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Whole-body positron emission tomography using ^{18}F-fluorodeoxyglucose compared to standard procedures for staging patients with Hodgkin's disease

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Background and Objectives. Accurate staging is essential in order to determine appropriate treatment in Hodgkin's disease (HD). ^{18}F-fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET) offers the advantage of metabolic imaging that is largely independent of morphologic criteria. In the present study we evaluated the role of ^{18}F-FDG PET compared to routine procedures for the staging of patients with HD.

Design and Methods. Thirty-three patients with HD underwent standard staging procedures (clinical examination, laboratory screening, chest X-ray, computed tomography (CT) of the chest and abdomen and bilateral bone marrow biopsies) and a whole-body ^{18}F-FDG PET study. In clinical examination, an isolated lymph node > 1 cm or multiple lymph nodes ≥ 1 cm in size were considered abnormal. Positive findings at both clinical examination or CT and ^{18}F-FDG PET were regarded as actual locations of disease. Negative findings with both methods were regarded as true negative (no involvement by HD). In cases of discrepancy, response to treatment and follow-up data were used to assess the overall accuracy of the patient's original evaluation.

Results. Completely concordant results in lymph node staging were observed in 20 patients. The two staging procedures indicated complementary information in 1 patient. Conventional staging indicated more pathologic lymph node areas in 6 patients (at least 1 false positive). ^{18}F-FDG PET showed more sites in 6 patients. The sensitivity of ^{18}F-FDG PET in detecting all known pathologic lymph nodes was 83% for peripheral lymph nodes, 91% for thoracic lymph nodes and 75% for abdominal and pelvic lymph nodes. Conventional staging procedures and ^{18}F-FDG PET indicated the same tumor stage in 26 patients. Based on ^{18}F-FDG PET, downstaging was suggested in 4 patients, including a biopsy-proven case. However in 1 of these cases this was incorrect. ^{18}F-FDG PET suggested upstaging in 3 patients. Based on conventional staging or ^{18}F-FDG PET the same treatment strategy was defined in 32 patients. In one patient ^{18}F-FDG PET downstaged disease extension (stage $III_A \rightarrow II_A$) that would have suggested radiotherapy as a possible treatment option.

Interpretation and Conclusions. ^{18}F-FDG PET provides an easy and efficient whole-body method for the evaluation of patients with HD. ^{18}F-FDG PET never missed tumor masses >1 cm. ^{18}F-FDG PET detected additional sites of disease not seen by conventional procedures and identified absence of disease in some sites suspected to be involved. However, in our patients this did not translate into changes in treatment strategy.

Key words: fluorine-18 fluorodeoxyglucose, Hodgkin's disease, positron emission tomography, radionuclide imaging, staging

In 2001, approximately 75-80% of all patients with HD should be cured of their disease. Accurate anatomic staging is essential for determining prognosis and appropriate treatment. Since 1970, staging of HD has been based on the Ann Arbor classification.[1] In 1989, a new international staging classification was proposed during a meeting held in the Cotswolds, England.[2] Routinely recommended procedures for staging of patients included medical history, clinical examination, laboratory tests, radiological procedures (plain film radiography, computed tomography) and bilateral bone marrow biopsy. One of the most controversial areas in the management of HD in recent years has been the role of staging laparotomy. Based on a possibly lower survival due to laparotomy-related death,[3] many international co-operative groups decided to abandon the strategy of routine staging laparotomy.[4] Whole-body ^{18}F-FDG PET is a new promising method in the staging, response evaluation and follow-up of lymphoma.[5-18] Increased glycolysis is one of the most distinctive biochemical features of malignant cells,[19] and results from amplification of the glucose transporter protein at the tumor cell surface as well as from increased activity of hexokinase. Like glucose, ^{18}F-FDG is transported into cells by a glucose transporter protein and rapidly converted into ^{18}F-FDG-6-phosphate. As the latter is not a substrate for glucose-6-phosphate isomerase, it is biochemically trapped in metabolizing tissues.[20] In the present study, we evaluat-

ed the role of ^{18}F-FDG PET compared to routine procedures for staging of patients with HD.

Design and Methods

Patients

Thirty-three consecutive patients with histologically verified HD were prospectively included between July 1994 and May 1998 in our study. The patients' characteristics are listed in Table 1. All patients gave oral informed consent for the PET study which was considered as a routine procedure in their staging.

