

Allen D. Elster, MD • James C. King, MD • Vincent P. Mathews, MD • Craig A. Hamilton, PhD

## Cranial Tissues: Appearance at Gadolinium-enhanced and Nonenhanced MR Imaging with Magnetization Transfer Contrast<sup>1</sup>

**PURPOSE:** To determine the relative contrast of normal cranial tissues at magnetization transfer (MT) spin-echo magnetic resonance (MR) imaging.

**MATERIALS AND METHODS:** MR imaging at 1.5 T was performed with conventional spin-echo techniques without and with off-resonance MT saturation pulses. The signal intensities of normal cranial tissues were measured in 10 healthy volunteers on spin-density- and T2-weighted images and in 10 patients on T1-weighted images obtained before and after administration of gadopentetate dimeglumine.

**RESULTS:** MT saturation produced a significant ( $P < .01$ ) reduction in signal from all tissues except cerebrospinal fluid and fat. Several gray matter structures had higher signal intensity than white matter on T1-weighted MT images. After administration of gadopentetate dimeglumine, imaging with the MT sequence increased visualization of normally enhancing structures.

**CONCLUSION:** MT saturation pulses produce new patterns of tissue contrast that differ substantially from those seen on conventional spin-echo images.

**Index terms:** Brain, MR, 10.121417 • Magnetic resonance (MR), magnetization transfer contrast

**Radiology 1994;** 190:541-546

<sup>1</sup> From the Department of Radiology, Bowman Gray School of Medicine, Wake Forest University, Medical Center Blvd, Winston-Salem, NC 27157-1088. From the 1993 RSNA scientific assembly. Received August 10, 1993; revision requested September 24; revision received October 4; accepted October 8. Address reprint requests to A.D.E.

© RSNA, 1994

See also the article by Mathews et al (pp 547-552) in this issue.

**M**AGNETIZATION transfer (MT) is a relatively new magnetic resonance (MR) imaging technique that allows suppression of signal from tissues in which macromolecular interactions with water molecules contribute substantially to relaxation (1-3). Although many variations of this method are possible, the usual MT technique consists of applying off-resonance radio-frequency saturation pulses selectively to saturate the pool of macromolecular protons (4,5). MT saturation of this macromolecular pool then modulates the MR signal from the nearby water molecules, presumably by means of dipolar cross-coupling and chemical-exchange interactions (6-8).

Findings in preliminary studies have demonstrated that the MT technique may be useful in several cranial imaging applications: for improving the visualization of small vessels at time-of-flight MR angiography (9-11); for increasing tissue contrast in gradient-echo imaging (12); for demonstrating the internal structure of the eye (13); for assessing the integrity of myelin (14-16); for detecting cerebral infarction (17); and for delineating a variety of intracranial mass lesions, with and without gadolinium enhancement (4,18-22). As MT techniques become more widely disseminated and used for general diagnostic purposes, it becomes increasingly important to recognize and document how these pulses alter the image contrast of *normal* intracranial tissues.

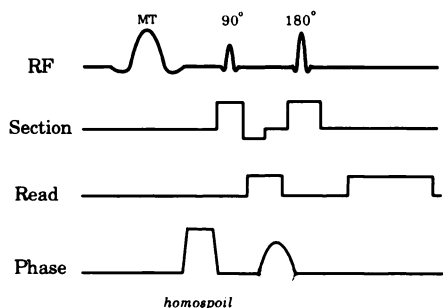
### MATERIALS AND METHODS

MR imaging was performed on a 1.5-T unit (Signa; GE Medical Systems, Milwaukee, Wis). An MT pulse was produced by modifying the standard chemical-shift selective saturation pulse available on this system (Fig 1). The resultant MT saturation pulse had a bandwidth of 220 Hz and an envelope composed of a 16-msec, apodized sinc function with two side lobes.

The frequency offset of this pulse was set at 1,200 Hz downfield from the water resonance. The pulse amplitude was maximized to produce a peak radio-frequency field flux density ( $B_1$ ) of 7.3  $\mu$ T. After each MT pulse, gradient homospoiling was performed by turning on the y-axis (phase-encoding) gradient to maximum amplitude for about 5 msec. (The purpose of this spoiling pulse was to prevent possible interference patterns with the next radio-frequency pulse.) Allowing for gradient ramp times, the interval between the end of the MT pulse and the beginning of the 90° pulse was approximately 6 msec.

