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Contrast-Enhanced Magnetization Transfer MR of the Brain: Importance of Precontrast Images

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PURPOSE: To determine the importance of obtaining precontrast T1-weighted magnetization transfer (MT) MR images for better interpretation contrast-enhanced T1-weighted MT images. **METHODS:** One hundred fifty-five patients referred for MR imaging of the brain were examined prospectively with noncontrast T1-weighted imaging, noncontrast T1-weighted imaging with MT, contrast-enhanced T1-weighted imaging, and contrast-enhanced T1-weighted imaging with MT. In the patients who had abnormally increased signal intensity on postcontrast images (with or without MT), the four imaging sequences were evaluated with regard to number of lesions and lesional signal intensity. For each of the sequences, two experienced neuroradiologists subjectively graded the lesions on a scale of 1 to 4 (4 being the most conspicuous) with regard to abnormally increased signal intensity. **RESULTS:** Twenty-two of the 155 patients had increased signal intensity on one or more of the postcontrast sequences. Eight of these 22 patients had increased signal intensity of one or more lesions on images without MT. All these lesions were seen better on images obtained with MT. An additional six of the 22 patients had increased signal intensity of one or more lesions on images obtained with MT that was not detected on images obtained without MT. Eight of the 22 patients had no high signal intensity on noncontrast images with or without MT. One of the eight had increased number and conspicuity of lesions on postcontrast MT images. **CONCLUSION:** A significant number of patients had increased signal intensity on noncontrast T1-weighted images with MT that was not seen on noncontrast T1-weighted images without MT. This high signal intensity was also visible on postcontrast MT images, and would have been mistaken for pathologic enhancement if noncontrast MT images had not been available for comparison.

Index terms: Brain, magnetic resonance; Magnetic resonance, magnetization transfer

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Magnetization transfer (MT) is an increasingly popular magnetic resonance (MR) imaging technique that produces patterns of tissue contrast that differ substantially from those obtained with conventional spin-echo imaging. Several investigators have suggested that MT combined with paramagnetic contrast agents improves the detection of enhancing lesions, such as intracranial tumors, infection, and infarction (1-6). More specifically, several investigators have documented significant increases in contrast-to-noise ratios of

contrast-enhanced T1-weighted images with MT as compared with those of contrast-enhanced T1-weighted images without MT (1, 5, 6). Recently, others have observed significantly increased signal intensity on noncontrast T1-weighted images with MT in tuberous sclerosis and pediatric brain tumors (7, 8). This effect has the potential to influence the interpretation of contrast-enhanced MT images, because high signal intensity due to MT could be misinterpreted as pathologic contrast enhancement. The purpose of this study was to determine the importance of obtaining noncontrast T1-weighted MT images of the brain for the interpretation of contrast-enhanced T1-weighted MT images.

Patients and Methods

One hundred fifty-five patients referred for contrast-enhanced imaging of the brain were examined prospec-

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tively with the following protocol: T1-weighted MR imaging; T1-weighted MR imaging with MT; injection of a standardized dose of gadopentetate dimeglumine (0.1 mmol/kg); 5-minute delay; contrast-enhanced T1-weighted imaging; and contrast-enhanced T1-weighted imaging with MT. Imaging was performed with three different MR units, and multisection spin-echo T1-weighted sequences were obtained with the following parameters. Scanner 1 (1.5 T): 747/15/2 (repetition time/echo time/excitations), 5-mm-thick sections, and a 218×256 matrix; scanner 2 (1.5 T): 760/15/2, 5-mm-thick sections, and a 230×256 matrix; and scanner 3 (1.0 T): 760/15/2, 5-mm-thick sections, and a 230×256 matrix. The MT pulse was applied before each section excitation pulse. Scanner 1 used a 1-2-1 binomial pulse and scanners 2 and 3 used a 7.68-millisecond gaussian-based pulse offset by 1.5 kHz. The power levels of the radio-frequency (RF) pulses were automatically set by the manufacturer and were within allowable limits of the specific absorption rate. To confirm adequate MT contrast on the three MR units, the percentage of MT $(1 - S_{MT}/S_0) \times 100$ was calculated for white matter and gray matter in four patients on each machine.

