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MR of Intracranial Tumors: Combined Use of Gadolinium and Magnetization Transfer

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PURPOSE: To study the potential combined application of gadolinium and magnetization transfer in the MR imaging of intracranial tumors. **METHODS:** Twenty-two patients were imaged at low field strength (0.1 T). Corresponding gradient-echo partial saturation images without and with magnetization transfer pulse were produced. Images with intermediate repetition times were obtained in 18 cases; five different sequences were produced in 4 cases. Gadopentetate dimeglumine was used at a dose of 0.1 mmol/kg. **RESULTS:** Magnetization transfer effect increased the contrast between enhancing lesion and normal brain and the contrast between edema and normal brain; the contrast between enhancing lesion and edema was not significantly changed. On intermediate-repetition-time magnetization transfer images the contrast between enhancing tumor and normal brain and the contrast between edema and normal brain were superior to short-repetition-time magnetization transfer images, but the differentiation between enhancing tumor and edema was poorer. **CONCLUSION:** Magnetization transfer can be used to improve contrast in Gd-enhanced MR imaging. Combining magnetization transfer with an intermediate-repetition-time image provides the possibility for displaying both enhancing and nonenhancing lesions on a single MR image.

Index terms: Magnetic resonance, contrast enhancement; Magnetic resonance, technique; Brain, magnetic resonance; Brain, neoplasms

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The contrast in conventional magnetic resonance (MR) imaging relies mainly on the differences in T1 and T2 relaxation times. Paramagnetic contrast agents such as gadopentetate dimeglumine, which shorten relaxation times, can be used to improve contrast in T1-weighted sequences. Recent studies have demonstrated the possibility of exploiting a new contrast method, magnetization transfer, in MR imaging (1, 2). Clinical investigations have shown that magnetization transfer combined with traditional sequences can be used to improve contrast in MR imaging (3–7). Furthermore, magnetization transfer may provide a useful tool in tissue characterization (8–10).

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Synergistic enhancement with gadolinium and magnetization transfer effect has been demonstrated in clinical imaging (5–7). In magnetization transfer the magnetization decreases during an off-resonance saturation pulse; the decline in most nonenhanced tissues is greater than in Gd-enhanced structures, which improves contrast between Gd-enhanced and nonenhanced tissues. The contrast obtained with magnetization transfer increases with the duration of the magnetization transfer pulse. So far, the combination of Gd and magnetization transfer contrast has been exploited in sequences with short repetition times (TRs). However, these sequences do not allow the use of a sufficiently long magnetization transfer pulse to obtain a strong magnetization transfer effect. Magnetization transfer effect can be increased with a longer TR and off-resonance pulse, although this may decrease the T1 contrast.

We studied the use of magnetization transfer contrast in the imaging of intracranial tumors. The aim was to compare contrast in Gd-

enhanced sequences with different TR and magnetization transfer pulse lengths. Additional studies were performed to investigate the applicability of intermediate TR and long magnetization transfer pulse in Gd-enhanced imaging.

Patients and Methods

The study group consisted of 22 patients with intracranial tumors at the Department of Neurosurgery. The diagnosis was in all cases confirmed surgically and histologically. Fully informed consent was obtained from every patient.

The imaging was performed at 0.1 T by using a double-saddle transmit-receive head coil with quadrature detection. Routine T2-weighted multiple-section spin-echo 2100/120/1 (TR/echo time/excitations) imaging and T1-weighted three-dimensional partial-saturation 50/20/1 imaging were performed; the partial-saturation 3-D imaging was repeated after injection of gadopentetate dimeglumine.

A representative section with tumor was chosen for single-section magnetization transfer imaging. In magnetization transfer imaging the off-resonance pulse was applied immediately before the 90° pulse. The sequences without and with off-resonance pulses were repeated in every phase-encoding step. Corresponding images without and with magnetization transfer effect were produced. A magnetization transfer pulse with a narrow bandwidth superior to the frequency of mobile water was used; the amplitude of the off-resonance pulse was 25 μT.

In four cases the following gradient-echo sequences without and with saturation pulses were performed after injection of gadopentetate dimeglumine: partial saturation 50/20/1 (magnetization transfer pulse, 0 milliseconds); partial saturation 100/20/1 (magnetization transfer pulse, 60 milliseconds); partial saturation 200/20/1 (magnetization transfer pulse, 160 milliseconds); partial saturation 400/20/1 (magnetization transfer pulse, 360 milliseconds); and partial saturation 600/20/1 (magnetization transfer pulse, 560 milliseconds). The TRs of the sequences varied from short (standard T1-weighted) to intermediate (between standard T1-weighted and spin density–weighted). For each different pulse sequence, the pulse width of the saturation pulse was maximized. The duration of the saturation pulse, however, varied with each pulse sequence because of the different TR values and the time required for other pulse sequence operations. The saturation pulse width thus varied from 0 milliseconds at a TR of 50 milliseconds to 560 milliseconds at a TR of 600 milliseconds. The single-section sequences were produced after the routine multisection partial-saturation 3-D imaging; the imaging time for the partial-saturation 3-D images was 3 minutes 25 seconds and for the single-section sequences altogether 16 minutes 39 seconds. In two cases the single-section sequences were produced in the above-mentioned order; in two cases the reverse order was used to exclude error caused by a temporal change in enhancement level after injection of contrast. The section thickness was 7 mm, the data acquisition matrix 192 × 256, and the frequency offset 4 kHz.

