Eur J Nucl Med Mol Imaging (2007) 34:704–714
DOI 10.1007/s00259-006-0290-4

ORIGINAL ARTICLE

Diagnostic value of ^{18}F-FDG PET/CT in trauma patients with suspected chronic osteomyelitis

Anna Hartmann · Karim Eid · Claudio Dora · Otmar Trentz · Gustav K. von Schulthess · Katrin D. M. Stumpe

Received: 10 July 2006 / Accepted: 8 September 2006 / Published online: 29 November 2006

Abstract
Purpose To retrospectively evaluate the diagnostic value of ^{18}F-FDG PET/CT in trauma patients with suspected chronic osteomyelitis.
Methods Thirty-three partial body ^{18}F-FDG PET/CT scans were performed in 33 patients with trauma suspected of having chronic osteomyelitis. In 10 and 23 patients, infection was suspected in the axial and appendicular skeleton, respectively. In 18 patients, PET/CT was performed in the presence of metallic implants. Histopathology or bacteriological culture was used as the standard of reference. For statistical analysis, sensitivity, specificity and accuracy were calculated in relation to findings of the reference standard.
Results Of 33 PET/CT scans, 17 were true positive, 13 true negative, two false positive and one false negative. Eighteen patients had chronic osteomyelitis and 15 had no osseous infection according to the reference standard. Sensitivity, specificity and accuracy for ^{18}F-FDG PET/CT was 94%, 87% and 91% for the whole group, 88%, 100% and 90% for the axial skeleton and 100%, 85% and 91% for the appendicular skeleton, respectively.
Conclusion ^{18}F-FDG PET/CT is a highly sensitive and specific method for the evaluation of chronic infection in the axial and appendicular skeleton in patients with trauma. PET/CT allows precise anatomical localisation and characterisation of the infectious focus and demonstrates the extent of chronic osteomyelitis with a high degree of accuracy.

Keywords ^{18}F-FDG · PET/CT · Chronic osteomyelitis · Axial skeleton · Appendicular skeleton

A. Hartmann · G. K. von Schulthess · K. D. M. Stumpe (✉)
Department of Medical Radiology, Division of Nuclear Medicine,
University Hospital,
8091 Zurich, Switzerland
e-mail: katrin.stumpe@usz.ch

K. Eid · O. Trentz
Department of Surgery, Division of Trauma Surgery,
University Hospital,
Zurich, Switzerland

C. Dora
Department of Orthopedic Surgery,
Orthopedic University Hospital Balgrist,
Zurich, Switzerland

Introduction

In traumatology, establishing the diagnosis of chronic osteomyelitis and differentiating soft tissue infection, bone infection and fracture non-union is often difficult with the current imaging techniques, especially if normal bone anatomy has been altered by previous infections or bone regeneration. White blood cell count, C-reactive protein and erythrocyte sedimentation rate lack sensitivity, particularly in low-grade infection. Thus more reliable investigations are needed for precise diagnosis and to assist in decision making about further therapy [1, 2]. The treatment of chronic osteomyelitis is primarily surgical because the complete debridement of all devitalised bone and soft tissue is essential for cure [3].

The diagnosis of musculoskeletal infections entails a variety of imaging methods. Magnetic resonance imaging (MRI) is currently the most widely used imaging method and it provides anatomical details as well as visualising abnormalities of bone marrow, joints and surrounding soft tissues with high sensitivity [4]. Computed tomography (CT) has proven to be a useful adjunct to MRI. However, MRI and CT are of limited value in the presence of metallic implants owing to susceptibility and beam-hardening arte-

facts [5, 6]. Three-phase bone scan has been the accepted examination for the initial evaluation for osteomyelitis, but its findings can be complicated by previous surgery and trauma. Combined ^{111}In-labelled leucocyte scintigraphy and complementary ^{99m}Tc-sulphur colloid marrow scintigraphy is the method of choice for post-traumatic infection imaging. Sensitivities of 100% and specificities ranging from 91% to 94% have been described [7, 8].

^{18}F-fluorodeoxyglucose positron emission tomography (FDG PET) imaging has been reported to be highly sensitive and specific in the diagnosis and exclusion of chronic osteomyelitis [9–13]. Unlike MRI and CT, FDG PET images do not show substantial implant-associated artefacts or tissue oedema, which can interfere with image interpretation in trauma patients with osteosynthetic metallic implants [12]. FDG PET has shown excellent results in imaging the axial skeleton as physiological uptake of FDG in bone and bone marrow is relatively low and FDG is only taken up into activated white blood cells.

In comparison with PET imaging alone, combined PET/CT imaging is supposed to have further advantages in providing additional anatomical information and characterisation of the infectious lesion, which is important for surgical planning. However, data are still missing.

Therefore the purpose of this study was to evaluate the diagnostic value of ^{18}F-FDG PET/CT in patients with trauma and suspected chronic osteomyelitis in the axial and appendicular skeleton.

Materials and methods

Patients

Between March 2003 and March 2005, 38 partial body ^{18}F-FDG PET/CT scans were obtained in 37 patients with trauma who were suspected of having chronic osteomyelitis. Of the 37 eligible patients, four were excluded owing to missing histopathological findings and/or microbiological evaluation of the suspected area of infection. In the remaining 33 patients (33 PET/CT scans), the site of infection was located in 10 and 23 patients in the axial and appendicular skeleton, respectively. Nineteen patients were referred to PET/CT by the Department of Surgery, Division of Trauma Surgery, University Hospital Zurich, nine patients by the Department of Orthopaedic Surgery, Orthopaedic University Hospital Balgrist, Zurich, and five by smaller peripheral hospitals. Seven women and 26 men were included in the study (age range 17–80 years, mean age 50). Eighteen of the patients had metallic implants close to the suspected infectious focus when PET/CT was performed. Three of them had prosthetic devices. On the basis of PET findings reported in the literature [14, 15], any patients who had experienced trauma or had undergone a surgical intervention on affected bone during the 6 months prior to the PET/CT examination were to be excluded; however, this applied to none of the 33 patients. None of the examined patients was receiving antibiotic treatment at the time of PET/CT scanning. None of the examined patients were immunocompromised.

The indication for the PET/CT investigation was based on clinical signs and laboratory findings. Inclusion criteria were: suspected chronic osteomyelitis with symptoms of infection lasting more than 6 weeks or presence of recurrent osteomyelitis [9, 10]. All of the 33 included patients had presented with pain at motion or rest for more than 6 weeks. Seven of the 33 patients were suspected to have a relapse of a previously treated osteomyelitis. Four patients presented with a fistula and one with a soft tissue ulcer.

The records of all patients were reviewed (A.H., K.E., C. D.) in accordance with the ethical guidelines of the hospital institutional review board. The clinical influence on management of FDG PET/CT was assessed retrospectively by two orthopaedic staff surgeons (K.E., C.D.).

PET/CT imaging protocol

Imaging was performed using an integrated PET/CT in-line system (Discovery LS, GE Medical Systems, Waukesha, WI, USA). A GE Advance NXi PET scanner and a multislice helical CT (LightSpeed plus scanner) were integrated in this dedicated system. The axes of both systems were mechanically aligned to coincide perfectly. The offset between the CT and PET scanner sensitive fields of view along the table axis was 60 cm. The same table was used to acquire PET and CT images. The table excursion permitted scanning of six contiguous PET sections covering 867 mm. In all examined patients at least four contiguous PET sections were acquired to image the involved bone. The PET and CT data sets were acquired on two independent computer consoles, which were connected by an interface to transfer CT data to the PET scanner.

