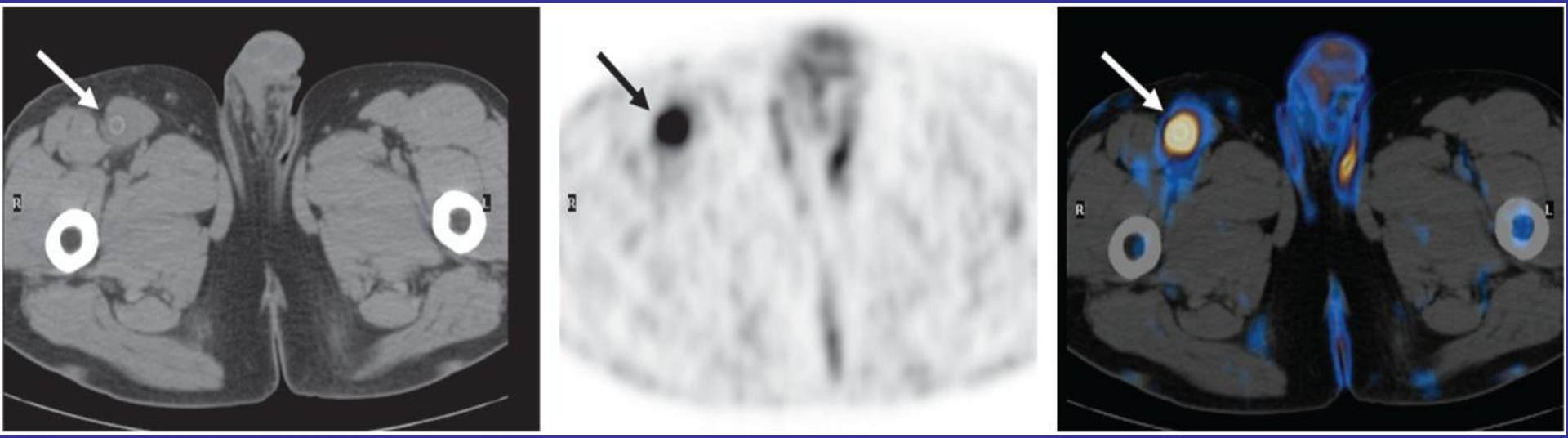


FIGURE 1. A 54-y-old man who had received right femoropopliteal bypass graft 3 mo previously. Infection was clinically suspected because of fever and local pain in right groin. 18F-FDG PET (center) demonstrates focus of increased tracer uptake in right groin (arrow), localized by PET/CT (right) to right femoropopliteal vascular graft as seen on CT (left, arrow). Graft was considered to be involved by infectious process. Diagnosis was confirmed at surgery, and infected graft was removed.

Wasselius et al, J Nucl Med 2008;49:1601-1605

FDG PET(-CT) IMAGING IN ENDOVASCULAR GRAFT INFECTION

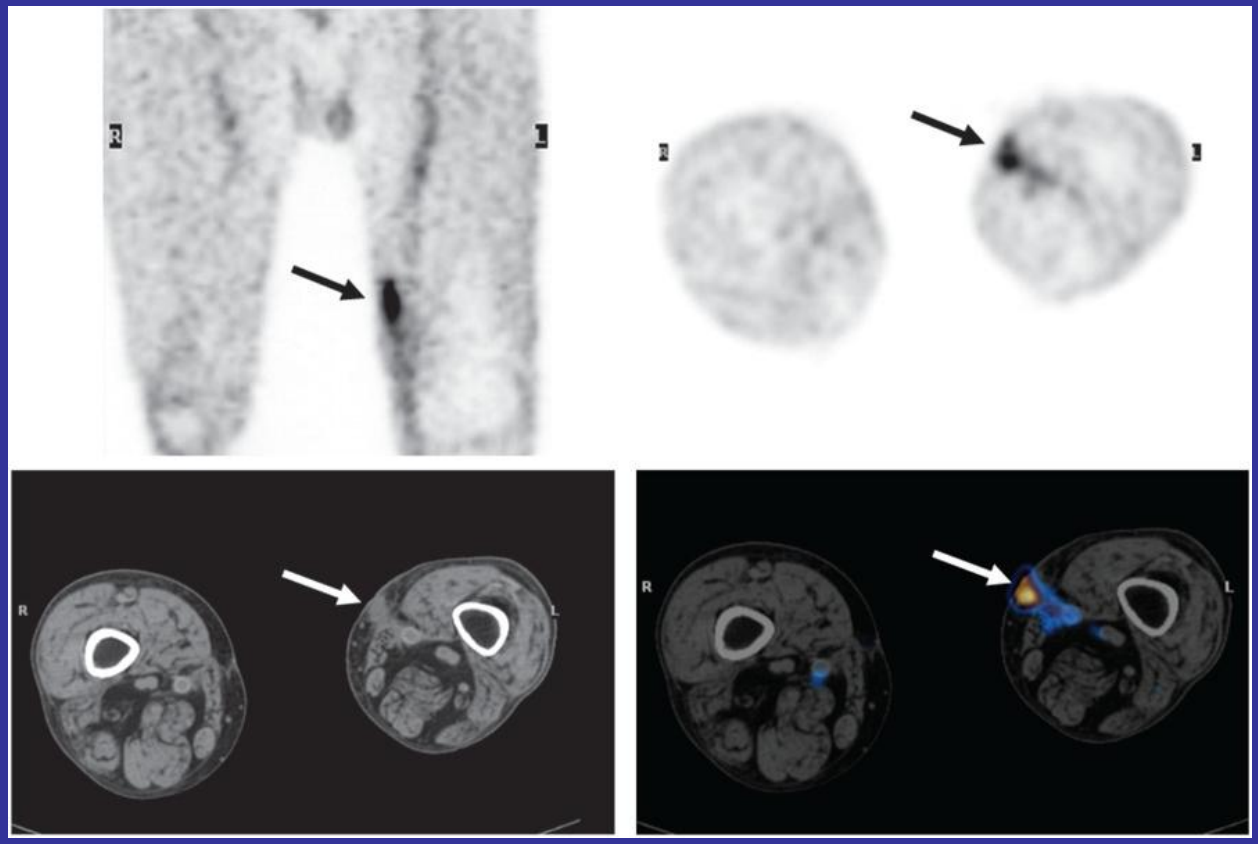


FIGURE 2. A 68-y-old man who had received left femoropopliteal bypass graft 18 mo previously. Infection was clinically suspected because of fever and infected surgical wound in medial aspect of left distal thigh. Coronal (top left) and transaxial (top right) 18F-FDG PET images show area of increased uptake in (arrows), localized by
PET/CT image (bottom right) to softtissue swelling (arrow) adjacent to left femoropopliteal graft as seen on CT (bottom left). Patient responded rapidly to antibiotic therapy, and no vascular graft infection was evident on long-term follow-up of 14 mo.

