The role of FDG-PET scanning in assessing lymphoma in 2012

C. Bodet-Milin\textsuperscript{a,\ast,e}, T. Eugène\textsuperscript{a}, T. Gastinne\textsuperscript{b}, C. Bailly\textsuperscript{a}, S. Le Gouill\textsuperscript{b,e}, B. Dupas\textsuperscript{c}, F. Kraeber-Bodéré\textsuperscript{a,d,e}

\textsuperscript{a} Nuclear medicine department, Hôtel-Dieu, Nantes University Hospital, 1, place Alexis-Ricordeau, 44093 Nantes cedex 1, France
\textsuperscript{b} Haematology department, Hôtel-Dieu, Nantes University Hospital, 1, place Alexis-Ricordeau, 44093 Nantes cedex 1, France
\textsuperscript{c} Radiology department, Hôtel-Dieu, Nantes University Hospital, 1, place Alexis-Ricordeau, 44093 Nantes cedex 1, France
\textsuperscript{d} Nuclear medicine department, René-Gauducheau Centre, boulevard Jacques-Monod, 44805 Nantes St-Herblain cedex, France
\textsuperscript{e} CRCNA (Nantes/Angers cancer research centre), Inserm UMR 892, 9 quai Moncousu, 44093 Nantes cedex 1, France

**Abstract** Positron emission tomography (PET) has a proven role in the assessment diffuse large B-cell lymphoma (DLBCL) and Hodgkin’s lymphoma (HL). The clinical impact of PET carried out at the end of the patient’s course of treatment is undeniable and recommendations must be followed in the interpretation of these examinations. PET is highly recommended as part of the initial investigations of these diseases because it can be used as a reference for the interpretation at treatment completion and allows disease spread to be assessed with greater sensitivity and specificity than when computed tomography (CT) is used. It seems to be certain that PET is useful for interim examinations too, in terms of assessing prognosis in DLBCL and HL, although its impact in terms of early changes to treatment is still to be determined. The criteria for interpreting the results of these early assessments are still evolving and the annual meetings in Menton, France, of groups of experts are leading towards a uniform interpretation method. In other types of lymphoma, PET can be useful for confirming local disease staging, especially in follicular lymphoma, and for guiding biopsy in patients with low-grade lymphoma that is suspicious for transformation into more aggressive disease. Several studies are in agreement that PET is valuable for assessing prognosis at treatment completion in FL and mantle cell lymphoma, but prospective studies are needed for this new indication to be validated.

\textsuperscript{\ast} Corresponding author.  
E-mail address: caroline.milin@chu-nantes.fr (C. Bodet-Milin).

\textcopyright{} 2012 Éditions françaises de radiologie. Published by Elsevier Masson SAS. All rights reserved.

2211-5684/$ – see front matter © 2012 Éditions françaises de radiologie. Published by Elsevier Masson SAS. All rights reserved.  
http://dx.doi.org/10.1016/j.diii.2012.12.005
Since the early 2000s, the assessment of lymphoma has been essentially based on results from clinical examination, computed tomography (CT), and bone marrow biopsy (BMB). These investigations allow clinicians to determine the initial stage of the disease according to the Ann Arbor classification and to assess therapeutic response based on the standardised international criteria brought together by Cheson et al. in the Journal of Clinical Oncology in 1999 [1]. CT has relatively high sensitivity and specificity for pretreatment staging, but low specificity for post-treatment evaluation due to the high frequency of residual masses (RM), especially if there is initially bulky disease [2–5]. Therapeutic response, based on the dimensions of lymphoma masses measured using CT, is classed either as partial response (PR) (the longest transverse diameter of the six largest nodes or nodal masses has decreased by 50% or more), complete response unconfirmed (CRu) (residual lymph node mass larger than 1.5 cm in the greatest transverse diameter has regressed by more than 75%, nodes that were confluent have regressed by more than 75% in their greatest transverse diameter) and complete response (CR) (disappearance of all radiological signs of disease, all nodes and nodal masses must have regressed to normal size: below or equal to 1.5 cm for lymph nodes that measured over 1.5 cm before treatment, involved nodes that measured 1.1 to 1.5 cm in their greatest transverse diameter before treatment must not measure more than 1 cm after treatment or they must have decreased by 75% or more) [1]. These criteria clearly have limitations in terms of the characterisation of RM in patients with PR or CRu, and these are found in over 60% of patients with Hodgkin’s lymphoma (HL) and probably 40% of patients with aggressive non-Hodgkin’s lymphoma (NHL) [2,5,6].

