# Improved MR Angiography: Magnetization Transfer Suppression with Variable Flip Angle Excitation and Increased Resolution[1]

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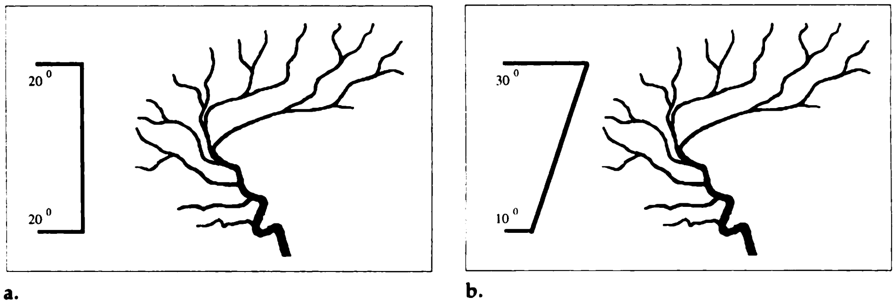
**Results at conventional magnetic resonance (MR) angiography were compared with results at MR imaging with a sequence combining optimized magnetization transfer (MT) saturation and tilted optimized nonsaturating excitation (TONE). Forty images were obtained of five healthy volunteers and five patients with known intracranial vascular abnormalities (four men and six women, aged 22–72 years). Four blinded readers found improved vessel penetration, enhanced vessel-to-background contrast, and better vessel detail in the MT saturation–TONE images than in the conventional three-dimensional time-of-flight MR angiograms.**

**Index terms:** Blood vessels, MR, 17.1214 • Brain, MR, 10.1214 • Cerebral blood vessels, MR, 17.1214 • Magnetic resonance (MR), magnetization transfer contrast • Magnetic resonance (MR), vascular studies, 17.1214

**Radiology 1994;** 190:890–894



a. b.

**Figure 1.** Simplified representations of the intracerebral vasculature demonstrate positioning of an excitation slab for a three-dimensional acquisition. **(a)** Schematic representation of the standard radio-frequency excitation, in which a constant 20° flip angle is applied across a transverse slab. In this example, the radio-frequency energy is applied uniformly over the vasculature within the slab. Experiencing more radio-frequency power over time, upward flowing spins exhibit saturation and a loss of contrast distally. **(b)** Schematic shows flip angle of 10°–30° over the slab of excitation, with a nominal flip angle of 20° at the center of the slab. The effect is reduction in distal saturation by exposure of the incoming flow to lower radio-frequency power than in **a**. Note: The reduced flip angle at the inlet (10° vs 20°) can also result in reduced vessel-to-background contrast compared with that in **a**.

MAGNETIC resonance (MR) angiography is gaining wide acceptance as a screening modality for the intracranial vasculature (1). The noninvasive nature, relatively rapid imaging times, and three-dimensional volume acquisitions of MR angiography make it an attractive technique in the clinical setting. MR angiographic data can be readily combined with findings at conventional MR imaging to correlate soft-tissue pathologic conditions and associated blood flow abnormalities. MR angiography, while widely used clinically, is still an evolving technique.

Three-dimensional time-of-flight MR angiography has been hampered by two effects: limited contrast from incomplete suppression of background tissues and saturation of flowing spin signals (2,3). The combination of these two effects reduces vessel-to-background contrast and available vessel detail.

When imaging with short repetition times and relatively high flip angles, as is done in most time-of-flight MR angiography, the background signal is driven into a state of reduced signal, or saturation. While use of higher flip angles produces better background suppression and a higher signal-to-noise ratio for fresh inflowing spins, it also tends to saturate any flowing blood that lies within the plane of excitation for any length of time.

Suppression of background signal while minimizing saturation of flowing spins can also be accomplished with other means. Given that differences in the resonant frequencies of tissues exist, unwanted background signals can be removed by applying presaturation pulses to frequencies away from that of flowing blood. The most commonly used pulse is spectral presaturation of lipids, or fat. Unfortunately, the brain parenchyma typically contains few suppressible lipid components, a condition that limits the benefits of fat saturation to those areas of the scalp and orbit that may obscure vessel signals on projection.