Routine staging procedures

Routine staging methods at diagnosis included at least clinical examination, laboratory screening, chest X-ray, CT of the chest, abdomen and pelvis and bilateral bone marrow biopsy. In clinical examinations, an isolated lymph node > 1 cm or multiple lymph nodes with a minimal diameter of 1 cm were arbitrarily defined as lymph nodes suspected to be infiltrated by lymphoma. Intravenous contrast enhancement was used in every CT examination. The chest, abdomen and pelvis were systematically investigated. Standard size criteria were used to discriminate pathologic lymph nodes on CT scans.[21,22]

^{18}F-FDG PET studies

Whole-body PET using ^{18}F-FDG was performed with a Penn Pet 240-H Scanner (UGM, Philadelphia, PA, USA). ^{18}F-FDG was produced using an automated synthesizer marketed by Coincidence Company (Liège, Belgium). A dose of 200-300 MBq of ^{18}F-FDG was administered intravenously and emission scans were recorded 45-90 minutes later. All patients were asked to fast for at least 6 hours prior to the study. A whole-body acquisition was performed from the cervical to the inguinal region. It consisted of 10-12 separate overlapping acquisitions each covering 12.8 cm and performed during 4 minutes. Each subsequent acquisition was performed after a 6.4 cm displacement of the table. The total time of image acquisition was about 50 minutes. Images were reconstructed using filtered back projection with a Hanning filter and were reoriented in transverse, coronal and sagittal planes. A 4 mm voxel size was used. Isotropic 3D resolution was better than 8 mm. PET interpretation was performed in a qualitative manner without attenuation correction for most patients (23/33). Recently, we also performed transmission scans for attenuation correction (10/33 patients). All PET images were analyzed by a physician in the division of nuclear medicine and then reviewed by one investigator (GJ) without previous knowledge of the results of conventional procedures. Any focus of increased ^{18}F-FDG uptake over background not located in areas of normal ^{18}F-FDG uptake (central nervous system, heart, digestive tract, thyroid, muscles) and/or excretion (urinary tract) was considered positive for tumor. The reference area (background) is taken in an area symmetrical to the one with the lesion, preferably in the same transverse plane; alternatively, when the structure or presence of another organ makes it impossible, we use the same coronal plane. As shown by Lowe *et al.*,[23] the human eye is as good as semi-quantitative evaluation at discriminating between malignant and benign focal abnormalities. The ratio between abnormal accumulation and a reference area is a minimum of 1.5 and most frequently more than 2, as judged by reference to the color scale (black and white). Furosemide (20 mg in slow intravenous injection) was administered to patients with suspected pelvic abnormalities to enhance ^{18}F-FDG urinary elimination. These patients were studied later (60-90 minutes) and after voiding. Diazepam (5 mg) was given orally before ^{18}F-FDG administration in most patients to prevent muscular uptake.

Table 1. Patients' characteristics.

No. of cases	33
Mean age, years (range 13 to 71 years)	33
Sex	
Male	13
Female	20
Disease status	
Initial diagnosis	24
First relapse	9
Histology (REAL classification)	
Lymphocyte-rich classic disease	1
Nodular sclerosis	26
Mixed cellularity	5
Lymphocyte depletion	1
Ann Arbor clinical stage (conventional staging procedures)	
I	9
II	16
III	6
IV	2
Treatment	
Chemotherapy	23
Radiotherapy	7
Chemotherapy + radiotherapy	3

Standard of reference

We examined the concordance between routine staging procedures and ^{18}F-FDG PET. All studies were done within one week. A lymph node biopsy was performed for histologic diagnosis but for ethical reasons, systematic biopsy of the various sites was not performed for staging, except when considered clinically necessary. Since the pathologic verification of every node or abnormal lesion was not possible (gold standard) we used clinical examination and CT as the standard of reference. Positive findings at both clinical examination or CT and ^{18}F-FDG PET were regarded as actual locations of disease. Negative findings at both methods were regarded as true negative (no involvement by HD). In cases of discrepancy, response to treatment and follow-up data were used to assess the overall accuracy of the patient's original evaluation.

Table 2. Comparison of conventional staging with PET on a patient-by-patient basis at various sites.