Images were evaluated by two neuroradiologists, in concert and by consensus, for areas of abnormally increased signal intensity on each of the four sequences. Lesions were graded on a qualitative scale of 1 to 4, where 1 was minimally increased signal; 2 was mildly increased signal; 3 was moderately increased signal; and 4, markedly increased signal intensity relative to normal brain. The sequences were reviewed in the following order: noncontrast non-MT images, contrast-enhanced non-MT images, noncontrast images with MT, and contrast-enhanced images with MT.

Results

Eighty-six patients were studied at 1.5 T (52 on scanner 2 and 34 on scanner 1) and 69 patients were studied at 1.0 T, on scanner 3. The amount of MT contrast was averaged over four patients on each scanner. In the deep gray matter, MT contrast was 23% with scanner 1, 13% with scanner 2, and 12% with scanner 3. The white matter had an MT contrast of 36% on scanner 1, 18% on scanner 2, and 17% on scanner 3.

Twenty-two patients had increased signal intensity on one or more of the contrast-enhanced sequences. This group comprised 11 men and 11 women (mean age, 52 years) with a total of 76 lesions. Eight of these patients also had increased signal intensity of one or more lesions on the noncontrast non-MT images, and one had an additional area of high signal in a lesion noted on a noncontrast image with MT. All areas of increased signal intensity had higher

scores on noncontrast images with MT than on noncontrast images without MT. Definite abnormal enhancement was noted in five of eight lesions when comparing noncontrast and contrast-enhanced images without MT and when comparing noncontrast and contrast-enhanced images with MT. Three of the eight patients had increased signal intensity on contrast-enhanced MT images that might have been confused with pathologic enhancement if similar high signal had not been observed on the noncontrast MT images. These included two patients who were being examined for recurrent tumor and one patient with a chronic cortical infarction (Figs 1 and 2). Mean signal intensity scores for the contrast-enhanced images with and without MT are shown in Figure 3.

An additional six patients had increased signal intensity of one or more lesions on noncontrast MT images that was not detected on images obtained without MT. Two of these were related to underlying high signal intensity in infarcts, two were due to white matter disease (progressive multifocal leukoencephalopathy and multiple sclerosis), and two were associated with hemorrhage (Fig 4). Five of the six did not show abnormal enhancement in comparisons of noncontrast with contrast-enhanced non-MT images and in comparisons of noncontrast with contrast-enhanced images with MT. One of the six had abnormal enhancement. Mean signal intensity scores for the contrast-enhanced images with and without MT are shown in Figure 5.

The third group consisted of an additional eight patients who had no high signal intensity lesions on noncontrast images with or without MT. All the lesions were seen as well or better on contrast-enhanced images with MT. Only one of the eight patients had an increased number and conspicuity of multiple brain lesions, and these were due to cysticercosis (Fig 6).

Discussion

MT contrast occurs because biological tissues contain varying amounts of mobile and immobile hydrogen (9-11). The immobile (restricted) hydrogen pool consists of protons bound to macromolecules. These restricted protons have a short T2 signal, which leads to a very broad line width and makes them nearly invisible to standard imaging methods. On the

