Evaluation of Therapy for Lymphoma

Guy Jerusalem, MD, PhD,* Roland Hustinx, MD, PhD,† Yves Beguin, MD, PhD,* and Georges Fillet, MD, PhD*

Positron emission tomography (PET) using 18F-fluorodeoxyglucose (18F-FDG) is the best noninvasive imaging technique for to assess response in patients suffering from lymphoma. Early response evaluation (“interim PET”) after one, a few cycles, or at midtreatment can predict response, progression-free survival, and overall survival. We calculated from data of 7 studies an overall sensitivity to predict treatment failure of 79%, a specificity of 92%, a positive predictive value (PPV) of 90%, a negative predictive value (NPV) of 81%, and an accuracy of 85%. Although it is not yet indicated to change patient management based on residual 18F-FDG uptake on interim scan in chemotherapy-sensitive patients, prospective studies evaluating the role of an interim PET in patient management clearly are warranted. 18F-FDG PET also has an important prognostic role in relapsing patients after reinduction chemotherapy before high-dose chemotherapy (HCT) followed by autologous stem cell transplantation (ASCT). However, all chemotherapy-sensitive patients remain candidates for HCT followed by ASCT, even if 18F-FDG PET showed residual 18F-FDG uptake. We calculated from data of 3 studies an overestimated risk of relapse in 16% of all PET-positive patients. Some patients with residual 18F-FDG uptake will have a good outcome after HCT followed by ASCT. 18F-FDG PET is the imaging technique of choice for end-of-treatment evaluation. However, 18F-FDG is not specific for tumoral tissue. Active inflammatory lesions and infectious processes can be falsely interpreted as malignant residual cells. However, a negative 18F-FDG PET cannot exclude minimal residual disease. Consequently, it is always indicated to correlate PET findings with clinical data, other imaging modalities, and/or a biopsy. We calculated, from data of 17 studies in end-of-treatment evaluation, a sensitivity of 76%, a specificity of 94%, a PPV of 82%, a NPV 92%, and an accuracy of 89%.

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Patients suffering from Hodgkin’s disease (HD) or non-Hodgkin’s lymphoma (NHL) can be cured by appropriate radiotherapy and/or chemotherapy. Long-term survival rates are as high as 90% for subgroups of patients with HD and 50% for those with high-grade NHL. Relapsing patients can be cured by second-line salvage treatments, including most times high-dose chemotherapy (HCT) followed by autologous stem cell transplantation (ASCT). Accurate staging and restaging allows the optimal selection of treatment options. Shorter treatment cycles are the goal of ongoing research in a subgroup of low-risk patients in an attempt to minimize side effects related to treatment. High-risk patients or those with persisting disease after first-line therapy may benefit from more aggressive treatments. The assessment of response to treatment is one of the most challenging aspects in the imaging of patients suffering from lymphoma. It is reasonable to use salvage therapy at the time of minimal residual disease rather than at the time of a clinically overt relapse. Furthermore, the earlier discontinuation of an unsuccessful treatment would avoid the associated toxicity. The presence of a residual mass during or after treatment is an important clinical issue. Unfortunately, computed tomography (CT) and magnetic resonance imaging (MRI) are unable to differentiate residual disease from fibrosis.

Until recently, gallium-67 (67Ga) scintigraphy was the imaging technique of choice to assess response to treatment in HD and in high-grade NHL. However, it suffers from low spatial resolution and a lack of specificity. Its sensitivity is low in infradiaphragmatic disease because of physiological uptake in the abdomen. Its limitations in low-grade NHL also are well known. Moreover, a 67Ga scintigraphy should always be performed before treatment to determine whether the individual patient has a gallium-avid lymphoma. Positron emission tomography (PET) using 18F-fluorodeoxyglucose

*Division of Medical Oncology, Department of Medicine, University of Liège, Liège, Belgium.
†Division of Nuclear Medicine, Department of Medicine, University of Liège, Liège, Belgium.
Address reprint requests to Guy Jerusalem, MD, PhD, Medical Oncology, CHU Sart Tilman, B35, B-4000 - Liège 1, Belgium. E-mail: g.jerusalem@chu.ulg.ac.be
(18F-FDG) is now widely used in the management of malignant tumors including lymphoma. Despite the important role of 67Ga scintigraphy in response evaluation, it appears now that 18F-FDG PET is more sensitive for the detection of nodal and extranodal sites of disease. Furthermore, 18F-FDG PET also is considered to be more convenient than 67Ga scintigraphy because a PET study can be performed 1 hour after the injection of 18F-FDG whereas the scintigraphy must be performed several days after the administration of 67Ga. 18F-FDG PET is without any doubt the best noninvasive imaging technique for response assessment in patients suffering from lymphoma.

