Teaching Editorial

Nuclear Magnetic Resonance Imaging

Nuclear magnetic resonance (NMR) is a phenomenon that has been used in physics and chemistry since the late 1940s. In the early 1970s, it was suggested that this phenomenon could be used to generate an image of the internal structure of the body. Now, after many years of research, NMR imaging is entering the hospital environment for clinical trial.

As this new technique becomes more widespread we will have to become familiar with its basic physics. A thorough understanding of NMR is only possible through the techniques of quantum mechanics. Since most of us in the medical world (including myself) do not understand quantum physics, I will attempt to explain the basics of NMR as it has been explained to me—in simple pictorial terms.

The nuclei of certain atoms possess intrinsic properties of spin and charge. Any atom with an odd number of protons in the nucleus is a potential candidate for NMR imaging. These atoms, therefore, will behave as small magnetic dipoles (similar to bar magnets). If they are subjected to an externally applied magnetic field, they tend to line up with that field. At any one instant in time the majority of the nuclei will line up with the field while the remainder of the nuclei will line up against it. The slight majority of nuclei lined up with the applied field result in a net magnetization of the specimen in the direction of the applied field. It is the ability to detect this net magnetization that forms the basis of NMR (Fig. 1A,B).

Although NMR experiments can be performed on many nuclei, hydrogen is the most common nucleus used for imaging. This is because the hydrogen nucleus or proton is the most abundant nucleus in the body and has a relatively large magnetic moment (spin). Because the NMR signal is inherently weak, use of hydrogen allows the largest signal with which to work.

A proton whose magnetic moment (spin) is not aligned with the field will precess around it. To understand the term "precession," imagine a child's spinning top, which not only spins around its own axis but also wobbles around a vertical axis (especially noticeable as the top slows down). This wobbling around the vertical axis is precession. The frequency of precession is dependent on the strength of the applied magnetic field and on the nucleus being examined. This is known as the Larmor frequency.

If energy is added to the system by supplying a radiofrequency pulse at the Larmor frequency, the protons are pushed out of alignment with the field. A short-time duration radiofrequency pulse will turn the protons 90° so that their spins are perpendicular to the direction of the applied magnetic field. They will then begin to precess about the field, thereby generating a detectable radiofrequency signal in a pickup coil—the so-called free induction (or free precession) signal (Fig. 1C,D). A pulse of longer duration will flip the protons 180° so that they are oriented opposite to the applied field.

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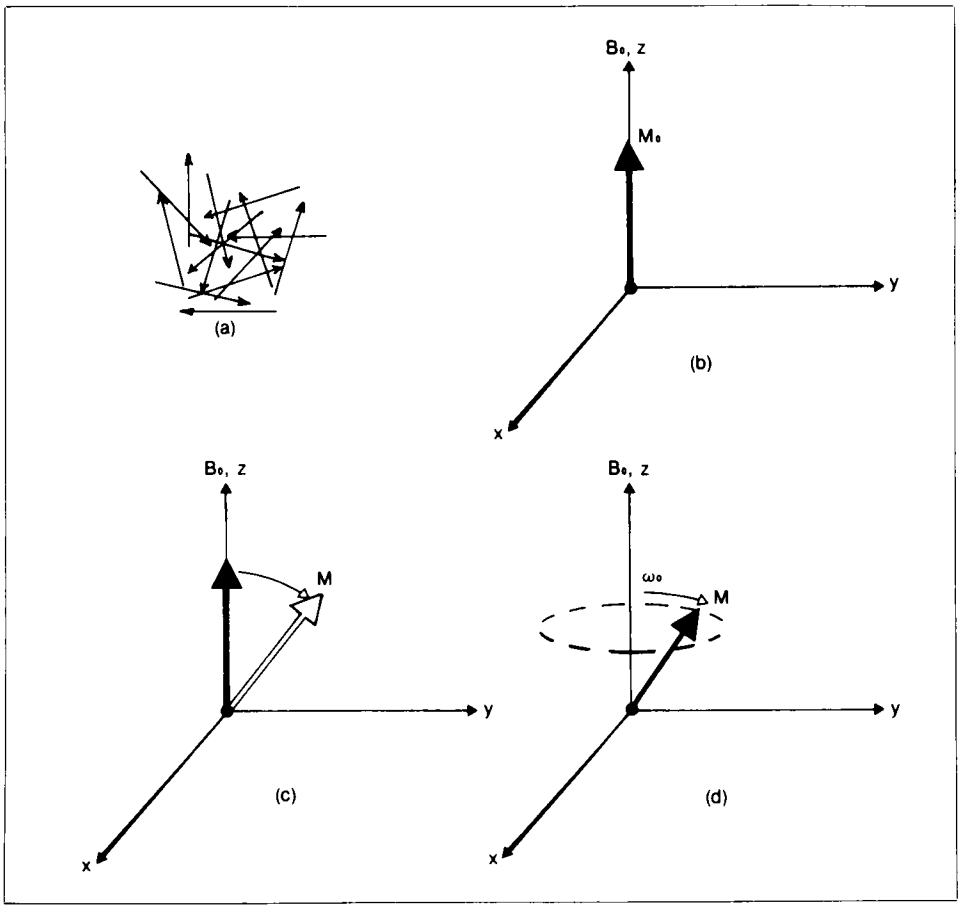