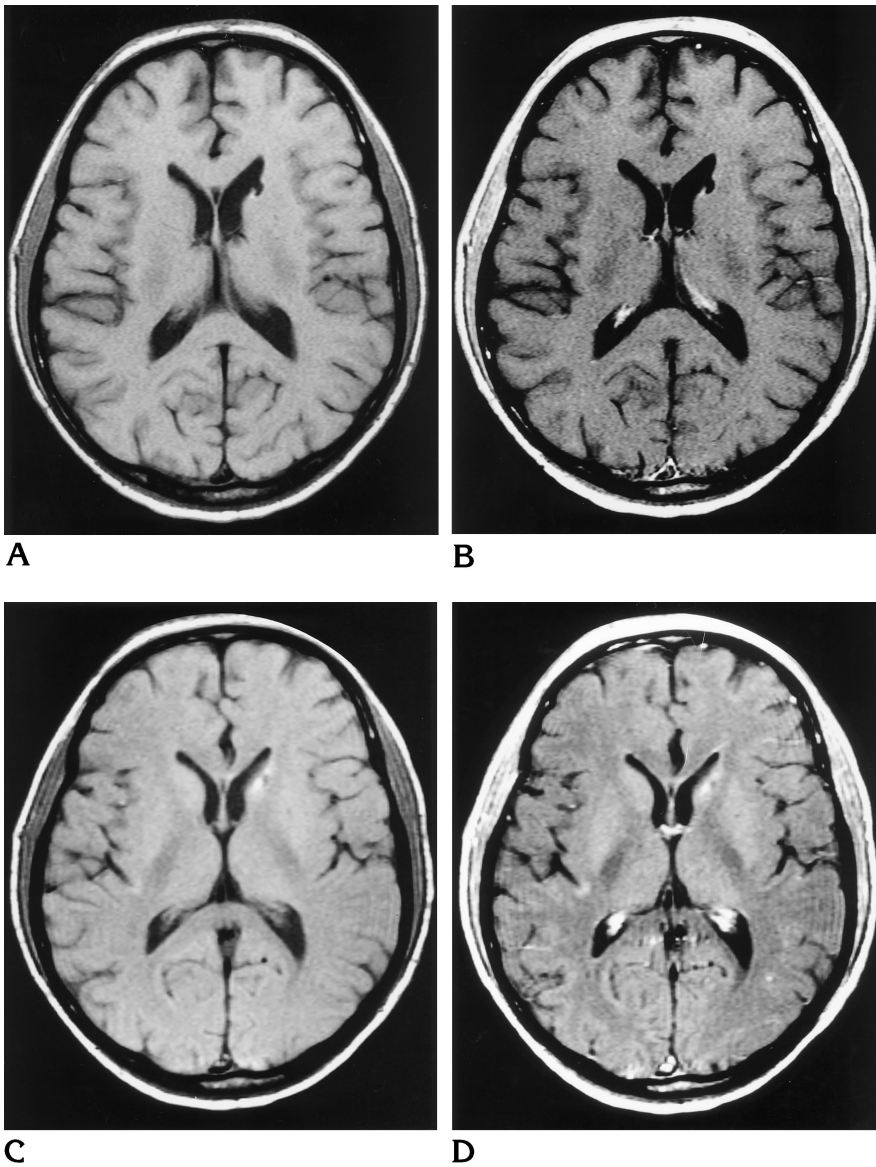


Fig 1. A 30-year-old man with history of treated CNS lymphoma.

A, Noncontrast T1-weighted image shows low signal abnormality in the head of the caudate nucleus on the left. Note subtle increased signal along periphery of the lesion. There is no evidence of mass effect along the frontal horn of the left lateral ventricle.

B, Contrast-enhanced T1-weighted image shows no evidence of abnormal contrast enhancement.

C, Noncontrast T1-weighted image with MT shows increased signal in the head of the caudate nucleus accounting for the signal abnormality on the contrast-enhanced MT image (D).

D, Contrast-enhanced T1-weighted image with MT shows increased signal intensity of the head of the caudate nucleus, which might suggest abnormal contrast enhancement if noncontrast MT image (C) were not available for comparison. Image at 6 month follow-up (not shown) showed new areas of lymphoma in the left occipital lobe without recurrence in the head of the caudate nucleus.

other hand, the mobile hydrogen pool has a very narrow line width (longer T2 signal), making it possible to image.

Conventional imaging sequences are capable of showing mobile hydrogen directly. MT sequences, on the other hand, image the restricted hydrogen pool indirectly. Saturation of the bound hydrogen pool with MT pulses results in decreased signal intensity from the free hydrogen pool by the exchange of longitudinal magnetization between the two groups (9–11). The net effect is greater suppression of signal from normal brain parenchyma (more bound protons) than from pathologic brain lesions (more free protons), which may result in increased lesion conspicuity.

The level of MT contrast depends on how it is applied, the power level used, and the off-resonance frequency response. MT contrast is generated by using either off- or on-resonance pulses. In our study, these methods generated different MT contrast ratios, as implemented on each scanner.

The off-resonance pulse selectively affects the restricted hydrogen pool. The pulse is applied far enough off resonance (>1 kHz) to achieve selective saturation yet near enough to resonance to reduce the amount of power required to saturate the bound pool (9). An advantage of this method is that it is simple to implement and generally more robust. Potential drawbacks of this technique include the long

Fig 2. A 35-year-old woman with history of resection of low-grade glioma.

A, Noncontrast T1-weighted image shows a postoperative defect and signal abnormality of the left posterior frontal lobe.

B, Contrast-enhanced T1-weighted image shows no evidence of abnormal contrast enhancement.

C, Noncontrast T1-weighted image with MT shows the same area of increased signal intensity as on the contrast-enhanced MT image (D).

D, Contrast-enhanced T1-weighted image with MT shows a distinct area of increased signal intensity along the anterior margin of the resection site, which might suggest the possibility of abnormal contrast enhancement if noncontrast MT images were not obtained.