Consequently, it is very important to take into account the shortcomings of 18F-FDG PET to avoid misinterpretation of PET findings. Current 18F-FDG PET instrumentation have a spatial resolution of approximately 5 to 8 mm. Radiotracer uptake in structures less than twice the spatial resolution of the tomograph can be underestimated (= partial volume effect). There is also a risk of temporarily reduced metabolic activity after chemotherapy. Early assessment of response is performed, whenever possible, the last day before or even the same day of a new cycle of chemotherapy. The best time for end of treatment evaluation remains unknown, but most investigators suggest waiting at least 1 month after the last day of chemotherapy and 3 months after the last dose of radiotherapy. It is important to understand that 18F-FDG PET can never exclude minimal residual disease, even if the spatial resolution of 18F-FDG PET improves in the future. It is not possible to decide to stop a treatment based only on a negative 18F-FDG PET. It may be indicated to repeat 18F-FDG PET during routine follow-up to overcome insecurities regarding the potential of residual tumor at the end of treatment. Residual lymphoma also may be missed or its extent underestimated because the lymphoma is not 18F-FDG avid or has very low-grade uptake, but this is extremely uncommon. However, positive findings on PET do not necessarily represent residual disease. Meticulous evaluation of PET images is mandatory to avoid false-positive PET findings associated with muscular tension or normal intestinal structures. Brown fat can avidly incorporate 18F-FDG, especially in lean patients. Physiological uptake can be misinterpreted, particularly by an inexperienced observer. 18F-FDG is not a tumorspecific radiotracer because antiinflammatory cells, such as activated macrophages, leukocytes or granulation tissues, show 18F-FDG avidity. Therefore, active inflammatory lesions and infectious processes can be falsely interpreted as malignant residual cells. Documented causes of false-positive PET studies in response assessment of lymphoma patients are shown in Table 1. A nuclear medicine physician experienced in 18F-FDG PET interpretation often will be able to recognize patterns of uptake as being caused by benign processes. He or she also will be able to recognize when benign uptake cannot be differentiated from malignant and, consequently, whether further workup is indicated.

### Early Response Evaluation

Early prediction of response to therapy could potentially identify those patients who will benefit most from stand-
assessment remains unknown. Early response evaluation by 18F-FDG PET (“interim PET”) after one, a few cycles, or at midtreatment can predict response, progression-free survival (PFS), and overall survival (OS) in lymphoma patients (Table 2).7,20,53-57 Most studies included only patients suffering from NHL.20,53,54,56 Two studies included a mixed patient population,55,57 and 1 study included only patients suffering from HD.7 Results in HD are very preliminary because 181 of the 217 patients included in these 7 studies suffered from NHL. In one study,55 a dual-head coincidence camera was used, whereas the others used dedicated PET systems. We calculate for PET an overall sensitivity of 79%, a specificity of 92%, a positive predictive value (PPV) of 90%, a negative predictive value (NPV) of 81%, and an accuracy of 85% (Table 2).