In 18 cases single-section gradient-echo partial-saturation 600/20/1 (between standard T1-weighted and spin density–weighted) (saturation pulse, 500 milliseconds) images were produced before and after injection of gadopentetate dimeglumine. The imaging time was 5 minutes 7 seconds. The imaging was performed after the routine partial-saturation 3-D sequence. The section thickness was 7 mm, the data acquisition matrix 256 × 256, and the frequency offset 8 kHz.

Gadopentetate dimeglumine was injected at a dose of 0.1 mmol/kg.

The region of interest method was used for signal intensity measurements. The regions of interest were identical in each sequence. Measurements were made in the enhancing nidus of the tumor, the nonenhancing tumor, edema, white matter, and gray matter. Additional region of interest analysis was performed in the extracranial fat and cerebrospinal fluid. Background noise was measured in the extracranial area.

Contrast indexes (the ratios of the signal intensities of the tissues) were calculated between enhancing tumor and white matter, between enhancing tumor and edema, and between edema and white matter. The magnetization transfer effect was quantified according to the following formula: $(S_0 - S_{MT})/S_0$, where S_0 and S_{MT} are the signal intensities without and with saturation pulse on the corresponding images. Student's paired *t* test was used to compare the contrast values without and with magnetization transfer.

Results

Four cases were studied to compare contrast between enhancing lesion, edema, and normal brain with different TR and magnetization transfer pulse lengths. Two meningiomas, one glioblastoma multiforme, and one arteriovenous malformation (misdiagnosed before surgery as an astrocytoma and used for our analysis as an enhancing lesion similar to neoplasms) were studied. The contrast between enhancing lesions and normal white matter in the different sequences in the absence and presence of magnetization transfer is presented in Figure 1. Without magnetization transfer the maximum contrast index was obtained in all four cases when TR was 100 milliseconds. With off-resonance pulse the contrast could be improved with increasing TR

