we wonder if the authors could comment. Second, as the authors correctly state, the increased specificity supposedly offered by PET assumes that the lack of focal <sup>18</sup>F-FDG uptake always indicates lack of a true lesion (which the authors disproved, like others, in their own paper). Therefore, in this study with few lesions overall, the true meaning of this increased specificity seems to remain a bit questionable. Third, we wonder if the reported level and frequency of discomfort at colonoscopy might be attributable to the type of sedation administered (midazolam and pethidine). Types of sedation vary worldwide and may not even be used in some centers (3,4). In the United States, propofol (Diprivan; AstraZeneca), a deep-sedative hypnotic, is being used more often. Patients seem to achieve greater comfort and less recollection of pain. One wonders if this would have changed the balance of preference. Fourth, it is hard to extrapolate Figure 7 from results in Figure 6. It seems that about the same number of patients rates each examination "well" or "fairly well" and yet most chose PET/CT colonography as more acceptable and as more desirable to undergo again. One wonders if there was some sort of recall bias or whether the entire equation comes down to the colonic preparation involved rather than the actual test itself. Do the authors have any sense for what part the preparation played in the rating? That is, is there a statistical way to separate out this component? Also 13 patients did not even return the questionnaire. Could they all have been utterly disgusted with both examinations? Fifth and finally, one disadvantage to which the authors allude but do not address is that if this minimal-preparation technique were to be implemented, patients who have a positive finding would have to undergo a full preparation for colonoscopy. In our study, patients went directly to colonoscopy. However, if in fact the negative predictive value of such a test in this population were shown to be high, patients could avoid a full preparation and a colonoscopy altogether-the obvious advantage.

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**REPLY:** We thank Drs. Gollub and Akhurst for their interest in our article (1) and acknowledge their work in this field.

We agree with their comment about the large volumes of  $CO_2$  insufflated. In the article, we report the volume of carbon dioxide insufflated in the supine position (3.1 L; range, 2.2–4.1 L) before

the supine CT acquisition and then the additional mean volume of gas insufflated just before the prone scan acquisition (based on assessment of the prone scout scan). We reported the volume in this manner to give readers a practical guide as to how we performed the technique—the total volume of gas insufflated over the whole hour is of less relevance. As to this total volume of carbon dioxide, we agree this volume can be very large because of absorption of the gas during the procedure. By reducing the pressure to 15 mm Hg, we obtained total volumes that were a little smaller than those experienced by Dr. Gollub but were in the range of 10–40 L.

The increase in specificity afforded by PET in our study does rely on the assumption that significant pathology would be PETavid, which we agree is not always the case. Reporting of colonic neoplasia during CT colonography is rarely a yes/no phenomenon. Readers take many factors into consideration when deciding whether to call a lesion real or not: for example, morphology, lesion movement, attenuation homogeneity, general state of bowel preparation, and distension. <sup>18</sup>F-FDG avidity or otherwise of the lesion is an additional factor that may aid the radiologist, and in our feasibility study we found that false-positives were reduced. It is perhaps more intuitive that PET would increase sensitivity in nonlaxative studies. We did not find this to be so, but as we discuss, we used an experienced reader to report the CT colonography component of the examination. It would seem likely that <sup>18</sup>F-FDG avidity would improve the sensitivity of less experienced CT colonography readers, somewhat akin to computer-aided-detection software, and further work on this possibility is under way.

A difference in sedation techniques may in part explain some of the patient discomfort during colonoscopy that we reported. Of course, heavy-sedation regimes are not without risk, particularly in older patients. In a recent study investigating the use of propofol and remifentanil during colonoscopy, oxygen saturation dropped to less than 90% in 5 of 25 patients, who required bag mask ventilation (2). Our endoscopists carefully titrated the amount of administered analgesia and sedation against patients' feeling of discomfort during colonoscopy to maximize both patient comfort and safety.

It is reassuring that patients generally tolerated both colonoscopy and PET/CT colonography reasonably well, and although we can only speculate on the views of questionnaire nonresponders, it would perhaps seem unlikely they were "disgusted"! It is absolutely correct that when assigning an overall preference between 2 tests, patients weigh many factors, not just the physical experience of the test itself. We believed that the convenience of bowel preparation for PET/CT colonography was a major factor, but there are many other facets more difficult to quantify, such as test environment, staff attitudes, posttest care, feedback of results, patients' assumptions on test performance, and fear of complications. We know, for example, that patients often assume that new, expensive imaging technologies must be "better" than conventional tests (3). Although quantitative questionnaires do have the benefit of speed and simplicity, in reality detailed qualitative studies are required to tease out which factors most influence patients' test preferences, and even then, these factors often differ widely between individuals.

