Bone involvement in patients with lymphoma: the role of FDG-PET/CT

Niklaus G. Schaefer[1, 2], Klaus Strobel[1], Christian Taverna[2], Thomas F. Hany[1]

[1] Department of Nuclear Medicine, University Hospital Zurich, Zurich, Switzerland
[2] Department of Internal Medicine, Clinic for Medical Oncology, University Hospital Zurich, Raemistrasse 100, 8091 Zurich, Switzerland

Received: 24 March 2006 / Accepted: 12 June 2006 / Published online: 22 September 2006

Abstract. *Purpose:* To evaluate the diagnostic impact and clinical significance of FDG-avid bone lesions detected by FDG-PET/CT in patients with lymphoma.
Methods: The study population comprised 50 consecutive patients (mean age 41.7±15.5 years; 27 female, 23 male; 41 staging, 9 restaging) with Hodgkin's disease (n=22) or aggressive non-Hodgkin's lymphoma (n=28) in whom FDG-avid bone lesions were detected by FDG-PET/CT. All patients had either direct biopsy of the FDG-avid bone lesion (n=18), standard bone marrow biopsy at the iliac crest (BMB; n=43) or both procedures (n=11). In 15 patients, additional MRI of the bone lesions was performed. All patients underwent FDG-PET/CT after the end of treatment. All CT images of FDG-PET/CT scans were analysed independently regarding morphological osseous changes and compared with FDG-PET results.
Results: In the 50 patients, 193 FDG-avid lesions were found by PET/CT. The mean standardised uptake value was 6.26 (±3.22). All direct bone biopsies (n=18) of the FDG-avid lesions proved the presence of lymphomatous infiltration. BMB (n=43) was positive in 12 patients (27.9%). In CT, 32 of 193 (16.6%) lesions were detected without the PET information. No additional morphological bone infiltration was detected on CT compared with FDG-PET. All morphological bone alterations on CT scans persisted after the end of therapy. Additional PET/CT information regarding uni- or multifocal bone involvement resulted in lymphoma upstaging in 21 (42%) patients compared with the combined information provided by CT and BMB.
Conclusion: In patients with FDG-avid bone lesions, FDG-PET is superior to CT alone or in combination with unilateral BMB in detecting bone marrow involvement, leading to upstaging in a relevant proportion of patients.

Niklaus G. Schaefer (✉)
Department of Internal Medicine, Clinic for Medical Oncology,
University Hospital Zurich,
Raemistrasse 100,
8091 Zurich, Switzerland
e-mail: niklaus.schaefer@usz.ch
Tel.: +41-44-2551111, Fax: +41-44-2559733

Keywords: FDG-PET/CT – Lymphoma – Bone – Bone marrow – Biopsy

Eur J Nucl Med Mol Imaging (2007) 34: 60–67
DOI 10.1007/s00259-006-0238-8

Introduction

Positron emission tomography (PET) using ^{18}F-fluorodeoxyglucose (FDG) has been used successfully for staging and follow-up examinations in patients with aggressive non-Hodgkin's lymphoma (NHL) and Hodgkin's disease (HD) [1–3]. Studies have proven that FDG-PET is more accurate than contrast-enhanced computed tomography (CT) in the staging and restaging of malignant lymphoma [1]. Few data are available regarding the diagnostic impact of FDG-PET in patients with malignant lymphoma and bone marrow involvement [4–6]. Data from patients with primary bone lymphoma suggest that FDG-PET scanning adds important information relevant to management decisions [7, 8].

It is still under discussion whether FDG-PET can reduce significantly the need for staging bone marrow biopsies (BMB) at the iliac crest [4, 5]. However, in a recent meta-analysis, a good, but not excellent correlation was demonstrated between FDG-PET and BMB in the detection of bone marrow involvement in the staging of patients with malignant lymphoma [6].

BMB is an invasive diagnostic procedure which allows the analysis of only a very limited area, and uni- or multifocal bone marrow involvement at locations other than the iliac crest can consequently be missed. In HD and NHL, unilateral iliac crest biopsy is false negative compared with bilateral iliac biopsy in up to 80% of the patients [9]. In view of these data, BMB cannot be regarded as a histological gold standard for bone involvement or bone marrow infiltration. Obviously, it is essential to have a routine diagnostic procedure, possibly consisting of a multi-step approach, to reliably assess bone marrow infiltration in patients with HD or NHL.

Table 1. Patient characteristics (total group)

Characteristics	No. of patients
Total no of patients	50
Sex	
Male	22
Female	28
Age, years	
Mean±SD	41.7 years (±15.5)
Range	14–75 years
Histology	
HD	22
NHL	28
Modality	
Initial staging	41
Restaging	9

The purpose of this study was to evaluate the diagnostic value and clinical significance of FDG-avid bone lesions diagnosed by FDG-PET/CT as the first step in staging of patients with lymphoma.