The MT pulse sequence was tested in 20 subjects: (a) 10 healthy volunteers (five men and five women, aged 24-27 years) who underwent noncontrast imaging only and (b) 10 patients (three men and seven women, aged 31-76 years) who underwent gadolinium-enhanced imaging as part of their work-up for suspected neurologic disease. The conventional precontrast MR images of these 10 patients were judged to be unequivocally normal by three experienced neuroradiologists (A.D.E., J.C.K., V.P.M.). Patients were enrolled for the contrast material-enhanced portion of the study so that volunteers would not be exposed to any possible risk, however small, of an adverse reaction to gadolinium. Overall, therefore, our cohort of 20 subjects comprised eight men and 12 women, aged 27-76 years (median, 38½ years). Informed consent for the administration of gadolinium and/or for the testing of the MT sequences was obtained from each subject. Approval was obtained from our local institutional review board and from GE Medical Systems to operate the MR imager in an investigational mode. Specific absorption rates were carefully monitored in every case and remained below limits mandated by the U.S. Food and Drug Administration (average, 3.2 W/kg for the whole head and 8.0 W/kg for any single gram of cranial tissue).

Spin-density- and T2-weighted spin-echo imaging were performed with and without MT pulses in the 10 volunteers, with use of the following parameters: plane of imaging, transaxial; repetition

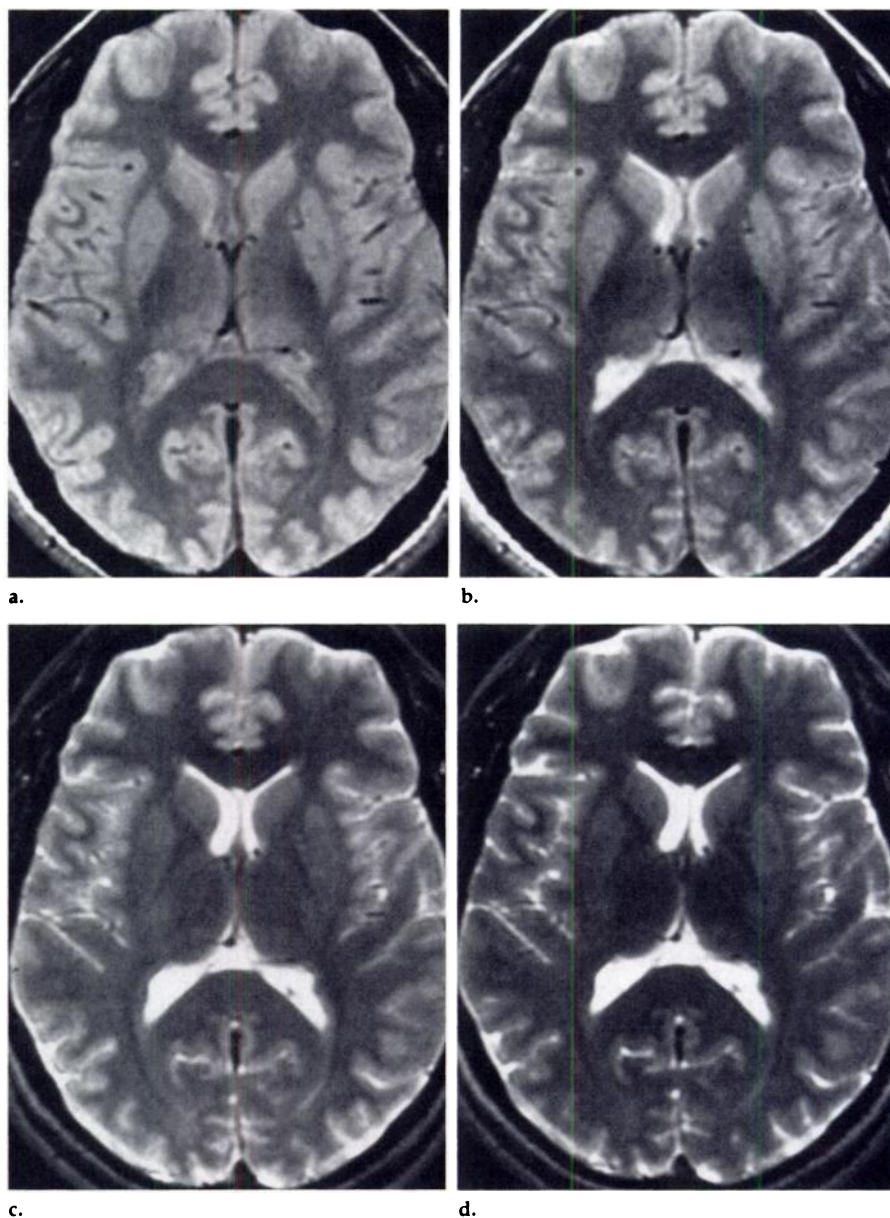


**Figure 1.** Diagram of the pulse timing of the MT spin-echo sequence. RF = radio frequency.

time, 3,000 msec; echo times, 30 and 90 msec; field of view, 22 cm; imaging matrix,  $192 \times 256$ ; 20 sections with thickness of 5 mm; intersection gap, 2 mm; and one signal averaged, with partial phase-conjugate symmetry. The total imaging time for both conventional spin-echo and MT-saturated long repetition time sequences was 7 minutes 48 seconds. Receive and transmit attenuator settings were maintained at constant levels within each pair of comparable pulse sequences for each subject.

