原 著 Three-dimensional cerebral tractography - An application of magnetization transfer ratio

Tatsuhiko Ito[1], Yasutomi Kinosada[2], Masao Kaneko[3]

Department of Radiology, Seirei Hamamatsu General Hospital[1],
Department of Radiology, Kyoto Prefectural University of Medicine[2],
Department of Radiology, Hamamatsu University, School of Medicine[3]

Summary

PURPOSE: To evaluate a use of the magnetization transfer ratio (MTR) in the delineation of neural tracts of the human brain. METHODS: Thirty-eight MR examinations were carried out with a 1.5 T clinical scanner. Three-dimensional spoiled gradient echo sequences with and without magnetization transfer (MT) saturation pulse were performed. MTRs were calculated and reconstructed into three-dimensional images after maximum-intensity-projection (MIP) processing (MIP-MTR). RESULTS: Three-dimensional MIP-MTR technique provided unique images. Those images were considered to be a map of myelin distribution, and thus, a tractography. CONCLUSION: MTR may create a novel form of image contrast; isolation of myelin distribution, and is considered to be a promising adjunct in the evaluation of normal and abnormal brain neural tracts.

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RESULTS

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Index terms

Brain, magnetic resonance; Magnetic resonance, technique; Magnetic resonance, magnetization transfer; Magnetic resonance, tissue characterization.

Materials and Methods

Thirty-eight subjects including thirty-six patients and healthy volunteers (13 women, 25 men; age range 0 to 84 years) were randomly selected. Patients were referred for clinical purposes of stroke, neoplasm, trauma, lupus, MG, encephalitis, epilepsy, asphyxia and developmental delay/error.

All MR imaging were performed with a 1.5 T clinical scanner (GE Medical Systems, Milwaukee, WI). Three-dimensional spoiled gradient echo (SPGR) images were obtained with the following parameters: TR of 50 msec, TE of 2.8 msec, one excitation, flip

Address reprint requests to Dr Tatsuhiko Ito, Department of Radiology, Seirei Hamamatsu General Hospital, 2-12-12 Sumiyoshi, Hamamatsu, Shizuoka 430-8558, Japan.
Daytime phone: +81/53-474-2222, FAX: +81/53-479-2663 E-mail: hopper@sis.seirei.or.jp.
別刷請求先：〒430-8558 静岡県浜松市住吉2-12-12 聖隷浜松病院放射線科 伊藤龍彦

