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NUCLEAR MAGNETIC RESONANCE IMAGING

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ABSTRACT — The physical principles involved in nuclear magnetic resonance and the five different methods used in nuclear magnetic resonance imaging are presented.

KEY WORDS — Physical principles, Sensitive point, Selective excitation, Fonar, Fourier imaging.

INTRODUCTION

The goal to image cross sections of human body non-invasively appears to be achievable in the very near future. Nuclear Magnetic Resonance (NMR) Imaging may quite well achieve this goal. The other modalities for medical imaging such as radiography, fluoroscopy, CT (computerized tomography) all use ionizing radiation exposing the patient to varying doses of ionizing radiation which is assumed to result in some risk to the patient. NMR imaging is still under development and preliminary clinical evaluation is being done in a few centers across the world.

Principles of NMR: NMR is not a new technique. NMR has been known over the past 30 years as a well established technique for analytical, structural and dynamic investigation of matter in many disciplines especially in physics and chemistry.[1]

The nuclei of hydrogen atoms are protons. Hydrogen is present abundantly in biological tissue. Protons possess two fundamental physical properties, (i) spin (L) and (ii) a small magnetic movement (μ). Therefore the atomic nuclei of hydrogen behave like tiny spinning magnets. Our earth is also an example of such a magnetic spinning top. When they are placed in a static magnetic field (Fig. 1), the nuclei align themselves parallel to the applied magnetic field. Because they spin, the protons experience a couple like a gyroscope and precess (spin like a top) about the direction of the magnetic field B as indicated in Fig. 2, just as a spinning top precesses about the vertical gravitational field. This precession occurs at a definite frequency proportional to the magnetic field intensity B. This frequency is a resonant frequency, known as the Larmor frequency which can be calculated by the following equation.

$$f = \gamma B \quad \ldots\ldots\ldots\ldots\ldots\ldots (1)$$

where the constant of proportionality γ depends on the gyromagnetic properties of the nuclei. For hydrogen nuclei in a magnetic field B of 1 tesla (10^4 gauss), the frequency f is 42.6 MHz. Therefore the nuclei are capable of absorbing or radiating electromagnetic energy at this particular shortwave radio frequency. They can be made to absorb energy by

Table 1. Elements present in the Body and their NMR Sensitivities*

Elements	Tissue Sensitivity in Decreasing Order
$^{1}_{H}$	1.00
$^{14}_{N}$	3.1×10^{-3}
$^{31}_{P}$	1.4×10^{-3}
$^{23}_{Na}$	1.0×10^{-3}
$^{17}_{O}$	4.9×10^{-4}
$^{13}_{C}$	2.5×10^{-4}
$^{39}_{K}$	1.1×10^{-4}
$^{35}_{Cl}$	8.4×10^{-5}
$^{19}_{F}$	6.3×10^{-5}
$^{2}_{H}$	6.2×10^{-5}

*Modified and adapted from Ref.(19).

irradiating them with a short pulse of resonant radio-frequency. As a result, they can be turned through 90° (this is called a 90° pulse) into a plane perpendicular to B, to give maximum transverse magnetization (Fig. 3). When the irradiating frequency is removed, they relax back to their normal equilibrium state with their magnetic moments along the field. In doing this they each radiate their surplus energy at the resonant frequency (Fig. 4). This emitted or induced radio frequency in a coil, can be amplified, detected and displayed on a video screen. This signal is called a *free inductin decay* (FID). This may last for several seconds. The time constant of this decay is called the *transverse relaxation time or spin-spin relaxation time* T2. In order to get this effect the applied radio frequency pulse has to be nearly the same frequency of the Larmor precession frequency, that is it has to be in resonance. Hence, this phenomenon is known as *Nuclear Magnetic Resonance*. If a Fourier transform of the free induction decay is taken, one gets the NMR spectrum of the hydrogen nuclei. In the conventional NMR system, the applied magnetic field is made very uniform, so that all parts of a sample placed in it have the same resonant frequency. If the sample is pure water, all the hydrogen protons emit a very narrow resonance spectral line, about 0.1 H2 to 5 H2 wide. NMR is thus a sharply resonant property which is especially true for liquids such as water.