In the 10 patients, T1-weighted images were obtained both with and without MT saturation pulses, with use of the following parameters: plane of imaging, transaxial; repetition time, 600 msec; echo time, 15 msec; field of view, 22 cm; imaging matrix,  $256 \times 192$ ; 20 sections with thickness of 5 mm; intersection gap, 2 mm; and one signal averaged. To obtain 20 sections with the MT pulse, two separate 10-section acquisitions were performed, each with a 35% MT duty cycle (ie, the fraction of time the MT pulse was activated during each repetition time interval). The imaging time for each conventional T1-weighted spin-echo study was therefore 2 minutes 4 seconds, whereas each MT-saturated study required 4 minutes 7 seconds. Gadopentetate dimeglumine (Magnevist; Berlex Laboratories, Wayne, NJ) was administered by slow intravenous infusion to each patient at a dose of 0.1 mmol/kg. After a delay of approximately 5 minutes, T1-weighted images were obtained with and without MT saturation; in five patients, T1-weighted images with MT were obtained first, and in the remaining five patients T1-weighted images without MT saturation were obtained first.

The images with each paired sequence were obtained with identical window and level settings and were visually assessed by the same three experienced neuroradiologists in side-by-side, nonblinded comparisons. To minimize the biases inherent in any such visually based evaluation, six anatomic regions of interest were selected for quantitative signal analysis: cerebrospinal fluid, scalp fat, cerebral white matter, caudate, and putamen (for the long repetition time images), with the addition of the pituitary gland (for the T1-weighted images only). These measurements were all obtained by a single investigator (J.C.K.), who, with use of conventional imager



**Figure 2.** MR images of 27-year-old female volunteer. (a) On spin-density-weighted image obtained without MT, cerebrospinal fluid has relatively low signal intensity and fat has relatively high signal intensity. (b) On spin-density-weighted image obtained with MT, both cerebrospinal fluid and scalp fat have relatively higher signal intensity compared with brain. The white matter (MT ratio = 28%) is also suppressed somewhat more than the deep gray matter nuclei (MT ratios = 20%–23%). (c) On T2-weighted image obtained without MT, cerebrospinal fluid has relatively high signal intensity and scalp fat has intermediate signal intensity. (d) On T2-weighted image obtained with MT, the brain parenchyma has lower signal intensity, making both cerebrospinal fluid and fat appear relatively brighter.

software, placed an oval cursor over each designated region of interest and obtained mean signal intensity measurements. The size and location of this region-of-interest cursor was not changed between each set of paired acquisitions; visual assessment of the images confirmed that no noticeable patient motion or image misregistration had occurred. For all quantitative determinations of signal intensity, the median of at least three independently obtained measurements was used.

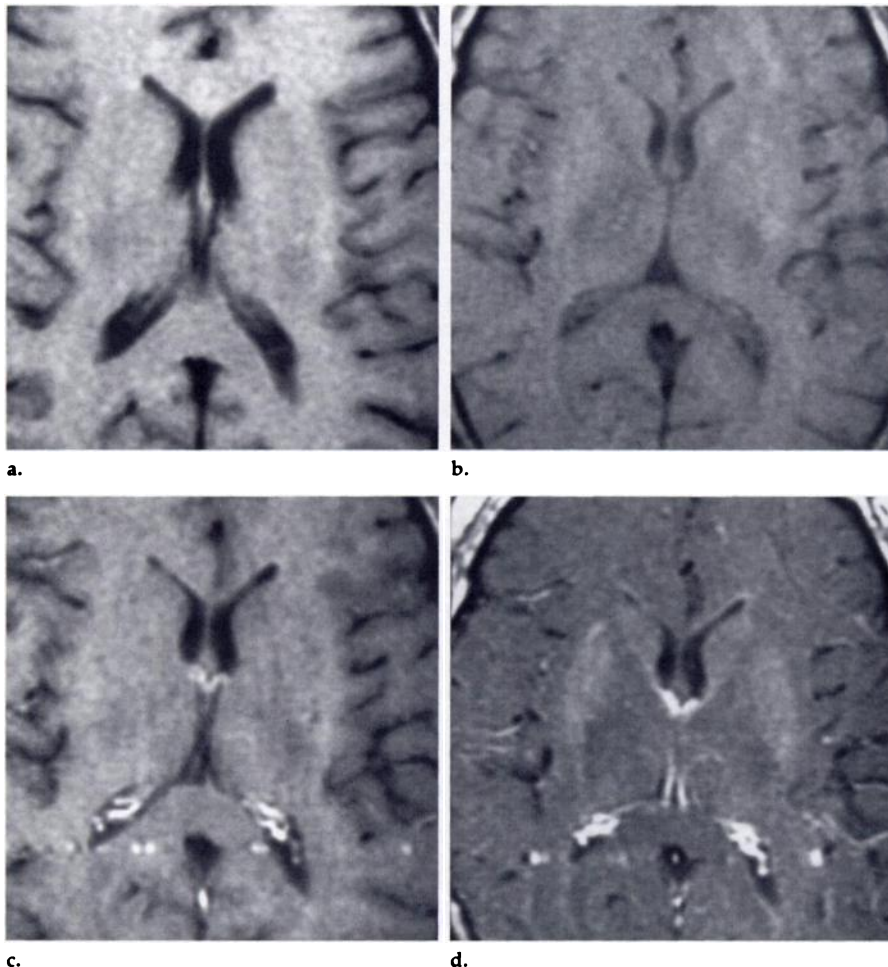
For each tissue and pulse sequence, an MT ratio was calculated with the formula  $MTR = (SI_0 - SI_m) / SI_0$ , where MTR is MT