Spaepen and coworkers56 showed that the predictive value of 18F-FDG PET is independent of conventional prognostic factors before treatment (International Prognostic Index: IPI). Kostakoglu and coworkers55 reported that PET findings obtained after the first cycle correlated better with PFS than 18F-FDG PET findings obtained after completion of chemotherapy. Most studies are oversimplified by defining only 2 categories of patients, either with or without residual 18F-FDG uptake in areas initially involved by lymphoma. Mikhaeel and coworkers53 described a third group of patients with minimal residual uptake on interim PET defined as low-grade, just above the background, in only one focus. The authors analyzed these patients together with PET-negative patients because they observed no relapse in all 4 patients presenting minimal residual uptake. Semiquantitative studies may be more appropriate but methodological problems remain to be resolved.58 A rapid decrease of tumor size may influence 18F-FDG uptake. Residual radioactivity concentration in structures less than twice the spatial resolution of the tomograph can be underestimated (partial volume effect). The use of SUV analysis also must take into account the influence of different imaging times over multiple bed positions because 18F-FDG uptake in lymphoma does not reach a plateau in the 3-hour postinjection time.

18F-FDG PET is the best noninvasive imaging technique for early response evaluation (Figs. 1-3). At this time it allows one to separate 2 categories of patients, either with or without residual 18F-FDG uptake. However, 18F-FDG PET is not a perfect indicator of response because some PET-positive patients will have a good outcome (Fig. 4). The probability that PET remains positive depends on the sensitivity of the tomograph (smallest lesion that can be detected), the biology of the tumor (more rapid response in aggressive tumors), the tumor mass at diagnosis (tumor shrinkage below the detection level, later in larger tumors), the drugs used (impact of monoclonal antibodies such as rituximab), the dose-intensity of chemotherapy (more rapid regression if higher doses), and the interval between the last day of chemotherapy and 18F-FDG PET (risk of temporarily reduced metabolic activity early after chemotherapy). Furthermore, Spaepen and coworkers59

<table>
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<tr>
<th>Authors</th>
<th>No. of Cycles Before Evaluation</th>
<th>Median Follow-Up (Months)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
<th>Accuracy</th>
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<td>Mikhaeel et al53</td>
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<td>90% (15/17)</td>
<td>72% (15/21)</td>
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<td>75% (13/18)</td>
<td>79% (16/21)</td>
</tr>
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<td>Kostakoglu et al55</td>
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<td>19</td>
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<td>85% (9/10)</td>
<td>85% (9/10)</td>
</tr>
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<td>3-4</td>
<td>36</td>
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<td>87% (14/16)</td>
<td>87% (14/16)</td>
<td>87% (14/16)</td>
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<td>94% (16/17)</td>
<td>94% (16/17)</td>
<td>94% (16/17)</td>
<td>94% (16/17)</td>
</tr>
<tr>
<td>Friedberg et al7</td>
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<td>92% (100/109)</td>
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<td>24</td>
<td>55% (22/40)</td>
<td>71% (29/41)</td>
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<td>71% (29/41)</td>
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</tbody>
</table>

Table 2 Predictive Value of Whole-Body 18F-FDG PET for Early Response Assessment (Adapted from Jerusalem and Hustinx19)
Figure 1  Stage II A high-grade NHL in a 53-year-old patient. $^{18}$F-FDG PET performed at diagnosis shows highly hypermetabolic lymph nodes in the left axillary and cervical areas (A, 3D projection image). PET performed after 3 courses of chemotherapy shows a complete metabolic response (B, 3D projection image). The patient is in complete clinical remission 6 months after completing the treatment.

Figure 2  Diffuse large B-cell NHL in a 49-year-old patient. $^{18}$F-FDG PET performed at baseline shows several foci of increased activity in the right cervical and infraclavicular areas, as well as in the spleen (arrows in A, 3D projection image). $^{18}$F-FDG PET performed after completion of induction chemotherapy (4 courses) shows a normal distribution of the tracer (B, 3D projection image). No relapse was observed (follow-up: 1 year).
**Figure 3** HD in a 56-year-old woman. $^{18}$F-FDG PET performed at baseline shows multiple foci of increased activity in cervical and mediastinal areas as well as right hilar and lung infiltration (A, 3D projection image). $^{18}$F-FDG PET performed after 2 cycles of polychemotherapy indicates residual $^{18}$F-FDG uptake in a right cervical lymph node (B, 3D projection image). Treatment failure was observed at the end of treatment (C, 3D projection image).