Table 2. Characteristics, histology and treatment of 22 HD patients with bone involvement

No.	Sex	Age (years)	Histology	Treatment
1	m	23	HD, mixed cell	ABVD
2	f	34	HD, nodular sclerosis	CBV
3	f	31	HD, nodular sclerosis	BEACOPP
4	m	47	HD, nodular sclerosis	EPOCH/CBV/radiation
5	m	31	HD, nodular sclerosis	ABVD
6	m	19	HD, nodular sclerosis	ABVD
7	f	37	HD, nodular sclerosis	ABVD
8	m	33	HD, nodular sclerosis	ABVD/radiation
9	m	14	HD, nodular sclerosis	ABVD
10	m	23	HD, nodular sclerosis	ABVD/radiation
11	m	17	HD, nodular sclerosis	ABVD
12	f	20	HD, nodular sclerosis	ABVD/radiation
13	f	21	HD, nodular sclerosis	ABVD
14	f	62	HD, nodular sclerosis	ABVD/radiation
15	m	31	HD, nodular sclerosis	ABVD
16	f	28	HD, nodular sclerosis	ABVD/radiation
17	m	19	HD, nodular sclerosis	CBV
18	f	28	HD, nodular sclerosis	ABVD/radiation
19	f	27	HD, nodular sclerosis	ABVD
20	f	35	HD, nodular sclerosis	ABVD
21	f	57	HD, nodular sclerosis	ABVD
22	m	24	HD, nodular sclerosis	ABVD

m Male; *f* female; *ABVD* adriamycin, bleomycin, vinblastin and dacarbazine; *CBV* cyclophosphamide, carmustine and etoposide; *EPOCH* etoposide, prednisone, Oncovin, cyclophosphamide and doxorubicin hydrochloride; *BEACOPP* bleomycin, etoposide, adriamycin, cyclophosphamide, Oncovin, procarbazine and prednisone

Materials and methods

Patients

All patients with HD or aggressive NHL who presented between January 2003 and November 2005 and who had uni- or multifocal FDG-avid lesions in the bone were analysed (mean age 41.69±15.53 years; 27 female, 23 male; 41 primary staging, 9 staging of recurrent disease). Patients had either direct bone marrow biopsy of the FDG-avid lesion (n=18), standard biopsy at the iliac crest (n=43) or both (n=11). In 15 patients, magnetic resonance imaging (MRI) of the bone lesions was additionally performed. All patients underwent FDG-PET/CT after the end of treatment. Patient characteristics are listed in Tables 1, 2 and 3.

All FDG-PET images and CT scans were analysed separately by one double board-certified nuclear medicine physician and radiologist and one board-certified radiologist with 3 years' experience in nuclear medicine. Suspected focal bone marrow infiltration by FDG-PET was compared with morphological changes in the corresponding CT scan.

Table 3. Characteristics, histology and treatment of 28 NHL patients with bone involvement

No.	Sex	Age (years)	Histology	Treatment
1	m	50	Anaplastic T cell lymphoma	CHOP
2	m	40	Diffuse large B cell lymphoma	R-EPOCH
3	m	59	Diffuse large B cell lymphoma	R-CHOP
4	m	34	Diffuse large B cell lymphoma	R-EPOCH
5	m	30	Diffuse large B cell lymphoma	R-CHOP
6	m	56	Diffuse large B cell lymphoma	R-EPOCH
7	m	68	Diffuse large B cell lymphoma	R-CHOP
8	m	71	Diffuse large B cell lymphoma	R-CHOP
9	f	62	Diffuse large B cell lymphoma	R-CHOP
10	f	36	Diffuse large B cell lymphoma	R-CHOP
11	f	70	Diffuse large B cell lymphoma	CHOP
12	m	33	Diffuse large B cell lymphoma	R-CHOP
13	m	62	Primary bone lymphoma	Radiation
14	m	69	Follicular lymphoma, grade III	R-CHOP
15	f	75	Follicular lymphoma, grade III	R-CHOP
16	f	71	Follicular lymphoma, grade II	R-CHOP
17	f	41	Primary B cell bone lymphoma	Radiation
18	m	39	EBV-associated B lymphoma	R
19	f	36	Diffuse large B cell lymphoma	R-CHOP
20	f	27	Diffuse large B cell lymphoma	R-CHOP
21	f	70	Diffuse large B cell lymphoma	R-CHOP
22	f	24	Anaplastic T cell lymphoma	CHOP
23	f	66	Follicular lymphoma, grade III	R-CHOP
24	f	28	Diffuse large B cell lymphoma	R-CHOP
25	f	47	Lymphoblastic B-NHL	R-HyperCVAD
26	f	59	Diffuse large B cell lymphoma	R-CHOP
27	f	57	Transformed follicular lymphoma, grade III	R-EPOCH
28	f	39	Follicular lymphoma, grade III	R-CHOP

m Male; *f* female; *CHOP* cyclophosphamide, hydroxydaunorubicin, vincristine and prednisone; *R* rituximab; *EPOCH* etoposide, prednisone, Oncovin, cyclophosphamide and doxorubicin hydrochloride; *HyperCVAD* hyperfractionated cyclophosphamide, vincristine, doxorubicin and dexamethasone

The FDG-PET/CT images of all patients were reviewed in accordance with the ethical guidelines of the hospital institutional review board after signed written informed consent had been obtained.

Imaging

All data were acquired on a combined PET/CT in-line system (Discovery LS, GE Healthcare, Waukesha, WI, USA). This dedicated system integrates a GE Advance NXi PET scanner with a multislice helical CT (LightSpeed plus) and permits the acquisition of co-registered CT and PET images in one session.