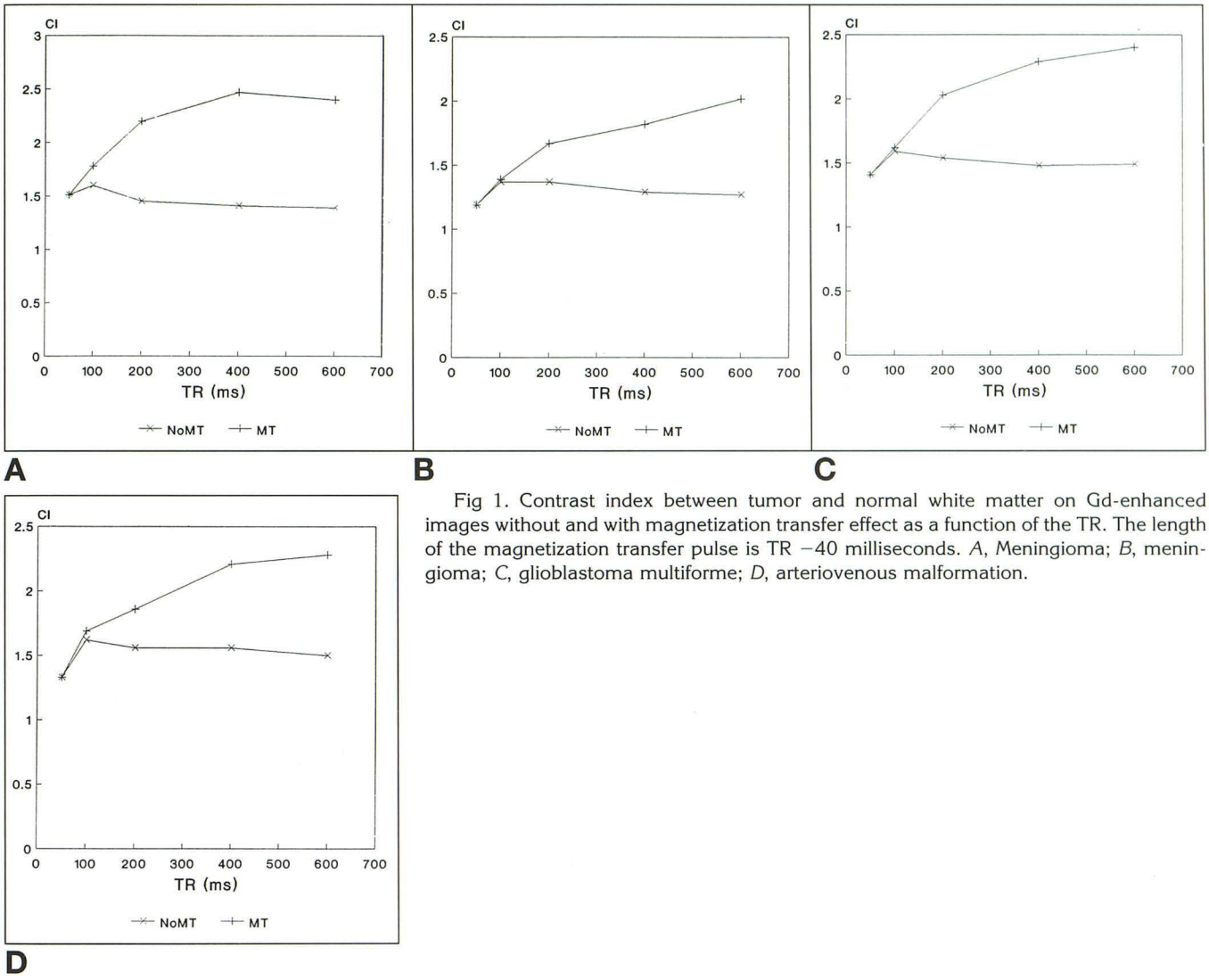


Fig 1. Contrast index between tumor and normal white matter on Gd-enhanced images without and with magnetization transfer effect as a function of the TR. The length of the magnetization transfer pulse is TR −40 milliseconds. *A*, Meningioma; *B*, meningioma; *C*, glioblastoma multiforme; *D*, arteriovenous malformation.

in three cases; in one case the maximum contrast index was found when TR was 400 milliseconds.

The mean contrast indexes between enhancing lesions and edema are presented in Figure 2. The maximum contrast was achieved in all cases when TR was 200 milliseconds both without and with magnetization transfer pulse. The contrast indexes between edema and white matter (Fig 3) increased with increasing TR, and magnetization transfer effect further increased the contrast index. Without magnetization transfer effect edema and white matter were relatively isointense at TR of 600 milliseconds; with magnetization transfer pulse the tissues became isointense at TR of 200 to 400 milliseconds, and edema was hyperintense at TR of 600 milliseconds (Fig 4).

Partial-Saturation 600/20 Magnetization Transfer Imaging

The tumors studied with intermediate-TR partial-saturation 600/20 magnetization transfer sequences included 7 astrocytomas, 7 meningiomas, 1 acoustic neurinoma, 1 brain lymphoma, 1 metastasis, and 1 malignant fibrotic histiocytoma. Significant contrast enhancement with gadopentetate dimeglumine was observed on the standard partial-saturation 3-D 50/20 images in 16 tumors. Six of the tumors were surrounded by marked edema.

The greatest magnetization transfer effect was observed on the unenhanced images in normal brain; magnetization transfer effect was clearly smaller in edema and tumors (Table 1). Magnetization transfer effect in tumors and in edema did not differ significantly. On

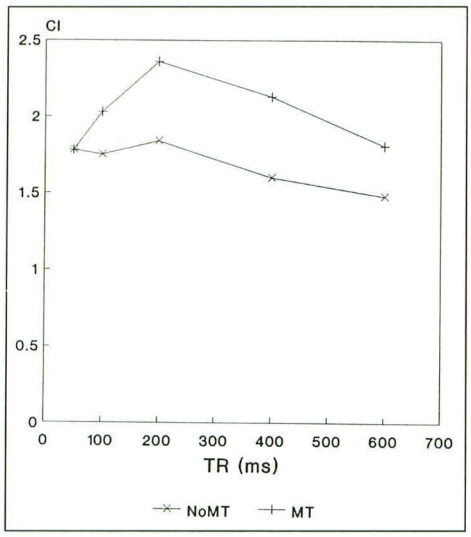


Fig 2. Contrast index (CI) between tumor and edema on Gd-enhanced images without (NoMT) and with (MT) magnetization transfer effect as a function of the TR. Contrast index is expressed as a mean value of four cases. The length of the magnetization transfer pulse is TR −40 milliseconds.

the Gd-enhanced images the magnetization transfer effect decreased clearly in enhancing tumors. The mean magnetization transfer effect in extracranial fat was 0.03 ± 0.01 (n = 14) and in cerebrospinal fluid 0.06 ± 0.05 (n = 7). The background noise was not affected by the magnetization transfer pulse.

On the unenhanced images the mean contrast index between enhancing tumor and white matter (Table 2) was 0.99 ± 0.13 without magnetization transfer and 1.20 ± 0.21 with magnetization transfer. On the Gd-enhanced images the mean contrast index was 1.13 ± 0.17 without magnetization transfer and 1.44 ± 0.25 with magnetization transfer. The increase in contrast index was significant both without and with contrast agent ($P < .001$). On the Gd-enhanced images the contrast index improved in all cases. Contrast improvement was most significant in tumors with prominent Gd enhancement, such as meningiomas (Figs 5 and 6).

The contrast index between enhancing tumor and edema was calculated in six cases with surrounding edema. On the unenhanced images the mean contrast index was 1.01 ± 0.06 without magnetization transfer and 1.01 ± 0.09 with magnetization transfer. On the Gd-enhanced images the mean contrast index was 1.20 ± 0.20 without magnetization transfer and 1.28 ± 0.29 with magnetization transfer. The change in contrast index with magnetization transfer pulse was not significant.