**Figure 4** High-grade gastric NHL in a 42-year-old man. In addition to the large gastric mass, $^{18}$F-FDG PET also shows increased activity in a celiac node (A, 3D projection image). Even though the PET study performed 5 weeks later, early on during treatment, showed complete remission (B, 3D projection image), a locoregional recurrence was observed 6 months later, as well as right para-aortic nodes (arrow in C, 3D projection image).
have shown in a tumor mouse model that a transient increase in inflammatory cells may result in overestimation of the fraction of viable cancer cells. Consequently, it is not yet indicated to change patient management based on residual 18F-FDG uptake on interim scan in chemotherapy-sensitive patients. However, prospective studies evaluating the role of interim PET in patient management are clearly warranted.

### Evaluation of Chemosensitivity Before High-Dose Chemotherapy

HCT followed by ASCT is the treatment of choice for patients who relapse from NHL after conventional chemotherapy but who remain chemotherapy-sensitive. It is also the best treatment option for most patients who suffer from relapsing or progressive HD after standard treatment. 18F-FDG PET may be able to better predict which chemosensitive patients might ultimately benefit from ASCT. Unfortunately, conventional diagnostic methods are not very accurate for the selection of patients who would benefit from ASCT. In fact, half of chemotherapy-sensitive patients suffering from NHL will relapse after ASCT, resulting in an overall survival in relapsed patients of only 25% to 30% at 2 years. 18F-FDG PET findings after induction chemotherapy are not discussed by the authors.

The prognostic value of 18F-FDG PET is higher at the end of induction chemotherapy than after transplantation. The sensitivity and NPV is lower after transplantation probably because of a transient reduction of tumoral glucose metabolism shortly after intense therapy. Interestingly, a similar prognostic value also was not obtained during the early phase of induction therapy. Cremerius and coworkers suggested that sequential 18F-FDG PET after 3 cycles and before HCT is indicated for response evaluation in patients undergoing 5 to 7 courses of induction chemotherapy. However, when the analysis was restricted to 18F-FDG PET findings after induction chemotherapy and before HCT, similar results were obtained: 5 of 15 patients with a negative PET relapsed compared with 7 of 9 patients with a positive PET (data included in Table 3). Unfortunately, this easier and less-expensive approach was not discussed by the authors.

Patients with a negative PET after the reinduction chemotherapy have a better prognosis and are good candidates for HCT followed by ASCT. However, it is not indicated to exclude chemotherapy-sensitive PET-positive patients from ASCT based on an overestimated risk of relapse in 16% of all PET-positive patients. Some patients with residual 18F-FDG uptake will have a good outcome after HCT followed by ASCT. 18F-FDG PET provides additional informations when compared with the IPI or with the age-adjusted IPI.

Spaepen and coworkers reported that 18F-FDG PET before transplantation is even a stronger prognostic factor than IPI. The standard uptake values (SUVs) in patients with a later relapse are higher than in patients remaining in clinical complete remission. There is also only a significant decrease of SUV after induction chemotherapy in patients who reached a clinical complete remission after ASCT. However, semiquantitative sequential studies add no useful prognostic information compared with a single 18F-FDG PET study (even without semiquantitative analysis) realized at the end of treatment. Cremerius and coworkers suggested that sequential 18F-FDG PET after 3 cycles and before HCT is indicated for response evaluation in patients undergoing 5 to 7 courses of induction chemotherapy. However, when the analysis was restricted to 18F-FDG PET findings after induction chemotherapy and before HCT, similar results were obtained: 5 of 15 patients with a negative PET relapsed compared with 7 of 9 patients with a positive PET (data included in Table 3). Unfortunately, this easier and less-expensive approach was not discussed by the authors.