FIG. 1. (A) Diagrammatic representation of randomly oriented nuclear dipoles. (B) Application of an external magnetic field B_0 along the z axis causes net magnetization M_0 along the z axis. (C) After an applied radiofrequency pulse the net magnetization is flipped from its equilibrium position. (D) Net magnetization precesses about the axis of the applied field at the Larmor frequency (W_0). (From David I. Holt)

In either of these excited or high-energy states the protons will attempt to achieve stability and return to their equilibrium position. The time that is taken to achieve equilibrium is called the relaxation time (T_1). In fact, two different processes occur as the nuclei return to equilibrium and so two times are measured; the so-called T_1 and T_2 times (Fig. 2). The T_1 time is also called the spin-lattice relaxation time as it is due to the nuclei losing energy to their environment or lattice. The spin-lattice relaxation time is dependent on the nature of the environment of the protons and the T_1 time is, therefore, a reflection of the environment of the proton. For instance, a proton in bone will have a different T_1 than a proton in muscle (which contains more fluid.). By appropriately timing the radiofrequency pulses, the T_1 of a specimen can be measured.

Another parameter, the T_2 relaxation time, can also be measured. Immediately after the radiofrequency pulse all the protons are precessing or wobbling in phase. With the passage of time some of the dipoles will precess faster and some slower, gradually reducing the signal until at some point there is no signal because they are sufficiently out of phase so that all net magnetic effects produced by one set of dipoles is cancelled by an equal and opposite effect by another group of dipoles. The time taken for the signal to stop is the