The clear value of molecular imaging in characterising RM lies in its potential to differentiate between necrotic and fibrotic tissue and viable tumour tissue. Biopsy is an option but it is an invasive procedure and only a positive result is useful, as it is always possible that the specimen was taken from an area of non-active disease. Furthermore, this exploration obviously does not take in the whole body. Molecular imaging has seen a considerable increase in popularity with the development of positron emission tomography (PET) using fluorodeoxyglucose labelled with fluorine 18 (FDG), which is a three-dimensional non-invasive imaging technique that offers a much improved diagnostic performance in terms of sensitivity and resolution compared to conventional nuclear medicine investigations. FDG, a glucose metabolism tracer, is effectively a tracer of cell viability. The technique has also benefited from the development of hybrid PET/CT systems. These fusion images mean that sites of abnormality can be localised and sensitivity and specificity are improved when compared to that of each technique used alone [2].

The contribution offered by FDG-PET has been demonstrated in lymphoma assessment and standardised assessment criteria integrating the molecular imaging approach were published in 2007 [7]. In order to validate this technique, the authors distinguished lymphomas by histological types and FDG uptake, while the treatment process was divided into four stages according to its goals: initial investigations, interim treatment assessment, final assessment of treatment, and post-treatment follow-up. Standardised criteria for interpreting PET carried out at treatment completion have been proposed [8]. Irrespective of the type of lymphoma, PET is not recommended for post-treatment follow-up. This is because, aside from the cost and even though the examination would certainly detect relapses sooner, the impact on the patient has not been established and its high sensitivity runs the risk of generating false positives (FP), which would mean that every finding of hypermetabolism suspicious for disease would need to be confirmed by histology [2–7].

**Positron emission tomography and the initial investigations**

In the initial investigations for HL and DLBCL, PET does not replace the standard Ann Arbor assessment using CT and bone marrow biopsy but it is highly recommended firstly for an improved evaluation of disease spread and secondly to facilitate exploration at treatment completion. This is because PET/CT assessment has over 95% sensitivity and specificity, which means that in 10 to 20% of cases changes can be made to staging, particularly in disease staged at I/II on CT [9–18], sometimes leading to changes in therapeutic management. PET/CT offers more information than CT in terms of assessing lymph node localisations smaller than one centimetre in size, as well as liver and spleen involvement, and it is better than BMB for assessing bone marrow localisations and detecting focal involvement (Fig. 1). However, BMB remains the reference investigation for confirming diffuse bone marrow invasion. For other histological types of lymphoma with strong FDG uptake, whether indolent (follicular lymphoma [FL]) or aggressive (mantle cell lymphoma [MCL]), PET can be considered both early on and at treatment completion as part of a clinical trial, if the lymphoma is FDG positive on initial investigations and when response rate is one of the primary endpoints.

**Positron emission tomography and treatment completion investigations in diffuse large B-cell lymphoma and Hodgkin’s lymphoma**