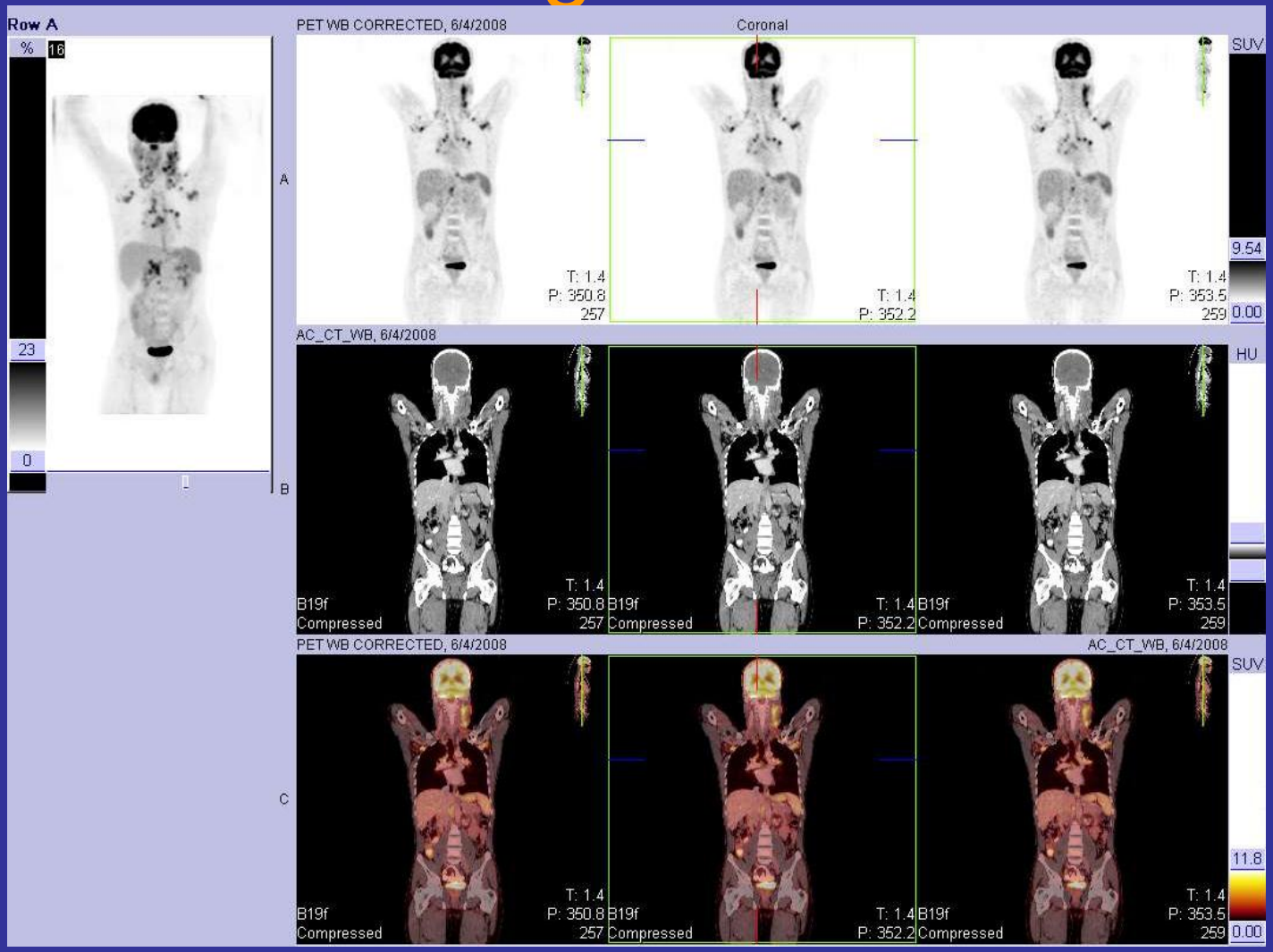
Wasselius et al, J Nucl Med 2008;49:1601-1605

FDG PET(-CT) IMAGING IN HIV

- In human:
  - Acute disease: lymphoid tissue activation in head and neck
  - Mid-stage: peripheral lymph node activation
  - Late disease: abdominal lymph nodes

