

Image Analysis Using Nuclear Magnetic Resonance with 9.4 Tesla of Static Magnet Field

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Abstract: Magnetic resonance image (MRI) is characteristic of a fine spatial resolution compared with Computer tomography and Ultrasonic tomography. The intensity of the external static magnet field of MRI is important factor on the spatial resolution. The tomogram depend on the conditions of measurements and intensity of the external static magnetic field. Further more, difference of measurement conditions depends on tissues. We show measurement conditions of chest and abdomen and the principle of MRI.

Key words: Image analysis, Mouse, Nuclear magnetic resonance, High magnet field

INTRODUCTION

We had previously reported investigations on the activities of transplanted human eccrine glands using various methodologies (Shimazu et al, 1996, Kosaka and Shimazu, 1997). From the view point of usage, NMR is divided into two functions; Magnetic Resonance Spectroscopy (MRS) and Magnetic Resonance Imaging (MRI) (Partain et al, 1983; Toung, 1984; Cohen, 1986; Kean & Smith, 1986; Sigal, 1988; Stark & Bradley, 1988). The establishment of Nuclear Magnetic Resonance facility for use in bioscience research at the Institute of Tropical Medicine was sponsored by the Japanese Government in 1996. Since then, we had used the facility to apply MRI to the investigations of activities of human eccrine gland tissue transplanted on heterologous nude-SCCIDE mouse. Even though there has not been substantial progress in terms of data acquisition, significant progress has been made in fully understanding the application of MRI in biomedical research. In this paper we discussed the various possibilities by which the principle of NMR can be applied to biomedical research.

METHODS

I. The principle of initiation of NMR signals

1. Magnetic characteristic of proton

An atom is composed of atomic nucleus and electrons, and the atomic nucleus of pro-

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tons and neutrons. The electron is negatively charged, where as the proton is positively charged. Electrical current is induced by the movement of free electrons. This charge transfer induces a magnetic field. The proton also produces a magnetic field by spinning with its positive charge. Therefore, a proton has characteristic similar to a micro magnet.

Seventy percent of biological tissue is composed of water. Therefore, on the basis of hydrogenic proton contained in water, biological image analysis is possible by the fine magnetism created by hydrogenic proton through MRI.

2. External static magnetic field

The direction of proton changes in random in two directions in the static external magnetic field. The direction of protons having low energy level is in parallel to the polarity of static external magnetic field. The direction of protons having high energy level is in the reverse. The number of protons having low energy level is higher than those having high energy level, but the difference is very small. Signal initiation depends on the difference in proton numbers moving in parallel and reverse direction because magnetization of proton is impressed by proton in other direction.

One way to initiate strong external magnetic field is to use super conduction magnets. These super conduction magnets are non-electric resistant at -269°C , so that electric current continually flows in them for ever. Further, the super conducting temperature of -269°C is always kept constant by cryogen which is supplied by liquid Helium and Nitrogen. If the temperature of super conduction magnet rises above the super conducting temperature due to decrease of cryogen, electric resistance occurs, and the super conducting magnet is rapidly destroyed by heat initiation.

3. Movement of proton in external static magnetic field

Proton in external magnetic field exerts itself by precession in addition to spin (Fig. 1). The frequency of the precession depends on the strength of the external magnetic field, and it is calculated by Larmor equation as follows:

Larmor equation

$$\omega_0 = \gamma B_0$$

where ω_0 : Frequency of precession

γ : Gyromagnetic ratio, Characteristics value of element

(Hydrogen Proton: $\gamma = 42.567 \text{ MHz/T}$)

B_0 : Unit of strength of External Magnetic field

G (Gauss), T (Tesla)

1 T = 10,000 G

B_0 of the MRI (NMR) used our experiments: 9.4 T

Therefore, frequency of precession of the hydrogen proton during MRI used in our experiments were calculated thus:

$$\omega_0 = \gamma B_0 = 42.567 \times 9.4 = 400.1298 \approx 400.13 \text{ MHz}$$

Fig. 2 shows the direction and polarity of protons, and a longitudinal magnetization induced by magnetization of protons as a vector. The X and Y component of magnetization induced by proton in precession is probably counterbalanced, therefore, only longitudinal magnetization is demonstrated in the figure.

