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Visualization of Brain Iron by Mid-Field MR

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Brain iron was visualized on a mid-field (0.5 T) scanner using a spin-echo pulse sequence. Methemoglobin was hyperintense on T1- and T2-weighted images. Deoxyhemoglobin, hemosiderin, and ferritin were seen as decreased intensity on T2-weighted images. The spin-echo pulse sequences were improved for identification of deoxyhemoglobin, hemosiderin, and ferritin by prolonging the TR to 3000 msec and the TE to 80–120 msec. Phase-encoding artifacts at the level of the sylvian fissures caused increased noise, obscuring the brain iron in the lentiform nuclei with the TE of 120 msec. This artifact was substantially reduced or eliminated by lowering the TE to 80 msec, changing the phase-encoding gradient to the Y axis, or using additional pulsing in the slice and read gradients.

Use of either the improved spin-echo or gradient-echo pulse sequences on a mid-field MR scanner provides improved evaluation of brain iron.

There are excellent articles describing imaging of brain iron on high-field MR scanners using spin-echo (SE) pulse sequences. Intracranial hematomas [1], occult cerebral vascular malformations [2], normal distribution of brain iron [3], hemorrhagic cortical infarction [4], and Parkinson plus syndromes [5] have all demonstrated brain iron on high-field (1.5 T) MR imagers. Brain iron can be easily seen on the high-field scanners [1–5].

A few articles have discussed imaging of brain iron on mid-field (0.5 T) MR scanners with SE pulse sequences. These include subarachnoid hemorrhage [6], occult vascular malformations [7], and multiple system atrophy [8].

Two recent articles have described factors that improve the visualization of deoxyhemoglobin, hemosiderin, and ferritin by shortening the T2 relaxation time [9, 10]. The effect is preferential loss of signal intensity on T2-weighted images in areas of deoxyhemoglobin, hemosiderin, and ferritin. The factors that increase the preferential T2 proton relaxation enhancement are: a stronger applied magnetic field, a greater concentration of intracellular paramagnetic substance, a prolonged echo time (TE), and an increased signal-to-noise ratio (S/N).

This paper reviews selected cases of brain iron abnormalities identified over the last 20 months to see if the factors suggested by Gomori and Grossman [9, 10] improved the visualization of brain iron on a mid-field MR scanner. Since various SE T2-weighted pulse sequences were employed over the last 20 months, we had the opportunity to determine if a longer TE and an increased S/N ratio would indeed improve visualization of brain iron on a mid-field MR scanner.

Subjects and Methods

To test the ability of the improved SE pulse sequence to visualize brain iron we selected prospective cases from over 3000 studies performed over the last 20 months. These included an acute intracerebral hematoma containing deoxyhemoglobin (Fig. 1), chronic hemorrhages with hemosiderin (Figs. 2–4), and abnormal distribution of ferritin in the lenticular nuclei (Fig. 5). These five cases were drawn from 44 patients studied specifically for abnormalities in

