There are some additional points that warrant discussion. As Kwee et al. correctly note, I did not address the disadvantages of labeled leukocyte imaging in the article. I assumed, perhaps mistakenly, that after more than 30 y of publications on labeled leukocyte imaging, it was unnecessary to reiterate the already well-known shortcomings of the procedure and that better use could be made of the allotted space.

Kwee et al. suggest that the issue of contradictory results for ^{18}F-FDG was based on one—in their opinion, flawed—investigation (*2*). To the contrary, contradictory results have been, and continue to be, reported for ^{18}F-FDG alone and in combination with bone or labeled leukocyte imaging. These results, both favorable and unfavorable, were summarized in my article (*1*).

Kwee et al. attribute the poor results of Love et al. (*2*) for ^{18}F-FDG to the use of coincidence detection rather than dedicated PET. A careful review of the literature, however, reveals investigations that used state-of-the-art PET or PET/CT to diagnose prosthetic joint infection, and their results for ^{18}F-FDG were no better, and in some cases were less satisfactory, than the results reported by Love et al. (*1–4*). Consequently, the argument that the data reported by Love et al. (*2*) are invalid, or flawed, because of the imaging device used is not tenable. Furthermore, this investigation was one of the very few in which the final diagnosis, in all cases, was based on histopathologic and microbiologic specimens obtained at the time of surgery (*2*).

Finally, Kwee et al. mention that recent consensus guidelines do not include leukocyte/marrow imaging for detecting prosthetic joint infection. One can presume that these guidelines do not include ^{18}F-FDG either, since Kwee et al. do not address this in their letter. According to the most recent revision of the American College of Radiology Appropriateness Criteria on imaging after total hip arthroplasty, labeled leukocyte/bone marrow imaging is the best imaging test for diagnosing infection (*5*).

In summary, given the inconsistent and at times contradictory results that have been reported for ^{18}F-FDG over more than 15 y of investigation, ^{18}F-FDG—its practical advantages notwithstanding—is not a suitable replacement for labeled leukocyte/marrow imaging for diagnosing prosthetic joint infection. For the moment, labeled leukocyte/marrow imaging is the best imaging test available for this indication.

REFERENCES

1. Palestro CJ. Radionuclide imaging of musculoskeletal infection: a review. *J Nucl Med.* 2016;57:1406–1412.
2. Love C, Marwin SE, Tomas MB, et al. Diagnosing infection in the failed joint replacement: a comparison of coincidence detection ^{18}F-FDG and ^{111}In-labeled leukocyte/^{99m}Tc-sulfur colloid marrow imaging. *J Nucl Med.* 2004;45:1864–1871.
3. Stumpe KD, Nötzli HP, Zanetti M, et al. FDG PET for differentiation of infection and aseptic loosening in total hip replacements: comparison with conventional radiography and three-phase bone scintigraphy. *Radiology.* 2004;231:333–341.
4. García-Barrecheguren E, Rodríguez Fraile M, Toledo Santana G, Valentí Nín JR, Richter Echevarría JA. FDG-PET: a new diagnostic approach in hip prosthetic replacement. *Rev Esp Med Nucl.* 2007;26:208–220.
5. Weissman BN, Palestro CJ, Appel M, et al. Imaging after total hip arthroplasty. ACR website. https://acsearch.acr.org/docs/3094200/Narrative/. Published 1998. Last reviewed 2015. Accessed September 26, 2016.

Christopher J. Palestro
Long Island Jewish Medical Center
270-05 76th Ave.
New Hyde Park, NY 11040
E-mail: palestro@northwell.edu