The patients were asked to fast for at least 4 h prior to the study and compliance was controlled by a blood glucose test value lower than 7 mmol/l. No patient had a history of diabetes. Fifty to 60 min prior to scanning, the patients received an intravenous injection of 300–400 MBq of FDG, which was produced in-house using a 17.8-MeV Cyclotron (PET Trace 2000; GE Medical Systems, Uppsala, Sweden) and automated FDG synthesis modules (PET Tracer Synthesizer; GE Nuclear Interface, Münster, Germany). Attenuation correction was performed using the built-in rotating ^{68}Ge sources. A multiplicative iterative reconstruction algorithm for improvement of image quality and reduction of computation time was employed [16].

For viewing the images, the PET and CT data sets were transferred to an independent, PC-based computer workstation by DICOM transfer. All viewing of co-registered images were performed with dedicated software (X-Xeleris workstation; GE Medical Healthcare, Waukesha, WI, USA).

Evaluation of PET/CT images

Two board-certified nuclear medicine physicians with extended CT experience (at least 6 years) evaluated the selected cases in consensus to ascertain the localisation and the degree of FDG uptake. They were blinded to the results of other imaging studies and the final diagnosis. Images were analysed as follows. First, physiological FDG uptake such as that in muscles was identified and excluded from further analysis. The intensity of FDG uptake was graded on a five-point scale as follows: a score of 0 indicated that FDG uptake was comparable to the background, of 1 that FDG uptake was low and comparable to uptake in inactive muscles and fat, of 2 that FDG uptake was moderate, clearly noticeable and distinctly higher than uptake into inactive muscles and fat, of 3 that FDG uptake was strong, but distinctly below FDG uptake noted in normal cerebral cortex or urinary bladder, and of 4 that FDG uptake was very strong and comparable to that in normal cerebral cortex or urinary bladder. This grading scale was adapted from Stumpe et al. [17, 18]. However, in contrast to the definition given there, we sometimes used the cerebral cortex and sometimes the bladder as an FDG uptake reference point, depending on the location of the affected bone. No patient had a history of renal failure. A receiver operating curve analysis using the above grading scale had shown that classifying grade 3 and 4 lesions as infectious foci yields the best discrimination between infected and non-infected lesions [12]. Therefore, we used increased FDG uptake of grade 3 and 4 as the criterion for infection in our study.

Attenuation-corrected images and non-attenuation-corrected images were used for image interpretation in order to avoid false positive findings due to metallic artefacts. The diagnosis of an artefact was made if increased FDG uptake was shown on the attenuation-corrected images without any uptake on the non-attenuation-corrected images. The diagnosis of infection was only made if grade 3 and 4 uptake was clearly visible on the attenuation-corrected and non-attenuation-corrected images.

From these data, sensitivities, specificities and accuracies were calculated for all data and for the axial and appendicular skeleton, respectively.

Standard of reference

The final diagnosis was made on the basis of the histopathological findings and microbiological evaluation of the surgical specimens. Histopathological features indicating chronic osteomyelitis included necrotic bone, new bone formation, leucocyte exudation joined by lymphocytes, histiocytes and occasional plasma cells.

Results

Of the 33 included patients with trauma and clinical suspicion of chronic osteomyelitis, 18 had osteomyelitis according to the reference standard. The 15 patients without a diagnosis of osteomyelitis presented with soft tissue infection (n=7), fracture non-union (n=3), a foreign body reaction against the metallic device (n=1) or without infection (n=4) (Table 1).

In 11 of the 18 patients with chronic osteomyelitis, microorganisms could be detected in culture and the diagnosis of infection was made. *Staphylococcus aureus* was identified in six patients, including two with multi-resistant *Staphylococcus aureus*, *Propionibacterium acnes* in four patients and *Bacillus subtilis* in one patient. In seven of the 18 patients with osteomyelitis, no microorganisms were found, and the diagnosis of infection was based on the presence of local abscess formation, neutrophilic granulocytes, an elevated CRP and clinical follow-up for at least 6 months. Three patients with an osteomyelitis presented with the additional diagnosis of a fracture non-union.

The overall sensitivity, specificity and accuracy were 94%, 87% and 91% (n=33). The sensitivity, specificity and accuracy for evaluation of the axial skeleton (n=10) were 88%, 100% and 90%, respectively. The corresponding values for the subgroup of 23 patients with suspected osteomyelitis in the appendicular skeleton were 100%, 85% and 91%, respectively.

All osseus infections except one were correctly identified as osteomyelitis at FDG PET/CT (Figs. 1, 2 and 3). There was one false negative result in the axial skeleton in a patient with osseous infection of the mandible showing osseous necrosis intraoperatively.

Thirteen of the 15 patients who had no osseous infection were classified as true negative at FDG PET/CT (Fig. 4). There were two false positive findings in the appendicular skeleton in the study. One false positive result was found in a patient with a foreign body reaction to the prosthetic device. The patient presented with a hemiarthroplasty of the hip. Polyethylene particles and metal wear particles were detected at the time of surgery.

The second false positive result was found in a patient with the diagnosis of a fracture non-union of the left distal femur and grade 3 FDG uptake on PET (Fig. 5). Although the CT part showed a fracture non-union, the latter case was classified as positive owing to strong FDG avidity within the area of the fracture in PET.

Table 1 Data of patients with suspected chronic osteomyelitis in the axial and peripheral skeleton

