Parametric Images for Quantitative Measurements of Regional Myocardial Blood Flow in Humans: A Step in the Right Direction

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In the March issue of the *Journal*, Choi and co-workers (*1*) described a useful method for obtaining parametric images of myocardial blood flow using Patlak graphical analysis (*2,3*) of dynamic PET ^{13}N-ammonia scans of the myocardium. The method, which originally was designed for applications involving brain imaging, was validated for myocardial scans by comparing results obtained with those of standard nonlinear least squares fitting of dynamic data to a compartmental model of ^{13}N myocardial tracer kinetics (*1,4*). Advantages, potential practical applications and limitations of this approach to the analysis of dynamic PET ^{13}N-ammonia myocardial perfusion studies are discussed below.

ADVANTAGES

The principal advantage of this approach for image analysis concerns its quantitative objective nature, the importance of which cannot be overstated. The ability to measure regional myocardial blood flow nonnivasively in humans represents an important methodological advance which has yet to be fully exploited. The convenience and simplicity of "eyeballing" single-photon nuclear images to a certain extent has been carried over to PET and undoubtedly has contributed to failure in fully exploiting its quantitative capabilities. Choi et al. may have helped to reverse this trend by providing a practical, rapid method for reducing the large amount of data in a dynamic PET study to a single easily understood parametric image of myocardial blood flow in the human heart. Accordingly, this approach to image analysis and others like it holds enormous potential.

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APPLICATIONS

A look at Figure 6 of Choi et al. quickly suggests a number of compelling reasons why it is important to make more extensive use of quantitative images of myocardial blood flow. In the top row of the figure, ^{13}N-ammonia uptake by the myocardium is shown in a normal dog at baseline (left panel) and during dipyridamole infusion (right panel). Several questions immediately spring to mind. Activity in most segments (save anterior) appears nearly equal in both images. Does that mean that myocardial blood flow is also equal? Almost certainly not. It is likely, although not stated, that the images have been normalized (each to itself) and we are thus unable to evaluate flow responses in a given zone between conditions (i.e., absolute coronary flow reserve (*5*) cannot be determined).

What about relative coronary flow reserve? There is a mild-to-moderate reduction in activity in the anterior segment vis-a-vis other regions in the dipyridamole image. The significance of the defect, however, is difficult to assess, especially since we can evaluate it only in terms of its percent activity versus other myocardial regions. Furthermore, we are forced to assume that flow responses in other myocardial regions are "normal," which may or may not be correct. Accordingly, a qualitative, relativistic approach to analysis of myocardial perfusion images forces us to make an incomplete and, in many cases, inadequate assessment of coronary flow responses to a variety of physiological conditions.

Now consider the bottom row of images. These scans map myocardial blood flow in absolute units (ml/min/g) in the same animal under the same conditions. Indeed, the blood flow images are computed from the uptake scans and the arterial blood (left ventricular region of interest) time-activity curve. It is now quickly apparent that resting blood flow is reduced versus dipyridamole in all regions. We also know the absolute levels of flow in each region under both conditions and thus are in a position to determine if prevailing levels of flow are appropriate for the conditions of the study. Resting blood flow values of 1–1.5 ml/min/g are considered "normal" for closed-chest sedated swine. A comparable number can and should be developed for normal unmedicated humans resting quietly in a PET scanner.

The myocardial flow response to dipyridamole in this animal is also interesting. Flow in the anterior segment appears to have increased from roughly 1 to only 2–2.5 ml/min/g whereas septal flow increased from about 1.2 to 3.5–4.0 ml/min/g. Myocardial blood flow in the inferior segment was even lower than that of anterior and septal segments at baseline, but increased to levels similar to those of the septum and lateral wall with dipyridamole. It also is worth noting that the observed flow responses could have been conveniently summarized and displayed in an anatomical format with appropriate subtraction and division images. Furthermore, it is important to determine if differences in myocardial blood flow and flow responses observed in this study represent true examples of flow heterogeneity (*6*) or if some other factor(s) is involved. Quantitative imaging permits us to formulate and potentially test hypotheses that address these and other interesting questions concerning coronary blood flow and its regulation in both health and disease.

Qualitative imaging cannot address issues such as absolute coronary flow reserve or appropriateness of a given level of flow to a particular set of physiological conditions. Accordingly, the ability to quantitate myocardial blood flow represents an opportunity to substantially enhance our ability to assess noninvasively the functional status of coronary circulation. Just as noninvasive measurement of left ventricular ejection fraction (*7*) provided a major tool for a host of clinical, epidemiological and physiological studies, so too can measurement of absolute levels of myocardial blood flow provide a similar opportunity.

