Regular Review

Magnetic resonance imaging—1: basic principles of image production

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Nuclear magnetic resonance has been a chemist's tool for determining the chemical composition of samples ever since the phenomenon was first described by Bloch *et al* and Purcell *et al*, work that gained them both the Nobel prize in 1952.[1,2] Such nuclear magnetic resonance data were, and usually still are, presented as a spectrum which, crudely speaking, indicates the relative quantities of the atomic nucleus of interest in various molecular configurations.

An important impetus for using nuclear magnetic resonance to create images grew out of Damadian's observation that nuclear relaxation times recorded from neoplastic tissues were different from those found in normal tissues.[3] Damadian's early work, however, provided numerical data without spatial information, but unless there is spatial information there can be no image. The vital breakthrough for creating images is credited to Paul Lauterbur. He suggested a method of localising the source of signals,[4] which led to a technological explosion, pioneered largely by British research groups in Nottingham,[5] Aberdeen[6] and the Hammersmith Hospital in London.[7,8] It switched the emphasis of magnetic resonance from numerical information to anatomical images. Relaxation times, even when spatially localised, were soon recognised to be of limited significance because many different pathological processes alter them similarly, and considerable overlap often exists between the values obtained from normal and pathological tissues. But it became abundantly clear that magnetic resonance imaging could provide exquisite anatomical information that rivalled, and in many cases exceeded, the capability of *x* ray computed tomography. Magnetic resonance imaging could also produce images without the risks of ionising radiation and with a minimum of discomfort to the patient.

This review is in two parts. In the first we provide a simple account of how such images are produced and in the second summarise the major clinical uses of magnetic resonance imaging today. The usual starting point when trying to explain magnetic resonance imaging is to compare it with computed tomography, because at first glance magnetic resonance and computed tomographic images seem similar. This is because both techniques show the same anatomy and both employ sectional images. But there are fundamental and important differences, the most important of which is that the computed tomographic image depends on *x* ray absorption whereas magnetic resonance imaging depends on the absorption of radiowaves by atomic nuclei within the body.

All current magnetic resonance images depend on the absorption of radiowaves by hydrogen nuclei. Imaging other nuclei with intrinsic spin, such as sodium-23 or phosphorus-31, is possible, but with current techniques of magnetic resonance imaging hydrogen is the only nucleus with intrinsic spin that is present in sufficient quantities to enable a useful image of the human body to be produced. Figure 1 shows the fundamental physical interactions responsible for a magnetic resonance image. A short burst of radiowaves, known as a radiofrequency pulse, is transmitted into the patient from an antenna within the machine referred to as a radiofrequency transmitter coil. This radiofrequency pulse is absorbed by hydrogen nuclei, which thereby gain energy. Re-emission of this energy gives rise to signals which can be received by the same radiofrequency coil or by a separate receiver coil.

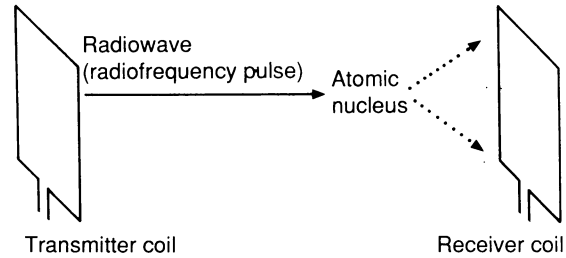

FIG 1—*Fundamental physical interactions responsible for magnetic resonance image. A radiofrequency pulse is transmitted into the patient and interacts with atomic nuclei (in current imaging the hydrogen nuclei). The hydrogen nuclei subsequently re-emit the energy they gained; the source of the signal can be localised and the signal itself measured*

The size of the signals depends largely on four factors. The first of these is proton density—in other words, the number of hydrogen nuclei per unit volume. (It is self evident that a magnetic resonance image will reflect the density of hydrogen in the section being displayed.) The three other factors are the spin-lattice (T1) and spin-spin (T2) relaxation times and the motion of protons, which are explained later.

Because information from magnetic resonance imaging depends on four factors whereas information from computed tomography depends on just two factors (the number of atoms in a given volume of tissue and the atomic number of those atoms) the potential information in a magnetic resonance image is between one and two orders of magnitude greater than that in a computed tomographic image. But the basic physics is similarly several orders of magnitude more difficult to understand.

Creating the magnetic resonance image

Magnetic resonance images depend on the distribution and concentration of hydrogen nuclei in the

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body and on the physicochemical environment of those nuclei. Hydrogen is a highly suitable element to image because it is so abundant in the human body, two hydrogen atoms being present in every water molecule, and hydrogen is a common atom in organic compounds. For the purpose of understanding magnetic resonance imaging hydrogen nuclei may be regarded as small bar magnets with north and south poles, which spin on their axes. As they spin the nuclei wobble, or, put more scientifically, they precess, rather like a spinning top wobbles as it starts to fall (fig 2).

