Review

Nuclear magnetic resonance imaging of the heart
Current status and future prospects

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SUMMARY The basic principles and current status of proton nuclear magnetic resonance imaging are outlined. Nuclear magnetic resonance images of the heart have improved in quality with advances in technique and better gating but clinical experience remains very limited. Myocardial infarction has been shown in animals and man, and plaques of atheroma have been seen with nuclear magnetic resonance flow studies.

Further improvements in image quality, faster examination times, ^{23}Na imaging, and the use of paramagnetic contrast agents are advances that are anticipated in the near future.

The medical application of nuclear magnetic resonance was pioneered by Odeblad, a Swedish physicist, who studied the properties of human tissues and fluids using proton spectroscopy during the 1950's and 1960's.[1,2] Later workers showed abnormal proton nuclear magnetic resonance properties of animals' tumours in 1971 and 1972.[3,4] The use of ^{31}P spectroscopy to study metabolism was first described in 1974[5] and has been applied to the study of skeletal muscle, brain, and myocardium with considerable success.[6]

The essential concept for nuclear magnetic resonance imaging of applying a magnetic field gradient in order to locate the position of nuclei by changing their response frequence was described by Lauterbur in 1973.[7] In vivo human proton heart images were first demonstrated in 1977 by Damadian *et al.*[8] Normal cardiac images have since been shown by other groups and technical advances including better cardiac gating have led to considerable improvement in image quality over the last two years.

The only other nucleus (apart from ^{1}H) which has been successfully imaged is ^{23}Na. Gated ^{23}Na images of a mouse heart were published in 1981.[9] The low natural abundance of ^{31}P in the body (one three-thousandth part of that of hydrogen) places severe constraints on phosphorus imaging and further comment in this paper will relate only to proton imaging.

Instrumentation

All nuclear magnetic resonance imaging machines are constructed around a large magnet which provides a uniform static magnetic field. Protons behave like tiny spinning magnets and this static magnetic field produces a net proton nuclear magnetisation in the patient (Fig. 1). Additional magnetic pulses oscillating at the spin frequency of the protons (several MegaHertz) are applied by means of a coil which surrounds the patient. These pulses rotate the nuclear magnetisation after which it relaxes or recovers back to its original position. For example, if a 90° pulse is applied, the nuclear magnetisation is rotated from the longitudinal direction into the transverse plane (Fig. 2). After this rotation the component of the magnetisation in the long axis of the patient recovers from zero to its original amplitude in an exponential way. This recovery is called longitudinal or spin-lattice relaxation; it is approximately exponential and is characterised by the time constant T_1. Relaxation of the component of the magnetisation in the transverse direction back to its original amplitude of zero is termed transverse relaxation or spin-spin relaxation and is also approximately exponential. It is characterised by the time constant T_2. A receiver coil surrounds the patient and the electrical signal detected by this coil after such a 90° pulse is known as the free
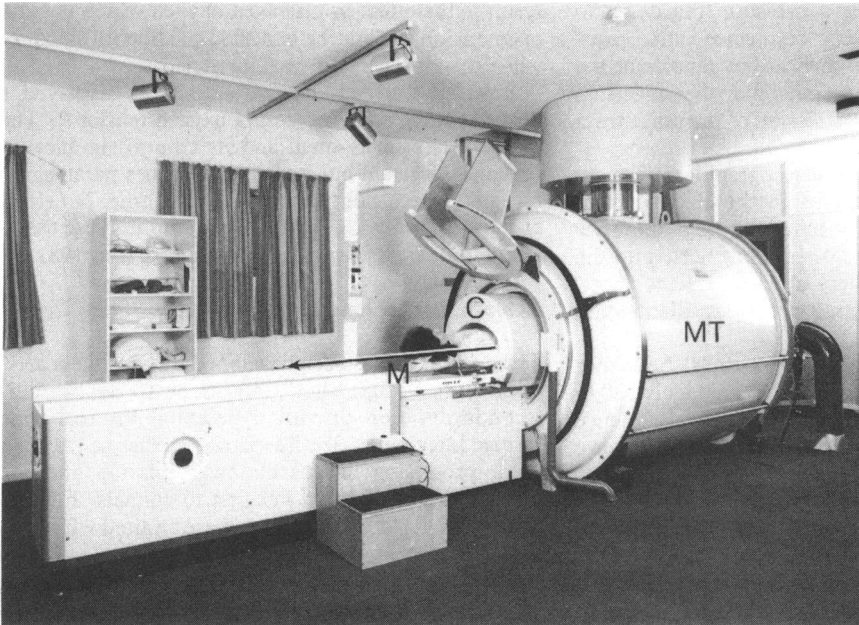
Fig. 1 *A nuclear magnetic resonance scanner. The machine is constructed around a large cryomagnet (MT). The patient is slid into the bore of this machine and surrounded by a transmitter and receiver coil (C). The magnet induces a net proton magnetisation (M) in the patient.*
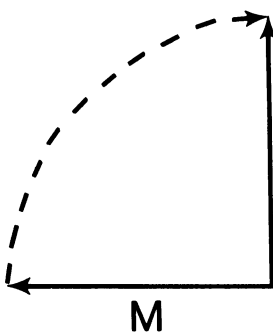