Localization	*No pathologic lymph nodes*	*Same pathologic lymph nodes*	*Only positive by PET*	*More sites positive by PET*	*Only positive by conventional staging procedures*	*More sites by conventional staging procedures*	*Complementary information*
Peripheral lymph nodes							
Cervical	19	9	3	0	1	1	0
Supraclavicular	23	8	0	0	1	1	0
Axillary	26	4	2	0	0	1	0
Inguinal	33	0	0	0	0	0	0
Overall	11	15	4	0	1	2	0
Thoracic lymph nodes							
Subclavicular	30	0	3	0	0	0	0
Mediastinal	7	21	3	0	2	0	0
Hilar	23	9	1	0	0	0	0
Overall	7	20	3	1	1	0	1
Abdominal and pelvic lymph nodes							
Intraperitoneal	27	4	0	0	2	0	0
Retroperitoneal	26	5	1	0	1	0	0
Iliac	30	3	0	0	0	0	0
Overall	24	6	1	0	2	0	0

"Complementary information" : some sites only positive by PET and other sites only positive by conventional procedures; "Only positive by": the other staging methods showed no lesions; "More sites positive by" : both methods showed lesions but this method showed more lesions than the other.

Comparison of PET and conventional staging

For each of the 3 broad regions of interest (peripheral, thoracic, or abdominal and pelvic), several sites were compared. For each site, left and right lymph node areas were considered as separate sites. Patients were classified into one of seven categories according to the result of the comparison of PET and conventional staging: no pathologic lymph nodes (both staging methods were negative), same pathologic lymph nodes (both staging methods indicated infiltration of the same lymph node areas), only positive by PET (conventional staging was negative), more sites positive by PET (both methods showed lesions but PET showed more lesions than conventional staging), only positive by conventional staging (PET was negative), more sites by conventional procedures (both methods showed lesions but conventional staging showed more lesions than PET) and complementary information (some sites only positive by PET and other sites only positive by conventional procedures). We considered the result of the comparison of PET and conventional procedures as concordant if both methods showed the same lesions or absence of lesions, the result as discordant if one of the two staging methods indicated fewer tumor sites (nodal or extranodal) without showing additional lesions in other sites, the result as complementary if some sites were only positive by PET and other sites only positive by conventional procedures.

To assess the degree of agreement between the standard of reference and ^{18}F-FDG PET we calculated Cohen's κ coefficient and its 95% confidence interval. This coefficient is equal to 0 in case of chance agreement and 1 when there is perfect concordance between the two methods.

Results

Lymph nodes

Peripheral lymph nodes. Table 2 compares staging with conventional procedures or PET on a patient-by-patient basis at various sites to determine whether more sites are positive by one of the two staging methods. Concordant results (negative or positive) were observed in 26 patients including 11 patients in whom no abnormal lymph nodes were detected and 15 patients in whom the same 21 lymph node areas were detected by the 2 methods. Discordant results were obtained in 7 patients: sites were detected by PET only in 4 patients; standard procedures showed more sites in 2 patients; standard procedures only were positive in 1 patient. Cohen's κ coefficient for agreement between the 2 staging methods was 0.57 (p=0.001, 95% confidence interval: 0.23-0.91).

Thoracic lymph nodes. CT and ^{18}F-FDG PET observations were concordant in 27 patients. Complementary information was obtained in 1 patient in whom CT indicated only mediastinal and ^{18}F-FDG PET only subclavicular lymph node involvement. Discordant results were obtained in 5 patients: 3 patients were only positive by ^{18}F-FDG PET; more sites were seen by PET in 1 patient; standard procedures only were positive in 1 patient. Cohen's κ coefficient for agreement between the 2 staging methods was 0.57 (p<0.001, 95% confidence interval: 0.23-0.91).

Abdominal and pelvic lymph nodes. The two techniques showed identical results in 30 patients. Lymph nodes were identified by ^{18}F-FDG PET only in 1 patient. Sites were identified by CT only in 2 patients. In one case, CT suggested the presence of a pathologic intra-

Table 3. Overall evaluation.

