

## REVIEW

# New trend of MRI diagnosis based on the function and metabolism in the central nervous system

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**Abstract :** The movement of a subject is a major problem in MRI experiments and diagnosis. At first, this review introduces a new technology named the "Propeller Technique" which can improve the motion artifact by changing the data sampling method in the K trajectory. Our experience of a case who underwent measurement by Propeller technique is reported and the effect of this technique is explained.

One of the recent hot topics is the appearance of the clinical 3T MR instrument, with its characteristic differences from that at 1.5T. The advantage of 3T is that it facilitates the evaluation of functional and metabolic information using MR spectroscopy (MRS) and functional MRI. The application of proton MRS in clinical cases is shown and the standard method to use proton MRS in a clinical setting is demonstrated. Furthermore, the new techniques, which can measure important metabolites in small amount such as neurotransmitters, was developed using a high signal to noise ratio and frequency resolution, which are advantages of 3T. *J. Med. Invest.* 53 : 199-203, August, 2006

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## INTRODUCTION

MRI devices and associated technology are improving and maturing rapidly. In addition, one of the recent hot topics is the appearance of the 3 Tesla (3T) instruments.

Though its licensing by the Japanese Government was slower than by Western countries, it is considered that its impact on clinical diagnosis will be huge when the high S/N ratio and effect of magnetic susceptibility are used effectively.

In this review, the utility of the "Propeller Technique" which is comparatively resistant to body movement

as one of the areas of progress in recent MRI technology is introduced, and the characteristics of 3T MRI are included concerning the development of applying metabolic changes and functional evaluations in the clinical diagnosis of the central nervous system.

### *1. Technology born from clinical need; the clinical utility of the Propeller Technique*

The shortening of measurement time is a goal of the recent MRI technology, and the efficient use of not only parallel imaging but also a multi-channel coil will shorten the measuring time drastically.

However, even if the measurement time is shortened using the new measurement technique, any body movement causes a larger artifact in the rapid MR scan due to there being less compensation for body movement than by classical MR imaging. Such an artifact can be especially problem-

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atic for the new technique of parallel imaging. This decline in image quality may lead to difficulty in diagnosis and, furthermore, artifacts may lead to misdiagnose. Thus, any reduction of measurement time will be meaningless.

So far, for unstable subjects, priority has been given to diagnostic imaging techniques such as CT, sedating patients when MRI was necessary. Nowadays, the "Propeller Technique" is one method which can be effectively applied for unstable patients. The basic theory behind this technique involves the gathering of much raw data on the center in the K space in which the contrast of the image is decided, and the Propeller Technique can minimize the influence of any position deviations due to body movement via the integration of adequate raw data.

When measurements cannot be completed due to the body movement of a subject, we are now applying this new technique in our facilities before resorting to sedation.

A case in which the Propeller Technique was employed in our facilities is shown in Figure 1, and the effectiveness of this new technique could be observed. This case had a large mass in the lateral ventricle and was complicated by obstructive hydrocephalus due to the circulatory failure of the cerebrospinal fluid caused by obstruction of the Monro foramen. CT demonstrated calcification in the mass.

When a decline in the level of consciousness was recognized, MRI was conducted, but there was a large artifact on conventional T2-WI due to head movement and the details weren't clear. Then, images of FLAIR and a T2-WI by the Propeller Technique were added and adequate images which could be used for diagnosis were acquired. The state of cystic degeneration, which was observed as a

low intensity signal with FLAIR, could be observed, and still a high intensity signal was thought to be useful for the qualitative diagnosis with T2-WI of the mass. As for the MRI diagnosis of the brain tumor, the examination time including FLAIR imaging and contrast enhanced T1-WI is usually long and it is considered lucky when the examination of an unstable patient can be conducted without sedation. It is also considered that this may greatly benefit radiologists by reducing the number of staff needed in the field of diagnostic radiology.