Patients fasted for at least 4 h prior to scanning, which started 40–60 min after the injection of a standard dose of 370 MBq of FDG. In addition, oral CT contrast agent (Micropaque Scanner, Guerbet AG, Aulnay-sous-bois, France) was given starting 15 min before the injection of FDG. Patients were examined in the supine position. No intravenous contrast agent was given. Initially, the CT scan was acquired starting at the level of the head using the following parameters: 80 mA, 140 kV, 0.5 s/tube rotation, slice thickness 4.25 mm, scan length 867 mm, data acquisition time 22.5 s. The CT

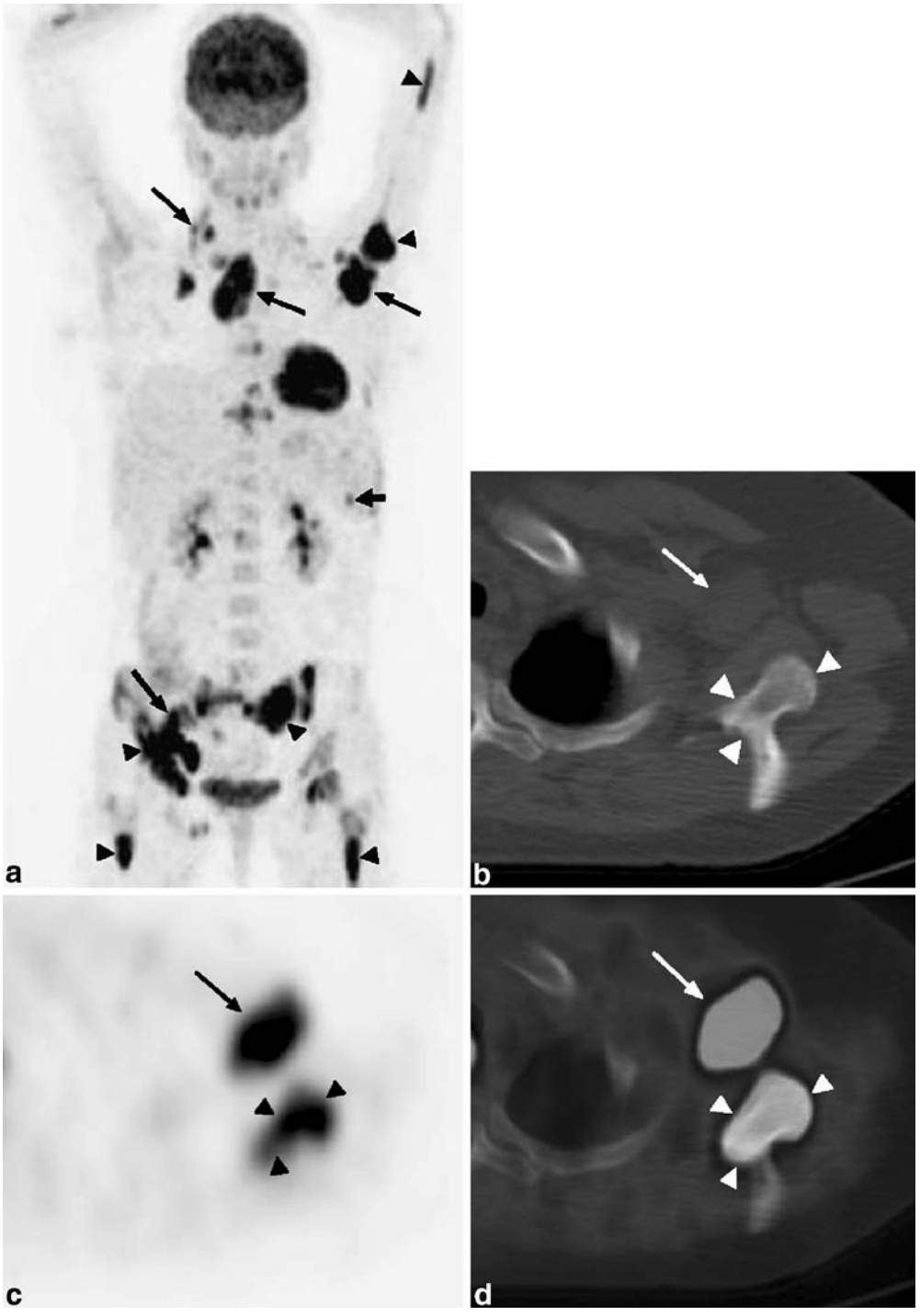

Fig. 1. PET/CT images for restaging in a 32-year-old woman with recurrence of HD. **a** Coronal maximum intensity projection image showing intense FDG uptake in cervical (*upper arrow*), mediastinal (*lower arrow*), axillary (*arrow at the left axilla*) and iliac (*lowest arrow*) lymph nodes as well as an FDG-avid lesion in the spleen (*short arrow*). There are multiple lesions with FDG uptake in the bones (*arrowheads*; left humerus, pelvis, both proximal femora). **b** Bone window of the axial CT image at the level of the upper thorax shows enlarged axillary lymph nodes (*arrow*) but normal bone structure of the scapula (*arrowheads*). **c, d** Corresponding axial PET image (**c**) and fused PET/CT image (**d**) demonstrate intense FDG uptake in enlarged axillary lymph nodes (*arrow*) and the scapula (*arrowheads*). BMB was negative in this patient

scan was acquired in breath hold in the normal expiration position and covered from the head to the pelvic floor.