Published online Sep. 22, 2016.
DOI: 10.2967/jnumed.116.181669

PET-Guided Stereotactic Irradiation of Prostate Cancer Lymph Node Metastases

TO THE EDITOR: We read with interest the study by Rauscher et al. reporting data about the short-axis diameter of prostate cancer lymph nodes detected by prostate-specific membrane antigen (PSMA) PET (*1*). The authors suggest that this imaging modality may be helpful for guiding salvage surgery (*1*). Such a paradigm is already being applied in radiation oncology, where noninvasive PET-guided salvage stereotactic body radiotherapy has entered routine clinical practice (*2*). Individual lymph nodes detected by choline or PSMA PET/CT can be irradiated in selected patients with oligometastatic prostate cancer. This avoids many of the risks associated with surgery, as well as the intraoperative challenge of locating a specific node. In keeping with Rauscher et al., our clinical impression was that the nodal metastases being detected with these scans were frequently under the 8- to 10-mm threshold in short-axis diameter used to identify nodes with a higher risk of being pathologic on conventional imaging (*3*). We therefore reviewed the plans of 46 PET-positive prostate cancer nodal metastases treated with salvage stereotactic body radiotherapy, 37 detected by choline and 9 by PSMA PET/CT. The median short axis on CT was 0.9 cm (range, 0.5–2.4 cm) for choline-detected nodes and 0.7 cm (range, 0.7–1.4 cm) for PSMA-detected nodes, with 10 of 37 (27%) and 24 of 37 (65%) choline-detected nodes and 5 of 9 (56%) and 7 of 9 (78%) PSMA-detected nodes having a short axis smaller than 8 and 10 mm, respectively. These results corroborate those of Rauscher et al. and indicate that nodal metastases identified by prostate cancer–specific PET imaging would frequently have been considered normal risk or low risk by size criteria alone (*1*). The median volume of choline- and PSMA-detected nodes was 1.3 cm^3 (range, 0.4–12.6 cm^3) and 0.6 cm^3 (range, 0.4–1.7 cm^3), respectively.

The authors mention the possibility of incorrectly allocating nodal fields in PET and surgical lymphadenectomy. Accurate targeting is also relevant in radiation oncology, especially when treating individual nodes as opposed to nodal regions. For example, if there are neighboring PET-negative nodes, it may not always be possible to differentiate the nodal metastasis on size or morphologic criteria. Therefore, coregistration of the diagnostic PET/CT scan with the radiotherapy-planning CT scan may be used to help identify the target node during treatment planning. In such situations it is important to verify the registration between the PET scan and the low-dose CT scan, to ensure that the region with enhanced uptake on PET corresponds to the correct node on CT and avoid possible misalignment of the PET and planning CT scans. A further challenge with small nodes can be good visualization on the imaging system (e.g., cone-beam CT) that is used to correctly position the node before irradiation. In our experience, if preset cone-beam CT options are not optimal, certain parameters (on the TrueBeam platform; Varian Medical Systems) may be adjusted by the user, improving image quality and facilitating accurate targeting.

Advances in diagnostic imaging are helping to drive new treatment options for patients and are enabling the detection of small metastases, with further reductions in the size threshold being likely (*4*). This is expected to present additional challenges to clinicians and to manufacturers of image-guided radiation therapy platforms that need to be able to accurately treat ever-smaller targets in the body.

DISCLOSURE

The Department of Radiation Oncology, VU University Medical Center, has research agreements with Varian Medical Systems. Ben Slotman and Max Dahele have received grants and personal fees from Varian Medical Systems outside the scope of this study. Ben Slotman (BrainLAB and ViewRay) and Max Dahele (BrainLAB) have received speaker honoraria outside the scope of this study. No other potential conflict of interest relevant to this article was reported.

REFERENCES

1. Rauscher I, Maurer T, Beer AJ, et al. Value of ^{68}Ga-PSMA HBED-CC PET for the assessment of lymph node metastases in prostate cancer patients with biochemical recurrence: comparison with histopathology after salvage lymphadenectomy. *J Nucl Med.* 2016;57:1713–1719.
2. Ploussard G, Almeras C, Briganti A, et al. Management of node only recurrence after primary local treatment for prostate cancer: a systematic review of the literature. *J Urol.* 2015;194:983–988.
3. McMahon CJ, Rofsky NM, Pedrosa I. Lymphatic metastases from pelvic tumors: anatomic classification, characterization, and staging. *Radiology.* 2010;254:31–46.
4. Fortuin A, de Rooij M, Zamecnik P, Haberkorn U, Barentsz J. Molecular and functional imaging for detection of lymph node metastases in prostate cancer. *Int J Mol Sci.* 2013;14:13842–13875.

Peter de Boer*
Anna H.M. Piet
Daniela E. Oprea-Lager
Ben J. Slotman
Max R. Dahele
**VU Medical Center*
Meibergdreef 9
Amsterdam, 1105AZ, The Netherlands
E-mail: m.dahele@vumc.nl.

Published online Aug. 18, 2016.
DOI: 10.2967/jnumed.116.181149

^{68}Ga-DOTATATE PET/CT Versus MRI: Why the Comparison of ^{68}Ga-DOTATATE PET/CT to an Appropriate MRI Protocol Is Essential

TO THE EDITOR: We read with interest the article by Janssen et al. (*1*) that analyzed the clinical utility of ^{68}Ga-DOTATATE PET/CT in the detection of head and neck paragangliomas (HNPGLs) compared with anatomic imaging using CT/MRI and with other functional imaging modalities, including ^{18}F-fluorohydroyphenylalanine (^{18}F-FDOPA) PET/CT, ^{18}F-FDG PET/CT, and ^{18}F-fluorodopamine PET/CT.

