In Vivo Measurement of Myocardial Mass Using Nuclear Magnetic Resonance Imaging

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To examine the accuracy of nuclear magnetic resonance imaging in measuring left ventricular mass, measurements of left ventricular mass made using this technique were compared with left ventricular weight in 10 mongrel dogs. Left ventricular myocardial volume was measured from five short-axis end-diastolic images that spanned the left ventricle. Left ventricular mass was calculated from left ventricular myocardial volume and compared with the left ventricular weight determined after formalin immersion-fixation.

Linear regression analysis yielded the following relation in grams: left ventricular mass determined using nuclear magnetic resonance imaging = (0.94) (left ventricular weight) + 9.1 (r = 0.98, SEE = 6.1 g). The small overestimation of left ventricular weight by nuclear magnetic resonance imaging was judged to be secondary to both difficulty with proper border definition and partial volume effects. Hence, this imaging technique can be used to obtain accurate measurements of left ventricular mass in dogs in vivo.

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The accurate measurement of myocardial mass is of importance in evaluating many forms of cardiac disease. Specifically, the detection of hypertrophy, by the direct measurement of left ventricular mass, can potentially provide important prognostic information in the patient with ischemic heart disease, valvular heart disease, congenital heart disease and hypertensive or hypertrophic heart disease (1–6). Previous investigations have demonstrated that left ventricular mass can be determined in vivo using a variety of imaging techniques, including contrast ventriculography (7), M-mode and two-dimensional echocardiography (8–11), computed tomography (12), single photon emission computed tomography (13) and the dynamic spatial reconstructor (14). However, many of these techniques involve the use of ionizing radiation or require significant assumptions regarding left ventricular geometry.

Nuclear magnetic resonance imaging is a relatively new imaging technique that 1) does not require ionizing radiation, 2) exhibits intrinsic contrast between chamber cavity and wall, and 3) offers high spatial resolution for imaging. In addition, left ventricular mass calculation by this technique does not require assumptions to be made concerning an analytic model of left ventricular shape. Recently, nuclear magnetic resonance imaging was used to calculate left ventricular mass in vitro (15) with encouraging results. This study was undertaken to determine whether this imaging technique can be used to accurately determine left ventricular mass in vivo.

Methods

Nuclear magnetic resonance imaging. Ten mongrel dogs weighing 5 to 30 kg were studied. Each dog was anesthetized before imaging with intravenous pentobarbital (20 to 25 mg/kg body weight). The dog was positioned in the magnet lying with its left side down. A 20 to 30° angulation of the dog's craniocaudal axis with respect to the long axis of the magnet was then performed. Then, paper shims were used to raise the anterior portion of the thorax so that the base of the heart was in the sagittal plane of the

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imaging device. With the dog breathing spontaneously, multiple imaging sequences were performed, followed by repeated repositioning of the animal so that the base to apex axis of the heart was as perpendicular as possible to both the long axis of the magnet and the imaging plane. Figure 1A is a typical scout view obtained in this iterative process of positioning the animal. With the dog in this position, coronal images were obtained through the animal, with the imaging slices perpendicular to the myocardial base to apex axis (Fig. 1B). Images obtained in this fashion are similar