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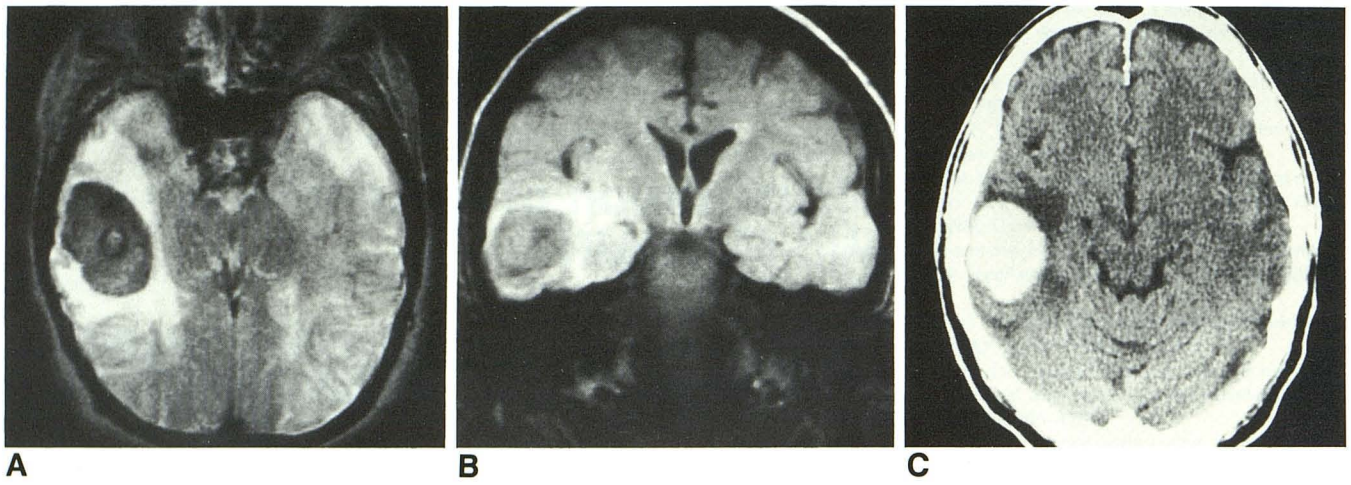

Fig. 1.—Deoxyhemoglobin. Acute intracranial hematoma in 71-year-old man.
***A*, Axial SE 3000/120 MR image obtained 6 days after acute attack shows area of decreased intensity (deoxyhemoglobin) in right temporal lobe surrounded by increased intensity (edema).**
***B*, Coronal SE 2000/40 MR image shows area of decreased signal (deoxyhemoglobin) in right temporal lobe.**
***C*, Nonenhanced CT scan obtained 2 days after MR. Hemorrhage surrounded by edema in right temporal lobe.**