Fig. 2 *Rotation of the proton magnetisation (M). Magnetic pulses are used to rotate the proton magnetisation into the transverse plane after which it recovers or relaxes back to its original orientation and magnitude.*

induction decay. It is this signal that is used to reconstruct the image.

Longitudinal relaxation (T_1) depends on the interaction of protons with surrounding nuclei and molecules (the "lattice") while transverse relaxation (T_2) depends on the interaction of protons with each other. Both T_1 and T_2 are sensitive indices of the local nuclear and molecular environment. By using a variety of pulse sequences it is possible to produce images with varying dependence on proton density (ρ), T_1 and T_2 (Table) The simplest of these is the repeated free induction decay sequence consisting of a succes-

Table *Nuclear magnetic resonance pulse recordings*

Pulse sequence	Principal image variables
Steady state free precession	Proton density, T_2/T_1
Repeated free induction decay	Proton density, T_1
Inversion recovery	Proton density, T_1
Spin echo	Proton density, T_2

sion of 90° pulses. The resulting image largely reflects proton density with a small dependence on T_1.

The inversion recovery sequence begins with a 180° pulse which inverts the direction of the magnetisation. The magnetisation is then allowed to recover for time τ after which a 90° pulse is applied and the data are collected. The image depends on proton density but contrast is very dependent on changes in T_1.

The spin echo sequence involves the use of a 90° pulse followed at time τ later by a 180° pulse. The signal is collected a further time τ later. The contrast in these images is largely dependent on changes in T_2.

A more detailed account of imaging techniques has been published by Pykett *et al*.[10]

Cardiac gating

After a pulse sequence, collection of nuclear magnetic resonance signal takes 10 to 30 ms. A delay (typically of about 1000 ms) is then necessary to allow the proton nuclear magnetisation to return to equilibrium. After this the pulse sequence is repeated. For the projection reconstruction technique the pulse sequence is typically repeated 180 times at 1° intervals in the transverse plane in order to acquire sufficient data to reconstruct an image.

It is possible to produce cardiac images in which the data are collected irrespective of the phases of the cardiac cycle. This produces images that are largely diastolic because of the higher proportion of the cardiac cycle occupied by diastole.

Synchronisation of data collection to the peripheral

pulse is achieved by using a pressure transducer to initiate the nuclear magnetic resonance pulse sequence. While this improves myocardial definition, the exact relation to cardiac events may be uncertain because of the delay in transmission of the pulse from the heart to the transducer.

