First-Pass Radionuclide Angiocardiography Using a Single-Crystal Gamma Camera: Are Count Statistics Actually the Limiting Factor?

TO THE EDITOR: In his editorial in the August 1994 issue of the *Journal* (*1*), Dr. Port reviewed the ups and downs of first-pass radionuclide angiography (FPRNA) as a function of both the design and performance of detectors. The editorial focuses on the reticence of a part of the nuclear medicine community to use this technique, which is probably the oldest clinical procedure in nuclear medicine (*2*). In the same issue, Nichols et al. validated FPRNA using a high-count rate single-crystal camera versus a multicrystal one. To obtain adequate counts statistics, they injected 740–925 MBq (20–25 mCi) and used a ultrahigh sensitivity collimator. In these conditions background-corrected end-diastolic counts were 5.0 ± 2.9 kcts.

Dr. Port agreed that a single-crystal FPRNA requires at least a 740-MBq (20 mCi) dose. This opinion, shared by some nuclear physicians and physicists, introduces a limitation for simultaneous assessment of function and perfusion at rest and during exercise in a single-day protocol, since a 370-MBq (10 mCi) dose is injected at rest. A strict approval of this threshold would then dissuade nuclear physicians from performing what is probably the most powerful noninvasive approach to diagnosing coronary artery disease today.

Other authors, however, (*4*) suggest that 2.0 background-corrected end-diastolic kilocounts should be adequate for reliable FPRNA. The question remains, which opinion should I follow if I am convinced that some of my patients would benefit from simultaneous function and perfusion assessment? The evaluation of systematic error on ejection fraction (EF) calculation due to statistic fluctuations inherent in the radioactive decay phenomenon could give part of the answer.

In our department, we routinely perform function perfusion studies with a single-crystal nuclear camera using a single-day MIBI protocol. The feasability of FPRNA with a 370-MBq dose and a high sensitivity collimator was first assessed in a group of 40 patients who underwent both FPRNA with this low dose and gated radionuclide angiocardiography. The study showed excellent correlation between both techniques in terms of EF measurement and regional wall motion assessment is not yet published.

Briefly, average background-corrected end-diastolic counts were 2.7 ± 1.3 kcs. The EF was calculated on the composite cycle using two end-diastolic and end-systolic regions of interest (ROIs) and a paraventricular end-diastolic background ROI.

In this situation, the EF is a function of:

$$f(x, y, z) = \frac{(x - az) - (y - bz)}{x - az}, \qquad \text{Eq. 1}$$

where x is the number of counts in the end-diastolic ROI, y is the number of counts in the end-systolic ROI, and z is the number of counts in the background ROI, a is the ratio of the number of pixels in the end-diastolic ROI to the number of pixels in the background ROI and b is the ratio of the number of pixels in the end-systolic ROI to the number of pixels in the background ROI.

The systematic error due to radioactive decay statistic fluctuations is:

$$\Delta f = \left|\frac{\partial f}{\partial x}\right| dx + \left|\frac{\partial f}{\partial y}\right| dy + \left|\frac{\partial f}{\partial z}\right| dz, \qquad \text{Eq. 2}$$

where dx, dy and dz are the standard deviations $\sqrt{x}$, $\sqrt{y}$, $\sqrt{z}$.

The differentials are:

$$\frac{\partial f}{\partial x} = \frac{y - bz}{(x - az)^2}, \quad \frac{\partial f}{\partial y} = -\frac{1}{(x - az)}, \quad \frac{\partial f}{\partial z} = \frac{bx - ay}{(x - az)^2}. \qquad \text{Eq. 3}$$

For example, the data from one of these patients are: x = 3.75 kcs, y = 1.69 kcs, z = 0.55 kcs; 195 end-diastolic ROI pixels, 110 end-systolic ROI pixels, 82 background ROI pixels, EF = 0.61. This corresponds to 2.44 background-corrected end-diastolic kilocounts. In these conditions, Δf = .031.

The same estimation on the same patient with 5.0 background-corrected end-diastolic kilocounts would be Δf = .02 which, as expected, is lower. It is doubtful, however, that this difference should have any clinical significance.

