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In Vivo Detection of Reperfused Myocardium by Nuclear Magnetic Resonance Imaging

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To assess the potential of in vivo nuclear magnetic resonance imaging for the detection of reperfused myocardium, in vivo T_2-weighted spin echo images were obtained of dogs at 0.15 tesla. Imaging was done during 3 hours of coronary occlusion (group I), and during 3 hours of coronary occlusion followed by 1 hour of reperfusion (group II). On sacrifice, the hearts were drained of blood and imaged in situ to determine the effect of in vivo imaging on myocardial signal intensity. The hearts were then excised and imaged at 1.4 tesla to compare the effect of high resolution imaging on image quality.

Of the six hearts in group I and the eight hearts in group II with a myocardial infarction and suitable image quality, four of the former hearts and six of the latter demonstrated a small but visible increase in infarct signal intensity at 3 hours of occlusion on the time to echo [TE] = 60 ms, single echo images. The T_2 (transverse) relaxation time of the infarct (measured in vitro by spectrometer) increased by 13% when compared with normal tissue. In contrast, the reperfused infarct was more easily visualized, with signal intensity increasing by 31 ± 17% and infarct T_2 increasing by 20%. Imaged at 1.4 tesla, the excised hearts showed the infarct to be subendocardial during occlusion and extending transmurally with reperfusion.

It is concluded that, although visualized, the increase in infarct signal intensity at 3 hours of coronary occlusion is small and this is consistent with the small increase in infarct signal intensity and T_2 relaxation. Reperfused infarct is more easily visualized, in association with an increase in these variables. Nuclear magnetic resonance imaging may, therefore, provide a method of distinguishing reperfused myocardium acutely.

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Williams et al. (1) first demonstrated the potential for nuclear magnetic resonance imaging to detect very early canine myocardial infarction. These investigators showed in vitro that myocardial T_1 (longitudinal) relaxation time rose as early as 1 hour after coronary occlusion; T_1 relaxation time increased slightly at 2 hours after occlusion. Our laboratory, in a study of excised canine hearts, reported an increase in myocardial T_1 and T_2 (transverse) relaxation times by 3 hours after coronary occlusion and these changes were associated with increased signal intensity on T_2-weighted spin echo images (2). One hour of reperfusion extended the region of increased signal intensity into the epicardium. In vivo images of canine myocardial infarction were obtained by Pflugfelder et al. (3) using a T_2-weighted spin echo pulse sequence. Their study demonstrated a gradual increase in signal intensity in the infarct region relative to the adjacent normal tissue during the first 4 hours after coronary ligation.

The aims of the present study were to 1) examine changes in infarct signal intensity as detected by in vivo, T_2-weighted spin echo imaging at 1, 2 and 3 hours after coronary occlusion; 2) compare these changes with changes in infarct signal intensity at 1 hour after reperfusion; 3) assess the effects of in vivo imaging on the appearance of myocardial infarction by imaging the nonbeating, drained heart; 4) assess the effect of magnetic field strength on image quality

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and the detection of infarct; and 5) compare infarct signal intensity with changes in magnetic resonance relaxation times as measured in a spectrometer.

Methods

Animal preparation. Twenty-seven mongrel dogs were anesthetized with intravenous pentobarbital, intubated and ventilated (Harvard Apparatus). The heart was exposed through a left thoracotomy (first 10 dogs) or a sternal thoracotomy (remaining dogs). Sternal exposure made it possible to place the heart in a pericardial cradle so that the left ventricular long axis approximated the direction of the magnet bore. This produced images that were oriented more along the short axis of the left ventricle. The chest remained open for the duration of the procedure with the exposed heart covered by a moist gauze. A 20 cm vinyl catheter was placed in the left atrium and used to inject microspheres for blood flow determinations. A second vinyl catheter was inserted into the femoral artery to monitor systemic pressure (p23Db transducers, Gould, Inc.). Electrocardiographic and hemodynamic monitoring was conducted for the duration of the in vivo study. A silk ligature was placed loosely about the proximal left anterior descending artery and the large collateral vessels entering the distribution of this vessel. The dog was placed on a pyrex carrier and positioned in the magnet with the use of a calibrated table. Ventilation was continued with the Harvard respirator. Dogs were hydrated before imaging by administering 1 to 2 liters of normal saline solution intravenously. This maneuver decreased the heart rate at rest without significantly altering mean arterial blood pressure.

After obtaining preocclusion images, the dog was removed from the magnet and the left anterior descending artery and collateral vessels were tied off. Postocclusion ventricular arrhythmias were controlled with repeated boluses of intravenous procainamide (Pronestyl), 100 mg, and lidocaine, 40 mg. Bretylium, 5 mg/kg, was given intravenously if arrhythmias were not adequately controlled with Pronestyl. Six dogs died within 30 minutes of occlusion. In the remaining dogs, arrhythmias were completely controlled within 30 to 45 minutes after occlusion and all dogs had sinus rhythm. The dog was then placed in its original position in the magnet using the calibrated table as a guide. Images were obtained at approximately 1, 2 and 3 hours after occlusion. On completion of 3 hours of occlusion, 8 dogs were killed (group I). In the remaining 13 dogs, the left anterior descending artery ligature was released to allow 1 hour of reperfusion (group II).