The contrast index between edema and normal white matter was 1.05 ± 0.15 on the unenhanced images without magnetization transfer and 1.35 ± 0.23 with magnetization transfer; the corresponding values on the Gd-enhanced images were 1.06 ± 0.15 and 1.35 ± 0.24, respectively. The difference between the magnetization transfer images and the standard images was significant ($P < .001$). The edema was hyperintense relative to white matter in all cases on the magnetization transfer images.

Discussion

The use of paramagnetic contrast agents has become a standard procedure in MR imaging of intracranial tumors. Paramagnetic substances reduce T1 and T2 relaxation times as a consequence of interactions between unpaired electrons of the paramagnetic ion and water protons (11). When gadopentetate dimeglumine is used at low concentrations, the T1 shortening predominates, resulting in increased signal on T1-weighted sequences. Because gadopentetate dimeglumine does not cross the blood-brain barrier, the normal brain tissue remains unenhanced (12, 13). Enhancement can be ob-

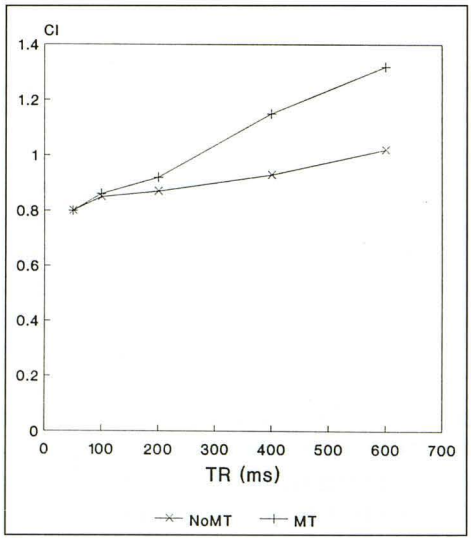


Fig 3. Contrast index (CI) between edema and white matter without (NoMT) and with (MT) magnetization transfer effect as a function of the TR. Contrast index is expressed as a mean value of four cases. The length of the magnetization transfer pulse is TR −40 milliseconds.