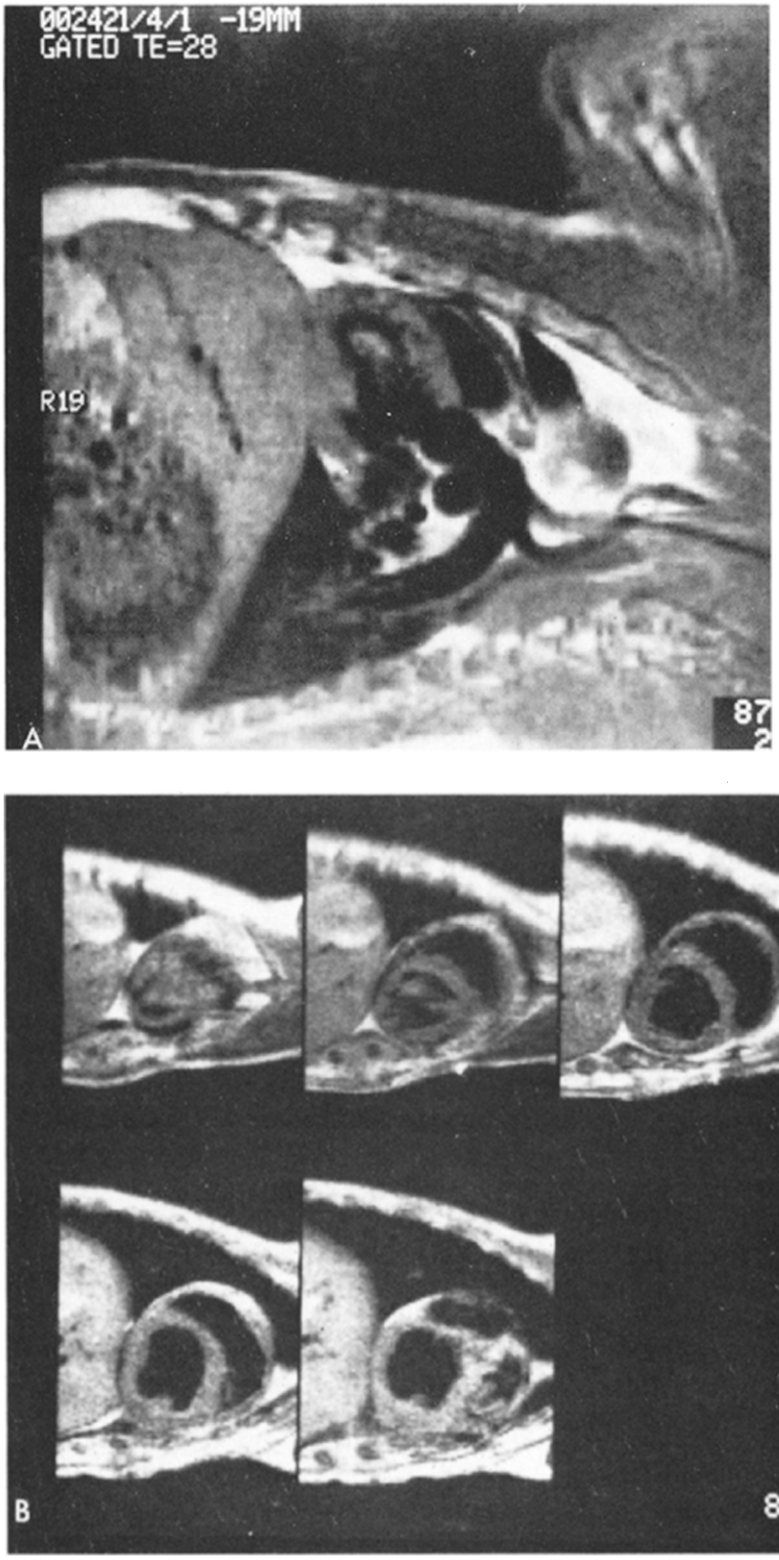


Figure 1. A, Sagittal image through one dog at the level of the left ventricle typical of the views used to aid in positioning. **B**, Coronal images obtained at five different levels of the ventricle at end-diastole in the same dog. Note the signal present in the ventricular cavity in the apical images (**upper left**).

to short-axis two-dimensional echocardiographic images or to images of a heart that has been sliced in a bread loaf fashion from the apex to the base.

Imaging was performed using a Diasonics 0.35 tesla nuclear magnetic resonance imaging device. A cardiac gated, double spin echo, multislice imaging pulse sequence was used without respiratory gating. Images were obtained at echo times of 28 and 56 ms. The time to repetition was between 500 and 1,000 ms with the actual value determined by the animal's heart rate. Images were 256 × 256 volume elements (voxels), and two signal acquisitions were averaged for each phase encoding step.