ratio,  $SI_0$  is the signal intensity of the tissue before the MT pulse has been applied, and  $SI_m$  is the signal intensity after the MT pulse has been applied. Calculation of the MT ratio has been used by a number of investigators (3,14,15,17) to quantify the extent of saturation experienced by a given tissue in an MT pulse sequence. The MT ratio indicates the percentage of signal loss that occurs during the irradiation of the immobile pool of protons and, consequently, is proportional to the pseudo-first-order rate constant for saturation transfer between two chemical species of Forsén and Hoffman (6). In general, the

MT Ratios for Cranial Structures on MR Images Obtained with Different Sequences

Structure	Sequence			
	T2-weighted	Proton-density-weighted	T1-weighted	Gadolinium-enhanced T1-weighted
Cerebrospinal fluid	0.0 ± 0.9	-1.0 ± 1.0	-1.0 ± 2.0	0.0 ± 2.3
Scalp fat	0.0 ± 1.2	9.0 ± 0.7	1.0 ± 0.8	0.0 ± 1.0
White matter	27.0 ± 0.7	28.0 ± 0.7	15.0 ± 0.8	16.0 ± 1.1
Caudate	22.0 ± 0.6	23.0 ± 0.9	7.0 ± 1.1	8.0 ± 1.4
Putamen	20.0 ± 1.0	20.0 ± 1.0	8.0 ± 0.8	8.0 ± 1.0
Pituitary gland	Not measured	Not measured	10.0 ± 1.0	2.0 ± 1.4

Note.—All measurements are MT ratio in percentage ± standard error. Larger MT ratios imply greater suppression and, therefore, decreased signal intensity.



**Figure 3.** MR images of a 42-year-old female patient. (a) Precontrast T1-weighted image obtained without MT shows the white matter with higher signal intensity than the gray matter. (b) Precontrast T1-weighted image obtained with MT shows the putamen and caudate head with higher signal intensity than the white matter. (c) Postcontrast T1-weighted image obtained without MT shows enhancement of choroid plexus and internal cerebral veins in addition to the higher signal intensity of white matter compared with gray matter. (d) Postcontrast T1-weighted image obtained with MT shows more conspicuous enhancement of choroid plexus, internal cerebral veins, subependymal veins, and cortical vessels, and higher signal intensity of the putamen and caudate head compared with white matter.

larger the MT ratio, the more suppressed (with lower signal) the tissue will be. Statistical analysis was performed with two-tailed *t* tests to compare MT ratios of pairs of structures, and a one-way analysis of variance with Bonferroni corrections was used for multiple comparisons of MT ratios.

## RESULTS

The appearance of the brain on spin-density- and T2-weighted images when MT pulses were used differed slightly from that expected on conventional spin-echo images (Fig 2). Specifically, MT pulses reduced the

signal from brain by 20% or more but had little effect on the signal from scalp fat or cerebrospinal fluid (Table). As a result of this differential suppression of signal, cerebrospinal fluid and fat appeared relatively brighter than brain on MT spin-echo images when compared with conventional (ie, non-MT) spin-echo images. Within the brain itself, we could demonstrate no visually apparent differences in the usual appearance of intrinsic structures on long repetition time MT images. Specifically, no statistically significant differences in suppression were noted between white matter and gray matter.

On T1-weighted images, however, qualitative differences in tissue contrast were more dramatic between the MT and conventional spin-echo images (Figs 3–5). As with the long repetition time MT sequences, the MR signals from all brain structures were decreased compared with fat, which therefore appeared to be abnormally bright. Moreover, even though brain signal was globally decreased, some brain structures were suppressed more than others. In particular, the white matter had the largest MT ratios and hence the greatest degree of signal suppression. As a result, certain brain components (gray matter of the central sulcus, putamen, caudate, aqueduct, and substantia nigra) were rendered significantly brighter than white matter and became conspicuous when MT pulses were used.

After administration of gadopentetate dimeglumine, several more differences were noted between the conventional and MT-saturated T1-weighted images. Structures that normally enhance with gadolinium (eg, choroid plexus, dural sinuses, pituitary, pineal) were rendered even more conspicuous than normal when MT pulses were used. Multiple small cortical veins, not seen to enhance appreciably on the conventional T1-weighted images, were well visualized on the MT images. Quantitative analysis of the MT ratios of pituitary tissue revealed a statistically significant reduction in MT saturation after administration of contrast material ( $P < .05$ ).