Regional myocardial blood flow. At 3 hours after occlusion and at 1 hour after reperfusion, approximately 4.5 million ruthenium-103 or scandium-46 microspheres (14 to 16 μ) (total dose 30 μCi, New England Nuclear Corporation) were injected into the left atrium. Arterial reference blood samples were collected from the femoral artery line for 2 minutes after the injection. To calculate regional myocardial blood flow, blood and tissue samples were measured in a well counter to approximately 10,000 counts for each isotope. Ruthenium-103 was counted in a 440 to 600 keV window and scandium-46 was counted in an 810 to 1,200 keV window. A computer program was applied to correct for activity spilling from one window into another. Regional myocardial blood flow (milliliters per minute per gram) was calculated from the sample activity and activity in the reference blood samples obtained during the administration of each isotope.

All dogs were killed by an intraatrial injection of potassium chloride. To determine the effect of in vivo imaging on myocardial signal intensity, the nonbeating, drained hearts were reimaged in situ in the same imaging system. For this procedure, both ventricles were drained of blood with use of a large bore (16 gauge) needle inserted through the myocardium; ventricular shape was maintained by reinjecting air into the ventricles. After imaging at 0.15 tesla, the heart was excised and infarct signal intensity was assessed at a higher magnetic field strength using a small bore, 1.4 tesla magnet. The excised hearts were wrapped in parafilm to prevent drying. High field imaging of the excised heart was obtained for two reasons. First, it provided the opportunity to demonstrate, under idealized conditions, potential differences between acutely occluded and reperfused hearts which may not be detected under the less optimal conditions of in vivo imaging. Second, it provided a comparison between visualization of acute infarction in vitro and its detection in vivo.

Tissue preparation. After the excised heart was imaged, it was carefully cut into 1 cm thick slices at an angle parallel to the atrioventricular groove. The slice located most centrally in the distribution of the left anterior descending coronary artery was removed. Four segments were resected from this slice, two from the central left anterior descending artery region (infarct zone) and two from the opposite myocardial wall (normal zone). Each sample was subdivided into endocardial and epicardial segments. These segments were used for measurement of relaxation times and regional myocardial blood flow. The delay from the time of the potassium chloride injection to the measurement of relaxation times was not considered excessive, because previous studies have shown T_1 relaxation time to be stable for 6 hours and T_2 relaxation time to be stable for 48 hours after removal from the animal (4). The two slices lying adjacent to this slice were soaked in triphenyltetrazolium chloride using a previously described technique (5). A preliminary study from our laboratory (6) found that triphenyltetrazolium chloride may alter relaxation times. Therefore, the slice located most centrally in the distribution of the left anterior descending artery was not stained for infarction until the four segments were removed.

Nuclear magnetic resonance imaging. *In vivo and in situ hearts.* Electrocardiographic-gated, in vivo cardiac imaging was obtained with a 0.15 tesla (6.26 MHz) resistive magnet with an access aperture of 28 cm (Technicare Corporation). Tomographs were 1 cm thick and the in-plane resolution was less than 0.25 cm. Gating was achieved using a Hewlett-Packard system with data acquisition triggered by the QRS complex. Wire leads 20 cm in length led to three standard electrocardiographic electrodes sutured into the skin by stainless steel sutures. Electrocardiographic pads were placed as near as possible to the heart to maximize the electrocardiographic signal without being within the imaging plane.

All nuclear magnetic resonance images were obtained as single slice acquisitions. Spin echo pulse sequences were used to acquire multiple echo (time to echo [TE] = 30/60 ms) images and single echo (odd echo, TE = 60 ms) images. The latter images were obtained in an effort to decrease the amount of signal caused by rephasing of slow intraventricular blood flow (7). Repetition time (TR) was determined by heart rate and was equal to one RR interval. Because of the effect of intravenous hydration, mean heart rate was lowered to 85 beats/min for group I and 87 beats/min for group II. Images were acquired with either two or four signal averages; image time for each data acquisition was 5 to 10 minutes. By noting the position of the radiofrequency spike on the electrocardiographic tracing, it was possible to approximate the time in the cardiac cycle at which the image was obtained. By adjusting the physiologic gate delay time, images were obtained in either systole or diastole. End-systole was considered to be at the peak of the T wave and end-diastole was during the QRS complex. Preocclusion images were acquired at 1 cm intervals from the apex to the base of the heart by moving the dog in and out of the magnet on the calibrated table. The pericardial cradle was suspended in such a way that the longitudinal axis of the heart was oriented as much as possible along the z axis of the magnet. The level chosen for serial imaging was located at the level of the papillary muscles. To maintain this level after coronary occlusion, the dog's position in the magnet usually required a slight adjustment. Just before 3 hours of occlusion, an image was acquired from either side of the papillary muscle plane to ascertain that the region of the infarction was maximally visualized. Reperfusion images were obtained during the last 15 minutes of reperfusion. Spin echo (TE = 30/60 ms, TR = 2,000 ms) images were also acquired of the nonbeating, in situ heart at the level of the papillary muscles. These images were slightly more T_2-weighted than the in vivo images, in which TR = heart rate.

Excised hearts. Excised hearts were imaged in an 8 cm, horizontal bore magnet at 1.4 tesla (61.4 MHz). Tomographs were 0.5 cm thick and the in-plane resolution was less than 0.1 cm. Hearts were positioned on a Pyrex carrier and placed with the anterior wall facing superiorly and the long axis of the left ventricle parallel to the magnet bore. Hearts were quickly imaged in the transverse plane using a short TR spin echo pulse sequence. From these images a slice was chosen that represented the best anatomic match in the in vivo image plane. This level was then imaged using a multiple echo spin echo pulse sequence with TE = 30/60 ms and TR = 2,000 ms. Single average acquisitions were obtained, each requiring approximately 5 minutes to acquire. The total time required to image the excised heart was approximately 25 minutes.