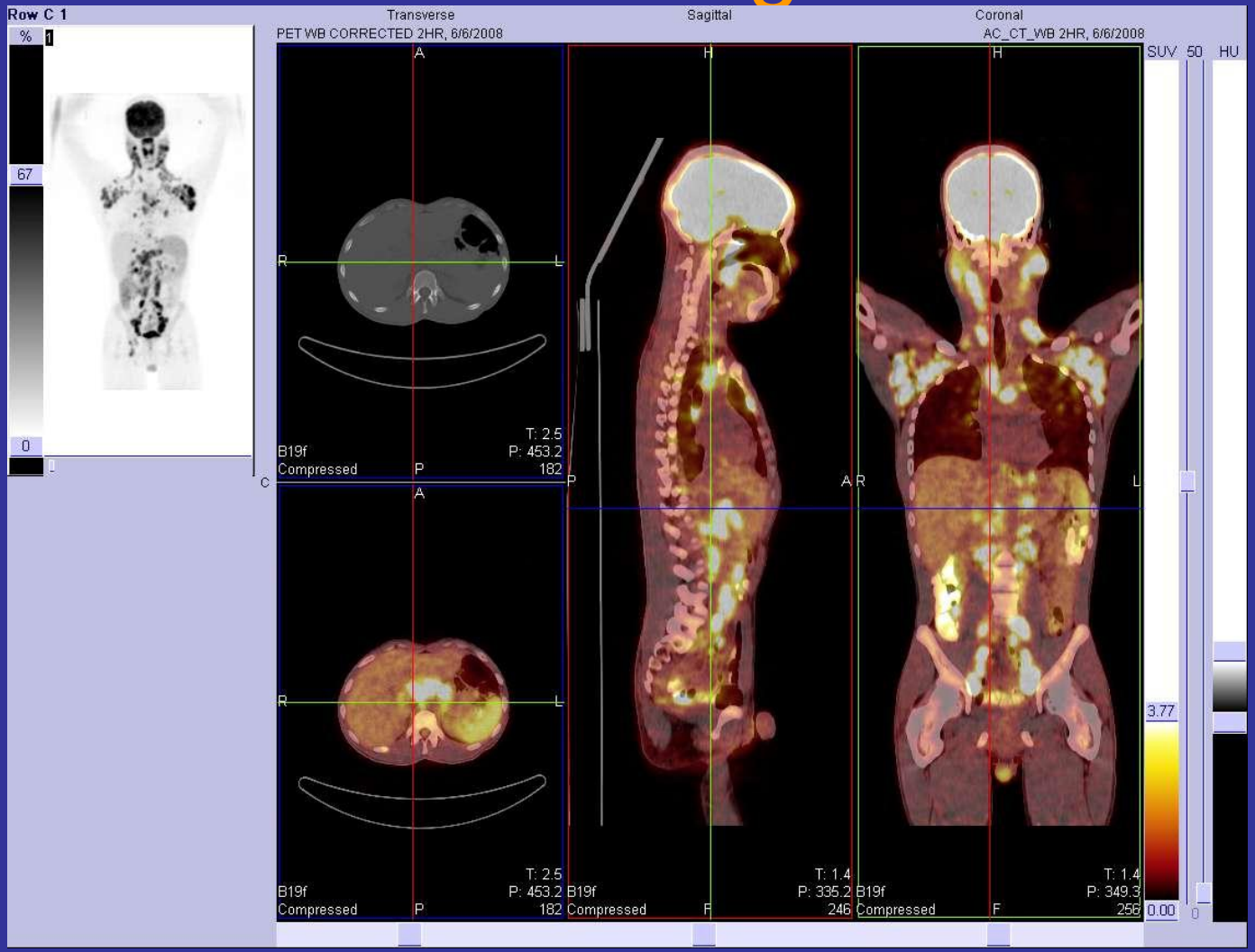
PREDICTABLE SEQUENCE

FDG PET(-CT) IMAGING IN early stage HIV



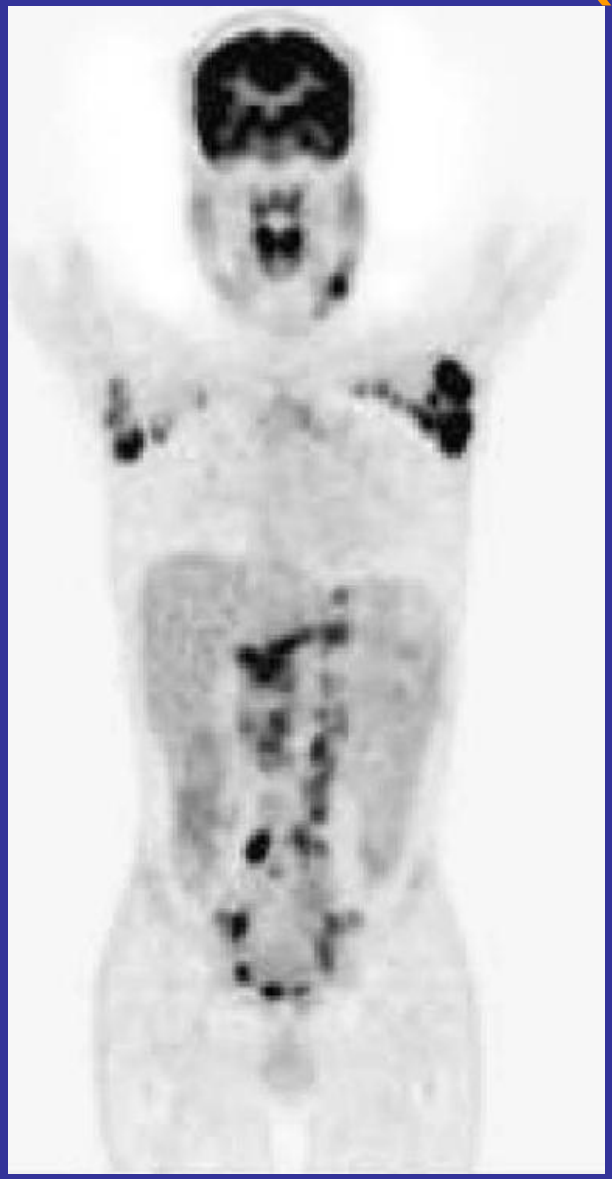
Courtesy of Sathekge

FDG PET(-CT) IMAGING IN late stage HIV



Courtesy of Sathekge

FDG PET(-CT) IMAGING IN HIV

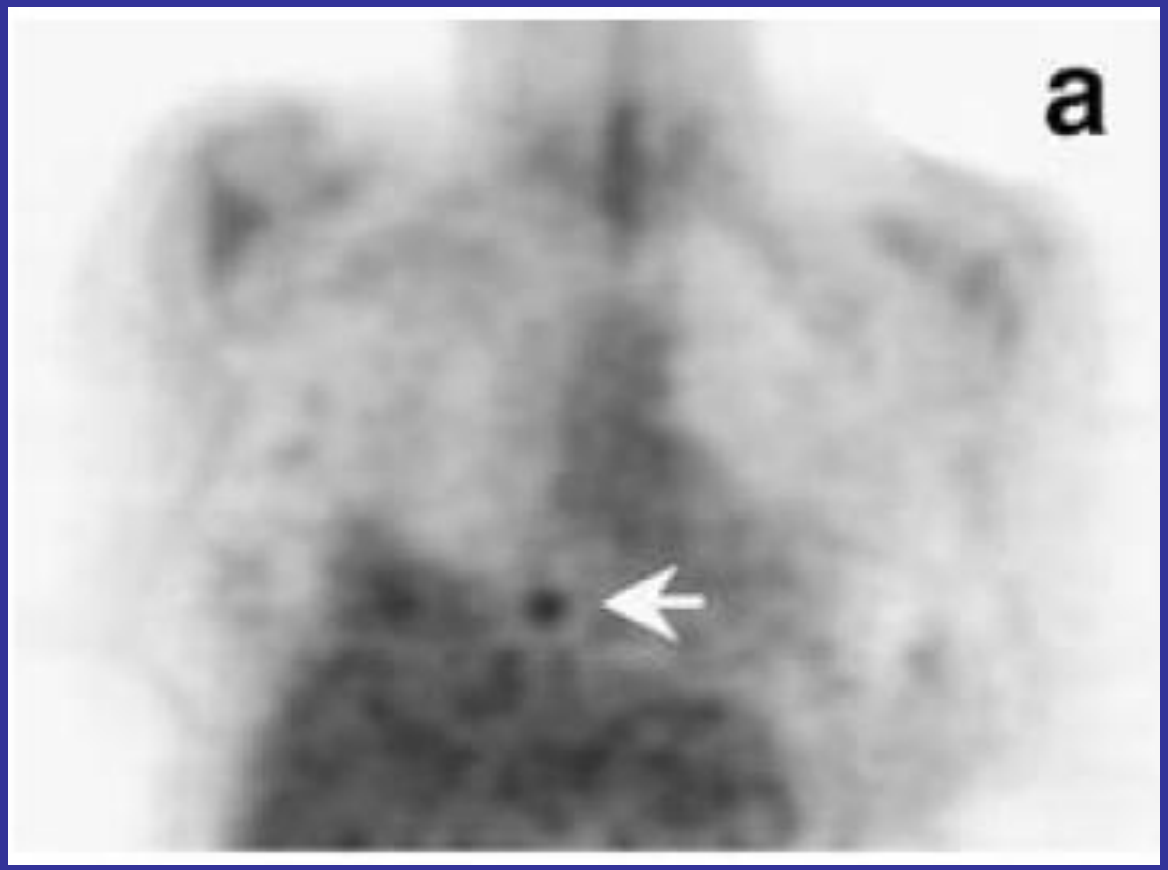


Multiple sites of lymph node involvement (cervical left-sided, axillary and abdominal) in a patient with HIV infection
Sathekge et al, EJNMI 2009;36:1176-1184