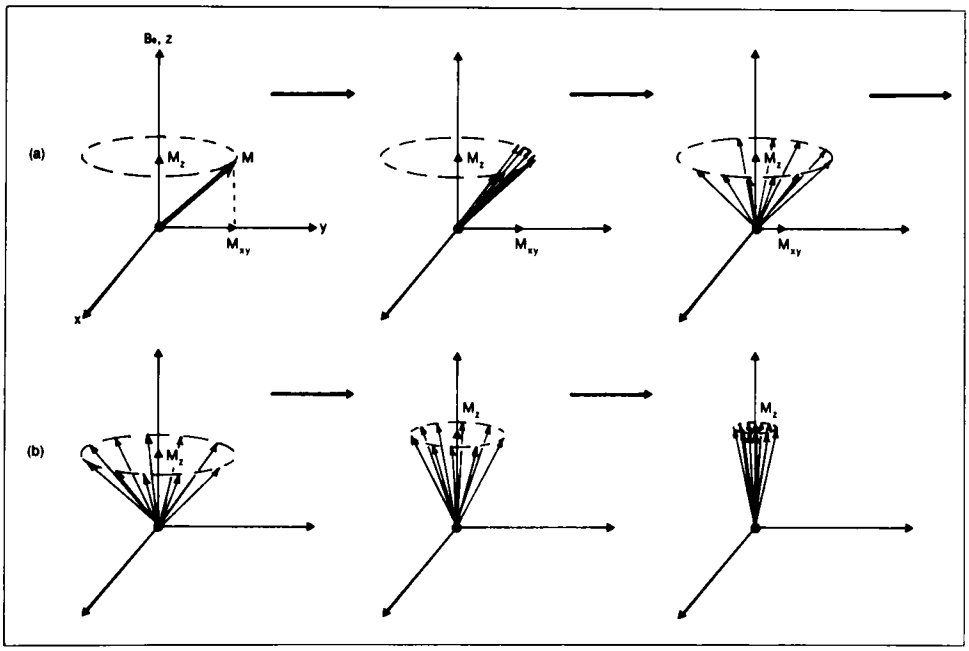

FIG. 2. (A) Diagrammatic representation of dephasing of nuclear magnetic movements caused by interaction with each other. The detected signal M_{xy} decays in time T_2, the spin-spin relaxation time. (B) The magnetization (M_z) recovers to its equilibrium position along the z axis in time T_1, the spin-lattice relaxation time. (From David I. Holt)

T_2 time. This is also called the spin-spin relaxation time as the gradual loss of signal is due to the interaction of the nuclear spins with one another.

The strength of the signal returning from the specimen is dependent on the total number of nuclei affected by the field and radiofrequency pulse.

Thus, three properties have been described that can be analyzed with NMR: the strength of the signal caused by the precession of the nuclei, which depends on the number of nuclei present; the spin-lattice relaxation time T_1; and the spin-spin relaxation time T_2. However, with this information alone it is not possible to form an image because there is no spatial information. We do not know where in space (or in the body) the signal is coming from. We do know, however, that the frequency of precession of a nucleus is directly dependent on the strength of the magnetic field that is affecting it. Superimposed field gradients in the X, Y, and Z axes of the magnet create different magnetic fields for each point in the X, Y, and Z coordinate grid. This is done by placing extra magnetic coils within the main magnet. Thus, each set of nuclei is subjected to a unique magnetic field within the main field and will precess at a slightly different frequency—thereby signalling (in effect) its location.

This explanation is somewhat simplified so that the concept can be more easily understood. In practice the radiofrequency signal used to stimulate the protons has a very wide band, (i.e., the signal is composed of many different frequencies), so protons situated in fields of differing strength will still be stimulated at the correct (Larmor) frequency. The received signal is also composed of a similarly wide band of frequencies. A mathematical technique called Fourier transformation is used to divide the signal into its component frequencies. Thus, for each point in the body an image can be created that reveals any one of the three basic parameters (signal strength, T_1, T_2).

Because the relaxation times reflect the interactions of the nucleus with its environment (T_1) and with other nuclei like itself (T_2), the NMR image is quite unlike anything we have ever seen. Images already produced show striking contrast between gray and white matter in the brain (Fig. 3). This is thought to be due to the fact that protons in gray matter are in water whereas protons in white matter are in the form of fat. This changes the T_1 of the protons enough to make the signal from white matter greatly different if the picture shows T_1 dependency. Pictures that reflect the total number of protons in the tissue do not show this contrast because the total number of protons in water and fat is similar. It has also been shown that several disease processes, for example, abscesses and some cancers, can be identified using NMR.

There are several different methods for reconstructing the data to form an NMR image. Each technique has advantages and disadvantages when compared with another and no technique has proved to be pre-eminent yet. Theoretical advantages may not prove to be advantageous clinically and only extensive clinical investigation will decide this question.

Radiologists already have very sophisiticated (and expensive) techniques to diagnose disease. What benefits does NMR offer? An obvious advantage of NMR imaging is that it does not use ionizing radiation to make an image. The energy deposited in the tissues in making an NMR image is very much less than the energy deposited when taking an x-ray or radioisotope scan. Therefore, NMR promises to be much safer.