## 2. Application of information on cerebral function and metabolism in clinical diagnosis

A method to obtain information on cerebral function and metabolic change was proposed even with an MRI device of 1.5T. In a high magnetic field, it is better to acquire information on function and metabolic change due through the increased S/N ratio, improvement in frequency resolution, and so on. Furthermore the examination time can be shortened by increasing the S/N ratio and an additional measurement for functional or metabolic examination can be afforded. This aspect brought about by high magnetic MRI has significant importance, especially in the clinical setting where time is distinctly limited. The purposes to add information on function and metabolism in clinical diagnosis can be divided roughly into the following :

1) The time when the lesion or abnormality in the brain is known :

The choice of therapy or the therapeutic plan will be improved by understanding the background and mechanism of the disease using functional or metabolic information derived from MRI. In addition, it is considered meaningful that such information will facilitate a prognosis prediction including the severity of the disease and the curative effects.

2) The time when the lesion or abnormality in the brain isn't clear :

Identification of the area or range of disease may be detected by functional or metabolic information and it will be useful to perform a differential diagnosis.

Although these two purposes cannot be distinguished strictly in the actual clinical setting, this classification is thought to provide a standard to add functional and metabolic information to anatomical information to facilitate easy understand-

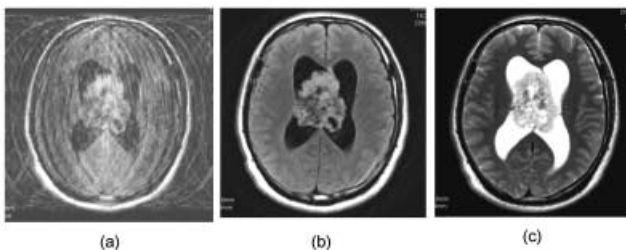


Fig. 1 : The utility of the "Propeller Technique" in an unstable subject with central neurocytoma  
 (a) conventional FLAIR image  
 (b) FLAIR image acquired with the Propeller Technique  
 (c) T2-WI acquired with the Propeller Technique

ing. Here, typical examples are introduced to help understand how to use the functional or metabolic information.

3) A case of the evaluation of functional and metabolic changes in MELAS :

A T2-WI and T1-WI of a 4-year-old child are shown in Figure 2. An abnormal signal can be observed in the occipital lobe containing the visual cortex and the surroundings of the central fissure of the primary motor area. This lesion showed a rather high intensity on diffusion-weighted imaging and hyperperfusion on FAIR imaging, which is one of the spin labeling perfusion MRI techniques (Figure 3).