Image quality. In vivo nuclear magnetic resonance image quality was rated as unsatisfactory for image interpretation if myocardial signal was markedly reduced because of the effects of motion, or if excessive spurious signal occurred along the phase encoding direction in the region of the heart. Only the odd echo, time to echo (TE) = 60 ms images were used to determine the presence of infarction. Images were examined prior to knowledge of signal intensity measurements and before the results of the triphenyltetrazolium chloride staining were known.

Signal intensity measurements. Signal intensity was measured in vivo from the odd echo, TE = 60 ms images before occlusion, 3 hours after occlusion and after 1 hour of reperfusion. Signal intensity was also determined in the nonbeating, in situ and excised hearts. For in vivo and nonbeating hearts, a region of interest, approximately 50 voxels in size, was fitted over a transmural region of the anterior wall in which there was increased signal intensity (infarct). A similarly sized region was outlined posteriorly (normal myocardium). In the absence of a visible increase in signal intensity, an infarct region of interest (50 voxels) was defined over the anterior wall. The percent change in signal intensity (SI) was calculated as [(infarct SI − normal SI)/normal SI] × 100%. For the excised hearts imaged at 1.4 tesla, the region of interest was placed over the endocardium.

T_1, T_2 calculations. Tissue relaxation times were measured using an International Business Machines 20 MHz minispectrometer (model PC-20) equipped with diode and phase-sensitive detectors. Ambient temperature was controlled at 40°. Tissue specimens were placed into glass tubes, capped and heated to 40° in a water bath before being placed into the PC-20 probe. The spectrometer frequency, 90° and 180° radiofrequency pulse widths and phase were first calibrated. T_1 (longitudinal) relaxation time was obtained using an inversion recovery pulse sequence at eight different time to conversion (TI) values ranging from 20 to 2,560 ms. The magnitudes of the magnetization vector for each TI value were automatically processed and T_1 was calculated. T_2 (transverse) relaxation values were obtained with the Carr-Purcell-Meiboom-Gill pulse sequence using 10 echoes. T_1 and T_2 were measured twice for each specimen and an average value obtained. The percent change in T_1 and T_2

was calculated as [(infarct relaxation − normal relaxation)/normal relaxation] × 100%.

Statistical analysis. Differences in relaxation times, signal intensity and blood flow were analyzed using an analysis of variance. The differences between epicardial and endocardial blood flow and normal and central zone relaxation times were examined using a Student t test. A probability of 5% or less was considered significant. Values are mean ± SD.

Results

Six dogs did not have a myocardial infarction by triphenyltetrazolium chloride staining and are subsequently referred to as the triphenyltetrazolium chloride-negative group. Two of these dogs were intended for group I (3 hours of occlusion) and four were intended for group II (3 hours of occlusion, 1 hour of reperfusion), leaving group I with six dogs and group II with nine dogs. These triphenyltetrazolium chloride-negative hearts served as a control group to compare with the infarcted hearts in group I and group II. All group I and II hearts demonstrated a subendocardial infarct by triphenyltetrazolium chloride staining in at least one of the adjacent myocardial slices. In each of these hearts, infarcted tissue was also detected in the slice that was previously subdivided for in vitro studies.

Regional myocardial blood flow (Fig. 1). Regional myocardial blood flow was calculated as a central/normal zone ratio. For group I, occlusion epicardial and endocardial ratios of 0.06 ± 0.07 and 0.06 ± 0.11, respectively, indicated a marked reduction in blood flow. For group II, occlusion epicardial and endocardial ratios of 0.23 ± 0.33 and 0.17 ± 0.34, respectively, were not significantly different from those in group I. With reperfusion, the epicardial and endocardial ratios rose significantly ($p < 0.05$ compared with occlusion) to 0.89 ± 0.49 and 0.77 ± 0.6, respectively. Epicardial and endocardial ratios of 0.49 ± 0.3 and

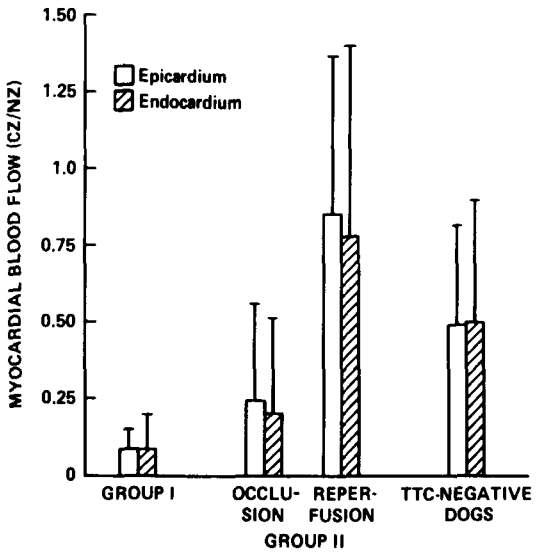

Figure 1. Regional myocardial blood flow for the three groups of dogs. Flow is shown as a ratio of central zone (CZ) to normal zone (NZ). Central zone refers to the region distal to the coronary occlusion and normal zone refers to the opposite wall. Reperfusion (group II) caused a significant ($p < 0.05$) increase in epicardial and endocardial flow compared with occlusion. Occlusion epicardial and endocardial blood flow was higher ($p < 0.01$) for the triphenyltetrazolium chloride (TTC)-negative group than for group I and group II. Values are mean ± SD.