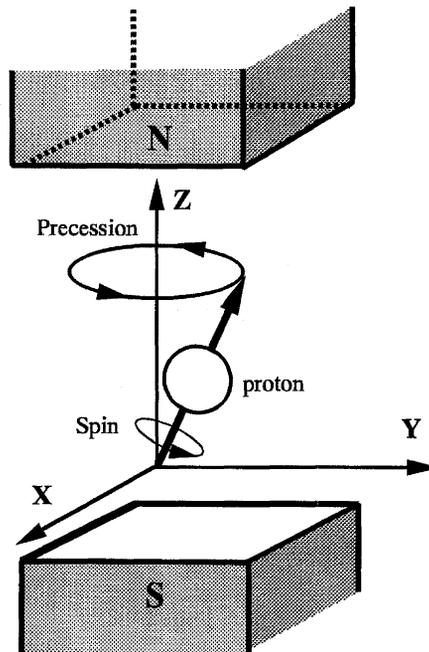


Fig. 1. Precession of a proton in static magnetic field

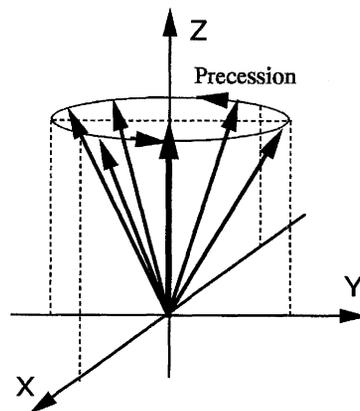


Fig. 2. Longitudinal magnetization

Thin arrows represent protons and the thick arrow represent longitudinal magnetization by protons.

4. Nuclear magnetic resonance phenomenon

Precessing proton is supplied with energy on application of electromagnetic wave for short time. However, it is possible for proton to take up energy by resonance phenomenon through the same frequency of precession of the proton. The 400.13 MHz of Radio frequency pulse (RF pulse) is effective for hydrogen proton at 9.4 T in the NMR used in our analysis. Therefore, the measurement device applied using nuclear magnetic resonance phenomenon is so-called NMR. There are two types of RF pulse used for measurement; one is 90° pulse and the other is 180° pulse. The effect of 90° pulse is that certain number of protons move toward reverse direction to external magnetic field because their energy level increase as result of absorption of energy from electromagnetic wave of RF pulse. On the other hand, 180° pulse is useful to synchronize phase of each protons. The effects of two RF pulses decrease the longitudinal magnetization and induce a high intensity transverse magnetization (Fig. 3). After cessation of RF pulse application, protons in the reverse direction recover to a stable and parallel direction as before the application. During this process, transverse magnetization decreases and longitudinal magnetization increases. The composition vectors of longitudinal and transverse magnetizations traces spiral and return to Z axis with only longitudinal magnetization (Fig 4). Micro electric current induced in the measurement coil by change of magnetism in recovering protons is attributed to signal of NMR. This phenomenon is well known in Faraday's law of electromagnetic induction.

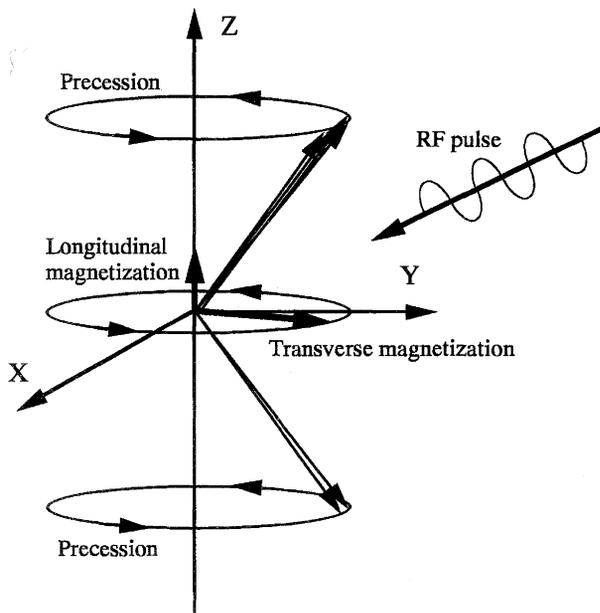


Fig. 3. Nuclear magnetic resonance

A creation of transverse magnetization due to irradiations of radio frequency pulse (RF pulse).