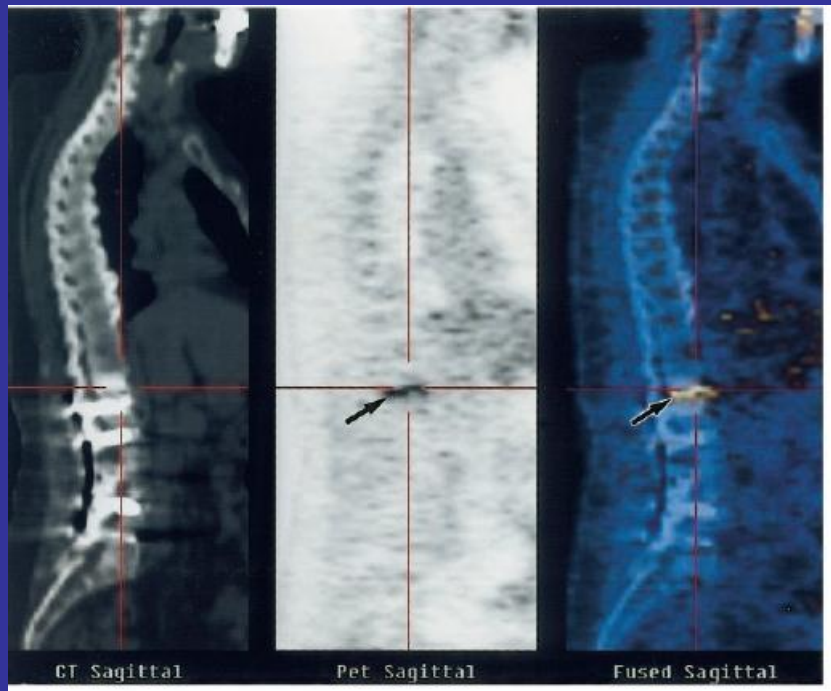
FDG PET(-CT) IMAGING IN INFECTION
other

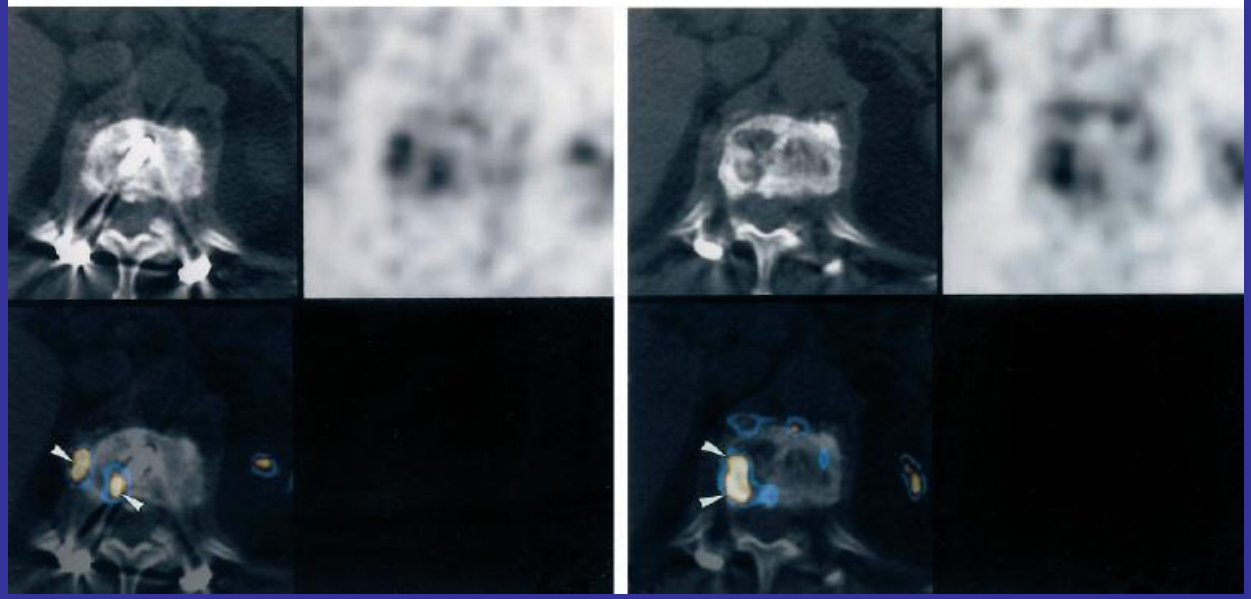
- Pacemaker lead infection
- Disc space infection
- Abcesses: hot rim, cold centre
- ….

Detection of infection of pacemaker epicardial electrode with FDG-PET



Vos et al, EJNMI 2006;33:1245





75-year old woman 2 years after lumbar decompression and spondylodesis of the lumbar spine, who was suspected of having a low-grade infection.
FDG uptake in the region of the right cranial screw in the L1 vertebral body.

Schiesser et al, Radiology 2003;226:391-98

FDG PET(-CT) IMAGING IN INFLAMMATION

- Vasculitis/ polymyalgia reumatica
- Sarcoidosis
- Brain inflammation
- Inflammatory bowel disease
- other

FDG PET(-CT) IMAGING IN POLYMYAGIA REUMATICA (PMR)

- Clinical syndrome of the elderly
- Symptoms
  - Pain
  - Stiffness in shoulders and pelvic girdle
  - Synovitis of the proximal joints and extra-articular synovial structures
- With/without giant cell arteritis

Repetitive 18F-FDG PET in isolated PMR

- N = 35 pts
- Elevated FDG-uptake in
  - Shoulders: 94%
  - Hips: 89%
  - Processi spinosi: 51%
  - Vascular uptake (<subclavian arteries): 31%

Blockmans et al, Repetitive 18F-FDG PET in isolated PMR, Rheumatology 2007; 46:672-7

