研 究 論 文

Tissue characterization by magnetization transfer ratio

– Evaluate of the MTRs in breast tunors, globus pallidus and nasopharyngeal tumors –

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Magnetization transfer ratios (MTRs) of tissues with different characteristics were investigated. Cross-relaxation rates of solutions with different protein concentrations were studied. We evaluated the MTRs of female breast tumors, the globus pallidus, and nasopharyngeal tumors, and assessed the usefulness of MTRs in determining tissue characteristics.

In phantom studies, we measured MTRs using gelatin and $MnCl_2$ solution with various concentrations of gelatin and $MnCl_2$. MTRs were measured using pairs of images obtained by conventional SPGR sequence and MT-prepared SPGR sequence. MTRs, defined as the percentage of signal loss between unsaturated and saturated images, were calculated using the equation (Mo-Ms) / Mo, where Mo is the measured signal intensity on the conventional SPGR images, and Ms is the measured signal intensity on the MT-prepared SPGR images. We investigated relationships between pathological findings and MTRs of breast tumors, between liver function and MTRs of globus pallidus, and between the DNA index and MTRs of nasopharyngeal tumors.

MTRs increased with increased gelatin concentration, but decreased as the $MnCl_2$ concentration increased. MTRs of breast carcinoma were higher than those of benign tumors. MTRs of globus pallidus showed a correlation with liver function (ChE: r = 0.79, PT: r = 0.75, ICGR15: r = -0.98). MTRs of aneuploid nasopharyngeal tumors had high MTRs. MTR is a good indicator of protein concentration and could be a new and useful parameter for tissue characterization.

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INTRODUCTION

In conventional MR imaging, image contrast is a function of inherent spin-lattice (T1) and spin-spin (T2) relaxation times of protons in the tissue water and fat molecules, as well as a function of proton density. However, the ability of MR imaging to obtain image contrast between different tissues on the basis of these factors is limited. Efforts to improve the contrast between tissues have recently led to the development of imaging with magnetization transfer contrast[1], which is sensitive to the extent of magnetization exchange, or cross relaxation in tissue[2-6].

This suggests that the magnetization transfer contrast technique could provide quantitative information on tissue relaxation. We performed phantom studies to determine whether the magnetization transfer ratios (MTRs) reflected cross relaxation rates. In the patient studies, MTR measurement was performed on breast tumors, the globus pallidus in patients with hepatocellular carcinoma, and nasopharyngeal tumors.

SUBJECTS AND METHODS

Subjects

We prepared gelatin (Gel-P) and $MnCl_2$ solution phantoms (Mn-P). The concentration of gelatin in the Gel-P varied from 0 to 30%. In the Mn-P, $MnCl_2$ was mixed in 20% gelatin, with the $MnCl_2$ concentrations ranging from 0.0 to 0.1mM. We measured MTRs and cross relaxation rate in these phantoms. In the patient studies, we measured MTRs of 40 breast lumps (the average ages: 52.8), 22 globus pallidus in patients (the average ages: 65.0) with hepatocellular carcinoma (HCC), and five nasopharyngeal carcinomas of stage IV. The forty breast lumps included 31 carcinomas, three mastopathies, two papilloma, and four cysts. To evaluate liver function, Prothrombin time (PT), cholinesterase (ChE), and ICGR15 were measured in the patients with HCC. The DNA index was measured in the five patients with nasopharyngeal carcinoma. The DNA indices were measured using the vindel ϕv method[11].

MR Imaging

The MR examinations were performed using a 1.5-T MR system (Signa; GE Medical Systems, Milwaukee, WI U.S.A.), with a head coil and a five-inch breast coil. We used an off-resonance technique for preferential saturation of the immobile protons to evaluate MTRs. Images were acquired with conventional spoiled-gradient-recalled acquisition in steady state (SPGR), MT-prepared SPGR sequence and calculated MTR. The single MT pulse consisted of 18 msec truncated-cycle sinc pulse with 1.2kHz off-water resonance frequency. MR imaging parameters were: TR = 50 msec; TE = 5 msec; flip angle = 30 degrees; matrix size = 256 x 192; and slice thickness = 5 mm. In the phantom study, the flip angles were varied from 1 to 40 degrees for measurement of cross relaxation rate.

