

## <sup>99m</sup>Tc-Tetrofosmin Scintigraphy in Management of Pulmonary Tuberculosis

**TO THE EDITOR:** We read with interest the article by Degirmenci et al. (1) exploring the role of <sup>99m</sup>Tc-tetrofosmin scintigraphy in pulmonary tuberculosis. The authors reported that tetrofosmin uptake was grade + in 15% and grade ++ in 85% of patients with active pulmonary tuberculosis (i.e., sputum culture was positive). There was no uptake in 5 of the 6 patients with inactive pulmonary tuberculosis. The decrease or disappearance of tetrofosmin uptake in 5 out of the 6 patients with active disease who were followed up after 9 mo of therapy correlated well with the clinical and radiologic findings. The authors assumed inactive tuberculosis in patients with negative sputum smears and cultures. Certain patients who were not producing more than 10–100 bacilli per milliliter of sputum (sputum smear and culture negative) still may have had active disease.

Pulmonary tuberculosis is an infection that is still rampant in developing countries and is making a comeback in developed countries, with the advent of AIDS. No single, simple test can definitively diagnose pulmonary tuberculosis; diagnosis is generally based on the correlation of clinical, laboratory (i.e., erythrocyte sedimentation rate, Mantoux test, sputum smears, and sputum culture for acid-fast bacillus [AFB]), radiologic findings, and, in some cases, a therapeutic trial of antitubercular treatment. Among laboratory tests, sputum cultures have a high specificity but there must be at least 10–100 *Mycobacterium tuberculosis* organisms per milliliter of sputum for detection by the culture method (2). Its use as a gold standard in the diagnosis of active pulmonary tuberculosis is questionable, because not all the active cases of tuberculosis would be producing the sufficient number of organisms in the sputum. Problems commonly faced by clinicians treating tuberculosis are difficulty in distinguishing between active and healed lesions in suspected cases of recurrence and assessment of response to therapy in cases of multidrug resistance. Two related studies have been published in *The Journal of Nuclear Medicine* (1,3) that explored the role of radiopharmaceuticals in the above-mentioned problems.

We performed <sup>99m</sup>Tc-tetrofosmin scanning in 30 adult patients (17 men, 13 women). Of the 30 patients, 20 had suspected cases of tuberculosis and 10 were control subjects. Of the 20 patients we believed had tuberculosis, 13 were suspected to have had active tuberculosis on the basis of clinical, laboratory, and radiologic criteria with no history of any antitubercular therapy; 5 patients had previously undergone 6 mo of therapy with no symptoms of active disease; and 2 patients who previously completed full therapy presented with symptoms of active disease. We used 10 patients with coronary artery disease who had presented for cardiac analysis but had no evidence of tubercular disease as control subjects. After 20 min of injecting 370 MBq <sup>99m</sup>Tc-tetrofosmin, we obtained an anterior view using a low-energy, all-purpose collimator. A chest radiograph was obtained within 7 d of scintigraphy. The radiotracer uptake in 12 of 13 (92%) patients with suspected active tuberculosis showed a high degree of correlation with the radiographic findings. In 1 patient (8%), there was bilateral radiotracer uptake (false-positive), whereas the radiograph showed a lesion on 1 side only. Of the 5 treated patients, 4 did not show any radiotracer

uptake and 1 had equivocal uptake. The chest radiographic findings in these treated patients were difficult to interpret definitively as healed or active lesions, and we were not able to differentiate between active lesion and tubercular sequelae in 2 patients with suspected relapse of active tubercular disease after full therapy 5 y before. Both these patients showed uptake on <sup>99m</sup>Tc-tetrofosmin scanning. Sputum cultures done subsequently showed positive results for AFB. All patients in the control group showed no radiotracer uptake.

We concluded that radiotracer uptake in active tuberculosis had a strong correlation with radiographic chest findings in untreated patients who had active tuberculosis. In cured cases of tuberculosis, there was no uptake of <sup>99m</sup>Tc-tetrofosmin. Radiotracer uptake can also be helpful in patients with recurrent symptoms for whom it is difficult to distinguish between active disease and tubercular sequelae.

Because sputum cultures normally take up to 2 mo for confirmation of disease, we believe that <sup>99m</sup>Tc-tetrofosmin scanning could be useful in distinguishing between active and healed lesions, which is not easily distinguished on chest radiographs. This may not be required in routine cases of pulmonary tuberculosis, as the 4-drug regimen generally used has a high cure rate. False-positive scans may result from pneumonitis in patients with suspected recurrence. This can be distinguished by a repeat scan after a 2-wk therapeutic trial of antibiotics. <sup>99m</sup>Tc-tetrofosmin scanning could have useful implications in the follow-up of patients who are on antitubercular therapy to determine the resolution of the active disease into healed lesions, particularly in the case of multidrug-resistant tuberculosis in which second-line drugs are commonly used. We propose to undertake a study of patients with active tuberculosis, in which the follow-up includes the response to therapy with serial scans at 3-mo intervals to see the changes on <sup>99m</sup>Tc-tetrofosmin scanning. This type of follow-up can be suggested in cases of multidrug-resistant tuberculosis for documenting disease control with therapy.