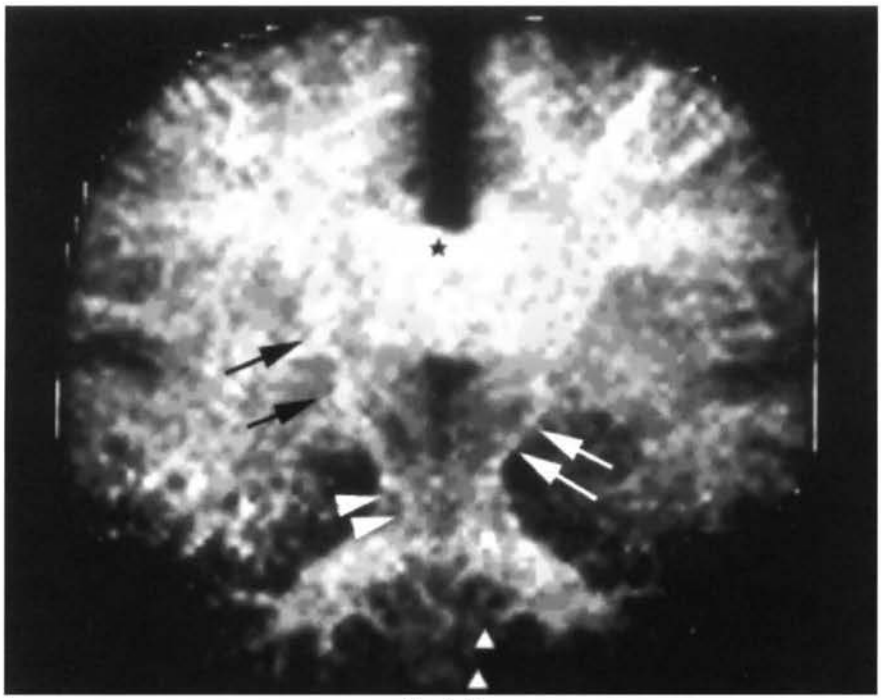

Fig.1-A

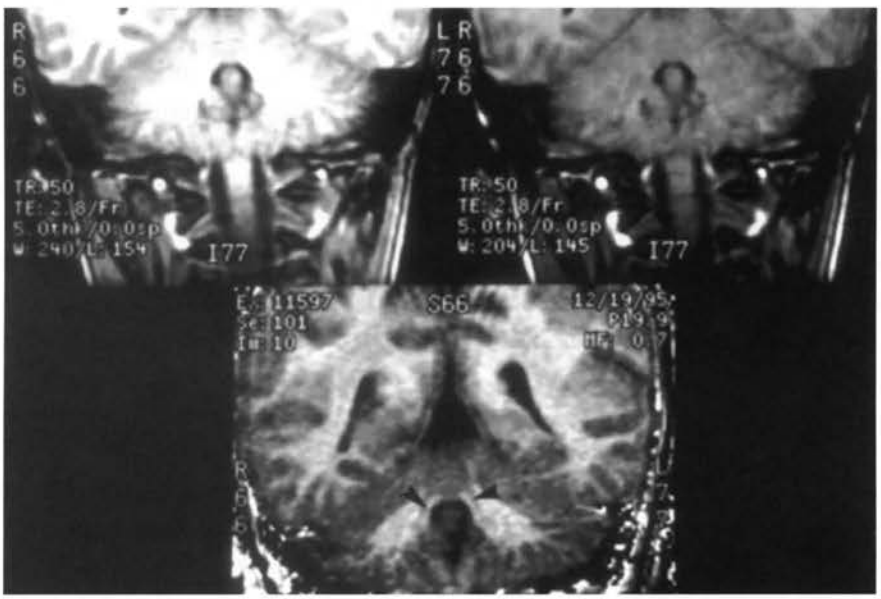

Fig.1-B

Figure 1 (A, B)

MIP-MTR image of a normal 22-year-old female. Hyperintense structures on this image are considered to have close relationship with myelin distribution (A: white arrows; corticospinal tract in the midbrain, white arrowheads; pontine corticospinal tract, white triangles; corticospinal tract in the medulla oblongata, black star; corpus callosum, black arrows; internal capsule).

A pre-MIP MTR image resembles to a T1-weighted spin echo image (B Bottom), but this is a map of MT sites. Arrowheads indicate superior cerebellar peduncles on this image. (SPGR image without saturation pulse; Upper left, SPGR with saturation pulse; Upper right))

