Annals of Oncology 20: 508–512, 2009
doi:10.1093/annonc/mdn657
Published online 12 January 2009

The majority of transformed lymphomas have high standardized uptake values (SUVs) on positron emission tomography (PET) scanning similar to diffuse large B-cell lymphoma (DLBCL)

A. Noy[1]*, H. Schöder[2], M. Gönen[3], M. Weissler[4], K. Ertelt[5], C. Cohler[6], C. Portlock[1], P. Hamlin[1] & H. W. D. Yeung[2]

[1]*Department of Medicine, Lymphoma Service;* [2]*Department of Radiology, Nuclear Medicine;* [3]*Department of Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, New York;* [4]*Department of Medicine, New York-Presbyterian, Weill-Cornell Medical Center, New York;* [5]*Humboldt University, Berlin, Germany;* [6]*University of Pennsylvania, Philadelphia, USA*

Received 4 May 2008; revised 18 August 2008; accepted 3 September 2008

Background: We previously correlated non-Hodgkin's lymphoma (NHL) histology with ^{18}fluoro-2-deoxyglucose–positron emission tomography (FDG–PET) intensity: a standardized uptake value (SUV) >10 predicted aggressive lymphoma with >80% certainty and an SUV >13, with >90% certainty.

Patients and methods: To evaluate SUV in transformed lymphoma, we identified all FDG–PET scans for NHL at Memorial Sloan-Kettering Cancer 1999–2007 with (i) biopsy-proven transformation, (ii) no therapy 60 days before PET scan and (iii) FDG–PET scans no more than 60 days before or 90 days after transformation.

Results: In 5 of 40 patients, the biopsy site was excised before PET; in two, only marrow was biopsied. In the remaining 33 patients, the SUV of the biopsy site ranged from 3 to 38, mean 14, median 12. Eighteen of 33 biopsies (55%) had an SUV >10 and 16 (48%) >13. The highest SUV in a transformed lymphoma PET scan ($SUV_{study\text{-}max}$) ranged from 3.2 to 40, mean 15, median 12. Twenty-five of 40 patients (63%) presented with an $SUV_{study\text{-}max}$ >10 and 20 (50%) >13.

Conclusions: Like *de novo* aggressive lymphomas, the majority of transformations have a high $SUV_{study\text{-}max}$ for a given pretreatment staging study, although many do not have very high values. Transformation should be suspected in indolent lymphoma with high SUVs on FDG–PET. Biopsies should be directed to the site of greatest FDG avidity.

Key words: ^{18}fluoro-2-deoxyglucose (FDG), lymphoma, positron emission tomography (PET), standardized uptake value (SUV), transformation

introduction

18-Fluorodeoxyglucose–positron emission tomography (FDG–PET) is increasingly recognized as an excellent tool in staging of newly diagnosed and recurrent non-Hodgkin's lymphomas (NHLs)[1–7]. FDG uptake in tumors is usually quantified by measuring the standardized uptake value (SUV). We have demonstrated that SUVs in FDG–PET can distinguish between indolent and aggressive NHL, with the highest uptake values being highly specific for aggressive disease. Midrange values are found in both indolent and aggressive lymphomas with the lowest values typically associated with indolent disease [8]. In patients previously known to have indolent disease, a PET scan with high uptake values raises the possibility of transformation and directs a biopsy toward the area of possibly the most aggressive disease [8]. Identification of transformed disease can influence therapy.

Our earlier report included eight patients with transformed lymphoma. Similar to the distribution of uptake values in the larger cohort of 63 patients with aggressive lymphoma, four patients in the transformed group had high uptake values. In the current report, we expand our dataset to 41 patients, including these eight initial patients, with transformed lymphoma to characterize better PET scanning in patients with transformation.

patients and methods

All FDG–PET studies carried out for an NHL indication at Memorial Sloan-Kettering Cancer (MSKCC) from 1999 to May 2007 were evaluated. A total of 40 patients met the following entry criteria: (i) histopathologic review by a dedicated MSKCC hematopathologist revealed an aggressive

Correspondence to: Dr A. Noy, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY 10065, USA. Tel: +1-212-639-7423; Fax: +1-646-422-2284; E-mail: noya@mskcc.org

NHL in a patient with prior biopsy-proven indolent NHL, (ii) an FDG–PET scan was carried out at the time of aggressive NHL at MSKCC ($n = 40$) or reviewed ($n = 1$) by a nuclear medicine physician at MSKCC, (iii) no therapy for 60 days before PET scan unless there was documented progression of disease after the last treatment, (iv) PET scans no more than 60 days before or 90 days after biopsy proven transformation and (v) no concurrent cancer diagnosis within 5 years of the PET scan.