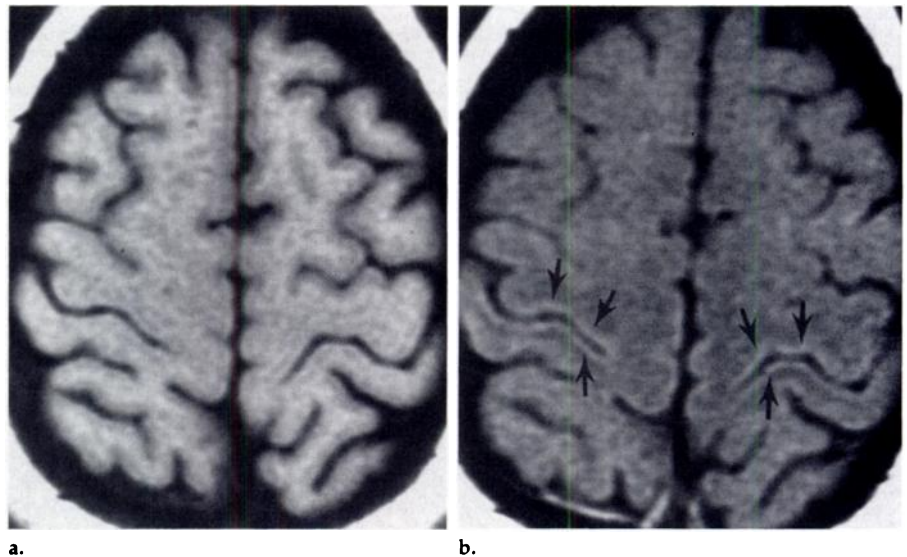
No significant differences were noted for the MT ratios of fat or cerebrospinal fluid on T1- or T2-weighted images. Both white matter and gray matter structures demonstrated significantly greater MT effect (greater MT ratios) on T2-weighted images than on T1-weighted images ( $P < .01$ ).

## DISCUSSION

MT imaging is a relatively new technique in which image contrast is thought to be manipulated through the selective saturation of a pool of protons on proteins, cell membranes, and other macromolecules that are in close thermal contact with a sphere of associated water molecules (1-3). These macromolecular protons were long considered to be invisible on clinical MR images because of their extremely short T2 values (which are measured in microseconds rather than in milliseconds) (23). Since the MR line width is inversely proportional to the T2 value, the macromolecular pool has a broad spectral density and can thus theoretically be stimulated over a wide range of radio frequencies. According to current theory, by selectively stimulating the macromolecular reservoir, saturation effects can be transferred to the associated water pool, thereby affecting the observed MR signal (7,8,24). Presumably this modulation of the water signal takes place with dipolar cross-coupling interactions and chemical exchange processes (2). However, much of the current MT theory remains highly speculative; other mechanisms (eg, water interactions with paramagnetic free radicals on protein surfaces, spin-lock relaxation effects, or chemical exchange reactions with a hot environment [the McConnell effect (25)]) may also be invoked to account for some of the effect of saturation on contrast observed in MT imaging.

Several methods of producing MT saturation have been proposed, including use of continuous-wave irradiation and pulse techniques (5). Because of considerations about specific absorption rates, continuous-wave methods are limited to use in low-field-strength systems (2,26,27). Application of the MT technique at high field strengths has generally involved use of pulse methods with which an MT saturation pulse of relatively low power is applied with a frequency offset of between several hundred and several thousand hertz from the water resonance. This off-resonance pulse is designed to have sufficient power to saturate protons in the immobile pool but with a frequency spectrum that will not directly stimulate protons in the free tissue water.

Use of the MT saturation pulse limits the time available for multisection acquisition and, hence, the number of allowed sections for a given repetition time. In addition, the number of sec-



**Figure 4.** MR images of a 31-year-old female patient. Compared with (a) the T1-weighted image obtained without MT, (b) the T1-weighted image obtained with MT demonstrates relative hyperintensity of gray matter adjacent to the central sulcus (arrows).