To justify the use of nonlaxative PET/CT colonography as a first-line test in the investigation of older patients, a high positive predictive value is essential, as Drs. Gollub and Akhurst correctly state, because patients with reported pathology must undergo invasive colonoscopy with bowel preparation. However, the test must also be sensitive (low false-negative rate) and so have a

DOI: 10.2967/jnumed.110.079632

high negative predictive value. Our study also showed this to be so for PET/CT colonography—indeed, by combining the attributes of CT colonography and PET, PET/CT colonography would seem to be a highly reliable test for classifying higher-risk symptomatic patients into those with or without significant colorectal neoplasia.

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DOI: 10.2967/jnumed.110.080374

# **VQ/SPECT**

**TO THE EDITOR:** In the December 2009 issue of *The Journal* of Nuclear Medicine, an invited perspective (1), a study (2), a continuing education paper on ventilation–perfusion (V/Q) SPECT (3), and a lung SPECT/CT image on the front cover can be found. These appeared shortly after the June (4) and July (5) 2009 publication of guidelines by the European Association of Nuclear Medicine detailing V/Q SPECT interpretation criteria. This amount of information seems to indicate that V/Q SPECT has gained much interest.

Several years ago, we compared V/Q SPECT with planar lung scanning in 95 patients who were suspected of recent pulmonary embolism but in whom planar lung scans had been nondiagnostic (6). CT angiography and lower-limb ultrasonography were used as independent reference standards. Using our own V/Q SPECT diagnosis criterion—that even a single subsegmental mismatch defect indicates pulmonary embolism—we found a negative predictive value of 0.94, which is similar to normal D-dimer plasma levels. Sensitivity, specificity, and accuracy were 0.79, 0.83, and 0.80, respectively. All discrepancies with final diagnosis were related to single subsegmental or nonoccluding segmental thrombi.

The tomographic mode enables more precise assessment of the shape of defects, and V/Q SPECT interpretation must overcome the simplistic criterion that a mismatch defect is always related to an underlying thrombus. Because a mismatch defect is not specific to pulmonary embolism, a careful visual analysis is mandatory. At the time that we submitted our manuscript, the topic of V/Q SPECT was considered of low priority and led us to publish our results (6) in a free-access journal (http://www.bentham.org/open/tomij/).

In their study, Gutte et al. (2) use low-dose CT in an elegant way to improve V/Q SPECT performance. There is no doubt that CT will greatly aid in the interpretation of V/Q studies. However, not all nuclear medicine departments have a hybrid  $\gamma$ -camera available to perform V/Q lung SPECT combined with CT.

According to our experience, a precise analysis of V/Q SPECT mismatch defects (location, shape, extent to fissure, presence and location of hot spots when using Technegas [Cyclopharm]) enables a diagnosis in 99% of patients without the use of CT. Illustrations given by Gutte et al. confirm this point.

In daily practice, V/Q lung scanning is used as the first imaging test in a few situations. This trend could be reversed if nuclear medicine physicians would routinely use tomographic instead of planar imaging. The addition of low-dose CT when feasible will probably help to shorten the learning curve for V/Q SPECT abnormalities significantly.

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DOI: 10.2967/jnumed.109.073627

## Additional Gains with Time-of-Flight PET at High Counting Rates: Lessons Learned from Early Time-of-Flight PET Systems

**TO THE EDITOR:** Recent publications on the new generation of time-of-flight (TOF) PET cameras by Lois at al (1), Surti et al. (2), and Karp et al. (3) very elegantly show the reduction in image noise and improvement in lesion detection with TOF PET positron cameras using phantoms and clinical studies. These new TOF PET cameras are optimized for high-resolution tumor detection using <sup>18</sup>F-FDG as the tracer and show that the highest improvement in signal-to-noise ratio in the image is obtained when imaging large 35- to 40-cm-diameter objects. Their noise reduction results are consistent with the published result by Yamamoto et al. (4) in 1982 for 35-cm-diameter objects scanned at low counting rates using the early Super PETT I TOF PET camera built at Washington University, Saint Louis, Missouri. However, Yamamoto et al. (4) also showed that, at high counting rates, there is an additional gain with TOF PET due to the way random coincidences are