projections, and does not have the radiation safety issues of ^{133}Xe. The downside is that in patients with chronic obstructive pulmonary disease, multiple central hot spots caused by turbulent airway flow are often seen, which can result in poor-quality and even nondiagnostic images. This becomes a particular problem with SPECT. ^{133}Xe is used at many institutions because the entire ventilator cycle can be viewed, hot spots are not a problem, and delayed washout is a sensitive indicator of obstructive lung disease, the most common alternative diagnosis to pulmonary embolism. Dr. Graham states that he uses ^{99m}Tc-sulfur colloid aerosol. ^{99m}Tc-sulfur colloid and ^{99m}Tc-pyrophosphate aerosols are used at very few institutions, and published data supporting their clinical use are extremely limited.

Technegas has been available in Australia and Europe for years. Since 1986, there have been approximately 180 scientific publications about this radiopharmaceutical, with overwhelmingly positive sentiment and data on its safety and clinical efficacy. Anyone who has seen images of ^{99m}Tc-Technegas compared with ^{99m}Tc-DTPA aerosol or ^{133}Xe readily appreciates the clear superiority of Technegas. The Australian manufacturer has been trying to obtain Food and Drug Administration (FDA) approval for Technegas in the United States for several years. However, the FDA has made this extremely difficult. Even though most imaging clinics in the United States use ^{99m}Tc-DTPA aerosol, the FDA will not allow a direct comparison between the two. The reason given is that the FDA never approved ^{99m}Tc-DTPA for ventilation studies. We presently use it on an off-label basis. Therefore, the FDA is requiring that Technegas be compared with ^{133}Xe, even though ^{133}Xe is used in a minority of imaging centers. In addition, the FDA has required a large multicenter protocol that must include at least 375 subjects with a final diagnosis positive for pulmonary embolism and 375 that are negative for pulmonary embolism. The protocol is complex, time-consuming, and expensive. As a result, the sponsor is having difficulty finding institutions willing to participate and patient accrual has been poor. Many predict that this study will never be completed and that we will not be able to use Technegas in the United States in the foreseeable future. The FDA is hindering good patient care in the United States and disregarding the extensive experience in Australia and Europe. A simple direct image comparison of Technegas with ^{133}Xe or ^{99m}Tc-DTPA aerosol is all that should be needed. Its safety has already been demonstrated by the experience worldwide.

I agree with Dr. Graham that V/Q SPECT should become the standard—that is, if we had a ventilation agent that would routinely provide good diagnostic SPECT images. Institutions with generally healthy patients who do not have cardiopulmonary disease may get away with using ^{99m}Tc-DTPA aerosol with SPECT in most patients, but for institutions with many cardiopulmonary disease patients, particularly those with chronic obstructive pulmonary disease or asthma, ^{99m}Tc-DTPA aerosol SPECT can be quite problematic.

The FDA should reexamine its complex protocol comparing Technegas and ^{133}Xe with the sponsor and devise a protocol that would simply examine the value of Technegas ventilation images versus ^{133}Xe or ^{99m}Tc-DTPA aerosol images, using a protocol that can be accomplished with a limited number of patients in a reasonably short time. The extensive literature should be part of the approval process.

In summary, I agree that SPECT, particularly SPECT/CT, is the future of V/Q imaging. However, we unfortunately are not there yet, mainly because the FDA has hindered that progress, and this has adversely affected state-of-the-art optimal patient care.

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REPLY: I thank Drs. Freeman and Ziessman for their comments on my editorial regarding SPECT V/Q imaging (*1*).

I understand Dr. Freeman's point that problems can arise if a test is too sensitive. It seems to me that there are two ways to approach the problem of detecting and reporting small emboli that are clinically insignificant and do not require therapy. One is to not detect them and the other is to appropriately report them. The use of a lower-sensitivity approach, such as planar ventilation–perfusion (V/Q) imaging, certainly will avoid detection of small emboli. However, there are moderate-sized emboli, particularly in more medial lung, that cannot be visualized with planar V/Q and are clinically significant. Currently, we really do not know much about the prognosis or the need for treatment of small emboli, and the only way this issue can be studied is by using V/Q SPECT. This is a significant point raised in the European Association of Nuclear Medicine guidelines (*2*). Once the significance of smaller pulmonary emboli is better established, V/Q SPECT guidelines will need to be refined to determine which patients need treatment. Even if the high sensitivity of V/Q SPECT results in a small number of people being treated for trivial disease, because of its higher specificity V/Q SPECT is also likely to result in a decreased number of patients being overtreated whose lung scans are "nondiagnostic," that is, not normal or high-probability (*3*). It is likely at Montefiore that few lung scans are nondiagnostic, but in the rest of the country this is not an uncommon outcome.