Patient no./ sex/age (yr)	Site of suspected infection	FDG grade[a]	Metallic implant	Final diagnosis	Type of diagnosis	FDG-PET/ CT result	Clinical findings
1/M/17	Lumbar spine	3	Yes	Osteomyelitis	Microbiological	TP	Pain, increasing infection parameters
2/M/80	Lumbar spine	0	Yes	No infection	Microbiological	TN	Pain, increased CRP
3/F/50	Mandible	1	Yes	Osteomyelitis with necrosis	Microbiological	FN	Pain, relapse
4/F/75	Lumbar spine	4	Yes	Osteomyelitis	Microbiological	TP	Pain
5/M/65	Tibia	4	Yes	Osteomyelitis	Microbiological	TP	Pain, relapse
6/M/49	Foot	1	No	Soft tissue infection	Microbiological	TN	Pain
7/M/38	Tibia	4	Yes	Osteomyelitis, fracture non- union	Microbiological	TP	Pain
8/M/31	Lower leg	2	No	Soft tissue infection	Microbiological	TN	Pain, secretion and fistula
9/M/41	Femur	4	No	Osteomyelitis	Microbiological	TP	Pain, fistula
10/F/26	Lower leg	1	No	Soft tissue infection	Microbiological	TN	Pain, fistula
11/M/48	Lower leg	4	No	Osteomyelitis	Microbiological	TP	Relapse, pain, tenderness
12/M/64	Lower leg	4	No	Osteomyelitis	Microbiological	TP	Pain, fistula, relapse
13/M/54	Femur	0	No	Soft tissue infection	Microbiological	TN	Pain
14/M/78	Lower leg	0	No	Soft tissue infection	Microbiological	TN	Pain, secretion from stump
15/M/48	Tibia	3	Yes	Osteomyelitis, fracture non- union	Microbiological	TP	Pain, improper healing
16/M/55	Femur	4	Yes	Foreign body granuloma	Microbiological	FP	Pain, increasing infection parameters
17/M/56	Lumbar spine	4	No	Osteomyelitis	Microbiological	TP	Pain
18/F/80	Lumbar spine	4	Yes	Osteomyelitis	Microbiological	TP	Pain, fever, sepsis, increasing infection parameters
19/M/72	Lumbar spine	4	Yes	Osteomyelitis	Microbiological	TP	Pain
20/M/72	Lumbar spine	3	No	Osteomyelitis	Microbiological	TP	Pain, relapse
21/M/32	Femur	3	Yes	Fracture non- union	Microbiological	FP	Pain
22/M/18	Lower leg	4	Yes	Osteomyelitis, fracture non- union	Microbiological	TP	Pain, fever, increasing infection parameters, relapse
23/F/67	Knee	4	Yes	Osteomyelitis	Microbiological	TP	Pain, increased infection parameters
24/F/45	Femur	0	Yes	No infection	Microbiological	TN	Pain
25/F/47	Foot	0	No	No infection	Microbiological	TN	Pain, recurrent erysipelas
26/M/60	Lower leg	0	Yes	Fracture non-union	Microbiological	TN	Pain
27/M/34	Lumbar spine	1	Yes	Soft tissue infection	Microbiological	TN	Pain
28/M/68	Humerus	0	Yes	Soft tissue infection	Microbiological	TN	Pain, fistula
29/M/41	Humerus	0	No	Fracture non-union	Microbiological	TN	Pain
30/M/37	Femur	4	No	Osteomyelitis	Microbiological	TP	Pain, relapse
31/M/55	Foot	4	No	Osteomyelitis	Microbiological	TP	Pain, soft tissue ulcer
32/M/62	Lumbar spine	4	Yes	Osteomyelitis	Microbiological	TP	Pain
33/M/58	Radius	1	No	No infection	Microbiological	TN	Pain

[a] Data are the grade assigned by both readers of the bone only

M male, *F* female, *TP* true positive, *FP* false positive, *TN* true negative, *FN* false negative, *CRP* C-reactive protein

PET results were not affected by attenuation correction artefacts due to the metallic implants (n=15) used in trauma surgery. In patients with prosthetic devices (n=3), the non-attenuation-corrected scans showed no FDG uptake at sites where the attenuation-corrected images were FDG positive. This can be explained by the lower photon absorption of the slender metallic instrumentation used in trauma surgery, in contrast to the joint arthroplasties with a high photon absorption used in orthopaedic surgery [12, 18, 19].

The surgeons analysed the clinical influence of FDG PET/CT retrospectively. In ten of the patients with the correct diagnosis of osteomyelitis on FDG PET/CT, the surgeons decided on a surgical intervention with removal or stabilisation of the osteosynthetic material, partial bone resection or

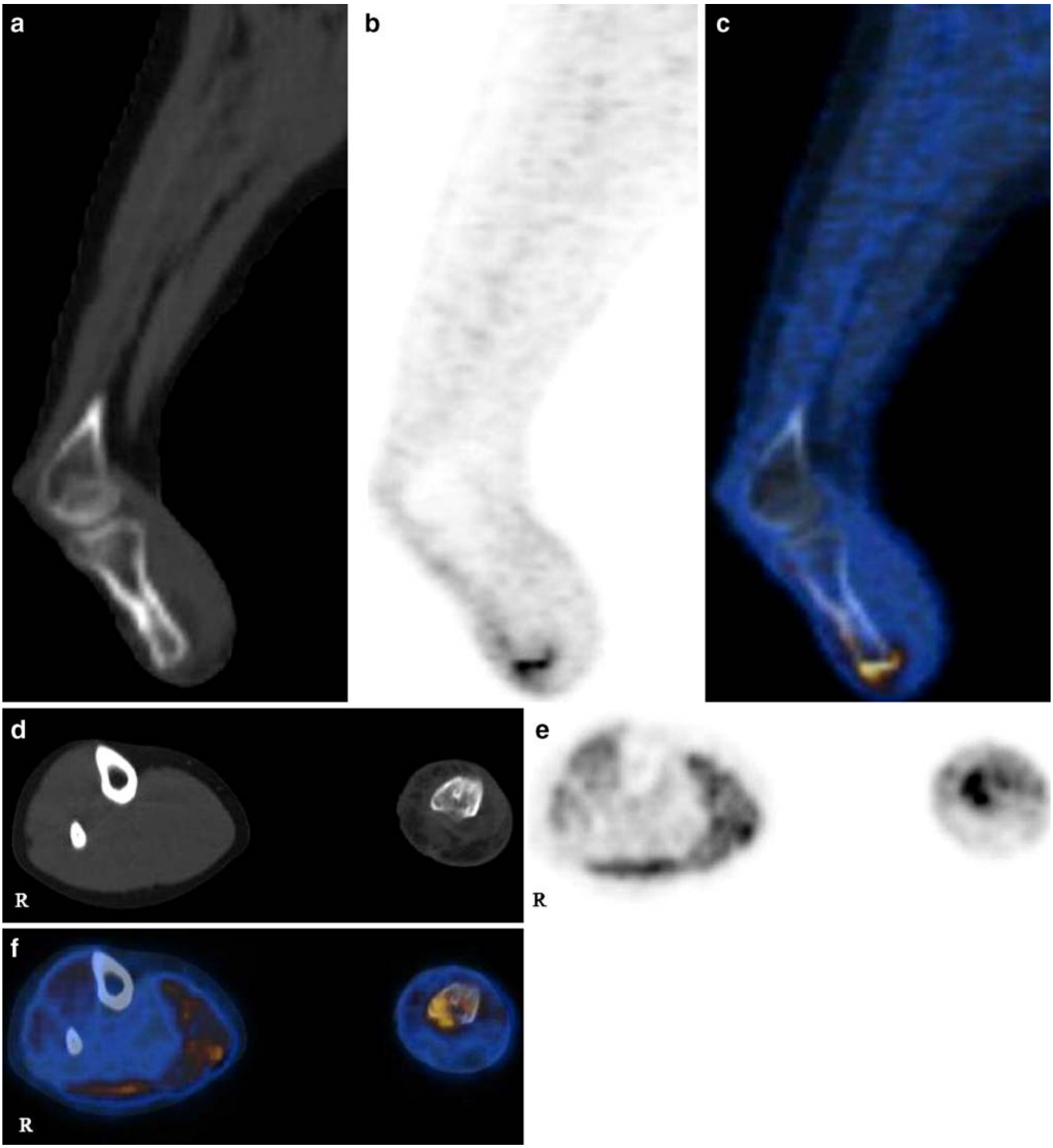

Fig. 1 A 48-year-old man with pain and tenderness of the left lower limb stump. Sagittal CT scan shows irregular cortical contours of the distal left tibial stump (**a**). Sagittal PET (**b**) and co-registered PET/CT (**c**) show increased osseous FDG uptake in the distal left tibial stump. On the axial CT image, compact bone is absent in the posterior parts of the distal tibial (**d**). Axial PET (**e**) and co-registered PET/CT (**f**) demonstrate increased osseous FDG uptake in the posteromedial parts of the distal stump, representing osteomyelitis. Compared with the contralateral side, muscle atrophy of the left lower extremity is seen. In contrast to PET imaging alone, co-registered PET/CT helps to confirm that FDG uptake involves the bone

osseous insertion of antibiotics. The precise anatomical localisation provided by, and the extent of increased FDG uptake detected on, combined PET/CT was especially useful for planning of surgery in the latter group of patients.