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## Left Ventricular Ejection Fraction and Gated SPECT

**TO THE EDITOR:** In the May 1999 issue of *The Journal of Nuclear Medicine*, the results of our study (1), which focused on

the accuracy of quantitative gated SPECT ([QGS] a commercially available software; Cedars-Sinai Medical Center, Los Angeles, CA) in patients with large perfusion defects, were criticized and the conclusion contested by Germano et al. (2). In our study (1), we found that (a) quantitative gated SPECT underestimated left ventricular ejection fraction (LVEF) by 5% on average and (b) the limits of agreement for the mean difference were large compared with standard equilibrium radionuclide angiography (ERNA) (95% confidence interval, -9.92 to 19.34) using Bland-Altman subsequent analysis (3) for technique comparison. These conclusions confirm our previous results using thallium-gated SPECT and another software configuration (4). We would like to emphasize that our conclusion underlined some evident restrictions of a technique that is based on edge detection in highly pathologic hearts. Originally, we decided to focus on a clinical setting that added critical conditions for the use of gated SPECT (i.e., large perfusion defects and impairment of left ventricular [LV] function).

In our study (1), the wide limits of agreement in QGS compared with equilibrium radionuclide angiography—and not only the underestimation of LVEF—are probably consistent with 8-frame gating (5). This latter point has not yet been clearly demonstrated. In their validation study, Germano et al. (6) found a 4% underestimation of LVEF when using 8-frame (obtained by compacting the 16-interval acquisition) compared with 16-frame gating. However, if the correlation to first-pass angiography is high, the limits of agreement between “compacted” 8-frame gated SPECT and first pass was not mentioned. Moreover, their population was quite different, because 40 of 65 (61%) patients had a history of myocardial infarction but only 9 of 65 (14%) had large infarcts.

Our conclusions do not suggest that routine evaluation of LVEF using QGS in patients with normal or moderately altered perfusion should be discarded. On the contrary, the performance of gated SPECT was similar to that reported with echocardiography and might be helpful in everyday practice by evaluating perfusion and function within the same study (and without additional cost). Furthermore, the relationship between LVEF and prognosis is not linear but exponential. This justifies the use of a reliable method of measurement, capable of correctly classifying the prognosis, particularly in patients with large infarction and LV dysfunction. The capabilities of both first-pass angiography and ERNA were proven in this clinical setting. Last, it remains unclear whether the increase of temporal sampling from 8- to 16-interval gating could improve the accuracy of gated SPECT LVEF in patients with severe perfusion defects. Whether 8-frame gating should be avoided and systematically replaced by 16-frame gating has yet to be shown clearly.

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**REPLY:** In the article by Manrique et al. (1), the authors concluded that “both  $^{201}\text{Tl}$  and  $^{99\text{m}}\text{Tc}$ -MIBI gated SPECT similarly and significantly underestimated LVEF in patients with LV dysfunction and large perfusion defects” and that “although the agreement between gated SPECT and ERNA appear sufficient for routine evaluation of LVEF, ERNA should be preferred when precise measurements are required.” We disagreed with that conclusion in an accompanying editorial (2) and suggested that the likely cause of the left ventricular ejection fraction (LVEF) underestimation by gated SPECT was not the presence of a perfusion defect per se but the use of 8-frame as opposed to 16-frame gating. This hypothesis is supported by our own data, as well as (and, perhaps, more interestingly) by an abstract by Manrique et al. (3), which focused on patients with large myocardial infarction and was submitted to the American College of Cardiology after the submission date of their previous article. In the abstract, Manrique et al. stated that “16-interval gating dramatically increased the correlation to ERNA, without underestimate [sic] LVEF, and should be preferred for LVEF measurement.” We, together with numerous other investigators, agree with the conclusion reached by Manrique et al. in this later abstract.

In their current Letter to the Editor, Manrique et al. appear to revert to their previous position, pointing out the “evident restrictions of a technique that is based on edge detection in highly pathologic hearts.” From the authors’ own statement that “these conclusions confirm our previous results using thallium-gated SPECT and another software configuration,” it can be inferred that the type of gated SPECT algorithm used for quantification is not the culprit for the LVEF underestimation. With respect to quantitative gated SPECT (Cedars-Sinai Medical Center, Los Angeles, CA) and the 2 sets of published data quoted in our editorial (2), 4 additional sets have since been published reporting accurate quantitative measurements of LVEF in patients with large perfusion defects (3,5–7). These results are similar to those reported by other investigators using gated SPECT quantitation algorithms that were not based on edge detection.

Again, we find it difficult to believe that any 2-dimensional imaging technique can be more accurate than 3-dimensional gated SPECT quantitation, particularly in the absence of widely used, clinically validated, and fully automatic quantitative algorithms for the 2-dimensional technique. Although the reproducibility of the equilibrium radionuclide angiography quantitative results may have been excellent at the institutions of Manrique et al., this simply cannot be assumed to be the case at most sites performing nuclear cardiology studies.

Last, we agree with Manrique et al. that “whether 8-frame gating