Repetitive 18F-FDG PET in isolated PMR

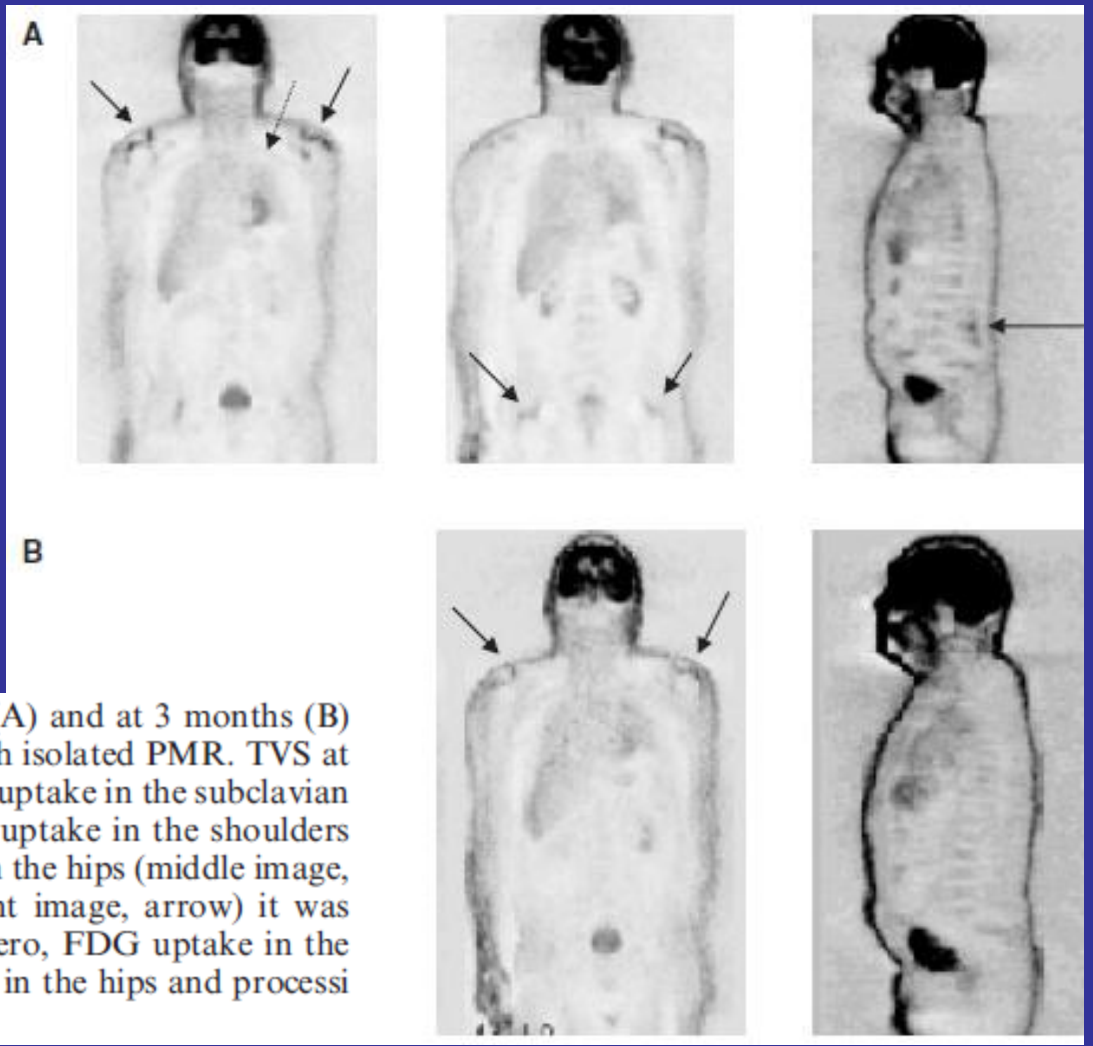


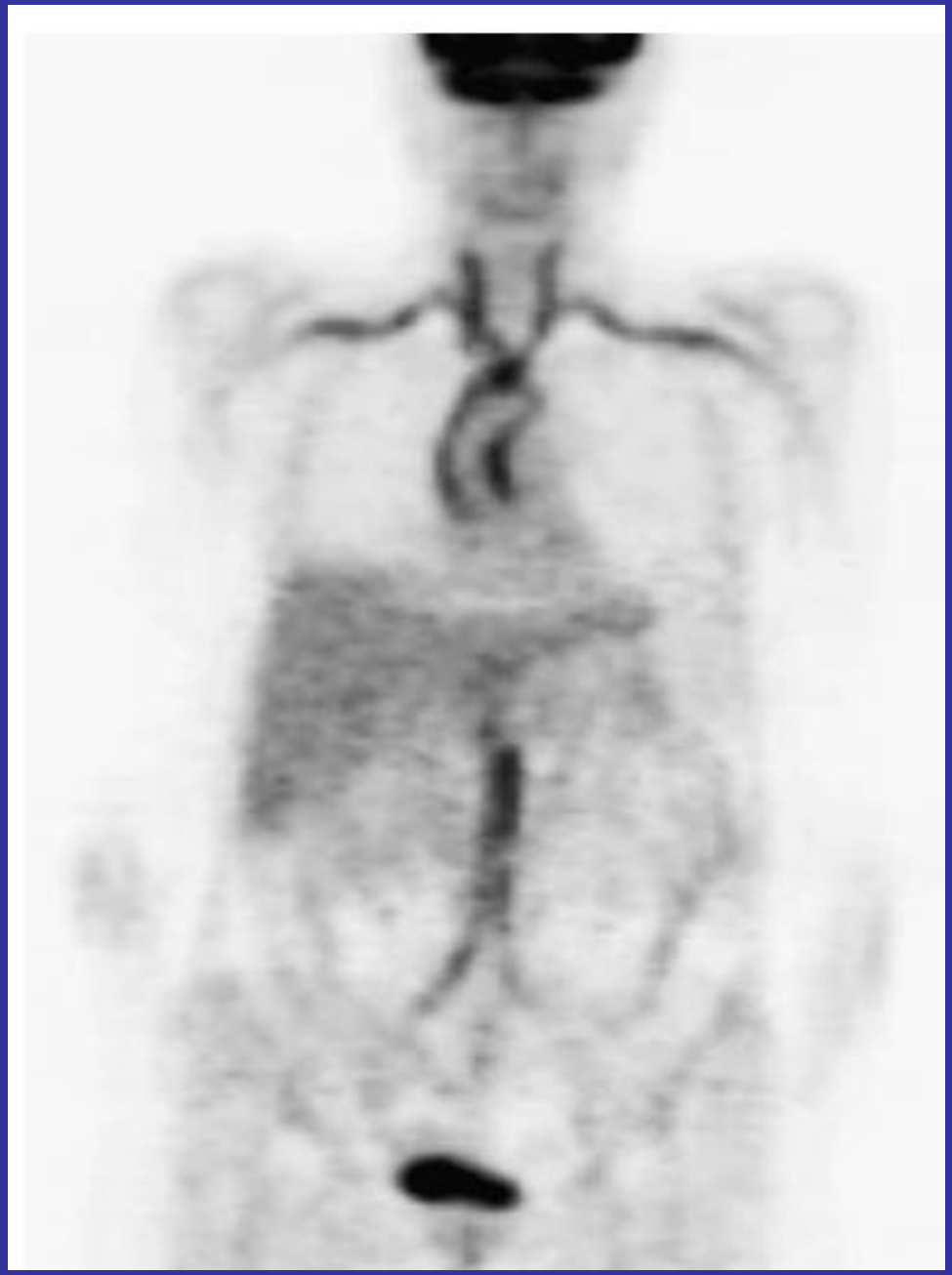
FIG. 3. FDG–PET pictures at diagnosis (A) and at 3 months (B) of therapy in a 63-yr-old male patient with isolated PMR. TVS at baseline was scored one (due to moderate uptake in the subclavian arteries: left image, dotted arrow), FDG uptake in the shoulders was scored two (left image, full arrows), in the hips (middle image, arrows) and in the processi spinosi (right image, arrow) it was scored 1. Three months later, TVS was zero, FDG uptake in the shoulders was scored 1 (arrows) and zero in the hips and processi spinosi.

Blockmans et al, Repetitive 18F-FDG PET in isolated PMR, Rheumatology 2007; 46:672-7

FDG-PET in patients with fever of unknown origin: the importance of diagnosing large vessel vasculitis

- 18F-FDG PET is sensitive (77%-92%) and highly specific in large vessel vasculitis in untreated pts with elevated inflammatory markers
- 18F-FDG uptake correlates well with markers of disease activity, especially in GCA (semiquantitatively)
- Typical 18F-FDG uptake pattern in PMR
- Cannot be used to diagnose or monitor inflammation of the temporal artery
- Highly effective in determing extent of disease in the whole body
- Suited for monitoring disease activity and response to therapy, expecially in GCA, earlier than MRI