If a resonant radio frequency pulse of twice the previous length is applied, then the nuclei can be rotated through 180° (this is called a 180° pulse) is completely inverted, pointing in the opposite direction to B (Fig. 3b). Thus the Nuclei are no longer in equilibrium. Interactions between the hydrogen nuclei and the molecular motions bring about a return to equilibrium. The time constant characterizing this exponential return to equilibrium is called the Spin-lattice relaxation time T1. T1 and T2 are equal for water and are several seconds. T1 and T2 are shorter for cellular water, several tenths of a second. There is experimental evidence that in cancerous tissue the values of T1 and T2 are about twic as long as in the corresponding normal tissue.[2] T1 and T2 depend upon the interaction (binding) of the atoms of molecules with their surroundings, that is, they are substance specific and thus of clinical interest.[3]

Principles of NMR Imaging: The basic components of NMR imaging system are shown in Fig. 5. An individual hydrogen atom gives off a very weak immeasurably small signal. On the other hand, a large collection of nuclei gives a strong signal which can be recorded. In the body the hydrogen atom concentration is about $6X10^{22}$ protons per ml. of water. As a result, the signal is of sufficient strength and permits imaging to be done.

At present there are five different methods available for NMR imaging. Lauterbur has produced two-dimensional NMR images by using the back projection and image reconstruction technique.[4,5] In this method, one dimensional profile of proton concentration with the magnetic field gradient applied at each of a series of equally spaced angles around the sample is obtained. The profiles are then compounded digitally using the well known principle of computer reconstruction tomography used in transmission and emission CT. Standard Reconstruction algorithm are used to form an image of the proton concentration in a transverse plane across the sample.

In all the methods of NMR imaging, an important requirement for the formation of an image is that the signals emitted by the object must be capable of being spatially resolved. To achieve this, the initially uniform magnetic field B, is superimposed in all three spatial dimensions with small gradient magnetic fields, Gx, Gy, Gz as shown in Fig. 6. The arrows of increasing thickness illustrate the linear increase in magnetic field strength. The field gradient is of the order of $10^{-2}Tm^{-1}$ or 1 gauss per cm. A gradient of the magnetic field labels different magnetic field strengths and hence different NMR frequencies (Fig. 7). A magnetic field gradient is essentially a one-dimensional probe of investigation, its orientation must either be moved round progressively , or switched rapidly along three orthogonal directions one after the other, or applied in all threee directions simultaneously but at different frequenceis. This means that the magnetic field strength is no longer identical at any point within the object, but, with the aid of the field gradients, can be selectively modified spatially. According to Equation 1, the precession frequency of the nuclei within the object differ from point to point. Accordingly, the measuring signal obtained presents as a frequency spectrum. If the measuring procedure is repeated a number of times, using different gradient fields, an analysis of all the frequency spectra thus obtained makes it possible to define each volume element of the object in terms of both its spin density and its relaxation time. If a large number of individual measurements is obtained then greater will be the power of resolution.

Sensitive point imaging: In this method three orthogonal field gradients, each modulated at a different non-conjugate low frequency, are applied to the object. The intersection of the three null planes of these three alternating gradients defines a small sensitive volume element whose signal is picked out by filtering and scanned selectively slice by slice through the object, successively, plotting out the NMR image of proton density of the slice. A stack of images of such slices constitutes a 3 dimensional image of the object.[6] This method is accelerated by using the multisensitive point method. In this method the NMR signal from selected regions of the sample is accepted while that from other regions is rejected.[7] In this technique a

time-dependent field gradient applied to the specimen makes the magnetic field in the sample time-dependent everywhere except on one plane which is normal to the direction of the field gradient. Thus NMR signals from that one "sensitive plane" or selected plane can be removed and processed. Similarly if two orthogonal time-dependent gradients are applied, say, in the X and Z directions, a "sensitive line" in the Y direction will result. As mentioned earlier, if three orthogonal time-dependent gradient are applied, this results in a "sensitive point" at the intersection of the three sensitive planes.

