INVITED COMMENTARY

Gated PET and Ventricular Volume

Cardiac research increasingly relies on small animals (rats and mice) in which the study of phenotypic expressions of genomic defects as well as the evaluation of gene therapies is possible. Accordingly, over the past few years new dedicated instruments have been developed that allow noninvasive imaging with ultrasound, magnetic resonance, and PET in small animals in vivo. These techniques can be used to monitor gene expression in vivo but can also simultaneously assess physiologic parameters such as myocardial blood flow in the same animal (*1*). Accurate measurement of physiologic parameters in small animals is challenging but is an essential term in the equation to define the phenotype of healthy and diseased animals and eventually to test the efficacy of any form of treatment.

PET is a well-established technique that is routinely used for the noninvasive imaging and quantification of myocardial metabolism, perfusion, and receptor density in humans (*2*). In addition, gated PET has been shown to accurately measure end-diastolic and end-systolic left ventricular (LV) volume and ejection fraction (EF) in healthy and diseased humans (*3*–*5*). In patients, end-diastolic volume, end-systolic volume, and EF are important predictors of prognosis and mortality after acute myocardial infarction. Furthermore, parameters of regional and global LV function are used to assess the efficacy of revascularization in patients with coronary artery disease and chronic but reversible LV dysfunction (hibernation). Therefore, application of these noninvasive measurements of LV function to small animals would be important to define normal values and to monitor the effect of different therapeutic strategies in disease models.

In this issue of *The Journal of Nuclear Medicine*, Croteau et al. (*6*) provide evidence that LV volume and EF can be measured noninvasively in rats by means of gated PET. The authors used a small-animal PET scanner for data acquisition and performed phantom experiments as well as animal experiments on control rats and on rats with heart failure. Cardiac ultrasound was used as the reference method for the assessment of LV volume and EF.

Overall, agreement was good between the volume measured by PET and the actual volume of the cardiac phantom. In healthy rats, agreement was good (r^2 = 0.96) between LV volume assessed by cardiac ultrasound and LV volume assessed by PET, although agreement was only "fair" in rats with heart failure (r^2 = 0.56). EF in normal rats was 83% ± 8% when measured with PET and 82% ± 6% with cardiac ultrasound. The authors concluded that both techniques can distinguish LV volume and EF in normal rats from those in the rats with heart failure.

The aim of the study is important and timely, and the study design is appropriate. However, some shortcomings limit the inferences that can be made from this investigation.

First, although, as stated by the authors, cardiac ultrasound is fast and convenient, the choice of this technique as a reference method for the assessment of LV volume is questionable. Assessment of LV volume with cardiac ultrasound relies on the use of geometric assumptions that work well in normal hearts with fairly standard shapes. However, these assumptions may not hold in dysfunctional and remodeled ventricles and may lead to less accurate estimates of LV volume. The latter issue probably explains why, in the present study, agreement was good between the 2 techniques in normal hearts but not in failing hearts. This worse agreement may therefore reflect the inadequacy of the cardiac ultrasound method rather than a reduced accuracy of PET.

Second, the LV volume measured in rats ranged from ~50 to ~800 μL, whereas in the phantom studies the smallest volume was 150 μL and the largest 1,000 μL. Therefore, although, as stated by the authors, technical limitations impeded the construction of phantoms of smaller volume, the range of volumes in the phantom experiments did not match well with the range in the animal experiments.

Finally, it is not entirely clear why the 4 rats with septic shock were included as a separate group.

In conclusion, this is an interesting study that provides further evidence of the feasibility of measuring physiologic parameters in small animals using noninvasive imaging. More studies of this kind will be needed to complement the results of gene studies in small animals.

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Received May 12, 2003; revision accepted May 22, 2003.

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