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}Tl and ^{99m}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

should be avoided and systematically replaced by 16-frame gating has yet to be shown clearly." This is particularly true when relatively low statistics studies are acquired, particularly in conjunction with single-detector cameras and low-dose injections.

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