FDG-PET, ^{99m}Tc-HMPAO white blood cell SPET and bone scintigraphy in the evaluation of painful total knee arthroplasties

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Received 17 April and in revised form 21 June 2001 / Published online: 17 August 2001

Abstract. Fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET), technetium-99m hexamethylpropylene amine oxime (HMPAO)-labelled white blood cell (WBC) scintigraphy and bone scintigraphy were used in the evaluation of total knee arthroplasties (TKAs). We prospectively included 21 patients who had a three-phase bone scan for exclusion of infection of TKAs. Four hours after injection of 185 MBq ^{99m}Tc-HMPAO-labelled WBCs, planar and single-photon emission tomographic (SPET) imaging was performed. Planar imaging was repeated at 24 h p.i. Consecutively images of the knees were obtained with a dedicated PET system 60 min following the injection of 370 MBq of FDG. Focal tracer uptake was scored on SPET and PET visually (0=no uptake, 4=intense uptake). In addition, SUV (standardised uptake value) per voxel was calculated from attenuation-corrected PET images using the MLAA algorithm. Focal uptake at the bone-prosthesis interface was used as the criterion for infection before and after correlation with the third phase of the bone scan. Final diagnosis was based on operative findings, culture and clinical outcome. In the infected TKAs, the WBC scan showed focal activity of grade 2 (n=2), 3 (n=1) or 4 (n=2). PET scan revealed focal activity of grade 4 (n=5) or 3 (n=1). WBC scan alone had a specificity for infection of 53% [positive predictive value (PPV) 42%, sensitivity 100%], compared with 73% for PET scan (PPV 60%, sensitivity 100%). Considering only lesions at the bone-prosthesis interface that were also present on the third phase of the bone scan, we found a specificity of 93% (PPV 83%) for WBC scan. Using these criteria, a specificity of 80% (PPV 67%) was obtained for PET scan. Two out of three false-positive PET scans were due to loosening of the TKA. It is concluded that WBC scintigraphy in combination with bone scintigraphy has a high specificity in the detection of infected TKAs. FDG-PET seems to offer no additional benefit.

Keywords: Arthroplasty – Infection – FDG – HMPAO

Eur J Nucl Med (2001) 28:1496–1504
DOI 10.1007/s002590100603

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Introduction

In a painful total knee arthroplasty (TKA) the exclusion of infection remains a diagnostic challenge. The incidence of infection after total knee replacement was reported to be 1.7% for arthrosis and 4.4% for rheumatoid arthritis in 12,118 TKAs [1]. After revision of a total joint arthroplasty, infection is more likely [2].

The diagnosis of an infected TKA has a major impact on the treatment. Systemic antibiotics alone are primarily used in most cases. Eventually resection and revision arthroplasties are performed in less than one-third of the patients, and arthrodesis in another third; amputation is seldom indicated [1]. Replacement of an infected TKA includes systemic (intravenous) and local antibiotic treatment for 6 weeks after removal of the infected TKA, followed by placement of a new TKA.

Clinical evaluation, erythrocyte sedimentation rate, peripheral leucocyte count and plain radiographs are not accurate in diagnosing an infected TKA [3, 4]. Preoperative joint aspiration appears to be the most useful single test in the workup of a painful total joint arthroplasty

(sensitivity of 67% for a positive intra-operative culture) [4]. However, even when intra-operative cultures are negative, the diagnosis of an infected TKA cannot be excluded and is often made on a clinical basis [5].

Bone scintigraphy is known to be very sensitive for infection and has a high negative predictive value in patients with a painful TKA [6]. However, the poor specificity (24%) limits its clinical value. Various additional techniques have been studied to increase the specificity. Gallium-67 in combination with technetium-99m methylene diphosphonate (MDP) bone scan was found to increase specificity to 81%, with a decrease in sensitivity to 66% [7]. Indium-111-labelled leucocyte scintigraphy was found to have a high sensitivity and specificity (88% and 73%, respectively) for the diagnosis of an infected orthopaedic prosthesis [5]. ^{111}In-labelled leucocyte scintigraphy seems to be superior to ^{67}Ga when compared in the same patient group [8]. ^{99m}Tc-hexamethylpropylene amine oxime (HMPAO)-labelled white blood cell (WBC) scintigraphy is reported to have a comparable sensitivity and specificity (100% and 86%, respectively) in respect of infected hip prostheses [9].

Recently more practicable techniques have been developed. In hip and knee prostheses, Sciuk et al. [6] found an overall sensitivity of 89% and an overall specificity of 84% using ^{99m}Tc- or iodine-123-labelled monoclonal mouse antibody. ^{99m}Tc-polyclonal human IgG scintigraphy in infected hip and knee prostheses has an overall sensitivity of 100% and a poor specificity of 41% [positive predictive value (PPV) 54%] [10].

