Imaging by nuclear magnetic resonance in patients with chronic ischemic heart disease

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ABSTRACT Cardiac anatomy was defined by gated nuclear magnetic resonance (NMR) imaging at a magnetic field strength of 3.5 kGauss in eight normal subjects and 10 patients with chronic myocardial infarctions. Multisectional imaging was performed with the spin-echo technique and encompassed most of the left ventricle in an imaging time of 5 to 12 min. In all subjects internal cardiac structure was well delineated without the use of any type of contrast medium. The myocardial wall-blood interface was sharply defined, resulting in visualization of trabeculations, papillary muscle, and chordal structures in both ventricles. In patients with ischemic heart disease, the extent of postinfarctional wall thinning, aneurysms, and mural thrombi were depicted on NMR images. Images obtained with the second spin-echo (delay time = 56 msec) demonstrated high signal intensity in regions of the left ventricular chamber adjacent to the site of aneurysms or infarctions; this finding suggested stasis of blood in a region of akinesis or dyskinesis. The results of this study show that gated NMR is feasible as a technique for imaging the human heart and is capable of demonstrating a variety of left ventricular abnormalities associated with chronic myocardial infarction. NMR is a completely noninvasive technique for clinical imaging of the cardiovascular system.


IMAGING by nuclear magnetic resonance (NMR) has emerged in the past few years as a completely noninvasive method for visualization of internal organs. Initial success in producing high-contrast images of the brain has now also been achieved in most other parts of the body.1-5 Because of the loss of NMR signal intensity by motional nuclei (hydrogen) with most proton NMR imaging techniques, flowing blood within the cardiovascular system generates little or no NMR signal; consequently, there is high natural contrast between blood and the walls of blood vessels or cardiac chambers.6,7 However, motion during imaging also complicates cardiac imaging, since signal is lost from the nuclei in the moving cardiac structures.8 This factor has caused some delay in the application of NMR imaging to cardiac diseases.

Distinct advantages of NMR imaging in relation to other imaging modalities are good contrast between soft tissues and the capability for characterization of specific tissues by estimation of magnetic relaxation times.9 These advantages, along with the fact that NMR imaging of the heart requires no contrast medium, may be particularly useful in the evaluation of ischemic heart disease. Early studies measuring relaxation times of myocardial tissues samples in vitro10 or studies imaging excised hearts11,12 suggest that NMR imaging may be capable of discriminating necrotic from normal myocardium.

The purpose of the current study was to determine whether gated NMR imaging could define the presence and site of previous myocardial infarctions and any complications of prior infarctions. The patients with ischemic heart disease were selected on the basis of distinct historical and electrocardiographic evidence of prior myocardial infarction. The NMR findings were corroborated by at least one other standard imaging modality. For comparisons, eight normal subjects were also imaged.

Methods

Study population. The study population consisted of eight normal subjects and 10 patients who were believed to have
previously suffered an acute myocardial infarction. There were two women in the former group and two women in the latter group. Ages of normal subjects ranged from 28 to 44 years and ages of patients ranged from 53 to 70 years. Each individual gave informed consent.

The diagnosis of a previous infarction was established by a typical history, Q waves on the electrocardiogram (ECG), and diagnostic elevation in myocardial enzymes in all but one of the patients. This single patient had allegedly suffered an infarction while residing in another country and his medical records could not be obtained for review. His current ECG did not show pathologic Q waves. The age and number of myocardial infarctions, left ventricular abnormalities, and the corroborative diagnostic imaging modality(ies) are detailed in table 1. For the left ventricular angiograms, an aneurysm was defined as a diastolic deformity of the left ventricle in diastole as well as systole.