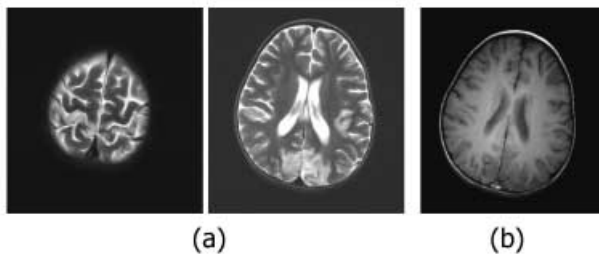


Fig. 2 : Anatomical images of a patient with MELAS (a)T2-WI (b)T1-WI

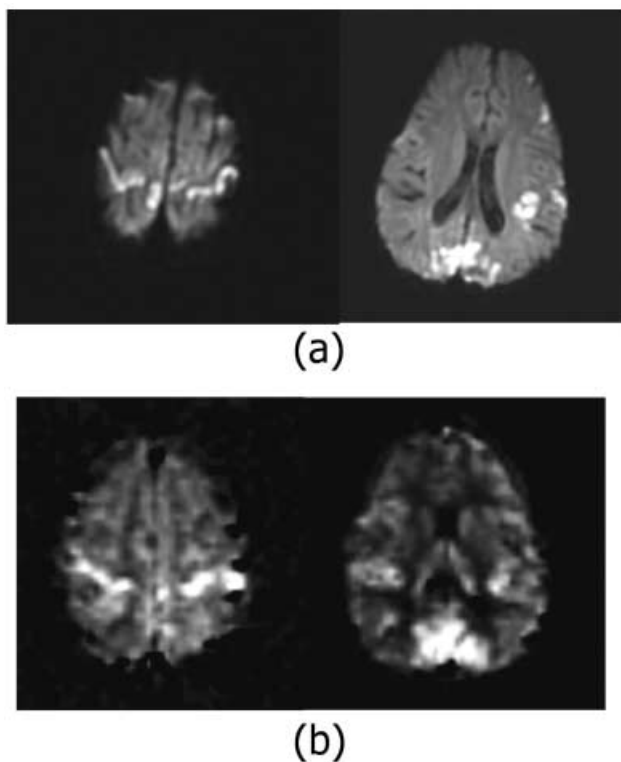


Fig. 3 : Diffusion-weighted images (a) and perfusion-weighted images (b) of a patient with MELAS  
The high intensity on DWI indicates a decrease in water diffusivity reflecting cytotoxic edema. The high intensity area on perfusion images show high flow rates in the lesion.

Proton MRS was measured by setting a region of interest (ROI) in the lesion showing abnormal intensity, revealing the decline of n-acetyl aspartate (NAA) and increase in lactate, and increase in the signal of macromolecules (MM) in the spectrum(Figure 4). It was considered that such signal changes in each metabolite suggested neuronal cell damage, an energy metabolism deficiency, and cellular destruction and necrosis.

From these results, it is considered that pathological changes in MELAS are based on energy metabolism deficiency in the mitochondria, which leads to a decreased oxygen utilization, and regional cerebral blood flow is increased by the vasogenic reactivity in order to compensate for energy failure. However, because energy failure does not occur via a shortage of blood or oxygen, damage and necrosis of neuronal cells still continues.

Therefore, it can be speculated that the local peripheral circulation and vasogenic reactivity as a function of the glial cells still remains at this stage even though the neuronal cell damage has progressed.

4) A case of multiple sclerosis showing a discrepancy between the symptom and anatomical abnormality on MRI :

The case was a 27-year-old female who had a past history of multiple sclerosis diagnosis and therapy, and a new symptom of incomplete paralysis of the right extremities, as shown in Figure 5. The relapse of multiple sclerosis was suspected and a brain examination by MRI was conducted. However, no remarkable new lesion was found on T2-WI and FLAIR images and a symptomatic cause wasn't clear with conventional MRI. The multivoxel measurement of proton MR spectroscopy, named Chemical Shift Imaging (CSI), in the brain was

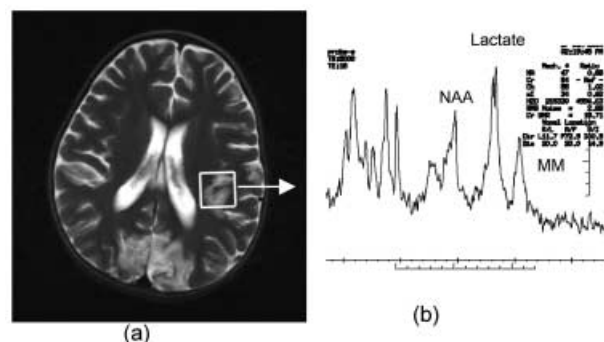


Fig. 4 : The ROI setting for acquiring proton MRS (a) and the obtained spectrum from a patient with MELAS  
The increase of lactate and decrease of NAA were revealed in this spectrum

added following conventional measurement by MRI. The result of CSI in this case is shown in Figure 6, and a decrease in NAA and increase in choline were found in the left hemisphere of the cerebrum compared to the maintained NAA peak in the right hemisphere. By constructing a metabolite ratio map by dividing NAA by Cho, a clear decline in the NAA/Cho ratio was noted in the left parietal lobe, as shown in Figure 6.