Fluorine-18 fluorodeoxyglucose (FDG) is known to accumulate at inflammatory sites. The usefulness of FDG positron emission tomography (PET) in infected knee prostheses has not yet been demonstrated. We conducted a prospective study to establish the clinical value of FDG-PET in comparison to WBC scintigraphy, in combination with the three-phase bone scan, in patients with a painful TKA. A PET scan was also performed in a control group to investigate the normal FDG distribution in asymptomatic TKA patients and to clarify whether there is a relationship between the intensity of FDG uptake (focal or diffuse) and the time interval between having a TKA and the PET scan. Knee phantom experiments were done to compare attenuation correction performed with and without transmission scan [11].

Materials and methods

Study population

Patient group

Twenty-one consecutive patients with a painful knee arthroplasty, who had a three-phase bone scan for exclusion of infection, were prospectively included in this study. There were 13 females and 8 males, aged 33–78 years (mean 66±10 years). They were operated on for gonarthrosis (n=19) or burnt-out septic arthritis (n=2) between 7 months and 9 years before the scintigraphic study (mean 35±23 months). Twelve patients had a cemented TKA (in three only cemented at the tibial component), while in nine patients a cementless TKA had been implanted. Sixteen patients had primary implants, and five had a revision. WBC scintigraphy was planned in all patients except one. A PET scan was performed in all patients the day after WBC scintigraphy.

Clinical, biochemical and radiological surveys were performed. Cultures were obtained during surgery in three patients or by needle aspiration in 12 patients. In patients who underwent surgery, prostheses were considered to be infected if micro-organisms grew in culture specimens, and uninfected if cultures were negative. In the absence of operative findings, the final diagnosis was based on long-term (at least 6 months) clinical evaluation (n=6) or on preoperative joint aspiration and culture (n=12).

Control group

In a second patient group without complaints 7 months to 6 years (29±16 months) after placement of a TKA, a bone scan was followed by a PET scan. The control group comprised 11 females and 6 males, aged 48–76 years (mean 67±7 years), with 26 TKAs, of which 15 were cemented. All patients were properly informed and cooperated voluntarily.

Imaging techniques

Bone scan

After i.v. injection of 740 MBq ^{99m}Tc-MDP, a three-phase bone scan was performed: dynamic phase (2 min, 120 1-s frames), blood pool phase (2 min, 2 min after i.v. tracer injection) and delayed phase [10 min anterior and posterior images of the knees 3 h after tracer administration, immediately followed by a single-photon emission tomographic (SPET) acquisition]. Ninety projections (15 s/projection, rotation step of 4°) were acquired over 360° using a 128×64 matrix. Transaxial slices 10.6 mm thick were reconstructed by an iterative reconstruction technique [12, 13]. Studies were performed with a large field of view gamma camera (Trionix, biad), equipped with a low-energy parallel-hole collimator (general purpose for the dynamic and blood pool phases, and ultra-resolution for the delayed phase), using a 20% window centred on the 140-keV photopeak.

WBC scintigraphy

Intravenous injection of 185 MBq ^{99m}Tc-HMPAO-labelled leucocytes was performed. The separation of WBCs and the labelling method with ^{99m}Tc-HMPAO have been described previously [14]. Planar anterior and posterior 10-min images of the knees were obtained at 4 h and 24 h post injection. The 4-h images were immediately followed by a 25-min SPET acquisition. Acquisition and processing parameters were identical to those for bone SPET (cf. above). Data were obtained for 20 s/projection.

FDG-PET scan

PET was performed with an ECAT Exact HR$^+$ scanner (Siemens Medical Systems) that produces slices of 4.6 mm thickness, with an axial field of view of 15 cm.

Knee phantom study. Within a box of Plexiglas, a knee prosthesis was fixed with a thin wooden frame (triplex). After filling this cylindrical volume (diameter 20.5 cm, height 18.5 cm, volume 6 l) with water, 22 MBq FDG was injected and dispersed with a water pump immediately before scanning. The knee phantom was scanned a second time after fixation of three radioactive sources simulating regions of focal tracer uptake. Three bottles (1 mm glass, 1 cm diameter and 3 cm length) were placed at the bone-prosthesis interface of the femoral component, of the tibial component and at the top of the femoral component. The bottle to background activity ratio was 5:1, 4:1 and 10:1, respectively. For the phantom studies, the cylinder was put in the PET camera, and an emission scan was acquired (10 min per bed position). After a one-night decay in the scanner, a transmission scan was acquired. Three methods were used for image reconstruction: (1) maximum likelihood expectation maximisation (MLEM) reconstruction without attenuation correction [12, 13], (2) MLEM reconstruction with attenuation correction using the cold transmission scan, (3) reconstruction with attenuation correction using the MLAA algorithm [11] (cf. below). Transmission-based attenuation correction was done by reprojection of a maximum a posteriori reconstruction as described in Nuyts et al. [15]. MLAA (maximum likelihood reconstruction of attenuation and activity) is an algorithm for reconstruction with attenuation correction but without use of a transmission scan. The MLAA algorithm uses only the emission scan to reconstruct both the activity and the linear attenuation coefficients in every pixel [11].