This retrospective data analysis was approved by the institutional review board and determined to be exempt research. Patient consent was not required.

lymphoma classification

The World Health Organization (WHO) classification for NHL was used for diagnosis and to subtype the lymphoma as indolent or aggressive [9, 10]. In cases where insufficient material precluded an accurate WHO classification, the pathologic description was recorded. The definition of transformation is controversial. We followed the definition described by Gine et al. [11]. Thus, any follicular lymphoma other than grade 3b or other indolent lymphoma was considered transformed if it progressed to an aggressive lymphoma with a diffuse growth pattern. Similarly to Gine et al, we accepted cytologic diagnosis with a uniform infiltrate of large cells if supported by the clinical scenario.

positron emission tomography

Patients were injected with 12–15 mCi (444–555 MBq) of ^{18}FDG i.v. Images were acquired from the level of the skull base to the upper thigh regions. The average time interval between FDG injection and image acquisition was 68 ± 11 min. Plasma glucose measurements were routinely obtained and ranged from 45 to 242 mg/dl (including three diabetic patients with plasma glucose >150 mg/dl), with a mean of 93 ± 33 mg/dl for the entire study population.

Early studies were carried out using the GE Advance (GE Medical Systems, Waukesha, WI) or HR plus (Siemens/CTI Knoxville, TN) PET tomographs. PET emission images were acquired for 3–4 min per bed position. On both tomographs, attenuation correction was carried out using Ge-68 transmission rods.

Since November 2001, studies were also acquired on combined PET/CTs either Biograph (Siemens/CTI, Nashville/TN) or Discovery LS (GE Medical Systems, Waukesha, WI). Both PET and computed tomography (CT) consist of a combination of a spiral CT with PET tomograph. The Discovery uses the Advance PET tomograph, and the Biograph uses the HR plus PET tomograph. With this equipment, a low-dose CT scan (120–130 kV, ~80 mA), which is used for attenuation correction of PET emission images as well as for anatomic localization of PET abnormalities, is acquired first. This is followed by acquisition of PET emission images of 3–4 min per bed position.

Regardless of the PET tomograph used, images were reconstructed using iterative algorithms. Attenuation correction was routinely applied. PET images of patients who met the above entry criteria were reviewed by one of the nuclear medicine physicians (HS, HWDY). Abnormal FDG uptake was defined as greater than background activity in surrounding tissue and unrelated to physiologic sites of tracer uptake (such as the myocardium) or excretion (such as excreted FDG in the ureters and urinary bladder). For the spleen, abnormal uptake was defined as FDG accumulation greater than in the liver, based on SUV measurements. Areas of abnormal FDG uptake were identified, and the intensity of FDG uptake was quantified by calculating the SUV. For the calculation of SUV, circular regions of interest (70 pixels) were drawn on transaxial images around the areas with increased FDG uptake. This was done on several slices, with window settings adjusted, to assure that indeed the slice with the highest FDG uptake was measured. The SUV was calculated as SUV = [decay corrected activity (kBq)/tissue volume (ml)]/[injected FDG activity (kBq)/body weight (g)]. The highest SUV within a given region of interest (SUV_{max}) was used for this analysis. The highest SUV of the entire study was defined as the $SUV_{study\text{-}max}$. All values reported are in g/ml.

statistical analysis

SUVs were summarized by using mean, median and range. Comparisons between groups were carried out using the Wilcoxon rank-sum test [12].

results

A total of 40 patients were included in the study. Each patient had evidence of biopsy-proven indolent as well as aggressive NHL. Among the indolent diagnoses ($n = 40$), the following specific histologies were identified: eight follicular lymphoma grade 1 (FL 1), nine follicular lymphoma grade 2 (FL 2), six small lymphocytic lymphoma/chronic lymphocytic leukemia (SLL/CLL), 11 marginal zone lymphoma (MZL) including one of mucosa-associated lymphoid tumor type, one mycoses fungoides and one each follicular lymphoma and indolent lymphoma otherwise not specified. Three follicular lymphomas grade 3 (FL 3) were considered indolent as they preceded a diagnosis of diffuse large B-cell lymphoma (DLBCL) by 7, 34 and 125 months.