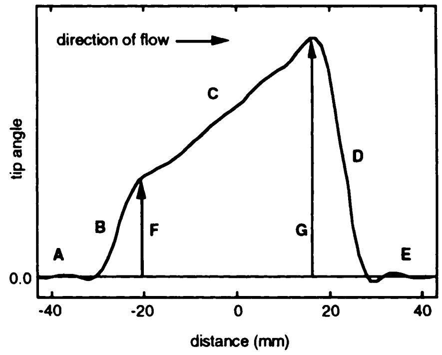


**Figure 2.** Graph simulates the variation in radio-frequency flip angle across the slab. This slab is located such that the flow direction is assumed to be toward the right. *A* and *E* represent background nonexcited regions, *F* and *G* indicate the flip angles at the defined edges of the slab, and *C* is a transition region between them. The optimization of this radio-frequency pulse involves compromises between minimizing the transition regions (*B* and *D*) and nonlinear variations along the slope (*C*).

Magnetization transfer (MT) contrast is another signal suppression technique that uses spectral presaturation. MT contrast significantly reduces brain (background) signal through the use of a second radio-frequency pulse tuned far off the resonances of water and lipid (4,5). Mobile free water (in vessels and tissues) has a much sharper resonance compared with the resonance of motionally restricted water found on macromolecules such as myelin membranes. This restricted, or bound, hydrogen resonates over a broad range of frequencies. By using the differences in frequency between the narrow "free"

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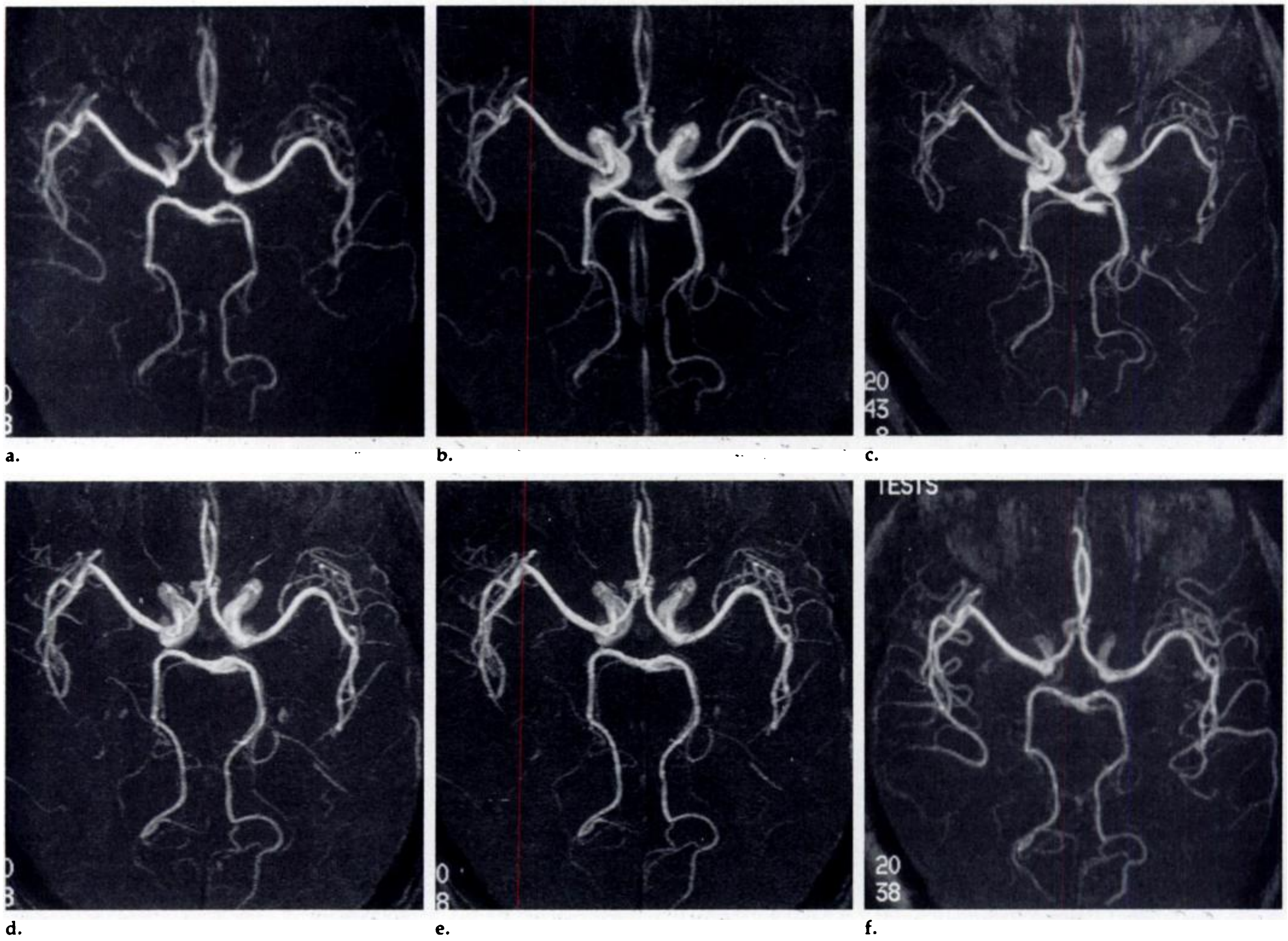