Clinical study. Patients fasted for at least 6 h before FDG administration. FDG was injected intravenously and the dose was adjusted to the body weight (dose in MBq = 37 × body weight in kg/8). Static emission scans were performed 60 min after FDG administration. The acquisition time for emission scans was 10 min per bed position. Two successive bed positions were scanned with the lower bed position starting just beneath the patellae. Image reconstruction was done without attenuation correction using MLEM and with attenuation correction using the MLAA algorithm. Standardised uptake values (SUVs) were calculated for each voxel with the MLAA algorithm, as indicated below:

$$SUV = \frac{decay\ corrected\ activity\ (kBq)/tissue(ml)}{injected\ FDG\ dose\ (kBq)/body\ weight\ (g)}$$

Image interpretation

Two nuclear medicine physicians without knowledge of the clinical, biochemical and radiological findings scored the images.

Bone scan

The dynamic and blood pool phases were scored as normal or abnormal, abnormal being any focal or diffuse uptake around the TKA. On the delayed phase any focal or diffuse tracer uptake was graded using a five-point scale [16]: grade 0 = no uptake to grade 4 = very high uptake, with grade 2 = uptake equal to the ipsilateral distal femoral cortex. SPET was used to locate any focal tracer uptake.

WBC scintigraphy

The 4-h and 24-h WBC images were evaluated for intensity of uptake and the pattern of activity (diffuse versus focal). As for the bone scan, a comparable five-point scale was used (grade 2 = uptake equal to the ipsilateral femoral bone marrow). SPET was used to locate any focal tracer uptake and to correlate this with the bone SPET findings.

FDG-PET scan

Non-attenuation-corrected and attenuation-corrected PET images were evaluated in the same way as the WBC images (intensity of uptake, pattern of uptake and the congruence of focal uptake with bone SPET). A five-point scale was used, and uptake as high as the popliteal artery was scored as grade 2. The maximum SUV per voxel was calculated for each focal or diffuse tracer uptake around the TKA.

Scintigraphic data analysis

Means were compared using the unpaired Student's *t* test; *P* values less than 0.05 were considered significant. Data were expressed as means±SD.

Results

Knee phantom study with FDG-PET

Figure 1 shows some maximum intensity projections from the reconstructed volumes. Figures 1a and 1b show the phantom containing a prosthesis surrounded by uniform activity in water. The transmission image obtained

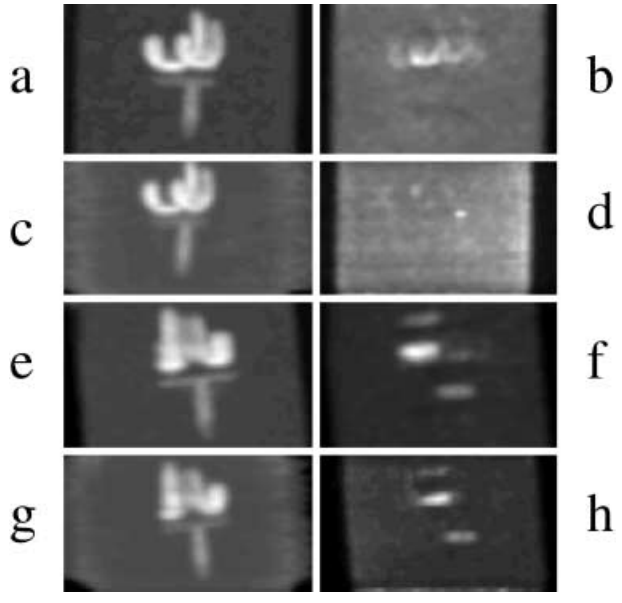


Fig. 1a–h. Maximum intensity projections from the phantom images. **a–d** Homogeneous phantom; **e–h** phantom with three hot tubes. Homogeneous phantom: **a** cold transmission image; **b** corresponding attenuation-corrected MLEM emission image; **c, d** attenuation and activity images by MLAA without transmission scan. Phantom with hot tubes: **e** cold transmission image; **f** corresponding attenuation-corrected MLEM image; **g**, **h** MLAA attenuation and activity images

Table 1. Object to background ratios for the three sources and the two reconstruction algorithms (MLEM with attenuation correction from cold transmission scan, MLAA without transmission scan)

	Source 1	Source 2	Source 3
True contrast	10	5	4
MLEM contrast	7.6	3.6	3.4
MLAA contrast	4.3	3.1	2.6

from the cold transmission scan clearly shows the shape of the prosthesis (Fig. 1a). The corresponding attenuation-corrected MLEM image shows increased tracer uptake near the prosthesis (Fig. 1b). This artefact consists of an 11-ml structure with an object to background ratio higher than 2. MLEM reconstruction without attenuation correction did not show apparent uptake near the prosthesis (image not shown). Figures 1c and 1d show the attenuation map and activity image obtained from the emission scan with MLAA. In the transmission image, the boundary of the cylinder is not well defined, but an excellent reconstruction of the prosthesis is obtained (Fig. 1c). The corresponding emission image did not suffer from the artefact, except for a very small hot spot between the femoral condyles (Fig. 1d). Figures 1e–h compare the images obtained from the phantom after fixation of three hot sources. These sources are clearly visible in the MLEM and MLAA images. Comparison of object to background ratios revealed that the recovery coefficient is lower for the MLAA images (Table 1).

