Does PET Offer Little Additional Value when Compared with SPECT?

TO THE EDITOR: It is rather embarrassing to write to the editors criticizing the article that the editors themselves have written, but in this case it probably should be done. We are referring to the commentary by Fischman and Strauss (*1*) concerning the comparison of PET and SPECT.

In their discussion of comparative myocardial perfusion studies with ^{82}Rb PET and ^{201}Tl SPECT, the authors fault the comparative study of Go et al. (*2*), which shows significantly higher sensitivity and accuracy with ^{82}Rb PET, by stating that, unfortunately, the ^{201}Tl SPECT studies were done by stress/redistribution rather than by stress/reinjection. The implication was that the SPECT sensitivity would be higher if the redistribution study were done with ^{201}Tl reinjection.

This statement is, of course, nonsense. Sensitivity of detection of coronary artery disease (CAD) is based entirely on the stress study and has nothing to do with the redistribution, reinjection or rest study. The latter measurement is performed to distinguish ischemia from scar, not normal subjects from abnormal subjects. In their own paper (*3*), in which the authors quote the "higher sensitivity" of the reinjection method, this higher sensitivity refers to the sensitivity in distinguishing ischemia from scar not higher sensitivity in identifying CAD.

In the authors' last sentence of that paragraph, they conclude that in the case for PET versus SPECT for myocardial perfusion, "the jury is still out" (*1*). The phase "only if the prosecutors are still confused" could be added.

The authors' views on the value of PET imaging for determining myocardial viability are also somewhat cavalier. Although the reports of Bonow et al. (*4*) and Tamaki et al. (*5*) were quoted, no mention was made of the work of Brunken et al. (*6*), where in twelve patients 58% of the segments with a fixed ^{201}Tl uptake showed myocardial glucose utilization, or Cook et al. (*7*), who reported that of 33 patients with fixed defects determined by a true resting ^{82}Rb myocardial perfusion procedure, nine patients (27%) demonstrated viable myocardium with ^{18}FDG. Of course, the work of Brunken et al. was done with 4-hr thallium redistribution so that some portion of the 58% could well be ischemic. Even if the reduction due to ischemia would be expected to be 31% of the fixed defect segments (*3*), myocardial glucose utilization would still be present in 28% of the remaining persistent segments.

Although no claims were made for identifying "all" viable regions, the superiority of FDG PET over any potassium analog reinjection or rest study appears well established. It is not clear how much additional work is necessary to convince the Committee on Advanced Cardiac Imaging and Technology of the Council on Clinical Cardiology of the American Heart Association (*8*) that these PET results are more than "tantalizing" (*1*).

REFERENCES

1. Fischman AJ, Strauss HW. Clinical PET—a modest proposal. *J Nucl Med* 1991;32:2351–2355.
2. Go RT, Marwick TH, MacIntyre WJ, et al. A prospective comparison of rubidium-82 PET and thallium-201 SPECT myocardial perfusion imaging utilizing a single dipyridamole stress in the diagnosis of coronary artery disease. *J Nucl Med* 1990;31:1899–1905.
3. Rocco TP, Dilsizian V, McKusick KA, Fischman AJ, Boucher CA, Strauss HW. Comparison of thallium redistribution with rest re-injection imaging for the detection of myocardial ischemia. *Am J Cardiol* 1990;66:158–163.
4. Bonow RO, Dilsizian V, Cuocolo A, Bachrach SL. Identification of viable myocardium in patients with coronary artery disease and left ventricular dysfunction. Comparison of thallium scintigraphy with reinjection and PET imaging with ^{18}F-fluorodeoxyglucose. *Circulation* 1991;83:26–37.
5. Tamaki N, Yonekura Y, Senda M, et al. Value and limitation of stress thallium-201 single photon emission computed tomography: comparison with nitrogen-13 ammonia positron emission tomography. *J Nucl Med* 1988;29:1181–1189.
6. Brunken R, Schwaiger M, Grover-McKay M, Phelps ME, Tillisch J, Schelbert HR. Positron emission tomography detects tissue metabolic activity in myocardial segments with persistent thallium perfusion defects. *J Am Coll Cardiol* 1987;10:557–567.
7. Cook SA, Go RT, MacIntyre WJ, et al. Use of rubidium-82 and F-18 FDG PET imaging in identifying viable myocardium [Abstract]. *J Nucl Med* 1991;32:968.
8. Bonow RO, Berman DS, Gibbons RJ, et al. Cardiac positron tomography. *Circulation* 1991;84:447–454.

