provides better diagnostic performance and prognostic stratification than does biopsy. *J Nucl Med.* 2013;54:1244–1250.
2. Khan AB, Barrington SF, Mikhaeel NG, et al. PET-CT staging of DLBCL accurately identifies and provides new insight into the clinical significance of bone marrow involvement. *Blood.* 2013;122:61–67.
3. Tsunoda S, Takagi S, Tanaka O, Miura Y. Clinical and prognostic significance of femoral marrow magnetic resonance imaging in patients with malignant lymphoma. *Blood.* 1997;89:286–290.
4. Adams HJ, Kwee TC, Vermoolen MA, et al. Whole-body MRI for the detection of bone marrow involvement in lymphoma: prospective study in 116 patients and comparison with FDG-PET. *Eur Radiol.* 2013;23:2271–2278.

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REPLY: We thank Adams et al. for their comments on our article (*1*). Their recent paper cited in their letter provides interesting results about the comparable performance of whole-body MR imaging and ^{18}F-FDG PET/CT for detection of bone marrow involvement in a mixed population of patients with newly diagnosed low-, intermediate-, and high-grade lymphoma (*2*). We agree with Adams et al. that the potential role of whole-body MR imaging for evaluation of lymphomatous bone marrow involvement in comparison or in association with ^{18}F-FDG PET/CT needs to be further explored.

However, ^{18}F-FDG PET/CT is now a standard procedure for initial staging and response assessment in patients with lymphoma, whereas whole-body MR imaging is still being evaluated for this indication (*3,4*). Under this current situation, our study was designed to answer a simple pragmatic question: in patients with newly diagnosed diffuse large B-cell lymphoma, is it still worthwhile to systematically perform a masked bone marrow biopsy when ^{18}F-FDG PET/CT, which is routinely performed for initial staging, has the potential to evaluate bone marrow status?

It seems that Khan et al. reached the same conclusions as we do (*1,5*). ^{18}F-FDG PET/CT provides better diagnostic performance regarding bone marrow involvement when compared with masked unilateral iliac crest bone marrow biopsy. Moreover, bone marrow involvement according to ^{18}F-FDG PET/CT yields a better prognostic stratification since patients with a negative result on bone marrow biopsy and a positive result on ^{18}F-FDG PET/CT for bone marrow involvement have a prognosis similar to that of patients with a positive bone marrow biopsy.

In this setting, the association of whole-body MR imaging with ^{18}F-FDG PET/CT could increase the diagnostic performance of noninvasive bone marrow status, particularly when PET/CT alone shows limited performance, such as in low-grade lymphomas and in diffuse or discordant bone marrow involvement (*6*). Thus, according to the diagnostic performance of both modalities, and to the lack of radiation exposure from MR imaging when compared with CT, we agree with Adams et al. that PET/MR imaging, despite its slow spread into clinical routine thus far, may evolve as an alternative for staging of lymphoma patients, including bone marrow status.

REFERENCES

1. Berthet L, Cochet A, Kanoun S, et al. In newly diagnosed diffuse large B-cell lymphoma, determination of bone marrow involvement with ^{18}F-FDG PET/CT provides better diagnostic performance and prognostic stratification than does biopsy. *J Nucl Med.* 2013;54:1244–1250.
2. Adams HJ, Kwee TC, Vermoolen MA, et al. Whole-body MRI for the detection of bone marrow involvement in lymphoma: prospective study in 116 patients and comparison with FDG-PET. *Eur Radiol.* 2013;23:2271–2278.
3. Lin C, Luciani A, Itti E, et al. Whole-body diffusion magnetic resonance imaging in the assessment of lymphoma. *Cancer Imaging.* 2012;12:403–408.
4. Juweid ME, Stroobants S, Hoekstra OS, et al. Use of positron emission tomography for response assessment of lymphoma: consensus of the Imaging Subcommittee of International Harmonization Project in Lymphoma. *J Clin Oncol.* 2007;25:571–578.
5. Khan AB, Barrington SF, Mikhaeel NG, et al. PET-CT staging of DLBCL accurately identifies and provides new insight into the clinical significance of bone marrow involvement. *Blood.* 2013;122:61–67.
6. Paone G, Itti E, Haioun C, et al. Bone marrow involvement in diffuse large B-cell lymphoma: correlation between FDG-PET uptake and type of cellular infiltrate. *Eur J Nucl Med.* 2009;36:745–750.

