# Enhanced and Unenhanced MR with Magnetization Transfer in Multiple Sclerosis

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**PURPOSE:** To evaluate the use of magnetization transfer and the apparent enhancement of lesions on contrast-enhanced MR images in patients with multiple sclerosis. **METHODS:** Contrast-enhanced T1-weighted spin-echo MR images obtained in 20 patients with relapsing-remitting multiple sclerosis, with and without magnetization transfer, were evaluated to determine the number of enhancing plaques. Comparison was made with unenhanced T1-weighted magnetization transfer images. Contrast-to-noise ratios were obtained for these lesions on both the enhanced and unenhanced magnetization transfer T1-weighted spin-echo MR images. **RESULTS:** Ten plaques were considered enhancing only when the enhanced magnetization transfer T1-weighted images (11% or more) were used; however, they were all hyperintense on unenhanced T1-weighted magnetization transfer images. The contrast-to-noise ratios of these lesions were 16.52 for the enhanced images and 15.65 for the unenhanced images. The two values were not statistically different. **CONCLUSIONS:** In patients with multiple sclerosis, examination with contrast-enhanced magnetization transfer MR images alone may overestimate the number of enhancing plaques.

**Index terms:** Magnetic resonance, contrast enhancement; Magnetic resonance, magnetization transfer; Sclerosis, multiple

*AJNR Am J Neuroradiol* 17:1837–1842, November 1996

The activity of multiple sclerosis (MS) is judged on magnetic resonance (MR) images by plaque enhancement after intravenous injection of contrast material (1, 2). Delayed MR imaging and administration of high doses of contrast agent increase the detection of enhancing lesions (3, 4). The magnetization transfer (MT) technique can improve the sensitivity of enhanced MR imaging (5–9) because the contrast-to-noise ratio (C/N) between enhancing lesions and white matter is more than doubled (7); however MT is able to modify the tissue contrast on unenhanced MR images as well (6). Grossman et al (10) have described better delineation of unenhancing MS plaques on T1-weighted sequences with MT and even correlated the activity of these lesions with their MT ratios.

The aim of our study was to ascertain whether on the enhanced MT images all the lesions of higher signal intensity than the suppressed white matter actually enhanced after administration of contrast material.

## Subjects and Methods

Fifty patients with relapsing-remitting MS were examined. All patients had a similar drug regimen, and all had both unenhanced and contrast-enhanced MR imaging performed on a 1.5-T system. Twenty patients were selected because of the presence of enhancing lesions on MR images.

### *Imaging Technique*

Contiguous axial spin-echo MT T1-weighted images covering the whole brain were obtained before injection of gadopentetate dimeglumine at the standard dose of 0.1 mmol/kg. The following parameters were used for MT T1-weighted MR images: 652/15/2 (repetition time/echo time/excitations); 90° flip angle; 5-mm-thick sections; 25-cm field of view; and an acquisition time of 7.09 minutes. With conventional T1-weighted images, the param-

Received February 27, 1996; accepted after revision June 22.

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AJNR 17:1837–1842, Nov 1996 0195-6108/96/1710–1837

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eters were 500/20/2; 90° flip angle; 5-mm-thick sections; 25-cm field of view; and an acquisition time of 5.29 minutes.

Five minutes after contrast injection the same spin-echo T1-weighted sequence was repeated with and without the MT pulse. To avoid the bias introduced by the time elapsing since injection, the sequences were acquired randomly.

The MT pulse used was a 50-millisecond sinc-gaussian pulse, cut off at the third zero crossing, with a duration of 15 milliseconds, an amplitude of 620°, power of 15.7 $\mu$T, bandwidth of 400 Hz, frequency offset of 2000 Hz, and off resonance. The MT pulse was applied before each excitation pulse.

### *Imaging Analysis*

Enhancing plaques were identified independently by two neuroradiologists who were blinded to the sequences. In case of disagreement, a third senior neuroradiologist reviewed the images and a final consensus was reached. The number of the enhancing lesions on both conventional and MT T1-weighted spin-echo images was determined.

C/Ns were obtained for those MS plaques considered enhancing only on the MT T1-weighted spin-echo images and for the corresponding areas seen on the MT T1-weighted spin-echo images obtained before contrast injection.

The C/N was defined as the difference in signal intensity (SI) between the enhanced lesion and the background white matter, divided by noise, according to the following formula: $C/N = (SI_{lesion} - SI_{WM})/noise$, where WM indicates white matter.