This result suggested that there was an inflammatory lesion in the normal appearing white matter which could not be recognized as an abnormal lesion by any conventional imaging modality. It is reported that the lesion is usually found as the existence of inflammatory or degeneration by histological examination, causing symptom or relapse phenomenon(1).

Even in the lesion which is difficult to identify as an anatomical abnormality, proton MRS showed such changes sensitively and with a high detectability of the pathological abnormality. As for the metabolite map including NAA, the understanding of the change is easier when presented visually, and it is considered that the metabolite

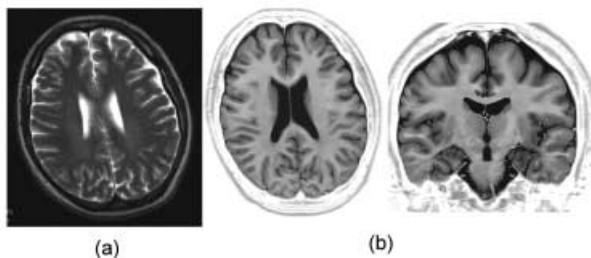


Fig. 5 : The anatomical images of a patient with multiple sclerosis. No remarkable abnormality can be found in these images.(a)T2-WI (b)High resolution and high contrast using the STIR technique

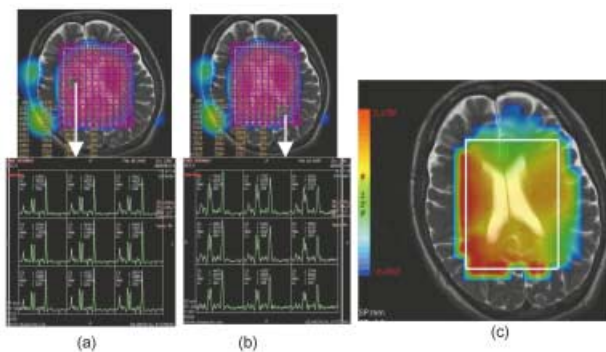


Fig. 6 : Chemical shift imaging of a patient with multiple sclerosis. (a)typical spectra obtained from the right hemisphere of the cerebrum ; (b)typical spectra obtained form the left hemisphere of the cerebrum ; (c)NAA/Cho map showing a decrease in the NAA/Cho ratio in the left hemisphere of the cerebrum.

map by the CSI is useful for the detection of normal appearing white matter.

5) For the routine use of the metabolite map by 3 :

The spectra of proton MRS of 1.5T and 3T in the same subject, obtained using the same measurement parameters, are shown in Figure 7. The spectrum of 3T showed not only a higher S/N ratio but also a better separation of each signal compared to 1.5T. The characteristics of 3T are a high resolution and high contrast images brought about by the increased S/N ratio, leading to a shortening of the measurement time for routine anatomical examinations. It is also expected that this shortening of the measurement time will bring about an environment in which the function or embolic information are easily added in the daily clinical use.

### 3. New metabolic information measured by the high magnetic field

The advantage of 3T is through its ability to detect a metabolite at a low concentration in tissue which is usually difficult to observe by 1.5T. Here, the example is introduced though the measurement of  $\gamma$ -aminobutyric acid (GABA), known as an amino acid related to neurotransmitters.

Glutamate is one of the constituent amino acids and it isn't formed only as a neurotransmitter though there are Glutamate and GABA as an amino acid which relates to the detectable neurotransmission by proton MRS. GABA is not a constituent amino acid and much exists in the neuron. It can be considered that GABA is more related to neurotransmitters than Glutamate.

However, Glutamate exists about 10mM in the brain, and only about 1 mM existed in GABA, and the signal of GABA piled up with the signal of the metabolite which concentration is high, and moreover, detailed evaluation was difficult with conventional proton MRS. Therefore, some ways of editing the signal of GABA selectively were proposed and we use the J difference method called MEGA-PRESS which takes the GABA signal at 3.0ppm for 3T MRI (2). The GABA signal can be recognized comparatively clearly in Figure 8 from the region of 27ml for about 10minutes. A change in the spectrum of GABA before and after drug administration in a healthy volunteer is given in Figure 9. On comparison with before medication, the GABA signal rose after two weeks medication with Li which cures depressive psychosis.