Selective excitation or irradiation method: 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 Δz within the sample is considered as shown in Fig. 8 which is part of an extended sample along the Z axis.[8]

The field gradient Gy alone is switched on and the spin within a narrow strip Δy at yo are selectively excited by applying a "tailored" radio frequency pulse to the specimen. The radio frequency components of the tailored pulse interact with spins in a narrow strip (shaded strip in Fig. 9), the linear magnetic field gradient Gy produced this interaction because 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 resonance 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 (Fig. 10). This Fourier transformed signal is directly proportional to the proton spin density at the point x, yo along the X 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.[9]

In summary, in the selective irradiation method the magnetic field gradient is switched rapidly, in time less than T1 and T2 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.

Fourier Imaging: This method for three-dimensional imaging has been developed by Kumar, et al.[10]

The sample is first irradiated with a 90° radio frequency pulse then subjected successively and rapidly to switched magnetic field gradients applied consecutively along the X, Y and Z directions for successively increasing time tx, ty, and tz (Fig. 11). Only the free precession signal which evolved in the period tz is sampled after each radio frequency pulse and stored in a computer for performing a three dimensional Fourier transform. It may be shown that a cross-sectional proton density image of the object is the three dimensional Fourier transform of the recorded Free Induction Decays (FID).

Focusing Nuclear Magnetic Resonance (FONAR) Imaging: This method originally conceived by Damadian[11] consists of focusing the nuclear magnetic resonance (NMR) signal within the interior of the live subject for data acquisition. The NMR signal of each anatomic region can be continuously monitored during date acquisition phase of the FONAR imaging process.

FONAR method depends on the shape of the magnetic field produced by the magnet that is used to focus on a given point within the live subject. This field is shaped somewhat like a saddle with the magnetic field strength varying with distance along its sloping surfaces. The exciting radio frequency is chosen so that it corresponds to the field strength at the small resonant window in the field center within the sample. The size of this resonance aperture varies from 1 to 3 mm and is approximately spherical.[12] Only this point will give a NMR signal because nuclei outside the focused point will be resonating at the wrong frequencies or because the field strength is sharply varying a signal cannot be produced. By moving this resonant window in ordered fashion through the live subject to be examined and determining the signal at each location as it is swept through a cross section of the subject, an image can be constructed.[13]

RESULTS

Cross sectional NMR images of the head of a normal patient are shown in Figure 12. Cross sectional NRM images of thorax of a normal patient are compared with a CT Scan in Figures 13-16.

DISCUSSION:

Other investigators 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.[13]

NMR imaging is non-invasive and painless and involved 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 NRM methods the patient is subjected to a static 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.[14,15] The major concern is that the oscillating magnetic field gradients could induce electric currents in the body which in turn may trigger ventricular fibrillation that can be fatal if not corrected within a few minutes.[13] Many researchers have rejected this possibility based on their own experiences as NMR imaging 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.[16]

Unlike radiographs which are shadow graph 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 to lung.[17]

In tissues where the proton density is the same, the tissue can be differentiated using the T1 and T2 relaxation times. For example it is very well known that both T1 and T2 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 2 hours 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.[18]

The human body contains many elements some of which are listed in Table I along with their NMR sensitivities. 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 diseases.[20] Thus ^{31}p NMR spectrometry and imaging have potential applications in the detection of heart attack, stroke, and measuring the size of the infarct and blood vessel disease.[21]

^{13}C constitutes only a small fraction of the naturally occurring carbon atoms. Compounds such as glucose labeled with 13C and the 13C NMR signal could be utilized for cellular and tissue metabolism.[22]