**NMR imager and imaging techniques.** The University of California, San Francisco, NMR imager uses a 3.5 kGauss superconducting magnet, giving a resonance frequency for hydrogend of 15 MHz. This imager has been described in detail previously. A multiple-plane selective irradiation technique was used for acquisition of data and sectional (plane) images were reconstructed with the two-dimensional Fourier transform technique. The reconstruction matrix was 128 vertical by 256 horizontal pixels. It was displayed in 256 gray levels, with the brightest area representing the tissues with the greatest NMR signal intensity. Spatial resolution was 1.6 mm.

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**TABLE 1**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (yr)</th>
<th>Myocardial infarction</th>
<th>LV abnormality</th>
<th>Corroborative imaging modality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient No.</td>
<td></td>
<td>Age</td>
<td>Number Site</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>65</td>
<td>20 yr, 5 yr</td>
<td>2 Anteroapical</td>
<td>Apical aneurysm; mimal thrombus</td>
</tr>
<tr>
<td>2</td>
<td>63</td>
<td>1 yr</td>
<td>1 Anteroapical</td>
<td>Anteroapical aneurysm</td>
</tr>
<tr>
<td>3</td>
<td>63</td>
<td>3 yr</td>
<td>2 Posterior</td>
<td>Posterior aneurysm; mitral regurgitation</td>
</tr>
<tr>
<td>4</td>
<td>60</td>
<td>2 yr</td>
<td>1 Anterior</td>
<td>Apical thrombus; apical dyskinesis</td>
</tr>
<tr>
<td>5</td>
<td>60</td>
<td>12 yr</td>
<td>1 Lateral &amp; posterior</td>
<td>Large posterolateral aneurysm; mitral regurgitation</td>
</tr>
<tr>
<td>6</td>
<td>53</td>
<td>1 yr, 3 mo</td>
<td>2 Anteroseptal</td>
<td>Anterior akinesis &amp; wall thinning</td>
</tr>
<tr>
<td>7</td>
<td>61</td>
<td>15 yr</td>
<td>1 Anterior</td>
<td>Anterior akinesis</td>
</tr>
<tr>
<td>8</td>
<td>70</td>
<td>2 yr</td>
<td>1 Anteroseptal</td>
<td>Anteroapical aneurysm</td>
</tr>
<tr>
<td>9</td>
<td>66</td>
<td>14 yr, 13 yr</td>
<td>2 Inferior</td>
<td>Global hypokinesis; more severe in inferobasal region</td>
</tr>
<tr>
<td>10</td>
<td>65</td>
<td>6 yr</td>
<td>1—</td>
<td>No evidence of myocardial segmental dysfunction; no myocardial scar at surgery</td>
</tr>
</tbody>
</table>

LV = left ventricular; 2D echo = two-dimensional echocardiography; CT = computerized tomography.

*History of prior myocardial infarction but no Q wave on current ECG or enzymatic evidence of infarct available. Hospitalization in foreign country from which no records are available.

The imaging sequence was spin-echo at echo delay times (TE) of 28 and 56 msec. The repetition rate for the sequences was determined by the subject's heart rate and the decision by the operator to initiate a sequence for every heart beat or for alternate heart beats. Total imaging time varied from 5 to 12 min; this was determined by the product of the RR interval of the ECG, the number of lines along the Y axis (vertical) of the reconstruction matrix, and the number of times the signal was averaged (four in the current study). Multisectional imaging was used by sequentially irradiating five adjacent 7.0 mm thick (Z axis) tissue sections at 100 msec intervals during each repetition interval (TR). Thus the imaging period for all five sections required approximately 500 msec. For most patients the heart rate was such that the repetition interval was 600 to 1000 msec, which easily accommodated the time necessary for imaging five separate sections.

**ECG gating technique.** An ECG gating technique was used in all 10 patients and in five of eight normal subjects. In one normal subject the physiologic signal was sensed with a volume pulse detector (Cardioline III Pulsorete), which operates on the principle of plethysmography. The cuff was applied to the arm and inflated to 10 mm Hg above the diastolic pressure during acquisition of NMR data. In two normal subjects a laser-Doppler system was used to obtain the physiologic gating signal. This was essentially a capillary perfusion meter, which operates on the principle of laser-Doppler velocimetry and detects the fluctuation in microcirculatory blood volume during
the cardiac cycle. The 1.8 mm diameter head of the light probe was attached to the person’s ear lobe or lip.