The prognostic value of 18F-FDG PET is higher at the end of induction chemotherapy than after transplantation. The sensitivity and NPV is lower after transplantation probably because of a transient reduction of tumoral glucose metabolism shortly after intense therapy. Interestingly, a similar prognostic value also was not obtained during the early phase of induction therapy. Cremerius and coworkers showed that only a sustained response to induction therapy is predictive of more favorable outcome. In contrast, sequential PET studies at baseline and after 3 of 5 to 7 cycles of induction therapy were not able to predict outcome. The results reported by Schot and coworkers in early response evaluation after 2 cycles of reinduction chemotherapy also are rather disappointing. If the analysis is restricted to patients who really undergo ASCT, they observed a sensitivity of 72% (13/18), a spec-

### Table 3 Predictive Value of Whole-Body 18F-FDG PET After Reinduction Chemotherapy Before Autologous Stem Cell Transplantation

<table>
<thead>
<tr>
<th>Authors</th>
<th>Median Follow-Up (Months)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
<th>Accuracy</th>
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<td>Becherer et al</td>
<td>13</td>
<td>100% (8/8)</td>
<td>71% (5/7)</td>
<td>80% (8/10)</td>
<td>100% (5/5)</td>
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<td>Cremerius et al</td>
<td>30</td>
<td>58% (7/12)</td>
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<td>67% (10/15)</td>
<td>71% (17/24)</td>
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<tr>
<td>Spaepen et al</td>
<td>50</td>
<td>90% (26/29)</td>
<td>86% (25/29)</td>
<td>87% (26/30)</td>
<td>89% (25/28)</td>
<td>88% (51/58)</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td>84% (41/49)</td>
<td>83% (40/48)</td>
<td>84% (41/49)</td>
<td>83% (40/48)</td>
<td>84% (81/97)</td>
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Table 4 Predictive Value of Whole-Body 18F-FDG PET for Post-Treatment Evaluation in a Mixed Patient Population (Adapted from Jerusalem and Hustinx19)

<table>
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<tr>
<th>Authors</th>
<th>Median Follow-Up (Months)</th>
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<td>de Wit et al20</td>
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<td>Jerusalem et al11</td>
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<tr>
<td>Zinzani et al35</td>
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<td>Mikhaeel et al76</td>
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<td>Naumann et al43</td>
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<td>12</td>
<td>100% (14/14)</td>
<td>97% (59/61)</td>
<td>87% (14/16)</td>
<td>100% (59/59)</td>
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<tr>
<td>Foo et al77</td>
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<td>57% (4/7)</td>
<td>100% (17/17)</td>
<td>100% (4/4)</td>
<td>85% (17/20)</td>
<td>87% (21/24)</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td>79% (67/85)</td>
<td>94% (257/272)</td>
<td>82% (67/82)</td>
<td>93% (257/275)</td>
<td>91% (324/357)</td>
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Achieving a complete remission is a major objective in patients with HD or NHL because it usually is associated with a longer progression-free survival than a partial remission.66 However, in as many as 64% of all HD cases67,68 and in 30% to 60% of all NHL cases,69 computed tomography or magnetic resonance imaging show abnormalities during restaging. Residual masses are observed more frequently in patients with an aggressive NHL and a large tumor mass at diagnosis and in patients suffering from scleranodular HD. Unfortunately, conventional imaging cannot differentiate between benign fibrous tissue, an inflammatory process, or persistent malignant disease. Only a maximum of 20% of residual masses at the completion of treatment are reported to be positive for lymphoma on biopsy and will eventually relapse.70-74 If the tumor is easily accessible, such as an enlarged peripheral lymph node, the questionable lesion should be excised and histologically analyzed. In other localizations, it is much more difficult to perform the biopsy. For example, a mediastinal tumor can only be biopsied by mediastinoscopy or open thoracic surgery. This procedure is associated with some morbidity and a high failure rate for a pathological diagnosis because of the relative small amount of tissue that can be resected.

Therefore, functional imaging techniques are of great interest in this situation.62 Ga scintigraphy has become a standard procedure to assess remission and the nature of residual masses.71 However, its sensitivity for staging lymphoma varies with the localization, the size, and the cell type of the lesion. Recent studies indicate the high accuracy of 18F-FDG PET for end-of-treatment response assessment.7,11,24-26,30,33,35,36,53,75-80 Two studies compare directly 18F-FDG PET and 67Ga scintigraphy.7,77 Friedberg and coworkers5 found a sensitivity of 80% for 18F-FDG PET compared with 40% for 67Ga scintigraphy. Foo and coworkers77 observed that 18F-FDG PET has superior accuracy in staging and restaging compared with gallium scans. The PPV of PET and gallium scans for relapse given a residual mass were 100% and 0%, respectively. The NPV was 76% and 70%, respectively. 18F-FDG PET is now considered the noninvasive imaging technique of choice for the detection of residual disease after treatment. According to the clinical situation, it allows either directed biopsies to be performed or further treatment to be administered. A positive 18F-FDG PET study after treatment is related in most patients to residual tumor cells accumulating the radiotracer.