Control group

Bone scan. In the patient group without complaints, focal uptake (always grade 3) was seen in six patients. In all except one this uptake was in a patellar location. The intensity of diffuse bone uptake was grade 2.15±0.73 (all patients).

FDG-PET scan. An example of a normal PET scan is shown in Fig. 2. The effects of the different attenuation correction techniques are indicated. In this patient with normal clinical and bone scan findings, focal FDG uptake was seen in the intercondylar space. This synovial uptake was probably falsely intensified after attenuation correction using the hot transmission scan. Attenuation correction using MLAA, however, showed less intense uptake.

Frequently we found diffuse synovial FDG uptake long after surgery. This physiological diffuse uptake did not correlate with the time interval between surgery and scan.

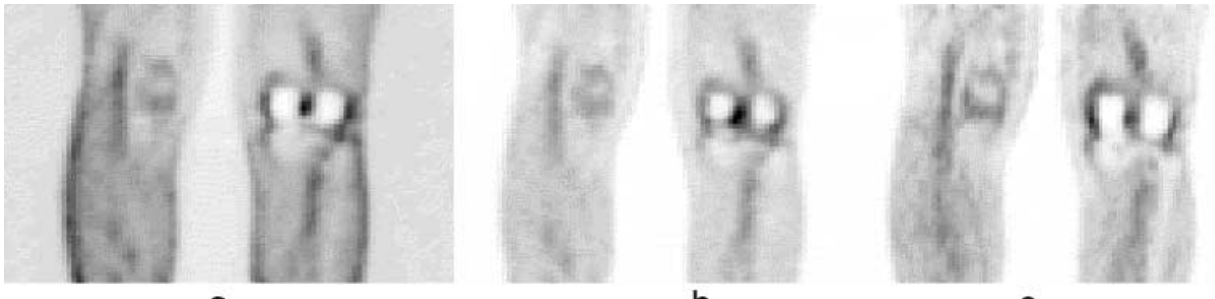
Postsurgical focal FDG uptake in the control group was seen mostly in the patellofemoral region in 9 of 17 patients 12–51 months after surgery. Ten focal lesions were detected in 26 TKAs on non-attenuation-corrected images, of which only four lesions in three patients were not located in the patellofemoral region (none of them had a correlate on bone scan). The highest SUVs of these three patients are presented in Fig. 5. These patients had a TKA implanted 34–36 months before the PET scan. We could not find a relation between the presence or the intensity of such a lesion and the time after surgery. On the attenuation-corrected images (MLAA), five of six patellofemoral lesions were confirmed, and one new (supra)patellar lesion congruent to a bone scan lesion was seen. Only two of the known non-patellar lesions were found clearly, and a new intercondylar lesion in another patient was visualised (normal bone scan findings).

Patient group

Six patients had an infected TKA (all primary implants, only one cementless TKA). The final diagnosis of infection was confirmed by microbiological culture in three (*Streptococcus milleri*, *Staphylococcus aureus* and *Enterococcus*) and by clinical follow-up of at least 6 months in the remaining three. The antibiotic treatment was efficient in five (four systemic and one local treatment), and in one patient the TKA had to be removed.

In six other patients loosening of the TKA was clinically suspected, of whom two required revision surgery. Symptoms in the remaining patients disappeared without operative intervention.

Fig. 2a–c. Patient without complaints in respect of his TKA. **a** Focal intercondylar lesion on emission scan. **b** The lesion is more intense on the attenuation-corrected image using the hot transmission scan. **c** The lesion is less intense on the attenuation-corrected image using only the emission data (MLAA)