The problems with electrocardiographic gating are the induced electrical currents in the electrocardiographic leads produced by magnetic field impulses and the introduction of radiofrequency noise into the system from outside. Filters are available to block outside interference, allowing precise cardiac gating timed in relation to the R wave.

Over a pulse range of about 60 to 90 beats per minute the duration of systole is approximately 380 to 400 ms[11] so that a typical inversion recovery sequence with the initial magnetic pulse triggered to the R wave produces a late systolic or early diastolic scan (sampling is performed 400 ms later just after the 90° pulse). An additional delay of 500 to 600 ms produces a later diastolic scan though the length of diastole is more variable than that of systole.

Effect of oxygen on T_1 of blood

Initial human studies displayed a decrease in relaxation time (T_1) of blood within the left ventricular cavity when subjects breathed 100% oxygen using ungated images. Studies of volunteers breathing 21%, 40%, 60%, 80%, and 100% oxygen showed a progressive decrease in T_1. A possible explanation for this

result is the effect of dissolved oxygen which is paramagnetic and would be expected to shorten blood T_1 when its concentration was increased.

Arterial blood studies on dogs also displayed a decrease in T_1 with increasing oxygen tension.[12] The effect of oxygen is small and its clinical significance remains uncertain but it is of interest as a paramagnetic agent which can change relaxation time. No effect of oxygen on myocardial T_1 was found in these cases, unlike the results reported by Doyle *et al.* in 1981.[13]

Echo-planar technique

This technique has been developed by Ordidge *et al.*[14] It involves "single shot" images of 10 to 20 milliseconds duration providing potential for real time cardiac imaging. A 32×32 matrix size has so far been used, producing images of low resolution and the magnet size has limited imaging to animals. Further developments of this techinique are awaited with considerable interest.

Experimental infarction

Studies with proton spectroscopy in dogs after myocardial infarction have shown an increase in T_1 which correlates well with increase in water content.[15 16]

Using a steady state free precession technique (a pulse sequence which produces images dependent on ρ and T_2/T_1) Buonanno *et al.*[17] were able to demon-
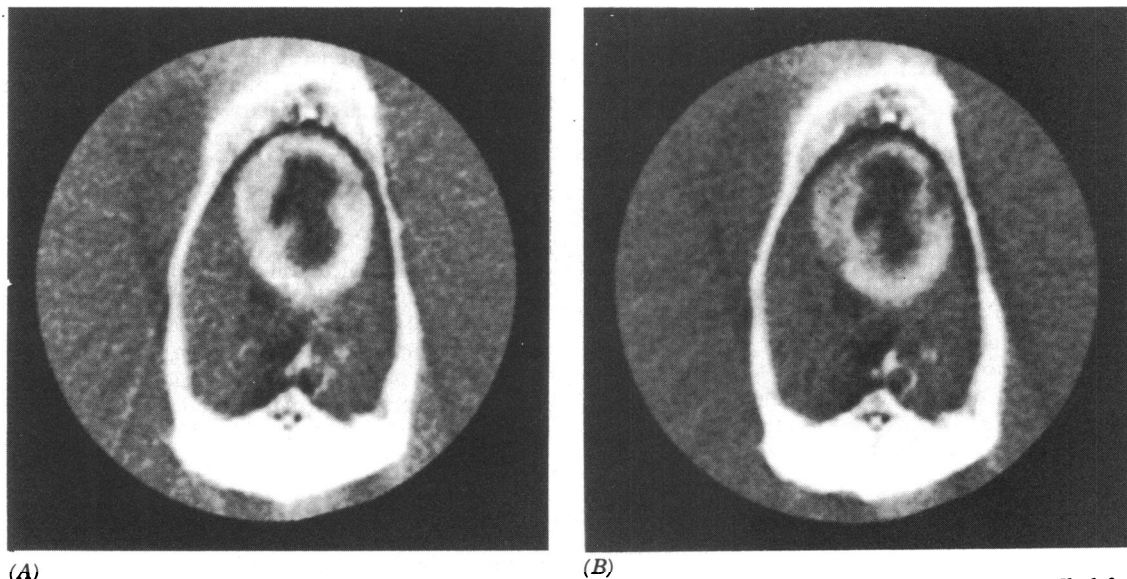
(A)   (B)