However, 18F-FDG uptake is not specific for tumoral tissue. In particular, when abnormal 18F-FDG uptake is observed outside the initially involved sites, infectious or inflammatory lesions have to be excluded. Consequently, it is always indicated to correlate PET findings with clinical data, other imaging modalities, and/or a biopsy before starting salvage therapy. However, a negative 18F-FDG PET study cannot exclude minimal residual disease leading later to a clini-
cal relapse. Tables 4 through 6 summarize the predictive value of whole-body PET in the end of treatment evaluation as reported in selected papers written in English. We are aware of the limitations of these studies. Patient populations were small and most times very heterogenous. The natural history of low-grade and high-grade NHL is very different, but all patients were analyzed together in some studies. The follow-up time also is a critical factor. However, these studies give us useful informations about the value of 18F-FDG PET in the end of treatment evaluation. In a mixed population of 357 patients (HD: 174, NHL: 18311,24,30,35,43,75-77 we calculated an overall sensitivity of 79%, a specificity of 94%, a PPV of 82%, a NPV of 93%, and an accuracy of 91%. Three articles31,81,82 were not included because only the region of interest (residual mass) instead of the whole-body was studied by 18F-FDG PET in most patients.

Lively and coworkers83 reported only PET findings in the areas initially involved by lymphoma. Furthermore, 12 of 40 patients received radiotherapy after 18F-FDG PET, potentially influencing outcome, explaining why this study was not included in Table 4. In a selected group of 257 patients suffering from HD (Table 5),7,25,26,33,36,78,79 we calculated a sensitivity of 80%, a specificity of 91%, a PPV of 74%, a NPV of 91%, and an accuracy of 89%. Two articles31,81 were not included because only the region of interest (residual mass) was studied instead of the whole-body PET in most patients.

Weihrauch et al25 28 67% (6/9) 80% (16/20) 60% (6/10) 84% (16/19) 76% (22/29)
Dittmann et al36 6 87% (7/8) 94% (17/18) 87% (7/8) 94% (17/18) 92% (24/26)
Guay et al79 16 79% (11/14) 97% (33/34) 92% (11/12) 92% (33/36) 92% (44/48)
Friedberg et al7 24 80% (4/5) 85% (23/27) 50% (4/8) 96% (23/24) 84% (27/32)
Panizo et al26 28 100% (9/9) 85% (17/20) 75% (9/12) 100% (17/17) 90% (26/29)
Overall 67% (35/52) 100% (86/86) 100% (35/35) 83% (86/103) 88% (121/138)

We explain the differences observed in our experience and in the literature according to histologic subtypes by the better prognosis in HD. Because a relapse is a rare event in HD, the impact of a false-positive PET on the PPV is more important in HD than in NHL. However, the NPV is lower in NHL than in HD. In fact, the risk of relapse is more important in patients with NHL and PET cannot exclude minimal residual disease. The predictive value of relapse depends not only on histologic subtype but also on the initial prognostic factors. The PPV will be higher and the NPV will be lower in a study population including more high-risk patients. Cremerius and coworkers85 observed a NPV of 90% in moderate-risk patients compared with 50% to 67% in high-risk patients. Patient selection criteria also have an impact on the results. Inclusion of patients with known or highly suspected relapse will improve the PPV. However, 18F-FDG PET is only clinically useful if relapse is not definitively known before the patient undergoes the functional imaging studies. Short follow-up will be in favor of a better NPV. To allow comparison between studies, it may be indicated to report 6-month and 1-year progression-free survival data. Most studies are oversimplified by reporting only positive or negative PET findings. However, in routine practice, it is not unusual to be confronted with questionable findings. Only 2 studies discussed this issue.43,85 Both studies found a higher accuracy if questionable lesions are analyzed as negative findings. We have some doubt in our center that accuracy is the most important issue. From a clinical point

