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Basic Principles of Magnetic Resonance Imaging

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The basic concepts which are necesary to understand the physical principles of Nuclear Magnetic Resonance (NMR) imaging are presented. It is intended as a primer for the physicians or scientists who are addressing the topic of NMR for the first time. The basis of the NMR phenomena is described with introduction of the concepts of magnetic moment, magnetic resonance, net magnetic moment of an object, NMR excitation and NMR emission. The equipment necessary to observe these NMR properties is summarized as well as the procedures for basic NMR experiments. The major scanning methods are reviewed, and the principles of technique are discussed. With major emphasis on repeated free induction decay (RFID) which yields proton image density, inversion-recovery (IR) which yields images weighter by tissue T− values, spin-echo (SE) which yields images weighted by tissue T{ values. Clinical applications of NMR imaging will be presented. Absence of known biological hazard, lack of moving parts, absence of ionizing radiation, and ability to measure multiple tissue parameters makes NMR the study of choice in many clinical situations particularly in early cancer diagnosis and in pathologic changes in the broad spectrum of disease within the brain. NMR's ability to create detailed tomographic images in any plane, with both anatomic detail and tissue specificity is revolutionizing diagnostic imaging. It has additional advantage of measuring metabolic processes in vivo which has great impact in understanding health and disease.

Introduction

This article is addressed to readers who are being exposed to nuclear magnetic resonance (NMR) imaging for the first time. For readers who are not interested in the mathematical description or who have a limited background in the physical sciences, the following conceptual approach is offered.

The Magnetic Moment

The nuclei of some atoms spin on their axis. Since they are spinning, these nuclei possess a certain amount of energy. This energy can do the work by virtue of its motion and is called **momentum.** The momentum possessed by a spinning object is called **angular momentum.** A very fast spinning top appears to defy the laws of gravity as it remains upright while poised on a single point. As the top loses speed of rotation, it begins to tilt over and slowly rotate[1] (Figure 1). This second motion is called precession. The spin axis precesses about the earth's gravitational field. As the top loses speed or angular momentum it begins to tilt away from the vertical (gravitational) axis at a larger angle. As a spinning top loses energy, one observes that the spin axis begins to tilt away from the vertical, the spin axis begins to precess, and the rate of precession or precession frequency increases. A top with a large angular momentum is said to be in a high-energy state; as ti loses this angular momentum, it goes through lower energy states until all motion stops. This lowest energy state is called the ground state.

The nucleus of the hydrogen atom is the proton, which has a positive electric charge. The spinning proton behaves like a small magnet, having a north and a south pole along the axis of rotation. Hence the proton has a **magnetic moment.**

In 1900, Larmor demonstrated that a magnet having angular momentum (a gyromagnetic system) will be set into precessional motion when placed in a magnetic field. This precession frequency is called Larmor frequency, w, given by the following equation:

$$w = YB \quad \ldots\ldots(1)$$

or

$$V = YB \quad \ldots\ldots(2)$$

where W is the Larmor frequency in radians per second
is the Larmor frequency is Hertz (Hz)
is the gyromagnetic ratio in radians per second per Tesla (10,000 Gauss). Y is characteristic nuclear constant different for each nucleus
is the magnetic flux density in Tesla (in vacuum the flux density B is equal to the magnetic field intensity H)

for protons $V = 42.6 \times B$ MHz if B is in Tesla.

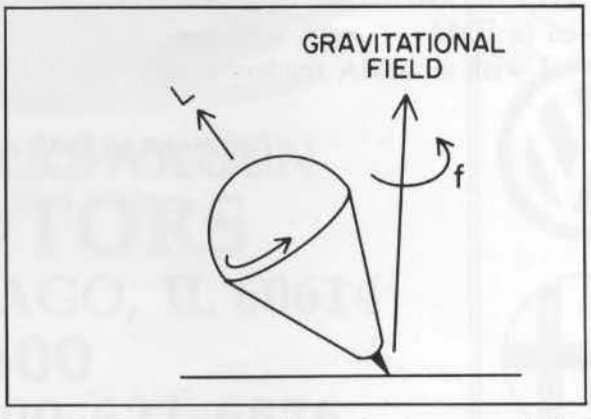

Figure 1: The precession of the nucleus in a magnetic field is similar to the precession of a spinning top in a gravitational field.