Because the "slice" in NMR is selected by applying a magnetic field gradient instead of physically changing the position of a machine or moving the patient, any plane of imaging can be chosen (Fig. 3). This has obvious advantages in dealing with patients who are relatively immobile. Also certain parts of the body are more easily examined in certain planes. For example, the relationship of the spinal cord to the vertebral body is more easily examined in the longitudinal (sagittal) section.

Another potential advantage of NMR imaging is the possibility of obtaining chemical information. Recall that the frequency of precession of a nucleus depends on the applied magnetic field and the nature of the nucleus itself. The frequency will also change

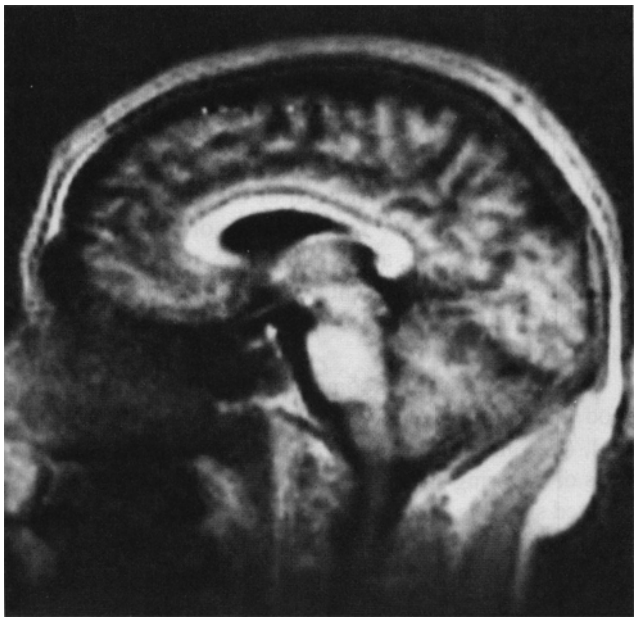

FIG. 3. Sagittal NMR scan of the brain. This scan demonstrates two advantages of NMR imaging. The high degree of gray–white matter diffrentiation is seen on the periphery of the brain; the gray matter appears gray and the white matter appears white. The sagittal scan is taken without moving the patient or the scanner. Note also the proximal spinal cord entering the spinal canal. (Courtesy of Dr. Graeme Bydder, Hammersmith Hospital, England.)

slightly depending on the chemical bonding of the atom. This is call the chemical shift and forms the basis for using NMR to investigate the structure of molecules. Although it has not yet been done, there is hope that an NMR image can be made that will show chemical information in an organ. Some nuclei that may be important for this determination are phosphorus, carbon, and sodium. However, they are far fewer in number in the body than hydrogen and give a much weaker signal. Therefore, significant technical problems will need to be overcome before images of those nuclei are readily available.

Until the introduction of NMR, computed tomography (CT) was the radiologic technique that produced pictures with a high degree of soft tissue contrast. Thus, the question of competition between the two modalities is often raised. It is impossible to make final judgments at this stage of development. It is possible to say that NMR has greater soft tissue contrast. In the brain this is manifested as great differentiation between gray and white matter. Certain diseases, such as multiple sclerosis, result in loss of white matter and it has been shown that NMR images of the brain reveal more of this white matter loss (demyelination) that CT images. For this one disease at least, NMR has a demonstrated advantage. Nuclear magnetic resonance has been able to identify disease in the brain, liver, pancreas, and kidney but in the majority of reported cases the lesion in question had also been identified by some other imaging modality.

Though the advances made by the investigators in the field of NMR imaging have been astounding, an enormous amount of information still needs to be gathered to decide what role NMR will play in medicine in the future. If the technique fulfills its promise, its role will be substantial.

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Glossary of Terms

Dipole. Object oppositely magnetized at two poles. Hence, North and South pole of a magnet.
Magnetic moment. The turning force exerted on a magnetic system placed in a magnetic field.
Larmor frequency. The frequency at which the resonance of the nucleus is excited.
T_1 relaxation time. The time taken for the nuclei to reach equilibrium with their environment. This is also referred to as the spin-lattice or longitudinal relaxation time.
T_2 relaxation time. The time taken by the nuclei to reach equilibrium with each other. This is also referred to as the spin-spin or transverse relaxation time.

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