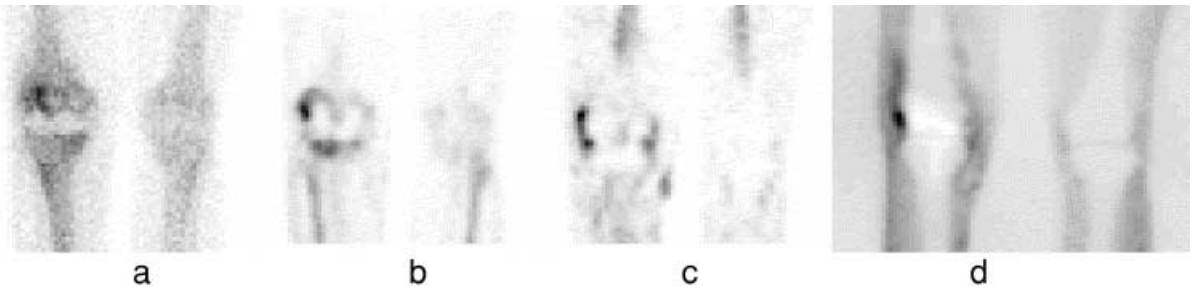


Fig. 3a–d. The infected TKA. **a** Planar bone imaging (focal uptake grade 2); **b** bone SPET; **c** congruent lesion on WBC SPET (grade 4); **d** congruent lesion on FDG-PET (grade 4, SUV 4.4)

Table 2. PPV and specificity for the detection of infected TKAs

Procedure	PPV (%)	Specificity (%)	TP/TN/FP/FN
WBC scan	42	53	5/8/7/0
+ bone scan	83	93	5/14/1/0
PET scan	60	73	6/11/4/0
+ bone scan	67	80	6/12/3/0

PPV, Positive predictive value; TP, True positive; TN, true negative; FP, false positive; FN, false negative

Bone scan. Blood flow was abnormal in 17 patients, showing a focal component in eight and diffuse uptake (mostly horseshoe pattern) in 14. In four studies no abnormal blood flow was found. If a TKA was infected, the blood flow and blood pool phases always showed a horseshoe pattern. On the delayed phase, focal uptake was seen in 17/21 patients. The intensity of uptake was grade 3.2±0.49 for focal lesions (n=27) and grade 2.7±0.70 for diffuse uptake (all patients). Among the six patients with an infected TKA, focal non-patellar tracer uptake of grade 2 was seen in one patient, of grade 3 in two and of grade 4 in two; diffuse uptake (grade 4) was observed in the remaining patient.

WBC scan. At 4 h p.i. focal uptake was seen in 12/20 patients (13 lesions), and in two others femoral bone marrow was clearly visualised. The uptake for focal lesions (all non-patellar) was grade 2.6±0.7, and for diffuse uptake, 1.5±0.8. At 24 h no additional lesions were detected. One patient with an infected TKA did not have a WBC scan for logistic reasons. All scanned infected TKAs showed focal increased uptake (grade 2 in two patients, grade 3 in one and grade 4 in two, cf. Fig. 3). In one patient the uptake increased from grade 2 to grade 3 at 24 h. Selecting focal uptake as the criterion for infection, a specificity of 53% was obtained (PPV 42%, sensitivity 100%).

Comparison between WBC and bone scan. Taking into account only those lesions on WBC scan that were also found on the third phase of the bone scan, the specificity increased to 93% (PPV 83%, sensitivity 100%; Table 2). The only false-positive scan left was probably due to loosening of the prosthesis.

Table 3. Results of WBC or PET scan in combination with bone scan in all patients, including time after surgery

Patient	Time interval (months)	WBC scan + bone scan	PET scan + bone scan
1	27	TN	FP
2	36	TN	TN
3	24[a]	TN	TN
4	7	TP	TP
5	58	TN	TN
6	23	TP	TP
7	12[a]	TN	FP
8	12	TN	TN
9	21	TN	TN
10	108	TN	TN
11	17	TN	TN
12	36[a]	TN	TN
13	60[a]	FP	TN
14	66	TN	TN
15	12[a]	TN	TN
16	16	TP	TP
17	14	TN	TN
18	60	TP	TP
19	84	TN	FP
20	41	TP	TP
21	29	NA	TP

TP, True positive; TN, true negative; FP, false positive; FN, false negative; NA, not available
[a] Revision surgery

FDG-PET scan. Without attenuation correction, focal FDG uptake was seen in 11/21 patients (15 lesions; visual grade 3.71±0.71); in two of these patients this uptake was in the patellofemoral region. The intensity of the diffuse uptake was 2.63±0.60 (all patients). Taking focal FDG uptake at the bone-prosthesis interface as the criterion for infection, a specificity of 73% was reached (PPV 60%, sensitivity 100%).