Magnetization Transfer

MTR is defined as the percentage of signal loss between unsaturated and saturated images. They are calculated with the equation:

$$MTR\ (\%) = 100 \times (Mo - Ms)\ /Mo,$$

where Mo is the measured signal intensity on the conventional SPGR images, and Ms is the measured signal intensity on the MT-prepared SPGR images. If the immobile protons are selectively saturated, MTR is given by the equation[1,7,8]

$$1/Tis = 1/T1^{*} \times MTR,$$

where 1/Tis is the cross-relaxation rate, and 1/T1* is the apparent T1 relaxation rate with MT pulse[9]. 1/Tis is given by the equation:

$$1/Tis = 1/T1^{*} - 1/T1,$$

where 1/T1 is the apparent T1 relaxation rate without MT pulse[9]. In the present study, 1/T1 and 1/T1* were calculated using the equation

$$S = [(1-E1)/(1/E1 \cos \alpha)] \times (MoE2 \sin \alpha),$$

where S = signal intensity, E1 = exp (−TR/T1), E2 = exp (−TE/T2), and α = flip angle[10].

RESULTS

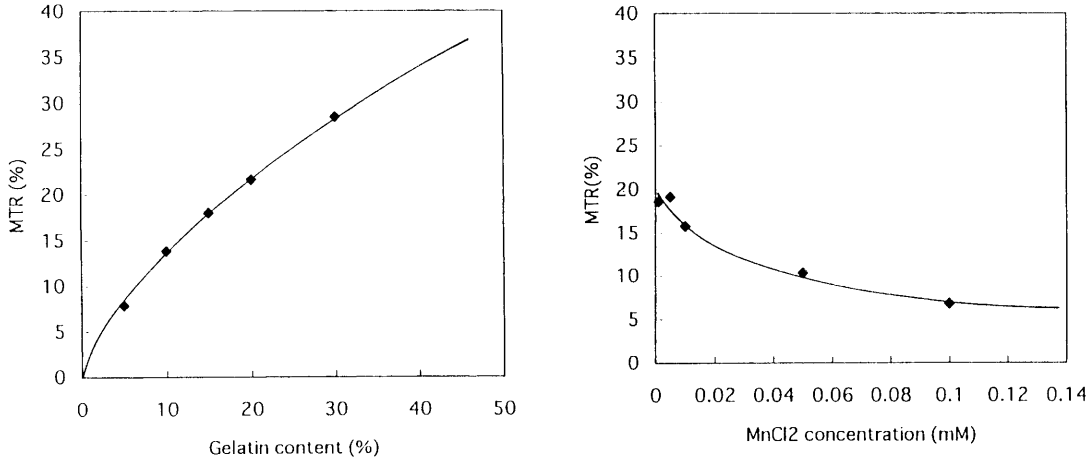
MTRs in Phantom Study

Figure 1 shows the MTR values for different gelatin concentrations and for different $MnCl_2$ concentrations dissolved in 20% gelatin gel. In the Gel-P, MTRs increased with increasing gelatin content, whereas in the Mn-P the MTRs decreased with increasing $MnCl_2$ concentrations. The solid lines indicate the second order approximation of the experimental values (correlation coefficient: R, Gel-P: R = 0.99, Mn-P: R = 0.98).

Figure 2 presents the correlation between cross relaxation rate and MTR. The solid lines are second order approximations of the experimentalvalues (Gel-P: R = 0.99, Mn-P: R = 0.98).

MTRs of Breast Tumors

Figure 3 shows the GD-DTPA contrast enhanced image of a tumor and the calculated MTR image in the breast carcinoma. On the calculated MTR image, the tumor and the intact mammary



(a) (b)

Fig.1 MTR values on phantoms with various concentrations.
(a) gelatin phantom.
(b) MnCl2 dissolved in 20% gelatin phantom.