Among the aggressive diagnoses ($n = 40$), the following specific histologies were identified: 35 DLBCL, one peripheral T-cell lymphoma large cell type and four large-cell lymphoma, not otherwise characterized on account of biopsy type or size. Patient 6 had a cytology showing a predominance of large cells. Patient 8 had a biopsied scalp lesion showing 'large-cell lymphoma' whereas a previous nodal biopsy showed FL 1. Patient 21 had a nodal biopsy showing a mixture of marginal zone lymphoma and large-cell lymphoma, but previous biopsies showed DLBCL. Finally, patient 10 with indolent follicular lymphoma for 8 years presented with a marrow replaced by large malignant B cells. In all four patients, the clinical impression was transformation.

SUV intensity in PET scans

FDG–PET scans were included if they were no more than 60 days before or 90 days after biopsy-proven transformation. SUV was measured at the biopsy site when possible ($n = 33$) (Table 1). In five patients, the biopsy size was completely excised before the PET scan and two underwent bone marrow biopsy only. SUV at the biopsy site ranged from 3.0 to 38.0, with a mean of 14 and median of 12. Of note, the patient with an SUV of 3.0 at the biopsy site had foci of Richter's transformation in a splenectomy specimen. These foci were likely too small to be seen on the PET scan as discrete lesions. Our previous work predicted an aggressive lymphoma with >80% certainty for an SUV >10 and >90% certainty for an SUV >13. Eighteen of 33 remaining biopsies (55%) had an SUV >10 and 16 (48%) >13.

The SUV at the site of biopsy was compared with the SUV range at different disease sites in a given patient (Table 1). In nine cases, the $SUV_{study\text{-}max}$ was not at the disease site that was actually biospied. The $SUV_{study\text{-}max}$ for a transformed aggressive lymphoma ranged from 3.2 to 40, with a mean of 15 and a median of 12. Twenty-five patients (63%) presented

Table 1. Indolent and transformed histopathological diagnosis and characteristics of PET at transformation

Patient	Indolent diagnosis	Transformed diagnosis	SUV range (g/dl)	SUV at biopsy site (g/dl)	$SUV_{study\text{-}max}$ (g/dl)
3	FL 1[a]	DLBCL	26.7	26.7	26.7
6	FL 1	LCL	10.9–22.5	22.5	22.5
8	FL 1	LCL	9–20.8	12.1	20.8
11	FL 1	DLBCL	1.9–5.3	5.3	5.3
16	FL 1	DLBCL	10–19.8	19.8	19.8
18	FL 1	DLBCL	7.6	7.6	7.6
36	FL 1	DLBCL	5.1–11.3	Marrow	11.3
40	FL 1	DLBCL	3.8–38	38	38
2	FL 2	DLBCL	4.9–11.5	Excised	11.5
10	FL 2	LCL[b]	4.3–9.7	4.3	9.7
20	FL 2	DLBCL	9.5–12.4	11.2	12.4
24	FL 2	DLBCL	7.4–30.2	7.4	30.2
27	FL 2	DLBCL	19.4–25.3	25.3	25.3
29	FL 2	DLBCL	2.8–8.2	Excised	8.2
30	FL 2	DLBCL	3–16.4	Bone marrow	16.4
34	FL 2	DLBCL	5.8–18.3	18.3	18.3
38	FL 2	DLBCL	2.6–8	Excised	8
1	FL 3	DLBCL	3.6–29.7	25.5	29.7
4	FL 3[a]	DLBCL	5.4–20.3	20.3	20.3
9	FL 3	DLBCL	7.4	7.4	7.4
35	FL, nos	DLBCL	4.1–13.2	13.2	13.2
14	SLL	DLBCL	4.5–7.6	7.6	7.6
15	SLL/CLL	DLBCL	2.7–3.2	3.2	3.2
19	CLL	DLBCL	12.8–13.3	13.3	13.3
22	SLL	DLBCL	8.7	8.7	8.7
28	CLL	DLBCL	9.5–9.9	9.9	9.9
31	SLL	DLBCL	8.1–40	34	40
7	MZL	DLBCL	2.9–8	2.9–3.5	8
12	MZL	DLBCL	9.7	9.7	9.7
17	MZL (MALT type)	DLBCL	2.6–7.1	7.1	7.1
21	MZL	Transformation to LCL[c]	3.2–10	10	10
25	MZL	DLBCL	3.9	Excised	3.9
26	MZL	DLBCL	5.8–10.2	Excised	10.2
32	MZL	DLBCL	2–15.2	15.2	15.2
33	MZL	DLBCL	6.2–22	17	22
37	MZL	DLBCL	9.7	9.7	9.7
39	MZL	DLBCL	2–13.8	13.8	13.8
41	MZL	DLBCL	4.7–23	23.1	23.1
5	Mycoses fungoides	PTCL	4.7–10.1	6.7	10.1
23	Indolent lymphoma	DLBCL	6.8–18.9	13.7	28.9