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Should Grade of Tracer Uptake on Somatostatin Receptor–Targeted Imaging Be the Major Determinant and Break the Barrier of Histopathologic Criteria for Determining the Suitability of Peptide Receptor Radionuclide Therapy?

TO THE EDITOR: The recently published joint practical guidance of the International Atomic Energy Agency, European Association of Nuclear Medicine, and Society of Nuclear Medicine and Molecular Imaging on peptide receptor radionuclide therapy (PRRT) in neuroendocrine tumors (*1*) is a nice conglomeration of data based on experience gained over the years by different centers across the world. In a systematic manner, the document has addressed the practical clinical issues with regard to important decision-making steps. PRRT has recently gained significant impetus among the nuclear medicine fraternity; a dramatic symptomatic response with better health-related quality of life has been one of the most gratifying experiences of the treating physicians in this domain. In the routine setting, it is not uncommon to experience patients, who have stable disease either radiologically or even biochemically, themselves volunteering for the subsequent cycles because of symptomatic improvement.

A prescribed indication for deciding on PRRT as an option has been grade 1 or 2 neuroendocrine tumor (corresponding to a low and intermediate grade, respectively, according to the recent 2010 classification of the World Health Organization). Histologically, grade 1 tumor corresponds to "<2 mitoses/10 hpf AND

< 3% Ki67 index" and grade II corresponds to "2−20 mitoses/10 hpf OR 3%–20% Ki67 index" (*2*). No doubt, the somatostatin receptor positivity reduces with higher-grade lesions, but in practice, one can encounter a situation in which the Ki67 index is more than 20% but may demonstrate multiple metastatic lesions that are highly positive on somatostatin receptor–targeted imaging (either with ^{68}Ga-DOTANOC/DOTATATE PET/CT or with ^{111}In-octreoscan/^{99m}Tc-HYNIC [hydrazinonicotinamide]-TOC). As stated in the document (*1*), the relatively documented success of the combination chemotherapeutic approach (with cisplatin etoposide) has been at best modest, ranging from 42% to 67% and for a short duration of 8–9 mo. Thus, an obvious practical question is whether, in a patient with high-grade tracer uptake on somatostatin receptor–based imaging, PRRT should be denied as an upfront therapeutic option because of a higher Ki67 index of the primary. The recently published clinical practice guidelines of the European Society for Medical Oncology (*3*) have made some interesting recommendations in this regard. First, the guidelines mention that "PRRT can be considered in both functioning and nonfunctioning neuroendocrine tumors with positive somatostatin receptor scintigraphy irrespective of the primary tumor site." Second, in the treatment algorithm table (Fig. 1 of the guidelines), the recommended upper limit of Ki67 for PRRT is extended to 30%. Although combination chemotherapy has been indicated in tumors with a Ki67 of more than 20%, PRRT is not precluded in the gray zone of tumors with a Ki67 index of 20%–30%, enabling this group of patients to be benefitted by this potentially useful targeted therapy.

REFERENCES

1. Zaknun JJ, Bodei L, Mueller-Brand J, et al. The joint IAEA, EANM, and SNMMI practical guidance on peptide receptor radionuclide therapy (PRRNT) in neuroendocrine tumours. *Eur J Nucl Med Mol Imaging*. 2013;40:800–816.
2. Klimstra DS, Modlin IR, Coppola D, Lloyd RV, Suster S. The pathologic classification of neuroendocrine tumors: a review of nomenclature, grading, and staging systems. *Pancreas.* 2010;39:707–712.
3. Öberg K, Knigge U, Kwekkeboom D, Perren A. Neuroendocrine gastro-entero-pancreatic tumors: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. ESMO Guidelines Working Group. *Ann Oncol.* 2012;23(suppl 7): vii124–vii130.

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