METHODOLOGIC ASPECTS OF MYOCARDIAL BLOOD FLOW QUANTIFICATION WITH 1-^{11}C-ACETATE PET

TO THE EDITOR: I have read with interest the article of Sciacca et al. (*1*) reporting on a comparison of $H_2{}^{15}O$ and 1-^{11}C-acetate for quantification of myocardial blood flow with PET. The aim of this study, to contribute to the validation of 1-^{11}C-acetate as a quantitative flow tracer in myocardial PET, is certainly important. However, the article exhibits methodologic problems concerning tracer kinetic modeling as well as correction of partial-volume effects.

The authors assume the rate of tissue clearance to be equal to perfusion, F (Fig. 1; Eqs. 1 and 2 (*1*)). This assumption is not justified: It is known from animal data (*2*) that within approximately 15 s after passage of a very short intraarterially injected bolus, tracer concentration drops to an approximately constant plateau of about 2- to 3-min duration (the initial drop corresponding to the finite first-pass extraction). Tissue clearance occurs only after this plateau phase and is numerically an order of magnitude smaller than F. Therefore, postulating a clearance rate equal to F seems inconsistent with the actual behavior of acetate, and parameter estimation bias can be expected. It would actually be less problematic to neglect tissue clearance altogether during the first 3 min. It should be noted, however, that restricting data evaluation to this time range leads to substantial loss of statistical accuracy of the perfusion estimates in comparison with using longer fitting intervals. I believe, therefore, that a 1-compartment model without parameter constraints (i.e., setting K_1 to zero and allowing for arbitrary clearance rates in Eqs. 1 and 2 (*1*)) would be a more adequate model. Such a model has the particular advantage of being able to fit the data over much longer time intervals (*3*,*4*).

Furthermore, I consider the described method for recovery correction to be questionable. Essentially, the F_{MM} (which can be identified with the recovery coefficients if fractional blood volume is neglected) are adjusted in such a way that the flow values derived with $H_2{}^{15}O$ and 1-^{11}C-acetate coincide if the individually adapted F_{MM} are used. The good agreement of the perfusion values is, therefore, no proof of adequacy of the recovery correction method. Rather, the derived F_{MM} empirically correct for all other sources of errors, such as model configuration and assumption of a constant extraction fraction. This conclusion is substantiated as follows. The general solution of Equations 1–3 (*1*) can be written as:

$$Q_{\text{tissue}}(t) = (F_{MM} \cdot E \cdot F) \times g(t) + F_{\text{BM}} \cdot C_a(t),$$

where E is the unidirectional extraction fraction, $g(t)$ describes the shape of the tissue signal, F_{BM} includes both spillover of counts from blood in the adjacent left ventricular cavity and counts from the fractional blood volume within the tissue region of interest, and $C_a(t)$ is the tracer concentration in arterial blood. The amplitude of $g(t)$ is given by:

$$A = F_{MM} \cdot E \cdot F. \qquad \text{Eq. 1}$$

This amplitude is an easily identifiable parameter, but as long as arbitrary tissue clearance is allowed for (no influence of F on $g(t)$), it is impossible to identify the individual factors contributing to A. Even under the assumptions used by Sciacca et al. (*1*) (i.e., clearance equal to flow) it is still impossible to differentiate between F_{MM} and E.

Because Sciacca et al. (*1*) found relatively large discrepancies in the flow estimates obtained with $H_2{}^{15}O$ and 1-^{11}C-acetate when using fixed values for E and F_{MM}, they describe a procedure for improving the recovery correction, which essentially is equivalent to solving Equation 1 for F_{MM} using the flow value determined in the $H_2{}^{15}O$ investigation for F. Correlating these individual adapted F_{MM} to echocardiographic findings is then performed to enable individual recovery correction. Thus, agreement of flow values derived with 1-^{11}C-acetate and $H_2{}^{15}O$ is enforced by the method.

Two other questions come immediately to mind in this context. Why did the authors not use the individual F_{MM} that have been apparently derived from the corresponding $H_2{}^{15}O$ scans? How do the F_{MM} derived by the authors' method compare with those obtained from the $H_2{}^{15}O$ scans?

In conclusion, I think that the data of Sciacca et al. (*1*) make a valuable contribution to the ongoing efforts to validate 1-^{11}C-acetate as a quantitative flow tracer, but the methods chosen to evaluate the acetate investigations seem to be inadequate. A modification of the model configuration, in combination with an implicit recovery correction as proposed, for instance, by Hutchins et al. (*5*), seems to be desirable.

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