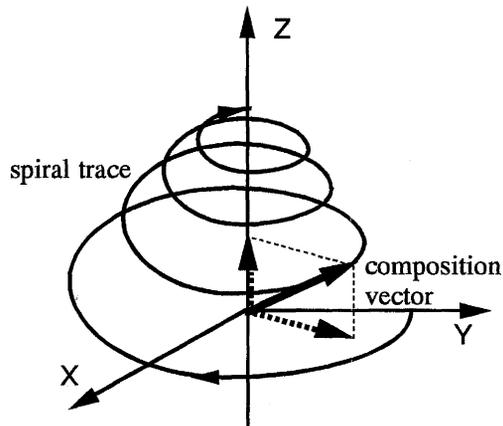


Fig. 4. A spiral trace of composition vector of transverse magnetization and longitudinal magnetization in recovery after stop the RF pulse

II. Principle of image analysis in MRI.

For image analysis, the position of proton initiating NMR signal must be determined. The location determination is achieved by gradient magnetic field. It is in addition to static magnetic field by gradient coil. There is a linear relationship between intensity of the magnetic field and the distance of reference point (Horowitz, 1989). Only the protons whose frequency of precession is the same as that of the RF pulse are excited, resulting to resonance signal. The frequency depends on the intensity of magnetic field as shown in Larmor equation. Therefore, the distance of reference point is determined from the intensity of magnetic field. The frequency is called resonance frequency.

To determine coordinates on X, Y and Z axis, three kinds of gradient magnetic fields are applied as follows (Friedmann et al, 1989; Schild, 1990),

- (1) Slice selecting gradient: determination coordinate of slice cross section on Z axis.
- (2) Frequency encoding gradient: to measure coordinate of signal spring point on X axis in the slice cross section.
- (3) Phase encoding gradient: to measure coordinate of signal spring point on Y axis in the slice cross section.

III. Specification and characteristic of established NMR facility.

NMR facility in this Institute is DWX400WB produced by BURUKER K.K. in Germany.

- (1) Super conduction magnet: 9.4 T < Intensity of static magnetic field
89 mm < Bohr diameter
- (2) Spatial resolution: Maximum spatial resolution > 5 μm
- (3) Gradient magnetic field: 25 mm diameter material > 90 G/cm
35 mm diameter material > 29 G/cm

- (4) Function of figure composition: New function of echo-planner figure and high speed gradient echo-figure
- (5) NMR spectrum: For solution measurement, 10mm in diameter polynuclear (^{109}Ag - ^{31}P) probe available for high analytical power spectrum.
- (6) Magnetic resonant spectrometer: Two channels band of proton resonance frequency (400 MHz) and polynuclear resonance frequency (6~243 MHz) and linear amplifier of 80W and 300W, respectively. Receiver has 451 MHz intermediate frequency, digital filter, and A/D converter wider than 16 bit/200 KHz spectrum.
- (7) Micro-imaging: Active shield intermediate imaging probe of maximum 25mm diameter and available for change 100°C . Multiple material usage of RF insert with minimum of 2mm in diameter RF insert is available.
- (8) Mini-imaging: For inner diameter 38mm material RF birdcage type resonator and material supporting apparatus are available. In figure 5, Block Diagram is demonstrated.