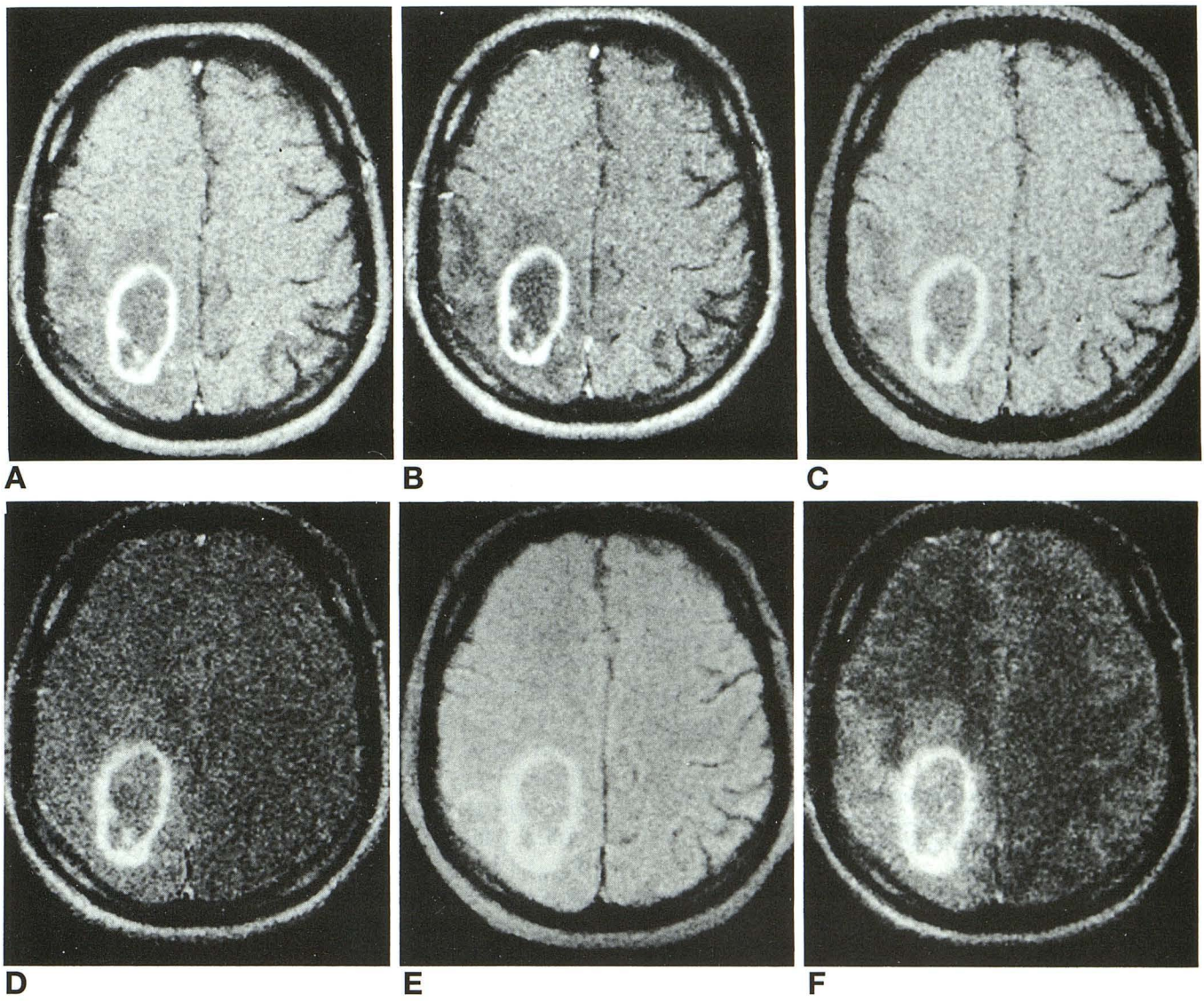


Fig 4. Glioblastoma multiforme. The Gd-enhanced images display ring enhancement, cystic or necrotic centers, and surrounding nonenhancing tumor or edema.

A, Partial-saturation 100/20 image.

B, Partial-saturation 100/20 magnetization transfer image. The contrast between enhancing tumor and brain is improved, and the edema and nonenhancing tumor portions are still hypointense.

C and *D*, The edema and the nonenhancing portions of the tumor are slightly hypointense on partial-saturation 400/20 image (*C*) and become slightly hyperintense on the corresponding magnetization transfer image (*D*).

E, Partial-saturation 600/20 image. The edema and the nonenhancing tumor are isointense relative to normal brain.

F, Partial-saturation 600/20 magnetization transfer image. The edema and the nonenhancing tumor become clearly hyperintense; normal brain tissue is prominently attenuated.

served only in vessels and structures that lack a blood-brain barrier, such as pituitary gland, dura, and choroid plexus. Most intracerebral tumors give rise to blood-brain barrier breakdown, and they enhance with gadopentetate dimeglumine if the perfusion is intact. Extraaxial tumors usually show prominent enhancement.

Dynamic changes in contrast enhancement can complicate to some degree the comparison between different sequences in vivo. Maximal Gd enhancement has been observed in many intracranial tumors about 5 minutes after intravenous injection, and the enhancement usually reduces slowly after that (14, 15). Our magnetization transfer and corresponding standard

TABLE 1: Magnetization transfer effect after a 500-millisecond saturation pulse on unenhanced and Gd-enhanced partial-saturation 600/20 images

Tissue (n)	Magnetization Transfer Value ± SD	
	Nonenhanced Images	Enhanced Images
All tumors (18)	0.30 ± 0.09	0.24 ± 0.06
Astrocytomas (7)	0.23 ± 0.07	0.20 ± 0.06
Meningiomas (7)	0.35 ± 0.04	0.27 ± 0.04
White matter (18)	0.43 ± 0.02	0.42 ± 0.02
Gray matter (18)	0.41 ± 0.03	0.40 ± 0.05
Edema (6)	0.26 ± 0.05	0.25 ± 0.04

images were produced by concurrent acquisition to minimize error possibilities. In the sequence comparison the different single-section images were obtained between 5 and 25 minutes after contrast administration. This period could be expected to provide the most stable enhancement. Because the reversed sequence order had no noticeable influence on the results, we can exclude time-dependent changes as significant causes of error in our results.

Magnetization transfer relies on interactions between two different proton pools of tissues,

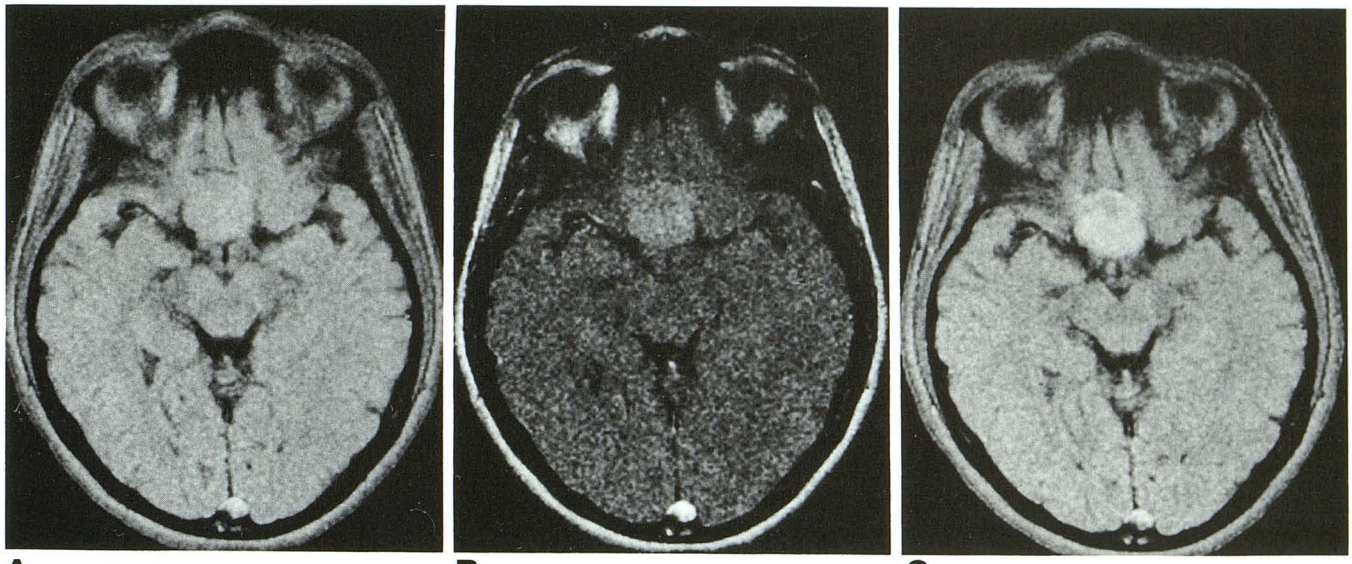
TABLE 2: Contrast indexes between tumors and normal white matter on unenhanced and Gd-enhanced partial-saturation 600/20 images without and with 500-millisecond magnetization transfer pulses