Meller et al, Q J Nucl Med Mol Imaging 2009; 53:51-63



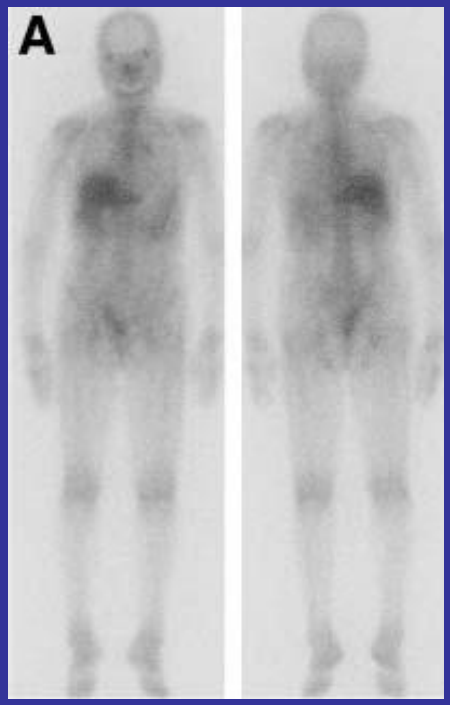
Bleeker-Rovers, EJNMI 2007; 34:694-703

FDG PET(-CT) IMAGING IN SARCOIDOSIS

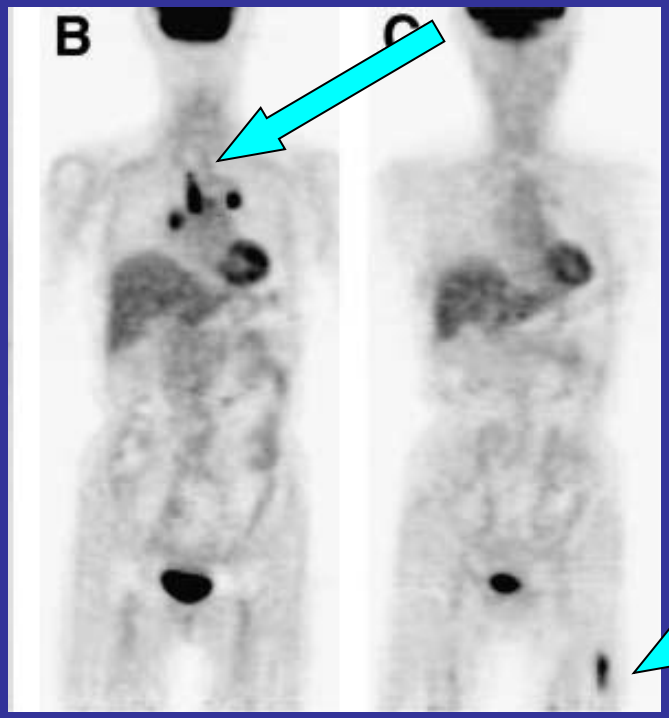
- Granulomatous non-caseating disease
- Unknown etiology
- Multisystem, preferentially intrathoracic and upper respiratory tract
- Staging
  - History and clinical examination
  - Endoscopy of rhinopharynx, pharynx, larynx and bronchy
  - Chest X-ray
  - CT
  - Pulmonary function test
  - Serum ACE, ANCA, urinary calcium
  - 67 Ga scintigraphy

Comparative evaluation of 18F-FDG PET an 67Ga scintigraphy in patients with sarcoidosis

- N = 18 pts, retrospectively
- Bioptic proven sarcoidosis, except for the heart (other lesions biopsies)
- Both FDG-PET/CT and 67Ga scintigraphy in each patient



67Ga scinti



FDG-PET

Nishiyama et al,JNM 2006;47: 1571-1576

Comparative evaluation of 18F-FDG PET an 67Ga scintigraphy in patients with sarcoidosis

- 18F-FDG PET appears to be more accurate and contributes to a better evaluation of extrapulmonary involvement in sarcoidosis patients as compared to Gallium

Nishiyama et al,JNM 2006;47: 1571-1576

18F-FDG PET/CT in sarcoidosis management: review and report of 20 cases

- N = 20 pts, retrospectively

- Diagnostic
  - 28 of 36 biopsy-proven sites of sarcoidosis correctly identified by FDG-PET/CT
    - (4 FN due to face skin sarcoidosis,1 pharyngolaryngeal, 1 labial, 1 gastric and 1 hepatic involvement)
  - 14 of 24 biopsy-proven sites of sarcoidosis correctly identified by 67Ga scintigraphy
  - Sensitivity of FDG-PET/CT from 78% to 87% after excluding skin involvement

- Therapeutic FU: evaluation of CS therapy
  - 5 pts: 1 CMR, 2PMR, 1 PD

Braun, EJNM 2008;35: 1537-1543

18F-FDG PET/CT in sarcoidosis management: review and report of 20 cases

Table 1 Sensitivity results of both ^{18}F-FDG PET/CT and Ga^{67} scintigraphy in detecting active sarcoidosis localizations determined, taking into account only biopsy-proven granulomatous disease

Location of biopsy-proven sarcoidosis involvement	^{18}F-FDG PET/CT			^{67}Ga scintigraphy		
	No. of examined patient	No. of biopsied sites	Sensitivity (%)	No. of examined patient	No. of biopsied sites	Sensitivity (%)
Thoracic	13	13	100	7	7	71
Sinonasal	5	5	100	4	4	75
Pharyngo-laryngeal	5	5	80	3	3	67
Thoracic + extra-thoracic[a]	20	31	87	12	21	67
Thoracic + extra-thoracic[a] (comparative analysis: ^{18}F-FDG vs. ^{67}Ga)	12	21	86	12	21	67