In five of seven patients with the diagnosis of a soft tissue infection but exclusion of osseous infection by FDG PET/CT, antibiotic treatment was started. In the last-mentioned group of patients, PET/CT improved the

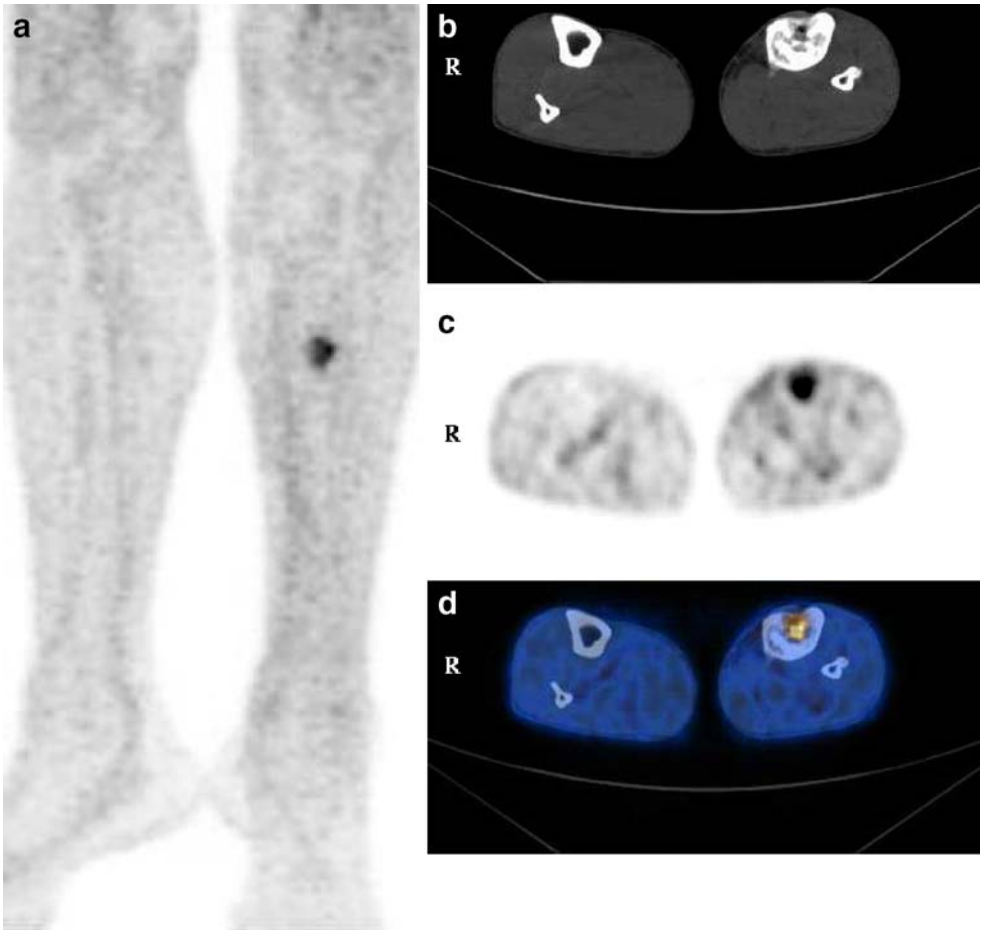

Fig. 2 A 64-year-old man with superficial fistulation and suspected periostitis in the left lower limb. Maximum intensity projection (MIP) PET scan (**a**) shows focally increased FDG uptake in the left lower leg. Axial CT image (**b**) demonstrates osteosclerotic changes of the left tibia with a bony defect anteriorly. Axial PET (**c**) and co-registered PET/CT (**d**) show increased osseous FDG uptake in the left tibia. PET/CT demonstrates the extent of the infection, showing osteomyelitis in the left tibia, where the anatomical information available on PET or CT images alone would not be sufficiently precise in localising the lesion

performance of FDG PET alone in discriminating or excluding osseous from soft tissue infection.

In three patients without osseous infection on PET/CT, the surgeons decided to remove the osteosynthetic material as PET/CT helped to exclude osteomyelitis.

Finally, in 18 patients the surgeons judged that relevant information was obtained with FDG PET/CT, while in 15 patients, they felt that no relevant information was provided by PET/CT.

Discussion

Although many techniques have been proposed for the non-invasive evaluation of chronic osteomyelitis, clinicians are still confronted with an indeterminate diagnosis in many patients, especially in cases of early infections. As preoperative planning in patients with suspected chronic osteomyelitis is difficult, the definitive surgical procedure required can often only be identified on the basis of intraoperative findings.

MRI is very sensitive for the detection of chronic osteomyelitis and can show sites with tissue oedema and increased regional perfusion. However, these changes can last for a long time after surgery and distinction between fibrovascular scarring and reactive infection is often difficult [20–22]. Delineation of the extent of the infectious lesion is important for the surgical procedure. MRI lacks specificity; thus Kaim et al. reported a sensitivity of 100%, a specificity of 60% and an accuracy of 79% for MRI in patients with chronic post-traumatic osteomyelitis of the lower extremities [22]. False positive MRI results occurred because of postoperative scarring and oedema in bone defects and soft tissues. In these situations, additional CT is required [23]. CT plays an important role in the evaluation of chronic osteomyelitis, demonstrating suspected fistula, bony fragments, mineralisation and extension of disease. However, CT quality is also degraded in the presence of metallic implants.

Three-phase bone scintigraphy combined with labelled leucocytes is used in the evaluation of chronic post-traumatic osteomyelitis [24–28]. Kaim et al. [22] examined combined bone scintigraphy and ^{99m}Tc-labelled antigranulocyte antibody scintigraphy in post-traumatic osteomyelitis of the lower extremities and found a sensitivity of 77%, a specificity of 50% and an accuracy of 61%. However, sensitivity is low in low-grade chronic infections and in the axial skeleton owing to physiological uptake in normal