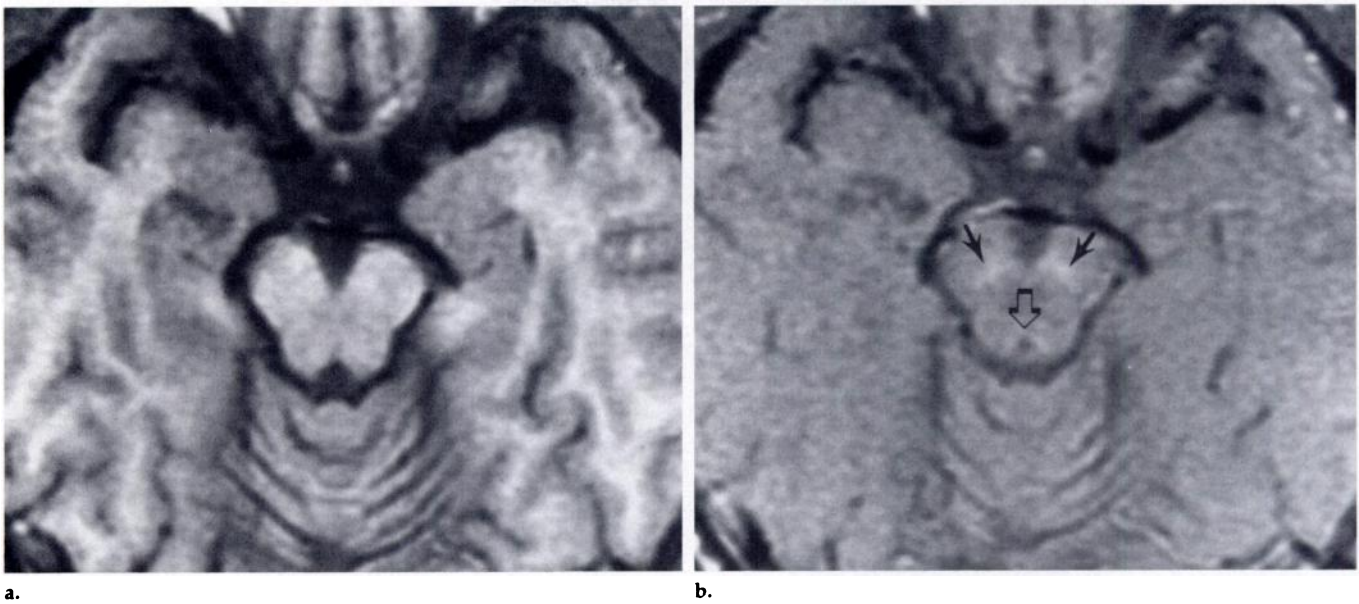
tions acquired may have to be further reduced to avoid exceeding limitations of specific absorption rates for tissue energy deposition. The precise penalty in multisection imaging depends on the repetition time: At 600 msec, for example, the number of available sections in our study was reduced by 40%, necessitating two separate acquisitions to cover the entire brain axially.

Preliminary research by several groups of investigators has demonstrated the usefulness of MT imaging in a variety of radiologic applications. Outside the nervous system, MT techniques have been used to image the knee (28), heart (29), liver (30), and breast (31). Many imaging applications for the central nervous system have also been proposed, the most important of which include suppression of background brain tissue at MR angiography (9-11), detection of demyelinating and degenerative lesions (14-16), and increased visibility of gadolinium enhancement (18-22). These applications of the MT technique encompass a wide range of imaging protocols; MT pulses will likely prove useful in conjunction with T1-, T2-, and spin-density-weighted imaging. To interpret MT-enhanced images of the brain properly, therefore, the radiologist must be aware of the expected patterns of tissue contrast likely to be encountered and how these patterns differ from those seen on conventional spin-echo images. Herein lies our motivation and justification for performing the present investigation.

Although the exact mechanisms

responsible for the generation of MT contrast remain unclear, a few simple concepts can reasonably explain many of the signal changes we observed in routine cranial imaging. First, MT effects should be most noticeable in tissues in which the interaction between water and macromolecules are the principal determinant of relaxation time. This is clearly the case for skeletal muscle and brain, for which several investigators (14,28,29) have measured MT ratios between 30% and 80%. Conversely, fluids with relatively low concentrations of macromolecules (eg, cerebrospinal fluid and blood) should experience little if any suppression of signal when MT pulses are applied. Our measurements of MT ratios in these tissues (Table) confirm this hypothesis.

The MT ratios we measured should not be taken as absolute values but rather as indexes of the relative suppression of tissues for a given pulse sequence and MT saturation method. Other investigators, with use of different MT pulses and imaging protocols, have reported different MT ratios for cranial tissues (14,20,27,29). Even in our own data, the MT ratios for brain tissue were two to three times larger for T2-weighted than for T1-weighted images. The precise explanation for this effect is unclear but may be a result of the fact that T1 weighting usually counteracts the contrast created with MT pulses. In addition, the MT ratio may be increased because of the increased number of sections acquired (with more nonselective MT pulses applied per image) and because of the off-



**Figure 5.** MR images of a 56-year-old female patient. Compared with (a) the T1-weighted image obtained without MT, (b) the T1-weighted image obtained with MT shows that the substantia nigra (black arrows) and the periaqueductal gray matter (open arrow) are relatively hyperintense.

resonance effects of  $180^\circ$  refocusing pulses used in the multiecho long repetition time sequence. Since twice as many refocusing pulses are used on a double-echo sequence compared with a single-echo sequence, one would expect a greater MT effect on the double-echo sequence. This MT effect of multiple  $180^\circ$  pulses has been documented in fast spin-echo imaging (32). An increase in MT effects in multisection (compared with single section) MR imaging has also been reported (33). The MT ratios we measured are proportional to and consistent with ratios measured in other studies and allow us to understand at a quantitative level the contrast differences between tissues that we observe visually.