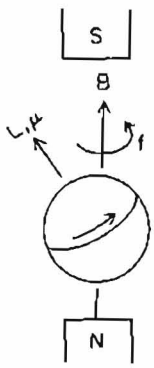

Figure 1

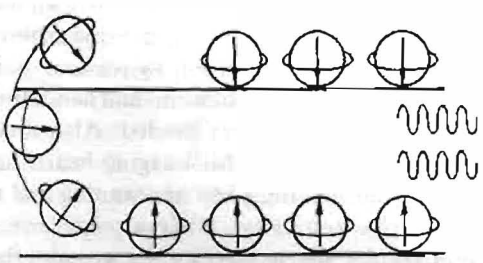

Figure 3(A)

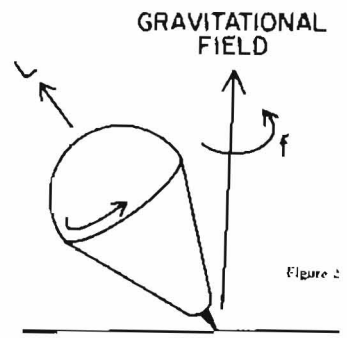

Figure 2

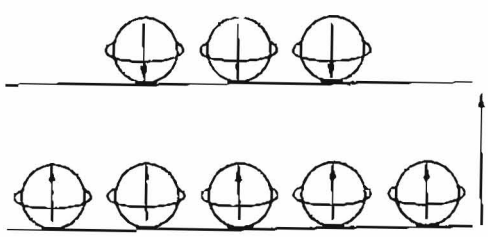

Figure 3B

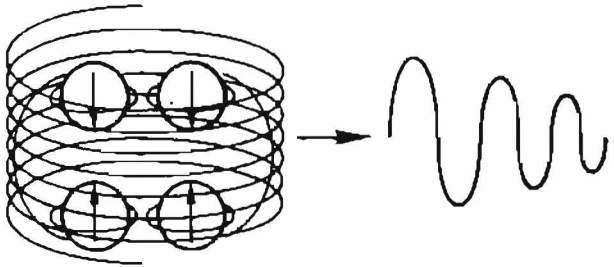

Figure 4

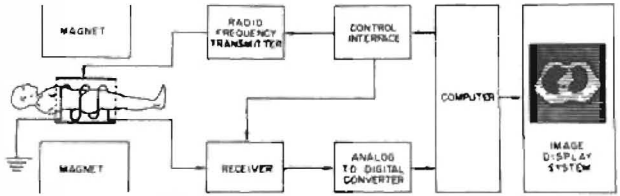

Figure 5 Components of an NMR imaging system

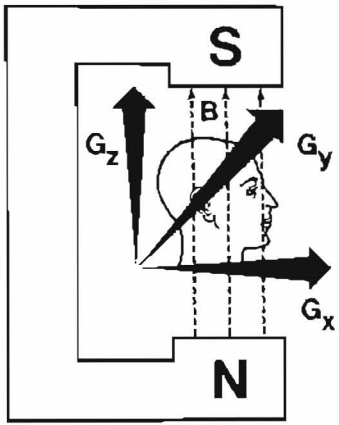

Figure 6

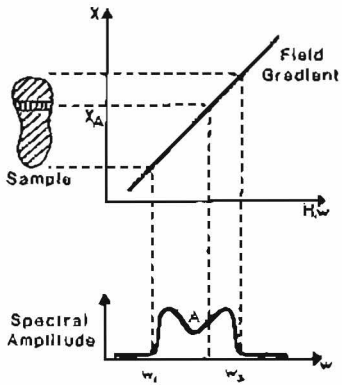

Figure 7

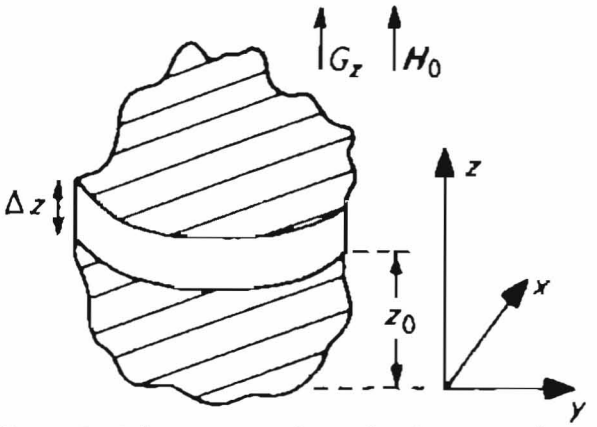

Figure 8 Initial preparation of a layer or slice of undisturbed spins. The shaded portion of the specimen corresponds to regions where the spin magnetization is saturated.

