Radiology of Magnetic Resonance Spectroscopy

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Abstract

The fundamental principles of MRS, one of the most powerful analytical tools in seience, is introduced as the promising methodology in the diagnostic radiology of medical science. A variety of applications of MRS indicates the possibility of more accurate and sensitive diagnosis in medicine. The combination of anatomical informations by MRI and biochemical informations by MRS provides the bright prospect in the diagnostic radiology.

Introduction

The first, pioneering Nobel-prize-wining nuclear magnetic resonance (NMR) experiments on atomic nuclei in liquids and solids were carried out in the 1940s by Purcell, Torey, and Pound[1] at Harvard University and by Bloch, Hansen, and Packard[2] at Stanford University. In 1950 Proctor[3] made the critical observation that the specific resonance frequency of a nucleus depended upon the nature of its chemical and magnetical environment. leaidng to the definition of this phenomenon as the chemical shift. Over the last decade, MNR spectroscopy has been evolved into one of the most valuable methods for investigation of the individual atomic nucleus and analysis of the various solution-state compounds, and extensively applied for a wide variety of applications including such areas as chemistry, biochemistry, physics, pharmacology, biomedical engineering and more recently for medicine, particulary diagnostic radiology. In medical field, NMR spectrosocpy is just called MR spectroscopy (MRS) since the word of "nuclear" itself made an undesirable impression on the general patients.

MRS is an analytical method that has been successfully employed in model systems to identify and quantitate the levels of biochemical compounds, and to investigate the metabolism and biochemistry of a variety of diseases and disorders. The development of MRS preceded the development of magnetic

resonance imaging (MRI) by several decades. However, MRS was recently applied in the medical area because of many sophisticated technical barriers like surface coils and localization problems.

As MRS employs much of the same instrumental components like MRI (i.e., magnet, radiofrequency pulse generator, gradient systems), it provides a rapid, quantitative, nondestructive, potentially risk-free method for the biochemical informations that can complement the results of MRI examinations in diagnostic radiology.

Background

The theoretical descriptions for MR phenomenon could be understood on the basis of the quantum mechanics and classical mechanics in physics. The three essential components of MR phenomenon consist of the external magnetic field, magnetic moment, and radiofrequency (RF) pulse. Many atomic nuclei possess angular momentum or spin, that causes them to behave like a spinning top or a gyroscope. As the spinning nucleus also possesses an electronic charge, a magnetic field is produced pointing vector along the rotating axis of the nucleus. This magnetic behavior is characterized by the magnetic moment, μ, which can have only a few specific values determined by the allowed values of angular momentum, as

$$\mu = \gamma \, (h/2\pi) \, (I(I+1))^{1/2}$$

where γ is called the gyromagnetic ratio, h is Planck constant, and I is called the spin quantum number. The summation of magnetic moment of each nuclei is defined as the net magnetization, M.

For many spin 1/2 nuclei such as ^1H and ^{21}P, the spins exist in the only two quantized energy states, with magnetic quantum number +1/2 or -1/2. The ratio between the spin populations of two energy levels is given by the Boltzmann distribution, $\exp(-\mu B/kT)$. The relative spin population difference will increase with magnetic field strength B, and decrease at higher temperature, T. k is defined as the Boltzmann constant.

For a change in the energy state of a spin to occur, the energy difference between the previous and the new energy level must be absorbed or released by the radiofrequency pulse. This event called quantum jump is stimulated by an oscillating magnetic field. The quantum jump can only occur when the energy of the applied oscillating magnetic field is exactly equal to the energy difference. This phenomenon is called magnetic resonance. The energy of radiation is given

by $E = h\nu$ where ν is the frequency, known as the resonance or Larmor frequency. The Larmor frequency is proportional to the external magnetic field and defined by