No site by either method	3
Same sites by both methods	19
Only sites by conventional procedures	0
More sites by conventional procedures	3
peripheral lymph nodes	2
abdominal lymph nodes	1
Only sites by ^{18}F-FDG PET	2
thoracic lymph nodes	1
peripheral and thoracic lymph nodes	1
More sites by ^{18}F-FDG PET	4
peripheral lymph nodes	1
thoracic lymph nodes	1
abdominal lymph nodes	1
peripheral and thoracic lymph nodes	1
Complementary information	2
more peripheral lymph nodes by PET, thoracic and abdominal lymph nodes only by CT	1
some thoracic lymph nodes by PET, other thoracic lymph nodes by CT and more peripheral lymph nodes by conventional staging	1

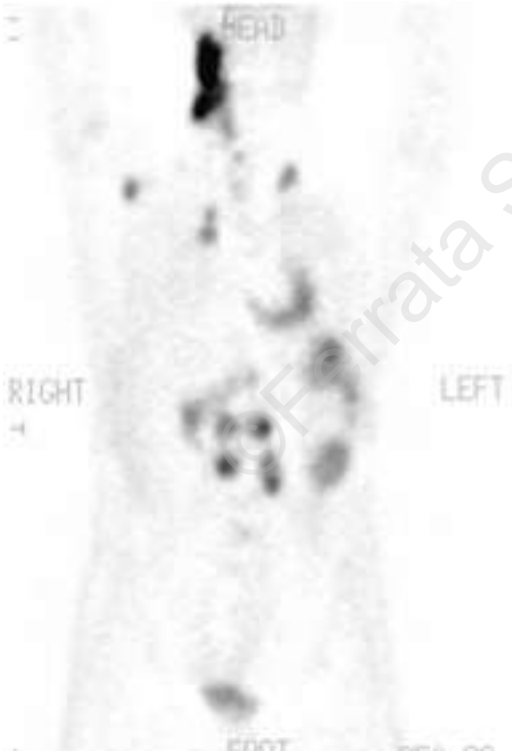

Figure 1. ^{18}F-FDG PET study of a patient with HD. Right cervical, right axillary, mediastinal, right hilar and retroperitoneal pathologic lymph nodes can be seen at diagnosis. ^{18}F-FDG PET also indicated splenic infiltration. Physiologic ^{18}F-FDG uptake was observed in the heart and the bladder. Results are completely concordant with clinical examination and CT studies of the thorax and abdomen (stage III$_S$).

peritoneal lymph node which was later proved by histology to be falsely positive. In the other, no biopsy was performed but follow-up CT scan showed disappearance upon treatment. Cohen's κ coefficient for agreement between the two staging methods was 0.74 (p<0.0001, 95% confidence interval: 0.4-1).

Overall results

Table 3 shows overall results of the evaluation of lymph node areas in the 33 patients. Completely concordant results were observed in 22 patients, among whom 3 had no lesion detected by either staging method after surgical removal of a single pathologic lymph node before the patients were referred to our center for staging and treatment. In 2 patients conventional procedures indicated more involved sites in some but fewer involved sites in other lymph node areas (complementary information by the two staging techniques). Conventional procedures indicated more pathologic lymph node areas in 3 patients. However, in 1 patient with a suspicion of intraperitoneal lymph node involvement by CT scan, staging laparotomy proved that this information was incorrect. In the other 2 patients with 1-cm lymph node areas, no biopsy was done. ^{18}F-FDG PET showed more involved sites in 4 patients and 2 patients were only positive by PET. ^{18}F-FDG PET never missed lymph nodes > 1 cm in size. Cohen's κ coefficient was 0.13 (p=0.46, 95% confidence interval: –0.21-0.47), indicating the absence of agreement between the standard of reference and ^{18}F-FDG PET. The two staging methods thus gave additional information.

Sensitivity of ^{18}F-FDG PET in detecting pathologic lymph nodes

We calculated the sensitivity of PET in detecting all pathologic lymph nodes shown by conventional procedures. This indicates the proportion of patients in whom PET would miss some pathologic areas if conventional staging procedures were not used. However, as biopsy of most lymph node areas to confirm the results of conventional procedures was not done and the results of conventional staging can thus be falsely positive, we also calculated the sensitivity in detecting at least some lymph nodes in a given region. Indeed, the impact of discordant results on the treatment strategy is more important if conventional staging procedures alone are positive (PET totally negative) than if they show more lesions than PET.

The sensitivity of ^{18}F-FDG PET in detecting all pathologic lymph nodes evidenced by standard procedures was calculated from data in Tables 2 and 3 by the ratio of the number of patients in groups *same pathologic lymph nodes + more sites positive by PET* over the total number of patients from among whom those with no pathologic lymph nodes and those only positive by PET were excluded. This sensitivity was 83% (15/18 patients) for peripheral lymph nodes, 91% (21/23 patients) for thoracic lymph nodes and 75% (6/8 patients) for abdominal and pelvic lymph nodes (Table 2). The sensitivity in detecting all pathologic lymph nodes in the

Table 4. Upstaging and downstaging by ^{18}F-FDG PET.