It is clear that it is in the treatment completion investigations for curable lymphomas that FDG-PET plays a decisive role because it allows residual disease to be assessed with 80 to 90% accuracy, outstripping CT which is no more than 40% accurate [19–23]. FDG-PET does this by distinguishing viable tumour tissue from the fibrotic tissue of RM that are often present in patients with no clinical signs or laboratory study results pointing to active disease. This led Juweid et al. in 2005 to compare the standard International Workshop Criteria (IWC) based on CT to an assessment incorporating CT and PET (IWC plus PET) in a series of 54 patients with DLBCL being treated with chemotherapy [19]. When the two classifications were integrated into one multivariate analysis, only the IWC plus PET classification was an independent predictor of progression-free survival (P = 0.008 vs. P = 0.72 for IWC). Some patients in PR according to the IWC were considered by IWC plus PET to be in CR, and this group had a progression-free survival that was no different from those in CR/CRu according to the IWC who were also in CR based on IWC plus
PET. This demonstrates that PET was able to define a group with a better prognosis among the patients in PR according to the IWC. In addition, new assessment criteria were published in 2007, in which CRu had been removed [7] and which considered metabolic response to be more decisive than morphologic response, with the exception of CT detection of progression in the form of small pulmonary lesions that were FDG-negative due to the partial volume effect. However, this situation remains rare in clinical practice and it is tending to become even more so due to technical advances in PET/CT equipment. Indeed, PET systems are able to achieve lower detection thresholds, on the one hand due to greater sensitivity of new generation machines but also due to increasing use of respiratory synchronisation systems that limit partial volume effects. With these systems, CR according to the IWC + PET criteria equates to the disappearance of any evidence of the disease with, for nodal masses with strong FDG uptake before treatment, no possibility of masses of any size if PET is negative and, for nodal masses with variable or negative uptake on PET, regression to normal dimensions seen on CT. For nodal masses with strong FDG uptake before treatment, PR is defined by the presence of at least one PET-positive lesion in an initially involved site, and for nodal masses with variable or negative uptake on PET, regression demonstrated on CT. The IWC + PET criteria have also been validated in HL in a series of 56 patients of which nine had relapsed and 47 were in remission after follow-up of nine years [24]. Using the IWC, responses were categorised as 15 in CR, 20 in CRu, 19 in RP and two with stable disease, with no significant difference in terms of outcome between the patients in CR/CRu and those in PR (P = 0.61). Based on IWC + PET, responses were categorised as 47 in CR, seven in PR and two with stable disease with no significant difference in terms of outcome between the patients in CR/CRu and those in PR (P = 0.61) with a shorter time to the next treatment for PR patients compared to those in CR (P = 0.01). Fig. 2 shows the images of a patient with a mediastinal HL, in metabolic CR according to the IWC + PET criteria, although there was a residual mediastinal mass on CT at the end of treatment. This patient was still in CR several months after treatment ended.

The completion of treatment assessment needs to take place after a suitable timeframe in order to mitigate against the impact of inflammatory phenomena: at least three weeks after chemotherapy has ended and 8 to 12 weeks after radiotherapy is complete [8]. There are some well-known pitfalls in the completion of therapy assessment: FP at the initial site of the disease due to thymus hyperplasia, post-treatment inflammation (especially in radiotherapy), or uptake in brown adipose tissue (Fig. 3); FP away from the initial site of the disease due to infection, overactive bone marrow or spleen after chemotherapy, or growth factors; false negatives (FN) for lesions smaller than 1 cm due to the partial volume effect. Beta-blockers can be administered prior to PET scanning in order to prevent brown adipose tissue uptake, as this can interfere with cervical mediastinal exploration in particular.

At the end of treatment the negative predictive value (NPV) of PET is in the region of 85% all studies considered, including both patients with DLBCL and HL. The rate of 15% FN is due to the inability of the modality to detect microscopic disease that will inevitably lead to relapse. By contrast the positive predictive value (PPV) is lower, especially in HL, barely exceeding 65%. The first studies allow us to consider that around 30 to 40% of patients treated for HL with a positive PET result at the end of treatment will not see disease progression. These FP, mainly due to minimal residual uptake (MRU), can probably be attributed to post-treatment inflammatory phenomena and suggest that MRU on PET should be interpreted or incorporated with clinical information differently depending on whether they occur in HL or DLBCL [23]. These results do however constitute,

**Figure 1.** Positron emission tomography/computed tomography from a patient’s initial investigations into diffuse large B-cell lymphoma. Pathological hypermetabolism of cervical (a) and retroperitoneal lymph nodes (b) smaller than one centimetre in size.
The role of FDG-PET scanning in assessing lymphoma in 2012

Figure 2. a: represents the positron emission tomography/computed tomography images seen in a patient’s initial investigations for mediastinal Hodgkin’s lymphoma; b: images in this same patient at the end of treatment: there is no longer any uptake abnormality in the mediastinum, meaning the patient is in metabolic CR according to the IWC+PET criteria. This patient was still in CR several months after treatment ended.