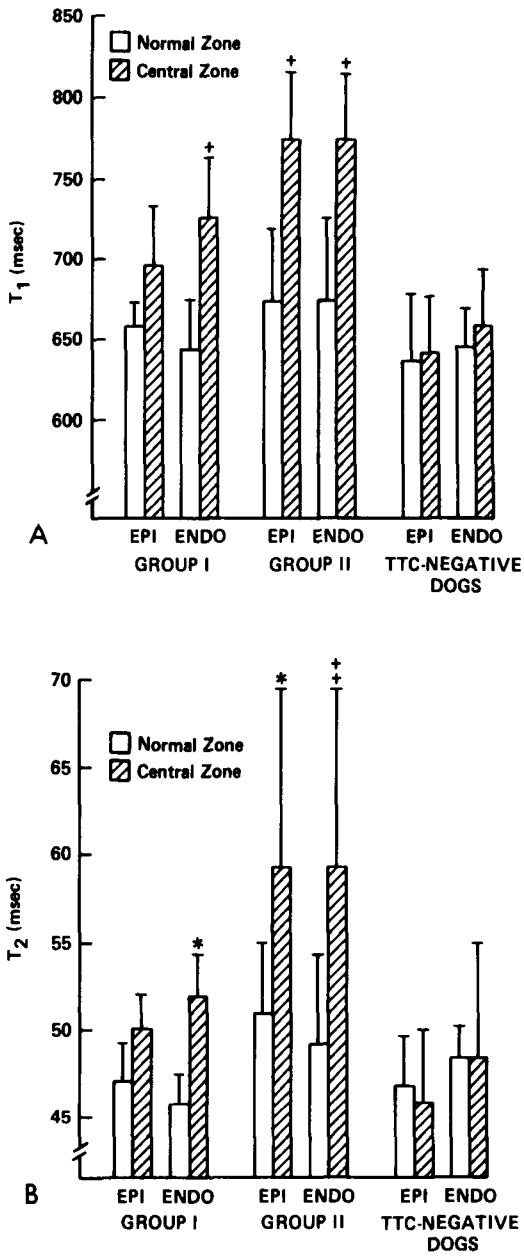

Figure 2. T_1 (longitudinal) (**A**) and T_2 (transverse) (**B**) relaxation times for the three groups of dogs. Epicardial (EPI) T_1 was higher ($p < 0.05$) for group II than for group I. Values are mean ± SD. *$p < 0.05$, + $p < 0.01$, + + $p < 0.001$ normal zone versus infarct zone. ENDO = endocardial; TTC = triphenyltetrazolium chloride.

0.50 ± 0.39, respectively, for the triphenyltetrazolium chloride-negative group were higher ($p < 0.01$) than values for group I or group II. There were no significant differences between epicardial and endocardial values for any group.

Spectrometer-measured relaxation times (Fig. 2). *T_1 changes (Fig. 2A).* Group I epicardial longitudinal relaxation time (T_1) did not change significantly (from 662 ± 13 ms [mean ± SD] in the normal zone to 693 ± 37 ms in the infarct zone); endocardial T_1 increased by 13% (from 643 ± 28 to 725 ± 33 ms in the respective zones; $p <$ 0.01). Group II epicardial T_1 increased by 15% (from 675 ± 48 to 774 ± 55 ms; $p < 0.01$); endocardial T_1 increased by 14% (from 678 ± 48 to 773 ± 49 ms; $p < 0.01$). Group II epicardial T_1 was higher than that in group I ($p < 0.05$).

T_2 changes (Fig. 2B). Group I epicardial transverse relaxation time (T_2) did not change significantly (from 47 ± 3 ms [mean ± SD] in the normal zone to 50 ± 2 ms in the infarct zone); endocardial T_2 increased by 13% (from 46 ± 2 to 52 ± 3 ms in the respective zones; $p < 0.05$). Group II epicardial T_2 increased by 16% (from 51 ± 4 to 59 ± 10 ms; $p < 0.05$); endocardial T_2 increased by 20% (from 49 ± 4 to 59 ± 10 ms; $p < 0.001$).

Triphenyltetrazolium chloride-negative group. In this group, the central zone relaxation times did not increase significantly compared with the normal zone. Epicardial T_1 was 634 ± 41 ms in the normal zone and 639 ± 34 ms in the central zone; endocardial T_1 was 647 ± 20 and 664 ± 38 ms, respectively. Epicardial T_2 was 47 ± 3 ms in the normal zone and 46 ± 4 ms in the central zone; endocardial T_2 was 48 ± 2 and 48 ± 7 ms, respectively.

Images (Fig. 3 and 4). *Group I (Fig. 3).* All group I images were considered to be of sufficient quality for interpretation. All demonstrated visible anterior myocardial wall systolic thinning 1 hour after occlusion; the wall remained thin in systole at 2 and 3 hours after occlusion. Although slight, infarct signal intensity was visibly increased (relative to normal myocardium) at 3 hours after occlusion on the TE = 60 ms odd echo images in four of the six group I dogs. However, there was little apparent hourly change in infarct signal intensity on these images; there was no increase in infarct signal intensity evident on the TE = 30 ms images. Infarct signal intensity calculated from the TE = 60 ms images was increased by 25 ± 14% at 3 hours of occlusion, compared with −3 ± 11% before occlusion (p = ns).