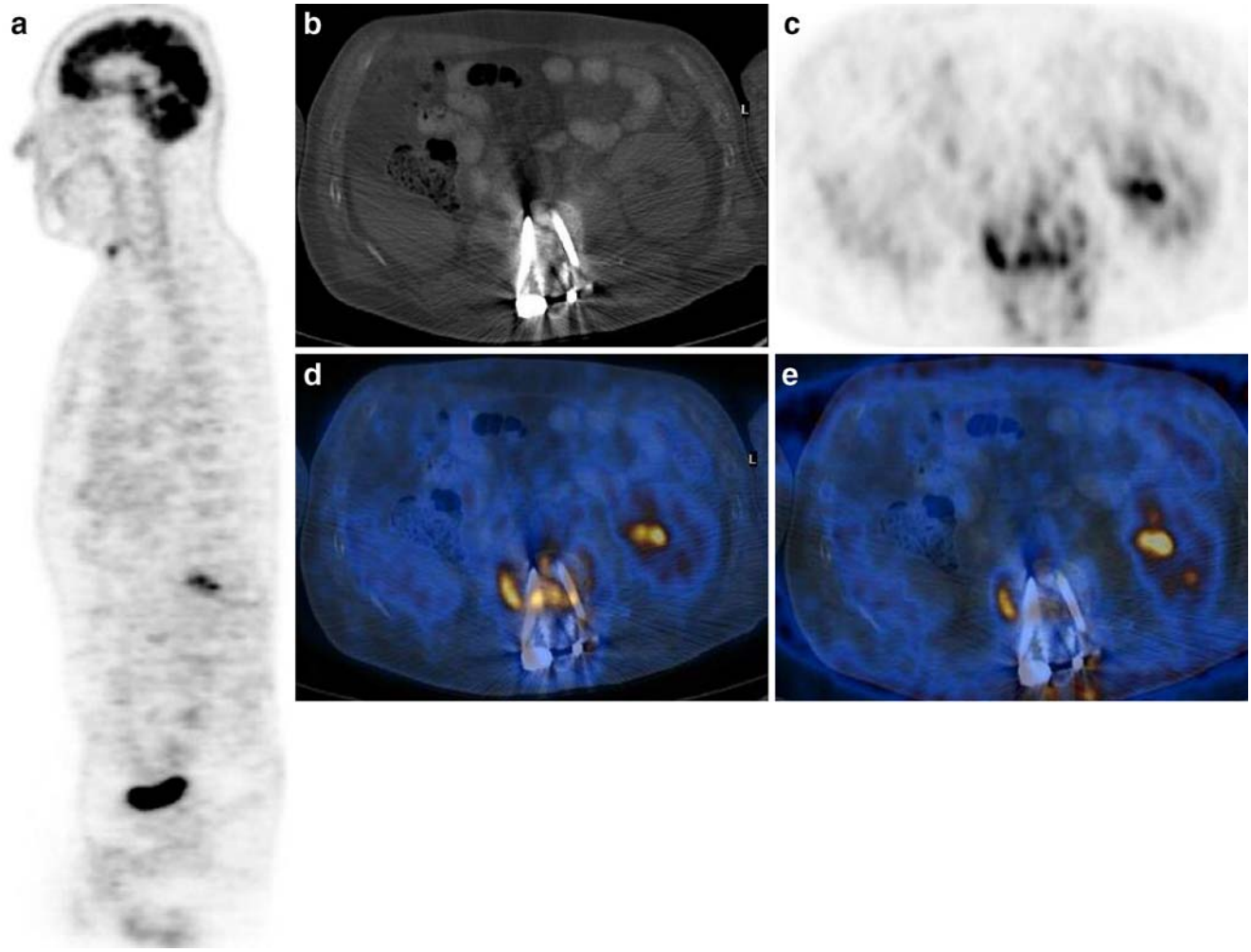

Fig. 3 A 62-year-old male with back pain after insertion of spinal hardware for an unstable fracture of L2. Sagittal PET scan (**a**) showing linear increased FDG uptake in the upper lumbar spine. On the axial CT image (**b**), artefacts are seen in the region of the spinal hardware. Axial PET (**c**) and axial attenuation-corrected co-registered PET/CT (**d**) show highly increased FDG uptake in the vertebral body (L2) and in the area of the pedicle screws. On the corresponding axial non-attenuation-corrected PET/CT scan (**e**), FDG uptake was confirmed and artefacts due to the pedicle screws could be excluded. On PET/CT, additional increased FDG accumulation in the adjacent soft tissues on the right side is seen. Diagnosis of osteomyelitis and infectious involvement of the adjacent soft tissues in association with spinal hardware was not possible with PET or CT alone

haematopoietic bone marrow, and specificity is low after trauma and surgery owing to the presence of ectopic haematopoietic bone marrow.

In the past decade, combined ^{111} In-labelled leucocyte and ^{99m} Tc bone marrow scintigraphy has been shown to be highly accurate for the diagnosis of various musculoskeletal infections after trauma or surgery in the presence of ectopic haematopoietic bone marrow [7, 8].

FDG PET has been reported to be an excellent tool in suspected implant-associated infections after trauma surgery and in musculoskeletal infections without prior surgery [11, 12, 29]. It is not only useful for the detection of acute infections, but is also the most accurate imaging modality for confirming or excluding the diagnosis of low-grade infection and chronic osteomyelitis [29]. In this setting, PET is useful because FDG is avidly taken up by activated macrophages which predominate in the chronic phase of infection.

Although leucocyte scintigraphy has adequate diagnostic accuracy in the appendicular skeleton, FDG PET is superior for detecting chronic osteomyelitis in the axial skeleton [29]. Our data confirm these results, with one false negative and no false positive findings in the axial skeleton.

FDG PET shows a sensitivity of up to 100% and a specificity in the range of 88–93% in the diagnosis of chronic musculoskeletal infections, including patients with and without metallic implants or prosthetic replacements [9, 11, 12]. In a study by de Winter et al. [11], the overall sensitivity, specificity and accuracy of FDG PET in suspected chronic musculoskeletal infection of the appendicular and axial skeleton (n=60) were 100%, 88% and 93%, respectively. Seventeen out of 34 patients presented