Immediately following the CT acquisition, a PET emission scan was acquired using an acquisition time of 3 min for the emission scan per bed position with a one-slice overlap. Six to seven bed positions from the pelvic floor to the head resulted in an acquisition time of approximately 18–21 min. The CT data were used for attenuation correction and images were reconstructed using a standard iterative algorithm (OSEM). The acquired images were viewed with a software providing multiplanar reformatted images of PET, CT and fused data with linked cursors (Xeleris workstation, version 1.0728; GE Healthcare, Waukesha, USA).

Analysis

As indicated above, PET/CT images were reviewed separately by one double board-certified nuclear medicine physician and radiologist and one board-certified radiologist with 3 years' experience in nuclear medicine for the presence of FDG-avid lesions located in the bone. All detected FDG-avid lesions in the bone were objectively analysed by measurement of the calculated standardised uptake value (SUV).

To assess the impact of PET/CT on staging of patients with lymphoma, all patients had either BMB at the iliac crest or a PET/CT-guided or open biopsy of the FDG-avid lesion or both procedures.

To assess the value of the CT scans, the presence of osteosclerotic, osteolytic or mixed bone changes was evaluated on the bone window of the CT images. Additionally, CT images were analysed for further osseous lesions without FDG uptake. To assess the impact of PET/CT on staging of patients with lymphoma, all information, including histology, BMB and non-contrast-enhanced CT information, was subsumed for staging and compared with the same information combined with FDG-PET/CT results. This method permitted assessment of the additional benefit of functional PET information without the bias of possible wrong localisation of FDG-avid lesions.

Results

In 50 consecutive patients, 193 skeletal FDG-avid lesions were found on PET/CT. No additional osseous, FDG-inactive lesion suspicious for bone involvement was found on any CT image. Localisation of the FDG-avid lesions was as follows: spine, $n=70$; pelvis, $n=57$; femur, $n=27$; humerus, $n=11$; ribs, $n=7$; sternum, $n=7$; scapula, $n=7$ (Fig. 1); clavicle, $n=5$; mandible, $n=2$. Mean SUV of the bone lesions was 6.26±3.22.

Of the 50 patients, 18 (36%) had direct biopsy of the FDG-avid lesion in the bone. All direct bone biopsies of the FDG-avid lesions revealed lymphomatous infiltration. In 11 of these patients, BMB was also performed, and was negative in seven (63.6%). In the other seven patients, only a direct osseous biopsy of the FDG-avid lesion without BMB was performed. In three of the aforementioned 18 patients, MRI was performed and revealed bone marrow alterations.

Table 4. Number of bone lesions, biopsy results and staging with PET/CT and CT alone in 22 HD patients

No.	Lesions on PET/CT[a]	Lesions on CT[a]	Iliac crest biopsy	Direct biopsy	Site of biopsy	MRI	Staging w/o FDG-PET	Staging with FDG-PET
1	2	0	Negative	Not performed		Not performed	III	IV
2	9	0	Positive	Positive	Femoral neck	Not performed	IV	IV
3	10	0	Negative	Not performed		Positive	IIIS	IV
4	1	1	Positive	Positive	Sternum	Not performed	IV	IV
5	10	0	Negative	Not performed		Not performed	IIIS	IV
6	2	2	Negative	Not performed		Not performed	IV	IV
7	3	2	Negative	Not performed		Not performed	IV	IV
8	1	1	Negative	Not performed		Not performed	IV	IV
9	4	0	Negative	Not performed		Positive	II	IV
10	1	1	Negative	Not performed		Positive	IV	IV
11	1	0	Positive	Not performed		Positive	III	IV
12	1	1	Negative	Not performed		Not performed	IV	IV
13	3	1	Negative	Positive		Positive	IV	IV
14	1	0	Negative	Positive	Trochanter	Not performed	I	IV
15	1	1	Not performed	Positive	Ileum	Not performed	IV	IV
16	1	0	Negative	Not performed		Positive	II	IV
17	1	0	Negative	Not performed		Not performed	III	IV
18	1	0	Negative	Not performed		Positive	II	IV
19	3	0	Negative	Not performed		Positive	III	IV
20	3	0	Negative	Not performed		Not performed	IV	IV
21	4	0	Negative	Not performed		Not performed	III	IV
22	1	1	Negative	Positive	Humerus	Not performed	IE	IE

MRI Magnetic resonance imaging, *w/o* without

[a] Number of detected lesions

In the remaining 32 patients, results from BMB were available, and eight patients (25%) had positive findings on histology. In three of these positive cases, MRI revealed bone marrow infiltration. In another nine patients with negative BMB, MRI revealed bone marrow infiltration.

Overall, BMB at the iliac crest was available in 43 patients and was positive in 12 (27.9%) patients. In five patients with positive BMB, no MRI or direct biopsy was performed additionally. In seven patients, positive BMB was confirmed by MRI (n=3), direct biopsy (n=3) or both (n=1).

The results of the other 31 biopsies were negative for lymphoma. In seven of these patients, direct biopsy was positive for lymphoma, which was also confirmed by MRI in two patients. In nine further patients, MRI showed focal bone marrow alterations. In the remaining 15 patients, no direct biopsy or MRI was available. However, in these patients, as well as in all the other patients, FDG-PET/CT after the end of treatment normalised without evidence of focal osseous FDG uptake.