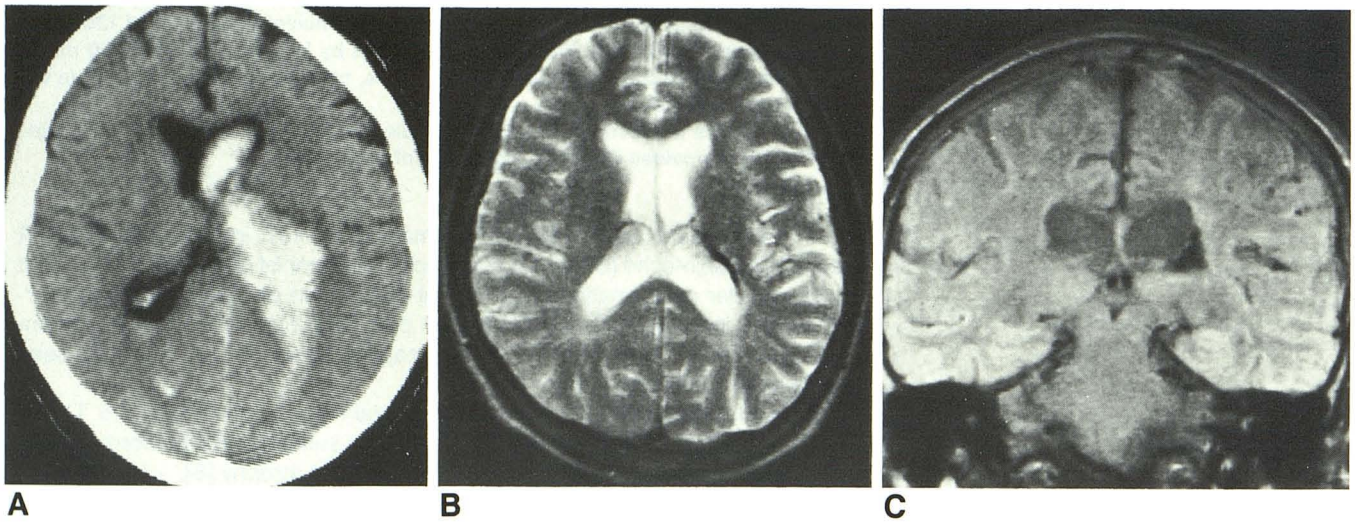

Fig. 2.—Hemosiderin. One-year-old large left subependymal hemorrhage in 57-year-old woman.
***A*, Nonenhanced CT scan obtained at time of hemorrhage. Large subependymal hemorrhage with blood in the ventricles.**
***B*, Axial T2-weighted SE 3000/120 MR image shows decreased intensity (hemosiderin) lateral to body of left lateral ventricle. Nonenhanced CT (not shown) performed within 1 week did not show calcifications.**
***C*, Coronal T2-weighted SE 2000/40 MR image shows enlargement of left lateral ventricle, but also an area of decreased intensity (hemosiderin).**

brain iron. The 44 patients included eight intracerebral hematomas (two spontaneous hematomas, four tumors with hemorrhages, two postsurgical hemorrhages), six arteriovenous malformations, two hemorrhagic cortical infarcts, and 29 Parkinson's patients.

The patients were examined on a 0.5-T Vista MR 2055 superconducting magnet.* All were studied with SE pulse sequences.

For the first 4 months of operation the brain-screening protocol included T2-weighted 10-mm axial sections with a repetition time (TR) of 3000 msec and a TE of 120 msec, and T2-weighted 5-mm coronal sections with a TR of 2000 msec and a TE of 40 msec. The longer TE (120 msec) images had a 128 × 256 matrix with two excitations and required 13 min. The shorter TE (40 msec) images had a 256 × 256 matrix with two excitations and required 17 min.

Later, the brain-screening protocol was changed by decreasing the TR to 2500 msec and the TE to 80 msec for the axial images. The matrix was maintained at 128 × 256, two excitations were used, and imaging required 10.6 min.

For the last 6 months we have been employing asymmetric multiecho sequences; that is, TR = 2500 msec, TE = 30/100 msec. The matrix was maintained at 128 × 256, two excitations were used, and imaging required 10.2 min.

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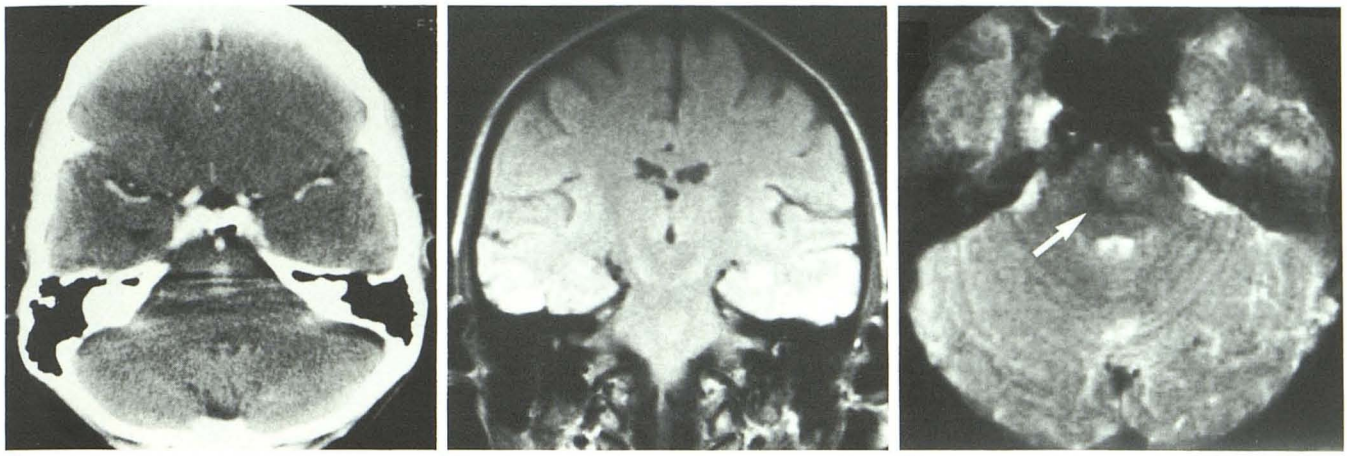