Fig. 3   *Dog heart before (A) and after (B) occlusion of the left anterior descending artery: ungated inversion recovery scans. The left ventricular muscle and cavity are well displayed in (A). After occlusion of the left anterior descending artery a dark rim (long T_1) is seen around the anterolateral aspect of the myocardium.*
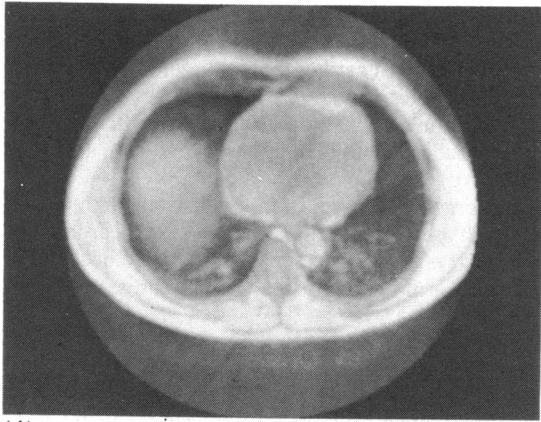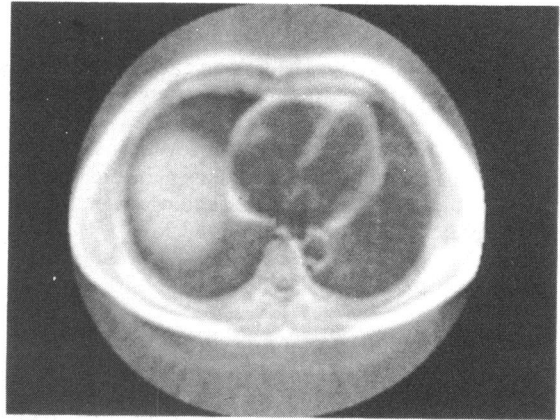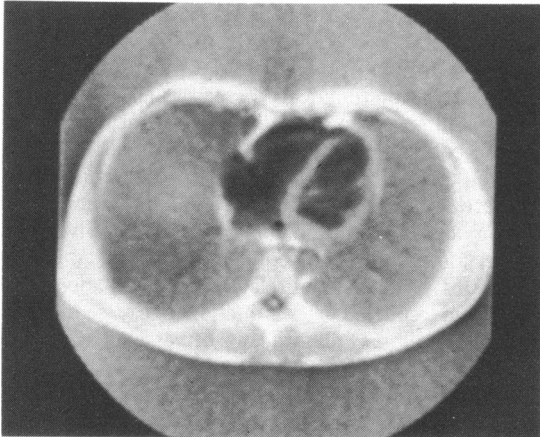
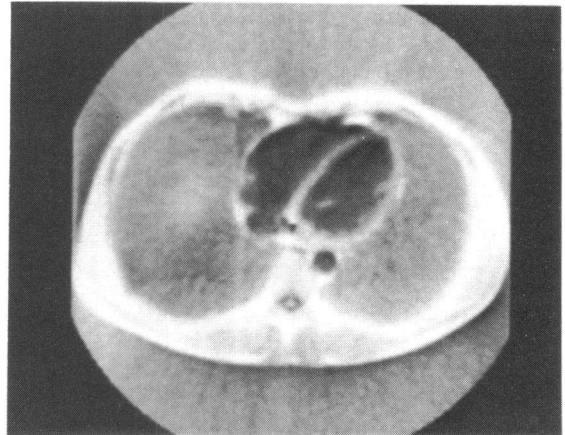(A)   (B)