Various measurement methods with NMR

1. Spin Echo single slice Hard/Soft (spin Echo method): the most easy to standardize and co-ordinate.
2. Gradient Echo single slice (gradient Echo method): usage for only gradient pulse short measurement time.
3. Spin Echo Multi slice (sems method): several possibilities. Possibly taking images at several different points.
4. Multi Echo Soft/Hard (mesh method): possibly taking images at several different times.
5. Multi Echo Multi slice (sems method): possibly taking images at several different places and times.
6. Chemical shift selective excitation (csse method): preparation of chemical shift image.

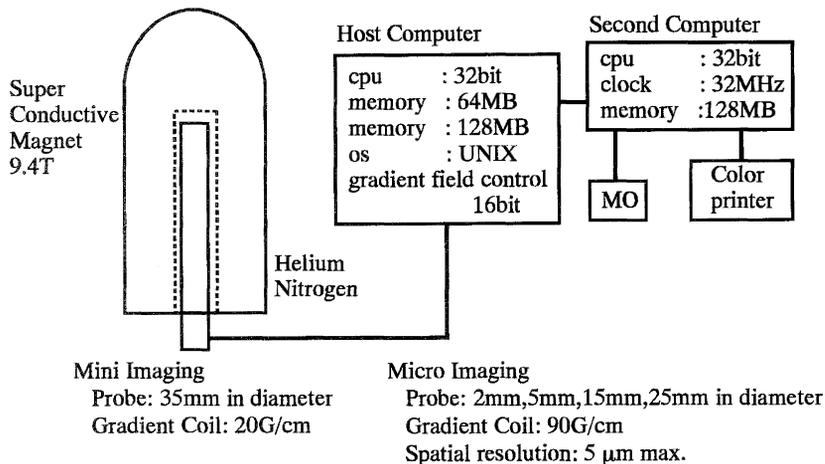


Fig. 5. Block diagram of the Nuclear magnetic resonance system device.

7. Chemical shift selective spin Echo single slice (sesscs method): possibly taking image of only chemical shift.
8. Spin Echo 3D (se3D method): stereo-structural method of spin Echo
9. Gradient Echo 3D (ge3D method): 3D structure of Gradient Echo method.
10. Chemical shift 3D (cs3D method): measurement from MRI.

Important parameters of using MRI

1. TR: Time to Repeat
Interval time to induce transverse magnetization.
2. TE: Time to Echo
Time from 90° pulse to measurement of MRI signal.
3. T_1 : Longitudinal relaxation time
This is the time that longitudinal magnetization recovers by 63%.
4. T_2 : Transverse relaxation time
This is the time that transverse magnetization decreases by 37%.

RESULTS

Figs. 6 and 7 show measurements of chest and abdomen of the mouse using MRI and variant organs are demonstrated in Fig. 8

The conditions of measurements in Figs. 6 and Fig. 7 are as follows;

In Fig. 6

Scan Name: msme, Matrix Dimension: 256
TR: 506 ms, TE: 11 ms, Number of Average: 6
Field of View: 5cm, Slice Thickness: 1mm

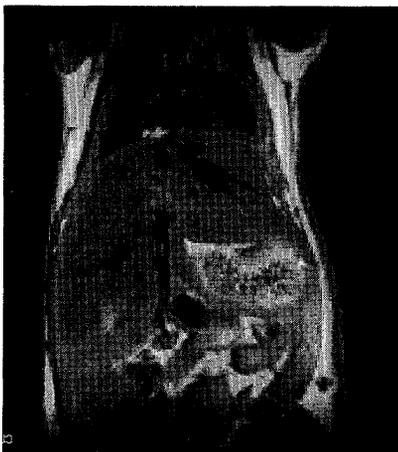


Fig. 6. Chest and abdomen of mouse using MRI on T_1 emphasis.



Fig. 7. Chest and abdomen of mouse using MRI on T_2 emphasis. At the same place as in Fig. 6

In Fig. 7

Scan Name: msme, Matrix Dimension: 256

TR: 2172 ms, TE: 44 ms, Number of Average: 6

Field of View: 5cm, Slice Thickness: 1mm

The figures show differentiations of organs and tissues on the basis of magnetic environment of proton. How do these differences shown occur in different tissues such as the liver and fat? When gradient magnetic field is macroscopically the same at a given point, an equivalent voltage must be induced by hydrogen proton. Therefore it is presumed that the differentiation of tissues mentioned above is the resultant effect. However, hydrogen atom environment is modified and deformed by effects of molecular structure, secreted substances, ion actions that result to fine changes in magnetic field. This makes the differentiations of different tissues and organs possible.