[a]FL diagnosis was not confirmed at MSKCC, but clinically evident by history.
[b]Diagnoses made in bone marrow.
[c]With background of MZL.
PET, positron emission tomography; SUV, standardized uptake value; FL, follicular lymphoma; DLBCL, diffuse large B-cell lymphoma; LCL, large-cell lymphoma; SLL, small lymphocytic lymphoma; CLL, chronic lymphocytic leukemia; MZL, marginal zone lymphoma; MALT, mucosa-associated lymphoid tumor; MSKCC, Memorial Sloan-Kettering Cancer; PTCL, peripheral T cell lymphoma.

$SUV_{study\text{-}max}$ >10 and 20 (50%) >13. In 13 patients (33%), the $SUV_{study\text{-}max}$ was >20. In cases where the biopsy site was also the $SUV_{study\text{-}max}$, it was not possible to state whether the surgeon or interventional radiologist took into account the FDG–PET scan findings when choosing a biopsy site. It would not have been the standard of care at the time.

SUVs were also organized by the type of indolent lymphoma from which transformation originated. For aggressive lymphomas developing from FL 1 ($n = 8$), the mean $SUV_{study\text{-}max}$ was 19; from FL 2 ($n = 9$) 16 and FL 3 ($n = 3$) 19 and 1 FL, not otherwise specified ($n = 1$) 13.2. In contrast, the mean $SUV_{study\text{-}max}$ from SLL/CLL was 13.8 and from marginal zone lymphoma was 12. When grouped as follicular lymphoma ($n = 21$) versus SLL/CLL and MZL ($n = 17$), there was a statistically significant difference between the mean values (17 versus 13) ($P = 0.02$, Wilcoxon test).

Finally, 12 patients had serial PET scans separately at the time of indolent and aggressive diagnosis (Table 2). In two patients, the biopsy site demonstrating DLBCL was excised before the PET scan. In the remaining 10 patients, the $SUV_{study\text{-}max}$

Table 2. Patients with serial PET scanning at indolent and aggressive diagnosis

UPIN	Indolent diagnosis	SUV range (g/dl)	SUV at biopsy site (g/dl)	$SUV_{study\text{-}max}$ (g/dl)	Subsequent transformed diagnosis	SUV range	SUV at biopsy site	$SUV_{study\text{-}max}$ (g/dl)
4	FL 3a	13	Excised	13	DLBCL	5.4–20.3	20.3	20.3
6	FL 1	1.5–3	Excised	3	LCL	10.9–22.5	22.5	22.5
8	FL 1	4.6–8.5	4.6–8.5	8.5	LCL	9–20.8	12.1	20.8
12	MZL	2.8–6.3	None	6.3	DLBCL	9.7	9.7	9.7
17	MZL (MALT type)	4.9–11.5	11.5	11.5	DLBCL	2.6–7.1	7.1	7.1
29	FL 2	2.5–10.5	6.8	10.5	DLBCL	2.8–8.2	Excised	8.2
30	FL 2	2–13.5	1.5	13.5	DLBC	3–16.4	16.4	16.4
31	SLL	5.5–14.5	5.5	14.5	DLBCL	8.1–40	33.5	40
32	MZL	2–7.1	6.2	7.1	DLBCL	2–15.2	15.2	15.2
37	MZL	3.4–6.2	Excised	6.2	DLBCL	9.7	9.7	9.7
38	FL 2	3.5–16.1	3.5	16.1	DLBCL	2.6–8	Excised	8
39	MZL	1.3–3.8	1.7	3.8	DLBCL	2–13.8	13.8	13.8

