
TO THE EDITOR: Presently, regional measurements of regional coronary arterial blood flow are not available in the clinic. These measurements are important because myocardial substrate oxidation is coupled to oxygen consumption in the processes of oxidative phosphorylation and electron transport. Similarly, substrate and O2 delivery is, of course, by regional blood flow. Since data obtained by positron emission tomography (PET) are, by definition, quantitative, one would expect that the computed regional values of nutritional flow and of oxidative metabolism may provide valuable information to the clinician. It would then be possible to address the issue of myocardial supply/demand needs following thrombolysis, angioplasty, and coronary revascularization.

Soufer and Zaret (1), correctly in my opinion, presented arguments for the use of oxygen-15(-15O) water when quantitation of myocardial blood flow is needed in cardiac PET studies. Two months later, an editorial in the JNM (2) asserted that nitrogen-13-ammonia (13N-ammonia) is equally fit to accomplish this purpose. What is the reader to believe?

Like thallium-201, rubidium-82, and radiopotassium, 13N-ammonia is extracted by the heart according to the fractional (myocardial) cardiac output. However, as expected, the extraction fraction of 13N-ammonia is nonlinear (in fact it plateau) as myocardial blood flow substantially increases following exercise (3) and dipyridamole challenges. Conversely, as per thallium-201, the extraction will exceed flow in low-flow regions. These flow-related changes in extraction are not present when 15O-water is used (4, 5).

Other characteristics that limit the use of 13N-ammonia for absolute quantitation of flow are:

1. Dependence of the kinetics of 13N-ammonia on myocardial metabolism (6).
2. Use of a kinetic model that does not take into account distributive parameters such as blood flow and the permeability-surface product (7).
3. Presence of substantial amounts of 13N-labeled metabolites (such as amino acids and urea) in blood, as early as 5 min after the intravenous delivery of 13N-ammonia (8). This complicates the computation of the input function.

Furthermore, the published PET 13N-ammonia data was never corrected for partial volume averaging, spillover effects (radioactivity crossover between blood pool and myocardium, and vice versa), and the linear effects of motion. Such corrections have been implemented in 15O-water studies (4).

Therefore, physiologic and instrumental limitations pose an unresolved challenge for determination of absolute nutritional coronary arterial flow using 13N-ammonia. If one spends several million dollars to build a PET center, one must remember that the conventional wisdom is that measurements of coronary flows with 15O have sound backing from experiment and from experience.

REFERENCES


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REPLY: The Letter to the Editor in response to our editorial in the Journal (1) asserts that only oxygen-15(-15O) labeled water permits the noninvasive quantification of regional myocardial blood flow. We agree on the suitability of 15O-water for such measurements, but disagree that they are the exclusive domain of 15O-water. We maintain that regional myocardial blood flow can be measured equally well and accurately with diffusible tracers as supported by several recent publications (2-5).

The authors cite “physiological and instrumental limitations” for blood flow measurements with, for example, nitrogen-13-ammonia (13N-ammonia) and infer that these limitations do not apply to 15O-water. Let us first consider “physiological limitations.” From a theoretical point of view, 15O-water seems indeed to be the favorite. Because it is relatively freely permeable across the capillary and cellular membranes, first-pass extraction fractions approach unity and are relatively insensitive to flow changes (6). The linear response of the