The methods proposed by Nusynowitz et al. cannot be recommended for evaluation of valvular regurgitations. Instead, the forward outputs of the two ventricles F_{rv} and F_{lv} can be compared to quantitate left-to-right (L-R) shunts. In particular, it holds:

$$\frac{\text{Pulmonary flow}}{\text{Systemic flow}} = \begin{cases} F_{rv}/\ F_{lv} \text{ in ASD} \\ F_{lv}/\ F_{rv} \text{ in PDA} \end{cases}, \qquad (6)$$

because in L-R shunting due to ASD the shunt flow avoids LV, but goes through the RV, contrary then in L-R ductal shunts.

References

1. Nusynowitz ML, Benedetto AR, Walsh RA, Starling MR. First-pass anger camera radioangiography: biventricular ejection fraction, flow and volume measurements. *J Nucl Med* 1987; 28:950–959.
2. Benedetto AR, Nusynowitz ML. Correlation of right and left ventricular ejection fraction and volume measurements. *J Nucl Med* 1988; 29:1114–1117.
3. Donato L. Basic concepts of radiocardiography. *Semin Nucl Med* 1973; 3:111–130.
4. Kelbaek H, Hartling OJ, Skagen K, Munck O, Henriksen O, Godtfredsen J. First-pass radionuclide determination of cardiac output: an improved gamma camera method. *J Nucl Med* 1987; 28:1330–1334.
5. Weber PM, Remedios LV, Jasko I. Quantitative radioisotopic angiocardiography. *J Nucl Med* 1972; 13:815–822.
6. Klepzig H Jr, Standke R, Nickelsen T, et al. Volumetric evaluation of aortic regurgitation by combined first-pass/equilibrium radionuclide ventriculography. *Eur Heart J* 1984; 5:317–325.
7. Klepzig H Jr, Standke R, Nickelsen T, et al. Combined first-pass and equlibrium radionuclide ventriculography and comparision with left-ventricular/right ventricular stroke count ratio in mitral and aortic regurgitation. *Am J Cardiol* 1985; 55:1048–1053.
8. Rigo P, Alderson PO, Robertson RM, Becker LC, Wagner HN Jr. Measurement of aortic and mitral regurgitation by gated cardiac blood pool scans. *Circulation* 1979; 60:306–312.
9. Sorensen SG, O'Rourke RA, Chaudhuri TK. Noninvasive quantitation of valvular regurgitation by gated equlibrium radionuclide angiography. *Circulation* 1980; 62:1089–1098.
10. Makler PT Jr, McCarthy DM, Velchik MG, Goldstein HA, Alavi A. Fourier amplitude ratio: a new way to assess valvular regurgitation. *J Nucl Med* 1983; 24:204–207.
11. Janowitz WR, Fester A. Quantitation of left ventricular regurgitant fraction by first pass radionuclide angiocardiography. *Am J Cardiol* 1982; 49:85–92.
12. Zierler KL. Equations for measuring blood flow by external measuring of radioisotopes. *Circ Res* 1965; 309–321.
13. Glass EC, Cohen HA, Mena I. Deconvolution of first-pass radionuclide angiograms for determination of forward ejection fraction [Abstract]. *Am J Cardiol* 1982; 49:P1032.
14. Philippe L, Mena I, Darcourt J, Frenh WJ. Evaluation of valvular regurgitation by factor analysis of first-pass angiography. *J Nucl Med* 1988; 29:159–167.

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REPLY: Eterović apparently misinterpreted our equations. He commented that "... they concluded that LV regurgitant flow is the difference in the apparent LV flow... and the 'corrected LV flow' ...". In fact, we stated that regurgitant flow is the difference between the pulmonary flow and the apparent (uncorrected) LV flow.