Statistical analysis of the data was performed with the paired Student's *t* test.

## Results

Ninety-four enhancing plaques were seen on the conventional T1-weighted spin-echo images (mean, 4.7) and 104 (mean, 5.2) on the MT T1-weighted spin-echo images (11% increase, $P < .05$).

Ten lesions were considered enhancing on the contrast-enhanced MT T1-weighted spin-echo images (Figs 1B, 2B, and 3B), but these lesions were also identified on unenhanced MT images as hyperintense areas (Figs 1C, 2C, and 3C). The mean C/N of these lesions was 16.65 (SD 3.22) on the enhanced MT images. The corresponding areas seen on the unenhanced MT T1-weighted spin-echo images showed a mean C/N of 15.52 (SD 2.97). The difference in C/N on the unenhanced and enhanced T1-weighted MT images was not statistically significant ($P < .59$). Results are reported in the Table.

## Discussion

The sensitivity of contrast-enhanced MR imaging in detecting active MS plaques is reported to be from five to 10 times higher than that of clinical evaluation (11). For this reason, contrast-enhanced MR imaging is used to observe patients undergoing new therapeutic trials (12). The use of high doses of contrast material (two or three times the usual dose) and delayed scanning can improve the sensitivity of MR imaging. Recent studies report that the sensitivity of MR imaging in detecting enhancing lesions greatly increases with a double dose of gadopentetate dimeglumine (3, 4, 13).

The MT pulse is able to modify the tissue contrast on MR images (6). When used with T1-weighted sequences after injection of contrast material, MT is reported to double the C/N between an enhancing lesion and white matter (7). Also, an increased number of enhancing lesions (such as metastases) can be seen on enhanced MT T1-weighted spin-echo images (7). Other studies have shown that MT images obtained with a single dose of contrast agent show areas of abnormal enhancement as effectively as those obtained with a triple dose of contrast and conventional T1-weighted spin-echo images (14, 15). In most of the studies evaluating the usefulness of the MT pulse in the detection of enhancing lesions, enhanced MT

**Number and contrast-to-noise ratios of enhancing lesions on MR images obtained with various techniques**

| Technique | No. of Lesions | Contrast-to-Noise Ratio (SD)* |
|---|---|---|
| Conventional T1-weighted SE | 94 | . . . |
| MT T1-weighted SE | 104 | . . . |
| Contrast-enhanced MT T1-weighted | 10 | 16.65 (3.22) |
| Unenhanced MT T1-weighted | 10 | 15.52 (2.97) |

Note.—MT indicates magnetization transfer; SE, spin-echo.

* $P < .59$ (paired Student's *t* test).