On CT, 32 of 193 (16.6%) lesions were detected without the PET information (8 osteolysis, 14 sclerosis, 10 mixed). In 161 lesions (83.4%), only focal increased uptake in the bone was observed on FDG-PET/CT, without morphological alteration of osseous structures on CT images. On a patient basis, no signs of osseous lymphomatous infiltration were seen in 28 of 50 patients (56%). Among 35 patients in whom lymphomatous infiltration was proven either by biopsy or by focal MRI changes, the CT scan was negative for bone infiltration in 18 (51.4%).

The additional PET/CT information regarding uni- or multifocal bone involvement upgraded the lymphoma stage in 21 (42%) patients compared with the combined information of CT alone and BMB. Seven (14%) patients had upstaging from an early (stage I/II) to an advanced stage (stage III/IV). In none of the 50 patients did CT show any additional bone lesion compared with FDG-PET. All patients with initial bone involvement on CT, seen as osteolytic, sclerotic or mixed lesions, had persistent bone alteration after the end of treatment. The results for each patient are listed in Tables 4 and 5. Examples are shown in Figs. 1, 2 and 3.

Table 5. Number of bone lesions, biopsy results and staging with PET/CT and CT alone in 28 NHL patients

No.	Lesions on PET/CT[a]	Lesions on CT[a]	Iliac crest biopsy	Direct biopsy	Site of biopsy	MRI	Staging w/o FDG-PET	Staging with FDG-PET
1	1	1	Not performed	Positive	Ileum	Not performed	IE	IE
2	3	0	Positive	Not performed		Positive	IV	IV
3	5	4	Not performed	Positive	Ileum	Not performed	IV	IV
4	2	1	Positive	Positive	Sacrum	Not performed	IV	IV
5	3	0	Negative	Positive	Humerus	Not performed	IIIS	IV
6	1	0	Negative	Not performed		Not performed	II	IV
7	8	0	Positive	Not performed		Not performed	IV	IV
8	2	0	Negative	Positive	Spine	Not performed	IIIS	IV
9	3	0	Negative	Not performed		Not performed	III	IV
10	1	0	Negative	Not performed		Not performed	I	IV
11	3	1	Negative	Positive	Femur	Not performed	IV	IV
12	1	0	Positive	Not performed		Not performed	IV	IV
13	1	1	Not performed	Positive	Sternum	Not performed	IE	IE
14	3	2	Negative	Autopsy	Lumbar spine	Positive	IV	IV
15	21	0	Not performed	Positive	Mandible	Not performed	III	IV
16	2	1	Negative	Not performed		Not performed	IV	IV
17	1	1	Not performed	Positive	Humerus	Not performed	IE	IE
18	3	0	Negative	Not performed		Not performed	III	IV
19	1	0	Negative	Not performed		Not performed	I	IV
20	15	3	Positive	Not performed		Not performed	IV	IV
21	3	1	Not performed	Positive	Femur	Not performed	IV	IV
22	1	0	Negative	Not performed		Positive	II	IV
23	10	0	Positive	Not performed		Not performed	IV	IV
24	11	2	Positive	Positive	Skull	Positive	IV	IV
25	15	0	Positive	Not performed		Positive	IV	IV
26	1	1	Negative	Not performed		Positive	IV	IV
27	6	2	Positive	Not performed		Not performed	IV	IV
28	2	0	Negative	Not performed		Positive	III	IV