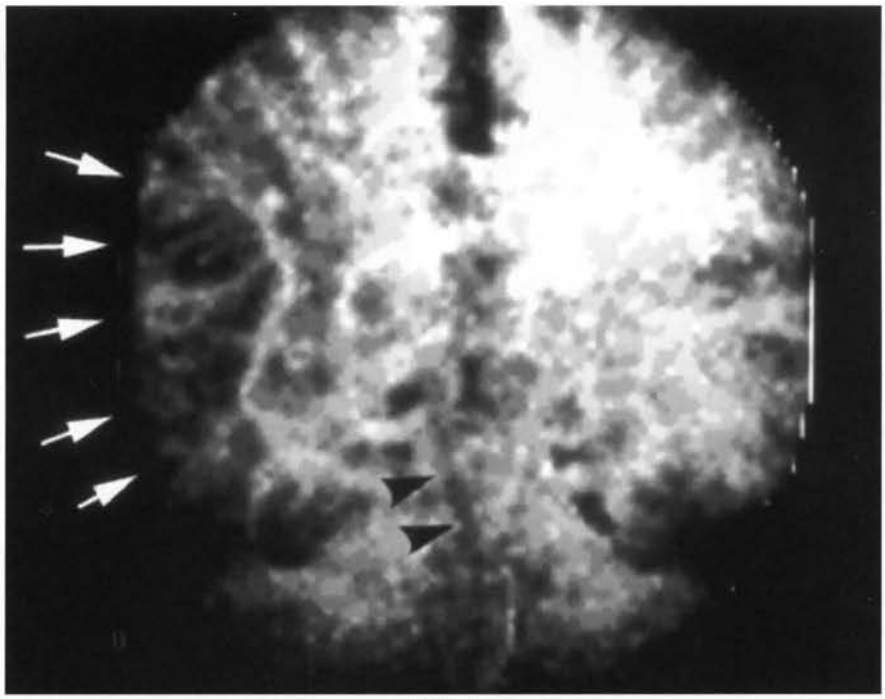

Fig.2-A

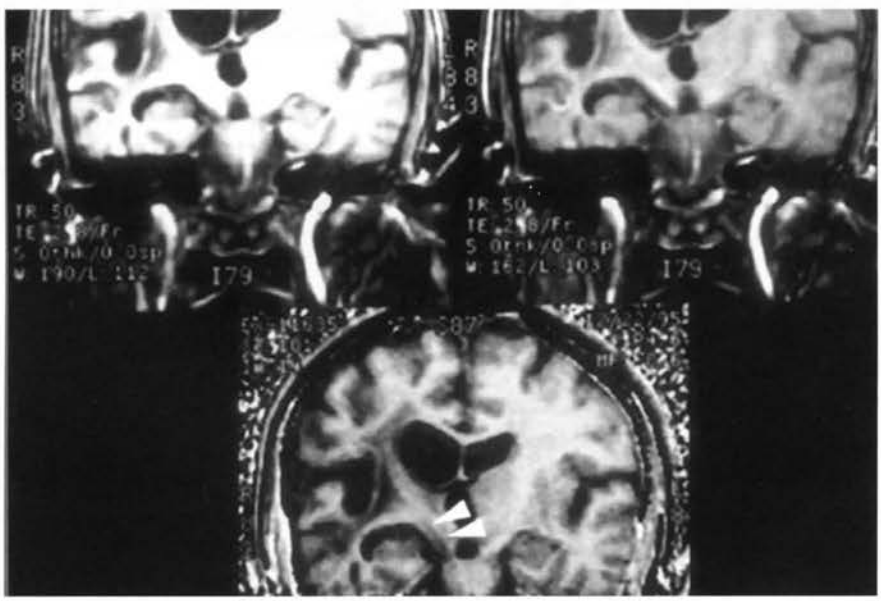

Fig.2-B

Figure 2 (A, B)

A 58-year-old male with chronic cerebral infarction. Destruction of the treelike structure is shown within and around the right basal ganglia and perisylvian region (A, white arrows). Also Wallerian degeneration of corticospinal tract is clearly shown (A, black arrowheads). This lesion is also revealed on pre-MIP MTR image (B Bottom; white arrowheads). (SPGR image without saturation pulse; Upper left, SPGR with saturation pulse; Upper right))