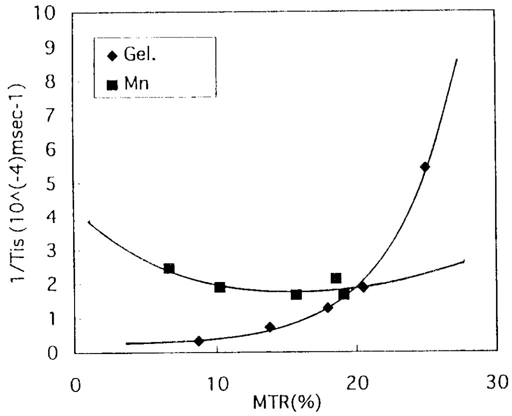
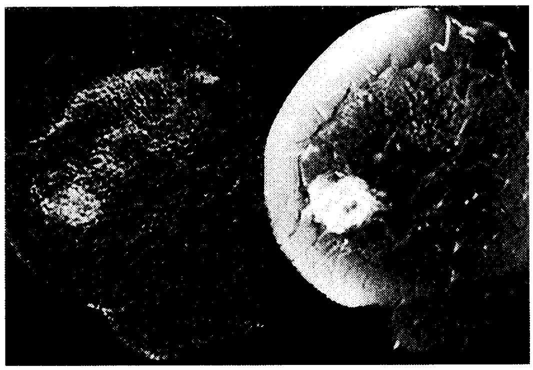


Fig.2 Correlation between cross relaxation rate and MTR



(a) (b)

Fig.3 MR images of breast carcinoma.
(a) Calculated MTR image.
(b) Gd-DTPA contrast enhanced image.

glands had high MTRs. The meansand standard deviations for MTRs of the normal breast structures and the tumors are shown in Fig. 4. In the normal structures, the lowest MTRs were for the fat tissue (1.0 [± 0.8%]), and increased in glandular tissue (12.4 [± 0.3%]) and muscle (15.1 [± 2.7%]). The MTRs of tumors increased in order from those found for cysts (4.24 [± 2.5%]), to mastopathy (16.4 [± 2.6%]), papilloma (17.6 [± 1.4%]), and carcinoma (24.2 [± 3.6%]).

MTRs of Globus Pallidus in Patients with Hepatocellular Carcinoma Figure 5 shows a conventional SPGR image, an MT-prepared SPGR image, and a calculated MTR image of the brain in patients with HCC. On both SPGR images, the globus pallidus exhibited higher signal intensity

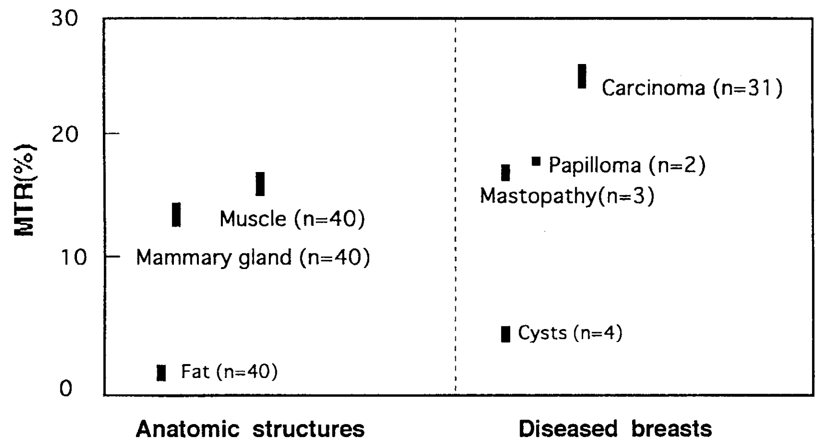


Fig.4 MTR values for breast.