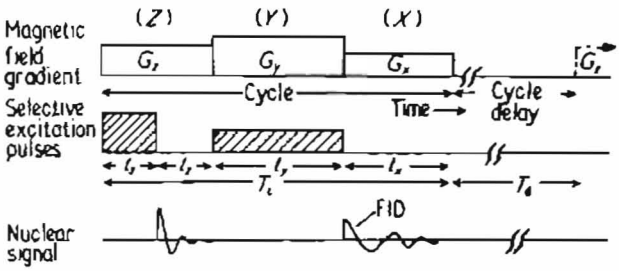

Figure 10 Switching sequence showing applied field gradients, the selective excitation sequence and the nuclear free induction decay (FID) signals following the (*Z*) and (*Y*) tailored pulses. Note that only the FID in *tx* is sampled in these experiments.

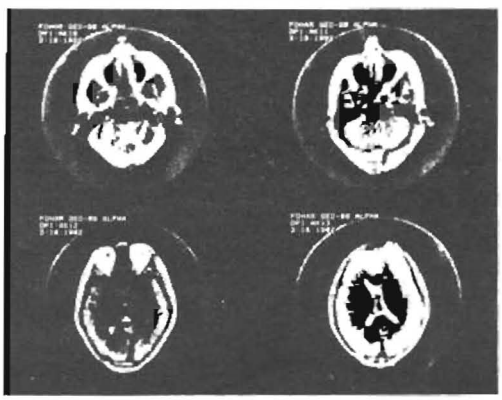

Figure 12

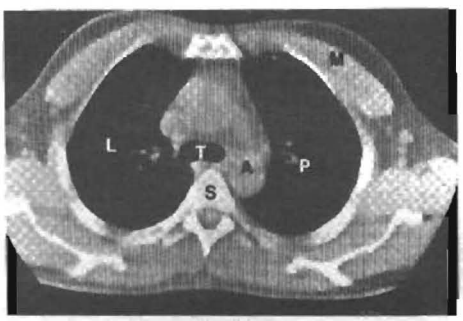

Figure 14

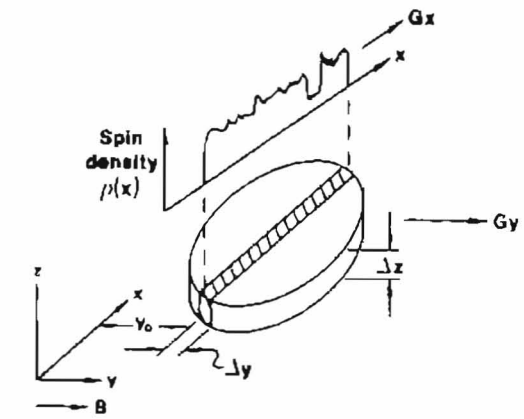

Figure 9 Sketch illustrating the principle of line scanning by selectively irradiating a narrow strip within an isolated slice of magnetization.