PET, positron emission tomography; SUV, standardized uptake value; FL, follicular lymphoma; DLBCL, diffuse large B-cell lymphoma; LCL, large-cell lymphoma; MZL, marginal zone lymphoma; MALT, mucosa-associated lymphoid tumor; UPIN, unique patient identification number.

increased between the first and second PET scan. In five patients, the $SUV_{study\text{-}max}$ in the first PET scan was ≤13, but rose >13 in the second scan at the time of transformation. In 9 of 12 patients, the $SUV_{study\text{-}max}$ at transformation exceeded the $SUV_{study\text{-}max}$ of FDG–PET scan done at the time of indolent lymphoma. In 8 of 12, the $SUV_{study\text{-}max}$ increased by > 50%. In three cases, it more than doubled.

discussion

In patients with indolent NHL, transformation to an aggressive phenotype is a defining moment in the natural history of their disease. It is often the harbinger of clinical decline and the impetus for more aggressive therapy. The size of a tumor mass is not a reliable predictor of transformation as indolent disease can accumulate slowly over a long time and present as a large mass. Patient morbidity would likely be reduced if a reliable, noninvasive test could alert the clinician to a transformation event before clinical symptoms were apparent or before a trial of inappropriate therapy is pursued. Our prior work has shown that a correlation between SUV and histology with an SUV >13 is 90% specific for aggressive lymphoma [8]. Our current work evaluated patients with transformed NHL in the hopes of defining an SUV value that was characteristic of transformation.

In our current study, the SUV of the biopsy-proven site of transformation ranged from 3 to 38, with a mean of 14 and median of 12. Eighteen of 33 remaining biopsies (55%) had an SUV >10 and 16 (48%) >13. The $SUV_{study\text{-}max}$ for a transformed aggressive lymphoma ranged from 3.2 to 40, with a mean of 15 and a median of 12. Twenty-five patients (63%) presented $SUV_{study\text{-}max}$ >10 and 20 (50%) >13.

This value parallels our prior results, which showed that an SUV >10 predicted an aggressive lymphoma with >80% certainty and an SUV >13 with >90% certainty (8). Of unclear significance is the finding that when the original lymphoma is follicular in nature, the $SUV_{study\text{-}max}$ of the transformation appears higher than when the cell of origin is CLL/SLL or MZL. This may suggest that PET scanning in these latter settings is less informative of a transformation. A larger series would be necessary for verification.

study limitations

In 5 of 14 patients whose biopsy preceded PET, no residual tissue was present in the biopsy location at the time of the PET scan. The $SUV_{study\text{-}max}$ for these five patients ranged from 3.9 to 11.5. It is possible that all the transformed lymphoma was removed during these biopsies and that the excised tissue would have had a higher SUV than the $SUV_{study\text{-}max}$ measured after the biopsy. Thus, our estimate of SUV for transformed lymphoma may be an underestimate. In contrast, the retrospective nature of our study could have overestimated the SUV of transformed NHL if particularly ill patients with very aggressive disease were referred for PET scanning.

Our study included three patients with blood glucose levels of >150 mg/dl and one with a glucose >200. Since normal blood glucose can interfere with FDG uptake in tumor lesions, the $SUV_{study\text{-}max}$ in these patients may have been underestimated. The blood glucose values and corresponding $SUV_{study\text{-}max}$ in these three patients were 151, $SUV_{study\text{-}max}$ 20.8; 173, $SUV_{study\text{-}max}$ 23 and 242, 3.9. We generally do not obtain PET scans in diabetic patients with blood glucose levels >200 mg/dl.

SUV measurements are influenced by a number of biologic and technical factors [13, 14]. In our own clinical practice with a standardized uptake period of ∼60 min and the equipment described, an SUV of 13 seemed to separate best between indolent and aggressive lymphomas. This number may be slightly higher or lower when other uptake times and scan parameters are used in other institutions. Nevertheless, this current analysis provides further emphasis that higher SUVs are characteristic of aggressive lymphoma and that a change from lower to higher SUVs in follow-up scans of indolent lymphoma patients should raise the suspicion for transformation to an aggressive phenotype.