TE = 60 ms images of the nonbeating hearts demonstrated a visible increase in infarct signal intensity in three of the four dogs having increased infarct signal intensity in vivo. The changes were slight, however, and to be demonstrated careful windowing of the image contrast was required. These images did not demonstrate an obviously greater increase in infarct signal intensity compared with the in vivo images, in spite of a slightly longer repetition time. Infarct signal intensity on these images increased by 18 ± 16%. One dog with an increase in infarct signal intensity in vivo did not demonstrate this increase when the heart was imaged in the nonbeating state. There were no instances in which the nonbeating heart showed an increase in anterior wall signal that was not present in vivo.

Group II (Fig. 4). Images from one dog were of insufficient quality for interpretation. Of the remaining eight dogs, six demonstrated a visible increase in infarct signal intensity in the odd echo TE = 60 ms images at 3 hours after occlusion (as with group I, these changes were slight and not easily appreciated) (Fig. 4a to D). Calculated infarct signal intensity for all the dogs increased by 22 ± 17%, compared with 4 ± 13% before occlusion (p = NS). Five of the six dogs with increased infarct signal intensity during occlusion demonstrated a greater increase (visibly and by measurement of signal intensity) with reperfusion (Fig. 4E). The two dogs with no increase in infarct signal intensity during occlusion had an increase with reperfusion. Calculated reperfused infarct signal intensity increased by 31 ± 17% ($p < 0.05$, compared with occlusion). The changes in reperfused infarct signal intensity were not clearly visible on the TE = 30 ms images. The only dog with no increase in reperfused infarct signal intensity compared to occlusion failed to demonstrate an increase in reperfusion blood flow.

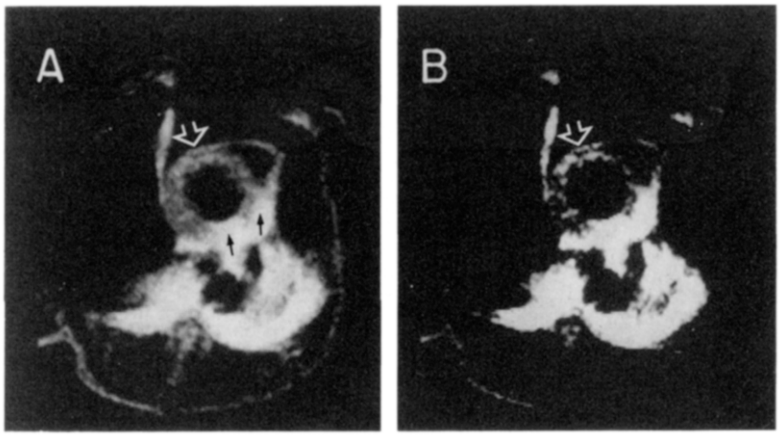

Figure 3. Effect of coronary occlusion on infarct signal intensity of a heart in Group I. The small changes caused at 3 hours after occlusion were most readily demonstrated in the nonbeating, drained hearts in which motion and flow signal were absent. **A**, Odd echo, TE = 60 image shows a slight increase in signal intensity in the anterior wall (**open arrow**). Residual blood remains in the right and left ventricles after draining (**closed arrows**). **B**, With careful windowing, contrast between the infarct (**arrow**) and normal tissue can be accentuated.