Fig. 4   Normal heart: ungated repeated free induction decay (A) and inversion recovery (B) scans. Little contrast is seen between blood and myocardium (A) but they are clearly distinguished in (B).
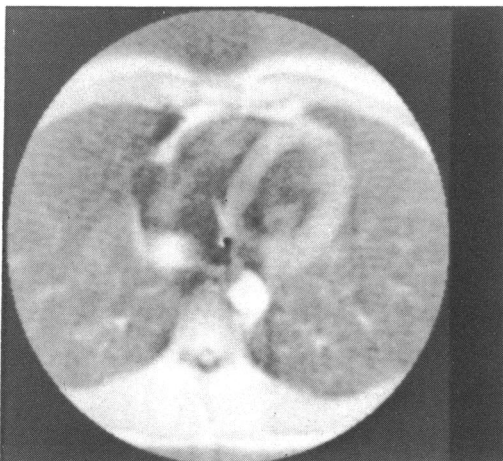

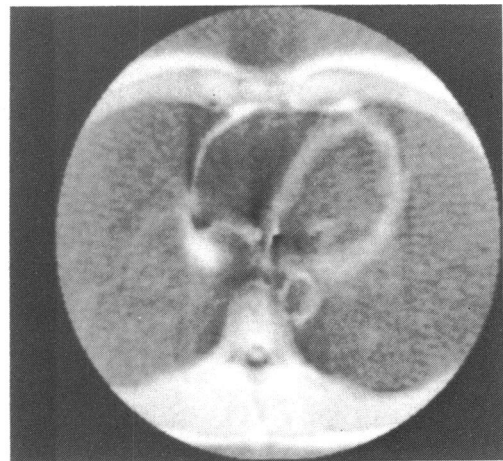(A)   (B)

Fig. 5   Normal heart: pulse gated inversion recovery scans in systole (A) and diastole (B). Definition of the myocardium is better than in Fig. 4B and the left ventricular cavity is seen to be larger in diastole.

(A)   (B)

Fig. 6   Normal heart: electrocardiogram gated inversion recovery scans in systole (A) and diastole (B). A further improvement in myocardial definition is seen with electrocardiograph gating, and the difference between systole and diastole is readily seen. The blood in the aorta appears light in (A) but dark in (B).

strate infarction in dogs, using manganese as a paramagnetic contrast agent; the infarct was not visible without it.

Using an ungated inversion recovery technique myocardial infarction has been shown in dogs after occlusion of the left anterior descending artery without the use of contrast agents (Fig. 3).

Normal appearances

Ungated human images have been produced by several investigators using techniques of selective excitation in which only the protons in the slice of interest are excited.[18-21] Direct coronal and sagittal imaging is also possible.

Three dimensional techniques involving simultaneous collection of data from a volume have also been used and combined with cardiac gating.[22-24]

Repeated free induction decay images show little contrast between blood and myocardium but the distinction is readily seen with inversion recovery images (Fig. 4). The image quality is improved with pulse gating (Fig. 5) and electrocardiographic gating (Fig. 6). Valves and papillary muscles are readily seen.

Rapidly flowing blood in the aorta and inferior vena cava may appear light or dark, depending on the phase of the cardiac cycle.

Clinical studies of heart

These have been limited. Many of the nuclear magnetic resonance machines presently in use are situated in factories or other clinically disadvantageous sites and most of these machines are research prototypes designed to explore the possibilities of nuclear magnetic resonance rather than for use on a routine basis.

Using electrocardiographic gated inversion recovery images, Go et al.[25] have shown evidence of old infarction and compared the results with dynamic isotope studies. Both techniques have shown a similar sensitivity.