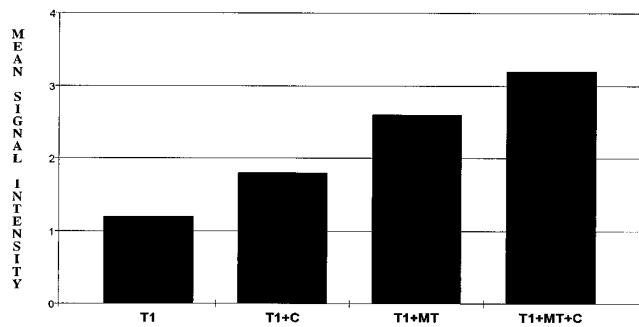
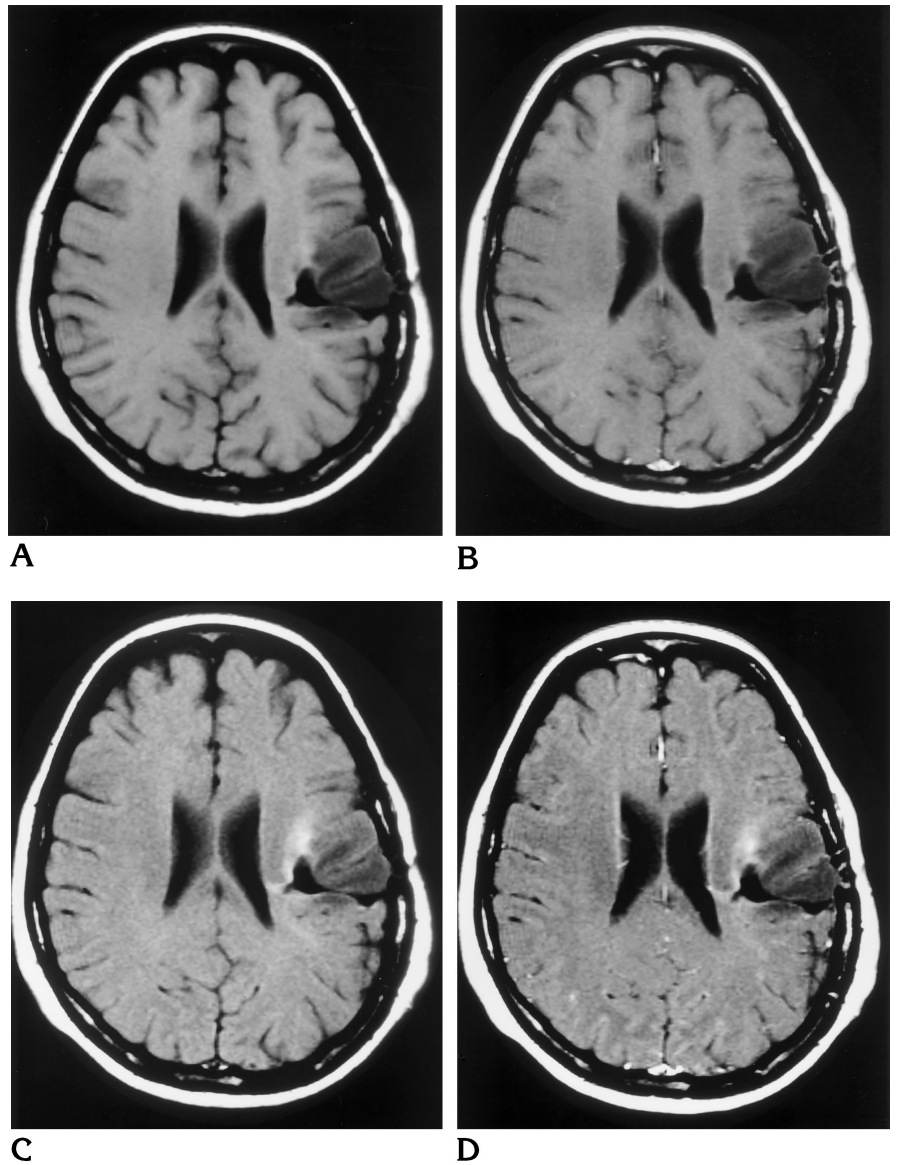


Fig 3. Mean signal intensity scores for contrast-enhanced (C) T1-weighted MR images with and without MT in eight patients who had increased signal intensity of one or more lesions on non-contrast images without MT.

duration of the pulse and the high power required to obtain proper contrast.