True voxel volume was determined with phantoms to be 1.6 × 1.6 × 9.0 mm with an interslice thickness of 13 mm. With this pulsing sequence five slices were obtained: the first slice imaging pulse sequence began 10 ms after the R wave; the second slice began 100 ms later and so forth so that the fifth slice was obtained 400 ms after the first slice. To obtain each slice at the same time in the cardiac cycle, the order of slice acquisition was repeatedly shifted by one for five consecutive acquisitions (16). This yielded five slices at five points during the cardiac cycle. Total acquisition time for each set of five slices was 5 to 8 minutes, making the total time for a full rotation (five sets of five slices) 25 to 40 minutes. During acquisition, small amounts of pentobarbital were administered to maintain adequate sedation.

Calculation of left ventricular mass. The images were analyzed using region of interest software available on the imager. A trackball was used to outline the left ventricular epicardium and endocardium on the five first echo (echo time = 28 ms) images obtained at end-diastole. The second echo image was used, when necessary, to help define the intracavitary signal and discriminate it from the myocardial signal. If a voxel demonstrated even echo rephasing (17) consistent with slowly flowing blood in the ventricular cavity, it was not included in the myocardium. When the epicardial border was drawn near the base or apex, epicardial fat and nonmyocardial structures were carefully excluded. The number of voxels between the epicardial and endocardial borders was then calculated. The borders were drawn three times and the mean number of voxels within the borders was determined.

Because of the presence of a gap between slices, the voxel volume was extrapolated to the total interslice distance. Hence, the voxel volume for the three interior slices was 1.6 × 1.6 × 13 mm. In the case of the two end slices, the slice was not extrapolated beyond the imaging volume, so that for these slices the voxel volume was 1.6 × 1.6 × 11 mm. The volume of myocardium in each slice was computed from the known voxel dimension using the average voxel count for each slice. The total volume of the left ventricular wall was obtained from these slice volumes using Simpson's rule. The mass of the left ventricle could then be directly calculated by multiplying the total myocardial volume by the density of myocardial tissue (1.05 g/cc). One observer (A.M.K) determined myocardial mass using this technique and repeated his measurements 1 month later to determine intraobserver variability. The average of these determinations was compared with those of a second observer (R.M.P.) to determine interobserver variability.

Postmortem determination of left ventricular weight. After imaging, the animals were killed with a lethal dose of pentobarbital and the hearts were excised and rinsed in saline solution. After dissecting off the free wall of the right ventricle, atrioventricular valves, great vessels, epicardial fat and atria, the heart was immersion-fixed in 10% neutral buffered formalin and weighed after fixation. In seven animals, left ventricular weight was obtained both before and after fixation. Values are reported as the weight of the left ventricle after fixation.

Statistical analysis. All correlations were made using standard linear regressions.

Results

Relation between left ventricular mass by nuclear magnetic resonance imaging and left ventricular weight. The left ventricular mass as determined with nuclear magnetic resonance imaging and the left ventricular weight for each animal are shown in Table 1. Linear regression analysis (Fig. 2) yielded the following relation: left ventricular mass determined using magnetic resonance imaging = (0.94) (left ventricular weight) + 9.1 (n = 10, r = 0.98, SEE = 6.1 g). The left ventricular weight ranged from 25 to 113 g (65.2 ± 30.9 g, mean ± SD). The left ventricular mass determined by magnetic resonance imaging ranged

Table 1. Comparisons of Left Ventricular Mass as Estimated by Nuclear Magnetic Resonance Imaging and True Left Ventricular Weight in 10 Dogs

		LV Weight	
Case	LV Mass by NMR	After Fixation	Before Fixation
1	107.1	113.0	—
2	105.3	102.0	—
3	91.2	84.3	86.7
4	60.7	64.3	66.1
5	60.3	55.7	57.6
6	31.8	27.4	28.7
7	41.2	30.7	32.4
8	79.6	68.4	—
9	29.8	25.0	27.0
10	94.5	81.3	84.6

LV Mass by NMR = left ventricular mass as determined using nuclear magnetic resonance imaging (the average value of the two mass determinations by one observer); LV weight after fixation = measured weight of the left ventricle after fixation in formalin; LV weight before fixation = left ventricular weight obtained before fixation in formalin.