**Figure 3.** Images were obtained to compare conventional time-of-flight MR angiograms with MR angiograms obtained with MT saturation, TONE, and MT saturation–TONE sequences in a healthy male volunteer (aged 36 years). Conventional MR angiograms (38/7) were each obtained in 7 minutes 49 seconds with **(a)** 192 × 256 and **(b)** 192 × 512 matrices. **(c)** MT saturation MR angiogram (43/7) was obtained with a 192 × 512 matrix in 8 minutes 47 seconds. **(d)** TONE 1:3 and **(e)** TONE 1:2 MR angiograms (38/7) were each obtained with a 192 × 512 matrix in 7 minutes 49 seconds. MT saturation–TONE 1:3 MR angiograms (43/7) were each obtained in 8 minutes 47 seconds with **(f)** 192 × 256 and **(g)** 192 × 512 matrices.

and broader "bound" water pools, a mechanism for selective suppression of one pool can be made. MT contrast, in our case, is accomplished by the application of a second off-resonance radio-frequency pulse with sufficient power to saturate primarily the macromolecule-bound water. By tuning the MT contrast radio-frequency pulse a few hundred Hertz off resonance, saturation of bulk water, such as is found in blood, can be minimized. In using MT pulses for MR angiographic applications, the generation of a tissue-specific MT contrast, per se, is not a defined goal. Rather, these MT pulses were added to the MR angiographic sequence to suppress the background signal (ie, MT suppression).

The time-of-flight effect in MR angiography is the result of inflowing unsaturated spins having a higher signal than the background. Yet after repeated application of radio-frequency pulses, these flowing spins (particularly those deep within the slab) become saturated and exhibit a reduction in intensity to the point of approaching the signal of the background. The result is a reduction in vessel-to-background contrast, especially for the distal vessels. Techniques to overcome this saturation include use of smaller flip angles, reduction of slab thickness, and use of gadolinium chelates to shorten the intravascular T1 times (6). Thin-section two-dimensional imaging methods are effective in minimizing flowing proton saturation, but they have a lower signal-to-noise ratio compared with three-dimensional methods and their use is limited to a practical section thickness of more than 2 mm (7). Multiple thin-slab three-dimensional methods are also possible (8,9). However, such methods necessitate overlapping to eliminate diminished signal at the slab edges, compromising their efficiency and lengthening the overall imaging time.