Sex/Age	Diagnosis	UE	UEMT	E	EMT
F/31	Astrocytoma II	0.84	1.05	0.85	1.09
F/30	Astrocytoma III	0.82	1.13	0.84	1.10
F/31	Astrocytoma III	0.92	1.55	1.07	1.68
F/33	Astrocytoma III	0.95	1.27	1.31	1.90
F/43	Astrocytoma III	1.34	1.79	1.37	1.87
M/24	Astrocytoma III	0.81	1.07	0.85	1.08
M/50	Astrocytoma III	0.96	1.23	1.00	1.32
F/33	Meningioma	1.06	1.28	1.30	1.70
F/43	Meningioma	1.05	1.15	1.17	1.39
F/49	Meningioma	0.90	0.98	1.02	1.32
F/53	Meningioma	1.07	1.39	1.31	1.78
F/71	Meningioma	1.01	1.05	1.22	1.42
M/39	Meningioma	1.21	1.23	1.24	1.41
M/70	Meningioma	0.91	1.02	1.19	1.48
F/36	Acoustic neurinoma	0.96	0.98	1.19	1.37
F/69	Lymphoma	0.96	1.17	1.04	1.29
F/66	Metastasis	0.93	1.18	1.40	2.06
M/37	Histiocytoma malignancy	1.04	1.04	1.18	1.33
Mean		0.99	1.20	1.13	1.44
SD		±0.13	±0.21	±0.17	±0.25

Note.—UE indicates unenhanced image; UEMT, unenhanced image with 500-millisecond magnetization transfer pulse; E, Gd-enhanced image; EMT, Gd-enhanced image with 500-millisecond magnetization transfer pulse.

the mobile water pool and the macromolecular pool of restricted motion (1, 16). The mobile water pool, which accounts for the signal in conventional MR imaging, has a narrow bandwidth. The macromolecular pool, which is not detectable in conventional MR imaging, has the same central resonant frequency as the water pool, but a broad bandwidth. Magnetization can transfer between these two pools through dipolar interactions. In conventional MR imaging the longitudinal relaxation of mobile water, which is described by relaxation time T1, consists of intrinsic longitudinal relaxation, magnetization transfer from water to macromolecules, and magnetization transfer from macromolecules to water. When the magnetization in the macromolecular pool is destroyed by an off-resonance saturation pulse, magnetization transfer from macromolecules to water decays. The magnetization in the water pool, M_0, decreases during an off-resonance pulse toward a steady state value, M_s; this exponential decrease is described by the apparent relaxation time in the presence of magnetization transfer pulse, $T1_a$ (3, 17, 18). The relaxation occurs both through intrinsic longitudinal relaxation (described by the relaxation time, $T1_w$) and through magnetization transfer to macromolecules (described by the cross-relaxation rate, R_{wm}) (3, 17, 18). The magnitude of magnetization transfer varies in different tissues, thus creating the contrast. The method has no effect on T2 relaxation times.

The rate of magnetization transfer effect has been demonstrated to provide a good source of contrast in brain MR imaging (6, 10). Magnetization transfer effect in normal brain is large in both white and gray matter. In cerebrospinal fluid the effect is small because of the small number of macromolecules. Magnetization transfer effect varies in different tumors, but it is smaller in most tumors than in normal brain (10). In edema the effect is reduced relative to normal brain tissue. In our study the mean magnetization transfer effect was larger in meningiomas than in astrocytomas, which is in accordance with previous results (10). The large magnetization transfer effect in meningiomas has been attributed to their high collagen content, which has been shown to give rise to large magnetization transfer effect (10). Magnetization transfer cannot be used to separate edema from nonenhancing tumor, because magnetiza-