MRI Magnetic resonance imaging, *w/o* without

[a] Number of detected lesions

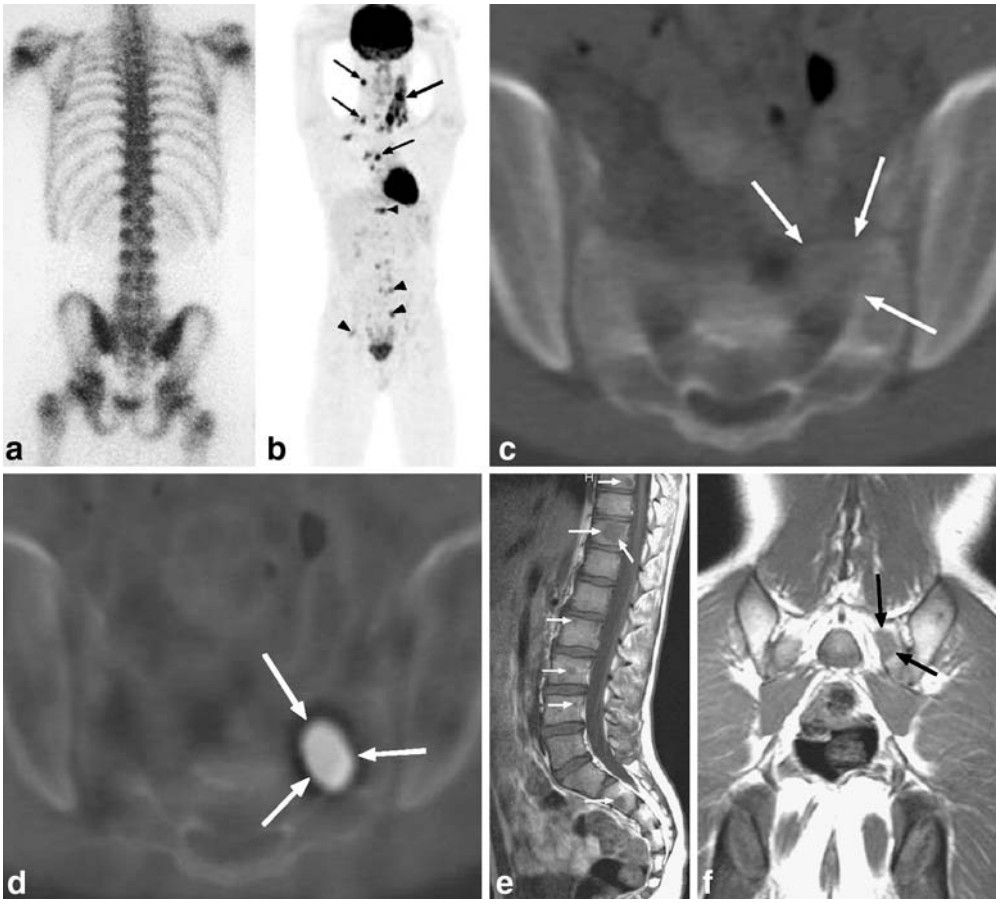

Fig. 2. Images for staging of a 14-year-old boy with HD. **a** BMB and bone scintigraphy were negative for bone involvement. **b** Coronal maximum intensity projection PET image shows increased FDG uptake in cervical and mediastinal lymph nodes (*arrows*) and multiple FDG-avid lesions in the bone (*arrowheads*; spine, sacrum). **c** Axial CT image at the level of the sacrum without alteration of the bony structures (*arrows*). **d** Axial PET/CT image with increased FDG uptake in the left sacrum. **e** Coronal T1-weighted MR image of the sacrum and **f** sagittal T1-weighted MR image of the lumbar spine showing multiple hypointense lesions (*arrows*), confirming the diagnosis of lymphomatous bone involvement

Discussion

The staging of lymphoma is essential in prognosis and therapy for patients with NHL and HD. The advanced stages III and IV correlate significantly with shorter overall or event-free survival and treatment may have to be modified accordingly [10]. In HD or NHL, multifocal bone marrow involvement places the patient in the most advanced disease stage IV. The European Society for Medical Oncology (ESMO) minimum clinical recommendations for diagnosis, treatment and follow-up of HD and NHL recommend a BMB in all patients [11, 12].

In HD, bone marrow infiltration by malignant cells in BMB occurs in up to 6.5% [13]. Various predictive factors, including B symptoms, peripheral low cellularity, age over 35 and inguinal involvement, have been established to predict possible bone marrow infiltration by HD [14]. However, BMB in HD has a low yield and BMI alone does not define a special high-risk group in which a different treatment approach is indicated [15]; accordingly, the need for BMB in all HD patients is questionable [16].

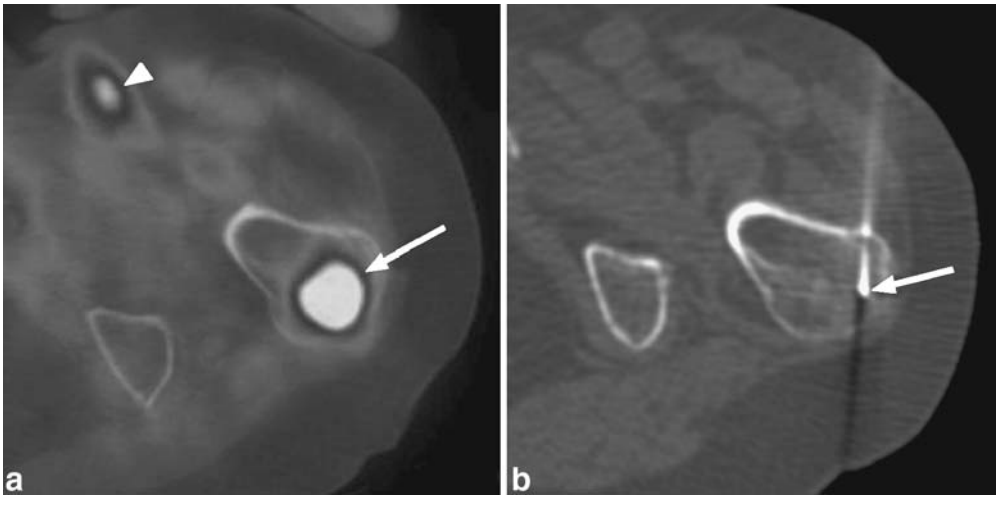

Fig. 3. PET/CT images of a 62-year-old women with recurrence of HD. **a** Axial PET/CT image showing increased FDG uptake in an inguinal lymph node (*arrowhead*) and the left proximal femur (*arrow*). **b** FDG uptake was used for planning the CT-guided percutaneous bone biopsy. The needle tip (*arrow*) is in the lesion. Histology was positive for lymphomatous infiltration

In NHL, bone marrow involvement occurs in 30%–50% and is more common in indolent histologies [17, 18]. Regarding the focal lymphomatous involvement of bone marrow, the value of unilateral versus bilateral BMB remains controversial. It has been shown that bilateral biopsy of the iliac crest enhances the diagnostic yield of BMB in HD (22 bilateral BMBs were positive, versus 14 unilateral BMBs) and NHL (237 bilateral BMBs were positive, versus 24 unilateral BMBs) [9]. These data show that focal bone marrow infiltrations in NHL and HD can pass undetected when using unilateral biopsy.