Fig. 3.—Hemosiderin. Suspected capillary telangiectasia in 55-year-old woman.
***A*, CT scan shows abnormal blush in pons after injection of IV contrast.**
***B*, Coronal T2-weighted SE 2000/40 MR image shows abnormal increased signal (edema) in pons.**
***C*, Axial T2-weighted SE 3000/120 MR image shows decreased intensity (hemosiderin) (*arrow*) posterior to area of increased signal (edema).**

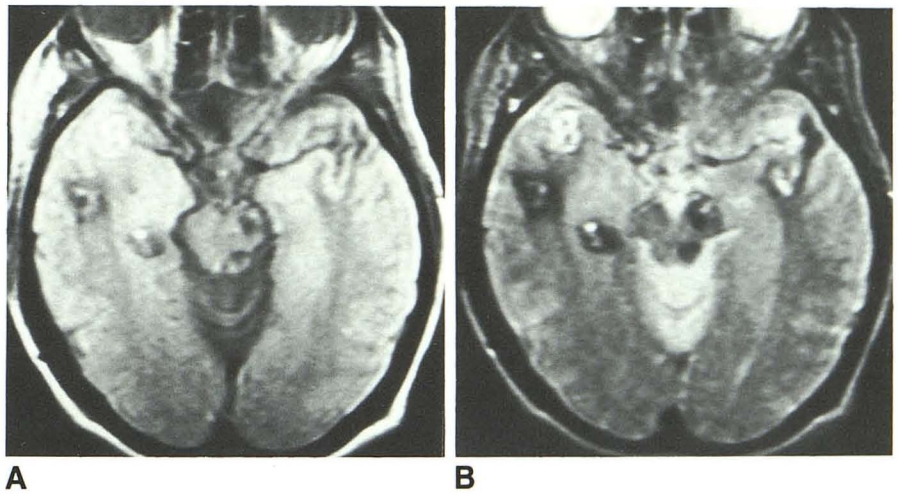


Fig. 4.—Hemosiderin. Multiple arteriovenous malformations (AVMs) in 44-year-old woman.
***A*, Axial T2-weighted SE 2500/30 MR image shows decreased intensity in AVMs from hemosiderin. Methemoglobin seen as areas of increased signal intensity.**
***B*, Axial T2-weighted SE 2500/100 MR image shows greater loss of signal intensity in AVMs with the longer TE.**

After reviewing the selected cases (Figs. 1–5) studied by various SE pulse sequences, we decided to use a TR of 3000 msec with a TE of 120 msec to improve T2 proton relaxation enhancement in visualizing brain iron. Thus, our brain-survey protocol remains SE 2500/30,100, but if there is a suspected abnormality related to brain iron the additional SE 3000/120 pulse sequence is used.

Results

Deoxyhemoglobin in an acute intracerebral hemorrhage was identified by its characteristic decreased intensity on T2-weighted images (Fig. 1). The decreased signal was more pronounced on the longer TE (120 msec) images than on the shorter TE (40 msec) images.

Hemosiderin was identified in an old subependymal hemorrhage as decreased intensity on both T2-weighted SE 2000/40 and SE 3000/120 images, but was lower in intensity on the longer TE (120 msec) images (Fig. 2). Hemosiderin was also identified in a suspected capillary telangiectasia in the pons of a patient who had recurrent brainstem symptoms for 10 years (Fig. 3). The decreased signal of hemosiderin was seen only on the TE (120 msec) images and not on the TE (40 msec) images. With asymmetric multiecho TR = 2500 msec, TE = 30/100 msec, the hemosiderin in a case of multiple arteriovenous malformations showed lower signal intensity on the longer TE (100 msec) images (Fig. 4).