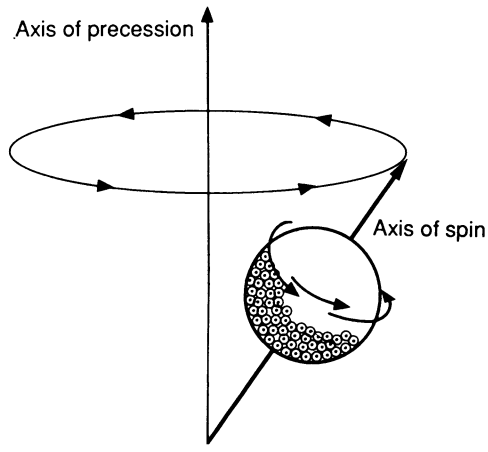

FIG 2—*Nuclear spin and precession. The hydrogen nucleus (proton) spins on its own axis and also precesses, rather like a spinning top wobbles as it starts to fall. The resulting magnetic vector lies along the axis of precession*

The reason precession is so important is that radiowaves with the same frequency as the frequency of precession of the hydrogen nuclei will transfer their energy to the nuclei. The word resonance in magnetic resonance imaging, or in nuclear magnetic resonance, comes from the fact that hydrogen nuclei will absorb the energy of radiofrequency pulses only if they are precessing at a frequency that is resonant with those radiofrequency pulses. Absorption of radiofrequency energy causes the net magnetic vector of the collection of hydrogen nuclei to tip through an angle that depends on the duration of the radiofrequency pulse. Maximum signal is obtained after a 90° pulse (fig 3).

In its new orientation the rotating magnetisation induces a measurable oscillating current in the receiving coils (remember that the protons may be regarded as tiny bar magnets). The magnetic resonance signals are, therefore, minute oscillating electrical currents induced in specially constructed receiving coils by the rotating magnetic vector resulting from the spinning, precessing hydrogen nuclei.

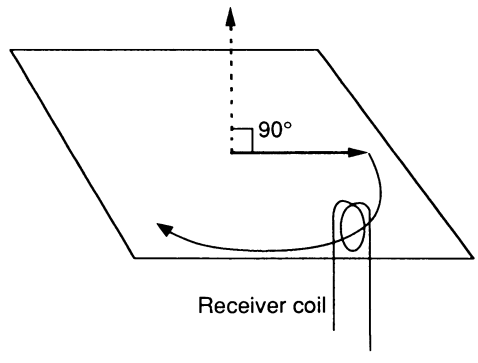

FIG 3—*How a rotating magnetic vector that has tipped (flipped) through 90° induces an oscillating current (signal) in the receiver coil*

A magnetic resonance image will be obtained only under quite specific circumstances, the most important of which is that the body part must be in a magnetic field. The resonant frequency of a nucleus is proportional to the strength of this field, which must therefore be known so that the frequency content of the radiofrequency pulse can be appropriately selected. The stronger the magnetic field the greater the proportion of nuclei that will line up in the direction of the field and thus the stronger the signal that can eventually be received. In clinical practice this field is extremely high; most magnets used in diagnostic imaging generate magnetic fields between 0·2 and 1·5 tesla. By way of comparison, the strength of the earth's magnetic field is about 0·00005 tesla. Provided that the spatial origin of the signals can be localised, an image can be created. The breakthrough for spatial localisation was provided by Lauterbur, who pointed out that as the frequency of precession of the hydrogen protons depended on the strength of the magnetic field to which they were subjected it should be possible to apply magnetic field gradients to achieve a different but predictable strength of magnetic field for each small picture element and so provide the spatial localisation needed to convert the signals into a recognisable anatomical image.[4]

A simple analogy, substituting sound waves for the less familiar radiowaves, illustrates how frequency may be used to localise signals. Imagine a room, at one end of which is a wine glass on a set of shelves. The glass and shelves are hidden from view behind a curtain. In walks an opera singer who sings a note at the resonant frequency of the glass. As the note is sung the glass resonates and we can then localise the position of the glass on the shelf by listening for that particular note coming from the glass, and, by using our ears, work out its position. Similarly, the position of multiple glasses, each with a different resonant frequency, could be localised by asking the singer to sing notes of those particular frequencies.