Pts.	*Disease status*	*Stage Conventional procedures*	*Stage ^{18}F-FDG PET*	*Adequacy of change in stage*	*Comment*
1	Initial diagnosis	III_A	II_A	proven	Laparotomy
2	Initial diagnosis	III_A	II_A	undetermined	CT indicated splenomegaly, laparotomy not performed; splenomegaly disappeared after polychemotherapy
3	Initial diagnosis	IV_A	III_B	undetermined	Bone marrow biopsy suggested very limited focal infiltration
4	Initial diagnosis	III_A	II_A	probably incorrect	Abdominal and retroperitoneal 1-cm lymph nodes not identified by PET, disappeared after chemotherapy
5	Initial diagnosis	I_A	II_A	probably correct	Mediastinal lymph nodes only identified by PET; patient in complete remission after radiotherapy
6	First relapse	II_A	IV_A	probably correct	Retroperitoneal lymph nodes and liver infiltration only identified by PET; ^{18}F-FDG PET was negative after a few cycles of polychemotherapy
7	First relapse	I_A	IV_A	probably correct	Isolated thyroid infiltration by standard procedures versus thyroid infiltration as well as cervical, subclavicular and mediastinal lymph nodes only identified by PET; ^{18}F-FDG PET was negative after salvage polychemotherapy

whole-body was 79% (23/28 patients) (Table 3). This calculation is a very conservative estimate of sensitivity because clinical examination and CT could falsely identify positive lymph nodes (as demonstrated by laparotomy in one of the patients) and PET could demonstrate abnormal lymph nodes not detected by conventional procedures.

We, therefore, calculated the sensitivity of ^{18}F-FDG PET in detecting at least some pathologic lymph nodes in a given region as the ratio of the number of patients in groups *same pathologic lymph nodes + more sites positive by PET + only positive by PET + more sites by conventional procedures + complementary information* over that of all patients excluding only those with concordant negative results. This sensitivity was 95% (21/22 patients) for peripheral nodes, 96% (25/26 patients) for thoracic nodes and 78% (7/9 patients) for abdominal and pelvic lymph nodes (underestimated because of one biopsy-proven false positive result by conventional staging) (Table 2). The sensitivity in detecting at least some pathologic lymph nodes in the whole-body was 100% (30/30 patients) (Table 3).

Alternatively, the sensitivity of standard procedures in detecting all pathologic lymph nodes detected by PET (ratio of the number of patients in groups *same pathologic lymph nodes + more sites by conventional staging procedures* over the total number of patients except those with no pathologic lymph nodes and those only positive by conventional procedures was 81% (17/21 patients) for peripheral lymph nodes, 80% (20/25 patients) for thoracic lymph nodes and 86% (6/7 patients) for abdominal and pelvic lymph nodes (Table 2). Overall this sensitivity was 73% (22/30 patients) (Table 3).

The sensitivity of standard procedures in detecting at least some pathologic lymph nodes in a given region was calculated as the ratio of the number of patients in groups *same pathologic lymph nodes + more sites positive by PET + more sites by conventional procedures + only positive by conventional procedures + complementary information* over that of all patients excluding only those with concordant negative results. This sensitivity was 82% (18/22 patients) for peripheral nodes, 88% (23/26 patients) for thoracic lymph nodes and 89% (8/9 patients) for abdominal and pelvic nodes (Table 2). Overall this sensitivity was 93% (28/30 patients) (Table 3).

Spleen and liver

Concordant results concerning spleen infiltration were observed in 5 patients. CT showed splenomegaly while ^{18}F-FDG PET indicated no abnormalities of the spleen in 1 patient. Laparotomy was not performed because chemotherapy was otherwise indicated. Focal liver infiltration was only detected by ^{18}F-FDG PET in 1 patient and it disappeared on follow-up studies after chemotherapy.

Bone marrow

Bilateral bone marrow biopsy indicated bone marrow infiltration in one patient. ^{18}F-FDG PET correctly identified this infiltration. Bone marrow biopsy also suggested a very focal infiltration in another patient. The ^{18}F-FDG PET study was negative in this patient.