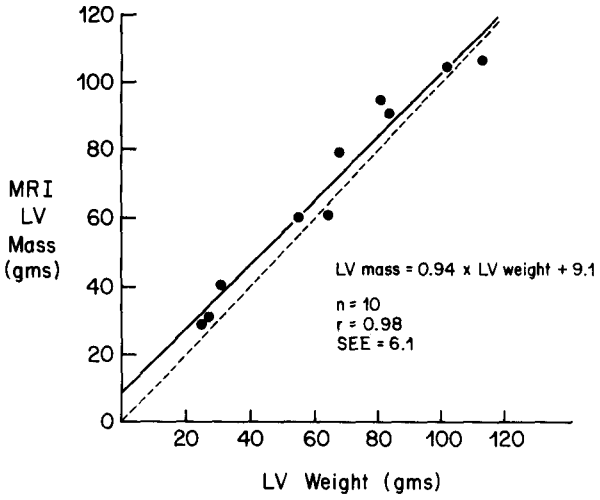
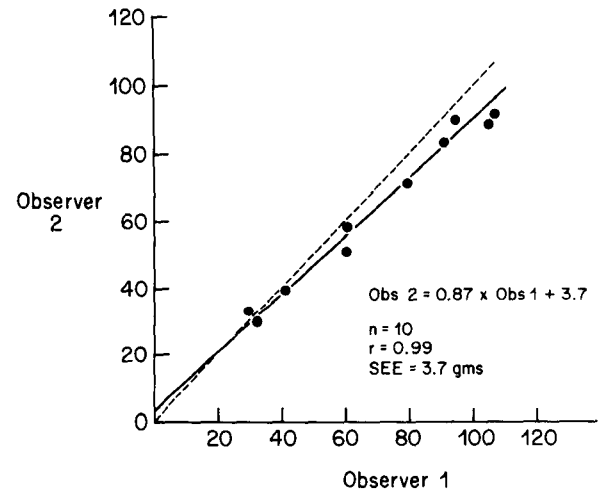


Figure 2. Relation between left ventricular mass determined from gated nuclear magnetic resonance imaging (MRI LV Mass) (**vertical axis**) and left ventricular weight (LV Weight) after formalin fixation (**horizontal axis**) for all 10 animals. The **dashed line** indicates the line of identity, whereas the **solid line** is the linear fit observed by least squares regression analysis.

from 29.7 to 107.0 g (mean 70.1 ± 29.5). The relation between prefixation and postfixation left ventricular weights for seven hearts was: prefixation left ventricular weight = (postfixation left ventricular weight) (1.02) + 1.1 (n = 7, r = 1.00, SEE = 0.5).

Reproducibility. Finally, mass measurements determined by nuclear magnetic resonance imaging were reproducible with an intraobserver correlation of r = 0.99 (n = 10, SEE = 3.8) and an interobserver correlation of r = 0.99 (n = 10, SEE = 3.7) (Fig. 3).

Figure 3. Plot of the left ventricular mass as determined by Observer 2 (Obs 2) (R.M.P.) versus that determined by Observer 1 (Obs 1) (A.M.K.) for each heart. The **dashed line** again indicates the line of identity, whereas the **solid line** indicates the linear fit obtained by least squares regression analysis.



Discussion

This study demonstrates that nuclear magnetic resonance imaging can be used to obtain accurate estimates of left ventricular mass in vivo in the dog. In addition, it appears to offer several advantages over methods presently used to determine left ventricular mass. In particular, it overcomes two important problems: 1) the need for an analytic model of ventricular shape, and 2) the need for the use of contrast material or ionizing radiation.

