nized this limitation and their reason for not randomizing these scans, the performance of an rhTSH scan first may result in a potential bias in favor of rhTSH scans relative to THW scans. This is so because the approximately 144 MBq (~4 mCi) of ^{131}I administered for the rhTSH scan may have stunned the uptake of metastases on the THW scan. The controversies involving stunning have been extensively discussed (*8*), and although the THW scans were performed at least 2 wk after the rhTSH scan, this interval does not necessarily eliminate potential stunning effects, which may result in a bias favoring the rhTSH scan. Nevertheless, Haugen et al. dismissed stunning as a potentially significant bias with their statement that 96% of the scans in their study were either equivalent or superior after THW, suggesting that any contribution of stunning may have been small. Of those 96% of scans, 80% were concordant, and we would submit that the mere fact that they were concordant (e.g., both scans showing no areas of uptake or both scans showing the same number and areas of uptake) does not rule out stunning. Stunning depends on many factors, and there may be metastatic sites that are not visually affected and other sites of metastatic disease that are stunned and hence potentially not visualized. If the THW scan had been performed first, the potential exists that more THW scans may have been superior to rhTSH scans, and if these are added to the other 8 THW scans that had already been demonstrated to be superior to rhTSH scans, statistical significance might have been achieved. Another limitation of the study by Haugen et al. was the lack of urinary iodine measurements. Although Haugen et al. stated that the use of a low-iodine diet was specifically recommended, that most investigators followed a low-iodine protocol, and that patients received the same dietary instructions for both scans, lower iodine intake before the rhTSH scan relative to the level of iodine intake before the THW scan could bias the scan results. Finally, an important limitation of the study of Haugen et al. is the imaging parameters used for the THW scans and rhTSH scans. The image parameters selected by Haugen et al. to help ensure that the THW scans had no unfair advantage relative to the rhTSH scans may in fact have given the rhTSH scans an unfair advantage relative to the THW scans. Haugen et al. stated that one of the purposes of their study was to address a significantly lower whole-body retention of radioiodine after rhTSH stimulation compared with THW. To compensate for this difference, they used a slower scanning speed or a minimum total-count number for each image rather than scanning for a defined period, thereby minimizing potential count-poor scans after rhTSH administration. Although the intent of compensating for poorer counting statistics is certainly reasonable, this method may have unfairly benefited the rhTSH scans. When one uses a slower scanning speed or a minimum total number of counts that must be obtained before the image is completed, one is obviously increasing total imaging time. In the situation where both the background activity and the lesional activity have decreased equally with rhTSH preparation relative to THW preparation, it may be arguably fair to increase the imaging time. However, in the situation where the background activity has decreased more rapidly than the activity in the lesion with rhTSH preparation, then the target-to-background ratio for a lesion could be higher for rhTSH. This, of course, would favor the rhTSH and is again arguably fair for rhTSH and an advantage for rhTSH. However, increasing the imaging time not only will increase the background and total counts in the image obtained after preparation with rhTSH but also will result in relatively more counts obtained from the target than from the background, in turn improving the counting statistics of the target and potentially building a bias into the study favoring rhTSH scans over THW scans. Verburg et al. overlook these inherent potential limitations of the report by Haugen et al. and simply accept the study as showing that the 2 modalities were comparable in their diagnostic yield.

In summary, we thank Verburg et al. for their thought-provoking letter. However, we believe that the results of our study remain important observations and that our original recommendation is appropriate—specifically that until more data become available, physicians should be cautious in using rhTSH for patient preparation before diagnostic scanning for the detection of DTC or treatment of distant metastases secondary to DTC with ^{131}I. Of course, both physicians and patients would like preparation by rhTSH injections to be as effective as THW in the management of patients with metastatic DTC, but convincing data free of the limitations inherent in prior studies will be required before we can be fully assured of that efficacy.