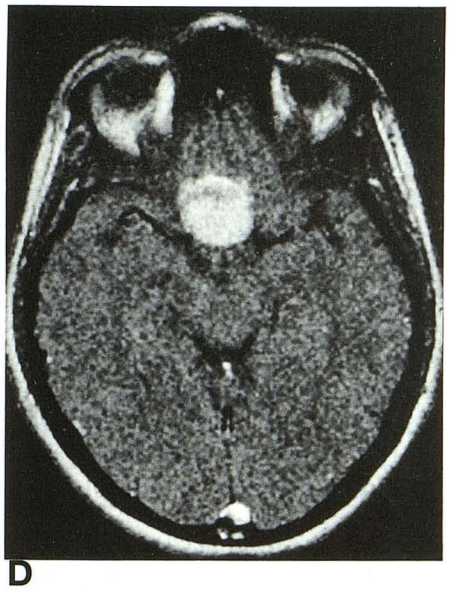


Fig 5. Meningioma.

A, Partial-saturation 600/20 image. The tumor is isointense relative to normal brain.

B, Partial-saturation 600/20 magnetization transfer image. The tumor becomes hyperintense.

C, Meningioma on Gd-enhanced partial-saturation 600/20 image.

D, Partial-saturation 600/20 magnetization transfer image. The contrast between enhancing tumor and normal brain is markedly improved.

tion transfer effect was not significantly different in these abnormalities.

In vitro studies have shown that paramagnetic substances reduce the longitudinal relaxation times, $T1_a$ and $T1_w$, and increase the magnetization, M_s, but have no effect on the cross-relaxation rate, R_{wm} (Hajnal JV, Young IR, The Combined Effects of Gd-DTPA and Magnetization Transfer: A Systematic Phantom Study, in: *Book of Abstracts: Society of Magnetic Resonance in Medicine*, 1992:1411; Yip V, Balaban R, The Effects of Magnetic Resonance Contrast Agents on Magnetization Transfer Contrast, in: *Book of Abstracts: Society of Magnetic Resonance in Medicine*, 1992:1412). The reduced relaxation times and increased available magnetization can be exploited to improve contrast between Gd-enhanced and nonenhanced tissues. Paramagnetic enhancement reduces magnetization transfer effect caused by these changes, thus intensifying paramagnetically enhanced lesions relative to most other structures. In our study the magnetization transfer effect in tumors was smaller on the Gd-enhanced images than on the nonenhanced images.

Previous studies have reported significant contrast enhancement between Gd-enhanced lesions and normal structures on T1-weighted sequences with off-resonance pulse (5–7). We could improve the contrast with magnetization transfer pulse in all cases; the contrast index

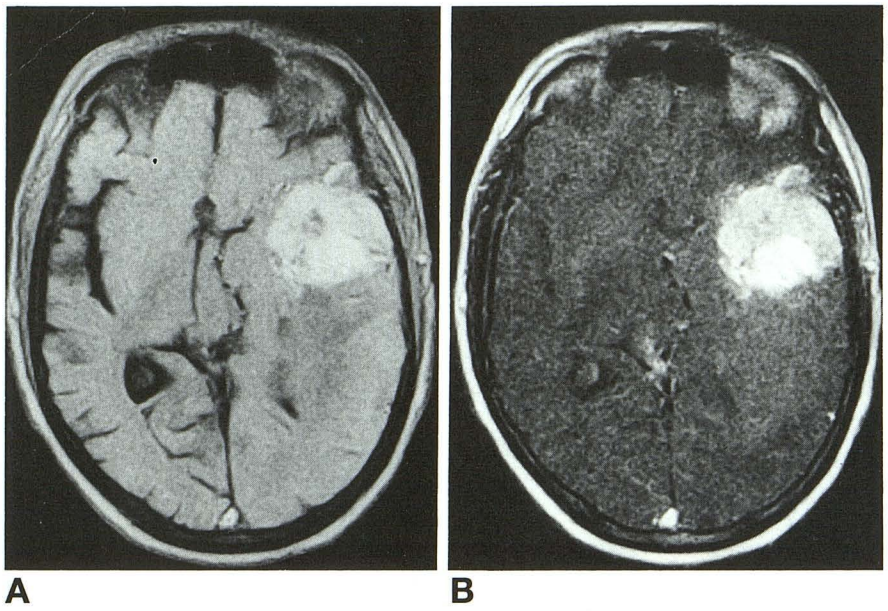


Fig 6. Meningioma.
A, Partial-saturation 600/20 Gd-enhanced image.
B, On the corresponding magnetization transfer image the contrast between enhancing tumor and brain is improved; edema is slightly hyperintense relative to white matter.

increased with longer TR and magnetization transfer pulse. The gained magnetization transfer contrast exceeded the loss of T1 contrast on the intermediate-TR images.