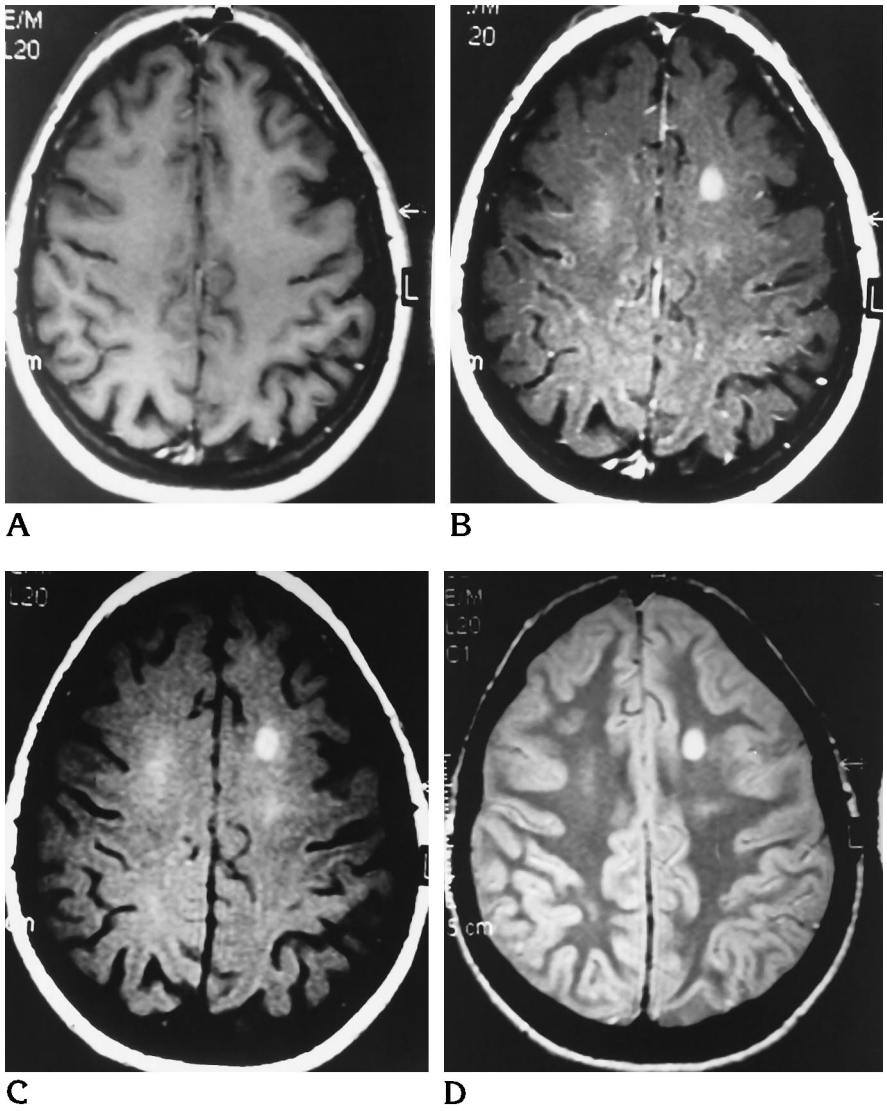

Fig 1. Contrast-enhanced conventional T1-weighted spin-echo MR image (*A*) and MT T1-weighted image (*B*). Note hyperintense round lesion in *B*, indicating the presence of an enhancing plaque. Other hyperintense areas are seen in the cerebral white matter. The round lesion, as well as the others, are not visible on the contrast-enhanced conventional image (*A*) but are clearly identified on the unenhanced MT T1-weighted image (*C*). This suggests a lower MT ratio of these lesions rather than true enhancement. The lesions are hyperintense on the proton density–weighted image as well (*D*).

images were compared with enhanced conventional images. Since noncontrast MT images were generally not obtained, the "real" increase of enhancement on MT images was never evaluated.

MT pulses produce patterns of tissue contrast that differ from those seen on conventional spin-echo images (6). The signal intensities of both normal brain structures and lesions are affected by the use of an MT pulse. Several gray matter structures have higher signal intensity than white matter on MT T1-weighted images. The differential MT ratios of unenhancing lesions and normal white matter may affect imaging contrast as well (7). Demyelinated white matter shows a lower MT ratio than the normal-appearing white matter (10, 16). The lowest MT ratios correspond to the histopathologic findings of myelin and axon destruction (17). Boorstein et al (18) described decreased MT ratios in the normal-appearing white matter around metastatic lesions in the brain. They suspected that this decrease resulted either from the destruction of myelin, which provides less available saturated immobile water protons for cross relaxation, or from increased extracellular fluid, such as vasogenic edema. Kucharczyk et al (19) demonstrated that, in vitro, galactocerebroside has the strongest effect on relaxivity and MT of all the major white matter lipids. They stated that the large number of hydroxyl groups in galactocerebroside and the conformation of the glycolipid head group at the membrane surface are responsible for these effects. Galactocerebroside is one of the components of myelin, and, along with other lipids, is known to be