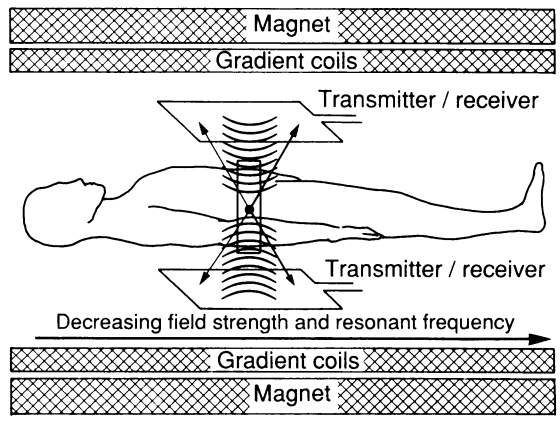

FIG 4—*Magnetic resonance imager. The patient lies within a "tunnel" formed by the magnet and radiofrequency coils. A high field magnet along with gradient coils creates a predictable but varied magnetic field. Radiofrequency coils transmit (waves) and receive (arrows) pulses of energy. The signal from within the selected "slice" of the patient (rectangle) can be measured, localised, and used to create the final image*

Figure 4 summarises simply how an image is created by a magnetic resonance imager. Each picture element in the final image represents the signal received from a specific position in the body; the signal intensity represents the combined effect of proton density, T1 relaxation, and T2 relaxation, together with any modification of the signal due to motion.

T1 and T2 relaxation times

T1 and T2 relaxation times depend on the physicochemical environment of the hydrogen protons. They reflect the rate at which the excited protons lose energy (their rate of relaxation). Protons lose energy by a variety of mechanisms, resulting in changes in the intensity of the signal that they produce. Every magnetic resonance image contains both T1 and T2 information, but by appropriate choice of the timing and length of the radiofrequency pulses the image can

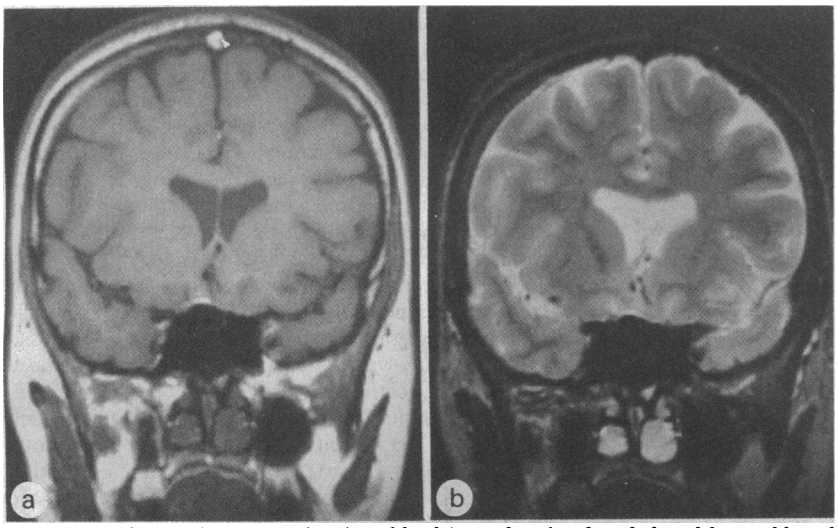

FIG 5—*Normal magnetic resonance imaging of head (coronal section through frontal horns of lateral ventricles) showing differences between T1 and T2 weighted images. (a) In the T1 weighted image cerebrospinal fluid shows low signal; grey matter appears grey; white matter appears whiter; and fat, which shows the highest signal intensity, appears white. (b) In the T2 weighted image cerebrospinal fluid in the lateral ventricles and subarachnoid space surrounding the brain is of high signal, grey matter appears whiter than white matter, and fat is of intermediate signal*

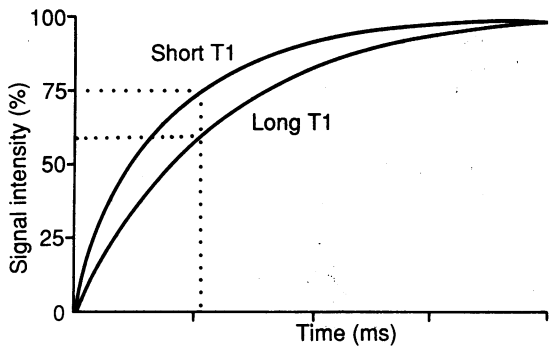

FIG 6—*T1 recovery curves. T1 recovery (realignment of the hydrogen protons with the magnetic field) is exponential in form. When measured at an appropriate time (vertical dotted line) the difference in signal intensity between a substance with a short T1 and a long T1 can be displayed on the final image as differing shades of grey. Thus, in this example, the substance with a short T1 (for example, white matter in the brain) will appear whiter (higher signal intensity) than the substance with a long T1 (for example, cerebrospinal fluid), which will appear greyer*

be weighted to depend mainly on one or other of these relaxation times (fig 5) or to represent mainly proton density.