FDG-PET is a whole-body imaging modality with high sensitivity and specificity for either HD or aggressive NHL. FDG-PET has been proven to be sensitive in lymph node staging and identification of organ involvement in these patients. However, only limited data are available regarding the impact of FDG-PET in patients with bone marrow involvement.

In a paper by Nakamoto et al., the authors evaluated the CT appearance of bone metastases of different tumours (mainly lung, breast and pancreatic cancers and melanoma). They demonstrated that CT images obtained as part of the PET/CT examination helped to localise bone lesions exactly. However, CT revealed morphological changes in only half of the bone lesions. Only 3 of the 179 evaluated lesions were caused by bone involvement by lymphoma [19]. Further, FDG-PET is superior to bone scintigraphy in detecting bone metastases of various malignancies such as non-small cell lung cancer [20]. Moog et al. reported that FDG-PET is more sensitive and specific than bone scintigraphy for identifying bone involvement by lymphoma and concluded that FDG-PET can replace bone scintigraphy in the primary staging of lymphoma [21].

MRI has been proven to be accurate in the staging of primary bone lymphomas [22, 23]. However, MRI cannot differentiate viable from non-viable tumour, is somewhat limited in its anatomical coverage owing to the rather long imaging time and is therefore currently not used as a standard staging procedure in patients with lymphoma. Recent technical developments, however, allow the acquisition of whole-body MRI in rather a short time. Preliminary data mainly available in paediatric patients are encouraging, in that they have shown STIR whole-body MRI to be a sensitive technique for evaluating lymphomatous involvement of bone marrow as well as non-marrow sites in a small number of patients [24].

In our patients, FDG-PET had higher diagnostic accuracy with regard to bone involvement and staging than BMB alone, CT alone or the combination of both. Only in 12 of 43 patients with FDG-avid bone lesions was BMB positive. In contrast, all 18 patients with PET/CT-guided biopsy of FDG-avid lesions had biopsy-proven lymphomatous infiltration. However, in the absence of histological confirmation of all FDG-avid lesions, the sensitivity and specificity of the PET or the CT cannot be calculated.

FDG-PET upstaged 21 patients (42%) in relation to the combined information from CT scanning and BMB at the iliac crest. Seven (14%) patients had upstaging from early (stages I/II) to advanced stages (stages III/IV), leading to modification of treatment and prognosis.

Of 193 lesions, 161 (83.41%) were detected only by FDG-PET. The corresponding lesion on CT was found in only 16.6% (32 of 193 lesions). These data suggest that FDG-PET has a much higher sensitivity than CT in the detection of bone involvement in patients with HD or aggressive NHL. Also, the administration of intravenous contrast material does not help to detect more bone lesions on CT. All of our patients with initial bone involvement on CT, seen as osteolytic, sclerotic or mixed lesions, had persistent bone alteration after the end of treatment. Our data also suggest that neither staging nor evaluation of therapy response is sufficient with CT alone in patients with HD or NHL and bone involvement.

Regarding the role of FDG-PET/CT, CT provided additional information in comparison with FDG-PET in terms of the correct anatomical localisation of FDG-avid lesions, but no further lesions were identified. In 18 patients, FDG-avid lesions were biopsied successfully under CT guidance, with the help of anatomical landmarks demonstrated on PET/CT. The high accuracy (95%) of percutaneous bone biopsy relies on cases with morphological changes [25]. Only limited experience exists with PET/CT-guided interventions [26]. The increasing availability of PET/CT and the detection of FDG-avid lesions without a morphological correlate will raise the need for PET/CT-guided interventions.

In conclusion, FDG-PET is superior to CT alone or in combination with unilateral BMB in detecting bone marrow involvement in HD and NHL patients and leads to upstaging in a relevant proportion of patients. In patients with FDG-avid bone lesions, direct PET/CT-guided bone biopsy seems to be more accurate than standard BMB in confirming bone involvement. In the future, the decision to perform a BMB in patients with HD or NHL and the type of biopsy procedure should thus be guided by the results of FDG-PET/CT as the initial staging procedure. In FDG-negative cases, a BMB is probably still warranted. FDG-positive bone lesions should be evaluated by direct bone biopsy or MRI.

References

1. Stumpe KD, Urbinelli M, Steinert HC, Glanzmann C, Buck A, von Schulthess GK. Whole-body positron emission tomography using fluorodeoxyglucose for staging of lymphoma: effectiveness and comparison with computed tomography. Eur J Nucl Med 1998;25:721–8.
2. Buchmann I, Moog F, Schirrmeister H, Reske SN. Positron emission tomography for detection and staging of malignant lymphoma. Recent Results Cancer Res 2000;156:78–89.
3. Kostakoglu L, Coleman M, Leonard JP, Kuji I, Zoe H, Goldsmith SJ. PET predicts prognosis after 1 cycle of chemotherapy in aggressive lymphoma and Hodgkin's disease. J Nucl Med 2002;43:1018–27.