As for the intracerebral tubercle with epilepsy, it

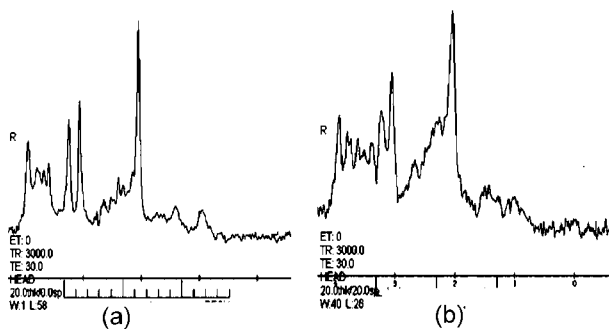


Fig. 7 : The difference in spectra between 3T (a) and 1.5T (b). The signal/noise ratio and resolution of the peaks are markedly different.

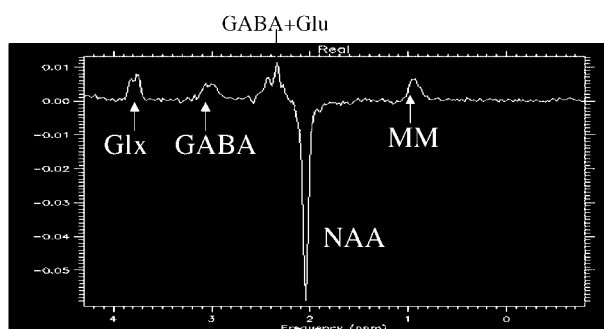


Fig. 8 : Typical spectrum measured by MEGA-PRESS showing the clear observation of GABA

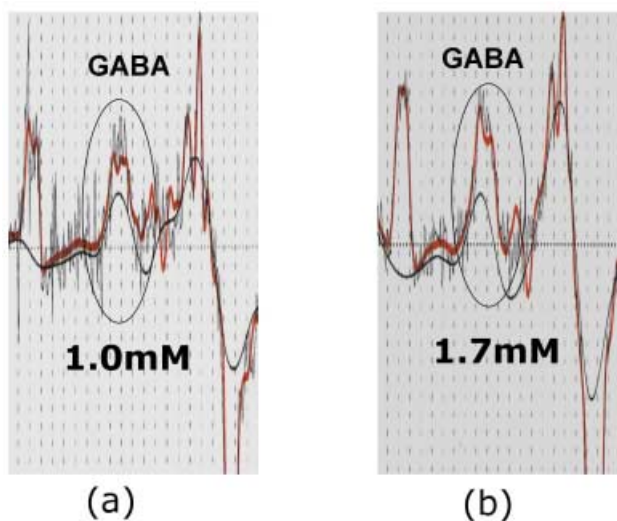


Fig. 9 : GABA signal changes by drug administration (a) before administration ; (b) after administration. An increase in the GABA peak is clearly observed by drug administration.

is recognized that GABA is present at high concentration in patients, with tuberous sclerosis in comparison with the healthy subjects suggesting a relation with the epileptic insult(3).

Because the relation with the neurotransmitter is so intimate, GABA is expected to become a new evaluation index of cerebral function and psychiatric disorder.

#### 4. Establishment of a new diagnostic system for brain imaging

The number of diseases recognized as causing functional changes in the brain have recently been increasing, including obsessive-compulsive disorder and autism, and anatomical observation sometimes shows limitations in functional evaluation.

The use of high magnetic field MRI clinically is thought to provide a good opportunity to evaluate metabolic or functional changes for practical use.

In the near future, if MRI facilitate a more detailed evaluation of brain function and metabolism, MRI may substitute positron emission tomography and the magnetoencephalogram or be used to complement these functional measurements.

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