Eterović asserts that indicator dilution flows are forward flows and are invariant to both regurgitation and bolus smearing. We disagree. Regurgitation can be viewed mathematically as a negative feedback, or as Lassen and Perl describe it, as "instant recirculation" (*2*). If one assumes monoexponential washout of indicator from a nonregurgitant LV, it can readily be shown that the effect of regurgitant flow (feedback) is to decrease the rate at which indicator leaves the LV. This slower rate translates into an indicator dilution curve downslope that is shallower than for the nonregurgitant case, and in turn the shallower downslope leads to an increased area under the indicator dilution curve. Since this area is in the denominator of the cardiac output equation (Eq. 1, Ref. 1), the increased area due to regurgitation leads to a decreased cardiac output; this decreased cardiac output is exactly in accord with our clinical observations.

Lassen and Perl (*3*) deal with the issue of bolus smearing in exacting mathematic detail. Briefly, note that, in Eq. (1) (*1*), the ratio of Ceq to the area under the curve is the reciprocal of the mean transit time. The total mean transit time represented by this term is the sum of the mean transit time of the system under consideration (LV, RV, or lungs) plus the mean transit time of the "injection". In the case of the RV, the bolus is very tight and the injection component is small. However, by the time the "bolus" has arrived in the LV, it has been smeared by the mean transit times of the RV and lungs. This smearing results in a much increased "injection" mean transit time as input into the LV and leads ultimately to an increased area under the indicator dilution curve. Convolution analysis has been proposed to deal with this effect, as suggested by Eterović's Ref. 13, but to date this type of analysis has been difficult to implement and has not lead to widely accepted improvement in data analysis. Thus, we disagree that flows calculated from this ratio (Ceq/Area) do not depend on "tempo of indicator input".

We agree that the lungs are not a perfect mixing model and that the entire volume of both lungs cannot be included in our regions of interest. However, we use as large a portion of the lungs as possible and we rely on the "convective spaghetti model" and bolus fractionation principle as described by Lassen and Perl (*4*), which states that the flow through a fraction of a larger volume is proportional to the flow through the entire volume if the various flow channels carry approximately equal flow. This is clearly an assumption that cannot be proved or disproved; we feel confident in making the assumption given the excellent correlations we observed (*1*).

Eterović has also misinterpreted our description of how we calculated EDV. We do *not* use forward flow. We use corrected (total) LV flow (forward plus regurgitant) to calculate SV and we use total (forward plus regurgitant) flow to calculate EF; thus, we are consistent. Eterović also asserts that F in his Eq. (2) is "widely recognized" as forward flow. We agree, so long as there is no regurgitation or shunting, or other process that might mimic them (e.g., bolus smearing).

Since we did not actually make the two errors suggested by

Eterović, we feel that the excellent correlations observed in our clinical data are prima facie evidence that our assumptions and simplifications are reasonable. In fact, we explicitly correct two terms in Eq. (1) (*1*), errors in which are neglected by many authors. First, calculation of total blood volume from peripheral hematocrit and a RISA plasma volume overestimates TBV by ~ 13% (*6*); we adjust the red cell volume by using a factor of 0.87 to account for the difference between peripheral and central hematocrit. Second, we correct LV parameters for bolus smearing; in nonregurgitant patients the average bolus smearing is ~ 12% (*1*) and its effect is to increase the area under the indicator dilution curve by that amount. Although the errors are roughly offsetting, they are errors nonetheless and should be taken into account explicitly, as we do.

We have found calculation of regurgitant fraction from the stroke counts obtained from a gated equilibrium study to be fraught with difficulty (e.g., selection of background areas, overlapping of heart chambers). Convolution analysis and factor analysis have been proposed and have not achieved widespread acceptance. We feel that first-pass techniques are the only reliable method currently available.

The comments by Eterović regarding shunts are interesting but are relevant to our paper only insofar as shunts and regurgitation are examples of "early" and "instant" recirculation, respectively (*2*).

References

1. Nusynowitz ML, Benedetto AR, Walsh RA, Starling MR. First-pass Anger camera radiocardiography: Biventricular ejection fraction, flow, and volume measurements. *J Nucl Med* 1987; 28:950–959.
2. Lassen NA, Perl W. Tracer kinetic methods in medical physiology. New York: Raven Press, 1979: 145–146.
3. Lassen and Perl, Tracer kinetic methods in medical physiology. New York: Raven Press, 1979: 86–88.
4. Lassen and Perl, Tracer kinetic methods in medical physiology. New York: Raven Press, 1979: 38–39.
5. Lassen and Perl, Tracer kinetic methods in medical physiology. New York: Raven Press, 1979: 85–86.
6. Nusynowitz ML, Blumhardt R. Estimation of true red cell volume from RISA red cell volume. *Am J Roentgenol* 1974; 120:549–552.