What would occur in a situation when both EF and end-diastolic counts would be low, which are two concomitant factors for higher systematic error on EF calculations? In one of our patients, the background-corrected end-diastolic counts were 1.53 kcs and EF was 0.38. In this patient, the entire bolus was not injected because of a misuse of the bolus syringe. From these data, we estimated that Δf was 0.07 and would have been 0.032 with 3.0 kcs. Now, the advantage of higher counts statistics is more decisive, although it would be needed to assess the clinical consequences. These unfavourable conditions are not, however, likely to combine often since the transit time of the bolus through cardiac chambers is longer and thus count statistics are higher when EF is depressed. In our study, all patients with a 0.4 or less EF had 2.1 or more background-corrected end-diastolic kilocounts. The Δf for a previous patient with 2.0 kcts background-corrected end-diastolic counts would be 0.04 compared to 0.032. Again, this should not significantly impair the clinical relevance.

I am not sure that counting statistic requirements accepted by one "camp of the clinical radionuclide imaging community" should be so drastic. I agree with Wackers et al. who recommend that background-corrected end-diastolic counts should not be less than 2.0 kcs.

Finally, I agree with Dr. Port's view that more work on FPRNA with single-crystal cameras is needed. Some questions to consider: Are the detectors and collimators optimal? Why should we not routinely use external jugular vein injection which, in our experience, is easy to perform, always gives optimal bolus and probably contributes to adequate count statistics? Which is the best acquisition mode: frame or list mode? For the latter, which is the best reframing procedure? Which is the most acceptable background substraction method? What are the right criteria for selecting the number of individual beats in the left ventricular phase? Each item of this nonexhaustive list interferes with FPRNA reliability. Counting statistics are only an additional problem that should be adequately solved, even with relatively low

doses and state-of-the-art nuclear cameras combined with the skill of necessarily well trained technologists and physicians.

It would be a shame if the dogma of the 20-mCi dose would discourage a part of our community from utilizing simultaneous function and perfusion assessment, a unique approach of imaging coronary artery disease by nuclear medicine.

REFERENCES

1. Port SC. The first-pass ventricular function study: why now? [Editorial]. *J Nucl Med* 1994;35:1301–1302.
2. Jones RH. Radionuclide angiocardiography revisited. *J Nucl Med* 1990;31: 1300–1302.
3. Nichols K, DePuey EG, Gooneratne N, Salensky H, Friedman M, Cochoff S. First-pass ventricular ejection fraction using a single-crystal nuclear camera. *J Nucl Med* 1994;35:1292–1300.
4. Wackers FJ, Sinusas A, Saari MA, Mattera JA. Is list mode ECG-gated first-pass LVEF accurate using a single-crystal gamma camera? Implications for ^{99m}Tc labeled perfusion imaging agents [Abstract]. *J Nucl Med* 1994;32(Suppl):939.

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REPLY: Esquerré and Coca raise several significant issues in their comments regarding first-pass radionuclide angiography (FPRNA) using single-crystal gamma cameras. Foremost of their concerns is the issue of the appropriate dose of ^{99m}Tc. Both our group (*1*) and Nichols et al. (*2*) have suggested that a 20-mCi (740 Mbq) dose is necessary to provide consistently reliable count rates during FPRNA on a single-crystal system. We also adhere to that recommendation even when using the multicrystal camera to avoid suboptimal clinical results. Esquerré and Coca are concerned that such a recommendation will inhibit the application of FPRNA during same-day sestamibi protocols where one dose must be 10 mCi (370 MBq). They suggest that, in their experience, FPRNA can be reliably performed with 10-mCi injections and average count rates of approximately half those reported by Gal et al. (*1*) and Nichols et al. (*2*) in previous studies using single-crystal systems.