William J. MacIntyre
Raymundo T. Go
Sebastian A. Cook
Cleveland Clinic Foundation
Cleveland, Ohio

Science Behind Clinical PET

TO THE EDITOR: Fischman and Strauss (*1*) have made an extremely important contribution to the subject of clinical PET. Their editorial is clear, concise and informative. They have furthermore addressed the issues up front.

The authors are correct in pointing out that it appears that nuclear physicians writing or talking about clinical PET are opponents or proponents. This unfortunate difference of philosophies is not with PET, but rather with the clinical application of PET at this period of time where cost/efficiency considerations dominate the opinion of nonphysicians about medical practice. Yet, nobody in nuclear medicine would disagree with the proposition, as correctly stated in the editorial, that PET is a unique modality in which our field can grow.

A most critical section in the editorial relates to a discussion on the additional value of PET when compared with SPECT. Of the 57 lines devoted to this section, 40 (= 70%) discuss nuclear cardiology issues. In consideration of myocardial perfusion imaging, the conclusion is that the jury is still out. I agree with the authors that the work of Gould has been enthusiastically performed. However, a key question in perfusion imaging still remains: given a patient with CAD, how is the decision made as to whom should be offered SPECT investigation and whom should be given a PET study? Consider the radioisotopes that are available: ^{20}Tl, ^{99m}Tc-hexamibi, ^{99m}Tc-teboroxime, ^{82}Rb, ^{13}N-ammonia, ^{62}Cu-PTSM and ^{15}O. Detectors available are planar Anger

camera, one or three-detector SPECT systems, PET cameras with no rings or with four or eight rings and septa present or absent (for optimized three-dimensional sampling). Finally, the intervention can be exercise, dipyridamole, adenosine or dobutamine. In this multidimensional decision matrix, there is indeed a pressing need for narrowing the duties of the jury!

Because of my NIH-sponsored research results, I have taken great pains to explore the science behind the detection of viable myocardium with FDG. We have published an editorial that addresses this matter directly and concludes with several scientific reservations on cardiac FDG studies (*2*). Of significance, Gropler and Bergmann (*3*) and Lear (*4*) have recently published editorials in *JNM* in which other reservations are voiced. Without being redundant, our consensus is that FDG does not yet pass scientific tests for being the gold standard for myocardial viability. At the recent meetings of the American Heart Association, Pohost concluded that SPECT scintigraphy is most costeffective for detection of myocardial viability. Among the agents for this purpose are ^{201}Tl, ^{99m}Tc-hexamibi and ^{99m}Tc-teboroxime. If FDG is to compete with SPECT scintigraphy, multicenter trials of the type recommended by the AHA (*5*) are needed to identify the subsets of CAD patients requiring FDG studies. Incidentally, echocardiography with dobutamine is another competing modality since it can also give viability information.

In a previous letter in this *Journal*, I stated that I disagreed with the position of the SNM and the ACNP that PET radionuclides should be exempt from efficacy appraisal by the Food and Drug Administration (FDA). If that were the case, then reimbursement, as discussed in the editorial, would be the only way for efficacy testing outside of the jurisdiction of FDA. That would be unfair to other radiopharmaceuticals, such as monoclonal antibodies, none of which have been approved for human use. Also, it is obvious that trials after reimbursement but without the FDA clinical phases process, might be biased since a $5 million PET investment is a strong incentive for obtaining positive results.

I think it is time for nuclear cardiologists to face the challenge and jointly establish the clinical utility of different modalities for assessing myocardial perfusion and viability.