The poor suppression of fat signal with MT pulses has been noted in several previous studies (11,27,29), in which computed MT ratios have not usually exceeded 5%. Adipose tissue contains numerous large intracellular deposits of lipid stored principally in the form of medium- and long-chain triglycerides. These triglycerides are of moderate size and mobility and hence have T2 relaxation times comparable to those of many other biologic tissues. Stored lipids, therefore, may not be considered to be macromolecules in the sense of being directly saturated with MT techniques. Furthermore, because stored lipids are hydrophobic and are loculated into self-contained droplets within adipose cells, stored fats have few direct interactions with free water.

MT effects are also minimized whenever high concentrations of a paramagnetic substance are present within tissue (2,18–22). Because contrast enhancement at MR imaging is due to a direct water-gadolinium ion interaction (34) (not to macromolecular cross relaxation), MT pulses will preferentially suppress the signal from background tissues and, hence, render gadolinium-enhanced areas more conspicuous. This use of MT pulses has been exploited at low field strength to increase the conspicuity of a variety of contrast-enhancing lesions (18,19). That such a phenomenon occurs is confirmed by our measurements of the pituitary gland and by our nonquantitative assessment of other structures such as veins, choroid plexus, and other tissues that normally enhance.

Within the brain parenchyma itself, we have discovered that a variety of structures are more conspicuous on T1-weighted images when MT pulses are used. The gray matter along the central sulcus, the basal ganglia, and substantia nigra are the most dramatic examples of this phenomenon. Our signal intensity measurements reveal that the gross MR signals from these structures are actually reduced by the MT pulses. However, the signals from these gray matter structures are *less* reduced than are those arising from the adjacent white matter; therefore, the gray matter structures are rendered *more* conspicuous on T1-weighted MT images. The reason is unknown for the differences in MT

ratio between white matter and gray matter and between different gray matter structures. The degree of myelination, iron deposition, and density of neurons may all play a role. We are now conducting research to determine how these effects vary with the age of the patient and with the type of MT pulse employed.

This pattern of relative prominence of the central sulcus and of the nuclei of deep gray matter must be recognized as a normal finding in the interpretation of T1-weighted MT images. When MT pulses are used in conjunction with gadolinium enhancement, the high signal from these gray matter structures must not be misconstrued as indicating a pathologic condition.

The prominence of the central sulcus is a curious and unexplained observation; one immediate practical benefit of this phenomenon is that it provides a method with which to determine easily the exact location of this sulcus on T1-weighted MT images. Potentially, this may prove helpful in at least three situations: (a) when general radiologists are not familiar enough with normal gyral anatomy to locate this structure with traditional means; (b) when coronal, oblique, or low axial images are obtained (when even expert neuroradiologists may find it difficult to locate the sulcus); and (c) whenever normal gyral landmarks are distorted by tumors, masses, or surgical change.

We conclude that in routine cranial imaging, MT saturation pulses produce new patterns of tissue contrast

that differ substantially from those expected on conventional spin-echo images. These patterns must be recognized for proper interpretation of pre- and postcontrast MR images that have been obtained with MT pulses. ■