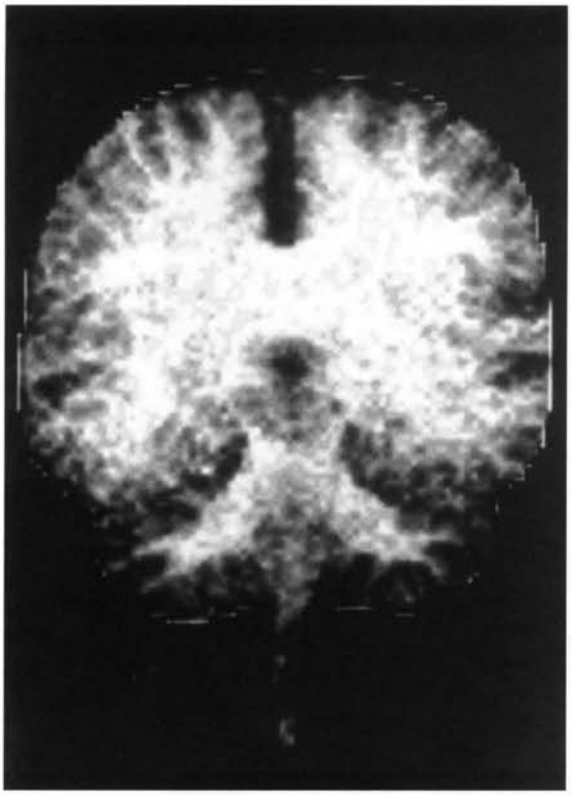

Fig.3-A

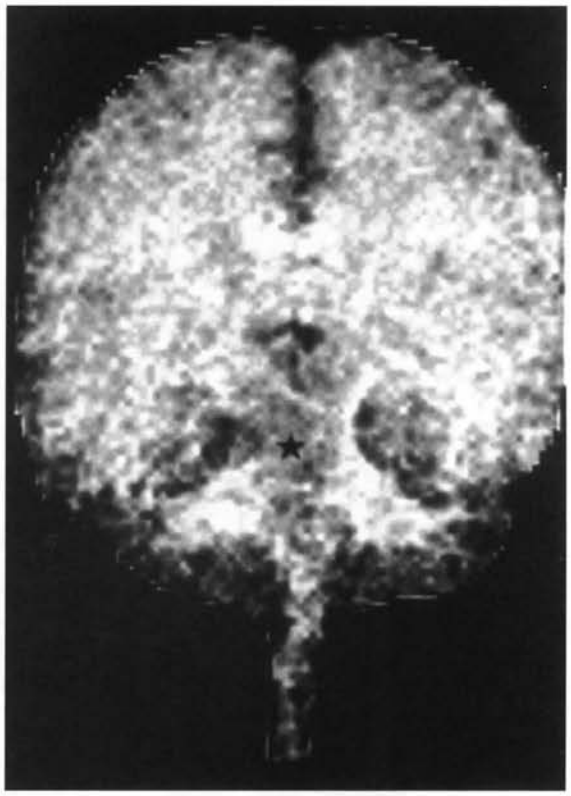

Fig.3-B

Figure 3 (A, B)

A normal three-year-old boy (A) and a 66-year-old male with right pontine hemorrhage (B star; hematoma). There is more detail of superficial regions in A than B. This may reflect immaturity of child's brain.

angle of 30 degrees, FOV of 20 cm, matrix of 256 x 128, partition thickness of 3 or 5 mm, single imaging slab of 28 partitions, in coronal or sagittal plane. All images were acquired with and without the saturation pulse for MT effect. The saturation pulse was applied with flip angle of 950 degrees, duration of 14,000 msec, 0.5 cycle of sinc pulse, offset frequency of 1,200 Hz.

From these batteries of SPGR data sets, MTRs were calculated on a workstation using the equation: MTR = (Mo-Ms) / Mo, where Mo is the signal amplitude without saturation pulse, Ms is signal amplitude with application of the saturation pulse.

Calculated MTRs were reconstructed to contiguous two-dimensional images. Then MIP technique was applied to these MTR images to obtain final images.

Results

Treelike high-intensity structures were clearly revealed in twenty-six MIP-MTR images **(Figure 1).** In another twelve cases, quality of MIP-MTRs was not excellent. The cause of image degradation was considered patients' movement between two scans; with and without MT pulse.

High-intensity structures revealed on images of excellent quality look to have close relationship with distribution of myelin. More precise anatomy was represented in periphery than deep regions of the brain. And more intense signal was seen in

densely packed tracts than loosely packed tracts.