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The top can possess any energy state, but the proton, by laws of quantum mechanics, exist only in two well-defined energy states, namely the excited state (with energy) and relaxed state or the ground state. In the ground state the nuclear magnetic vector is parallel to the direction of the applied magnetic field whereas in the excited state it is antiparallel to the direction of the applied magnetic field.

Spin Density Measurement

Nuclear spin density is the total number of nuclei of a given species in a given sample. To measure this, one has to measure the change in distribution. To effect the distribution some nuclei are raised to a a higher energy state (antiparallel state) by imparting energy to them. In a static magnetic field, nuclei precess at the Larmor frequency and they align themselves with the lines of magnetic induction. When a perpendicular alternating magnetic field (called the radio frequency or RF, field) that is alternating in synchrony with or in resonance with the nuclear magnets (hence the term "nuclear magnetic resonance") is applied to the sample, some of the nuclei are raised to a higher energy state or excited state. When the RF field is shut off, the nuclei fall from the excited state to the ground state by emitting energy in the form of a packet of electromagnetic energy and for proton, it is identical to radio waves. In fact, they have the same frequency as the Larmor frequency.

NMR phenomenon is measured either by measuring the energy that is absorbed when the RF field is turned on or by measuring the energy that is emitted when the RF field is turned off. The first technique is called **nuclear magnetic absorption** and it is widely used in NMR spectroscopy for the study of molecular structure. The second technique is called **free induction decay** (FID). In the first technique the RF source at a fixed frequency is maintained and the magnetic field strength is varied while monitoring the energy absorbed from the generator. A plot on the graph of absorption versus magnetic field strength, shows absorption peaks of the various atomic species within the sample. These peaks occur at different magnetic field strengths due to the electronic properties of the neighboring atoms. Such changes in peaks at different magnetic field strengths is referred to as a **chemical shift.** The relative heights of absorption peaks reflect the ratio of spin densities or number of protons in each banding configuration (Figure 2).

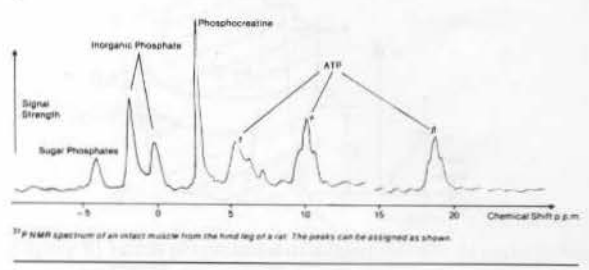

Figure 2: ^{31}P NMR spectrum of an intact muscle from hind leg of a rat. The peaks can be assigned as shown[3].

The total of all the nuclear magnets can be represented as one small magnetic vector (M) pointing in the direction of the applied static magnetic field (Z). This is also called resultant vector (M) or net magnetic moment or net nuclear magnetization vector (M). When a perpendicular RF field is applied, the nuclei becomes synchronized and the resultant vector begins to tilt through an angle and precesses (Figure 3). As long as the RF field is applied, the resultant vector continues to tilt and precesses until the nuclei distribution is totally inverted, at which time the resultant vector will be straight down and no further energy will be absorbed from the RF source. The sample is now said to be saturated. The RF pulse required to take a sample into saturation is referred to as a 180 degree pulse, since it causes the resultant vector to tilt through approximately 180 degrees. Similarly the RF pulse required to tilt the resultant vector to the horizontal position (x-y plane) is called a 90 degree pulse. After a 180 degree pulse is applied and RF field is turned off, the nuclei will return to their initial state and the resultant vector will return to its upright position or Z axis. As this resultant vector moves, RF energy will be emitted. The time required for 63% of the nuclei to return to the initial state is called the **spin-lattice relaxation time** or T_1. It is also called logitudinal relaxation time as it is the time constant that described the recovery of the Z component of M to its equilibrium value M_0, along the direction of the applied magnetic field. It characterizes the time for the perturbed nuclei to realign themselves with the existing lattice structure of the host material. The signal emitted from a 180 degree pulse is usually very small and beyond the detection capability of the present day detectors. When the resultant vector is rotated out of the Z direction by the RF signal, it represents an ensemble of magnets that are now in phase. When the RF signal is turned off, individual magnetic moments begin to dephase (some precessing faster than the resonant frequency and others