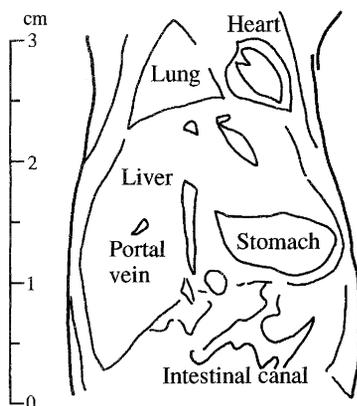


Fig. 8. Schematic illustration of the Photographs in Figs. 6 and 7.

DISCUSSION

On the value of T_1 , T_2 in transverse picture of abdomen in mouse, T_1 value in every one pixel along X axis was compared in several organs and tissues. For example, in the liver there is a wide variation which ranged between 1.09 to 20.0 ms. Mean value was 3.82 ms. The values in Fat were concentrated in a narrow range, 1.02~1.26 ms. This might be attributed to the composition differentiations of tissues in liver and fat. As to the experimental results obtained using T_1 emphasis and T_2 emphasis regarding the abdomen of mouse, there were scarcely any difference in the tissues between Figs. 6 and 7 except for intensity of signals. It is a typical occurrence between T_1 and T_2 emphasis that an image of tissues is reversed. However, it is impossible to reverse on every tissue, because difference between T_1 and T_2 values of tissues are a little. Therefore we should try to reverse only the target tissue clearly. Furthermore, a sample size also changes the condition of measurement (Lufkin, 1990), so further experiment needs to be done to determine the difference between mouse and human.

On a scale of Matrix: In order to record the precise image, the scale of Matrix should be larger and maximums of the scale of Matrix in the NMR we used was restricted to 512. If it is possible to double the value to 1024, four times of both memory and CPU clock are necessarily, however, CPU clock in our NMR is 132 MHz, therefore, 518 MHz (132 x 4) is enough and therefore used in our NMR. When 1024 scale of Matrix is used, more precise figure will be recorded in near future.

Number of Average and Gaseous anesthesia: In order to record a precise image, number of average should be larger. Here, maximum number is 6. In Nembutal anesthesia applied to the mouse, one hour anesthesia is maintained. However, differences occur and ranges can vary between one to three hours. For 3 D figure (three dimension figure), long time is required, therefore, a trial of gaseous anesthesia is necessary. However, there is difficulty in control of breathing as well as the difficulty to decide gasory and oxygen concentrations and their flow rates (Runge, 1989).

Chemical shift: The principle of image formation by proton magnetic field of hydrogen atom of water must be the objective in consideration. However, there are electrons around an atomic nucleus. Therefore, images must be affected by magnetic field induced by the movement of electrons. Whether there is an increase or decrease of magnetic field around proton due to electro magnetic field depends on the direction of proton, and the difference between numbers of parallel and reversed protons, which is known as "chemical shift". However, the location of the "chemical shift" is still experimentally not clear, therefore we shall try to determine that in future.

Regarding the present and future prospects for the usage of the NMR (particularly MRI) in the Institute of Tropical Medicine, Nagasaki University, this facility has been made available for cooperative research in various fields such as, Neuroscience, Environmental Physiology, Anatomy, Pathology, Pharmacology, Immunology, Dermatology, Anesthesiology, Plastic-orthoped-Transplant Surgery, Internal Medicine and so on. However, in the present, we are exploring all the possible functions of NMR (particularly MRI). We shall undoubtedly use this facility to improve on previous methodologies (Shimazu et al, 1996, Kosaka and Shimazu, 1997). This Strategic improvement will lead to well established and widened use of Magnetic Resonance Spectroscopy.

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