Dr. Ziessman is concerned that ^{99m}Tc-Technegas (Cyclomedica Ltd.) is required to obtain high-quality SPECT ventilation images that are needed as part of V/Q SPECT imaging. I agree with him that Technegas is the best agent, but aerosol imaging with ^{99m}Tc-sulfur colloid generates remarkably high-quality tomographic scans in most patients. The approach we use in Iowa results in a set of high-quality planar images as well as the tomographic images, so the interpreter can always fall back on evaluating the planar images. I agree that we need to try to convince the Food and Drug Administration to approve Technegas, but in the meantime we should move ahead with aerosol ventilation imaging and broadly adopt V/Q SPECT imaging.

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Qualitative ^{18}F-FDG PET/CT Response Evaluation After Chemotherapy or Radiotherapy for Head and Neck Squamous Cell Carcinoma: Is There an Equivocal Group?

TO THE EDITOR: We read with great interest the recent article by Marcus et al. (*1*). The objective of this retrospective study on 214 patients with head and neck squamous cell carcinoma was to validate qualitative interpretation criteria for ^{18}F-FDG PET/CT assessment of response after chemoradiotherapy or radiotherapy in terms of accuracy, reader reliability, and predictive value for survival outcomes. This is an area of particular interest because the use of ^{18}F-FDG PET/CT for response assessment of head and neck squamous cell carcinoma is becoming increasingly widespread (*2*). Their Hopkins criteria were used to assign a score of 1–5, with scores of 1–3 considered negative for residual disease. A score of 1 was for focal ^{18}F-FDG uptake less than activity in the internal jugular vein, a score of 2 was for focal ^{18}F-FDG uptake more than activity in the internal jugular vein but less than liver uptake, a score of 3 was for likely inflammatory changes, and scores of 4 and 5 were for focal uptake greater than liver uptake. The study demonstrated high interreader agreement and an overall negative predictive value of 91.1%.

The authors stated that "no established qualitative interpretation criteria...have been published" (*1*). However, Porceddu et al. reported final results in 2011 (*3*) of a high-quality prospective study on 112 patients evaluating an ^{18}F-FDG–directed policy for the management of patients with neck node–positive head and neck squamous cell carcinoma after chemoradiotherapy or radiotherapy using qualitative PET response criteria. With some similarity to the Hopkins criteria, these response criteria were prospectively implemented; focal uptake greater than liver background was considered positive, focal uptake less than liver but more than surrounding normal tissues was considered equivocal, and no uptake above background or diffuse uptake without underlying structural abnormality was considered negative. In this prospective study, PET-based nodal assessment had a negative predictive value of 98.1% (*3*). The most significant difference in this method of classification is the assignment of an equivocal response to focal uptake less than liver background, which would be assigned a score of 1 or 2 and considered negative according to the Hopkins criteria.

The management of this group of equivocal responders in neck lymph nodes in an era in which neck dissections are not routinely performed (*4*) is a particularly difficult clinical issue. In the study by Porceddu et al. (*3*), 11 of 112 patients had an equivocal response and 10 of these 11 patients became negative on a repeated PET scan performed within the study protocol after a 4- to 6-wk interval and were spared a neck dissection; None of these 10 patients had subsequent neck failure. We have previously reported our initial experience with ^{18}F-FDG PET for response assessment (*5*). In a recent update of our series (*6*), 10 of 105 patients had an equivocal response according to the reporting criteria published by Porceddu et al. (*3*); 2 of these 10 patients subsequently had clinicopathologic evidence of lymph node disease.

We believe that the clinical significance and optimal management of focal ^{18}F-FDG PET uptake below the level of liver background remains uncertain. In light of these differing qualitative response criteria and the higher negative predictive value reported by Porceddu et al. (*3*) for a negative PET scan, it is possible that the negative predictive value provided by the Hopkins criteria may be improved by separately considering patients with an equivocal response as defined by Porceddu et al. (*3*). We would be interested to learn whether there is any difference in the negative predictive value reported by Marcus et al. (*1*) comparing patients who scored a 1, 2, or 3 according to the Hopkins criteria and classified as having a negative scan.

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REPLY: We agree that having an equivocal group is a challenging clinical issue in assessing patients with head and neck squamous cell carcinoma after chemoradiation therapy. The Hopkins criteria (*1*) are a simple, standardized, qualitative method of assessing therapy,