REFERENCES

1. Van Nostrand D, Khorjekar GR, O'Neil J, et al. Recombinant human thyroid-stimulating hormone versus thyroid hormone withdrawal in the identification of metastasis in differentiated thyroid cancer with ^{131}I planar whole-body imaging and ^{124}I PET. *J Nucl Med.* 2012;53:359–362.
2. Van Nostrand D, Moreau S, Bandaru VV, et al. ^{124}I positron emission tomography versus ^{131}I planar imaging in the identification of residual thyroid tissue and/or metastasis in patients who have well-differentiated thyroid cancer. *Thyroid.* 2010;20:879–883.
3. Jentzen W, Schneider E, Freudenberg L, et al. Relationship between cumulative radiation dose and salivary gland uptake associated with radioiodine therapy of thyroid cancer. *Nucl Med Commun.* 2006;27:669–676.
4. Sgouros G, Hobbs RF, Atkins FB, Van Nostrand D, Ladenson PW, Wahl RL. Three-dimensional radiobiological dosimetry (3D-RD) with ^{124}I PET for ^{131}I therapy of thyroid cancer. *Eur J Nucl Med Mol Imaging.* 2011;38(suppl 1):S41–S47.
5. Klubo-Gwiezdzinska J, Burman KD, Van Nostrand D, Mete M, Jonklaas J, Wartofsky L. Radioiodine treatment of metastatic thyroid cancer: relative efficacy and side effect profile of preparation by thyroid hormone withdrawal versus recombinant human thyrotropin. *Thyroid.* 2012;22:310–317.
6. Freudenberg LS, Jentzen W, Petrich T, et al. Lesion dose in differentiated thyroid carcinoma metastases after rhTSH or thyroid hormone withdrawal: ^{124}I PET/CT dosimetric comparisons. *Eur J Nucl Med Mol Imaging.* 2010;37:2267–2276.
7. Haugen BR, Pacini F, Reiners C, et al. A comparison of recombinant human thyrotropin and thyroid hormone withdrawal for the detection of thyroid remnant or cancer. *J Clin Endocrinol Metab.* 1999;84:3877–3885.
8. Wartofsky L, Van Nostrand D, eds. *Thyroid Cancer: A Comprehensive Guide to Clinical Management.* 2nd ed. Totowa, NJ: Humana Press; 2006.

Douglas Van Nostrand*
Leonard Wartofsky
Frank Atkins
**Washington Hospital Center*
110 Irving St., N.W.
Washington, DC 20012
E-mail: douglas.van.nostrand@medstar.net

Published online Sep. 17, 2012.
DOI: 10.2967/jnumed.112.112094

Radiation Exposure Should Not Limit Bone Scintigraphy with ^{18}F-NaF

TO THE EDITOR: The article by Kurdziel et al. (*1*) focused mainly on the kinetics of ^{18}F-NaF and reproducibility of studies using PET scanners. In addition, the authors presented a dosimetric result that should be emphasized, in our opinion.

Based on the measured biodistribution of ^{18}F-NaF, the authors calculated organ doses using OLINDA. With the highest organ dose

being found in the urinary bladder wall (0.08 mGy/MBq), the mean effective dose for 8 patients was 0.017 mSv/MBq. The mean administered activity of 141 MBq corresponds to an effective dose of 2.4 mSv per ^{18}F-NaF examination. Hence, the effective dose is 20% lower than the effective dose for skeletal scintigraphy using ^{99m}Tc-methylene diphosphonate (MDP), that is, 2.95 mSv with a mean administered activity of 518 MBq (*2*). In this report, Grant et al. listed an effective dose of 3.99 mSv using 148 MBq of ^{18}F-NaF (*2*). The difference is related to the biokinetic data. As Kurdziel et al. explained, their measured urinary excretion fraction (15.3%) and biologic half-life (1.37 h) were lower than the data given in ICRP report 53 (50% excretion fraction) (*3*).

Our own experiences indicate a nearly 50% excretion fraction, too. Nevertheless, the effective dose might be less than the values obtained by Grant et al. based on the simple bladder model that is implemented in OLINDA. A more realistic dynamic urinary bladder model that considers different parameters such as initial bladder volume, initial voiding time, voiding interval, and bladder fill rate is described in MIRD pamphlet 14 (*4*).

Because of the detailed data on organ doses that Kurdziel et al. provide, we performed dose calculations using OLINDA and the dynamic urinary bladder model. For convenience, a software tool based on the dynamic urinary bladder model was developed (http://nuklearmedizin.uniklinikum-dresden.de/forschung-research/mird-14-dosis-kalkulator/). For ^{18}F-NaF, the bladder dose could be reduced by 25% if the voiding interval was shortened to 2 h with a first voiding at 60 min after injection. Additionally, a dose reduction of 70% can be achieved by increasing the initial bladder volume at the time of administration from 0 to 300 mL. Thus, optimizing the voiding scheme can reduce the effective dose significantly because the urinary bladder wall is the organ with the highest dose.

Assuming a clinical setup (300-mL initial bladder volume, first voiding at 60 min after injection, voiding interval of 2 h), the bladder dose is 30% lower than the dose calculated with OLINDA and results in an effective dose of 2.96 mSv per ^{18}F-NaF examination. The effective dose can be additionally reduced to 2.26 mSv by good hydration of the patients, as can be demonstrated in the model calculations by increasing the urine flow rate from 1 to 5 mL/min. These effects are less pronounced in ^{99m}Tc-MDP because of the different physical properties and different local dose depositions of γ-rays and positrons. Applying these considerations to clinical practice, the radiation exposure of the patients can be reduced remarkably when using ^{18}F-NaF as a radiotracer that provides better imaging properties than ^{99m}Tc-MDP (*5*).