REFERENCES

1. Fischman AJ, Strauss HW. Clinical PET—a modest proposal. *J Nucl Med* 1991;32:2351–2355.
2. Bianco JA, Wilson MA. Should F-18 deoxyglucose scans be indicated for care of patients with coronary artery disease? *Cardiology* 1991;79:219–226.
3. Gropler RJ, Bergmann SR. Myocardial viability—what is the definition? *J Nucl Med* 1991;32:10–12.
4. Lear JL. Relationship between myocardial clearance rates of carbon-11-acetate-derived radiolabel and oxidative metabolism: physiologic basis and clinical significance. *J Nucl Med* 1991;32:1957–1960.
5. Bonow RO, Berman DS, Gibbon RJ, et al. Cardiac positron tomography. *Circulation* 1991;84:447–454.

Jesus A. Bianco
University of Wisconsin
Madison, Wisconsin

Clinical PET: The Debate Continues

REPLY: The dichotomy of opinion of McIntyre et al. and Bianco about our editorial (*1*) highlights the need for a well-defined comparison of these radionuclide imaging modalities. We would like to thank MacIntyre et al. for pointing out an error in our editorial: only initial images are required for the detection of coronary artery disease with myocardial perfusion imaging.

It is clear from their comments that MacIntyre et al. are PET enthusiasts, convinced of the superiority of PET for cardiac applications. Based on theoretical considerations, review of the literature and our own personal experience, we tend to agree with them. However, it seems prudent to withhold our unconditional endorsement of cardiac PET for clinical decision making until irrefutable data on a large number of patients are available. Although measurements of resolution, statistical reliability and lack of attenuation artifacts suggest that PET based myocardial perfusion studies are superior to single-photon methods, the clinical community needs to know whether these technical advantages benefit patient care.

An area where PET could make a major contribution to nuclear cardiology is in differentiating areas of ischemic but viable myocardium from scar. Although we did not cite many references in this area, our discussion made the point that the quantity of supporting data for the utility PET for making this distinction is not overwhelming. Bianco is less enthusiastic about the future of clinical cardiac PET. He questions the use of ^{18}FDG as a "gold standard" for evaluating myocardial viability and suggests that a large multicenter trial will be required to define those clinical situations where PET studies are required. Overall, we agree that only the objective scientific observations of a multicenter trial can establish the clinical utility of PET.

Many questions remain about the use of FDG for quantifying myocardial viability. Should these studies be performed under fasting or glucose-loaded conditions? If glucose-loaded, should it be after a single bolus or under controlled "clamp" conditions? These questions suggest that an alternative to metabolic imaging should be sought. A quantitative myocardial perfusion study may provide information about viability. In this regard, we would like to mention the results of a recent study performed in our laboratory by Gewirtz (*2*). In a group of 28 patients with previous myocardial infarction, we compared the results of quantitative blood flow studies with $^{13}NH_3$ to ^{18}FDG studies (with glucose loading) for detecting viable myocardium. In this group of subjects, myocardial blood flow in regions of previous infarction (MI) was significantly lower than in zones of normal myocardium (NZ): 0.33 ± 0.24 versus 1.02 ± 0.48 ml/min/g, $p < 0.01$. Border zone regions (BZ) showed intermediate reductions in flow: 0.68 ± 0.34 ml/min/g ($p < 0.01$ versus MI and NZ). Mismatches of flow and FDG occurred in only six zones (five patients) of which five (4 BZ, 1 MI) had flows of greater than 0.40 (0.65 ± 0.08). Perfusion and FDG accumulation were well correlated in MI zones. This study suggests that in patients with previous MI, viable myocardium is unlikely to be present in areas in which flow is < 0.40 ml/min/g.

To end the speculation about PET, we need to work with funding agencies to organize and perform a multicenter trial to define the clinical utility of PET imaging procedures.

REFERENCES

1. Fischman AJ, Strauss HW. Clinical PET: a modest proposal. *J Nucl Med* 1991;32:2351–2355.
2. Gewirtz H, Fischman A, Strauss HW, Alpert N. Quantiative PET measurement of regional myocardial blood flow ($^{13}NH_3$) identifies non-viable