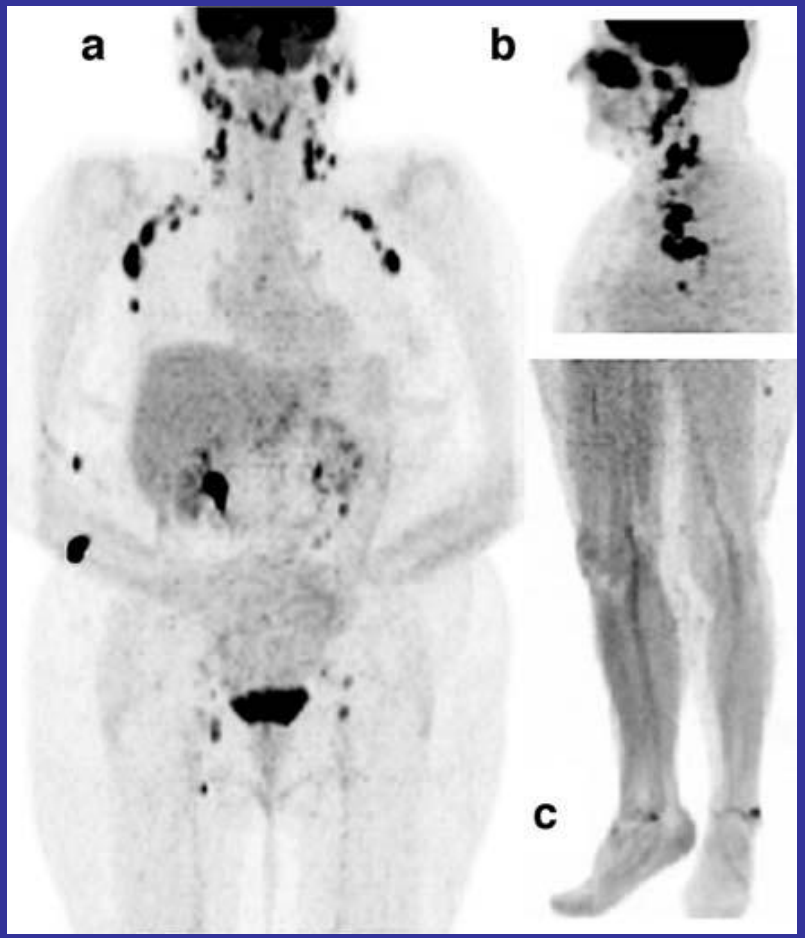
[a] Excluding skin involvement

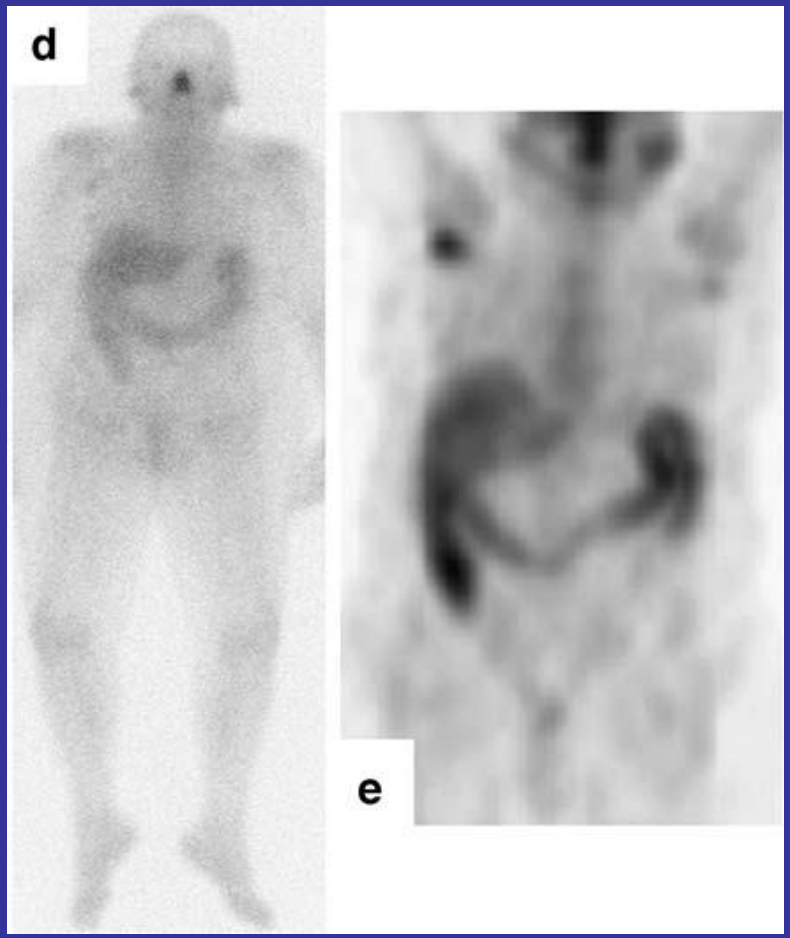
Braun, EJNM 2008;35: 1537-1543

Biopsy proven multiple site sarcoidosis in one patient: FDG-PET vs 67Ga scintigraphy

FDG-PET

67Ga-scintigraphy

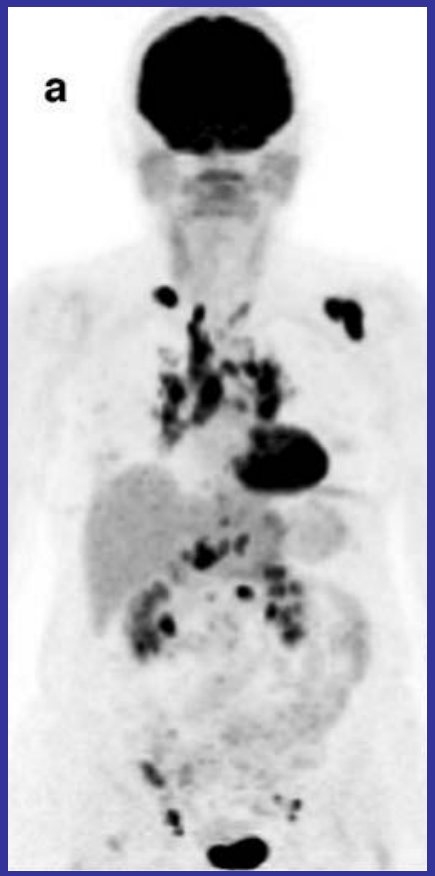




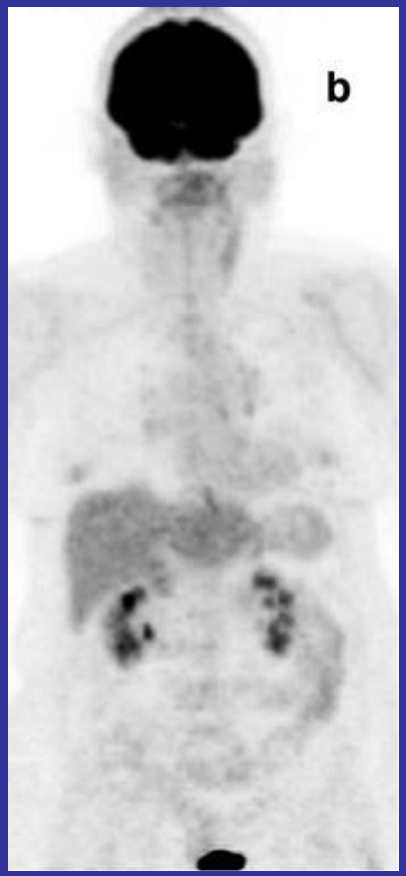
Braun, EJNM 2008;35: 1537-1543

Biopsy proven multiple site sarcoidosis in one patient: before and after corticosteroid treatment

FDG-PET baseline

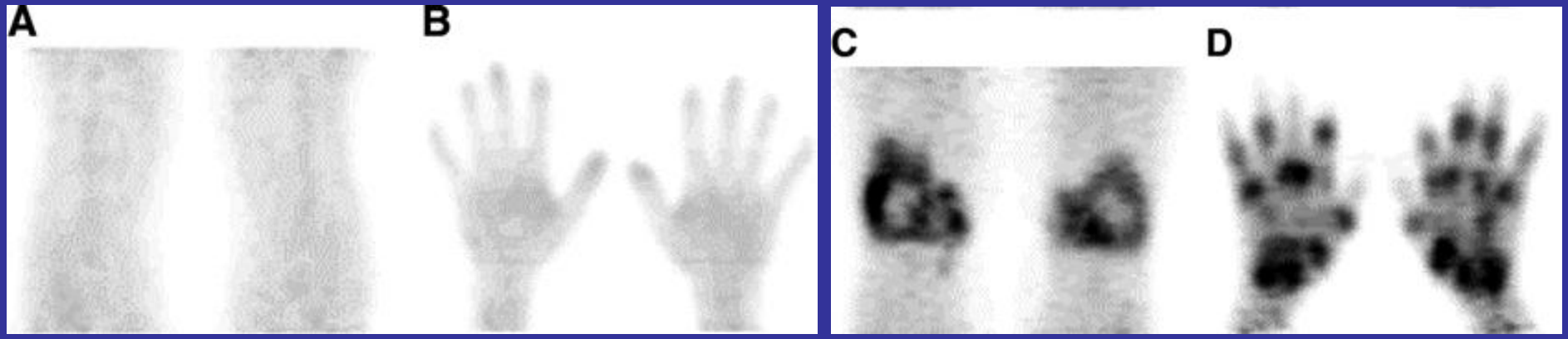


FDG-PET after CS treatment



Braun, EJNM 2008;35: 1537-1543

FDG PET(-CT) IMAGING IN REUMATOID ARTHRITIS



18F-FDG PET images of
- healthy control subject (A and B)
- RA patient with active disease (C and D)

- 18F-FDG PET is a unique imaging technique that can assess the metabolic activity of synovitis and measure the disease activity in RA.
- Corresponds well with clinical and ultrasound joints assessment
- Further studies are of course needed before 18F-FDG PET analysis of RA joints can be considered as an established method for diagnosis and therapeutic follow-up in rheumatology practice.