Finally, in the future PET with the thymidine analogue 3′-deoxy-3′-[^{18}F]fluorothymidine (FLT) may prove to be

a more accurate discriminator between indolent and aggressive lymphomas than FDG–PET [15], in which case additional work with transformed lymphoma would be indicated. Currently, however, FLT–PET is still a research tool.

conclusions

Roughly half the patients in our series with documented transformed NHL had an $SUV_{study\text{-}max}$ at transformation falling into a category reliably characteristic of aggressive NHL [8]. In patients with newly diagnosed indolent lymphoma, SUV numbers in the lower range may reduce the suspicion of transformation in disease sites that were not biopsied. Conversely, in patients with monitored indolent lymphoma, a PET scan with an uncharacteristically high $SUV_{study\text{-}max}$ may signal transformation to an aggressive lymphoma phenotype, warranting a biopsy directed at the site of highest SUV in the body. Identifying transformation as early as possible is likely to influence the anatomic spread of transformed lymphoma, and its effect on performance status, and hence prognosis [16].

references

1. Buchmann I, Reinhardt M, Elsner K et al. 2-(fluorine-18)fluoro-2-deoxy-D-glucose positron emission tomography in the detection and staging of malignant lymphoma. A bicenter trial. Cancer 2001; 91(5): 889–899.
2. Carr R, Barrington SF, Madan B et al. Detection of lymphoma in bone marrow by whole-body positron emission tomography. Blood 1998; 91(9): 3340–3346.
3. Hoh CK, Glaspy J, Rosen P et al. Whole-body FDG-PET imaging for staging of Hodgkin's disease and lymphoma. J Nucl Med 1997; 38(3): 343–348.
4. Jerusalem G, Beguin Y, Fassotte MF et al. Whole-body positron emission tomography using 18F-fluorodeoxyglucose for posttreatment evaluation in Hodgkin's disease and non-Hodgkin's lymphoma has higher diagnostic and prognostic value than classical computed tomography scan imaging. Blood 1999; 94(2): 429–433.
5. Romer W, Hanauske AR, Ziegler S et al. Positron emission tomography in non-Hodgkin's lymphoma: assessment of chemotherapy with fluorodeoxyglucose. Blood 1998; 91(12): 4464–4471.
6. Spaepen K, Stroobants S, Dupont P et al. Early restaging positron emission tomography with (18)F-fluorodeoxyglucose predicts outcome in patients with aggressive non-Hodgkin's lymphoma. Ann Oncol 2002; 13(9): 1356–1363.
7. Moog F, Bangerter M, Diederichs CG et al. Extranodal malignant lymphoma: detection with FDG PET versus CT. Radiology 1998; 206(2): 475–481.
8. Schoder H, Noy A, Gonen M et al. Intensity of 18fluorodeoxyglucose uptake in positron emission tomography distinguishes between indolent and aggressive non-Hodgkin's lymphoma. J Clin Oncol 2005; 23(21): 4643–4651.
9. Harris NL, Jaffe ES, Diebold J et al. Lymphoma classification—from controversy to consensus: the R.E.A.L. and WHO classification of lymphoid neoplasms. Ann Oncol 2000; 11 (Suppl 1): 3–10.
10. Harris NL, Jaffe ES, Diebold J et al. World Health Organization classification of neoplastic diseases of the hematopoietic and lymphoid tissues: report of the Clinical Advisory Committee meeting-Airlie House, Virginia, November 1997. J Clin Oncol 1999; 17(12): 3835–3849.
11. Gine E, Montoto S, Bosch F et al. The Follicular Lymphoma International Prognostic Index (FLIPI) and the histological subtype are the most important factors to predict histological transformation in follicular lymphoma. Ann Oncol 2006; 17(10): 1539–1545.
12. Conover W. Practical Nonparametric Statistics, 3rd edition. New York: Wiley 2001.
13. Huang SC. Anatomy of SUV. Standardized uptake value. Nucl Med Biol 2000; 27(7): 643–646.
14. Schoder H, Erdi YE, Chao K et al. Clinical implications of different image reconstruction parameters for interpretation of whole-body PET studies in cancer patients. J Nucl Med 2004; 45(4): 559–566.
15. Buck AK, Bommer M, Stilgenbauer S et al. Molecular imaging of proliferation in malignant lymphoma. Cancer Res 2006; 66(22): 11055–11061.
16. Yuen AR, Kamel OW, Halpern J, Horning SJ. Long-term survival after histologic transformation of low-grade follicular lymphoma. J Clin Oncol 1995; 13(7): 1726–1733.