A T1 relaxation curve represents the rate at which the excited protons realign with the field. These curves are exponential in form, and the number T1 represents the time it takes for 63% of the magnetisation due to the excited protons to realign with the field. In images of complex structures such as the brain there are, of course, many different tissues, each with its own individual T1 curve, but for the sake of simplicity figure 6 illustrates just two different T1 curves. One curve is from a substance with a long T1—for example, cerebrospinal fluid—and the other represents the T1 curve of a substance in which the hydrogen nuclei realign more quickly—for example, white matter in the brain. Differences in grey scale in the final image reflect the difference between the height of the T1 curves for these two tissues at the point in time corresponding to the rate at which radiofrequency excitation is repeated. This difference in signal intensity is referred to as T1 contrast.*

*The word "contrast" in this context needs to be clearly understood. All black and white images depend on two basic factors: contrast and spatial resolution. Contrast resolution refers to the comparative difference in blackness or whiteness between tissues in the final display, reflecting the difference in signal intensity of different portions of the image. Contrast information can be artificially changed with a contrast agent.

T2 is a relaxation time that reflects the rate of signal decay due to dephasing of the spinning protons. Dephasing is an important concept in magnetic resonance imaging. It is best explained with an analogy. Imagine a pond on which are floating innumerable small bar magnets all spinning at the same rate (fig 7(*a*)). If the bar magnets spin in phase—in other words, if all the north poles are pointing in the same direction—it is easy to see how a signal could be generated that would rise and fall as the north poles all swept around in phase with one another. If, on the other hand, all the poles were pointing in random directions there would be no coherent signal (fig 7(*b*)), even if the magnets were all spinning at the same frequency. In magnetic resonance scanning not only does the radiofrequency pulse excite the protons to a higher energy state but it also jerks them into phase, rather like a drill sergeant suddenly shouting to soldiers on a parade ground to line up and face left.

Once the pulse is switched off the protons start to dephase, and the rate at which they dephase is characterised by a time known as T2, representing the time it takes for 37% (100%−63%) of the magnetisation due to the spinning protons to decay due to dephasing. The contrast due to T2 decay in the final image depends on the difference in magnitude of the two T2 curves at the point in time when the signal is collected (fig 8).

So far we have discussed three of the four variables that are responsible for the contrast in a magnetic resonance image: proton density, T1, and T2. The final variable is motion. All motion affects the image, often in unwanted ways, but there are situations in which motion can be exploited for diagnostic information. A good example of useful information obtainable from the alteration of signal due to motion is in imaging flowing blood.

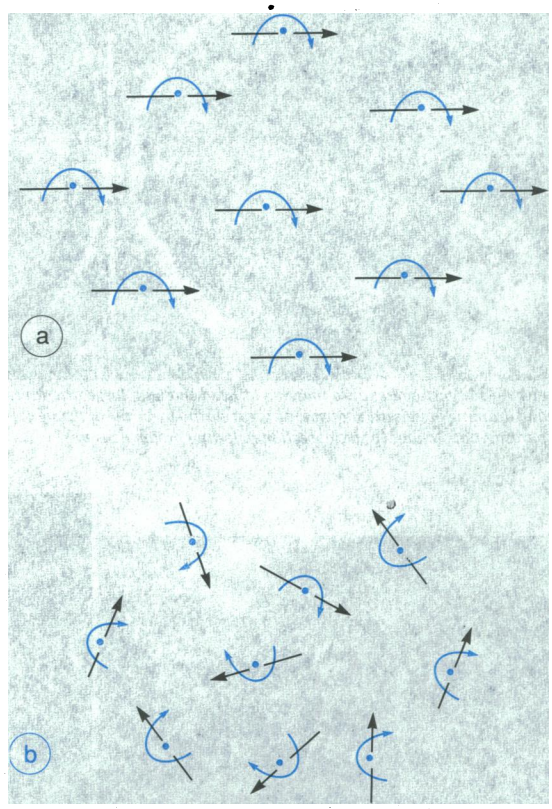

FIG 7—*Dephasing of nuclear "spins." (a) All the spins are in phase. The nuclei, which can be likened to small bar magnets, are spinning on their own axes but at any one point in time are all facing the same direction. (b) The spins are dephased: they all point in random directions and will therefore not induce a coherent signal in the receiver coil*