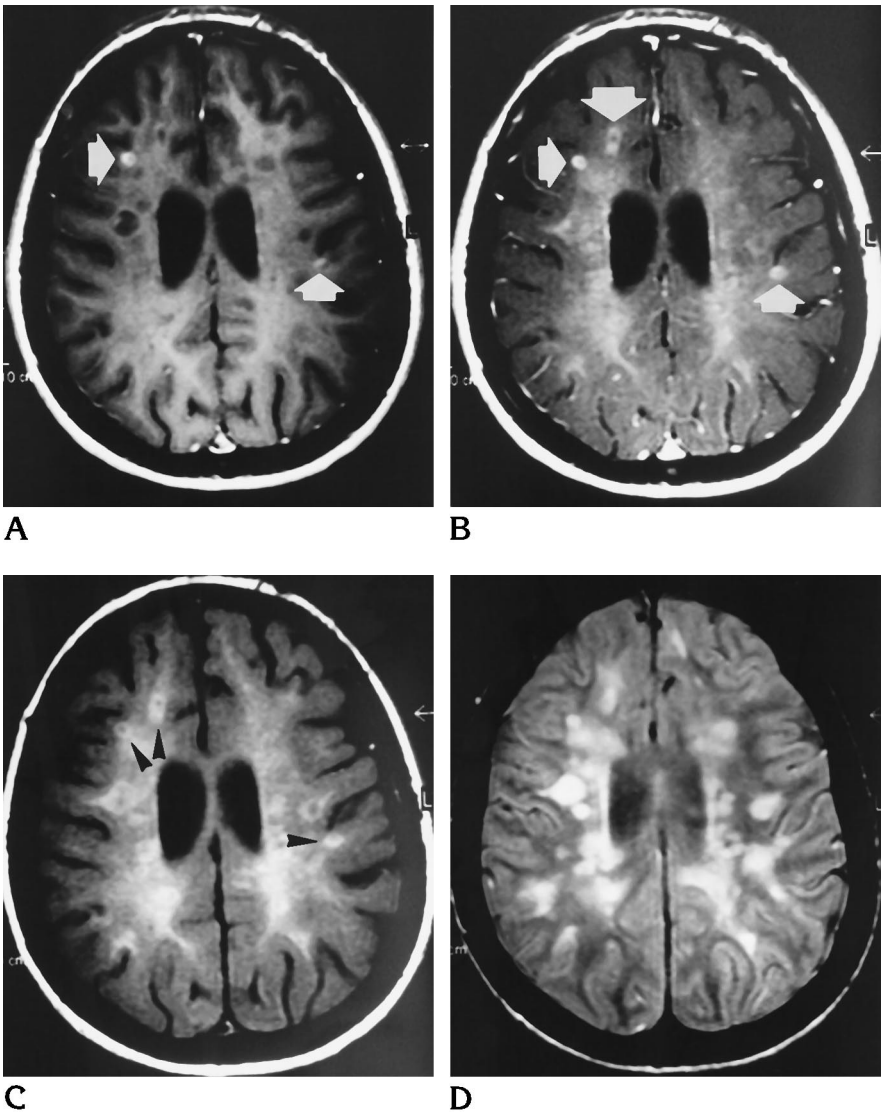


Fig 2. Contrast-enhanced conventional T1-weighted spin-echo MR image (*A*) and MT T1-weighted image (*B*). Two enhancing lesions are seen on the conventional spin-echo image (*arrows, A*), whereas three enhancing plaques are evident on the contrast-enhanced MT T1-weighted sequence (*arrows, B*). All lesions are clearly identified in on the unenhanced MT T1-weighted image (*arrowheads, C*). *D,* Proton density–weighted image of the same section.

decreased in MS plaques. Accordingly, Hiehle et al (8) suggested that diminished MT ratios may reflect diminished myelin content.

For these reasons, both enhancing and unenhancing MS plaques are more evident on MT T1-weighted images. The effect of the longer T1 and T2 relaxation times and increased proton density in reducing the MT ratio is not well known (7). Recently, Ulmer et al (20) stated that in off-resonance saturation imaging both spin-lock and MT effects are most likely involved at the frequency offset ranging from 300 to 2000 Hz from water resonance. Very long T1 and T2 relaxation times reduce the spin-lock effect. Parenchymal lesions with increased free water content and long T2 relaxation times (ie, demyelineated plaques) will be slightly hyperintense on saturated T1-weighted images because of the lack of suppression relative to normal brain tissue (Figs 1B and C, 2B and C, and 3B and C).

On this basis, we evaluated whether the signal intensity of some MS plaques, as observed on unenhanced MT T1-weighted spin-echo images, could be responsible for a false enhancement on contrast-enhanced MT T1-weighted images. Our data revealed that the MT pulse increases the number (by 11% or more) of hyperintense areas thought to be enhancing lesions (Figs 1, 2, and 3). This occurred with the use of a standard dose (0.1 mmol/kg) of contrast material. Importantly, all lesions considered enhancing on the MT T1-weighted images were clearly seen as hyperintense areas on the unenhanced MT images (Figs 1C, 2C, and 3C). The C/N of these lesions and the C/N of the