To avoid problems of flow saturation associated with a thick slab, we implemented a modified radio-frequency pulse that varies the power (and flip angle) across the slab (10). With use of a low flip angle on the inlet side, adequate high flow–to-background contrast can be maintained, while less saturation of flowing signal occurs. On the distal side, conversely, a higher flip angle is used to increase the blood signal, maintaining the blood-to-background contrast. The transition from lower to higher flip angles is accomplished with use of a linear ramp (tilted optimized nonsaturating excitation [TONE]) (Fig 1).

This study describes the implementation of this TONE pulse in combination with MT background suppression and compares MT saturation–TONE with existing time-of-flight MR angiographic protocols. Finally, to evaluate these methods and their ability to produce improved image quality with a finer spatial resolution, we compared images obtained with these techniques in both 256- and 512-pixel-matrix formats.

## Materials and Methods

All images were obtained with a standard circularly polarized head coil on a conventional 1.5-T imager (Magnetom 63SP; Siemens Medical Systems, Iselin, NJ). After localization, transverse MR angiography was performed with 64 partitions over a 64-mm slab, producing an effective partition thickness of 1.0 mm. A venous presaturation pulse was applied superiorly to the slab in all cases.

Conventional three-dimensional time-of-flight MR angiography used a flow-compensated sequence (fast imaging with steady-state precession, repetition time msec/echo time msec of 38/7, with a 20° flip angle). Comparisons were made with use of 192 × 256 and 192 × 512 matrices, both at a constant field of view of 160 × 210 mm. The acquisition time for these studies was 7 minutes 49 seconds.

The variable-flip-angle radio-frequency pulse varied the slab excitation linearly from 13° to 27° (TONE 1:2) and from 10° to 30° (TONE 1:3) (Fig 1b). In either case the effective flip angle at the center of the slab, the nominal flip angle, was 20° (Fig 2). This pulse replaced the standard excitation radio-frequency pulse and did not extend the repetition time of the sequence. The TONE pulses were positioned to accentuate moving spins in a superiorly flowing direction (ie, arterial spins first experience the lower flip angle on entering the slab). Since the TONE pulse replaced the standard radio-frequency pulse without lengthening the echo or repetition times, the TONE protocols were identical to the conventional protocols.

The MT saturation pulse in this study was Gaussian shaped, 8.192 msec in duration, and was applied 1.5 kHz off resonance, with a bandwidth of 250 Hz. Sufficient power was applied to produce an effective MT saturation flip angle of 550°. This additional pulse lengthened the repetition time to 43 msec, for a total imaging time of 8 minutes 47 seconds. The echo time remained constant at 7 msec. The MT saturation pulse was also combined with a TONE 1:3 sequence (43/7), and images were compared with both 192 × 256 and 192 × 512 matrices. Identical maximum-intensity-projection techniques were used in all protocols throughout the study.

All images were obtained under existing institutional review board guidelines, and imagers were operated with a local maximum specific absorption rate of 8 W/kg and a total body exposure of less than 3 W/kg. No contrast agents were used during the study.

This study was performed in two phases. The first phase was an optimization process. One reader (M.B.Z.) reviewed data from the images of four volunteers obtained with the large number of possible combinations of conventional, MT saturation, and TONE parameters. From this series, an optimum MT saturation–TONE technique was defined.

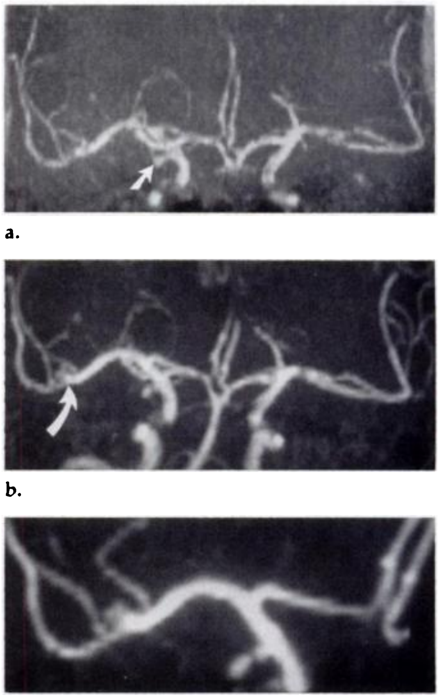
In the second part of the study, the optimized MT saturation–TONE technique was used for imaging in five healthy volunteers and in five patients with known intracranial vascular abnormalities. These subjects were examined with both the optimized MT saturation–TONE technique and conventional MR angiography. A blinded evaluation of all images was performed by four readers (M.B.Z., M.N., S.S., L.T.). Images were scored for vessel penetration, vessel-to-background contrast, small vessel visualization, artifact (background lipid signals from subcutaneous and periorbital regions), and overall image quality.