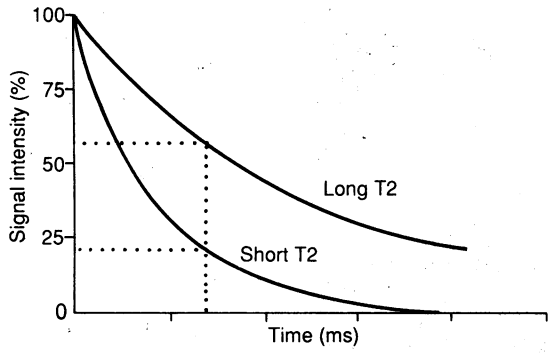

FIG 8—*T2 decay curves. The signal decay due to T2 (proton to proton interactions) is, like T1 recovery, exponential in form. When measured at the appropriate time the difference in signal intensity between a tissue with short T2 (for example, white matter in the brain) and long T2—(for example, cerebrospinal fluid) can be displayed so that the material with a long T2 appears whiter (higher signal intensity) than the substance with a short T2*

Flowing blood

With computerised tomographic images blood vessels either appear of similar density to muscle or, when intravenous contrast material has been given, they appear denser than muscle because the iodine of the contrast material shows up white. With magnetic resonance images the message is more complex. Flowing blood may be dark or white depending on the signal sequences and gradients and on the speed and turbulence of the blood flow.

Fast flowing blood does not generate any signal on most standard so called spin echo images. (To explain why would require an explanation of the spin echo method of obtaining magnetic resonance data, a topic that is beyond the scope of this review.) The explanation centres on timing—by the time the scanner is ready to collect the data the blood has moved on and no signal is recorded, or, expressed in magnetic resonance imaging jargon, there is a signal void. Figure 9 shows a highly practical application, where the signal void of fast flowing blood enables an arteriovenous malformation of the brain to be shown.

The different signal of flowing blood compared with stationary tissues holds out the promise of "magnetic resonance imaging angiography" (fig 10)[9]—the possibility of (*a*) showing vascular disease without the need for needles, catheters, or contrast media and (*b*) applying quantitative techniques for mapping such variables as the velocity and direction of blood flow, thereby deriving a variety of measurements reflecting disordered physiology. More recently suggestions have been made that measuring capillary perfusion and such factors as capillary permeability in each small picture element will be possible.[10 11]

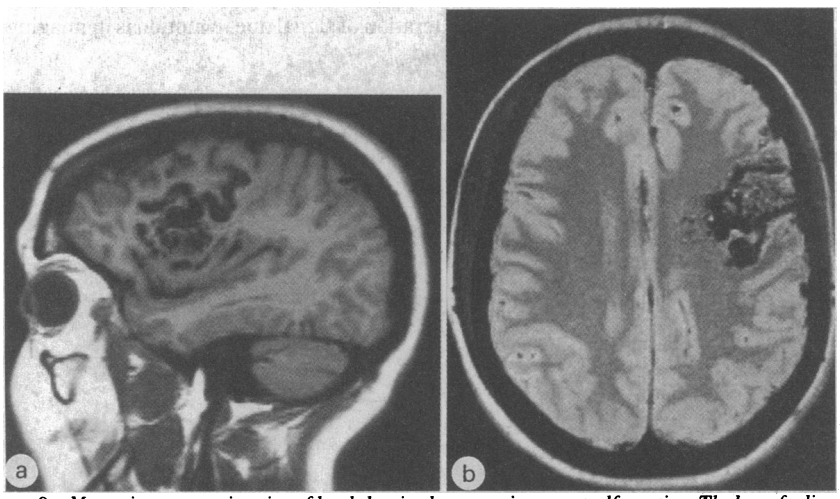

FIG 9—*Magnetic resonance imaging of head showing large arteriovenous malformation. The large feeding and draining vessels are shown with great clarity by virtue of the signal void of flowing blood (a) T1 weighted parasagittal section; (b) axial section reflecting proton density*

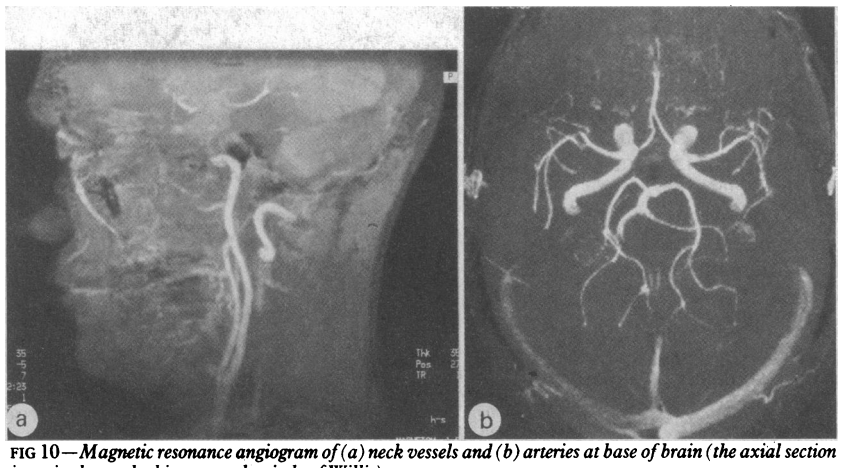

FIG 10—*Magnetic resonance angiogram of (a) neck vessels and (b) arteries at base of brain (the axial section is equivalent to looking up at the circle of Willis)*

Magnetic resonance contrast agents

Clearly a wealth of information can be obtained with magnetic resonance images relying only on the inherent or natural magnetic resonance contrast of the tissues of the body, but there are times when an artificial contrast medium is needed. A magnetic resonance contrast medium may be something drunk or injected, which will selectively alter the signal intensity of an organ or a pathological process.