## References

- Wolff SD, Balaban RS. Magnetization transfer contrast (MTC) and tissue water proton relaxation in vivo. *Magn Reson Med* 1989; 10: 135-144.
- Balaban RS, Ceckler TL. Magnetization transfer contrast in magnetic resonance imaging. *Mag Reson Q* 1992; 8:116-137.
- Eng J, Ceckler TL, Balaban RS. Quantitative <sup>1</sup>H magnetization transfer imaging in vivo. *J Magn Reson* 1991; 17:304-314.
- Hajnal JV, Baudouin CJ, Oatridge A, Young IR, Bydder GM. Design and implementation of magnetization transfer pulse sequences for clinical use. *J Comput Assist Tomogr* 1992; 16:7-18.
- Schneider E, Probst RW, Glover GH. Pulsed magnetization transfer versus continuous wave irradiation for tissue contrast enhancement. *JMRI* 1993; 3:417-423.
- Forsén S, Hoffman RA. Study of moderately rapid chemical exchange reactions by means of nuclear magnetic double resonance. *J Chem Phys* 1963; 39:2892-2901.
- Koenig SH, Bryant RG, Halenga K, Jacob GS. Magnetic cross relaxation among protons in protein solution. *Biochemistry* 1978; 17:4348-4358.
- Edzes HT, Samulski ET. Cross relaxation and spin diffusion in the proton NMR of hydrated collagen. *Nature* 1977; 265:521-523.
- Pike GB, Hu BS, Glover GH, Enzmann DR. Magnetization transfer time-of-flight magnetic resonance angiography. *Magn Reson Med* 1992; 25:372-379.
- Edelman RR, Ahn SS, Chien D, et al. Improved time-of-flight MR angiography of the brain with magnetization transfer contrast. *Radiology* 1992; 184:395-399.
- Lin W, Tkach JA, Haacke EM, Masaryk TJ. Intracranial MR angiography: application of magnetization transfer contrast and fat saturation to short gradient-echo, velocity-compensated sequences. *Radiology* 1993; 186:753-761.
- Wolff SD, Eng J, Balaban RS. Magnetization transfer contrast: method for improving contrast in gradient-recalled-echo images. *Radiology* 1991; 179:133-137.
- Ceckler TL, Karino K, Kador PF, Balaban RS. Magnetic resonance imaging of the rabbit eye: improved anatomical detail using magnetization transfer contrast. *Invest Ophthalmol Vis Sci* 1991; 32:3109-3113.
- Doussot V, Grossman RI, Ramer KN, et al. Experimental allergic encephalomyelitis and multiple sclerosis: lesion characterization with magnetization transfer imaging. *Radiology* 1992; 182:483-491.
- Lexa FJ, Galetta SL, Grossman RI. Phasic changes in magnetization-transfer rate in human visual pathways after unilateral enucleation (abstr). *Radiology* 1992; 185(P): 199.
- Chew WM, Rowley HA, Barkovich JA. Magnetization transfer contrast imaging in pediatric patients (abstr). *Radiology* 1992; 185(P):281.
- Ordidge RJ, Helpen JA, Knight RA, Qing Z, Welch KMA. Investigation of cerebral ischemia using magnetization transfer contrast (MTC) MR imaging. *Magn Reson Imaging* 1991; 9:895-902.
- Tanttu JI, Sepponen RE, Lipton MJ, Kuusela T. Synergistic enhancement of MRI with Gd-DTPA and magnetization transfer. *J Comput Assist Tomogr* 1992; 16:19-24.
- Kurki TJI, Niemi PT, Lundbom N. Gadolinium-enhanced magnetization transfer contrast imaging of intracranial tumors. *JMRI* 1992; 2:401-406.
- Finelli DA, Hurst GC, Gullapali RP, Bellon EM. Improved contrast of enhancing brain lesions on postgadolinium, T1-weighted spin-echo images with use of magnetization transfer. *Radiology* 1994; 190:553-559.
- Mathews VM, King JC, Elster AD, Hamilton CA. Cerebral infarction: effects of dose and magnetization transfer contrast at gadolinium-enhanced MR imaging. *Radiology* 1994; 190:547-552.
- Elster AD, King JC, Mathews VP, Hamilton C. Improved detection of gadolinium enhancement using magnetization transfer imaging. *Neuroimaging Clin North Am* (in press).
- Bottomley PA, Foster TH, Argersinger RE, et al. A review of normal tissue hydrogen relaxation times and relaxation mechanisms from 1-100 MHz: dependence on tissue type, NMR frequency, temperature, species, excision, and age. *Med Phys* 1984; 11:425-449.
- Koenig SH, Brown RD III, Ugolini R. Magnetization transfer in cross-linked bovine serum albumin solutions at 200 MHz: a model for tissue. *Magn Reson Med* 1993; 29:311-316.
- McConnell HM. Relaxation rates by nuclear magnetic resonance. *J Chem Phys* 1958; 28:430-431.
- Niemi PT, Komu MES, Koskinen SK. Tissue specificity of low-field-strength magnetization transfer contrast imaging. *JMRI* 1992; 2:197-201.
- Swallow CE, Kahn CE Jr, Halbach RE, Tanttu JI, Sepponen RE. Magnetization transfer imaging of the human leg at 0.1 T: preliminary study. *Magn Reson Imaging* 1992; 10:361-364.
- Wolff SD, Chesnick S, Frank JA, Lim KO, Balaban RS. Magnetization transfer contrast: MR imaging of the knee. *Radiology* 1991; 179:623-628.
- Balaban RS, Chesnick S, Hedges K, Samaha F, Heineman FW. Magnetization transfer contrast in MR imaging of the heart. *Radiology* 1991; 180:671-675.
- Outwater E, Schnall MD, Braitman LE, Dinsmore BJ, Kressel HY. Magnetization transfer of hepatic lesions: evaluation of a novel contrast technique in the abdomen. *Radiology* 1992; 182:535-540.
- Pierce WB, Harms SE, Flamig DP, Griffey RH, Evans WP, Hagans JE. Three-dimensional gadolinium-enhanced MR imaging of the breast: pulse sequence with fat suppression and magnetization transfer contrast—work in progress. *Radiology* 1991; 181:757-763.
- Listerud J, Einstein S, Outwater E, Kressel HY. First principles of fast spin echo. *Magn Reson Q* 1992; 8:199-214.
- Dixon WT, Engels H, Castillo M, Sardashti M. Incidental magnetization transfer contrast in standard multislice imaging. *Magn Reson Imaging* 1990; 8:417-422.
- Wood ML, Hardy PA. Proton relaxation enhancement. *JMRI* 1993; 3:149-156.