Appearances arising from cardiac aneurysm and muscle hypertrophy (Fig. 7) have also been shown with nuclear magnetic resonance but its clinical application in cardiology remains virtually unexplored.[26]

Vascular studies

The flow dependence of the nuclear magnetic resonance signal has been recognised for a long time and attempts to produce a quantitative assessment of flow have been in progress for over 20 years.[27] The flow dependence of the signal from the aorta in systole and diastole can be appreciated from Fig. 6 and flow profiles at different phases of the cardiac cycle can be produced.[28] Atheroma can be seen as an obstruction to flow and may also display a high signal because of its lipid content.[29]

In the thorax there may be difficulty in distinguishing between vascular structures and tumours. The lack of signal from flowing blood using inversion recovery and spin echo sequences is very helpful in this regard.[30] The lack of relative signal enhancement with rapid repeated free induction decay sequences may also be used as an indicator of vessel obstruction or occlusion.

It is also worth noting that exercise may produce obvious changes in the appearance of skeletal muscle. This is mainly an effect of increased blood flow to muscle[31] (Fig. 8), and may be relevant in the interpretation of T_1 changes in myocardium.
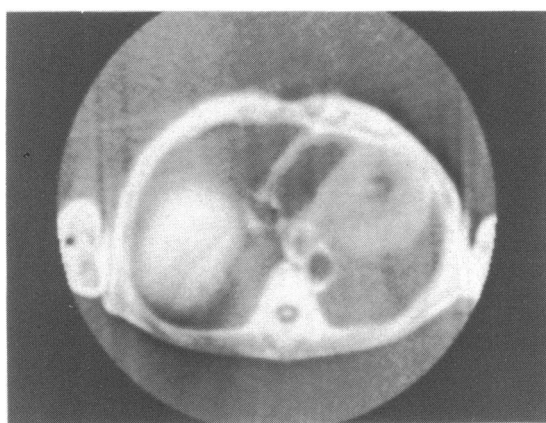
(A)   (B)

Fig. 7   *Left ventricular hypertrophy (A) and hypertrophic obstructive cardiomyopathy (B): ungated inversion recovery scans. The enlarged ventricular wall and different contours of the ventricular cavities are evident.*
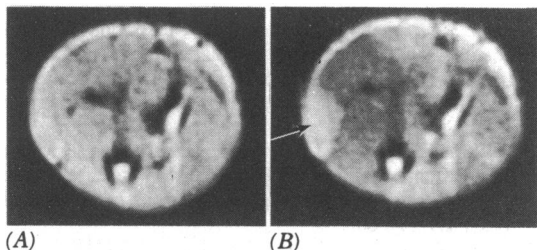
(A)   (B)

Fig. 8 *Normal forearm: inversion recovery scans before (A) and during (B) exercise. After finger flexion the flexors of the fingers appear dark (long T_1). Flexor carpi ulnaris (arrow) is unchanged.*

Future developments

Without doubt improvements in image quality will continue though probably not at the rate seen over the past two years.

The development of organic paramagnetic agents such as the nitroxide stable free radicles is an important advance.[32] These so-called "spin labels" have been used in chemistry for many years. They appear to be non-toxic in animals and shorten relaxation time. They can be linked to metabolites or other substances of interest and appear to have considerable potential though it will take some time to assess toxicity before these agents can be considered for human use.

Much interest surrounds the possibility of obtaining clinically useful proton images and ^{31}P spectra on the same nuclear magnetic resonance machine. In order to obtain images the field must be low to avoid magnetic pulse absorption but for the production of spectra with good separation of peaks the field should be high. It is hoped that a compromise may be possible at a field strength of about 15 Kilogauss and work in this direction is proceeding at several centres.

^{23}Na images of the rat brain have been produced demonstrating brain infarction. These latter images displayed considerable contrast between normal and abnormal regions and the technique may have application in the human heart.[33]

With nuclear magnetic resonance still in a rapid phase of development assessment of its likely clinical role is not possible but the initial results are promising and this area of research is likely to be a source of considerable interest over the next few years.

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