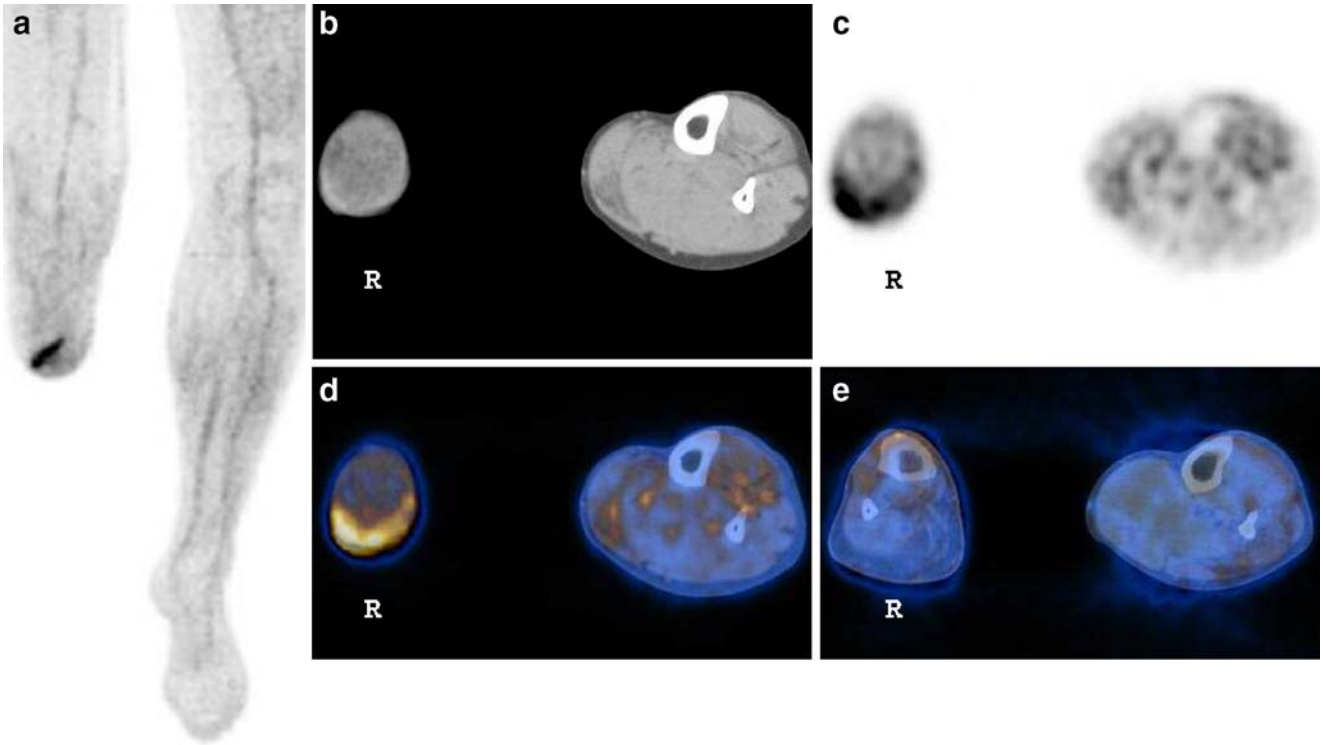

Fig. 4 A 78-year-old male with pain and secretion of the right lower limb stump. MIP PET scan (**a**) demonstrates linear increased FDG uptake in the distal end of the right lower limb stump. Axial CT image (**b**) shows muscle atrophy of the right lower limb. Axial PET scan (**c**) shows increased cutaneous and subcutaneous FDG uptake in the dorsal part of the right stump. Axial PET/CT scans (**d**, **e**) demonstrate increased FDG uptake in the soft tissues but no uptake within the bone of the right tibial stump. On PET/CT, differentiation between soft tissue and bone infection was possible

with infections around metallic devices used in trauma surgery. Two of four false positive findings were related to recent surgery within the previous 6 months. In concordance with these results, Schiesser et al. [12] showed a sensitivity of 100% and a specificity of 93% for FDG PET in the diagnosis of metallic implant-associated chronic infections in trauma patients (n=22). The latter group emphasised that FDG PET was not affected by artefacts from metallic implants used for fixation of fractures, which corresponds to our data and previously reported studies [9, 30]. Schiesser et al. [12] found one single false positive finding in the soft tissue of a patient 6 weeks after surgery. No false negative findings were seen. In the current study we only included patients who had undergone open fracture fixation or implantation of arthroplasty at the affected bone at least 6 months prior to the PET/CT examination to eliminate false positive findings due to recent surgery.

Guhlmann et al. [9] performed FDG PET in six patients with suspected metallic implant-associated infection among a group of 31 patients with suspected chronic osteomyelitis. The overall sensitivity, specificity and accuracy were 100%, 92% and 97%, respectively. The only false positive finding was a patient with a soft tissue infection which on PET was assigned to bone because of missing anatomical landmarks. With the use of PET/CT in our study, the additional information provided by CT enabled accurate differentiation between osteomyelitis and soft tissue infection (Fig. 4).

Zhuang et al. [31] demonstrated a sensitivity of 100%, a specificity of 87.5% and an accuracy of 90.9% in 22 patients with suspected chronic osteomyelitis. One of two false positives had a tibial non-union and one, an osteotomy. Several authors have reported [12, 30] that FDG uptake at the sites of fractures and non-unions (failure of union after 6 months) is significantly lower than that at the sites of infections, thereby facilitating differentiation. These data were not confirmed by our study. It is well known that postoperative reparative tissue and fractures may present with increased FDG uptake [32–34]. Increased FDG uptake normalises at around 4 months after traumatic or surgical fractures [15]. The healing process demonstrates most of the cellular components that are present in inflammation [35]. We had one patient with a false positive finding due to a non-union fracture of the femur with improper fracture consolidation after 9 months that showed grade 3 uptake on FDG PET/CT (Fig. 5). Microbiological results were negative for infection. In the last-mentioned patient, the CT part of the scan yielded the diagnosis of a non-union, demonstrating prominent cortical bone within the marrow cavity. One of the main causes of delayed fracture healing is infection [36, 37]. To date, no studies