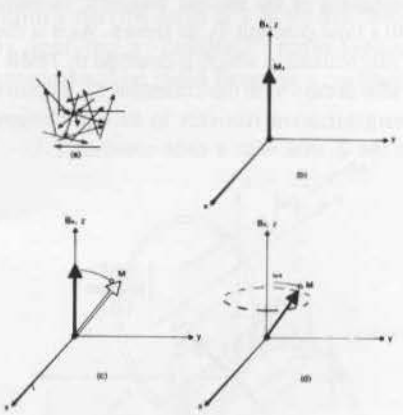

Figure 3: The application of an external magnetic field causes the nuclear magnetic moments to align themselves, producing a net moment M_0. If this magnetization is flipped from its equilibrium position, it precesses about the external field direction at a high angular frequency which is proportional to the field strength[3].

a bit slower) with one another. This decay of signal due to dephasing has a time constant related to T_2, the **spin-spin relaxation time.** It is also known as transverse relaxation time as it describes the decay of the component of the resultant vector, M, in the x-y or horizontal plane which is be definition transverse or perpendicular to the Z axis or direction of the static magnetic field (Figure 4). T_2 is usually much shorter than T_1.

Free Induction Decay (FID)

When a 90 degree pulse is applied, the resultant vector rotates in the horizontal plane. If the pulse is then turned off, the vector continues to rotate freely in this plane and it will at times be parallel to, and then antiparallel to, the RF coil. The effect of this alternating magnetic vector on the coil is the induction of an electric current in the coil and thus the signal is called the "free induction decay" (FID). The 90 degree pulse provides an FID of maximum amplitude since it is only the x, y component or the projection of the resultant vector in the horizontal plane that contributes to the emitted signal. The emitted NMR signals are usually detected by the same coil which transmitted the RF pulse, although a separate receiver coil is sometimes used (Figure 5).

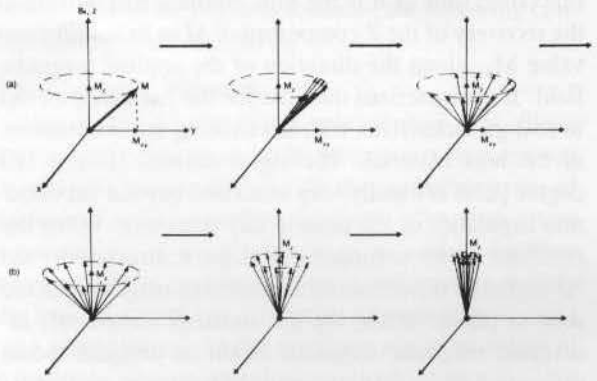

Figure 4: The magnetization decays in two ways. In Figure (a), the dephasing of the nuclear magnetic moments, which occurs with a time constant T_2, is shown. As it is the xy component of magnetization which is detected by NMR receiver, the signal also decays with time constant T_2. Figure (b) shows how the magnetization recovers to its equilibrium position parallel to the Z axis with a time constant T_1[3].

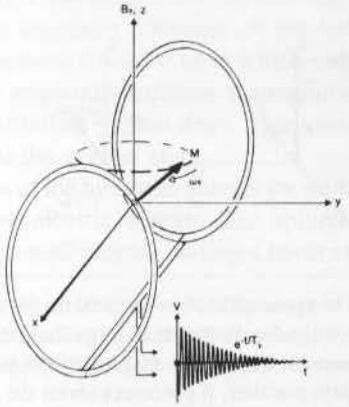

Figure 5: The precessing nuclear magnetization induces a small voltage in pick-up coils placed around the sample, which can be recorded and analyzed[3].

Fourier Transformation

NMR signals constitute a complex wave form in which multiple frequencies are present; the wave form appears as an oscillating sine wave signal (Figure 6) which decreases in amplitude in an exponential fashion with time. Figure 6 shows signal amplitude on the ordinate and time is represented on the abscissa. It is necessary to determine the amount of signal strength at each frequency in order to produce an image, and this is achieved using a process called **Fourier** transformation. Fourier transformation is a mathematical manipulation which allows the curve to be transformed from one representing signal strength versus time into one representing signal strength versus frequency (Figure 6). The amplitude of each signal to each frequency can be determined from the new curve. Fourier transformation of the FID yields the NMR frequency spectrum.