Figure 3. a: shows uptake in the brown adipose tissue of the neck and mediastinum that interferes with interpretation of the examination; b: positron emission tomography images recorded in the same patient a few days later after premedication with 40 mg of propanolol.

Undeniable progress when compared to CT assessment, which has been the source of a significantly higher number of FP caused by RM. Recently, in a large study of advanced HL, German researchers have confirmed the high NPV of PET for detecting early relapse or progression in patients presenting an RM at completion of their first line of treatment [25].

An international harmonisation project (IHP) has resulted in proposed recommendations with standardised treatment completion interpretation criteria, their specific goal being to reduce FP due to MRU identified on end of treatment assessment [8]. The interpretation criteria, also known as the IHP 2007 criteria, are based on visually analysing PET
images. The criteria suggest that a different interpretation should be made of uptake in an RM measuring 2 cm or more and an RM of between 1.1 and 1.9 cm in which uptake may be underestimated due to a possible partial volume effect. This means that PET must be interpreted as positive in the case of an RM measuring at least 2 cm if activity can visibly be said to exceed that seen in the mediastinal blood pool reference background, and in the case of an RM measuring between 1.1 and 1.9 cm if activity can visibly be said to exceed that of adjacent reference tissue. Specific criteria have been put forward for analysing the spleen, liver, lungs, and areas of bone marrow. In pulmonary lesions, it is important to watch out for common FP due to infection and inflammation, especially if there was no initial involvement in this area. New nodules larger than or equal to 1.5 cm are considered to be positive on PET if their activity exceeds that of the mediastinal blood pool reference background, while new nodules smaller than 1.5 cm are considered to be positive irrespective of uptake. Lesions of the spleen and liver are analysed by comparison to the organ itself. Diffuse overactivity of the spleen can be triggered by growth factor administration. Focal involvement in the bone marrow is interpreted as positive on PET and diffuse involvement is considered to be above all reactive. A negative result on PET does not exclude the presence of mild to moderate invasion and BMB remains the standard diagnostic investigation even if it does only explore a very limited area.

An initial validation of these criteria has been made using a series of 50 patients (26 with Hodgkin’s lymphoma (HL), and 24 with aggressive NHL) and their results on CT/PET carried out 3 to 12 weeks after they completed their treatment and after follow-up at 1 year [26]. Fifty-five RM were detected on CT in 29 patients, 31 of which measured at least 2 cm. Event-free survival was 0% at one year in patients presenting a positive RM result based on the IHP criteria and 96% in patients who had a negative RM result.

### Positron emission tomography and interim monitoring of diffuse large B-cell lymphoma and Hodgkin’s lymphoma

In spite of numerous publications demonstrating the value of FDG-PET for interim therapeutic assessment after one to four cycles of chemotherapy or chemoradiotherapy and immunotherapy [27–36], the current advice is to carry out interim monitoring (after two and/or four cycles) following the IHP recommendations, i.e. when the appropriate length of time has elapsed after the last cycle (between day 17 and 21 for 21-day cycles and between day 10 and 14 for 14-day cycles) and only within the context of a clinical trial. Furthermore, it has not yet been clearly demonstrated that changes in treatment based on PET results are beneficial.

It is well demonstrated in the literature that MRU found on early assessments do not have the same predictive value in both DLBCL and HL [30–35] and the international recommendations suggest that interim PET scan monitoring should be interpreted differently in DLBCL and HL. The interpretation criteria have significantly moved on in recent years and while semi-quantitative methods are today indicated in interim monitoring of DLBCL as the work of the Créteil team suggests [37], a visual assessment remains the reference method for interpreting PET results in HL.