Gadolinium diethylenetriaminepenta-acetic acid (DTPA), the first contrast agent to be introduced for clinical use in magnetic resonance imaging, is a paramagnetic substance. The distribution of gadolinium DTPA after intravenous injection is similar to that seen with the conventional iodinated contrast media used for computed tomography and angiography. At standard tissue concentrations gadolinium acts as a T1 shortening agent, and thus tissues containing gadolinium appear bright on T1 weighted images.

Many potential applications of contrast enhanced magnetic resonance exist—for example, distinguishing tumour tissue from surrounding oedema or active inflammation from established scar tissue, and finding very small tumours, either by altering the signal in the normal background tissue or by altering the signal of the tumour itself.

Figure 11 shows an example of the use of gadolinium DTPA to diagnose a small tumour. The images taken after injection of gadolinium DTPA show very high signal in a tiny acoustic neuroma lying within the internal auditory canal, whereas before the gadolinium was given the tumour was undiagnosable. The presence of gadolinium DTPA within the lesion made it possible to show the size, shape, and position of an extremely small tumour with great confidence. Little doubt exists that contrast media will be more widely used and, in the future, further agents will be introduced.

Fast magnetic resonance imaging

One of the reasons why conventional magnetic resonance images of the head and bones are so impressive is that patients can keep their heads and their skeleton relatively still for long periods. Conventional spin echo images take several minutes and, on occasions, as long as 10-15 minutes to acquire. But it is not possible for patients to keep their chests or abdomens still for several minutes. They breathe, their hearts beat, and their intestines move. Consequently, images of the chest or abdomen are degraded

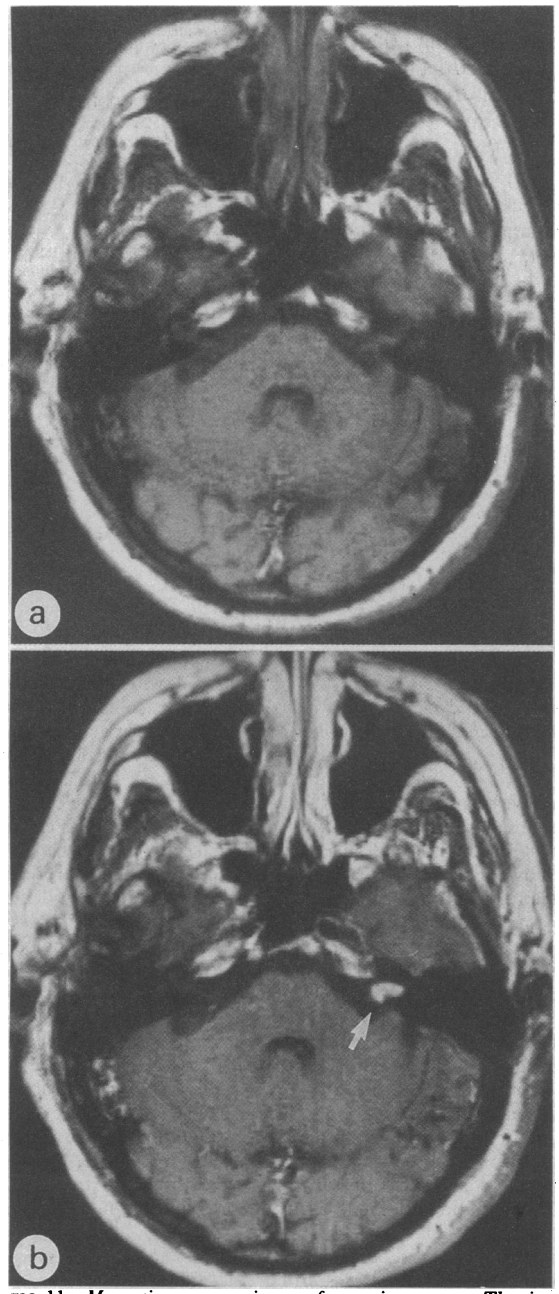

FIG 11—*Magnetic resonance image of acoustic neuroma. The tiny acoustic neuroma in the left internal auditory canal (arrow) is identifiable only in (b), taken after an intravenous injection of gadolinium DTPA. Both images are T1 weighted axial sections through exactly the same level*