Beckers et al, Journal of Nuclear Medicine 2004 Jun; 45 (6): 956-964

FDG PET(-CT) IMAGING IN INFLAMMATORY BOWEL DISEASE

- Role of scintigraphy in inflammatory bowel disease

  Stathaki et al, World J of Gastroenterology June 2009

- HMPAO labelled white blood cells
- 99m Tc pentavalent DMSA: FU and assessment of disease activity
- FDG-PET: proposed by Bicik in Lancet 1997

FDG PET(-CT) IMAGING IN INFLAMMATORY BOWEL DISEASE

Neurath et al, Am J Gastroenterol. 2002; 6:851-855

Noninvasive assessment of Crohn's disease activity: comparison of 18F-FDG PET, hydromagnetic resonance imaging and scintigraphy with labeled antibodies

	Sensitivity	**Specifcitiy**
FDG-PET	85%	85%
Hydro MRI	67%	93%
99mTc BW 250/183	41%	100%

FDG PET(-CT) IMAGING IN INFLAMMATORY BOWEL DISEASE

Löffler et al, Ann N Y Acad Sci. 2006 Aug;1072:379-85

High diagnostic value of 18F-FDG PET in pediatric patients with chronic inflammatory bowel disease

	Sensitivity	**Specificity**	**Accuracy**
FDG-PET Large bowel	98%	68%	83%
FDG-PET Small bowel	100%	86%	90%
Endoscopy	90%	75%	82%
US	56%	92%	75%

- FDG-PET is an excellent, noninvasive diagnostic tool for IBD.
- Depicting inflammation in the whole bowel, while being not traumatic, it is attractive for use especially in children.
- FDG-PET is especially reliable for the small bowel and can inform application of topical therapy.

FDG PET(-CT) IMAGING IN INFLAMMATORY BOWEL DISEASE

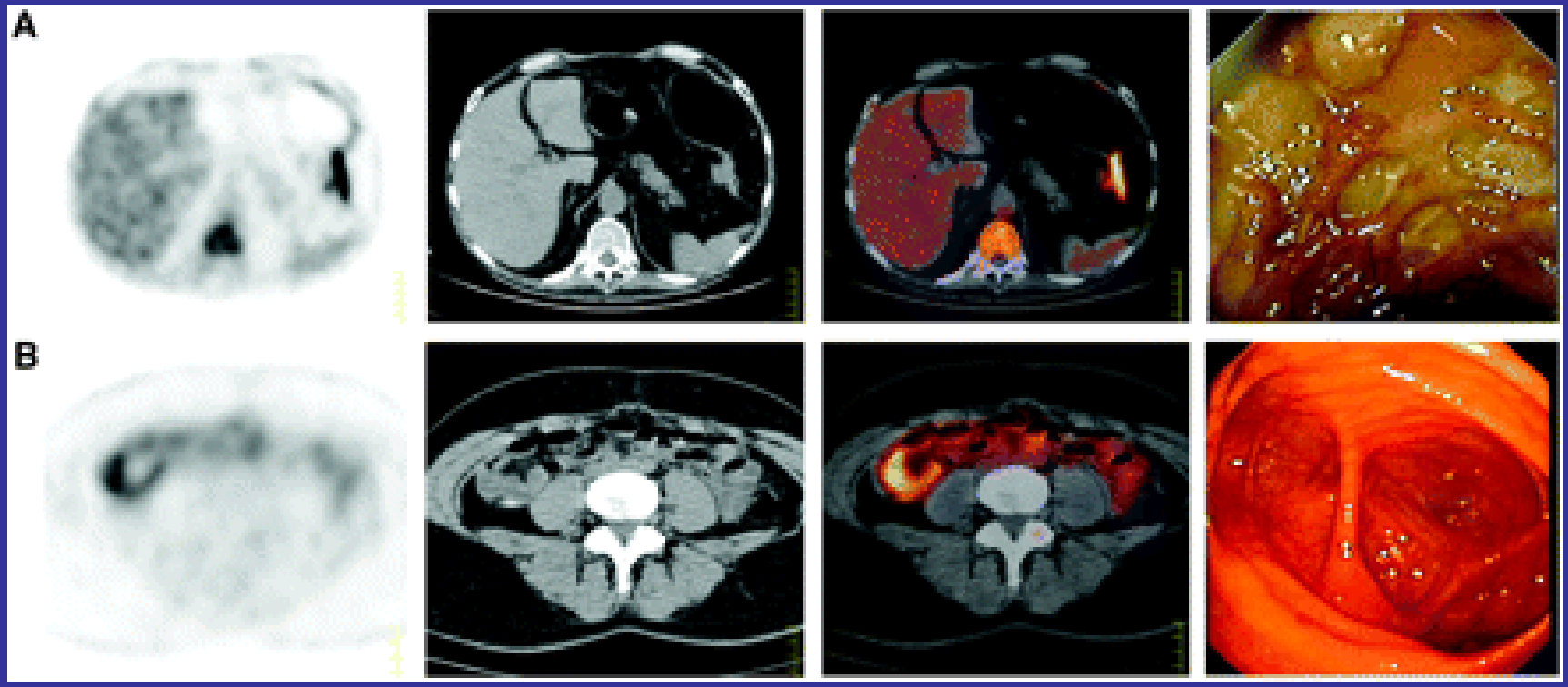


FIGURE 1. From left to right, examples of PET, CT, PET/CT, and corresponding endoscopic appearance. (A) Deep ulcers with cobblestones in left colon, appearing as thickened segment with prominent increase of 18F-FDG uptake on PET/CT. (B) No endoscopic lesion in cecum, contrasting with thickening of bowel wall and increased uptake of FDG on PET/CT

Louis et al.

FDG PET(-CT) IMAGING
Conclusions

- FDG-PET can be used :
  - Chronic osteomyelitis
  - FUO
  - Graft infection
  - Vasculitis
  - Polymyalgia
  - Sarcoidosis
- FDG-PET still in debate :
  - Diabetic foot
  - Infected prosthesis
  - Reumatoid arthritis
  - Inflammatory bowel disease
  - Other?

Future perspectives of nuclear medicine in infection/inflammation

- Labelled WBC
  - 64-Cu
  - 18-F
- Radiolabeled
  - Chemotactic peptides
  - Liposomes
  - Avidin-mediated imaging
  - Antibiotics

Imaging with FDG labeled leukocytes: is it clincally useful?

TABLE I.—*Summary of the results of FDG-labeled leukocyte imaging in two patient's studies in terms of sensitivity, specificity, and accuracy.*

	Sensitivity (%)	Specificity (%)	Accuracy (%)
Dumarey *et al.*[15] (PET/CT)	86	86	86
Rini *et al.*[16] (coincidence PET)	87	82	84

21 pts
43 pts

Dumarey et al, Q J NUCL MOL IMAGING 2009;53:89-94

Imaging with FDG labeled leukocytes: is it clincally useful?

- Advantages
  - absence of significant gastrointestinal and renal uptake
  - only faint uptake in brain and myocardium
  - FDG-leukocytes reveal active diapedesis of granulocytes through chemotactic processes
  - No concern about possible immunological side effects
  - Can be repeated

- Disadvantages
  - Limited by neutrophilic concentration in the patient's peripheral blood
  - Variable labeling efficiency, on site cyclotron
  - Leukocyte accumulation can be seen in sterile inflammation