An electrocardiographic signal was obtained with low-resistance electrocardiographic leads designed for safe use and for minimal noise generation on the images when used in the presence of high magnetic fields and rapidly changing radiofrequency pulses. This was achieved by transmitting the ECG signal from a preamplifier via fiber optics to the main amplifier and trigger circuits outside the radiofrequency screen room. The physiologic or ECG signal was the input signal to the NMR triggering module, which then activated the initiation of imaging sequences. An operator-controlled time delay between the input signal and activation of the imaging sequence was available.

Results

Normal findings. Cardiac chambers and the great vessels were sharply defined on gated NMR images (figure 1). There was generally no NMR signal intensity within the cardiac chambers. However, occasionally the images formed with the longer echo delay time (TE = 56 msec) showed some intraluminal signal within a small portion of the left ventricle (figure 1). Moreover, high signal intensity was observed within the lumina of the pulmonary artery and the aorta in late diastole. This presumably reflected slow blood flow velocity or static blood occurring in late diastole.

Cardiac NMR images clearly demonstrated the endocardial interface between intraluminal blood and the myocardial wall (figure 1). The interface between myocardium and pericardial fat or lung was also clearly defined. On gated NMR images, pericardial fat, like subcutaneous fat, generates the highest (brightest)

FIGURE 1. Four transverse images beginning at the level of the great vessels (A) and proceeding toward the apical portion of the ventricles (C and D) in a normal subject. These ECG-gated images display normal internal cardiac structure, including the trabecular and papillary muscle pattern. Three images were produced from the first spin-echo (A to C; TE = 28 msec). The image in D was produced from the second spin-echo (TE = 56 msec) and shows some intraluminal signal in small regions of the left ventricle (arrow).
NMR signal with the spin-echo technique. Thickness of the myocardial wall was evident because of these sharp endocardial and epicardial contrast interfaces. This is an intrinsic advantage of NMR imaging, which obviates the need for intravascular contrast media.

Internal cardiac structure was also demonstrated without the need for contrast media. Axial NMR images displayed the moderator band of the right ventricle, the chordal papillary muscle apparatus of the left ventricle, and portions of the atrioventricular valves (figures 1 and 2). Portions of the coronary artery were also demonstrated; the right coronary artery at its origin from the aorta and within the right atrioventricular groove was most evident because of the high contrast provided by the adjacent fat (figure 2).

**Prior myocardial infarction.** Regions of prior myocardial infarction could be discerned as a result of the clear demonstration of wall thinning on NMR images (figures 3 to 7). The transition between normal myocardial wall thickness and wall thinning was well defined (figures 3 to 6); this provided an estimate of the extent of the left ventricle involved by the previous infarct. In eight of the 10 patients with a history of previous infarction, the region of wall thinning was demonstrated on NMR images. The NMR findings correlated with the corroborative left ventricular angiogram and/or sector scan echocardiogram in nine patients (table 1). One patient (No. 10) had no evidence of wall thinning on NMR images and no contractile abnormality on the left ventricular angiogram or echocardiogram. The final patient (No. 9) had global left ventricular hypokinesis but showed no discernible wall thinning on the NMR images.

Gated NMR images displayed regions of extreme wall thinning and bulging of segments of the left ventricle in each of the four patients with aneurysm demonstrated on left ventriculograms or echocardiograms (table 1, figures 3, 5, and 6). Figure 5 displays the extreme wall thinning in a large aneurysm of the lateral and posterior segments of the left ventricle. Figure 6 shows transverse NMR images through the apical region of the left ventricle in a patient with an anteroposterior aneurysm. Wall thinning and deformity extending over the anterior segment and into the anterior septum at this level were clearly discerned on NMR images.