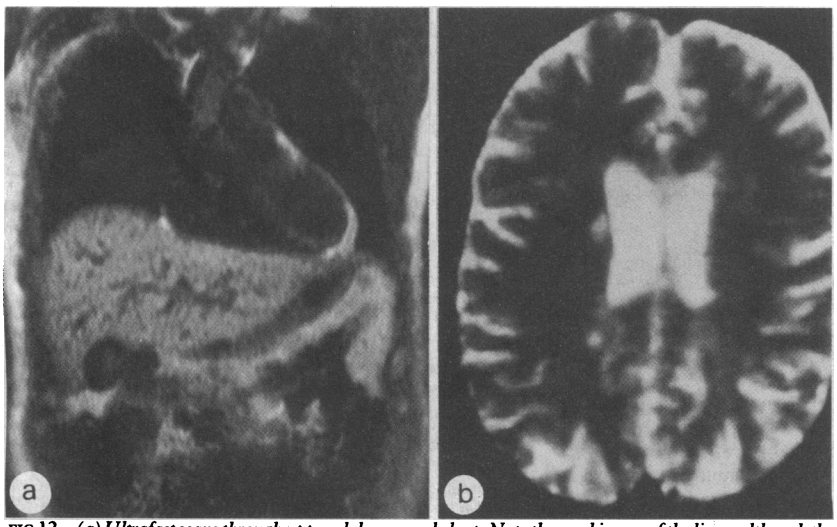

FIG 12—*(a) Ultrafast scans through upper abdomen and chest. Note the good image of the liver, although the total time for this image was a few milliseconds. (b) Echoplanar image of T2 weighted axial section through the head. This image was acquired in just 40 ms (courtesy of GE Corporation)*

by motion artefact. What that means in practice is that the differences in contrast that are inherently present cannot be displayed at an acceptable spatial resolution—the images appear blurred. Many different approaches have been tried to overcome the degradation of images due to motion. Cardiac gating of the data collection (acquiring the signal in defined blocks of time according to the phases of the patient's electrocardiograph) is widely used and is very successful for providing images of the heart and larger arteries. But cardiac gating prolongs total imaging times and requires expert implementation.

Respiratory gating, which doubles or triples scanning time, has proved impracticable to implement routinely for various reasons. An alternative approach is to repeat the data acquisitions in an attempt to average out motion artefacts, but when applied to structures such as the liver this particular technique inevitably requires relatively thick sections and substantially limits the choice of pulse sequences that may be used—for example, with spin echo imaging it is really practicable to use only heavily T1 weighted sequences.

In many other forms of imaging, including conventional photography, the main method used to overcome motion artefacts is to take the images quickly—if possible so fast that the image becomes a stop action photograph. Most computed tomography scanners produce images with exposure times of two seconds, so that a section of the liver, for example, may be obtained during a single breath hold. Conventional radiographs such as chest radiographs, angiograms, and so on, are obtained with exposure times of 30 ms or less, and at this speed the effects of movement are greatly reduced.

Clearly, the aim of physicists and engineers working in magnetic resonance imaging has been to provide machines that can acquire images in less than a second, preferably in less than 100 ms. Such ultrafast imaging has been under development since the early days of magnetic resonance scanning. Only recently, however, have machines capable of producing ultrafast images become commercially available. Several methods are being pursued. The first to be introduced on to the market tips (flips) the protons through very small angles (low flip angle techniques), thus saving time, and does so repetitively with extremely short time intervals (fig 12 (*a*)).[12 13] Another, known as echoplanar imaging[14] (fig 12 (*b*)) has very demanding hardware requirements and is not yet commercially available.

Fast imaging has many other potential advantages. Magnetic resonance imaging machines are very expensive to buy and run, but clearly the cost of imaging one patient depends critically on how long it takes to perform the examination. Faster imaging could translate to more patients being examined each working day and, therefore, to less expensive individual examinations. Also, faster imaging makes it practicable to image data from a whole volume of tissue instead of just one section through a predetermined axis; the computer can then be programmed to reconstruct many different sections in a variety of different planes retrospectively.

The concept of volume imaging was first put forward in the early days of magnetic resonance imaging, but the problem was that it took so long to acquire a volume image that it proved to be impractical. Fast imaging has now enabled volume imaging to become a practical proposition. Other applications of fast imaging include cine-imaging and real time flow imaging.[15]

Figure 12 shows what may currently be achieved by using commercially available equipment with imaging times of only a few hundredths of a second. Figure 12 (*a*) is almost a stop action picture of the heart and liver, and figure 12 (*b*) is an image of the brain obtained in three hundredths of a second. The images them-

selves are not better than the conventional images shown earlier; the point is that even though they were acquired in just three to four hundredths of a second they show acceptable anatomical information, almost as good as with conventional techniques.