$$\nu = \gamma B_o / 2\pi.$$

Table I lists some of the more frequently used nuclear spin properties with their gyromagnetic ratios which also correspond to their resonance frequencies at a field of 1.5 Tesla. The description of the spin behavior in MRS is most easily visualized by the vector diagram, with regard to the net magnetization. When a RF pulse, a second magnetic field B_1 is applied along a direction perpendicular B_o oscillating at the same rate as the Larmor frequency, this B_1 field will apply torque on the nuclei causing them to rotate in a plane perpendicular B_1 with the rate of rotation in this plane depending on the strength of the B_1 field and the spin gyromagnetic ratio. The angle of rotation θ, is determined by the length of time that the B_1 field is applied, τ_p, as

$$\theta = \gamma B_1 \tau_p.$$

Table I. Some nuclear spin properties for clinical studies

Nucleus	Spin	Natural abundance (%)	Gyromagnetic ratio ($rad.T^{-1}s^{-1}$)	Relative sensitivity[a]	MR frequency at 1.5T (Hz)
^{1}H	1/2	99.98	26.75	1.0	63.89
^{13}C	1/2	1.18	6.73	2.5×10^{-4}	16.06
^{15}N	1/2	0.37	-2.71	1.0×10^{-3}	6.47
^{17}O	5/2	0.04	-3.63	2.9×10^{-2}	8.66
^{19}F	1/2	100.00	25.18	0.85	60.08
^{23}Na	3/2	100.00	7.08	0.13	16.89
^{31}P	1/2	100.00	10.84	8.3×10^{-2}	25.85

Theoretical analysis of the behavior of the spinning atomic nucleus in a magnetic field led to the development of the Bloch equations, which form a classical basis for a description of the phenomenon[4-6]. The followings are the rotating frame Bloch equations

$$dM_x / dt = -M_x / T_2$$
$$dM_y / dt = -M_y / T_2$$
$$dM_z / dt = -(M_z - M_o) / T_1$$

where T_1 is referred as the spin-lattice or longitudinal relaxation time, T_2 is referred as the spin-spin or transverse relaxation time, and M_o is the thermal equilibrium value of the net magnetization. The behavior of the net magnetization observed on resonance is called the free induction decay(FID) that is the signal variation with time. The Fourier transform (FT) of FID produces the MR spectrum with frequency domain. The characteristic MR parameters defined by the MR spectrum are the chemical shift (ppm), area and line width. The relaxation mechanisms are followed a RF pulse.

Practical Application

The recent development of spatial localization methods that sample the relative levels of mobile metabolites from a volume of interest defined from an MR image, has provided the valuable biochemical data base for integrating the anatomical and pathological informations obtained from MRI. This combination of metabolic and anatomic informations offers a new means for understanding the origins and the time course of progression in a variety of diseases. Table I shows the models used *in vitro* and *in vivo* MRS studies of medical science. Although any nucleus possessed a nuclear spin can give rise to an MRS absorption signal, the initial chemical and biological MRS studies focused on proton spectra exclusively.

Table II. Models used in *in vitro* and *in vivo* MRS studies of medical science.

in vitro MRS	solution:body fluids(blood plasma, urine,amniotic fluid, ascites fluid,etc.),extracts cell:cultured cells,red blood cells, isolated myocytes and hepatocytes tissue:cultured tissue,muscle and heart tissue
in vivo MRS	intact animals:brain,heart,liver,muscle,kidney humans:brain,liver,muscle,kidney,bone

Protons were initially selected because of the highest natural abundance, the high relative receptivity in the biological systems, and the determination of the three-dimensional macromolecular structures on the basis of nuclesar Overhauser effect. In most of ^1H MRS studies, MRS was used to investigate the aspects of cellular processes in isolation or the influences of different processes in isolation on the resonance of water in intact cells. In 1959, Odeblad reported on ^1H MRS studies of the chemical shift and relaxation times of water in human vaginal epithelial cells[7]. However, *in vivo* proton MRS confronted many problems because of the large number of metabolites producing many overlapping peaks and the very complex spectra. Coupling effect between the spins of particular protons

causes resonances to occur as doublets, triplets, or more complicated multiplets. In the past the application MRS to the study of living tissue has been disturbed by the technical problems posed by the presence of 110 molar concentration of the water signal. The relative size of this signal can now be reduced substantially by a variety of water suppression pulse sequences, such as PRESS (Point RESolved Spectroscopy) and STEAM (STimulated Echo Acquisition Method)pulse sequences[8]. A large number of proton-containing metabolites can be detected when these methods are employed.