### Positron emission tomography and early assessment of Hodgkin’s lymphoma

Progress in terms of treatment and the development of new chemotherapy regimens has considerably improved survival rates in HL, even in advanced forms, with survival at 5 years of over 90%. However, incidences of post-chemotherapy complications, affecting the cardiovascular system in particular, and of secondary cancers are constantly on the increase, especially when intensive BEACOPP-type regimens are used. The goal today in this curable disease is to define treatment protocols that are most suited to each stage and to how aggressive the disease is, as well as how sensitive it is to chemotherapy. The Ann Arbor staging system and international prognosis score (IPS) are currently the most widely used tools for defining therapeutic management but they are based on criteria defined at diagnosis without taking into account either therapeutic response or how sensitive to chemotherapy the patient’s disease is. In 2007, Gallamini et al. were among the first researchers to prospectively demonstrate the predictive value of PET after two cycles of chemotherapy. In this joint Italian and Danish study that included 260 patients newly diagnosed with HL (190 patients at stages IIb – IVB and 70 at stage IIA with factors for a poor prognosis), the patients were treated with the standard protocol of ABVD followed by radiotherapy when they presented bulky disease or RM [36] and they underwent PET assessment after two cycles of ABVD. The treatment was not changed based on the results of the PET assessment after two cycles. PET results were interpreted visually with RM considered to be positive when residual uptake slightly exceeded uptake in the mediastinum. Progression-free survival at two years was at 12.8% for patients with a positive result on PET and 95.0% for patients with a negative result on PET (P < 0.0001).

The predictive value of PET was an independent predictive factor of the IPS prognostic factors. In a meta-analysis published in 2010, Terasawa et al. [38] subsequently reviewed the prognostic value of early PET taking into account the results from 13 studies covering 360 patients. This meta-analysis found that PET had an overall sensitivity of 81% and specificity of 97%. However, the populations of the different studies brought together in this meta-analysis were not homogenous (localised disease stage/widespread disease), and they were treated using different protocols, with their PET assessments carried out at different points (after two cycles or four cycles), and most importantly these were interpreted using criteria that varied from study to study.

In a 2011 study, Le Roux et al. [39] retrospectively compared the various interpretation criteria that have been successively proposed. Based on the 90 patients included in this study, the NPV remained high irrespective of the criteria used (between 95 and 96%), while the PPV was clearly influenced by the choice of criteria with values of 16% for the initial criteria, 19% for the IHP criteria, 25% for the Gallamini criteria, and 50% for the London scale (threshold for a positive result > 4). However, the validity of these results is limited because interim PET results interpreted using the initial criteria could change how treatment continues.
The role of FDG-PET scanning in assessing lymphoma in 2012

The process PET-scan interpretation study: the patients in this International RM practices. The experts who came together in 2009 at the first International Workshop on Interim PET in Deauville, France, drew up a visual interpretation scale that was initially called the London scale, then renamed the Deauville scale during this meeting and it was decided that studies should be set up to validate this tool (IVS study). This group were concerned that results should be reproducible so they agreed on a threshold of 4 for a result to be considered positive, which was further adapted depending on the study question: if the objective of a study was to find a high positive predictive value with a view to treatment escalation, the threshold for a positive result would be RM uptake ≥ 4. In contrast, if the objective of the study was to find a high negative predictive value with a view to de-escalation, the threshold for a positive result would be lowered so that RM uptake is considered to be positive from 3.

The first results from the IVS study using this visual interpretation scale were presented in September 2011 at the Third International Workshop on Interim Lymphoma in Menton, France. This retrospective validation study covered 261 patients treated between 2001 and 2009 in 17 national and international centres, with HL at an advanced stage or at a local stage with factors for a poor prognosis, who had all been treated with ABVD and had undergone PET assessment at their initial diagnosis and after two cycles. The PET results would not lead to any change in therapeutical management and each examination was reassessed in a centralised process by six reviewers. The first conclusions of this study, which has not yet been published, seem to show that there is significantly higher progression-free survival at 5 years in patients who had a negative PET result at two cycles (taking residual uptake of ≥ 4 as the threshold for a positive result, in line with the Deauville scale) with rates of progression-free survival at five years of 95% for patients with a negative PET-scan at two cycles versus 35% for those with a positive PET-scan, and this finding is independent of the IPS status at diagnosis. These first results are also thought to show that in HL a semi-quantitative analysis, as things stand and based on the SUVmax, has no advantages over a visual analysis [40]. Several prospective treatment escalation and de-escalation studies are currently ongoing in Europe and the USA, so that the impact on survival of treatment changes based on PET results may be more accurately understood.