Acknowledgments

This review is based on the inaugural lecture given by P Armstrong. SFK is supported by the Bunzl Gift Fund.

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ANY QUESTIONS

For how long should chemotherapy with rifampicin and thiazine (a combination of isoniazid and thiacetazone) be given to a middle aged woman with tuberculous lymphadenitis living in tropical Africa?

Few randomised clinical trials have been conducted on the chemotherapy of tuberculous lymphadenitis. The British Thoracic Society has shown that nine months of isoniazid and rifampicin, supplemented by ethambutol for the first eight weeks, is as highly effective as the same regimen continued for 18 months,[1] and a report on a non-randomised series suggests that a six month regimen of isoniazid, rifampicin, and pyrazinamide for two months, followed by isoniazid and rifampicin for four months, is equally good.[2] Indeed, the committee on treatment of the International Union Against Tuberculosis and Lung Disease recommends this latter regimen.[3] The regimen mentioned by the questioner is, however, less effective as it does not contain pyrazinamide. In the absence of data from randomised trials the committee therefore recommends that such a regimen be continued for nine months. If rifampicin is stopped after the first two months the treatment should be continued for a year.

In populations in which the prevalence of tuberculosis is high, as is the case in tropical Africa, most cases of tuberculous lymphadenitis are indeed caused by *Mycobacterium tuberculosis*. In contrast, in populations with a low prevalence other mycobacteria are more likely to be the cause. Surgical resection is usually the treatment of choice in such cases.—DAVID J GIRLING, *senior scientific staff, Medical Research Council, London*

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Botulinum toxin in great dilution is used to reduce blepharospasm. Is there any evidence that the toxin would be of value in restoring anal muscle function after the muscle has been stretched for the treatment of haemorrhoids or anal fissure?

Clostridium botulinum type A toxin in very dilute solution (3 ng) is used clinically. The toxin produces muscle paralysis by blocking the release of acetylcholine from motor neurones. It is used by ophthalmologists to treat strabismus and essential blepharospasm and to paralyse the levator palpebrae in treating retraction of the upper lid associated with thyrotoxicosis. It has also been used to treat torticollis and facial spasm. Larger doses are required when larger muscles are treated (up to 40 ng).[1] In ophthalmology the dose is approximately 3 ng. There is a report of its use in treating anismus, a condition in which there is inappropriate contraction of the anal sphincters, causing constipation.[2] Paralysis of the puborectalis part of the anal sphincter mechanism can give good results.

There are, however, complications associated with using this potentially lethal agent. Paralysis can be reversed only by the early administration of botulinus antitoxin. This will not be effective unless given soon after the toxin, so permanent paresis is a danger. There may also be spread of paralysis to adjacent muscles or generalised systemic effects. There seems to be no evidence that the toxin has been used to relieve the muscle spasm associated with anal fissures or haemorrhoidal prolapse. This is presumably because of the risk of causing permanent incontinence if the sphincters are inadvertently permanently paralysed. The toxin would be of no value in restoring anal muscle function after the muscle has been stretched for the treatment of haemorrhoids or anal fissures.—DONALD REID, *consultant surgeon, Brighton*

1 Humphrey RC. Botulinum toxin: a new ally of an old adversary. *BMJ* 1989;**298**:136-7.
2 Hallan RI, Melling J, Womack NR, Williams NS, Waldron DJ, Morrison JFB. Treatment of anismus in intractable constipation with botulinum A toxin. *Lancet* 1988;ii:714-7.

Are people who adhere strictly to "prudent diets"—designed to reduce fat intake to very low amounts—at risk of deficiency of fat soluble vitamins?

No. The advice to reduce fat intake applies to adults, not infants or young children, and it is associated with advice to increase consumption of vegetables.[1] Dietary vitamin A is obtained from fats, especially fatty fish, and (in the form of carotene) from green vegetables and especially carrots. Fifty grams of carrots or 100 g of leafy green vegetables would supply the adult requirements even if the fat intake was zero. In fact, fat intake is unlikely to fall below 80 g a day, and this amount of vitaminised margarine would also supply daily requirements. Vitamin D requirements in adults can normally be met by synthesis in the skin under the influence of sunlight, but fatty fish and fortified margarine are also good dietary sources. Excessive intake of fat soluble vitamins is potentially dangerous.—J S GARROW, *professor of human nutrition, London*

1 National Advisory Council on Health Education. *Proposals for nutritional guidelines for health education in Britain 1983.* London: Health Education Council, 1983:40.