The on-resonance approach uses a series of nonselective RF pulses with pulse amplitudes described by the binomial expansion to produce the desired effect (12, 13). The simplest version of these jump-and-return pulses is the 1 – 1 pulse ($90_x - \tau - 90_{-x}$). The first pulse rotates all magnetization into the transverse plane. The delay time, τ , between the pulses is short, several hundred microseconds, but due to the extremely short T2 of the bound protons they dephase immediately relative to the free protons. The “return” RF pulse rotates the free protons back to the longitudinal axis, ready to be

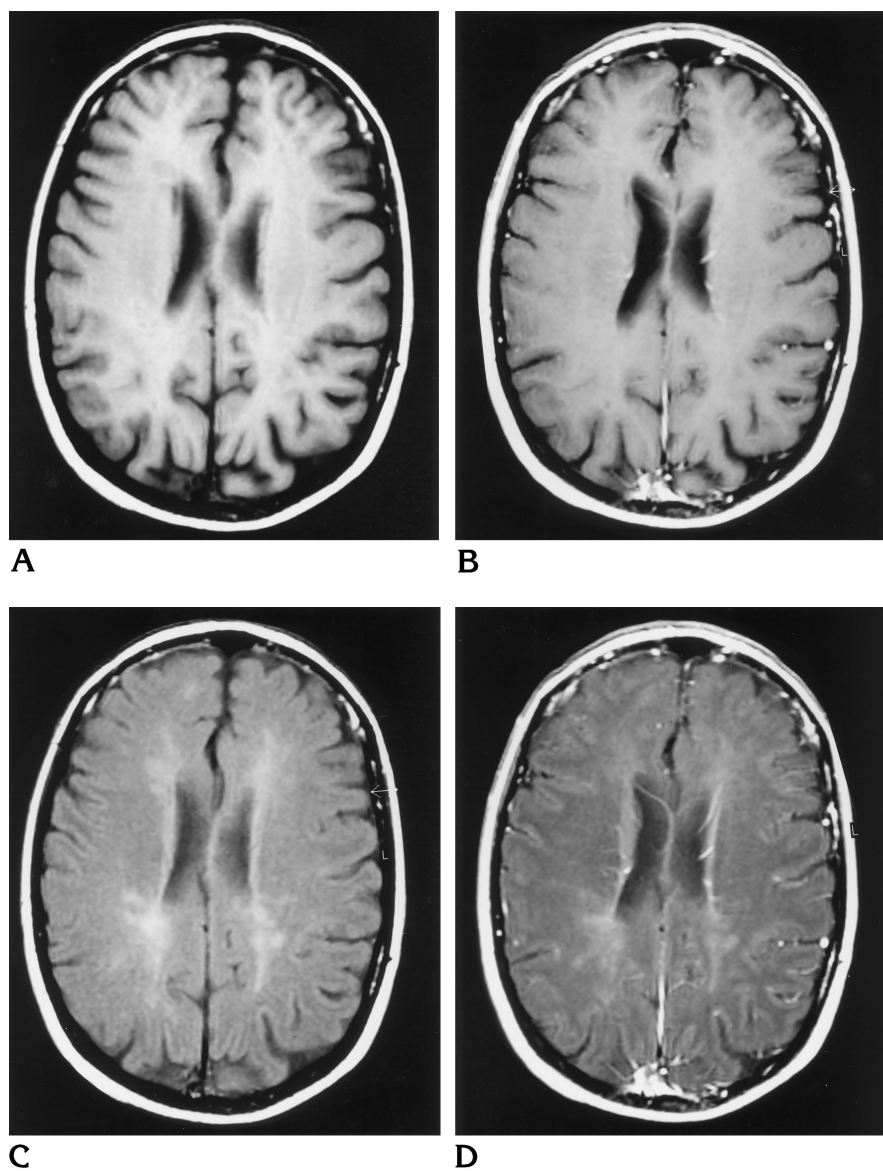


Fig 4. A 53-year-old woman with long-standing history of multiple sclerosis. A, Noncontrast T1-weighted image shows several low signal abnormalities in the centrum semiovale, right greater than left. Note subtle increased signal in the periphery of two of these lesions on the right.

B, Contrast-enhanced T1-weighted image does not show definite abnormal contrast enhancement of the lesions.