Figure 1 shows the T1-weighted axial MR image of a normal volunteer defining the VOI (Volume Of Interest) selected for localized proton MR spectroscopy using the ^{1}H bird cage head coil. The size of VOI is $2 \times 2 \times 2\,cm^3$ corresponding to a volume of 8 ml. A typical water-suppressed proton MR spectrum obtained from the brain of a normal volunteer is shown in Figure 2. MRI/MRS were performed at GE 1.5T Signa Advantage MR instrument. Resonance assignments were made to major metabolites such as N-acetyl aspartate (NAA), creatine (Cr) and choline-containing compounds (Cho) in Figure 2. Resonance frequencies are referenced to the strong singlet methyl group from NAA at 2.0 ppm. The ^{1}H spectra from most tumors are very different from those in normal brain[9]. The specific features of most brain tumor spectra show a decrease of the NAA signal and an increase of the Cho signal relative to normal brain spectra. Other spectral abnormalities have been reported in various types of brain neoplasms[10-13].

Phosphorus-31 is a very useful nucleus for biological investigations, because it is present as 100% of the naturally occurring phosphorus and is found in only a
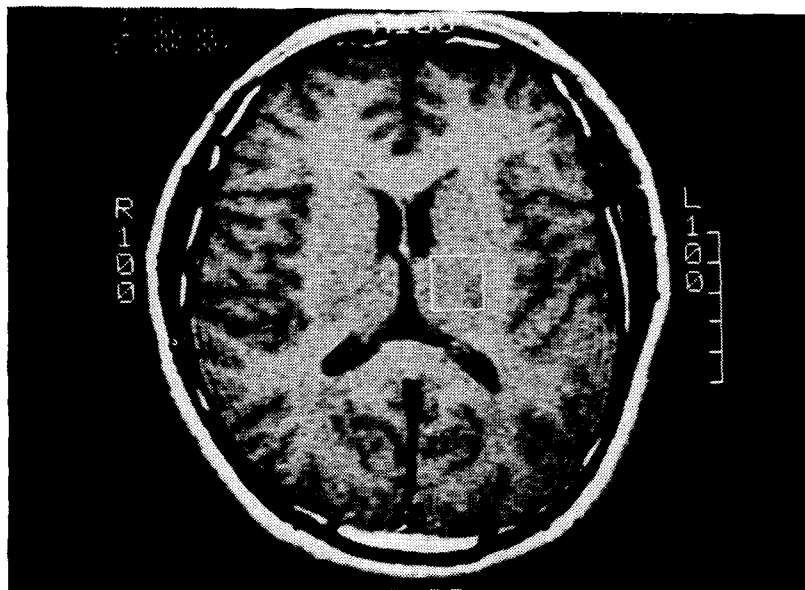