Comparison between FDG-PET and bone scan. When a PET lesion of grade 3 with no correlate on the third phase of the bone scan was classified as true negative, a specificity of 80% was obtained (PPV 67%, cf. Fig. 3 and Table 2). In Table 3 the results in all patients of

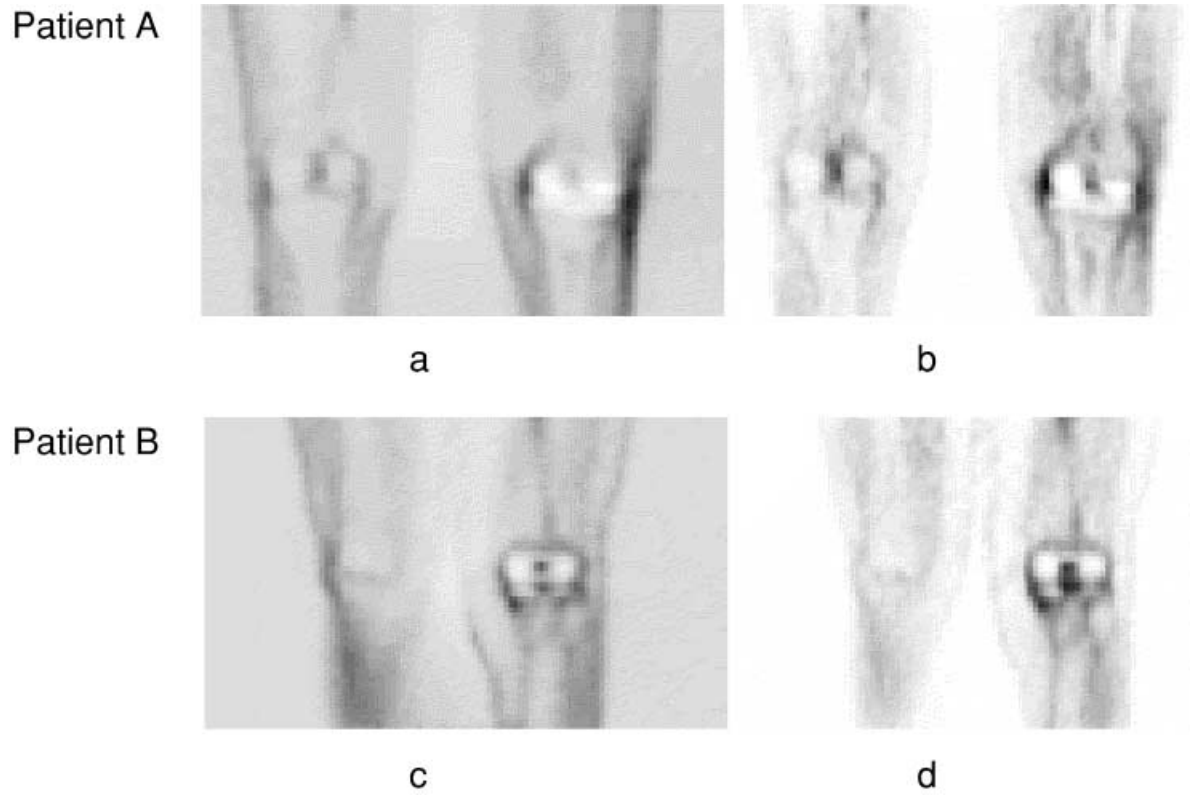


Fig. 4. Non-attenuation-corrected (**a, c**) versus attenuation-corrected PET images (**b, d**) in two patients. In patient A a focal lesion at the medial femoral condyle in an infected TKA was missed on attenuation-corrected images owing to synovial uptake. In patient B a focal lesion at the medial side of the tibial plateau was only seen clearly on attenuation-corrected images, creating a false-positive result

WBC and PET scan in combination with the bone scan are summarised, including the time after surgery. Two of the three remaining false-positive PET studies were performed 1 and 5 years after revision surgery in patients suspected to have a loosened TKA. The third false-positive lesion was found 7 years after placement of a primary implant. Neither clinical nor biochemical evaluations up to 1 year after the PET scan revealed the true nature of this lesion.

Attenuation-corrected FDG-PET. Attenuation-corrected images (MLAA) showed 18 focal lesions in 11/21 patients, although in one infected TKA no focal uptake was observed owing to intensified adjacent synovial uptake (patient A in Fig. 4). Four additional lesions at the bone-prosthesis interface were seen in three patients as compared to the non-attenuation-corrected images (cf. patient B in Fig. 4). Not one of these lesions had a congruent lesion on the bone scan. In comparison to non-attenuation-corrected images, the intensity of the FDG uptake scored visually was significantly lower for focal lesions (grade 2.75±0.45; P=0.0009), but comparable for diffuse uptake (grade 2.62±0.51; P=0.47). The mean SUV for