Basic NMR Apparatus:

The basic components necessary for a magnetic resonance measurement are the subject or sample, magnetic field, radio frequency transmitter and radio frequency receiver, sequencer, signal processor, and display[2].

Of these components, the most important and usually the most expensive is the magnet to create the magnetic field. This can be either a permanent magnet or an electromagnet. The electromagnets are either resistive magnets or super-conducting magnets. In a resistive magnet a standard wire is wound and operates at the room temperature. In the case of a super conducting magnet, the coil winding must be cooled to liquid helium or liquid nitrogen temperatures to eliminate electrical resistance. Cryogenic or super conducting magnets provide great stability and high field strengths which result in the best possible signal to noise ratio. However they have a high initial cost and high maintenance.

The radio frequency transmitter provides an RF signal to the sample coil usually at the resonant frequency determined by the selected nuclear species and magnetic

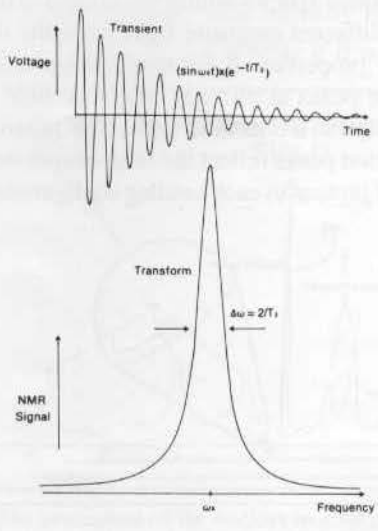

Figure 6: Fourier transformation of the recorded signal produces a characteristic lorentzian line whose width at half height is a measure of the spin-spin relaxation time T_2[3]

field strength. The radio frequency receiver is switched on after the excitation pulse to detect the radio frequency emissions from the sample. The receiver is usually tuned to the resonant frequency of the sample and the simplest type of experiment delivers the FID signal to the signal processor from where it goes to an oscilloscope display or video monitor.

NMR Imaging

The basic principle of the NMR imaging or zeugmatography is quite simple, the dominant relationship in magnetic resonance is the proportionality of the Larmor frequency to the strength of the main field B_0. If that field varies spatially as shown on Figure 7, so does frequency[3]. This is called superimposition of a linear magnetic field gradient G. Now the resonant nuclei at one side of the sample will experience a lower total magnetic field than those at the other side. There will then exist a linear distribution of resonant frequencies across the sample. The spectrum will therefore be broadened to the shape shown in the Figure 7, which in fact corresponds to a one-dimensional projection of the nuclear spin density onto the frequency axis. Such projection data contain information analogous to that obtained from a translate-rotate x-ray CT scanner during one translation and as the CT scanner rotates the direction of the translating beam, so the magnetic field gradient G may be electronicallly rotated in an NMR imaging instrument to obtain another projection from a slightly different angle. Subsequent computer analysis of many such projections allows reconstruction of the image. This was put forward in an article in Nature in 1973 by Paul Lauterbur[4]. There are many methods used to generate NMR images[5].

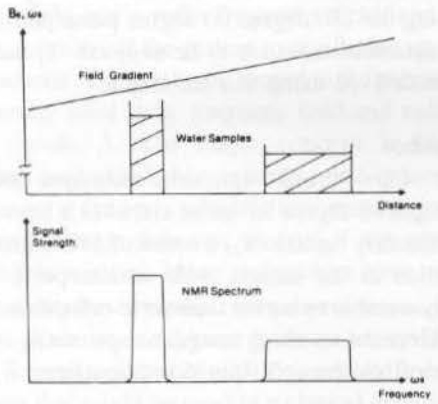

Figure 7: The zeugmatographic principle: The word zeugma means "a yoke" or "that which is used for joining together." In this case, the field gradient couples frequency and distance, and so an NMR spectrum becomes a graph of concentration versus distance[3]