Figure. 1 T1-weighted axial brain MR image of a normal volunteer defining the VOI
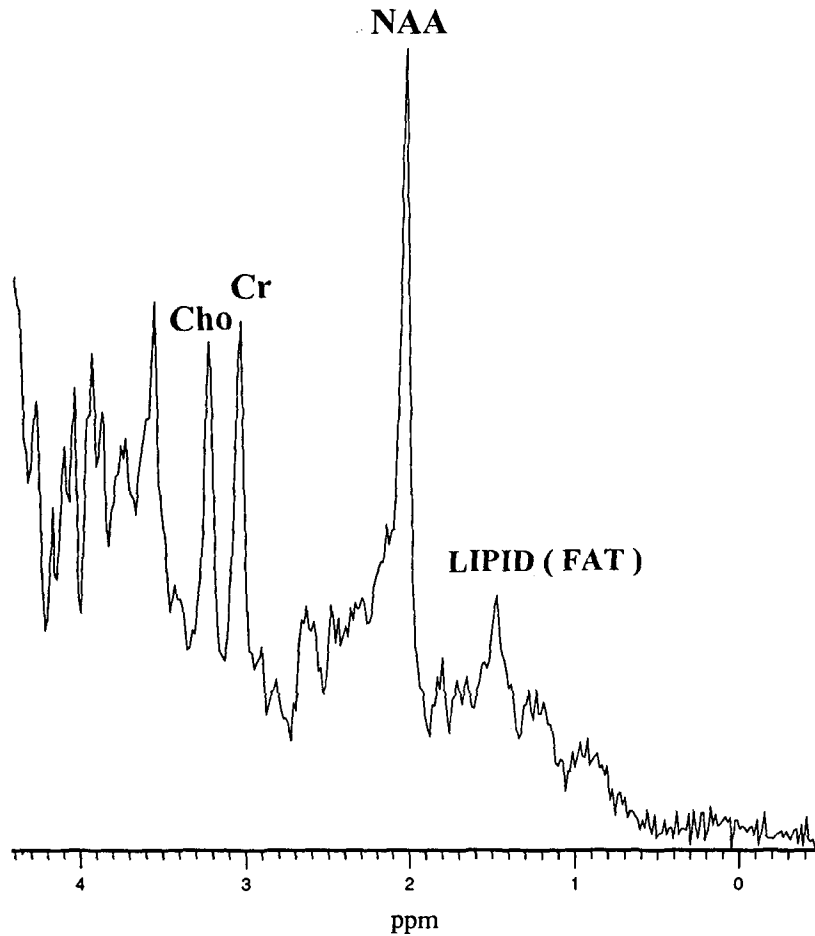
Figure. 2 A typical water-suppressed ¹H MR spectrum obtained from the brain of a normal volunteer.