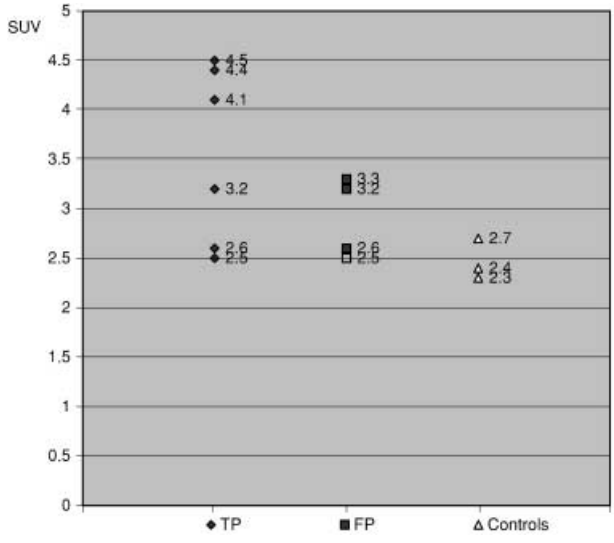


Fig. 5. Semi-quantitative analysis (SUV value) of non-patellar focal FDG uptake in TKAs (symptomatic patients and controls). One false-positive lesion could be classified as true negative after correlation with the bone scan findings (SUV 2.5, represented by a *hollow cube*). Focal FDG uptake in asymptomatic patients (*Controls*) never had a correlate on bone scan. *TP*, True positive; *FP*, false positive

focal lesions seen on non-attenuation-corrected FDG images (n=17) was 3.72±1.22, and for non-patellar focal lesions (n=13), 3.29±0.79. Figure 5 divides non-patellar focal lesions into true-positive and false-positive lesions for infection. In one true-positive case only the highest SUV of two lesions is depicted. One false-positive lesion

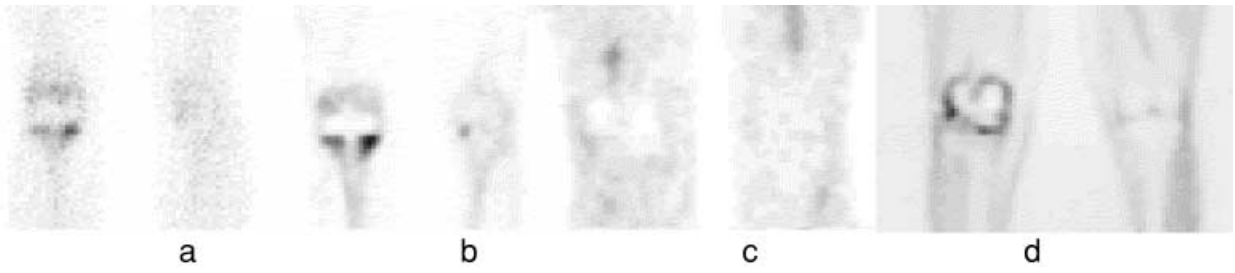


Fig. 6a–d. Loosening of a TKA. **a** Focal MDP uptake of grade 4 around the tibial neck of the prosthesis; **b** congruent focal lesion on MDP SPET; **c** no focal uptake on WBC SPET; **d** false-positive congruent lesion on PET (grade 4, SUV 3.2)

could be classified as true negative after correlation with the bone scan findings (SUV 2.5, represented by a hollow cube in Fig. 5). Two false-positive studies due to loosening of a revised TKA had SUVs of 3.2 and 3.3. The third false-positive lesion in the primary implant had an SUV of 2.6.

Loosening of a TKA

Bone scan. Among those patients in whom TKA loosening was suspected clinically, bone scan revealed focal uptake of grade 3 in three and of grade 4 in three. In four of these six patients, focal uptake at the tibial tip and/or neck of the prosthesis was seen (Fig. 6).

WBC scan. Suspected loosening of the knee prosthesis presented with focal uptake in four patients (grade 2 in two and grade 3 in two) and with diffuse uptake in two patients (grade 1 or 2). Only one lesion also showed increased focal uptake on bone scan.

FDG-PET scan. Among those patients in whom loosening was suspected, FDG-PET scan showed diffuse uptake of grade 3 in four patients, and focal uptake of grade 3 or 4 in the other two (Fig. 6). These two patients had congruent lesions on bone scan.

Discussion

Knee phantom study

The artefacts observed in the phantom experiment were probably due to mismatches between the transmission and emission scans. Two types of mismatch can occur: mismatch in resolution and mismatch in position. Because of the different geometrical situation, the resolution of a transmission scan is never identical to that of the emission scan. Normally, this resolution mismatch has no dramatic effects. However, near the edge of a material with a very high attenuation coefficient, any blurring leads to severe overcorrection in the low-attenuation medium and undercorrection in the high-attenuation material. In the evaluation of TKAs, the undercorrection is not a problem because there is no activity in the prosthesis. In contrast, overcorrecting can be problematic, since it generates an apparent increase in tracer uptake near the prosthesis, which is exactly the signal we are looking for. Similar and probably far more severe artefacts occur in the case of patient motion between the emission and transmission scans. Even with post-injection transmission scanning, patient motion cannot be excluded. The MLAA algorithm derives the attenuation coefficients directly from the attenuated emission scan, ensuring a perfect match between attenuation coefficients and activity and elimination of the artefact. MLAA produced a virtually exact reconstruction of the prosthesis.

The phantom experiment indicated that MLAA-reconstructed images are sufficiently sensitive (the small hot source with a lesion to background ratio of 4 was clearly visible) and more specific than the MLEM images (there were almost no hot artefacts).