Given the small size of distal vessels, no numerical calculations were performed to quantitate the contrast-to-noise ratio at these vessels. Rather, we relied on the presence and characteristics of vessels in combination with a score based on a grading scale to compare methods.

Admittedly, this method may not be as scientifically rigorous as is a numerical calculation of pixel values with each method. However, this method of analysis probably reflects the clinical situation more realistically, because the comparison is more subjective.

## Results

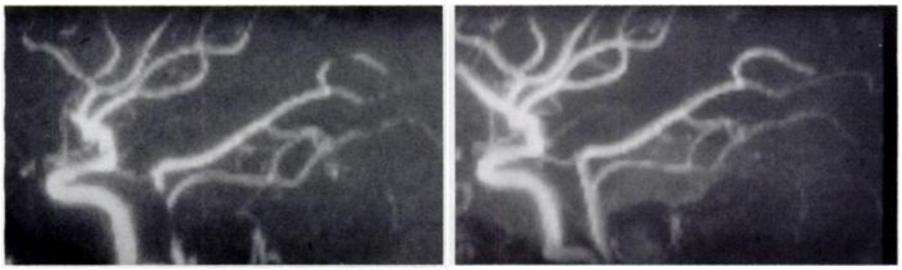
Satisfactory quality was obtained in all images. The MR angiographic techniques were well tolerated by all subjects. Figure 3 demonstrates the conventional, MT saturation, and TONE images obtained in a healthy volunteer. In reviewing the final maximum-intensity-projection images, the combination of a 192 × 512 matrix with an MT satu-


a.

b.

c.

**Figure 4.** Images are of a 72-year-old female patient with history of intracranial aneurysm. **(a)** Conventional three-dimensional time-of-flight MR angiogram demonstrates the presence of a 4-mm-diameter aneurysm at the junction of the right inferior cerebral artery and the right posterior communicating artery (arrow). **(b)** MT saturation–TONE 1:3 MR angiogram was obtained 7 months later. The original aneurysm is seen again, as well as a second aneurysm at the trifurcation of the right middle cerebral artery (arrow). **(c)** Detailed view of **b,** obtained with reduced maximum-intensity-projection field, more clearly depicts both aneurysms.


a.

b.

**Figure 5.** **(a)** Lateral maximum-intensity-projection image was obtained with conventional parameters. **(b)** Lateral maximum-intensity-projection image was obtained with optimized parameters incorporating the MT saturation–TONE pulses. Note the improved depiction of small vessel detail, including demonstration of the anterior choroidal artery.

ration and TONE pulse ratio of 1:3 at a nominal flip angle of 20° produced the best overall image quality (Fig 3g). This combination was used for later clinical comparison studies.

In our initial comparison series, MT saturation and TONE pulses were implemented separately with a standard sequence. Each was judged to result in improvement over the conventional acquisition scheme. With an MT saturation pulse alone (Fig 3c), background brain signal was markedly reduced compared with imaging performed with the standard fast-imaging-with-steady-state-precession sequence (Fig 3b), showing overall increased vessel conspicuity. Since the MT saturation pulse is far from the lipid resonance, both the MT saturation and the non–MT saturation images demonstrated the presence of fat signal from regions around the orbits and subcutaneous tissues. Imaging with the TONE pulses alone was effective in reducing blood saturation of distal vessels and in increasing visualization. Brain parenchyma-to-fat contrast was unchanged with the TONE only series.