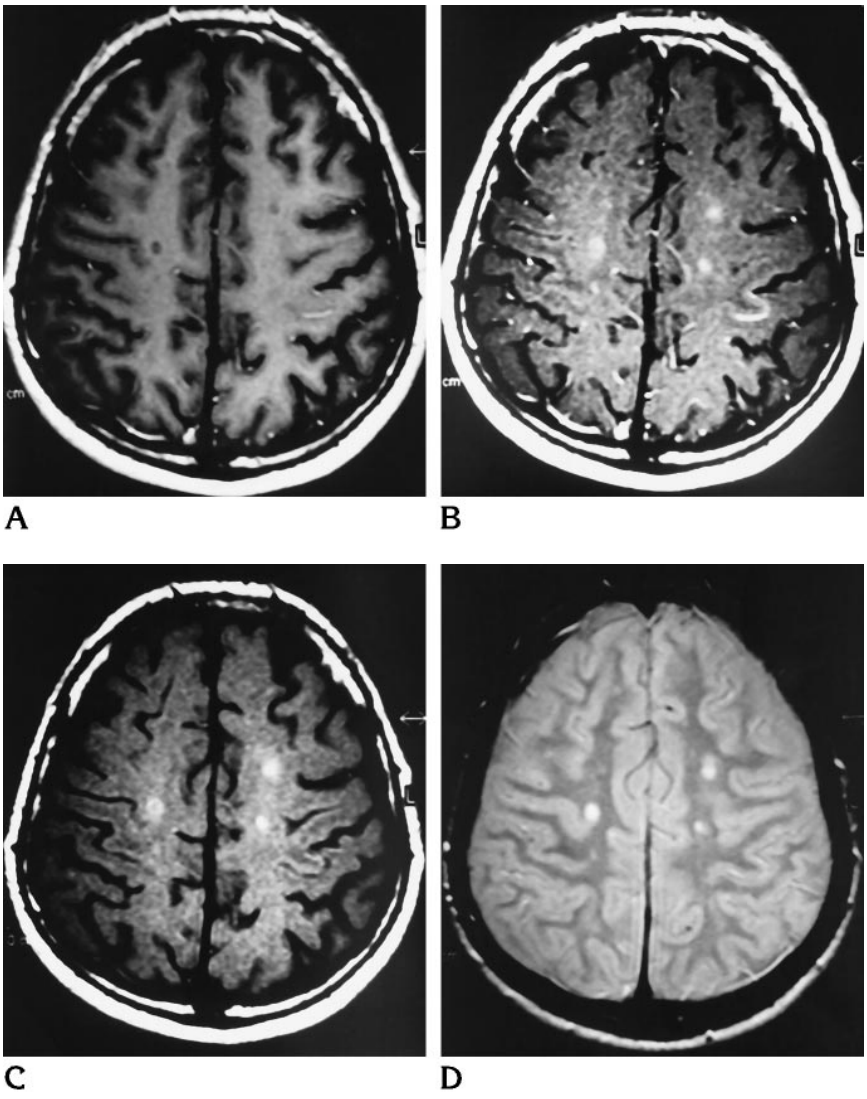


Fig 3. No enhancing plaques are present on the contrast-enhanced conventional T1-weighted spin-echo MR image (*A*). Three enhancing lesions are seen on the MT T1-weighted image (*B*); however, they are also seen on the unenhanced MT T1-weighted sequence (*C*). On the proton density–weighted image, all the lesions appear hyperintense (*D*).

corresponding areas on unenhanced MT T1-weighted images were not statistically different ($P < .6$). The mean value of C/N was 16.65 on the enhanced MT images and 15.52 on the unenhanced MT images. This suggests that the increased signal of some of these plaques on enhanced MT T1-weighted spin-echo images is mostly related to the lower MT ratio of the plaques itself rather than to real enhancement (Fig 1). These lesions could represent areas with more myelin destruction. Whether they carry a poorer prognosis or have other clinical significance is an intriguing matter that should be assessed.

In conclusion, our study confirms that the use of an off-resonance MT pulse increases the signal intensity of unenhancing plaques because of their lower MT ratio. This may cause false enhancement of plaques that are not in the acute, inflammatory enhancing phase. Thus, in patients with MS, MT T1-weighted spin-echo images should always be obtained before and after administration of contrast material to avoid overestimation of disease activity.

## Acknowledgment

We thank Carmelita Marinelli for her helpful technical assistance.

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