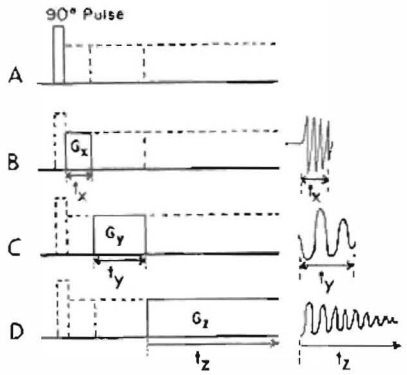

Figure 11

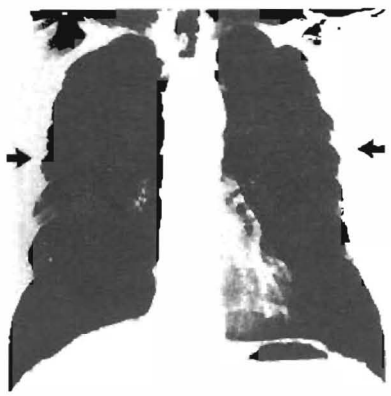

Figure 13

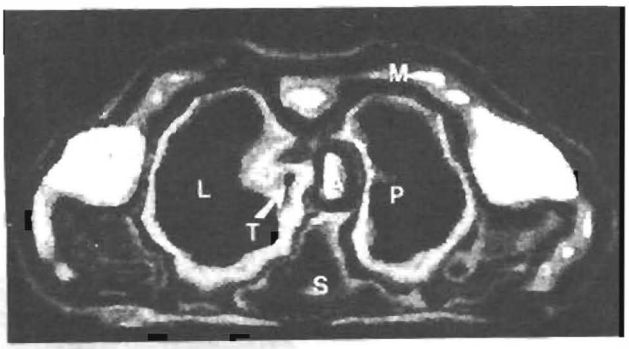

Figure 15

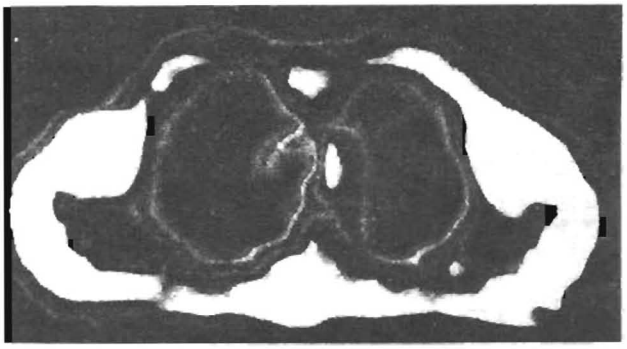

Figure 16

Images based on the resonance of 19F nucleus have been published.[23] The abundance of 19F in most biological tissue is negligible. Hence fluorine bearing compounds can be introduced, such as fluorocarbons as blood substitutes.[7]

Fossel[21] et al utilized 23Na 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.[12]

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 diseases such as cirrhosis, NMR is proving superior to CT.[24]

In conclusion NRM 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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LEGEND TO THE FIGURES

Figure 1: The precession of a spinning nucleus (such as a proton) in an applied magnetic field of strength B. (modified and adapted from Mallard, J. et al, *Journal of Biomedical Engineering*, 1979, *1*, 153-160, by permission of the publishers, IPC Business Press Ltd. ©).

Figure 2: The precession of the nucleus in a magnetic field is similar to the precession of a spinning top in a gravitational field. (modified and adapted from Mallard, J. et al, *Journal of Biomedical Engineering*, 1979, *1*, 153-160, by permission of the publishers, IPC Business press, Ltd. ©).

Figure 3: Atomic nuclei in a magnetic field absorb energy when they are irradiated with a short pulse of resonant radio-frequency. (Reproduced with permission of the Fonar Corp., Plainview, N.Y.).

Figure 3B: When a 180° resonant radio frequency is applied, the nuclei are completely inverted, pointing in the opposite direction to the applied magnetic field B. (Reproduced with permission of the Fonar Corp., Plainview, N.Y.).