C, Noncontrast T1-weighted image with MT shows hyperintense lesions of the periventricular white matter, accounting for the signal changes noted on the post-contrast T1-weighted image with MT (D).

D, Contrast-enhanced T1-weighted image with MT shows prominent hyperintense periventricular lesions that correspond well to abnormalities shown on proton density-weighted images. Without noncontrast MT images, it would be unclear whether these lesions represented abnormal contrast enhancement.

imaged. The bound proton signal is sufficiently decreased owing to the dephasing that occurs during the mixing period. More complicated pulse schemes can be used for optimal saturation effects. The advantage of the on-resonance pulse is that it is considerably shorter in duration than the off-resonance method and may be more energy efficient. However, the sensitivity to field homogeneity and chemical-shift differences may result in direct saturation of the fat or water peaks. The improved efficiency of the on-resonance pulse may account for the increase in MT contrast ratios observed for scanner 1.

Clinically, MT sequences have been shown to improve small-vessel conspicuity on time-of-

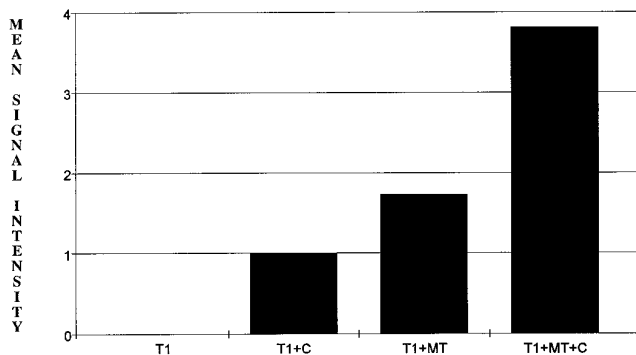


Fig 5. Mean signal intensity scores for contrast-enhanced (C) T1-weighted images with and without MT in six patients who had increased signal intensity of one or more lesions on noncontrast images with MT that was not detected on images without MT.

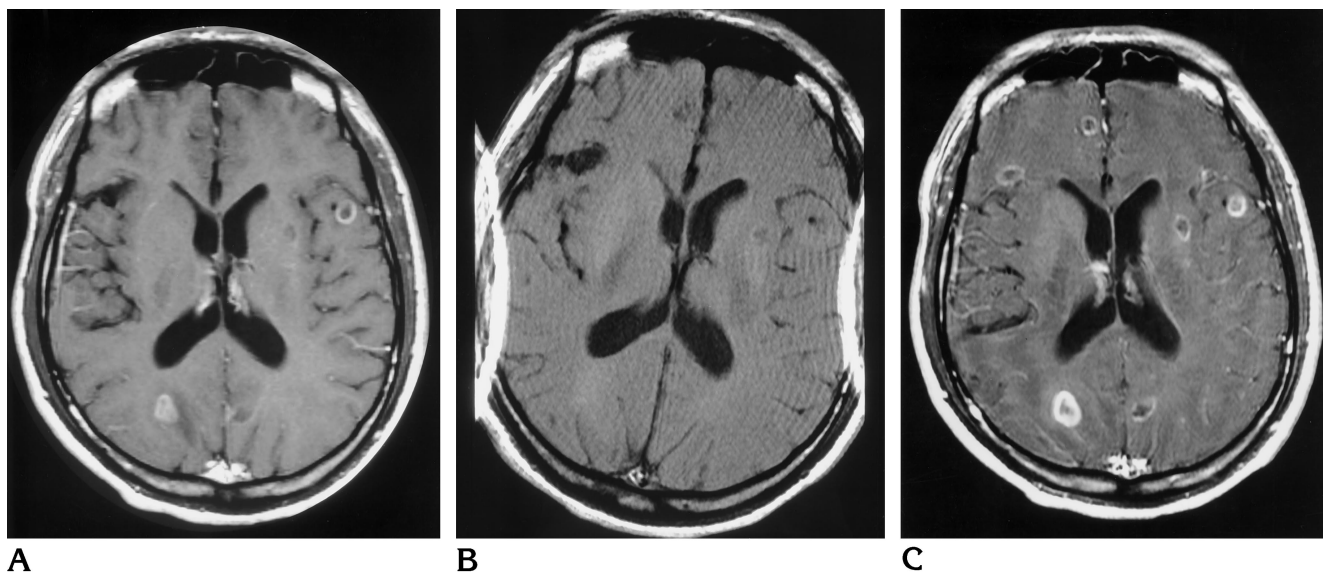


Fig 6. A 26-year-old woman with cysticercosis.