4. Carr R, Barrington SF, Madan B, O'Doherty MJ, Saunders CA, van der Walt J, et al. Detection of lymphoma in bone marrow by whole-body positron emission tomography. Blood 1998; 91:3340–6.
5. Moog F, Bangerter M, Kotzerke J, Guhlmann A, Frickhofen N, Reske SN. 18-F-fluorodeoxyglucose-positron emission tomography as a new approach to detect lymphomatous bone marrow. J Clin Oncol 1998;16:603–9.
6. Pakos EE, Fotopoulos AD, Ioannidis JP. ^{18}F-FDG PET for evaluation of bone marrow infiltration in staging of lymphoma: a meta-analysis. J Nucl Med 2005;46:958–63.
7. Park YH, Kim S, Choi SJ, Ryoo BY, Yang SH, Cheon GJ, et al. Clinical impact of whole-body FDG-PET for evaluation of response and therapeutic decision-making of primary lymphoma of bone. Ann Oncol 2005;16:1401–2.
8. Park YH, Choi SJ, Ryoo BY, Kim HT. PET imaging with F-18 fluorodeoxyglucose for primary lymphoma of bone. Clin Nucl Med 2005;30:131–4.
9. Wang J, Weiss LM, Chang KL, Slovak ML, Gaal K, Forman SJ, et al. Diagnostic utility of bilateral bone marrow examination: significance of morphologic and ancillary technique study in malignancy. Cancer 2002;94:1522–31.
10. A predictive model for aggressive non-Hodgkin's lymphoma. The International Non-Hodgkin's Lymphoma Prognostic Factors Project. N Engl J Med 1993;329:987–94.
11. Jost LM, Kloke O, Stahel RA. ESMO minimum clinical recommendations for diagnosis, treatment and follow-up of newly diagnosed large cell non-Hodgkin's lymphoma. Ann Oncol 2005;16 Suppl 1:i58–9.
12. Jost LM, Stahel RA. ESMO minimum clinical recommendations for diagnosis, treatment and follow-up of Hodgkin's disease. Ann Oncol 2005;16 Suppl 1:i54–5.
13. Macintyre EA, Vaughan Hudson B, Linch DC, Vaughan Hudson G, Jelliffe AM, et al. The value of staging bone marrow trephine biopsy in Hodgkin's disease. Eur J Haematol 1987;39:66.
14. Vassilakopoulos TP, Angelopoulou MK, Constantinou N, Karmiris T, Repoussis P, Roussou P, et al. Development and validation of a clinical prediction rule for bone marrow involvement in patients with Hodgkin lymphoma. Blood 2005;105:1875–80.
15. Munker R, Hasenclever D, Brosteanu O, Hiller E, Diehl V. Bone marrow involvement in Hodgkin's disease: an analysis of 135 consecutive cases. German Hodgkin's Lymphoma Study Group. J Clin Oncol 1995;13:403.
16. Howard MR, Taylor PR, Lucraft HH, Taylor MJ, Proctor SJ. Bone marrow examination in newly diagnosed Hodgkin's disease: current practice in the United Kingdom. Br J Cancer 1995;71:210–2.
17. Foucar K, McKenna RW, Frizzera G, Brunning RD. Bone marrow and blood involvement by lymphoma in relationship to the Lukes-Collins classification. Cancer 1982;49:888.
18. Conlan MG, Bast, M, Armitage JO, Weisenburger DD. Bone marrow involvement by non-Hodgkin's lymphoma: The clinical significance of morphologic discordance between the lymph node and bone marrow. Nebraska Lymphoma Study Group. J Clin Oncol 1990;8:1163.
19. Nakamoto Y, Cohade C, Tatsumi M, Hammoud D, Wahl RL. CT appearance of bone metastases detected with FDG PET as part of the same PET/CT examination. Radiology 2005;237:627–34.
20. Bury T, Barreto A, Daenen F, Barthelemy N, Ghaye B, Rigo P. Fluorine-18 deoxyglucose positron emission tomography for the detection of bone metastases in patients with non-small cell lung cancer. Eur J Nucl Med 1998;25:1244–7.
21. Moog F, Kotzerke J, Reske SN. FDG PET can replace bone scintigraphy in primary staging of malignant lymphoma. J Nucl Med 1999;40:1407–13.
22. Mengiardi B, Honegger H, Hodler J, Exner UG, Csherhati MD, Bruhlmann W. Primary lymphoma of bone: MRI and CT characteristics during and after successful treatment. Am J Roentgenol 2005;184:185–92.
23. Stiglbauer R, Augustin I, Kramer J, Schurawitzki H, Imhof H, Radaszkiewicz T. MRI in the diagnosis of primary lymphoma of bone: correlation with histopathology. J Comput Assist Tomogr 1992;16:248–53.
24. Kellenberger CJ, Miller SF, Khan M, Gilday DL, Weitzman S, Babyn PS. Initial experience with FSE STIR whole-body MR imaging for staging lymphoma in children. Eur Radiol 2004;14:1829–41.
25. Mink J. Percutaneous bone biopsy in the patient with known or suspected osseous metastasis. Radiology 1986;161:191–4.
26. Kaim AH, Burger C, Ganter CC, Goerres GW, Kamel E, Weishaupt D, et al. PET-CT-guided percutaneous puncture of an infected cyst in autosomal dominant polycystic kidney disease: case report. Radiology 2001;221:818–21.