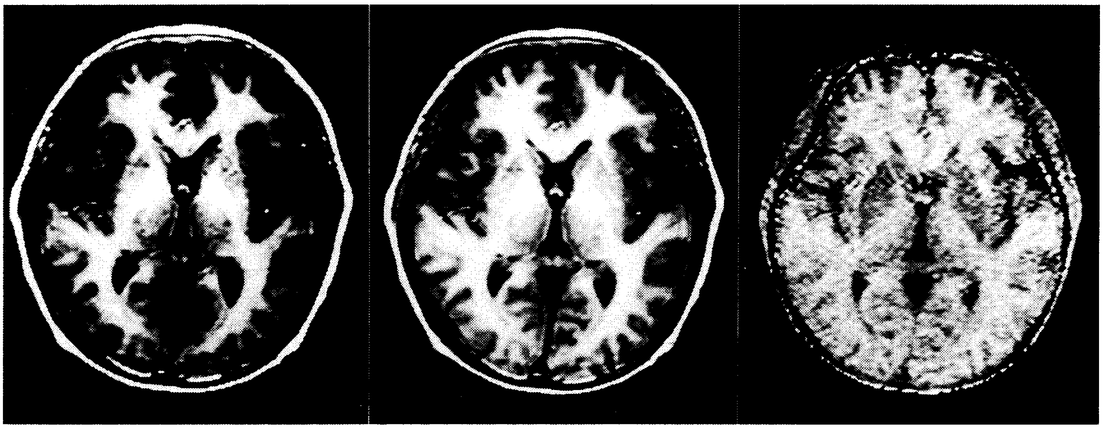
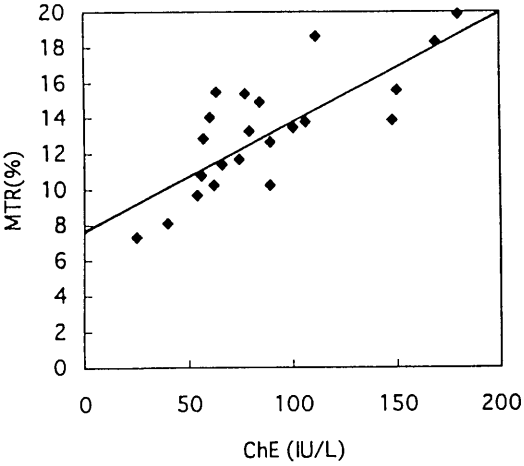


Fig.5 MR images of basal ganglia in patients with hepatocellular carcinoma.
(a) MT－prepared SPGR image.
(b) Conventional SPGR image.
(c) Calculated MTR image.

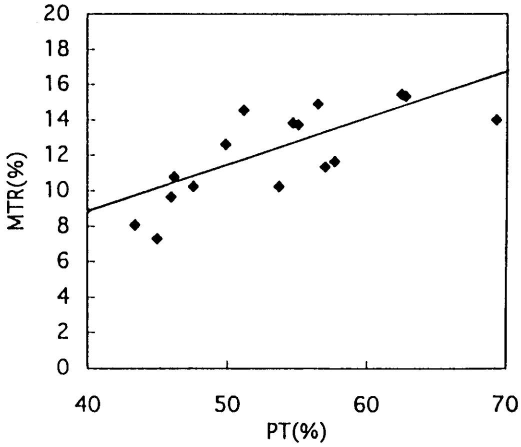
than the white matter. On the calculated MTR image, these portions had a lower value than the white matter. Figure 6 shows a relation between liver function and MTRs of the globus pallidus. To evaluate liver function, 22 cases ChE, 16 cases PT, six cases ICGR15 were measured in the patients with HCC. The MTRs of globus pallidus did show a correlation with liver function.

MTRs for Nasopharyngeal Tumors

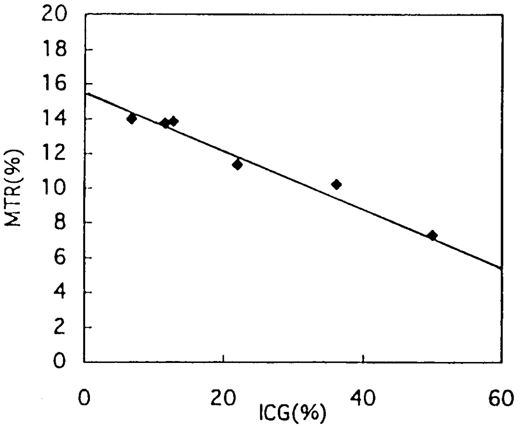
Table 1 shows a relation between the DNA index and MTRs in patients with nasopharyngeal carcinoma of stage IV. The aneuploid tumor had higher the DNA index. Two of five cases were of aneuploid type, and had high MTR values.