Comparison of images generated form the first spin-echo (TE = 28 msec) with those from the second spin-echo (TE = 56 msec) showed areas of high NMR signal intensity within the left ventricular chamber on the latter image in patients with left ventricular aneurysms (figures 5 and 6). This anomalous signal pattern within the region of the left ventricular aneurysm suggests the presence of blood flow stasis as a consequence of regional akinesis or dyskinesis. This signal from blood adjacent to a dysfunctional region of the left ventricle was only evident on images generated with the longer delay time (TE = 56 msec).

Left ventricular thrombus was demonstrated on NMR images in the two patients shown to have this abnormality on the corroborative imaging studies (figure 7). Mural thrombus was noted on NMR images as structures of medium signal intensity projecting in the signal void of the left ventricular chamber. The signal intensity of the thrombus increased on the images formed with the second spin-echo (TE = 56 msec).
FIGURE 3. Sequential transverse NMR images extending from cranial (upper left) to caudal (lower right) levels through the heart of a woman with chronic anteroseptal myocardial infarction. The images at the level of the aortic root show the right ventricular outflow tract, aorta, junction of the superior vena cava and right atrium, and the left atrium. Caudal transverse levels reveal the wall thinning of the anterior portion of the septum and the anterior segment. Note the sharp transition between myocardium of normal thickness and the thinned myocardium demonstrating the extent of necrotic myocardium.

Discussion

Proton NMR images reflect the density distribution of protons, i.e., hydrogen, in tissues and provide further tissue characterization by showing the variation in T1 and T2 relaxation times of tissues.9,15 The spin-echo technique used to generate images in the current study is responsive to both T1 and T2 relaxation times as well as to proton density. The multidimensional nature of NMR imaging, derived from the ability to accentuate the contribution of these three factors in producing differential contrast between soft tissues, is achieved by varying the pulse sequence. For instance, a short interpulse delay (TR = 0.5 sec) accentuates T1 differences between tissues, while at any TR value T2 differences are emphasized on images generated by a long echo delay (TE = 56 msec) compared with those generated by the short echo delay (TE = 28 msec).

An important concept for NMR imaging of the cardiovascular system is that the chamber of the normal heart and lumina of blood vessels possessing blood flow at normal velocity have an NMR signal intensity approaching background intensity and appear black (flow void) on most NMR images.6,7 This absence of signal results in maximum contrast between the lumen and the walls of the cardiovascular system and consequently does not require the use of contrast media. Thus NMR imaging, like ultrasonography but in distinction to computed tomography and digital subtraction angiography, is a completely noninvasive technique for imaging the cardiovascular system.

The effect of blood flow on NMR images has been examined with preparations in vitro.6,16 Generally,
blood flowing in a laminar fashion at normal velocity (10 to 15 cm/sec) causes no NMR signal. The loss or reduction in signal intensity depends on the fraction of hydrogen nuclei that are mobile and the velocity of motion. However, even in normal young individuals prominent signals may be observed at the first cross-sectional level (entrance level) of the imaged volume into which blood is flowing. At lower velocities of flow, the signal generated from blood at the entrance level of an imaged volume may be greater than that produced by stationary blood. The signal from slowly flowing blood is most prominent on images formed from the second spin-echo (TE = 56 msec).

It has been proposed that some pathologic flow patterns produce intraluminal signals. These are sluggish flow (stimulated nuclei remain within the cross-sectional volume during an imaging sequence) and possibly turbulent flow. With turbulent flow some nuclei remain within the imaged voxel during the imaging sequence and consequently produce an NMR signal within the lumen. In the current study, prominent signal intensity of intracavitary blood was noted in the regions of large contraction abnormalities of the left ventricle. These empirical observations are consistent with the above hypothesis. However, this interpretation must be tentative at the current time and awaits confirmation by further clinical experience with NMR imaging of the heart.