Prior methods. Estimates of left ventricular mass have been made using a variety of imaging techniques that can generally be divided into those that define an analytic formula for left ventricular mass based on assumptions regarding left ventricular shape and those that do not. Contrast angiography using the prolate ellipsoid model has been used to estimate myocardial mass and this method can yield useful results (7). However, it is inherently limited by the model, particularly in patients with ischemic heart disease and asymmetric cardiomyopathy. Similarly, echocardiography, as it is applied clinically, also utilizes assumptions regarding left ventricular geometry (8–11). In addition, with echocardiography, reliable measurements are dependent on the quality of the study which may vary considerably from one patient to another.

Mass estimation using thallium-201 single photon emission computed tomography requires no assumptions regarding left ventricular geometry, but does require normal myocardial perfusion for thallium-201 distribution, which limits its usefulness in patients with ischemic heart disease (13). Measurements of left ventricular mass using computed tomography also do not rely on an analytic model of left ventricular shape and have been shown to correlate well with measurements of left ventricular weight (12). The dynamic spatial reconstructor allows image acquisition similar to that of computed tomography in simultaneous multiple slices and is the most accurate method for estimating left ventricular mass (14). However, both of these techniques require the use of significant doses of ionizing radiation and the administration of intravenous contrast agents. In addition, the dynamic spatial reconstructor is not widely available.

Advantages. The overall correlation of r = 0.98 between left ventricular weight and left ventricular mass determined with nuclear magnetic resonance imaging is better than that obtained in a similar model with either a count-based method using thallium-201 single photon emission computed tomography or a Simpson's rule method using two-dimensional echocardiography (10,13). Schiller et al. (11) reported a correlation similar to that obtained in this study using echocardiography. However, that study utilized a complex analytic model of left ventricular geometry that required a number of assumptions and was validated only in litter-matched beagle pups. The correlation using nuclear magnetic resonance imaging compares favorably with that

of computed tomography and approaches the accuracy obtained only with the dynamic spatial reconstructor (12,14). In addition, magnetic resonance imaging offers advantages over all of these techniques in that 1) it does not require the use of ionizing radiation or contrast material, 2) it does not require an analytic model of left ventricular shape, and 3) it is not dependent on tissue perfusion. It is also rapidly becoming widely available.

Limitations. Over the range of myocardial weights examined, nuclear magnetic resonance imaging overestimated myocardial mass. The most likely reasons for this overestimation are partial volume effects and improper border definition. Hand-drawn regions of interest can potentially include voxels that are not totally composed of myocardium. This is especially likely to occur in areas of significant curvature involving the epicardium or endocardium, especially near the apex of the heart. Partial volume effects would also be greater if the heart was not carefully positioned and oblique sections were obtained. Because these voxels would be counted as being filled with myocardium, the mass would be overestimated. Partial volume effects have been suggested as a major cause of magnetic resonance imaging overestimation of myocardial mass in excised hearts (15). One could potentially correct for this by including voxels at the border in the region of interest only if their intensity were similar to that of voxels from the center of the myocardium. Imaging with thinner slices would also reduce partial volume effects, but this could significantly increase the acquisition time because more slices would be required to scan over the same volume. A second reason for overestimation is improper border definition, especially where signal intensity is similar to that of myocardium from surrounding structures either outside the heart or within the cavity. Border definition can be improved, particularly at the apex, with the use of the second echo image to help differentiate the signal in the ventricular cavity from endocardium.

In the largest hearts, multiple steps of careful positioning were required to ensure that the heart was completely spanned by the five imaging planes. To apply this method to even larger hearts, more planes or thicker slices would be necessary.

Clinical application. The application of this technique to the measurement of left ventricular mass in humans is straightforward. One group (18) has described orienting patients in the imager to obtain short-axis views of the heart. Recently, it has become possible to perform these variations of the imaging plane electronically (19), obviating the need for patient rotation.

Conclusions. We have demonstrated that nuclear magnetic resonance imaging can accurately assess the myocardial mass in vivo in a canine model. Magnetic resonance imaging tended to overestimate myocardial mass and this is thought to be due primarily to partial volume effects and difficulty with border definition. The high accuracy, safety and availability of this imaging technique suggest that it may become an important tool in the assessment of myocardial mass in patients with cardiac disease.

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