The Value of ^{18}F-FDG PET/CT in the Assessment of Cardiac Malignancy Remains to Be Defined

TO THE EDITOR: We read with great interest the recent article by Rahbar et al. titled "Differentiation of Malignant and Benign Cardiac Tumors Using ^{18}F-FDG PET/CT" (*1*). The paper is interesting because diagnosis of cardiac malignancy is difficult and poorly defined. For example, it has been estimated that in most melanoma patients with cardiac metastases, the metastases remain undiagnosed (*2*). However, several concerns in this paper need to be discussed and clarified.

The first is that special patient preparation is required for detecting cardiac malignancy. It is well known that ^{18}F-FDG uptake in the heart is highly heterogeneous. Fasting for 6 h, as used in the study of Rahbar et al., is not enough to significantly suppress physiologic ^{18}F-FDG uptake of the heart and thus does not offer the ability to differentiate malignancy from physiologic activity (*3*). We personally examined the ^{18}F-FDG PET/CT images of 27 patients who had fasted overnight (10–14 h), and we found that ^{18}F-FDG uptake in the myocardium (the lateral wall of the left ventricle) varied significantly, with maximum standardized uptake value (SUV) ranging from 2.1 to 27.15 (mean ± SD, 11.22 ± 7.71; with 13/27 having an SUV > 10 and only 8/27 having an SUV < 5), consistent with reports in the literature (*3,4*). It is likely that the difference between benign and malignant cardiac tumors is less than the variation in myocardial ^{18}F-FDG uptake in healthy persons. To solve this problem, a low-carbohydrate, high-fat, high-protein diet has been proposed in addition to overnight fasting to minimize background ^{18}F-FDG uptake in the myocardium (*2,5–7*). This diet significantly reduces but still does not allow complete suppression of myocardial ^{18}F-FDG uptake.

The authors performed a receiver-operating-characteristic analysis and obtained cutoff maximum SUVs of 3.5 (with a sensitivity of 100% and specificity of 86%) and 4.6 (with a sensitivity of 94% and specificity of 100%) with high diagnostic accuracy. The authors did not specify for what category the sensitivity and specificity were, and we assume that these sensitivity and specificity values were for identifying malignant cases from a total of benign and malignant cardiac tumor cases. However, these seemingly excellent results are misleading and have limited clinical value. The receiver-operating-characteristic analysis was performed on patients with known cardiac tumors. As such, the sensitivity and specificity obtained in this paper are applicable only to a patient population with known cardiac tumors and cannot be applied to a general patient population or even to patients with suspected cardiac malignancy. Because the prevalence of cardiac malignancy is low in the general patient population, these cutoff SUVs as described in this article would lead to high false-positive results, although use of these criteria in patients highly suspected of having cardiac malignancy is possible and worth further investigation. Even in patients prepared with a low-carbohydrate, high-fat, high-protein diet and overnight fasting, variation in ^{18}F-FDG uptake in the heart remains high. For example, Williams et al. (*5*) reported a cardiac maximum SUV of 3.9 ± 3.6 (average ± SD) in 60 patients, with 16 patients (26.7%) having a maximum SUV above 4 and 3 patients (5%) having a maximum SUV above 15. The heterogeneity of cardiac ^{18}F-FDG uptake and the low prevalence of cardiac tumors make the accurate detection of cardiac tumors (either benign or malignant) on ^{18}F-FDG PET problematic. More useful would be a receiver-operating-characteristic analysis performed on a patient population representative of clinical practice.

Other causes of increased cardiac ^{18}F-FDG uptake should also be considered. For example, sarcoidosis lesions often have increased ^{18}F-FDG uptake comparable to that of malignancy. With an estimated prevalence of cardiac involvement of at least 25% (*8*), cardiac sarcoidosis is probably a more common cause of increased uptake in the heart, further complicating the interpretation of an ^{18}F-FDG PET study of the heart. Correlation with the patient's history and other imaging findings will be critical for accurate diagnosis on ^{18}F-FDG PET.

Finally, the authors did not clarify whether biopsy of heart lesions was performed on all patients and whether biopsy was performed before or after ^{18}F-FDG PET. The authors stated that the grouping of patients was based on "the histologic characterization of the surgically resected cardiac tumors or tumor biopsies." Apparently, then, the pathologic findings were available for this analysis, which may lead to significant bias in this study.

REFERENCES

1. Rahbar K, Seifarth H, Schäfers M, et al. Differentiation of malignant and benign cardiac tumors using ^{18}F-FDG PET/CT. *J Nucl Med.* 2012;53:856–863.
2. Cheng G, Newberg A, Alavi A. Metastatic melanoma causing complete atrioventricular block—the role of FDG PET/CT in diagnosis. *Clin Imaging.* 2011;35:312–314.
3. Kaneta T, Hakamatsuka T, Takanami K, et al. Evaluation of the relationship between physiological FDG uptake in the heart and age, blood glucose level, fasting period, and hospitalization. *Ann Nucl Med.* 2006;20:203–208.
4. Inglese E, Leva L, Matheoud R, et al. Spatial and temporal heterogeneity of regional myocardial uptake in patients without heart disease under fasting conditions on repeated whole-body ^{18}F-FDG PET/CT. *J Nucl Med.* 2007;48:1662–1669.
5. Williams G, Kolodny GM. Suppression of myocardial ^{18}F-FDG uptake by preparing patients with a high-fat, low-carbohydrate diet. *AJR.* 2008;190:W151–W156.
6. Wykrzykowska J, Lehman S, Williams G, et al. Imaging of inflamed and vulnerable plaque in coronary arteries with ^{18}F-FDG PET/CT in patients with suppression of myocardial uptake using a low-carbohydrate, high-fat preparation. *J Nucl Med.* 2009;50:563–568.
7. Harisankar CNB, Mittal BR, Agrawal KL, Abrar ML, Bhattacharya A. Utility of high fat and low carbohydrate diet in suppressing myocardial FDG uptake. *J Nucl Cardiol.* 2011;18:926–936.
8. Youssef G, Leung E, Mylonas I, et al. The use of ^{18}F-FDG PET in the diagnosis of cardiac sarcoidosis: a systematic review and metaanalysis including the Ontario experience. *J Nucl Med.* 2012;53:241–248.