A patient with multisystem atrophy was identified as having Shy-Drager syndrome when MR showed an increase of ferritin (decreased intensity) in the putamen as compared with the globus pallidus (Fig. 5). The increased ferritin was seen better on the T2-weighted SE 3000/120 images than on the T2-weighted SE 2500/80 images.

A review of our images using a long TE of 120 msec showed increased phase-encoding artifacts at the level of the globus pallidus and putamen on the axial sections (Fig. 6). The phase-encoding artifacts occurred only when there was

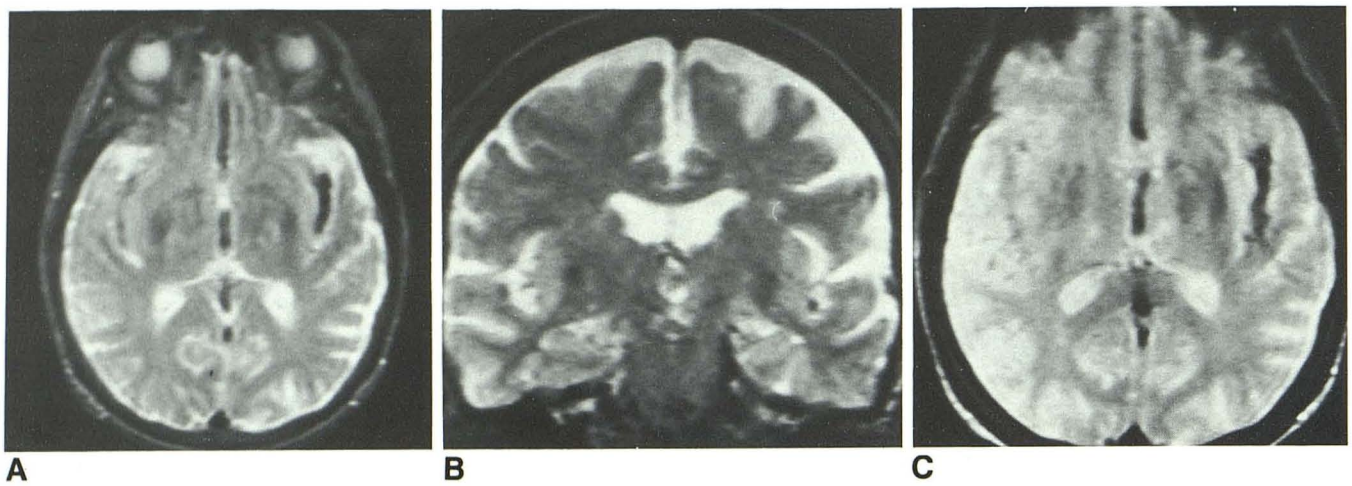


Fig. 5.—Ferritin. Shy-Drager syndrome in 78-year-old woman.
A, Axial T2-weighted SE 3000/120 MR image shows decreased signal in putamen (increased ferritin) compared with the globus pallidus. Signal-void artifact in left sylvian fissure.
B, Coronal T2-weighted SE 3000/120 MR image confirms decreased signal in putamen.
C, Axial T2-weighted SE 2500/80 MR image also shows increased ferritin in putamen. Signal-void artifact in left sylvian fissure.