The "SNM Practice Guideline for Sodium ^{18}F-Fluoride PET/CT Bone Scans 1.0" (*6*) points out that conventional bone scans cause lower radiation doses than ^{18}F-NaF bone scans (effective dose of 8.9 mSv compared with 5.3 mSv); however, the above-mentioned details have not been taken into consideration. Additionally, the administered activity may be reduced. As Kurdziel et al. stated, they obtained high-quality images by administering only 111–185 MBq of ^{18}F-NaF (*1*).

From the view of radiation protection, ^{18}F-NaF ought to replace ^{99m}Tc-MDP wherever available, and the imaging should be performed with a prefilled urinary bladder.

REFERENCES

1. Kurdziel KA, Shih JH, Apolo AB, et al. The kinetics and reproducibility of ^{18}F-sodium fluoride for oncology using current PET camera technology. *J Nucl Med.* 2012;53:1175–1184.
2. Grant FD, Fahey FH, Packard AB, et al. Skeletal PET with ^{18}F-fluoride: applying new technology to an old tracer. *J Nucl Med.* 2008;49:68–78.
3. Radiation dose to patients from radiopharmaceuticals: ICRP publication 53. *Ann ICRP.* 1988;18(1–4).
4. Thomas SR, Stabin MG, Chen CT, et al. MIRD pamphlet no. 14 revised: a dynamic urinary bladder model for radiation dose calculations—Task Group of the MIRD Committee, Society of Nuclear Medicine. *J Nucl Med.* 1999;40 (suppl):102S–123S.
5. Schirrmeister H, Guhlmann A, Elsner K, et al. Sensitivity in detecting osseous lesions depends on anatomic localization: planar bone scintigraphy versus ^{18}F PET. *J Nucl Med.* 1999;40:1623–1629.
6. Segall G, Delbeke D, Stabin MG, et al. SNM practice guideline for sodium ^{18}F-fluoride PET/CT bone scans 1.0. *J Nucl Med.* 2010;51:1813–1820.

Robert Freudenberg*
Liane Oehme
Joerg Kotzerke
**Universitätsklinikum Carl Gustav Carus Dresden*
Fetscherstrasse 74
Dresden 01307, Germany
E-mail: robert.freudenberg@uniklinikum-dresden.de

Published online Sep. 6, 2012.
DOI: 10.2967/jnumed.112.111195

REPLY: I would like to thank Drs. Freudenberg, Oehme, and Kotzerke for their insightful comments and for sharing their software tool for implementation of the dynamic bladder model.

I am uncertain why our urinary fraction (calculated as the fraction of total activity within an expanded volume of interest encompassing the bladder) with respect to the total activity within the torso (calculated as the total activity within an expanded volume of interest encompassing the torso) differs from Drs. Freudenberg, Oehme, and Kotzerke's experience. Retrospectively, analyzing the first 20 patients of our dataset (as opposed to the initial 8 used for dosimetry) who underwent continuous 3-time-point serial imaging, the mean urinary fraction was 0.16 ± 0.04 with a range of 0.05–0.27. Our patients were requested to maintain good hydration for the 24 h before imaging, likely increasing the urine flow rate. This precaution should increase the urinary clearance rate but may not have a large effect on the urinary fraction (because of the rapid skeletal uptake).

Contrary to prior reports, the radiation dose for ^{18}F-NaF PET is lower than that for ^{99m}Tc-methylene diphosphonate (MDP) or similar planar bone scans. By our calculations, using ICRP 103 weighting factors, the effective dose of a 740-MBq (20-mCi) ^{99m}Tc-MDP scan is 5.0 mSv (*1*) and that of a 185-MBq (5-mCi) ^{18}F-NaF PET scan is 3.1 mSv (*2*). It is the addition of the whole-body (vertex to toes) low-dose CT transmission scan, which in our clinic is 4.5 mSv (whole-body Phillips Gemini PET/CT scanner using the ImPACT CT patient dosimetry calculator, version 0.99x 20/01/06, for an adult subject, a pitch of 1.438, 60 mAs, 120 kV, and collimation of 24) (*3*), that increases the radiation exposure. In our experience, in prostate cancer and multiple myeloma, the transmission CT increases reader confidence in interpretation as it better defines areas of degenerative disease. If ^{99m}Tc-MDP SPECT/CT were performed, the combined effective dose would be 9.5 mSv (as compared with 7.6 mSv for ^{18}F-NaF PET/CT). The real question is whether the CT adds sufficient medical benefit to warrant the increased radiation exposure.

Thus, it is important that when we compare PET and conventional bone scans we appropriately consider the CT compo-