(a)



(b)



(c)

Fig.6 Liver function and MTRs of globus pallidus in patients with hepatocellular carcinoma. Prothrombin time (PT) and cholinesterase (ChE) decrease with poor liver function. ICGR15 increases with poor liver function.
(a) Relationship between MTR and ChE. (r = 0.79, n = 22)
(b) Relationship between MTR and PT. (r = 0.75, n = 16)
(c) Relationship between MTR and ICGR15. (r = −0.98, n = 6)

Table 1 MTRs of nasopharyngeal tumor and DNA index.

age/sex	pathology	MTR (%)	DNA index
60/F	squamous cell carcinoma	17.7	1.78
40/F	undifferentiated carcinoma	15.2	1.13
40/F	undifferentiated carcinoma	14.2	1.00
64/M	squamous cell carcinoma	13.9	1.00
60/M	undifferentiated carcinoma	13.4	1.00

DISCUSSION

Magnetization transfer links the immobile proton pool to the protons in water present[1,7,8]. The MTRs were, therefore, sensitive to the extent of magnetization exchange, and to the cross relaxation in the tissue. We performed phantom studies to examine the quality of the MT method.

Changes in the MTRs were shown to correlate the concentration of gelatin and $MnCl_2$ with cross relaxation rate. However, Comparing Gel－P and Mn－P, the relation between MTRs and concentration was inverse (Fig.1). The reasons for these differences were presumably due to their respective relaxation mechanisms. In the Gel－P, the relaxation mechanismis possibly dominated by cross relaxation[3], whereas in the Mn－P the relaxation mechanism may have been dominated by paramagnetic effects. Changes in the MTRs reflected differences in the dominant relaxation mechanisms. Therefore, the present phantom study has provided proof of the quality of our MT method.

We assessed the tissue characteristics using MTR values for female breast, globus pallidus, and nasopharynx tissue. We measured MTRs of normal anatomic structures of the breast. Muscle tissues had the highest MTRs due to their high macromolecular protein content. MTRs of the mammary glands varied more than those of other normal tissues in the breast, presumably because of the variable amount of fat and fibrous tissue. Fat tissue had the lowest MTR, because of non－magnetization transfer in the fat tissue. In the breast tumor, the lowest MTR value was in the cystic tumor, with values progressively increasing for mastopathy, papilloma, and carcinoma. Mastopathy and papilloma exhibited MTRs similar to those of the mammary glands. The carcinomas showed higher MTRs than those of the mammary glands. The prognosis of breast cancer depends on collagen concentrations[12]. In the meningiomas, these MTR values were correlation with collagen concentrations[13]. In the breast tumors, these MTR values increased in a pattern similar to that of the Gel－P MTR values. We think that changes in MTRs had a close relation with the collagen concentrations. The MTRs of breast tumor can be a new indicator for pathological malignity.

MTRs of the globus pallidus in patients with HCC showed a correlation with liver function. There are numerous reports concerning the high signal intensity in T1－weighted images of the globus pallidus in patients with chronic liver disease[14-17]. These changes are believed to be due to deposits of manganese in the globus pallidus[14]. We speculate that, although the causes are unknown, manganese had been deposited in the globus pallidus of patients with poor liver function. If we combine the results of our phantom studies with these ideas concerning manganese deposits, we might be able to estimate the concentration of manganese in the globus pallidus.

The aneuploid nasopharyngeal tumor showed high MTR values. Although the number of cases was small, we think that the MTRs reflected differences in the amount of nuclear material and the existence of abnormal protein in the tumor cells.

The present study suggests that the MTRs increased with the number of immobile protons; it also suggests that the MTRs increased as the cross relaxation rate increased. MTRs may be a new and useful parameter for tissue characterization.

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