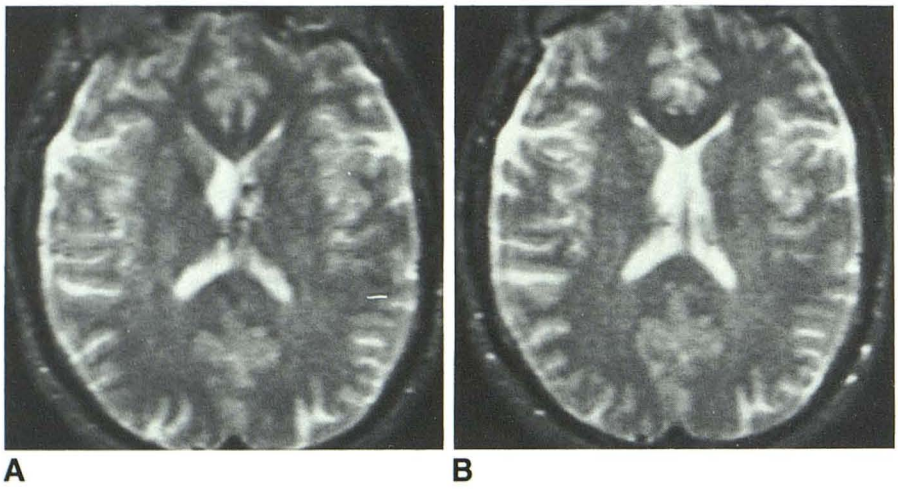


Fig. 6.—Phase-encoding artifacts.
A, Phase-encoding artifacts at level of globus pallidus and genu of internal capsule with long TE (SE 3000/120). Artifacts seen as misregistration of blood vessels between ventricles and increased signal in lenticular nuclei and internal capsule.
B, Eliminating phase-encoding artifacts by MAST® (Motion Artifacts Suppression Technique) (SE 3000/120).

atrophy in the sylvian fissures—the sylvian fissures being at the same level as the lenticular nuclei. These phase-encoding artifacts could be partially corrected by decreasing the TE to 80 msec. The artifacts were eliminated with a new pulse sequence using additional pulses in the slice and read gradients [11]. Incorporation of this technique allows continued use of the longer TE of 120 msec with production of artifact-free images and optimal visualization of the lentiform nuclei. The lentiform nuclei can also be visualized without the motion artifact if the phase-encoding gradient is changed to the Y axis. The motion artifact is then projected through the temporal cortex.

Discussion

Previous articles have shown that both mid- and high-field MR scanners can easily identify methemoglobin with SE pulse sequences [1, 6]. We therefore did not have to optimize our SE pulse sequences to visualize methemoglobin. On T1-weighted images methemoglobin in the intact red blood cells will have an increased intensity. After lysis of the red blood cells, the free methemoglobin will be hyperintense on T2-weighted images [1, 4].

Deoxyhemoglobin, hemosiderin, and ferritin can be seen on T2-weighted images as areas of decreased intensity [1, 3] . Mid-field scanners can image brain iron, but the quality of the image will depend on several factors other than field strength. Gomori and Grossman [9, 10] outlined the other factors, which include (1) the concentration of the intracellular paramagnetic molecules, (2) the signal-to-noise ratio, and (3) the echo delay, TE.

First, a greater concentration of the intracellular paramagnetic molecules causes a greater decrease in the T2-weighted signal [9, 10, 12]. The greater concentration of the super-