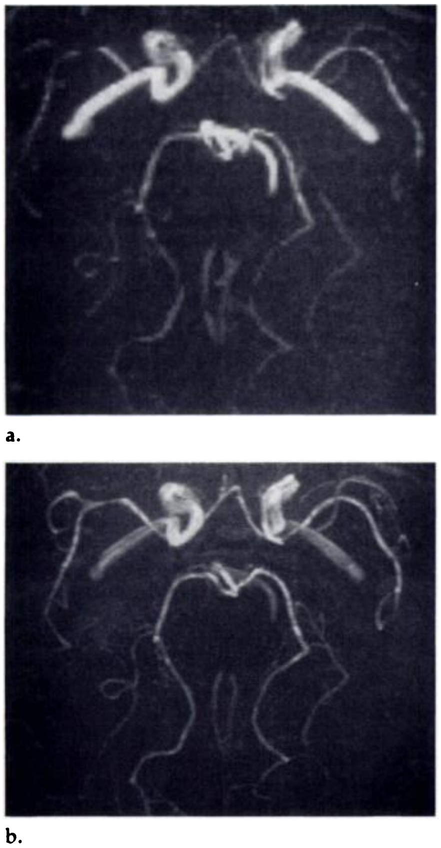


**Figure 6.** Images are of a 46-year-old female patient who was being treated with steroids for inflammatory bowel disease and who experienced severe headaches and left hemiparesis. MR brain studies (not shown) depicted subacute hemorrhagic infarcts and enhancement along the distribution of the posterior cerebral artery. **(a)** Conventional time-of-flight MR angiogram demonstrates irregular vasculature of the right middle cerebral artery. There is a suggestion of irregularity and beading of the posterior cerebral vessels. **(b)** MT saturation–TONE 1:3 MR angiogram of the same area (obtained with a 192 × 512 matrix) shows the areas of irregularity and stenosis of the middle cerebal artery to be less severe, with better visualization of the true lumen. The irregularity of the posterior cerebral vessels is less severe than was suggested on the conventional image.

The use of a TONE 1:2 pulse produced image quality similar to that obtained with the TONE 1:3 pulse, but with a slight reduction in distal vessel contrast (Fig 3d, 3e). Overall, the TONE pulses by themselves did not result in as good image quality as was obtained with the MT saturation–TONE pulses.

Imaging with the standard fast-imaging-with-steady-state-precession technique, with limited vessel-to-background contrast, resulted in only slightly improved vessel detail conspicuity when the matrix size was increased to 512 (Fig 3a, 3b). In comparison, imaging with the MT saturation–TONE combination at a 512 matrix resulted in enhanced vessel detail and conspicuity (Fig 3f, 3g).

In comparing the volunteer and patient images, the readers judged that images obtained with the optimized MT saturation–TONE technique showed improved vessel penetration (38 of 40 images). In 33 of the 40 MT saturation–TONE images, vessel contrast was gauged to be as good as or better than that seen in the conventional images. The readers noted in 35 of the 40 images that vessel detail improved with the optimized technique. In one-half (20 of 40) of the images, visualization of the proximal carotid artery was worse in the MT saturation–TONE images. The reviewers indicated also in 35 of the 40 images that the visualization of periorbital and subcutaneous fat was more noticeable with MT saturation–TONE imaging.

Small aneurysms were more accurately displayed with the MT saturation–TONE technique (Fig 4). Small anatomic structures, such as the anterior choroidal artery, were better visualized with the MT saturation–TONE technique at a 512 matrix (Fig 5). Intracranial vasculitis was more accurately displayed with MT saturation–TONE imaging. In comparison, conventional three-dimensional time-of-flight MR angiography (Fig 6) tended to exaggerate the flow restrictions.

## Discussion

MR imaging with combined MT saturation and TONE sequences has the potential to enhance the quality of conventional three-dimensional time-of-flight MR angiography of the intracranial vessels, without major modification of existing MR imaging equipment.

Other groups have shown that the application of an MT suppression prepulse alone can improve overall vessel contrast by suppressing background signal (4,5,11). Further improvements have been proposed to improve the efficiency of the MT pulses to reduce background signal (12,13) and to improve MR angiography by the addition of a weak section-selection gradient to remove venous signal (14). These potential improvements were not tested in this study.