Positron emission tomography and early assessment in diffuse large B-cell lymphoma

The prognostic value of early PET has also been widely demonstrated in DLBCL. For example, in a retrospective study published very recently, Zinzani et al. [41] used the interpretation criteria defined by Gallamini in 2007 [36] and found that PFS at 5 years was 75% for PET+ patients as against 18% for PET-patients in a population of 91 patients with DLBCL. In 2005, Haioun et al. established the prognostic value of PET carried out after two cycles of anthracycline-containing induction chemotherapy, combined with rituximab in 41% of cases, in a population of 90 patients with aggressive NHL (94% of these had DLBCL) [29]. The PET result was considered to be negative in 54 patients. The prognoses for the PET negative patients and PET-positive patients were significantly different, with event-free survival at two years estimated at 82% and 43% respectively (P < 0.001) and overall survival of 90% and 61% respectively (P = 0.006). The predictive value of PET was reported in the International Prognostic Index (IPI) lower and higher risk groups. In the Terasawa meta-analysis [38] discussed above, the overall sensitivity and specificity values of early PET were in the region of 64% and 87% respectively in 313 patients with DLBCL. However, the same criticism stands as for the HL strand, in that the various studies covered in this meta-analysis took in populations that were not homogenous, who had been treated according to varying therapeutic protocols (the majority without immunotherapy), and who had undergone PET assessment either after two or four cycles, to which different interpretation criteria were applied, although they were essentially based on visual analysis.

In 2009, Itti et al. showed, in a retrospective study of 92 patients treated for DLBCL, that the value of Δ SUV after two cycles was decisive in terms of PFS at two years but also in terms of PPV, with the PPV of PET exceeding 50% when a visual analysis was used in the same patient group that showed a Δ SUV of 85%. In this study, a SUV corresponded to the percentage reduction between the SUVmax of the tumour at diagnosis (PET0) and the SUVmax of the residual tumour after two cycles (even if PET0) [42]. In 2010, the same team used the same 92 patients as before to demonstrate that using the mediastinal as a reference background above which a result on early PET assessment was considered to be positive did not allow a distinction to be made between patients who responded to treatment and those who did not. By contrast, when the liver was used as the reference tissue for a positive result, PFS at 2 years was statistically higher in PET negative patients than in PET-positive patients (82% compared to 52%) [43]. Fig. 4 illustrates the case of a patient carrying a mediastinal DLBCL, with an insufficient response after four cycles of chemotherapy according to visual analysis and Δ SUV. This patient showed no objective response to chemotherapy and died a few months later.

Just as with HL and always with the goal in mind of harmonising practices, the experts who came together at the first and second International Workshops on Interim PET in Deauville in 2009 and then Menton in 2010 decided to set up studies to validate this method of quantitative analysis (IVS study). The first results of the IVS study using these new criteria in DLBCL were presented at the Third International Workshop on Interim Lymphoma and published in the journal Blood in 2011 [44]. This was done using these interpretation criteria in a centralised process of reinterpreting the PET results of 85 patients with DLBCL who had been included in the LNH2007-3B trial. In this study, Casasnovas et al. confirmed that Δ SUV reductions of 66% after two cycles and 70% after four cycles were decisive in terms of survival at 2 years and, more importantly, that the semi-quantitative analysis
Figure 4. Female patient with a mediastinal B-cell lymphoma: a: positron emission tomography/computed tomography at initial investigations showing hypermetabolism of the anterior mediastinal mass; b: PET/CT after four cycles of chemotherapy showing intense hypermetabolism of mediastinal tumour residue, which translates into an insufficient response, while morphologic imaging points to a complete response unconfirmed (CRu); c: PET/CT after six cycles of chemotherapy showing increased mediastinal hypermetabolism, which translates into disease progression that is also visible on morphologic imaging. The patient passed away after several lines of chemotherapy.
was more decisive in terms of prognosis than visual analysis using the IHP treatment completion criteria, and this result was found independently of IPI status and was highly reproducible between individuals. The experts were therefore able to put this quantitative interpretation method after two and four cycles of chemotherapy in the new treatment protocols, whilst putting forward a few caveats, notably that for patients whose SUVmax value was ≤10 at diagnosis, quite a rare situation in clinical practice, the ΔSUV method was probably not terribly suitable.