The appropriate dose for a first-pass study depends on several factors, including the sensitivity of the camera-computer system, the collimation, the acquisition matrix, the body habitus of the subject, the number of sinus beats available for analysis during the left ventricular phase, the range of statistical reliability that the operator is willing to accept and the objective of the study. Esquerré and Coca do not provide enough information in their letter for us to assess those variables in their data. They report an average of 2.7–1.3 kcts at end-diastole in the representative cycle. The statistical error in the measurement of left ventricular ejection fraction (LVEF) increases as both the counts and the LVEF decrease. At 2.7 kcts, the error in an LVEF that is 0.50 is ±0.05, whereas the error in an LVEF of 0.30 is ±0.10 (*3*). When the LVEF is in the normal range, the exact identification of the end-diastolic peaks and end-systolic troughs becomes less critical and the count rate is much more forgiving. When the LVEF is low, small errors in the calculation of end-diastolic and end-systolic counts make much larger differences in the calculated LVEF. Fortunately, at low LVEFs, the chambers are usually large and there are frequently more beats for analysis, so there are usually adequate count statistics. Clinically, however, it is the measurement of intermediate range LVEFs that is so critical prognostically, because survival is fairly stable at LVEFs above 0.50 and consistently poor at LVEFs less than 0.30. Prognosis varies dramatically, however, when the LVEF is in the range of 0.35–0.50 (*4*). One of the examples given by Esquerré and Coca of a patient with an intermediate range LVEF and only 1.53 kcts at end-diastole is important since it points out how very low count rates can occur despite the best intentions of the operator. The error in the calculated LVEF of 0.38 was 0.06 LVEF units. In other words, the true LVEF could have been 0.32–0.44, which is clinically unacceptable. The prognosis of a 0.32 LVEF is much different than that of a 0.44 LVEF.

The objective of the study is also important in determining the necessary count rate and dose. When performed adjunctively with perfusion imaging, some clinicians are only interested in obtaining the prognostic information contained in the LVEF. For that purpose, it may not be mandatory to get the absolutely highest count rates possible. For diagnostic quality, however, in regional wall motion assessment, the count rate requirement is higher than that for the measurement of LVEF alone. We routinely use collimation that provides an acceptable compromise between count rate and spatial resolution so that we may analyze regional wall motion confidently. Parametric image analysis is also highly dependent upon the count density of the data.

The count density is also lower when the acquisition matrix is 64 × 64 as is so typical of FPRNA on many single-crystal systems. Unfortunately, at the average count rate of 2.7 kcts recorded by Esquerré and Coca on a 64 × 64 matrix, one should expect suboptimal and occasionally uninterpretable end-systolic images due to the low count densities per pixel. That problem has been our experience and our main concern with low-dose FPRNA on both single- and multicrystal systems and we never use a matrix larger than 32 × 32.

In making recommendations for the general application of FPRNA, we have always believed that if it is important enough to do the study, it is equally important to ensure adequate statistics. We have no doubt that the 10-mCi study will frequently be technically acceptable when all conditions (patient size, camera, collimator, acquisition matrix, bolus and number of beats) are favorable. Unfortunately, there are too many instances where those conditions are not met and the data become marginal at best and frequently unacceptable. The higher dose study can accommodate a larger patient, fewer available beats, a delayed bolus and even somewhat higher resolution collimation.

I would certainly not dissuade Esquerré and Coca from pursuing low-dose FPRNA in their laboratory, but the onus is on them to prove to the imaging community that the low-dose, first-pass study, especially when acquired on a single-crystal system, is consistently clinically reliable both at rest and during exercise. Those of us interested in first-pass studies would welcome a manuscript from Esquerré and Coca that documents their experience.

REFERENCES

1. Gal R, Grenier RP, Carpenter J, Schmidt DH, Port SC. High count rate first-pass radionuclide angiography using a digital gamma camera. *J Nucl Med* 1986;27:198–206.
2. Nichols K, DePuey EG, Gooneratne N, Salensky H et al. First-pass ventricular ejection fraction using a single crystal nuclear camera. *J Nucl Med* 1984;35:1292–1300.
3. Wackers JFTh. First-pass radionuclide anigocardiography. In: Gerson M, ed. *Cardiac nuclear medicine*. New York: McGraw Hill; 1987:58.
4. Pryor DB, Harrel FE, Lee KL, et al. Prognostic indicators from radionu-