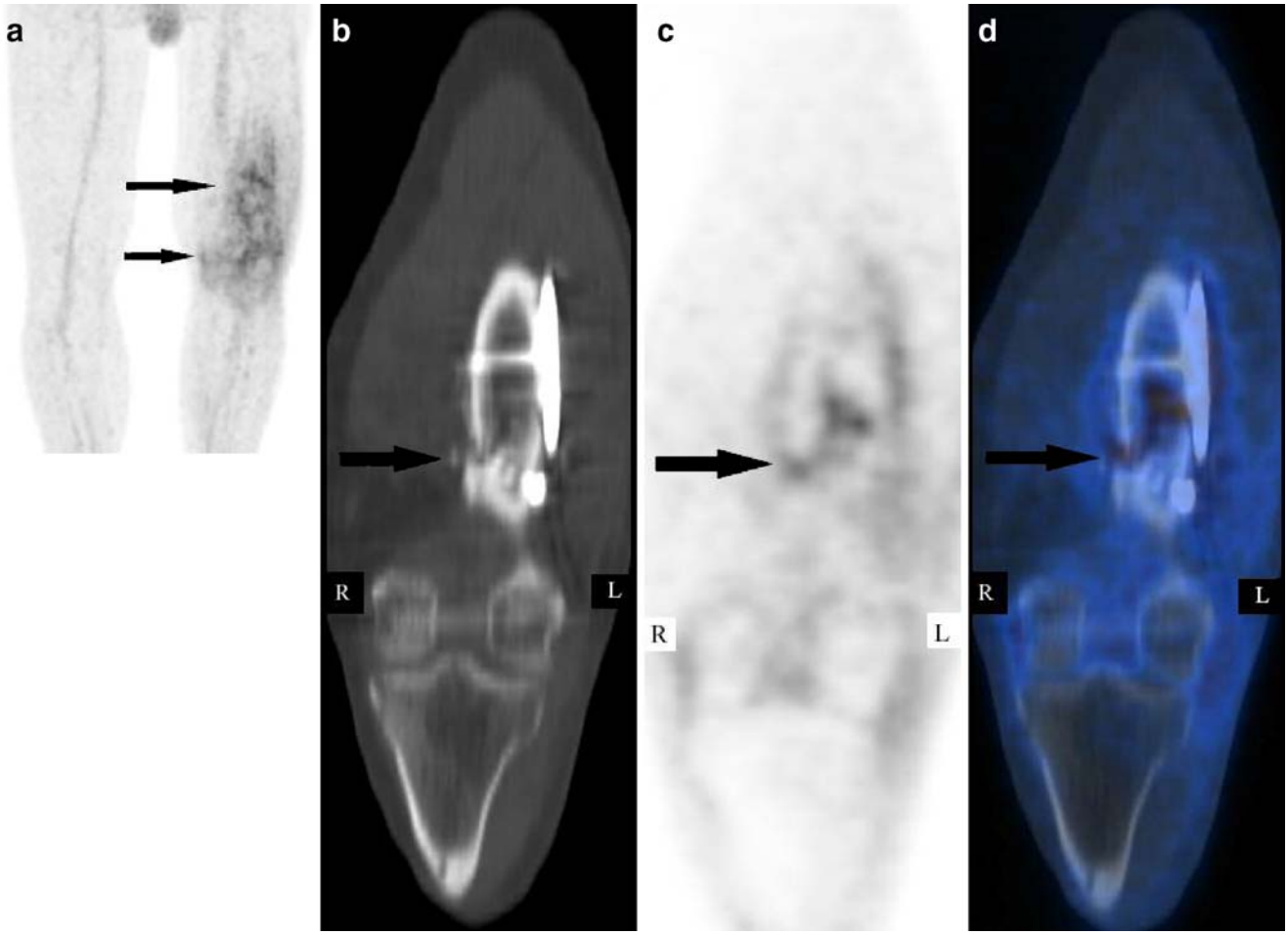

Fig. 5 A 32-year-old male 9 months after grade 2 open intra-articular fracture of the distal femur and insertion of metallic implants. MIP PET (**a**) shows diffusely increased FDG uptake in the left thigh including the knee (*arrows*). Coronal CT image (**b**) demonstrates osteopenia of the left distal femur with distraction of femoral fragments (*arrow*). In addition, CT shows sclerosis of distal femoral fragments and bony fragments adjacent to lower screws. Coronal PET (**c**) scan shows increased FDG uptake in left thigh (*arrow*). In a coronal co-registered PET/CT scan (**d**), FDG uptake could be localised precisely at the fracture site (*arrow*)

have assessed the clinical value of FDG PET or FDG PET/CT in patients with fracture non-union. Different forms of fracture non-unions may be responsible for various FDG uptake patterns. CT has proved to be a useful imaging method in the evaluation of patients with fracture non-unions [38, 39]. An imaging technique that can reliably differentiate infection from fracture non-union would be a useful adjunct for therapeutic management of these patients.

The second false positive finding occurred in a patient with a hemi-arthroplasty of the hip. Histopathological specimens showed granulomatous tissue with giant cells and macrophages resulting from a foreign body reaction at the prosthesis–bone interface. Polyethylene particles and metal wear particles were found in this patient and seemed to be responsible for this reaction. Both giant cells and macrophages accumulate FDG, as shown in previous studies in patients with prosthetic devices [11, 18, 40].

Several authors have concluded that it is questionable whether FDG PET is able to differentiate between aseptic and septic prosthetic loosening because of the remarkably similar histopathological morphology [8, 11, 18, 40].

The single false negative result in this series, a very small (<5 mm) osseous infectious lesion in the mandible, is difficult to explain but was presumably due to the limited spatial resolution of the PET/CT scanner. Robiller et al. [13] reported a patient with increased FDG uptake within a necrotic, poorly vascularised fibular transplant, whereas ^{99m}Tc-labelled leucocyte scintigraphy was false negative. The authors emphasised that the small FDG molecule was still able to enter poorly perfused areas rapidly, in contrast to labelled granulocytes, which required delayed imaging after at least 24 h because of the slow accumulation kinetics of the tracer.

A general limitation of FDG PET is that it provides only a restricted amount of anatomical information. The data available thus far suggest that FDG PET is better than conventional scintigraphic techniques at distinguishing between osseous and soft tissue infection owing to its

better spatial resolution and inherently tomographic capabilities [9, 12]. PET/CT data in respect of bone infections are still very limited. A single FDG PET/CT study has been performed so far, by Keidar et al. [41], who investigated 14 patients with clinical suspicion of diabetes-related osteomyelitis of the foot. The authors concluded that FDG PET/CT is useful for the diagnosis of diabetes-related infection as it accurately differentiated between osteomyelitis and soft tissue infection. PET/CT adds important anatomical details, which are relevant to the surgeon, as the operative approach differs greatly when osteomyelitis is present. This was confirmed in our study, in which surgeons retrospectively assessed the influence of FDG PET/CT on their treatment decisions and found that PET/CT influenced the clinical decision-making process in approximately 50% of patients. The addition of the CT part to the PET scan provided complementary information relevant to surgical planning, which reduced the surgical intervention to a minimum. Furthermore, PET/CT enabled the surgeon to determine the precise extent of resection and therefore to anticipate the appropriate surgical approach (e.g. external fixation or cement spacer).

Our study has limitations. We performed a retrospective study in a small number of patients. Our data are promising, but larger prospective series of patients are needed before clinical use of this method can be recommended. A prospective comparison between PET imaging alone and integrated PET/CT should be performed, together with an evaluation of their impact on the surgical management.

Our data suggest that FDG PET/CT is sensitive and specific for the detection of chronic osteomyelitis in trauma patients in both the axial and the appendicular skeleton. Especially in the axial skeleton, FDG PET/CT is an important imaging technique in the diagnosis and exclusion of chronic osteomyelitis, showing superior accuracy to other radionuclide imaging modalities. Although its role is still evolving, in the future FDG PET/CT may permit more precise delineation and characterisation of the infectious focus in patients with and without metallic devices. Differentiation between osteomyelitis and infection of the adjacent soft tissues can be accurately obtained with FDG PET/CT because of the high lesion-to-background contrast and because of the less severe artefacts arising from metallic implants compared with CT. It can be anticipated that the new diagnostic imaging technique of FDG PET/CT will improve the rate of detection of chronic post-traumatic osteomyelitis.