While reduced background signal improves the quality of MR angiography, saturation of inflowing spins can still be problematic in three-dimensional time-of-flight applications. Distal vessels may show poor conspicuity despite the reduced signal of background. Even though this limitation may be overcome by using multiple thin-section three-dimensional acquisitions (eg, multiple overlapping thin-slab acquisitions) such methods use imaging time inefficiently because of the large overlaps (50%) required to eliminate slab-edge effects.

Signal saturation of moving blood may be reduced by the introduction of a contrast agent that shortens T1 time, such as gadolinium chelates. Studies have shown that use of contrast agents improves blood-tissue differentiation, particularly in situations of slow flow (6,15). However, the use of contrast media adds to both cost and examination time, produces a confusing tangle of vessels as a result of enhancement of venous and arterial vessels (16), and results in a maximum-intensity-projection image that may be obscured by areas of gadolinium-enhanced tissues and lesions.

Reduced signal saturation and thus improved distal vessel visualization may be achieved by the introduction of a TONE pulse. Replacement of the existing radio-frequency slab excitation with an excitation sequence tailored for spatially varying flip angles does not increase the echo or repetition times. Nevertheless TONE-only images, while improving vessel visualization, are limited in their small vessel detail, as background signal still exists. As noted by the readers in this study, a potential problem exists when the inlet side of the slab is placed too close to the carotid siphon. Since the inlet side of the slab has a low flip angle, contrast of the intraluminal carotid siphon was reduced (due to inadequate background suppresion) when in close proximity to the edge of the slab. When the slab was placed so that its lower edge was below the siphon, no similar findings were observed.

To avoid production of excessive background signals, specific postprocessing methods have also been used. Targeted, or volume-specific, maximum-intensity-projection imaging can eliminate unwanted background signal intensities (17). Use of vessel tracking algorithms can improve vessel-to-background contrast by selecting only the vessels of interest and their neighboring tissues (18). The resultant maximum-intensity projections of these vessels avoid the noise contained in spurious structures. To address the objections of our readers regarding the depiction of subcutaneous and periorbital fat, we have implemented use of a simple postprocessing method that edits out undesired areas. This editing was done manually over the entire data set and took about 1 minute. The initial results showed a reduction in extraneous background signal intensity on some images, with increased vessel visualization and no additional loss of vessel detail.

Depiction of increased vascular detail is one goal in MR angiography. Toward that end, imaging sequences have evolved that allow use of smaller fields of view, thinner three-dimensional sections, lower bandwidths (with better signal-to-noise ratio), and high-resolution matrices. These technical improvements can be well appreciated in imaging of the intracranial vasculature, in which multiple small vessels exist, vascular motion is minimal, and the head coil provides an increased signal-to-noise ratio. While 512-pixel-matrix imaging, per se, is possible with conventional three-dimensional time-of-flight MR angiography, the poorer background suppression and saturation of distal vessels limit its capacity to effect improved imaging (Fig 3a, 3b). Compared with conventional 256-pixel-matrix MR angiography, the optimized MT saturation–TONE approach with 512-pixel matrices makes a clinically attractive replacement for existing protocols (Fig 3g vs 3b). This small-vessel detail may be useful in increasing diagnostic confidence in the definition of small lesions or structures. Similar to the application of MT saturation and TONE sequences, imaging with 512-pixel matrices should be possible with most existing MR imagers and postprocessing methods. However, the increased size of data sets and the longer processing time may require use of additional computer resources to be clinically useful.

In this study, the combination of MT saturation and TONE sequences produced the best overall MR angiographic quality for intracranial vessels. Particularly, small vessel extent and detail were enhanced with the combined MT saturation–TONE approach. We have since implemented this optimized technique as our routine angiographic protocol. With the existing MR angiographic techniques, disease states such as vasculitis, arterial spasm, and small aneurysms have been difficult to identify. Imaging with the combination of higher-resolution matrices and the MT saturation–TONE sequences may be useful in these cases. ■

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