few biological molecules. Moreover, many phosphorus-containing compounds are involved in the process that either produce or consume energy for cell. Because of the large range of chemical shifts present in the different phosphorus-containing species, the ^{31}P MR spectroscopy has been widely used to study cellular metabolism, to monitor the metabolic state of a variety of tissues, and to investigate the biochemical basis for diseases[14-15]. The ^{31}P MR spectroscopy recently plays a important role to evaluate the chemo and radio therapy[16-18]. The typical MR image and ^{31}P spectrum obtained from the muscle tissue of the right thigh of a normal volunteer is shown in Figures 3 and 4. respectively. using the ¹H and ^{31}P doubly tuned extremity surface coil. In order to increase the signal to noise ratio for ^{31}P. the size of VOI located within the muscle is 5x5x5 cm³ corresponding to a volume of 125 ml. The in $vivo$ ^{31}P spectrum of a tissue generally exhibits seven distinct resonances:phosphomonoesters (PME),
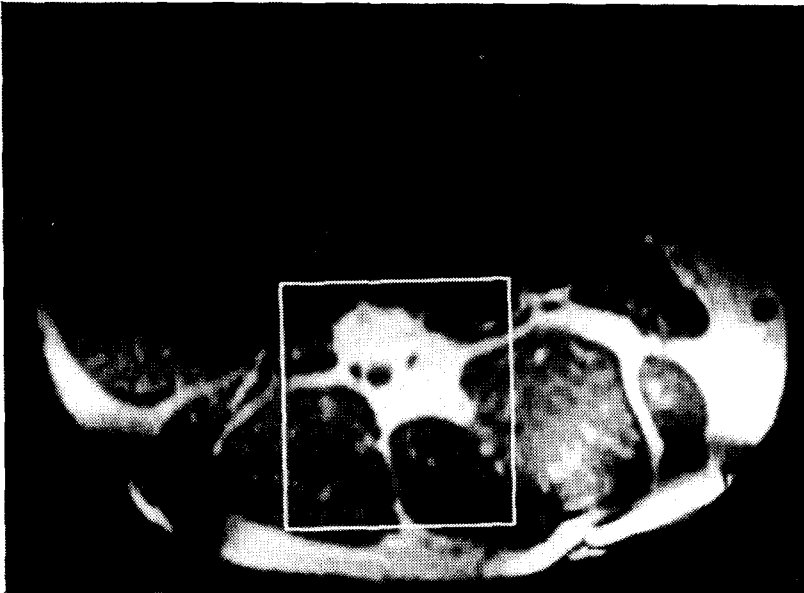
Figure. 3 T1-weighted MR image obtained form the muscle tissue of the right thigh of a normal volunteer defining the VOI. The size of VOI located within the muscle is 5×5×5 cm².
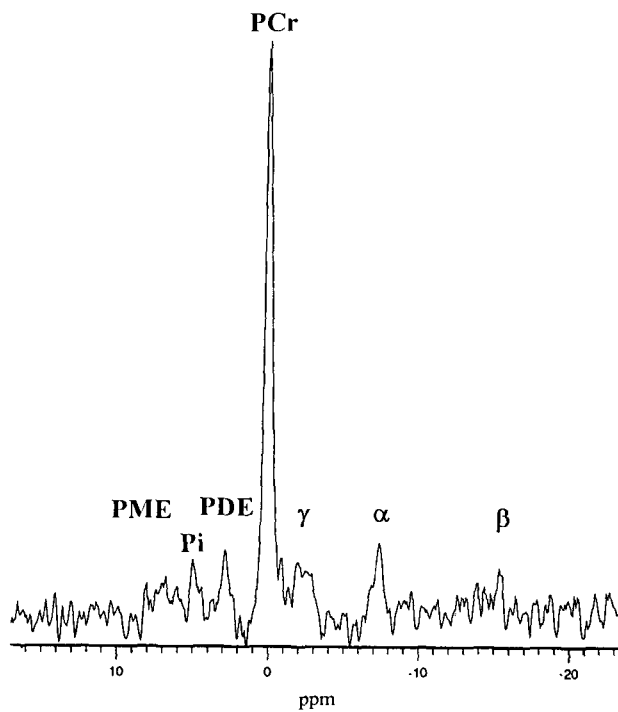

Figure. 4 A typical ³¹P spectrum obtained from the muscle tissue of the right thigh of a normal volunteer.

inorganic phosphate (Pi), phosphodiesters (PDE), phosphocreatine (PCr), and the alpha, beta, gamma phosphorus atoms of adenosine triphosphate(ATP).

The proton and phosphorus spectra contain the different informations concerning the metabolite state of the tissue being sampled. It is believed that the acquisition of the spatially localized metabolic informations available form either a proton, a phosphorus, or both spectra can be correlated with the informations available form magnetic resonance imaging (MRI). These correlations may lead to the development of a set of physiological, anatomical, and biochemical indices that will provide a valuable approach for investigating the underlying basis for many clinical diseases and disorders.

Conclusion

It is clear that *in vivo* MRS offers the new biochemical insights *in vivo* as well as clinical applications to various states of metabolic or biochemical disorders and the best and possibly the only hope for performing a noninvasive biopsy[19-20]. The extra dimension of *in vivo* MRS has both genuine clinical value for diagnosing disease and evaluating therapy, and scientific value as a new source of functional informations about the nature of disease states in patient.

Acknowledgments

References

1. E. M. Purcell:H. C. Torrey:R. V. Pound:Resonance absorption by nuclear magnetic moments in solids:Phys Rev, 69, 37-38(1946).
2. R. Bloch:W. W. Hansen:M. Packard:Nuclear induction:Phys Rev, 69, 127(1946).
3. W. G. Procter:F. C. Yu:The dependence of nuclear magnetic resonance frequency upon chemical compound:Pys Rev, 70, 717(1950).
4. A. Abragam:The Principles of Nuclear Magnetism:Oxford, Clarendon Press,

(1961).