Clinical study

Accurate diagnosis is essential for the effective management of suspected infection of a TKA. Labelled leucocyte scintigraphy is the preferred imaging technique for the evaluation of orthopaedic infections [17]. In the search for a more convenient and faster imaging tool we evaluated the usefulness of FDG-PET in detecting infected TKAs.

Bone scan. In the infected TKAs, the dynamic and blood pool phases always showed diffuse uptake (horseshoe pattern), masking focal uptake. Delayed bone imaging in patients with infected TKAs revealed focal uptake in all but one. It should be noted that SPET allowed clearer visualisation of lesions (cf. Fig. 3). Based on a visual scoring system we found a low specificity (33%) of the delayed phase for infected TKAs, as has been reported in the literature (25%) [7]. In patients without complaints, however, we found only one case of focal non-patellar uptake in 26 TKAs.

HMPAO WBC scan. Using focal uptake as a criterion for infection, a specificity of 53% was obtained (sensitivity 100%). When only lesions also seen on bone scan were taken into account, the specificity increased to 93%

without any loss in sensitivity. Loosening also presented with focal uptake in four out of six patients, but only one had a congruent lesion on the bone scan. Around a loosened TKA, focal inflammation can be seen without involvement of the bone itself. This emphasises the need to correlate WBC scan findings with bone scan abnormalities. Visual grading and 24-h imaging did not allow further differentiation. Femoral bone marrow did not interfere because of the anatomical distance from the bone-prosthesis interface.

FDG-PET scan. Focal uptake at the bone-prosthesis interface on non-attenuation-corrected images gave a sensitivity of 100% and a specificity of 73% (PPV 60%). Focal non-patellar FDG uptake of grade 3 was seen in asymptotic TKAs until 36 months after surgery, also suggesting a lack of specificity of FDG for infection. In this group no time-dependent typical FDG uptake was seen. In the patient group, correlation with the third phase of a bone scan increased the specificity of FDG-PET to 80% (PPV 67%). Two out of three false-positive results left were due to loosening of the TKA. Comparison of PET images with the bone scan findings also facilitated the detection of focal FDG uptake at the bone-prosthesis interface, which is easily overlooked owing to intensified adjacent synovial uptake. Attenuation correction (MLAA) showed comparable diffuse uptake but significantly less intense focal uptake (visual grade 2.75±0.45 vs 3.71±0.71; P=0.0009). One lesion in an infected TKA was not identified on attenuation-corrected images, probably due to intensified adjacent synovial uptake (cf. patient A in Fig. 4), and in another patient a lesion was seen more clearly, creating one false-positive result (cf. patient B in Fig. 4). No other lesions at the bone-prosthesis interface only seen on attenuation-corrected images had a correlate on bone scanning. Therefore, attenuation correction does not seem to be required for the detection of infected TKAs.

These findings confirm the high sensitivity of FDG-PET reported by others [18]. Increased uptake at the bone-prosthesis interface was observed in all six infected hip arthroplasties and in five of six infected knee arthroplasties.

The same authors also mentioned a high rate of false-positive focal FDG uptake, especially in TKAs (3/9, specificity 67% compared with 88% for hip arthroplasties). In our study, false-positive focal FDG uptake was seen in three patients with aseptic loosening and in another patient probably due to focal synovitis near the bone-prosthesis interface. Focal FDG uptake was also seen in asymptomatic prostheses, although a correlate on the bone scan was never found. Manthey et al. [19] studied 24 patients in a comparable clinical setting to ours (15 hip and 14 knee prostheses). High glucose uptake at the bone-prosthesis interface was considered indicative of infection, and intermediate uptake as suspect for loosening. All five infected arthroplasties were correctly identified, as were four out of six loosened arthroplasties. Manthey et al. also noted that synovitis (FDG uptake in the synovia only) was frequently found in TKAs (eight TKAs versus four hip prostheses).

Loosening of a TKA. In four out of six patients with clinically suspected TKA loosening, we found the same pattern of uptake on the third phase of the bone scan as is depicted in Fig. 6. Only two patients showed a congruent lesion on PET scan. Semiquantitative analysis using SUVs did not allow differentiation between infected and loosened arthroplasties. In hip prostheses a comparable pattern (increased uptake adjacent to the femoral neck of the prosthesis) has been described as suggestive for loosening [20].

In WBC scintigraphy, leucocyte migration is visualised, resulting in a high specificity for infected TKAs. Using FDG as a marker of glucose metabolism, a totally different and probably less specific mechanism involved in inflammation is depicted.

In conclusion, WBC scan in combination with bone scan revealed a high specificity for the detection of infected TKAs. FDG-PET offers no added value. Especially loosened TKAs also show focal FDG uptake, probably due to sterile inflammation. Attenuation-corrected PET images and SUV analysis did not improve the results.

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