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Role of Technetium-99m Phosphonate Bone and Indium-111 Leukocyte Scanning for Detecting the Infected Hip Prosthesis

TO THE EDITOR: A recent report by Johnson et al. described the use of technetium-99m (^{99m}Tc) hydroxymethylene diphosphonate (HDP) bone scanning and indium-111 (^{111}In) labeled leukocyte scanning (ILLS) for detecting infected joint prostheses (*1*). They found an increased specificity and accuracy for the two types of scan taken in sequence compared to ILLS alone. Although their study included 21 total hip arthroplasties, the authors made no reference to our report of 50 painful prosthetic hip joints investigated with a [^{99m}Tc]methylene diphosphonate (MDP) bone scan and an ILLS, 32 of whom also had a gallium-67 (^{67}Ga) citrate scan (*2*).

In our study, [^{99m}Tc]MDP bone scans were classified into the following distributions of radioactivity around the prosthesis: normal uptake, focally abnormal uptake, diffusely abnormal uptake, and focal superimposed on diffusely abnormal uptake (the captions to Figure 1 (c) and (d) in Ref. (2) should be interchanged). We classified ILLS and ^{67}Ga scans as abnormal if they demonstrated hyperactivity in any distribution (i.e., by the first of the two ways described by Johnson et al.). Infection was absent in all cases of normal and focal uptake in the [^{99m}Tc]MDP bone scans, and was present in five out of six cases of diffuse uptake. The false-positive diffuse uptake occurred in a case of nonseptic synovitis which also produced a false-positive ILLS. In the 26 prosthetic hips which had focal superimposed on diffuse uptake, infection was present in six cases. Thus for the normal, focal, and diffuse types of ^{99m}Tc uptake, the ILLS was unnecessary. Consequently, the policy in this department is to conduct a [^{99m}Tc]MDP bone scan first and proceed to an ILLS only if the uptake in the former is classified as focal superimposed on diffuse.

Subsequent to conducting our review and before implementing the above policy, we obtained follow-up on a further 11 painful prosthetic hips imaged with [^{99m}Tc]MDP and [^{111}In] leukocytes that endorsed our earlier conclusions. Focal superimposed on diffuse ^{99m}Tc uptake was produced in seven cases. There were two cases of proven infection which were the only cases with diffuse ^{99m}Tc uptake and the only cases with an abnormal ILLS. For completeness, these results have been added to those already published (*2*) and the combined data are given in Table 1.

The implication of Johnson et al.'s study is that all patients investigated for a painful prosthetic hip require an ILLS. If the ^{99m}Tc bone scan is performed first and classified as above, it is our experience that only about half of the patients referred routinely for investigation will require a subsequent ILLS (Table 1). The costly and time-consuming procedure of labeling leukocytes with ^{111}In can be avoided for the remainder.

Applying our method to the two prosthetic hip cases illustrated by Johnson et al., the [^{99m}Tc]HDP bone scan given in their Figure 1 would be classified as focally abnormal and interpreted as uninfected, an ILLS would not have been performed, and the result agrees with their clinical finding of negative for infection by intraoperative cultures. The uptake in the [^{99m}Tc]HDP bone scan shown in their Figure 2 would be classified as diffusely abnormal which would be interpreted as infected, an ILLS would not have been performed, and the result again would agree with their clinical finding of positive for infection by intraoperative cultures.

TABLE 1
Combined Results from Ref. (2) and the Review of 11 Further Cases of [^{99m}Tc]MDP for Detecting Infection Around a Hip Prosthesis

[^{99m}Tc]MDP bone scan uptake	With infection	Without infection
Normal	0	3
Focal	0	17
Diffuse	7	1
Focal + diffuse	6	27