Comparison of all standard procedures vs. ^{18}F-FDG PET

Conventional staging procedures and ^{18}F-FDG PET indicated the same tumor stage in 26 patients, including 7 stage I, 15 stage II, 3 stage III and 1 stage IV patients. Based on ^{18}F-FDG PET a downstaging was suggested in

4 patients including one case of biopsy-proven appropriate downstaging (Table 4). However, in three of these cases this may have been incorrect. In one case, splenomegaly and in another 1-cm abdominal lymph nodes were not identified but disappeared after chemotherapy (no biopsy performed). In addition, PET did not detect a possible very focal bone marrow infiltration but evidence of this latter was not compelling. This patient did not have attenuation-corrected imaging (see Discussion). ^{18}F-FDG PET suggested an upstaging in 3 patients. Based on conventional staging or ^{18}F-FDG PET the same treatment strategy was defined in 32 patients: 23 patients were treated by chemotherapy, 7 by radiotherapy, and 3 by the 2 combined modalities. In the patient with abdominal lymph nodes not detected by PET, ^{18}F-FDG PET would have incorrectly suggested radiotherapy as an appropriate treatment option for stage IIA supradiaphragmatic disease.

Comparison of attenuation-corrected and non-attenuation-corrected ^{18}F-FDG PET studies

The sensitivity of ^{18}F-FDG PET was not better in the 10 patients who had attenuation correction compared to those who did not. Comparison of standard procedures versus attenuation-corrected ^{18}F-FDG PET yielded the same pattern of identification of lymph node infiltration in 8 patients. Conventional procedures alone showed cervical and supraclavicular lymph nodes in 1 patient and ^{18}F-FDG PET alone indicated retroperitoneal lymph nodes and hepatic infiltration in 1 patient.

Discussion

The use of ^{18}F-FDG PET provides an interesting alternative to conventional imaging procedures in patients with malignant disease. Indeed, the use of increased ^{18}F-FDG metabolism as an indication of disease makes PET independent of morphologic abnormalities. As reported by several authors, intermediate and high-grade non-Hodgkin's lymphomas (NHL) demonstrate high ^{18}F-FDG uptake and this can be used to depict disease involvement, detect recurrences and assess the results of therapy.[5-18] Preliminary data published by Newman *et al*.[5] suggested an excellent accuracy for ^{18}F-FDG PET imaging of thoraco-abdominal lymph nodes. Sixteen patients (11 NHL, 5 HD) prospectively underwent ^{18}F-FDG PET and CT. All sites of adenopathy seen at CT were also detected by attenuation-corrected ^{18}F-FDG PET images. Hoh *et al*.[7] evaluated whole-body ^{18}F-FDG PET as an imaging modality for the initial staging or restaging of 7 HD and 11 NHL patients. Whole-body PET images were obtained without tissue attenuation correction. Accurate staging was achieved in 17 of the 18 patients using a PET-based staging algorithm compared to in 15 when conventional staging was used. In 5 patients, whole-body PET showed additional sites not detected by conventional procedures, whereas conventional staging demonstrated additional sites in 4 patients. The disease was upstaged by PET in 3 patients whereas in 1 NHL patient the clinical stage would have been incorrectly underestimated. Stumpe *et al*.[9] studied 10 patients with HD at diagnosis by non-attenuation-corrected ^{18}F-FDG PET. ^{18}F-FDG PET missed no sites seen on CT, but additional sites were found in one patient. In another patient CT falsely suggested more extensive disease than PET, without resulting in a change in patient management. The value of ^{18}F-FDG PET in staging of patients with HD is a little difficult to assess in these small series of patients, often including NHL patients. Weidmann *et al*.[11] reported that PET could be considered sufficient for staging the majority of 20 patients with HD, but that PET may have disadvantages in the evaluation of extranodal lymphoma. Attenuation correction was not usually performed in their study. Extranodal manifestations were detected only by conventional staging in 3 patients and only by PET in 2 patients. More advanced stages were documented by PET in 3 patients. Bangerter *et al*.[8] compared attenuation-corrected ^{18}F-FDG PET images with conventional methods (CT, ultrasound, bone scanning, bone marrow biopsy, liver biopsy, laparotomy) in a larger group of patients. ^{18}F-FDG PET was positive in 38 of 44 (86%) patients at sites of documented disease. As a consequence of PET findings 5 patients had to be upstaged and 1 patient had to be downstaged (6/44 = 14%) resulting in changes in treatment strategy in all 6 patients. ^{18}F-FDG PET failed to visualize sites of HD in 4 patients. A false positive result was obtained in 2 patients.