**Positron emission tomography and other histological types of lymphoma**

In other histological types of lymphoma, FDG-PET can be considered at the end of treatment when identifying the objective response rate, especially the rate of patients in CR, is one of the endpoints of the study [2,7]. The recommendation is that a PET scan should be carried out as part of the inclusion investigations, especially when FDG uptake is variable for the type of lymphoma. The role for interim assessment remains to be determined depending on the treatment plan and the histological type. In FL, PET shows high sensitivity (94–100%) for disease staging and restaging except for when bone marrow involvement is being studied [45–47]. PET may be useful for making a distinction between focal and diffuse involvement. Furthermore, Schöder et al. have showed that since 2005 the different levels of FDG uptake demonstrated by low-grade lymphomas and aggressive lymphomas on metabolic imaging exploring the whole body had been considered to be a useful tool for assessing the transformation of a low-grade lymphoma to more aggressive disease [48]. A prospective study was carried out with the intention of assessing the value of FDG-PET for guiding biopsies in patients with a low-grade lymphoma with clinical signs or laboratory results suspicious for transformation [49]. A semi-quantitative study of SUVmax meant that suspicion for transformation could be established with a PPV and NPV both exceeding 94% (Fig. 5). By contrast, the size of lesions seen on CT was not predictive for Richter’s syndrome (P=0.094). In the same way as for HL and DLBCL, recent studies have suggested that a positive result on PET at the end of treatment for FL was a factor for a poor prognosis, pointing to a risk of early recurrence. In other less common histological types such as mantle cell lymphoma, our group has demonstrated in 44 patients following their first line of treatment that the SUVmax together with the IPI enables patients to be divided into three groups according to their prognosis and that the PFS of patients found to be PET+ using the IHP criteria at the end of chemotherapy was significantly poorer than those who had a negative PET result (P=0.0001) [50]. A second retrospective study into 53 patients confirmed the prognostic value of a negative PET result at treatment completion (IHP criteria used) in patients with mantle cell lymphoma, with significantly better PFS at three years (P=0.0001) [51].

**Conclusion**

In conclusion, the value of FDG-PET for assessing DLBCL and HL has been demonstrated. When PET is carried out at the end of the treatment process, its prognostic impact is
undeniable and the IHP criteria remain the reference criteria at treatment completion. PET is highly recommended as part of initial disease assessment because it is a reference examination that allows an end of treatment assessment to be made, as well as allowing disease spread to be evaluated with greater sensitivity and specificity than when CT is used. It seems certain that interim examinations are useful for prognosis, although different interpretation criteria are used depending on whether the patient has HL or DLBCL. However, the impact of early treatment changes based on PET results remains to be confirmed. The group of experts convening at the International Workshop on Interim Lymphoma were in this way able to validate in 2011 use of visual analysis using the Deauville scale for HL and a semi-quantitative analysis using a SUV for DLBCL. However, further results from prospective international studies will be needed in order for us to understand the impact on prognosis of early treatment changes based on PET results and to thus validate the use of interim PET in clinical practice. For other types of lymphomas, PET may be useful to confirm local disease staging, especially in FL, and to guide the biopsy in a patient with a low-grade lymphoma suspicious for transformation to aggressive disease. PET also seems to have prognostic value at treatment completion in FL and mantle cell lymphoma, although prospective studies will be essential to back up these data.

Disclosure of interest
The authors declare that they have no conflicts of interest concerning this article.

References


The role of FDG-PET scanning in assessing lymphoma in 2012