Gang Cheng*
Abass Alavi
**Philadelphia VA Medical Center*
3900 Woodland Ave.
Philadelphia, PA 19104
E-mail: gangcheng99@yahoo.com

Published online Aug. 22, 2012.
DOI: 10.2967/jnumed.112.109611

REPLY: We thank Drs. Cheng and Alavi for adding and corroborating interesting points of discussion. We completely agree with the authors that the sensitivity and specificity of ^{18}F-FDG PET would be much lower in patients without a prior diagnosis of a cardiac tumor by morphologic imaging. Our results are restricted to patients with known cardiac tumors. ^{18}F-FDG PET is certainly not going to be the first-line procedure for excluding cardiac involvement in patients with known or suspected malignancy elsewhere.

Physiologic myocardial uptake was not so great an obstacle as suggested in the letter. It has to be kept in mind that the location

of the tumor was known by morphologic imaging. In some cases, regional physiologic uptake in the myocardium was observed, but as reported, the vicinity of the tumors showed a mean myocardial uptake of as low as 2.1 ± 0.6 standardized uptake value (SUV) (*1*). Peritumoral myocardial dysfunction might be discussed as an explanation of this finding, but in the absence of further evidence this assumption was not discussed in the article.

Nevertheless, we support the concept of a prolonged fasting period.

Sarcoidosis is certainly a condition that may mimic malignant disease. Patient inclusion criteria were primarily based on morphologic imaging. The probability of sarcoidosis was low according to imaging and clinical information. The differential diagnosis was therefore no major problem in this series of patients. In that context it has to be emphasized that sufficient results in functional imaging can be obtained only with state-of-the-art morphologic imaging techniques in the background.

Tumor biopsy was performed before ^{18}F-FDG PET/CT in 3 of 24 patients: almost 2 mo before PET/CT in one of these patients and within 1 wk in the other two. In all patients, the tumors had a malignant histology, and the smallest tumor had a maximum diameter of 5.6 cm. There is no evidence that inclusion of these 3 patients systematically affect the results of the study.

We completely agree with Drs. Cheng and Alavi that the proposed cutoff of 3.5 SUV cannot be applied to an unselected population to screen for myocardial malignancy. Maximum SUV depends on many factors such as scanner resolution, lesion size, scan delay after injection, and the use of motion correction. The cutoff is valid only in the technical and clinical setting described in detail in the article. We thank Drs. Cheng and Alavi for emphasizing this important issue.

REFERENCE

1. Rahbar K, Seifarth H, Schäfers M, et al. Differentiation of malignant and benign cardiac tumors using ^{18}F-FDG PET/CT. *J Nucl Med.* 2012;53:856–863.

Kambiz Rahbar*
Otmar Schober
Matthias Weckesser
**University Hospital Münster*
Albert-Schweitzer-Campus 1
48149 Münster, Germany
E-mail: rahbar@uni-muenster.de

Published online Aug. 23, 2012.
DOI: 10.2967/jnumed.112.110676

Erratum

The authors of "Impact of Dynamic ^{18}F-FDG PET on the Early Prediction of Therapy Outcome in Patients with High-Rish Soft-Tissue Sarcomas After Neoadjuvant Chemotherapy: A Feasibility Study" (Dimitrakopoulou-Strauss et al. *J Nucl Med.* 2010;51:551–558) regret that Table 2 contained some errors. The corrected table appears below.

TABLE 2
Results of Linear Discriminant Analysis with Equal Prior Probabilities Based on ^{18}F-FDG Parameters of First PET Study (1) or Second PET Study (2) or Combination of Both Studies

Parameter	PPV	NPV	Sensitivity	Specificity	Accuracy
1: SUV	9/15 (60.00%)	7/10 (70.00%)	9/12 (75.00%)	7/13 (54.00%)	16/25 (64.00%)
1: SUV, VB, k1, k3, FD	9/11 (81.81%)	11/14 (78.57%)	9/12 (75.00%)	11/13 (84.62%)	20/25 (80.00%)
2: SUV	10/16 (62.5%)	6/8 (75.00%)	10/12 (83.33%)	6/12 (50.00%)	16/24 (66.70%)
2: SUV, influx	8/10 (80.00%)	10/14 (71.43%)	8/12 (67.00%)	10/12 (83.30%)	18/24 (75.00%)
2: FD, k4	9/11 (81.81%)	10/13 (76.92%)	9/12 (75.00%)	10/12 (83.30%)	19/24 (79.20%)
1 + 2: SUV	9/14 (64.30%)	7/10 (70.00%)	9/12 (75.00%)	7/12 (58.33%)	16/24 (66.70%)
1 + 2: SUV, influx	11/14 (78.60%)	9/10 (90.00%)	11/12 (91.67%)	9/12 (75.00%)	20/24 (83.33%)
% change SUVmax	8/14 (57.14%)	6/10 (60.00%)	8/12 (66.67%)	6/12 (50.00%)	14/24 (58.33%)

Groups were defined according to histologic classification of 10% variable tumor tissue.
PPV = positive predictive value; NPV = negative predictive value.