Our study is the second largest one to evaluate the value of PET in the initial staging of patients with HD. Excluding incorrect or undetermined cases, we observed a downstaging in 1 patient and an upstaging in 3 patients (4/33 = 12%) (Table 4). However, in our study the treatment strategy was not changed solely based on ^{18}F-FDG PET findings, explaining why confirmation by biopsy of unknown sites was only obtained in 1 patient. A biopsy was not performed for ethical reasons in the other patients. Two of the three patients who presented more advanced disease on ^{18}F-FDG PET were relapsed patients. Re-induction chemotherapy followed by high-dose chemotherapy and autologous stem cell transplantation was thus indicated independently of disease extension. Treatment with polychemotherapy alone is internationally recognized as a standard treatment for most patients with Hodgkin's disease.[24] However, the treatment strategy for early stage HD could change in the near future.[4,25] Brief chemotherapy and involved field irradiation could become the treatment of choice. In the study published by Bangerter *et al*.[8] one patient was upstaged from stage I to II, three patients from stage II to IV and another patient from stage III to IV. The treatment strategy had to be changed in each case based on the management of HD at the University of Ulm (Germany).

In our study non-attenuation-corrected ^{18}F-FDG PET failed to visualize abdominal and retroperitoneal 1-cm lymph nodes in one patient and very limited focal bone marrow infiltration in another patient (Table 4). Incorrectly, radiotherapy was suggested by ^{18}F-FDG PET as an appropriate treatment option in the former of these 2 patients. However, actual treatment was always based

on conventional staging alone. Treatment would have been inappropriate if it were based only on PET (stage IIA by PET, stage IIIA by conventional staging procedures). Treatment strategy based on ^{18}F-FDG PET alone was not analyzed by Bangerter *et al*.[8] However, incorrect management of some patients in this study is probable because 4 false negative and 2 false positive results in some sites of HD were reported. The technical conditions of our study have to be considered. We have not performed attenuation correction until recently when we acquired a new system using a single photon source (cesium-137) for transmission studies.[26] However, it remains to be demonstrated that attenuation correction must be tried out for the primary staging of malignant lymphoma by ^{18}F-FDG PET. Kotzerke *et al*.[27] retrospectively evaluated 51 untreated patients with either NHL (n=29) or HD (n=22). In this study, attenuation correction did not improve the diagnostic accuracy of ^{18}F-FDG PET in the detection of lymph node or organ involvement during the primary staging of lymphoma. Bengel *et al*.[28] also concluded that attenuation correction was not necessary for lesion detection in a study of 34 patients undergoing PET for the staging of malignancies. In our study, the sensitivity of PET was not better in the 10 patients who had attenuation correction compared to in those who did not.

One of the main uses of ^{18}F-FDG PET in the future is likely to be the assessment of viable tumor in patients with residual masses after treatment for lymphoma.[17,18] We compared ^{18}F-FDG PET to CT in the post-treatment evaluation of 54 patients with HD (n=19) or intermediate/high-grade NHL (n=35). The detection of viable tumor by ^{18}F-FDG PET after the end of treatment had a higher predictive value for relapse than classical CT scan imaging (positive predictive value: 100% versus 42%, retrospectively). This could help identify patients requiring intensification immediately after completion of chemotherapy.

In conclusion, ^{18}F-FDG PET provides an easy and efficient whole-body method for the evaluation of patients with HD. ^{18}F-FDG PET never missed tumor masses >1 cm. ^{18}F-FDG PET detected additional sites of disease not seen by conventional procedures and identified absence of disease in sites suspected of involvement by HD based on conventional procedures. However, in our patient group, it did not determine changes in therapy.

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All the authors participated actively in the design, execution, analysis and writing up of the study. GJ, YB, MFF and GF were involved in the clinical diagnosis and treatment of patients and in the collection of clinical data. FN, PP and PR were involved in all practical aspects of nuclear medicine from image acquisition to interpretation. All seven authors actively participated in correlating clinical and imaging data. They approved the content of the manuscript. They accepted the order of authorship. The order of authorship is related to the importance of their contribution to the analysis, writing up and revision of the manuscript.

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Potential implications for clinical practice

^{18}F-FDG PET provides an easy and efficient whole-body method for the staging of patients with HD; ^{18}F-FDG PET gives additional information to conventional staging procedures; further studies are warranted to determine the impact of PET on treatment strategy; one main use of ^{18}F-FDG PET in the future is likely to be the assessment of viable tumor after treatment for HD.

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