Besides the qualitative identification of abnormal flow patterns shown in these clinical examples, noninvasive quantitation of blood flow by NMR imaging may be possible. A number of techniques have been suggested for this, including measurement of transit of time of excited nuclei and the generation of "flow graphs" that plot the number of nuclei flowing within the various velocity intervals.

For the full potential of NMR imaging of the heart to be achieved, gating is required. The most clinically useful mode of gating in our initial experience was synchronization of the imaging sequence to the R wave of the ECG. As shown in the current study, this technique is a reliable method for producing diagnostic quality NMR images of the heart. Previous studies have also shown anecdotal examples of NMR images of the human heart and have displayed adequate images of mediastinal vascular structures beyond the
heart on nongated images.\textsuperscript{19,20} In contradistinction to computed tomographic scans, motion of the heart does not cause artifacts but does cause loss of signal from the beating cardiac structures on nongated images.

The current study indicates that gated NMR imaging clearly depicts anatomic abnormalities of the left ventricle in patients with remote myocardial infarctions. Animal studies have also explored the capability of

FIGURE 5. NMR image in a patient with a huge posterolateral aneurysm of the left ventricle. The image produced from the first spin-echo (top; TE = 28 msec) shows no intraluminal signal within the aneurysm. This pattern of images is indicative of slowing blood flow or relative stasis of blood within the left ventricular aneurysm. Bottom, Image produced from the second spin-echo (TE = 56 msec).

FIGURE 6. Transverse NMR images of the apical portion of the left ventricle in a patient with an anteroapical left ventricular aneurysm. The image produced from the first spin-echo (\textit{A}; TE = 28 msec) has essentially no signal in the lumen, while the one from the second spin-echo (\textit{B}; TE = 56 msec) shows an area of high signal intensity within the aneurysm. This pattern indicates slowly moving blood within the aneurysm.
NMR imaging for detecting and characterizing acute myocardial infarctions relative to normal myocardium. An early report\textsuperscript{11} on NMR imaging of excised hearts with acute infarctions suggested that infarcts could not be discerned from normal myocardium without the use of a paramagnetic perfusion marker (contrast media). More recent experiences from our own laboratory\textsuperscript{12} and later experience from the above-referenced group\textsuperscript{21} have shown that acute myocardial infarctions can be shown on NMR images and that myocardium in the early phase of infarction has significant differences in relaxation times compared with normal myocardium.

Although contrast media are not required to delineate the blood-tissue interface of the cardiovascular systems, it may prove useful as a myocardial perfusion marker. It has not been determined whether myocardial ischemia without infarction can be detected by gated proton NMR imaging. Paramagnetic contrast media have been used to differentiate normally perfused myocardium from jeopardized myocardium after coronary occlusion in canine and lapine excised hearts.\textsuperscript{11,22}

The eventual role of NMR imaging relative to other imaging modalities for the evaluation of ischemic heart disease is unclear at present. The interest, design, and number of patients are not such that any conclusion can be drawn regarding comparative clinical efficacy of NMR imaging in ischemic heart disease. It does seem clear that advantages will have to be shown for this technique in order for it to have extensive clinical efficacy in relation to less expensive modalities such as echocardiography. However, even at this early stage in its development and evaluation, NMR imaging offers three intriguing insights into the assessment of ischemic heart disease and the response to therapeutic interventions, direct tissue characterization,\textsuperscript{9,12,15} noninvasive regional blood flow measurements,\textsuperscript{17,18} and assessment of regional myocardial metabolism in vitro.\textsuperscript{23}

The magnetic relaxation times (T1 and T2 times) of protons in different tissues are currently the basis for tissue characterization. These relaxation times and their diagnostic implications are poorly understood.
Nevertheless, both normal and pathologic tissues have been shown to have combinations of T1 and T2 values that fall in a characteristic range for a specific tissue. These specific relaxation times for various tissues have been estimated in experimental animals and in man. Various disease processes, including ischemia, have been found to alter the magnetic relaxation times of tissues and organs.

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