LIMITATIONS

Aside from economic and regulatory issues which apply to PET imaging in general, what are the limitations of the approach to myocardial image analysis described by Choi et al. (*1*)? First, it is clear that endocardial and epicardial blood flow cannot be measured by this or any other PET technique because of limited spatial resolution (10 mm in-plane and 7 mm axial). Assessment of endocardial epicardial distribution of blood flow and flow responses to vasodilator stimuli represents an important but as yet clinically unattained component of the evaluation of problems such as functional severity of coronary artery stenoses, myocardial viability and myocardial hibernation (*8–10*). Current efforts to address these issues with PET perfusion and/or metabolic imaging must rely on transmural measurements which may obscure important differences in endocardial epicardial distribution of flow or metabolism. Accordingly, truly complete parametric images of myocardial blood flow and its distribution are still lacking and must await future technical advances.

Second, since parametric images are about quantitation of myocardial blood flow, it is important to note in the paper by Choi et al. (*1*) that absolute values of flow determined by Patlak analysis (*2,3*) in humans were sensitive both to time points over which the data were analyzed and to constraints placed on the intercept and therefore the slope of the plot (their Figure 8). Since the slope of the plot reflects K1 (flow∗extraction fraction), it is understandable why constraints on the intercept influence the computed absolute value of flow. Furthermore, the compartmental model used by Choi et al. employed only the first 2 min of data and assumed that $k2 = 0$. Accordingly, limits placed by Choi et al. on both the tracer kinetic compartmental model and Patlak analysis need to be recognized and understood before implementation of their method.

SUMMARY

Choi et al. (*1*) describe a useful method for producing parametric images of myocardial blood flow from dynamic PET ^{13}N-ammonia images of the myocardium. The method is important because it provides a convenient vehicle for quickly displaying anatomically oriented information about absolute values of myocardial blood flow in humans. Absolute values of myocardial blood flow will enhance our ability to assess relative coronary flow reserve and will make it possible to noninvasively and routinely measure absolute coronary flow reserve. In addition, absolute measurements of myocardial blood flow will be useful in addressing important clinical problems, such as myocardial viability, stunning and hibernation. We look forward to the time when technical advances make it possible to obtain accurate parametric images not only of transmural but also endocardial epicardial distribution of blood flow.

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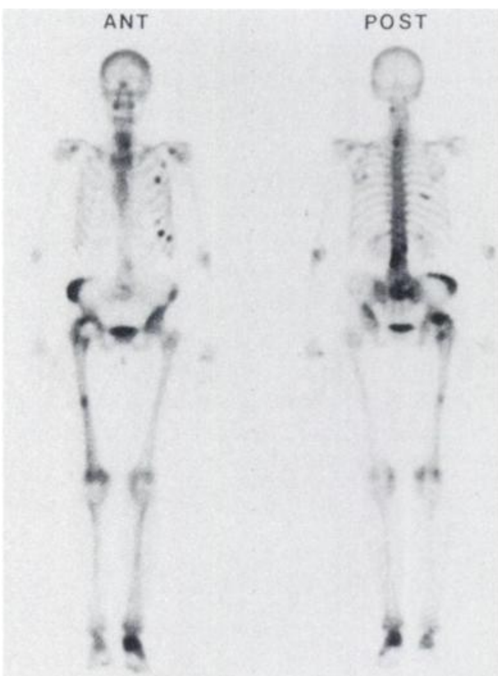
FIRST IMPRESSIONS



PURPOSE

A 59-yr-old woman with a history of breast cancer, metastatic to bone, received irradiation to the sacrum and hormonal therapy. She was referred for a bone scan to evaluate the status of her skeletal metastases. On first impression, the images were consistent with widespread metastases. However, by history and physical and radiographic examination, she was found to have a right femoral metastatic lesion (not a loose prosthesis), heterotopic ossification in the right hip, traumatic left rib fractures, reflex sympathetic dystrophy syndrome of the left lower extremity, and Paget's disease in the right iliac spine, as well as other skeletal metastases to explain the remaining foci of abnormal uptake.

TRACER

Technetium-99m-MDP.

ROUTE OF ADMINISTRATION

Intravenous injection of an antecubital vein.

TIME AFTER INJECTION

Three hours.

INSTRUMENTATION

Siemens Bodyscan whole-body scanner.

CONTRIBUTORS

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INSTITUTION

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