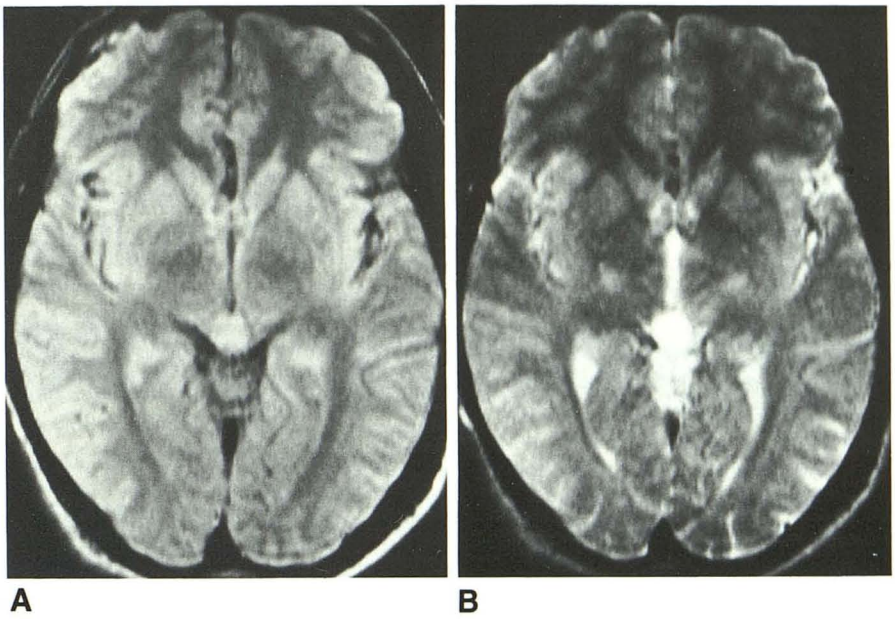


Fig. 7.—Dephasing of water protons by long TE.

***A*, SE 2000/40 MR image shows increased intensity of globus pallidus and putamen.**

***B*, SE 2000/120 MR image allows more dephasing of protons in globus pallidus compared with putamen, due to long TE.**

paramagnetic deoxyhemoglobin, hemosiderin, or ferritin causes a more rapid dephasing of the water molecules [1, 12]. In our study of two patients with large intracerebral hemorrhages, both the acute stage (deoxyhemoglobin) (Fig. 1) and the chronic stage (hemosiderin) (Fig. 2) were easily observed as areas of decreased intensity on all T2-weighted images. However, the brain iron was seen better on the longer TE images (Figs. 1 and 2). In a suspected small arteriovenous malformation in the pons, a small chronic hemorrhage (hemosiderin) could only be seen as a faint decrease in signal on the longer TE images (Fig. 3). In Shy-Drager syndrome, the putamen has been found to have a higher concentration of paramagnetic molecules (ferritin) than the globus pallidus [5, 8]. Our studies supported this finding by showing a greater loss of signal on the T2-weighted images in the putamen compared with the globus pallidus (Fig. 5). This finding was again seen better on the longer TE images.

The second factor cited by Gomori and Grossman [9, 10] to improve visualization of deoxyhemoglobin, hemosiderin, and ferritin is an increase in the signal-to-noise ratio. The signal in the normal tissues of the brain can be increased by increasing the TR [12]. We therefore elected to increase the TR from 2500 msec to 3000 msec. The longer TR images provide better contrast for the areas of decreased signal due to the paramagnetic molecules. The superparamagnetic areas (areas of increased magnetic susceptibility) are seen as black on a background of normal white brain. With a shorter TR of 2500 msec superparamagnetic areas appear as black on a gray background. This decreased contrast with a shorter TR makes it more difficult to identify areas of increased magnetic susceptibility.

Third, a long TE is necessary to visualize the preferential T2 proton relaxation enhancement caused by the superparamagnetic deoxyhemoglobin, hemosiderin, and ferritin [9, 10, 12]. Adequate time is needed to allow dephasing of the intracellular water protons by the local heterogeneous magnetic fields caused by deoxyhemoglobin, hemosiderin, and ferritin. A long TR, short TE sequence (SE 2000/40) shows the globus pallidus and putamen with increased signal intensity (Fig. 7). By prolonging the TE to 120 msec, there is a greater signal loss in the globus pallidus compared with the putamen, because of the greater concentration of ferritin in

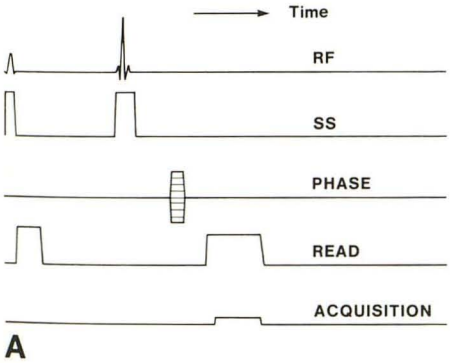
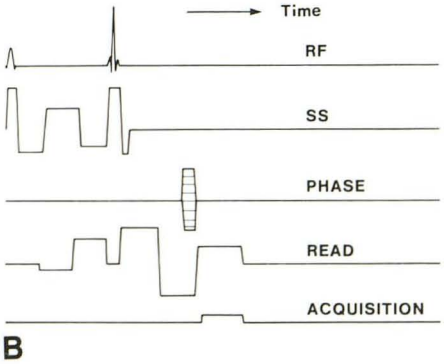


Fig. 8.—Gradient modification pulse sequence (RF = radiofrequency, SS = slice select gradient, PHASE = phase-encoding gradient, READ = readout gradient, ACQUISITION = signal measurement).