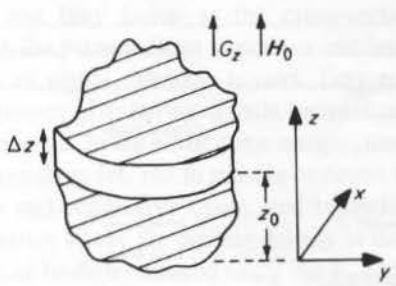

Figure 8: Initial preparation of a layer or slice of undisturbed spins. The shaded portion of the specimen corresponds to regions where the spin magnetization is saturated (From 6) by permission of the authors and publishers. Copyright material of the Institute of Physics, Bristol, England).

The next question is how to provide axial discrimination in order to obtain information from only a thin slice of the body? There are several solutions to this problem[5], and one that is used presently in a number of scanner designs is selective excitation or irradiation.

Selective Excitation or Irradiation Method

Principle:

This technique requires two gradients for each projection. First, a gradient is applied along the X axis or direction of the magnetic field during the RF excitation pulse and a second gradient in the x-y plane during the emission phase. By creating a magnetic field gradient along the Z axis during excitation and transmitting only a single resonant frequency with the RF transmitter, a thin cross-section of the patient is excited. During the emission phase, the Z gradient is eliminated and a gradient in the x-y plane is created. This entire procedure must then be repeated many times (typically 180) to form the different projections necessary for the reconstruction.

In this method the specimen is placed in a large static magnetic field B which polarizes all nuclear spins. In addition to this field, switched linear magnetic field gradients (obtained by using magnetic coils) are applied along three principal coordinate axes. First a thin disc or slice of magnetization of thickness A Z within the sample is considered as shown in Figure 8, which is part of an extended sample along the Z axis[6].

The field gradient Gy alone is switched on and the spin within a narrow strip A y at yo are selectively excited by applying a "tailored" radio frequency pulse to the specimen. The radio frequency components of the

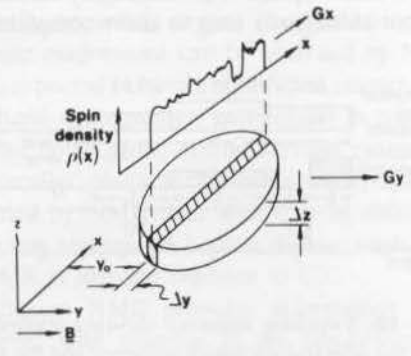

Figure 9: Sketch illustrating the principle of the scanning by selectively irradiating a narrow strip within an isolated slice of magnetization. (Reproduced from Mansfield P, Mandsley AA[6]: BJR 50: 188-194, 1977 by permission of the authors and the editor of BJR).

tailored pulse interact with spins in a narrow strip (shaded strip in Figure 9). The linear magnetic field gradient Gy produced this interaction because of the spins within the slice of material have a range of nuclear Larmor frequencies. Therefore, the spins in the shaded strip having the right Larmor sesonance frequency respond to the selective radio frequency pulse.

Immediately after this excitation pulse, the magnetic field gradient is switched from Gy to Gx and the free induction decay (FID) or spin response signal is recorded and Fourier transformed (Figure 10). This Fourier transfored signal is directly proportional to the proton spin density at the point X, Y_0 along the axis. Thus using the Fourier transformed signals for each strip of the specimen, a cross-sectional picture of the object is constructed and displayed on a television screen.

In summary, in the selective irradiation method the magnetic field gradient is switched rapidly, in time less than T_1 and T_2 from Y to the X and then to the Z direction. Specific planes and lines in the object are imaged by the use of pulse sequences whose radio frequency spectrum covers the carefully selected band of frequencies required to excite the nuclei in the layer or plane of interest.

As well as employing a diversity of image reconstruction techniques, NMR imaging systems often differ with respect to the pattern of stimulating RF pulses applied to the sample; indeed, a given system may be designed with sufficient flexibility to allow use of many different pulse sequences. The extent to which the nuclear spin density (p) and relaxation times (T_1 and T_2) affect image intensity is strongly dependent on the RF pulse sequence used, and careful selection of sequence parameters helps achieve optimal contrast resolution in the final image. By use of a variety of pulse sequences, it is possible to produce images with varing dependence on proton density (p), T_1, and T_2. Several commonly used pulse sequences designed to do this are summarized in Table 1.