5. C. P. Slichter:Principles of Magnetic Resonance:2nd edition. Berlin. Springer. (1978).

6. R. R. Ernst:G. Bodenhausen:A. Wokaun:Principles of Nuclear Magnetic Resonance in One and Two Dimensions:Clarendon Press. Oxford.(1987).

7. E. Odeblad:G. Lindstrom:Some preliminary observations on the proton magnetic resonance in biological samples:Acta Radiol. 43, 469–476(1966).

8. W. P. Aue:Localization methods for *in vivo* nuclear magnetic resonance spectroscopy:Rev. Magn Reson Med 1:21–72(1996).

9. P. A. Bottomley:Human *in vivo* NMP spectroscopy in diagnostic medicine: clinical tool or research probe?:Radiology 170:1–15(1989).

10. C. M. Segebarth:D. F. Baleriaux:P. R. Luyten:J. den Hollander:Detection of metabolic heterogeneity of human intracranial tumors *in vivo* by ^{1}H NMR spectroscopic imaging:Magn Reson Med 13:62–76(1990).

11. D. L. Arnold:P. M. Matthews:G. Francis:J. Antel:Proton Magnetic Resonance Spectroscopy of human brain *in vivo* in the evaluation of multiple sclerosis: Assessment of the load of disease:Magn Reson Med 14:154–159(1990).

12. R. Kreis:B. D. Ross:N. A. Farrow:Z. Ackerman:Metabolic Disorders of the brain in chronic hepatic encephalopathy detected with H-1 MR spectroscopy: Radiology 182:19–27(1992).

13. J. D. Duijin:G. B. M   on:A. A. Maudsley:J. W. Hugg:M. W. Weiner:Human Brain Infarction:Proton MR spectroscopy:Radiology 183:711–718(1992).

14. M. W. Weiner:The promise of magnetic resonance spectroscopy for medical diagnosis:Invest Radiol. 23, 253–261(1988).

15. G. K. Rádda:B. Rajagopalan:D. J. Taylor:Biochemistry *in vivo*:an appraisal of clinical magnetic resonance spectroscopy:Magn Reson Q. 5, 122–151(1989).

16. C. M. Christoph:D. F. Baleriaux:D. L. Arnold:P. R. Luyten:J. A. Hollander: MR image-guided P-31 MR spectrosocpy in the evaluation of brain tumor treatment:Radiology. 165. 215–219(1987).

17. W. Semmler:G. Gademann:P. Bachert-Baumann:H. Zabel:W. J. Lorenz:G. van Kaick:Monitoring human tumor response to therapy by means of P-31 MR spectroscopy:Radiology. 166, 533–539(1988).

18. B. Hubesch:D. Sappey-Marinier:K. Roth:D. J. Meyerhoff:G. B. Matson:M. W. Weiner:P-31 MR spectroscopy of normal human brain and brain tumors: Radiology. 174, 401–409(1990).

19. J. Frahm:H. Bruhn:M. L. Gyngell:K. D. Merboldt:W. Hanicke:R. Sauter: Localized high-resolution proton NMR spectroscopy using stimulated echos: Initial applications to human brain *in vivo*:Magn Reson Med. 9:79–93(1989).

20. M. J. Berridge:R. F. Irvine:Nature(London)312:315(1984).

진단방사선에서의 자기공명분광

최 보 영

가톨릭대학교 의과대학 방사선과학교실

과학분야에서 가장 획기적인 방법중의 하나로 각광받는 자기공명분광의 기본적인 원리가 의학분야의 진단방사선에서 유망한 방법론으로 소개되었다. 자기공명의 다양한 응용은 의학에서 보다 정확하고 민감한 정밀 진단의 가능성을 시사한다. 자기공명영상의 해부학적 정보와 자기공명분광의 생화학적 정보의 결합은 진단방사선의 밝은 전망을 제시한다.