In this study, ^{68}Ga-DOTATATE PET/CT was able to detect more lesions (38/38) than any other imaging modality, with only 23 lesions being identified by CT/MRI ($P < 0.01$). On the basis of those results, the authors concluded that ^{68}Ga-DOTATATE PET/CT may become the preferred functional imaging modality for HNPGLs. Although ^{68}Ga-DOTATATE PET/CT seems a more efficient imaging modality than ^{18}F-FDOPA PET/CT, ^{18}F-FDG PET/CT, or ^{18}F-fluorodopamine PET/CT, we believe that the comparison with MRI is not valid.

First, the MRI protocol used in the study of Janssen et al. was suboptimal because of the lack of contrast-enhanced angio-MRI (CE-MRA) covering the head and neck area. CE-MRA is known to be the key sequence for the detection of HNPGLs (*2–4*) and is now broadly used in radiology departments. Paragangliomas are highly vascularized tumors, and the arterial enhancement of HNPGLs highlighted by CE-MRA, in combination with localization of the lesion, makes MRI—unlike what the authors state—a highly specific imaging modality, with specificity exceeding 94% (*2–4*). Furthermore, detection rates of MRI in the study are not consistent with the current literature, because sensitivity and specificity reach 90% or more with a proper MRI protocol (*2–4*).

Second, CT and MRI were evaluated together as a single imaging modality even though 3 patients did not undergo head and neck MRI. This may have biased the results by underestimating the detection rates of CT/MRI, because MRI has long been known to be superior to CT for the detection of HNPGLs (*5*).

The authors also state that ^{68}Ga-DOTATATE PET/CT, unlike MRI, provides the advantage of whole-body imaging. Yet, whole-body MRI is feasible and is currently recommended by the Endocrine Society and by the European Society of Endocrinology for the follow-up of genetically predisposed patients (*6–8*).

To our knowledge, only one study showed a higher detection rate for ^{68}Ga-DOTATATE PET/CT than for a proper MRI protocol that included CE-MRA (*9*).

We acknowledge that ^{68}Ga-DOTATATE PET/CT is a promising imaging modality for the detection of HNPGLs. However, the superiority of ^{68}Ga-DOTATATE PET/CT over MRI cannot be asserted by this study and should be confirmed by further studies comparing ^{68}Ga-DOTATATE PET/CT with an appropriate MRI protocol including CE-MRA.

REFERENCES

1. Janssen I, Chen CC, Taieb D, et al. ^{68}Ga-DOTATATE PET/CT in the localization of head and neck paragangliomas compared with other functional imaging modalities and CT/MRI. *J Nucl Med.* 2016;57:186–191.
2. Neves F, Huwart L, Jourdan G, et al. Head and neck paragangliomas: value of contrast-enhanced 3D MR angiography. *AJNR.* 2008;29:883–889.
3. Gimenez-Roqueplo A-P, Caumont-Prim A, Houzard C, et al. Imaging work-up for screening of paraganglioma and pheochromocytoma in SDHx mutation carriers: a multicenter prospective study from the PGL.EVA investigators. *J Clin Endocrinol Metab.* 2013;98:E162–E173.
4. Gravel G, Niccoli P, Rohmer V, et al. The value of a rapid contrast-enhanced angio-MRI protocol in the detection of head and neck paragangliomas in SDHx mutations carriers: a retrospective study on behalf of the PGL.EVA investigators. *Eur Radiol.* 2016;26:1696–1704.
5. Vogl T, Brüning R, Schedel H, et al. Paragangliomas of the jugular bulb and carotid body: MR imaging with short sequences and Gd-DTPA enhancement. *AJR.* 1989;153:583–587.
6. Lenders JWM, Duh Q-Y, Eisenhofer G, et al. Pheochromocytoma and paraganglioma: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2014;99:1915–1942.
7. Plouin PF, Amar L, Dekkers OM, et al. European Society of Endocrinology Clinical Practice Guideline for long-term follow-up of patients operated on for a phaeochromocytoma or a paraganglioma. *Eur J Endocrinol.* 2016;174:G1–G10.
8. Favier J, Amar L, Gimenez-Roqueplo A-P. Paraganglioma and phaeochromocytoma: from genetics to personalized medicine. *Nat Rev Endocrinol.* 2015;11:101–111.
9. Archier A, Varoquaux A, Garrigue P, et al. Prospective comparison of ^{68}Ga-DOTATATE and ^{18}F-FDOPA PET/CT in patients with various pheochromocytomas and paragangliomas with emphasis on sporadic cases. *Eur J Nucl Med Mol Imaging.* 2016;43:1248–1257.