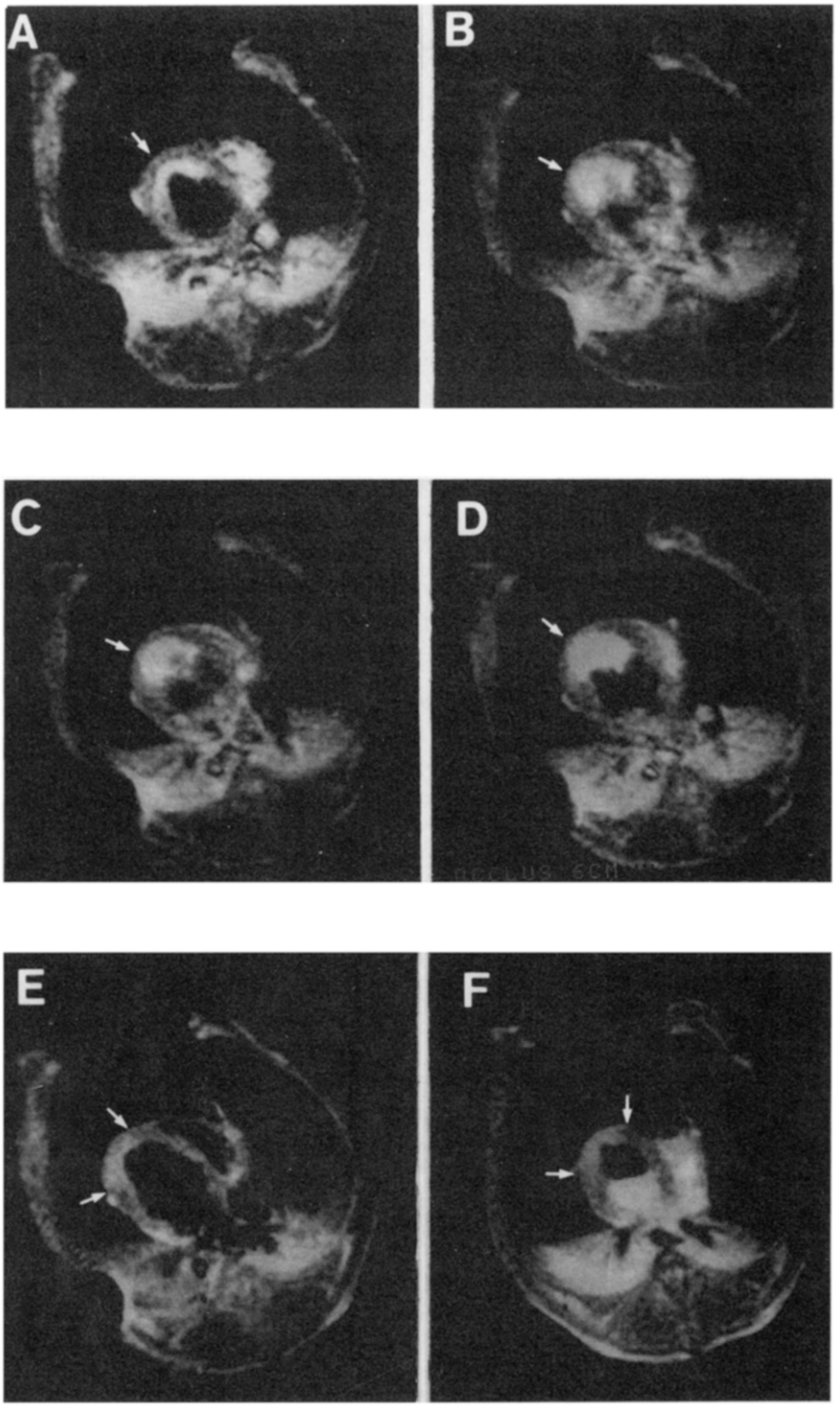

Figure 4. Serial, odd echo TE = 60 ms images of a heart from group II. All images were acquired in diastole. A large anterior wall infarction was detected by triphenyltetrazolium chloride staining. **A**, Preocclusion image demonstrating flow signal adjacent to the anterior wall. Anterior wall signal intensity is not increased (**arrow**). **B**, At 1 hour after occlusion, intraventricular flow signal is increased and the anterior wall appears thinner. **C**, 2 hours postocclusion and **D**, 3 hours postocclusion; the slight increase in anterior wall signal intensity during occlusion is difficult to appreciate. **E**, After 1 hour of reperfusion, infarct signal intensity is visibly increased and the infarct is delineated from surrounding normal tissue (**arrows**). **F**, A similar increase in infarct signal intensity in the nonbeating heart suggests that the signal change observed in the beating heart is due to tissue changes, not abnormal wall motion. Note the increase in signal from residual blood lying in the ventricles.

TE = 60 ms images of the nonbeating, reperfused hearts demonstrated an increase in signal intensity in all the hearts which had reperfusion changes in vivo (Fig. 4F). Infarct signal intensity increased by 25 ± 10%. As with group I, there were no instances in which the nonbeating heart demonstrated an increase in anterior wall signal intensity that was not present in vivo. Overall, the images of the nonbeating heart were useful in demonstrating that the changes in signal intensity observed in vivo in the present study represented changes in myocardial signal intensity and were not likely to be due to slowly flowing blood, diminished tissue perfusion or altered wall motion.

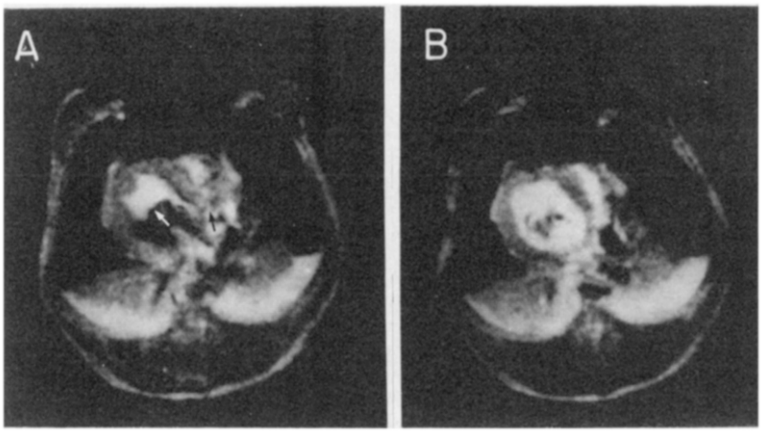

Figure 5. Effect of slow flow on intraventricular signal. **A**, Preocclusion, TE = 60 ms even echo image shows an increase in signal intensity anteriorly (**white arrow**), presumably because of slow flow at end-diastole. The signal is also increased in the right ventricle (**black arrow**). **B**, At 1 hour after occlusion (also end-diastole), intraventricular flow signal is greater, presumably because of left ventricular dysfunction. The right ventricular signal is also increased.

Triphenyltetrazolium chloride-negative group. Heart rate for these six dogs was not significantly different from that in group I or group II. One dog (intended for group II) demonstrated a visible increase in signal intensity in the central zone on the TE = 60 ms odd echo image at 3 hours of occlusion; signal intensity did not increase further with reperfusion and the change in signal intensity was not evident on the nonbeating heart. For the remaining three dogs intended for group II, there was no visible increase in central zone signal intensity during occlusion or with reperfusion.

Slow flow (Fig. 5 to 7). Slow ventricular blood flow caused an increase in left and right intraventricular signal intensity, especially on the even echo, TE = 60 ms images. It was greater after occlusion (Fig. 5), presumably as a result of impaired left ventricular function. Blood flow signal adjacent to the occluded zone was occasionally difficult to distinguish from the signal of myocardial infarction. This effect was particularly troublesome when the image was obtained near end-systole and the occluded zone was maximally thinned. The odd echo, TE = 60 pulse sequence greatly reduced the amount of signal produced from slowly moving blood, but did not always eliminate it completely (Fig. 6). Reperfusion also caused a reduction in intraventricular signal (Fig. 7).