Most prominent structures were pontine corticospinal tract, corpus callosum and brachium pontis. Cephalad part of internal capsule and corona radiata were hard to recognize. Basal ganglia were also hard to recognize.

In four cases of old infarction, lesions appeared as hypointense regions and lost well-organized treelike pattern. In one case of stage IV Wallerian degeneration, ipsilateral pontine corticospinal tract definitely lost its signal intensity i.e. loss of magnetization transfer **(Figure 2)**.

Superficial regions had more details in children compared to older patients **(Figure3)**.This tendency was considered, at least partly, to have relationship with patients' age, i.e. degree of maturation.

Discussion

Due to its complex structure, human brain is unique as a target organ in the field of medical imaging. It is hard to recognize each neural tract correctly on routine spin echo or gradient echo MR images even if they are of best quality.

Usually radiologists recognize the location of the lesion according to several well-delineated references such as basal ganglia, cortical sulci, ventricular system and so on. Sometimes more precise localization is performed based on the stereotactic methodology. But direct visualization of the neural tracts is not possible. Correct mapping of the neural tract is important not only in the clinical medicine but also in the basic neuroscience.

Magnetization transfer has been recognized as an important concept in MR imaging. Although it may often work as a degrading parameter in MR signal generation, sometimes it can provide valuable information about physiochemical environment of the organs.

Most MR images, even MR angiography, are maps of distribution of density or relaxation time of spins. But MTR depends on completely different parameters.MTR measurements offer information not obtainable with standard MR imaging. Its utility is twofold: as a new contrast method and to detect changes in structural integrity **(2)**.MTR imaging may be more useful than other MR measures, such as T2 mapping and spectroscopy **(3)**, and should create novel forms of contrast on MR imaging **(4)**.

Many authors reported the usefulness of MTR measurement in multiple sclerosis, brain injury, optic neuritis, infarction, infection and tumor **(5, 6, 7, 8)**. Usually the theme of investigation is a decreased MTR and loss of neuronal integrity **(9)**. We considered that MTR would be a useful tool in delineation of normal brain neural tract and this is the aim of this work.

The structure of myelin is represented by a fluid mosaic, which consists of a lipid bilayer and macromolecular proteins **(10)**. Lipid bilayers may contribute to the generation of MTR contrast, and so, MTR-weighted images may be utilized as a density map of myelin-bound cholesterol, thus, tractography.

The effect of cholesterol on magnetization exchange is consistent with an increase in dipolar cross relaxation between the lipid protons (^1H_r) and bulk water protons (^1H_f). Cholesterol could increase the correlation time of the lipid-water complex, where the dipolar interaction would occur. Increased magnetization transfer by both chemical exchange and through space dipole-dipole interactions may result from increased affinity of water for the bilayer. This could be manifested as an increase in the number of water interaction sites or as an increase in the residency time of water per site on the lipid. The addition of cholesterol to lipid has been shown to organize more water at the bilayer surface, possibly through direct interaction of the water with the cholesterol hydroxyl group. Simple addition of cholesterol hydroxyls to the lipid surface is not adequate to catalyze the exchange process. Most likely, both an increase in bilayer correlation time and an increase in the amount of water associated with the bilayer as a function of cholesterol result in the magnetization exchange effects. Shortly, cholesterol-dependent magnetization exchange occurs

between bulk water and the macromolecular matrix. Cholesterol may modulate this interaction by increasing the correlation time of the lipid-water complex, by organizing more water at the bilayer surface, or by a combination of these effects. MTC and other water relaxation differences observed in tissues with high phospholipid / cholesterol content may result from this cross-relaxational pathway **(11)**.