A, Contrast-enhanced T1-weighted image shows enhancing lesions in the right occipital lobe and superficial to the left insula. Possible areas of enhancement are noted in the left basal ganglia and left occipital lobe. A low-signal lesion is noted along the right frontal operculum.

B, Noncontrast T1-weighted image with MT shows areas of low signal intensity in the left basal ganglia, right frontal lobe, and right frontal operculum.

C, Contrast-enhanced T1-weighted image with MT shows several additional ring-enhancing lesions. Note the increased conspicuity of the occipital lesions compared with postcontrast T1-weighted image without MT.

flight intracranial MR angiograms; improve contrast on gradient-echo images of the cervical spine; provide tissue characterization in head and neck cancer, meningiomas, intracranial hemorrhage, wallerian degeneration in the feline visual system, and multiple sclerosis lesions; and improve detection of pathologic contrast enhancement on MR images (14–18).

It is well documented that MT sequences improve the conspicuity of contrast enhancement by suppressing background tissue signal intensity. This effect has been shown to be both dose related and synergistic (5, 19). Finelli et al (20) reported similar relative contrast improvement with triple-dose contrast-enhanced non-MT images compared with single-dose contrast-enhanced images with MT suppression. The synergistic effect is due to the fact that paramagnetic contrast agents decrease the MT effect within enhancing lesions, thereby further accentuating differences between enhancing lesions and background tissues (19). Therefore, the signal intensity of enhancing lesions is only minimally decreased with MT, much less than the background brain, which experiences a more pronounced reduction in signal intensity.

MT sequences are also highly sensitive to

differential MT ratios in normal brain and in nonenhancing pathologic brain lesions. Differential MT ratios in normal brain account for the typical gray/white matter reversal and high signal intensity of the basal ganglia observed on noncontrast T1-weighted images with MT (21). Similarly, differential MT ratios of pathologic brain lesions have recently been shown to be highly sensitive for detection of tuberous sclerosis and some brain tumors on noncontrast T1-weighted images with MT (7, 8).

A recent study by Mehta et al (6) suggested that MT pulses had little effect on noncontrast T1-weighted images in the first 14 patients of their 86-patient series. For time and cost considerations, they eliminated the noncontrast MT images in the remainder of their series. Our results differ from theirs in that a significant number of our patients (six of 22) had increased signal intensity on images obtained with MT that were not present on images obtained without MT, which influenced the qualitative interpretation of the contrast-enhanced MT images. Furthermore, eight of 22 patients had more pronounced increased signal intensity on the MT images than on the non-MT images, and this also influenced the qualitative interpretation of the contrast-enhanced MT images. This in-

creased signal intensity was related solely to the MT effect of nonenhancing tissue.

High signal on noncontrast images due to the MT effect on pathologic tissues is potentially problematic when interpreting contrast-enhanced images for the presence of abnormal enhancement. In our first group, in which the mean lesional signal intensity scores on unenhanced MT images were higher than on unenhanced non-MT images, a comparison of enhanced with unenhanced non-MT images is misleading. Simply documenting higher signal intensity on the contrast-enhanced MT images did not necessarily correlate with contrast enhancement. Rather, the mean signal intensity ratings show that a significant percentage of the signal change was due to MT effect alone.

The noncontrast MT effect was potentially even more problematic in the second group (six of 22 patients), in which high signal intensity on noncontrast images was seen only on those obtained with MT. Without a noncontrast MT image, all areas of increased signal intensity on contrast-enhanced MT images could be incorrectly attributed to enhancement, which could result in misdiagnosis of enhancement, as seen in three of six cases in which contrast-enhanced MT images showed increased signal intensity without high signal intensity on contrast-enhanced non-MT images. This might adversely affect diagnosis and treatment planning in a variety of pathologic conditions, including multiple sclerosis, brain infarction, and tumors.

Our study demonstrates the importance of comparing noncontrast with contrast-enhanced MT images. A significant number of patients had increased signal intensity on unenhanced MT images that was not identified on images obtained without MT. This increased signal contributes to the signal intensity on contrast-enhanced MT images, and could have been mistaken for enhancement if noncontrast MT images had not been available for comparison. Caution should be exercised when comparing postcontrast T1-weighted images without MT with postcontrast T1-weighted images with MT because of the potential for misdiagnosis resulting from false identification of contrast enhancement.

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