Excised hearts (Fig. 8). The greater signal obtained at 1.4 tesla, along with the lack of cardiac and respiratory motion, produced high quality images. Group I hearts (Fig. 8A) all showed an increase in infarct signal intensity relative to normal in the anterior, subendocardial region, although the degree of change ranged from easy to difficult to visualize. All group II excised hearts demonstrated a well defined transmural region of increased infarct signal intensity not apparent in group I (Fig. 8B). However, triphenyltetrazolium chloride staining in both groups of dogs showed only endocardial infarction. Infarct signal intensity increased by 19 ± 14% and 26 ± 12%, respectively, when compared with normal. The triphenyltetrazolium chloride-negative group did not demonstrate a definite increase in signal intensity in the occluded region.

Discussion

Changes in myocardial signal intensity during coronary occlusion and reperfusion. The present study used T_2-weighted (TE [time to echo] = 60 ms) spin echo imaging to examine infarct signal intensity during 3 hours of experimental coronary occlusion (group I) and after 1 hour of reperfusion (group II). Transverse relaxation time (T_2) weighting was essential for the demonstration of image contrast in association with prolongation of T_2 in the infarct region. In vivo images obtained during occlusion demonstrated a small increase in visualized infarct signal intensity.

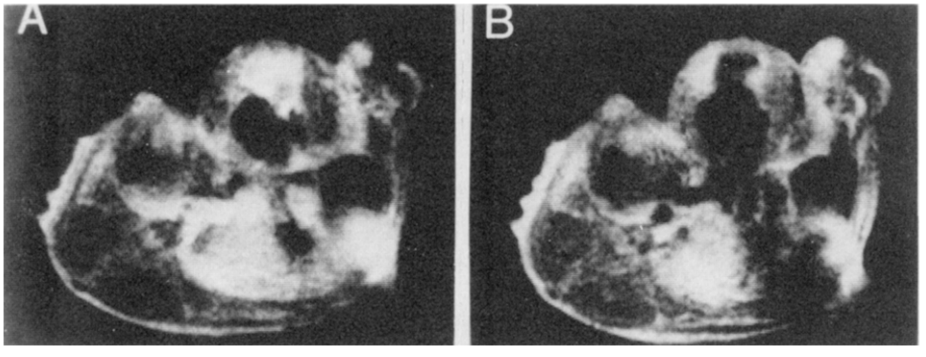

Figure 6. Effect of odd echo imaging on intraventricular flow signal. **A**, TE = 60 ms, even echo diastolic image at 3 hours after occlusion. An increase in signal intensity in the anterior endocardial wall would be difficult to separate from the slow flow signal. **B**, The flow signal is less on the TE = 60 ms, odd echo image. However, the slow flow signal may not be completely eliminated, making precise definition of the endocardial border difficult.

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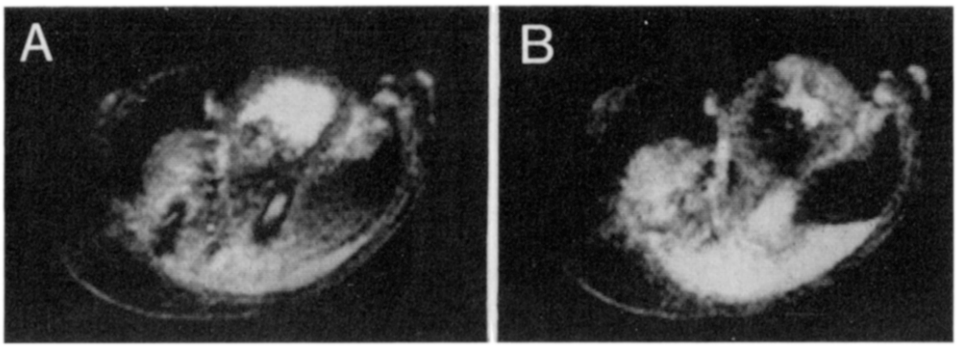


Figure 7. Effect of reperfusion on the intraventricular flow signal. **A**, The TE = 60 ms, even echo diastolic image obtained at 3 hours after occlusion shows the entire ventricular chamber obscured by the signal of slow flow. **B**, The TE = 60 ms, even echo diastolic image obtained during 1 hour of reperfusion shows an increase in infarct signal intensity and a reduction in intraventricular flow signal compared with the occlusion image. The anterior wall also appears thicker.

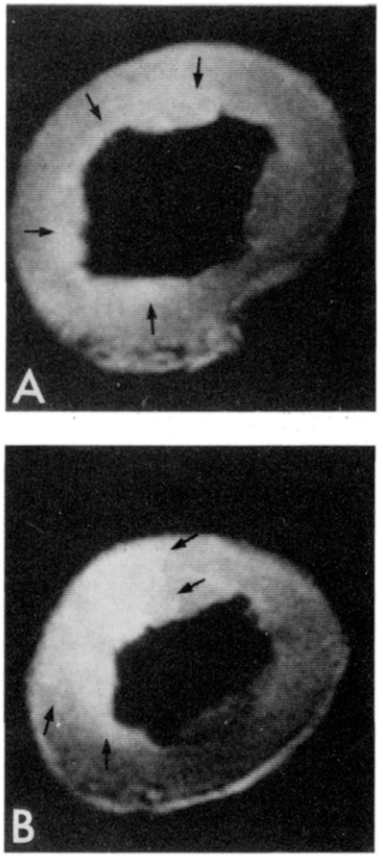
These changes were consistent with the small (13%) increase in infarct T_2 measured by spectrometer. For the seven hearts that were successfully reperfused and had images of satisfactory quality, the infarct region was more easily visualized after reperfusion than during occlusion; the observed change in signal intensity was also consistent with the increase (20%) in tissue T_2 as measured in the spectrometer.