The myelin acts as a lipid-water interface in which a representative water molecule experiences a sevenfold greater interaction than at a typical protein-water interface. The potholes at the cholesterol locations in the myelin lipid surfaces are presumably filled with water molecules that could form an extended network of hydrogen bonded waters. The influence of myelin on the relaxation rate of myelin water must truly be at the lipid-water interface, with a significant contribution from cross-relaxation. The relaxation properties of myelinated white matter are unique and are evidenced at physiological temperatures because of a rapid mixing of axonal water with the water of myelin **(12)**.

In our investigation, pre-MIP MTR images resemble to T1-weighted spin echo images, but it should be emphasized that this is not a map of water proton but a map of MT sites. Signal differences derived from water proton distribution were cancelled during image processing.

Possible explanations for such MTR variation in the different regions include possible differences in fiber packing density, degree of myelination, tissue hydration, and vascularity **(1)**.

MTR images is considered to be a density map of the spatial distribution of myelin-bound cholesterol and, only to the extent that the two are correlated, the extent of myelination **(1)**

Conclusion

MTR may create a novel form of image contrast; isolation of myelin distribution.

Three-dimensional MIP-MTR images may provide unique information and is considered to be a promising adjunct in the evaluation of normal and abnormal brain neural tracts.

Acknowledgment

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References

1. Silver NC, Barker GJ, MacManus DG, et al. Magnetization transfer ratio of normal brain white matter: a normative database spanning four decades of life. Journal of Neurology, Neurosurgery, and Psychiatry 1997;62:223-228
2. Koenig SH. Cholesterol of Myelin Is the Determinant of Gray-White Contrast in MRI of Brain. Magnetic Resonance in Medicine 1991;20:285-291
3. Grossman RI, Gomori JM, Ramer KN, et al. Magnetization Transfer: Theory and Clinical Applications in Neuroradiology. Radiographics 1994;14:279-290
4. Balaban RS, Ceckler TL. Magnetization Transfer Contrast in Magnetic Resonance Imaging. Magnetic Resonance Quarterly 1992;8(2):116-137
5. Lexa FJ, Grossman RI, Rosenquist AC. MR of Wallerian Degeneration in the Feline Visual System: Characterization by Magnetization Transfer Rate with Histopathologic Correlation. AJNR 1994;15:201-212
6. Kimura H, Meaney DF, McGowan JC, et al. Magnetization Transfer Imaging of Diffuse Axonal Injury Following Experimental Brain Injury in the Pig: Characterization by Magnetization Transfer Ratio with Histopathologic Correlation. Journal of Computer Assisted Tomography 1996;20(4):540-546
7. Thorpe JW, Barker GJ, Jones SJ, et al. Magnetization transfer ratios and transverse magnetization decay curves in optic neuritis: correlation with clinical findings and electrophysiology. Journal of Neurology, Neurosurgery, and Psychiatry 1995;59:487-492

8. Dousset V, Grossman RI, Ramer KN, et al. Experimental Allergic Encephalomyelitis and Multiple Sclerosis:Lesion Characterization with Magnetization Transfer Imaging. Radiology 1992;182:483-491
9. Hiehle JF, Lenkinski RE, Grossman RI, et al. Correlation of Spectroscopy and Magnetization Transfer Imaging in the Evaluation of Demyelinating Lesions and Normal Appearing White Matter in Multiple Sclerosis. Magnetic Resonance in Medicine 1994;32:285-293
10. Kimura H, Grossman RI, Lenkinski RE, et al. Proton MR Spectroscopy and Magnetization Transfer Ratio in Multiple Sclerosis:Correlative Findings of Active versus Irreversible Plaque Disease. AJNR 1996;17:1539-1547
11. Mehta RC, Pike GB, Enzmann DR. Improved Detection of Enhancing and Nonenhancing Lesions of Multiple Sclerosis with Magnetization Transfer. AJNR 1995;16:1771-1778
12. Fralix TA, Ceckler TL, Wolfe SD, et al. Lipid Bilayer and Water Proton Magnetization Transfer Effect of Cholesterol. Magnetic Resonance in Medicine 1991;18:214-223