***A*, Standard TE (120 msec). Two pulses are obtained in slice-select and readout gradient. Interval between slice-select and readout pulses and the phase-encoding pulse allows dephasing to occur.**

***B*, Motion-desensitized TE (120 msec). Additional pulses in slice-select and readout gradients prevent dephasing in phase-encoding gradient.**



the globus pallidus (Fig. 7) [3]. The greater loss of signal intensity in a T2-weighted image with a longer TE can also be seen in a patient with multiple arteriovenous malformations studied with asymmetric echoes (TE = 30/100 msec) (Fig. 4). Therefore, a long TR (3000 msec) allows adequate signal from normal tissue, while the long TE (120 msec) allows adequate loss of phase coherence of water protons adjacent to superparamagnetic molecules. The long TE sequence would explain the better visualization of deoxyhemoglobin and hemosiderin in the heavier T2-weighted images (SE 3000/120) in Figures 1–3.

With a long TE of 120 msec, motion artifacts appeared along the phase-encoding axis at the level of the globus pallidus, putamen, and sylvian fissures, which are at the same level as the globus pallidus and putamen (Fig. 5). The artifacts were corrected in patients without atrophy in the sylvian fissure regions by decreasing the TE to 80 msec. The artifacts were not totally eliminated in patients with sylvian area atrophy. The widened sulci allowed significant motion of CSF, which then created the phase-encoding artifacts [13]. A new pulse sequence eliminates the phase-encoding artifacts by applying additional pulsing to the read and slice gradients. As can be seen in Figure 8, the usual SE pulse sequence with the long TE of 120 msec allows significant time for dephasing between the 90° pulse and the 180° rephasing pulse. With the new motion-desensitized pulse sequence, repetitive pulsing of the read and slice gradients maintains the protons in phase thereby eliminating phase-encoding artifacts. The new pulse sequence is MAST® (*M*otion *A*rtifact *S*uppression *T*echnique) [11]. If MAST® or a similar pulse sequence is not available, the TE of 120 msec can still be used to identify brain iron in the lentiform nuclei by changing the phase-encoding gradient to the Y axis. The motion artifact will be projected through the temporal cortex.

Recently, a gradient-echo pulse sequence, instead of an SE pulse sequence, was used to identify acute and subacute hemorrhage on a mid-field MR scanner [14]. The gradient-echo pulse sequence showed an increased sensitivity in identifying hemorrhage compared with SE pulse sequences. This sensitivity is due to dephasing of protons caused by both the nonuniformity of the external magnetic field and the local variations of internal fields [12, 14]. Since the external magnetic field is stronger, this will cause a greater dephasing of protons compared with local internal fields. In SE, the effect of nonuniformity of the external magnetic field is compensated for by the refocusing 180° pulse [12]. Therefore, in SE, the dephasing of protons (signal decay) is governed by local variations in stationary internal fields. We have shown that this dephasing in SE pulse sequences can be visualized better by prolonging the TR and TE.

Our own experience with gradient echo has been limited to a short TE to reduce motion artifacts in liver and spine imaging. To evaluate brain iron with gradient echo the T2-weighted images are obtained by using a small pulse tip angle and prolonging the TE [15]. We are undertaking a comparison of the improved SE 3000/120 pulse sequence and the gradient-echo pulse sequence for evaluating brain iron.

In conclusion, use of either the improved spin-echo or gradient-echo pulse sequences on a mid-field MR scanner provides improved evaluation of brain iron.

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