Saturation Recovery:

The simples pulse sequence is one in which a series of equally spaced 90 degree pulses is applied to the sample with an interpulse interval roughly the same length as T_1 but sufficiently long to allow complete spin-spin relaxation (T_2) to occur in each pulse interval. The amplitude of free induction decay signals will reach a steady state value that is dependent on both the value of T_1 and proton density. The image intensity will be reduced in regions of the sample where T_1 values are long.

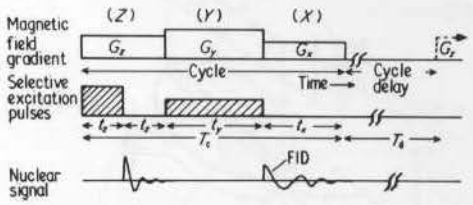

Figure 10: Switching sequence showing applied field gradients, the selective excitation sequence and the nuclear free induction decay (FID) signals following the (Z) and (Y) tailored pulses. Note that only the FID in tx is sampled in these experiments. (From 6, by permission of the authors and publishers. Copyright material of the Institute of Physics, Bristol , England).

Since T_1 is a much more sensitive soft tissue contrast parameter than is pure mobile proton concentration, and since T_1 is important in characterising various disease states, such discrimination in NMR images is extremely valuable. If two or more images are obtained for different interpulse intervals, the contribution of spin (proton) density and T_1 to image intensity can be separated mathematically and displayed as T_1 maps or spin (proton) density maps.

Inversion Recovery:

In the inversion-recovery technique, a 180 degree pulse is first applied to invert the spin system. After a delay time approximately equal to T_1, during which some spin-lattice relaxation will occur, a 90 degree ''read'' pulse is applied. The FID following this second pulse is used to generate the image. This pulse sequence gives an image contrast resolution superior to that obtained by the saturation recovery technique, but the penalty is a longer imaging time (or reduced spatial resolution, since a delay of at least $3T_1$ should be allowed to elapse before repeating the 180 degree 90 degree pulse-pair if errors in T_1 determinations are to be avoided. T_1 maps may also be derived using this technique.

Spin-echo:

The ''Carr-Purcell'' spin echo technique consists of applying a 90 degree RF pulse and after a lapse of time approximately equal to T_2, a series of 180 degree pulses is applied to the sample with an interpulse interval roughly equal to twice the transverse relaxation time (or $2T_2$). Here the resulting images are primarily or solely dependent on the spin-spin relaxation time, T_2.

Steady-State-Free Precession:

In this technique a regularly spaced string of RF pulses is rapidly applied to the sample and results in the generation of images of very high spatial resolution. In SSFP,

Table 1. PULSE SEQUENCES AND CORRESPONDING IMAGE PARAMETERS

PULSE SEQUENCES	PRINCIPAL IMAGE PARAMETERS
1. Repeated Free Induction Decay (RFID)	T_1, Proton Density
or	
Saturation Recovery	
2. Inversion - Recovery (IR)	T_1, Proton Density
3. Spin-Echo (SE)	T_2, Proton Density
4. Steady - State - Free Precession (SFFP)	T_2, Proton Density $\frac{}{T_1}$

T_1 = Longitudinal relaxation time

T_2 = Transverse relaxation time

the pulse interval is much shorter than the relaxation times T_2 and T_1, and the image intensity function is a much more complicated function that precludes straightforward extraction of T_1 or T_2 values for the sample. Image interpretation is therefore, not simple, but nonetheless some very high quality images have been obtained using SSFP.

Discussion

Other investigator such as David Hoult of the Biomedical and Instrumentation Branch of the Division of Research Services of the National Institutes of Health (USA) and Richard Ernst of the Eidgenoessiche Technische Hochuschule in Zurich (Switzerland) have developed their own methods for imaging the NMR signals generated from planes.

NMR imaging is non-invasive and painless and involves no ionizing radiation and hence the tests may be repeated as often as needed. Also imaging time could be long except for imaging heart, lung, etc. It involves no moving parts as scanning and imaging is done electronically whereas in computerized tomography the gantry moves around the patient. Furthermore, transverse, coronal, and sagittal images could be obtained without repositioning the patient or the gantry.