Signal intensity after 1 hour of reperfusion was significantly greater than during occlusion in the same hearts (31 ± 17% compared with 22 ± 17%, respectively). Images of the excised hearts obtained with the small bore, high field magnet showed that reperfusion caused extension of the increased signal intensity into the epicardium. This may have been due to reperfusion-induced capillary damage and cell rupture in tissue that was already severely ischemic and destined for irreversible damage. In addition to changes in tissue signal intensity, reperfusion also caused a decrease in intraventricular flow signal. This was probably due to two factors: improved contractility and loss of systolic expansion in the ischemic region (8). Our study did not determine the ability of nuclear magnetic resonance imaging to distinguish reversibly injured from irreversibly injured myocardium. Assessment of tissue viability by nuclear magnetic resonance will be required before the usefulness of this technique can be determined in the patient after reperfusion.

Intraventricular flow signal. In the present study, the effect of coronary occlusion on intraventricular flow was most readily demonstrated on the even echo images. This was most evident in the region adjacent to the akinetic anterior myocardial wall where flow was slowest. Visualization of slow flow from even echo data was described by Waluch and Bradley (7). Although flow signal was greatly reduced by odd echo imaging, we found that for some hearts, flow may be sufficiently slow to prevent complete elimination of signal from the ventricular chamber. Flow signal was also detected, albeit to a lesser degree, in the preocclusion images. Presumably, if the image is acquired at a time in the cardiac cycle when intraventricular flow is slow, an increase in signal intensity will result.

In contrast to our study, an early study (3) reported no difficulty in detecting the change in signal intensity associated with coronary occlusion. Pflugfelder et al. (3) calculated a marked increase in signal intensity in the infarct region, with signal increasing progressively on the TE = 60 ms images from 35% at 1 to 60 minutes to 116% at 3

Figure 8. Excised heart images obtained at 1.4 tesla. **A**, A TE = 60 ms image from group I shows the greatest increase in signal intensity in the infarcted endocardium (**arrows**). The increase in epicardial signal is less intense. **B**, A TE = 60 ms image from group II shows a greater increase in signal intensity in the epicardium compared with that in group I (**arrows**).



to 4 hours. The change at 3 to 4 hours was significant compared with the intensity before occlusion. If one assumes that normal myocardial T_2 is 48 ms (mean of group I and II endocardial values), then a rise of 116% in signal intensity is consistent with an infarct T_2 of approximately 125 ms. These findings contrast with our present data, in which changes in infarct signal were difficult to detect at 3 hours of occlusion and T_2 rose only slightly to 52 ms. It is possible that flow signal in the study by Pflugfelder et al. made it difficult to distinguish the precise location of the infarct. This group did not compare their in vivo findings with images of the drained, nonbeating heart and the presence of infarction was not documented by triphenyltetrazolium chloride staining. Notable in both their study and the present one was the high intersubject variability in signal intensity measurements; this degree of variability may limit the detection of small changes in signal intensity.

Value of nuclear magnetic resonance imaging in acute myocardial infarction. A reduction in sensitivity of in vivo nuclear magnetic resonance imaging for detecting early myocardial infarction was suggested in our study by the observation that in vivo infarct signal intensity did not increase appreciably in four (29%) of the dogs with infarction. In comparison, sensitivity after reperfusion would appear to be high, with all reperfused infarcts being detected during in vivo imaging. A reduction in specificity was suggested by the observation that infarct signal intensity was increased in 2 of the 20 dogs (1 from group I and 1 from the noninfarct group) during in vivo imaging, but not in images of the nonbeating, drained heart. Abnormal wall motion, signal from slow intraventricular flow or, possibly, altered tissue perfusion could have contributed to the in vivo signal changes. It is important to note that the changes in signal intensity observed during coronary occlusion in this study reflect only the changes occurring up to 3 hours after occlusion. During the less acute period of infarction, beginning at approximately 3 days after infarction, the changes in signal intensity may be greater (9,10).

Possible improvements aimed at enhancing the detection of infarction. Several changes could be implemented to enhance the in vivo detection of injured tissue very early after myocardial infarction. 1) Pulse sequences could be optimized for maximal tissue contrast (11). 2) A decrease in the effects of motion by careful attention to cardiac and respiratory gating (12) together with special postacquisition data processing (13) should enhance image quality. 3) Ongoing improvements in nuclear magnetic resonance imaging systems by the commercial manufacturers are increasing the contrast to noise ratio and producing better images. 4) Paramagnetic contrast agents could be used to increase tissue contrast between the occluded zone and normal tissue (14). Although in vivo T_2 tissue contrast will not improve by increasing the magnetic field strength, the images of the excised heart in our study obtained at 1.4 tesla demonstrate that greater spatial resolution may aid in visualizing the infarct.

Summary. In vivo cardiac images obtained at 3 hours of coronary occlusion in the dog demonstrated only a small increase in infarct signal intensity on T_2-weighted (TE = 60 ms) spin echo images. In comparison, infarct signal intensity was clearly visualized following reperfusion; these observations demonstrate the potential of nuclear magnetic resonance imaging to detect and characterize reperfused infarction in man.

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