Table 5 Predictive Value of Whole-Body 18F-FDG PET for Post-Treatment Evaluation in HD (Adapted from Jerusalem et al19,87)

<table>
<thead>
<tr>
<th>Authors</th>
<th>Median Follow-Up (Months)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
<th>Accuracy</th>
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<tr>
<td>de Wit et al23</td>
<td>26</td>
<td>100% (10/10)</td>
<td>78% (18/23)</td>
<td>67% (10/15)</td>
<td>100% (18/18)</td>
<td>85% (28/33)</td>
</tr>
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<td>94% (17/18)</td>
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<td>94% (17/18)</td>
<td>92% (24/26)</td>
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<td>Spaepen et al78</td>
<td>32</td>
<td>50% (5/10)</td>
<td>100% (50/50)</td>
<td>100% (5/5)</td>
<td>91% (50/55)</td>
<td>92% (55/60)</td>
</tr>
<tr>
<td>Weihrauch et al25</td>
<td>28</td>
<td>67% (6/9)</td>
<td>80% (16/20)</td>
<td>60% (6/10)</td>
<td>84% (16/19)</td>
<td>76% (22/29)</td>
</tr>
<tr>
<td>Guay et al79</td>
<td>16</td>
<td>79% (11/14)</td>
<td>97% (33/34)</td>
<td>92% (11/12)</td>
<td>92% (33/36)</td>
<td>92% (44/48)</td>
</tr>
<tr>
<td>Friedberg et al7</td>
<td>24</td>
<td>80% (4/5)</td>
<td>85% (23/27)</td>
<td>50% (4/8)</td>
<td>96% (23/24)</td>
<td>84% (27/32)</td>
</tr>
<tr>
<td>Panizo et al26</td>
<td>28</td>
<td>100% (9/9)</td>
<td>85% (17/20)</td>
<td>75% (9/12)</td>
<td>100% (17/17)</td>
<td>90% (26/29)</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td>80% (52/65)</td>
<td>91% (174/192)</td>
<td>74% (52/70)</td>
<td>93% (174/187)</td>
<td>88% (226/257)</td>
</tr>
</tbody>
</table>

Table 6 Predictive Value of Whole-Body 18F-FDG PET for Post-Treatment Evaluation in NHL (Adapted from Jerusalem and Hustinx19)

<table>
<thead>
<tr>
<th>Authors</th>
<th>Median Follow-Up (Months)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mikhaeel et al53</td>
<td>30</td>
<td>60% (9/15)</td>
<td>100% (30/30)</td>
<td>100% (9/9)</td>
<td>83% (30/36)</td>
<td>87% (39/45)</td>
</tr>
<tr>
<td>Spaepen et al80</td>
<td>21</td>
<td>70% (26/37)</td>
<td>100% (56/56)</td>
<td>100% (26/26)</td>
<td>84% (56/67)</td>
<td>88% (62/93)</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td>67% (35/52)</td>
<td>100% (86/86)</td>
<td>100% (35/35)</td>
<td>83% (86/103)</td>
<td>88% (121/138)</td>
</tr>
</tbody>
</table>
of view we are in favor of a more sensitive interpretation, allowing earlier salvage therapy in the case of residual disease. To improve specificity we correlate in a second time our findings with clinical informations and other imaging modalities encouraging also, whenever possible, a multidisciplinary interpretation.

Response Assessment After Radioimmunotherapy (RIT)

RIT is a new treatment option in NHL. The antitumor mechanism is based on immunologic effects and radiation damage. Torizuka and coworkers showed in a small study population (14 low- or intermediate-grade NHL) that 18F-FDG PET findings obtained 1 to 2 months after RIT correlated well with the ultimate best response of NHL to RIT. In contrast, earlier 18F-FDG PET findings 5 to 7 days after RIT may fail to reliably assess the long-term therapeutic effect. Further studies are clearly warranted before using 18F-FDG PET routinely for monitoring response to RIT.

References


emission tomography (PET) in the management of lymphoma patients. Ann Oncol 10:1181-1184, 1999