However, there is some concern on NMR's safety. In all NMR methods the patient is subjected to a statis magnetic field and a radio frequency field, and many of them also subject the patient to oscillating magnetic field gradients. There is some hazard to the patient from the currently used static magnetic field and radio frequency levels,[7],[8]. The major concern is that the oscillating magnetic field gradients could induce electric currents in the body which in turn may trigger ventricular fibrillation than can be fatal if not corrected within a few minutes. Many researchers have rejected this possibility based on their own experiences as NMR subjects. Also when Chinese hamster ovary cells in culture were exposed to 24 to 800 times NMR imaging exposures that might be used in a clinical situation, no chromosomal aberrations or genetic damage was detected[9].

Unlike radiographs which are shadow graphs with poor definition for soft tissue regions, the NMR images give precise spatial discrimination rejecting the variation of proton density distribution of free or nearly free water and fatty tissue as the cross-sectional slices through the patient. Bone structures are detectable due to lack of signal, whereas tumors, fatty regions, and other tissues give strong signals because of their free water content. In the NMR color images, usually yellow corresponds to fat, red to muscle or organ tissue, blue to skin and connective tissue, and black lung.

In tissues where the protein density is the same, the tissue can be differentiated using the T_1 and T_2 relaxation times. For example it is very well known that both T_1 and T_2 are longer in cancerous tissue compared with normal tissue. This offers great promise for cancer detection. Unlike computerized tomography (CT) where it takes only # 2 # seconds to scan a cross-section, the NMR scan time per picture varies from 1.5 min. to 15 min. depending on the imaging method used. Although anatomic resolution may be equal to that of C.T., the great advantage of NMR over CT is its ability to produce multiplane (axial transverse, coronal, sagittal) tomograms due to electronic scanning mechanism. Also repeated scans can be performed on the patient without over-dosing.

Promising areas of NMR imaging are blood flow measurement, circulation problem-myocardial ischemia, cerebral ischemia, hepatic ischemia, renal ischemia, cerebral edema, pulmonary edema. More than 50 potential medical uses of NMR scanning are listed by one of the commercial developers.

The human body contains many elements. Because of their low sensitivity compared to hydrogen, it is difficult to apply their NMR signals for imaging purposes. However, by measuring the concentration of elements like ^{31}P, the changes in the chemical status of the cell and abnormalities in basic cellular metabolism can be related to particular disease. Thus ^{31}P NMR sectrometry and imaging have potential applications in the detection of heart attack, stroke, and measuring the size of the infarct and blood vessel disease[10].

^{13}C constitutes only a small fraction of the naturally occurring carbon atoms. Compounds such as glucose labeled with ^{13}C and the ^{13}C NMR signal could be utilized for cellular and tissue metabolism.

Images based on the resonance of ^{19}F nucleus have been published[11]. The abundance of ^{19}F in most biological tissue is negligible. Hence fluorine bearing compounds can be introduced, such as fluoro-carbons as blood substitutes.

Fossel et al[10] utilized ^{23}Na NMR spectra using a high resolution NMR spectrometer and constructed gated planar images at two points in the cardiac cycle. They calculated the ejection fraction of the heart from these images. A sensitive indicator of healthy tissue is its ability to maintain low sodium levels to the blood perfusing it. In case of ischemia and infarction, the myocardium will fail to maintain low sodium levels. Utilizing ^{23}Na images of the heart, one can hope to detect the above conditions with high specificity.

Thus, all of the major biologically active elements except naturally occurring oxygen (oxygen-16 does not have nuclear magnetism) can be analyzed by NMR.

NMR is expected to have a significant impact on CT (computerized tomography), particularly in providing the anatomic detail of the central nervous system. For example smaller plaques of multiple sclerosis were demonstrated by NMR than with CT. In delineating kidney lesions and certain hepatic disease such as cirrhosis, NMR is proving superior to CT.

In conclusion NMR provides information at the cellular level with promise in the physiologic and metabolic areas. NMR imaging is successful and sometimes superior to CT in providing anatomical details due to its advantage of soft tissue contrast.

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