References

1. Perry M. Erythrocyte sedimentation rate and C reactive protein in the assessment of suspected bone infection—are they reliable indices? J R Coll Surg Edinb 1996;41:116–8.
2. Lew DP, Waldvogel FA. Osteomyelitis. N Engl J Med 1997;336:999–1007.
3. Eckardt JJ, Wirganowicz PZ, Mar T. An aggressive surgical approach to the management of chronic osteomyelitis. Clin Orthop Relat Res 1994:229–39.
4. Santiago Restrepo C, Gimenez CR, McCarthy K. Imaging of osteomyelitis and musculoskeletal soft tissue infections: current concepts. Rheum Dis Clin North Am 2003;29:89–109.
5. Ma LD, Frassica FJ, Bluemke DA, Fishman EK. CT and MRI evaluation of musculoskeletal infection. Crit Rev Diagn Imaging 1997;38:535–68.
6. Unger E, Moldofsky P, Gatenby R, Hartz W, Broder G. Diagnosis of osteomyelitis by MR imaging. AJR Am J Roentgenol 1988;150:605–10.
7. Palestro CJ, Roumanas P, Swyer AJ, Kim CK, Goldsmith SJ. Diagnosis of musculoskeletal infection using combined In-111 labeled leukocyte and Tc-99m SC marrow imaging. Clin Nucl Med 1992;17:269–73.
8. Love C, Marwin SE, Tomas MB, Krauss ES, Tronco GG, Bhargava KK, et al. Diagnosing infection in the failed joint replacement: a comparison of coincidence detection ^{18}F-FDG and ^{111}In-labeled leucocyte/^{99m}Tc-sulfur colloid marrow imaging. J Nucl Med 2004;45:1864–71.
9. Guhlmann A, Brecht-Krauss D, Suger G, Glatting G, Kotzerke J, Kinzl L, et al. Chronic osteomyelitis: detection with FDG PET and correlation with histopathologic findings. Radiology 1998;206:749–54.
10. Guhlmann A, Brecht-Krauss D, Suger G, Glatting G, Kotzerke J, Kinzl L, et al. Fluorine-18-FDG PET and technetium-99m antigranulocyte antibody scintigraphy in chronic osteomyelitis. J Nucl Med 1998;39:2145–52.
11. de Winter F, van de Wiele C, Vogelaers D, de Smet K, Verdonk R, Dierckx RA. Fluorine-18 fluorodeoxyglucose-position emission tomography: a highly accurate imaging modality for the diagnosis of chronic musculoskeletal infections. J Bone Joint Surg Am 2001;83:651–60.
12. Schiesser M, Stumpe KD, Trentz O, Kossmann T, Von Schulthess GK. Detection of metallic implant-associated infections with FDG PET in patients with trauma: correlation with microbiologic results. Radiology 2003;226:391–8.
13. Robiller FC, Stumpe KD, Kossmann T, Weisshaupt D, Bruder E, von Schulthess GK. Chronic osteomyelitis of the femur: value of PET imaging. Eur Radiol 2000;10:855–8.
14. Zhuang H, Sam JW, Chacko TK, Duarte PS, Hickeson M, Feng Q, et al. Rapid normalization of osseous FDG uptake following traumatic or surgical fractures. Eur J Nucl Med Mol Imaging 2003;30:1096–103.
15. Kaim AH, Gross T, von Schulthess GK. Imaging of chronic posttraumatic osteomyelitis. Eur Radiol 2002;12:1193–202.
16. Schmidlin P. Improved iterative image reconstruction using variable projection binning and abbreviated convolution. Eur J Nucl Med 1994;21:930–6.
17. Stumpe KD, Dazzi H, Schaffner A, von Schulthess GK. Infection imaging using whole-body FDG-PET. Eur J Nucl Med 2000;27:822–32.
18. Stumpe KD, Notzli HP, Zanetti M, Kamel EM, Hany TF, Gorres GW, et al. FDG PET for differentiation of infection and aseptic loosening in total hip replacements: comparison with conventional radiography and three-phase bone scintigraphy. Radiology 2004;231:333–41.
19. Goerres GW, Ziegler SI, Burger C, Berthold T, Von Schulthess GK, Buck A. Artifacts at PET and PET/CT caused by metallic hip prosthetic material. Radiology 2003;226:577–84.
20. Erdman WA, Tamburro F, Jayson HT, Weatherall PT, Ferry KB, Peshock RM. Osteomyelitis: characteristics and pitfalls of diagnosis with MR imaging. Radiology 1991;180:533–9.

21. Seabold JE, Nepola JV. Imaging techniques for evaluation of postoperative orthopedic infections. Q J Nucl Med 1999;43:21–8.
22. Kaim A, Ledermann HP, Bongartz G, Messmer P, Muller-Brand J, Steinbrich W. Chronic post-traumatic osteomyelitis of the lower extremity: comparison of magnetic resonance imaging and combined bone scintigraphy/immunoscintigraphy with radiolabelled monoclonal antigranulocyte antibodies. Skeletal Radiol 2000;29:378–86.
23. Gold RH, Hawkins RA, Katz RD. Bacterial osteomyelitis: findings on plain radiography, CT, MR, and scintigraphy. AJR Am J Roentgenol 1991;157:365–70.
24. Seabold JE, Nepola JV, Conrad GR, Marsh JL, Montgomery WJ, Bricker JA, et al. Detection of osteomyelitis at fracture nonunion sites: comparison of two scintigraphic methods. AJR Am J Roentgenol 1989;152:1021–7.
25. Kim EE, Pjura GA, Lowry PA, Gobuty AH, Traina JF. Osteomyelitis complicating fracture: pitfalls of ^{111}In leukocyte scintigraphy. AJR Am J Roentgenol 1987;148:927–30.
26. Schauwecker DS. The scintigraphic diagnosis of osteomyelitis. AJR Am J Roentgenol 1992;158:9–18.
27. Datz FL. Indium-111-labeled leukocytes for the detection of infection: current status. Semin Nucl Med 1994;24:92–109.
28. Palestro CJ, Torres MA. Radionuclide imaging in orthopedic infections. Semin Nucl Med 1997;27:334–45.
29. Termaat MF, Raijmakers PG, Scholten HJ, Bakker FC, Patka P, Haarman HJ. The accuracy of diagnostic imaging for the assessment of chronic osteomyelitis: a systematic review and meta-analysis. J Bone Joint Surg Am 2005;87:2464–71.
30. Kalicke T, Schmitz A, Risse JH, Arens S, Keller E, Hansis M, et al. Fluorine-18 fluorodeoxyglucose PET in infectious bone diseases: results of histologically confirmed cases. Eur J Nucl Med 2000;27:524–8.
31. Zhuang H, Duarte PS, Pourdehand M, Shnier D, Alavi A. Exclusion of chronic osteomyelitis with F-18 fluorodeoxyglucose positron emission tomographic imaging. Clin Nucl Med 2000;25:281–4.
32. Meyer M, Gast T, Raja S, Hubner K. Increased F-18 FDG accumulation in an acute fracture. Clin Nucl Med 1994;19:13–4.
33. Fayad LM, Cohade C, Wahl RL, Fishman EK. Sacral fractures: a potential pitfall of FDG positron emission tomography. AJR Am J Roentgenol 2003;181:1239–43.
34. Fayad LM, Kawamoto S, Kamel IR, Bluemke DA, Eng J, Frassica FJ, et al. Distinction of long bone stress fractures from pathologic fractures on cross-sectional imaging: how successful are we? AJR Am J Roentgenol 2005;185:915–24.
35. Henry G, Garner WL. Inflammatory mediators in wound healing. Surg Clin North Am 2003;83:483–507.
36. Nicoll EA. Fractures of the tibial shaft. A survey of 705 cases. J Bone Joint Surg Br 1964;46:373–87.
37. Heiple KG, Herndon CH. The pathologic physiology of nonunion. Clin Orthop Relat Res 1965;43:11–21.
38. Lang P, Genant HK, Chafetz N, Steiger P, Morris JM. Three-dimensional computed tomography and multiplanar reformations in the assessment of pseudarthrosis in posterior lumbar fusion patients. Spine 1988;13:69–75.
39. Frahm R, Lowka K, Vinee P. Computerized tomography diagnosis of scaphoid fracture and pseudarthrosis in comparison with roentgen image. Handchir Mikrochir Plast Chir 1992;24:62–6.
40. Love C, Tomas MB, Marwin SE, Pugliese PV, Palestro CJ. Role of nuclear medicine in diagnosis of the infected joint replacement. Radiographics 2001;21:1229–38.
41. Keidar Z, Militianu D, Melamed E, Bar-Shalom R, Israel O. The diabetic foot: initial experience with ^{18}F-FDG PET/CT. J Nucl Med 2005;46:444–9.