Figure 4: When the irradiating frequency is removed, the nuclei relax back to their normal equilibrium state and in doing this they each radiate their surplus energy at the resonant frequency. This emitted signal or induced frequency in a coil is called free induction decay (FID). (Reproduced with permission of Fonar Corp., Plainview, N.Y.).

Figure 5: Components of an NMR imaging system (Reproduced from Partain, C.L. et al, *Radiology, 136*, 767-770, 1980 by permission of authors and publishers of *Radiology*).

Figure 6: The uniform magnetic field B, is superimposed in all three spatial dimensions with small gradient magnetic fields Gx, Gy and Gz. (Modified and adapted from Zeitler, E. and Schiltenhelm, *Electromedica*, *49*, 2-11, 1981).

Figure 7: A gradient of the magnetic field labels different magnetic field strengths and hence different NMR frequencies related to proton concentration spatial distribution. (Reproduced from Mallard, J. et al, *Journal of Biomedical Engineering*, 1979, *1*, 153-160, by permission of the publishers, IPC Business Press, Ltd. ©

Figure 8: See Figure 8 Captions.
(Reproduced from Mansfield, P. et al, *Journal of Physics E: Scientific Instruments*, *9*: 271-278, 1976, by permission of the authors and publishers. Copyright material of the Institute of Physics, Bristol, England).

Figure 9: See Figure 9 Captions.
(Reproduced from Mansfield, P and Maudsley, A.A. *British Journal of Radiology*, *50*, pp. 188-194, 1977, by permission of the authors and the editor of the *British Journal of Radiology*)

Figure 10: See Figure 10 Captions.
(Reproduced from Mansfield, P. et al, *Journal of Physics E: Scientific Instruments*, *9*: 271-278, 1976, by permission of the authors and publishers. Copyright material of the Institute of Physics, Bristol, England).

Figure 11: Principle of Fourier imaging is illustrated here.

A. Sample is first irradiated with a 90° radio frequency pulse.
B. Sample is subjected to switched magnetic field gradient applied along the X direction for time t_x.
C. Sample is subjected to switched magnetic field gradient applied along the Y direction for time t_y.
D. Sample is subjected to switched magnetic field gradient applied along the Z direction for time t_z

modified and adapted from Kumar, A. Welti, D., and Ernst, R.R., 1975, *Journal of Magnetic* Resonance, 18, 69-83.

Figure 12: Top left shows NMR transverse scan of the head through the atlas and dens.
Top right shows NMR transverse scan of the head 1 cm. above the previous cut- and 1.5 below the orbit; the scan is through the Reid's base line.
Bottom left shows NMR transverse scan through the orbit and basal skull region.
Bottom right shows NMR transverse scan through the mid-brain. (Reproduced with permission of the Fonar Corporation, Plainview, N.Y.).

Figure 13: Chest radiograph. The arrows show the transverse scanning levels for CT and NMR. (Reproduced from Partain, C.L., et al. *Radiology, 136*, 767-770, 1980, by permission of the authors and publishers of *Radiology*).

Figure 14. CT Scan. L = lung, T = trachea, S = spine, A = aorta, P = pulmonary artery, M = thoracic muscle. (Reproduced from Partain, C.L., et al, *Radiology, 136*, 767-770, 1980, by permission of the authors and publishers of *Radiology*).

Figure 15: NMR Scan obtained using a 256 x 256 image matrix. The anatomical labels are same as shown in Figure 14. (Reproduced from Partain, C.L., et al, *Radiology, 136*, 767-770, 1980, by permission of the authors and publishers of *Radiology*).

Figure 16: NMR Scan. Same image as in Figure 15, but obtained using a 512 x 512 image matrix. Computer smoothing was provided by linear interpolation between data points in the 256 x 256 matrix array. (Reproduced from Partain, C.L., et al, *Radiology, 136*, 767-770, 1980, by permission of the authors and publishers of *Radiology*).

Sayings of the Prophet (p.b.u.h.)

From the report of Anas:

"He who goes out in search of knowledge is in God's path till he returns." — Tirmidhi and Darimi