On routine T1-weighted sequences the edema and nonenhancing tumors are hypointense relative to normal white matter because of longer T1 relaxation times. If TR is increased, the sequence becomes more spin-density weighted, and the lesion becomes first isointense and then hyperintense. Magnetization transfer pulse intensifies the signal from abnormalities relative to normal brain. This leads to impaired contrast between them on short-TR magnetization transfer images, but on intermediate-TR magnetization transfer images edema and nonenhancing tumor become hyperintense relative to normal brain (Fig 4). The best contrast between enhancing tumor and edema or nonenhancing tumor is obtained in short-TR imaging. Magnetization transfer effect varies greatly in tumors and edema; the contrast may be improved or impaired on magnetization transfer images. The contrast between enhancing tumor and edema is impaired on intermediate- or long-TR images. In practice, the separation between enhancing tumor and edema can be difficult if

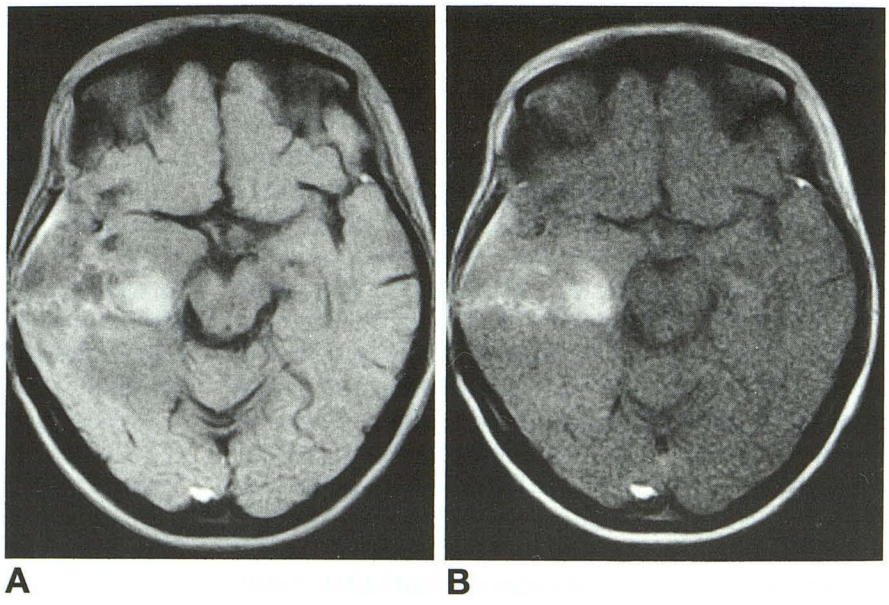


Fig 7. Astrocytoma grade III.
A, Partial-saturation 600/20 image reveals heterogenous enhancement pattern with cystic or necrotic components.
B, On the corresponding magnetization transfer image the contrast between enhancing tumor parts and normal brain is improved. Also, the nonenhancing tumor components are slightly hyperintense, and the separation between Gd-enhanced and nonenhanced tumor portions may be impaired.

the enhancement is very slight. Also, the differentiation between areas within a tumor presenting different degrees of enhancement may be more difficult (Fig 7).

Magnetization transfer contrast resembles in most tissues T2 contrast with two exceptions: the fat and the tissues containing paramagnetic substances. In brain imaging the use of magnetization transfer contrast in Gd-enhanced T1-weighted sequences often presents problems, because the combination of T1 contrast and T2-like contrast can impair the visibility of unenhanced lesions.

There are two possibilities for exploiting magnetization transfer contrast on Gd-enhanced images without losing the visibility of edema and nonenhancing tumor: short-TR imaging with short magnetization transfer pulse (TR less than 150 at 0.1 T) and intermediate-TR imaging with long magnetization transfer pulse (TR greater than 400 at 0.1 T). In short-TR magnetization transfer imaging the contrast between tumor and normal brain is moderately improved, and edema or nonenhancing tumor remains hypointense relative to white matter. Actually, this kind of contrast is obtained in standard T1-weighted multiple-section imaging, which is affected by the magnetization transfer phenomenon (19). In intermediate-TR magnetization transfer imaging a prominent contrast between enhancing lesion and normal brain can be achieved. The edema and nonenhancing tumor, which are hyperintense relative to normal brain, can be separated from normal brain better than with short-TR magnetization transfer imaging. However, the differentiation between enhancing tumor and nonenhancing abnormalities may be inferior to that with short-TR imaging.

T2-weighted or spin density–weighted imaging is usually performed before administration of contrast media. However, T2-weighted or spin density–weighted images after contrast administration have been reported to be beneficial, because they provide the ability to display both enhancing lesion and edema or gliosis on a single image (20). Our results indicate that magnetization transfer sequence demonstrates edema as hyperintense relative to normal brain with shorter TR than conventional sequences; the contrast between enhancing lesion and normal brain on these magnetization transfer images is superior to standard images.

We have demonstrated that magnetization transfer effect improves the contrast between paramagnetically enhanced lesions and normal brain. When magnetization transfer is used in short-TR imaging, the contrast is moderately improved. In intermediate-TR imaging the contrast is markedly improved, and also the nonenhancing lesions are clearly demonstrated. However, intermediate-TR magnetization transfer images probably cannot replace short-TR images, because the differentiation between enhancing and nonenhancing lesions is better on short-TR images. Gd-enhanced intermediate-TR magnetization transfer can be used as an additional sequence, or it may replace the conventional T2-weighted or spin density–weighted sequences.

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