There have now been several reports regarding the use of nuclear magnetic resonance imaging (NMRI, also referred to as magnetic resonance imaging) in the evaluation of various stroke syndromes. Acute (within hours to 2 days) and chronic (within weeks) infarcts have been noted to have prolonged T1 and T2 relaxation times. NMRI studies in hemorrhagic infarction have been based on plain (i.e., not contrast-enhanced) computed tomography (CT) showing bright, speckled areas in areas of superimposed infarction. NMRI in such cases has shown T1 and T2 relaxation times between the short T1 of hemorrage and the long T1 and T2 of infarction. Acute hemorrhages have had short T1 and T2 relaxation times, while chronic hemorrhages have had short T1 and long T2 relaxation times. In the few reported instances, subarachnoid hemorrhage (SAH) detected by x-ray CT has gone undetected by NMRI, only rarely showing as a region of shortened T1 relaxation time or as a region of long T2 relaxation time corresponding to subarachnoid clot.

Reports of areas of prolonged T2 relaxation time (bright areas on T2-weighted spin-echo images) surrounding areas of chronic infarction, as documented by x-ray CT, have raised the question of whether NMRI could be detecting the "ischemic penumbra." In addition, areas representing prolongation of the T2 relaxation time on spin-echo scans have been noted in periventricular regions (so-called "rimming" or "capping"). It has been suggested that these changes represent subcortical zones of infarction as might occur in arteriosclerotic encephalopathy or Binswanger's disease. However, similar lesions have been seen both in patients who clinically do not fit this syndrome and in some normal individuals.

To date, there has been no comparative study correlating the NMRI alterations in cerebrovascular disease with the actual gross and microscopic pathoanatomic examination. We report here our early NMRI findings in 3 cases studied pathologically.

Subjects and Methods

Postmortem NMRI was performed on 2 patients within 12 hours of death. A prototype 0.147 tesla (t) imager manufactured by Technicare (Solon, Ohio) was used to obtain true, three-dimensional volume acquisition data that allowed subsequent reconstruction of images at 3-mm thick planes to match the plane of actual brain slices. The "IR-T1" pulse sequence was used to obtain both qualitative morphologic images and quantitative T1 data. With this combination pulse sequence, quantification is achieved by manipulation of 2 independent signals (S-1 and S-2) obtained during the imaging; the S-2 signal contains T1-weighted inversion recovery (IR) imaging data obtained with a 180–90 degree interpulse spacing of 400 msec, whereas the S-1 signal contains saturation recovery (SR)-type imaging data, in which the image intensity approximates the mobile proton density. The total three-dimensional data collection time was 39 minutes. Computer manipulation of the 2 signals, using an

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appropriate equation, generates a pure T1 rate (1/T1) image, from which regional T1 values (in milliseconds) were obtained. A Carr-Purcell-Meiboom-Gill (CPMG) spin-echo pulse sequence furnished T2-weighted images generated from each of 4 spin-echoes obtained at multiples of 61.4 msec following the initial 90-degree pulse; the total three-dimensional data collection time for this technique was 34.4 minutes. The T2 values were derived from a 4-point monoexponential least-squares curve fit to signal intensity data.

Postmortem examination was performed after completion of the NMRI studies. Brain sections were examined macroscopically for lesions. In the first 2 cases, where three-dimensional volume acquisition had been possible, images were reconstructed at levels exactly matching the macroscopic sections. Thereafter, large hemisections were obtained of histologic preparations including the areas of interest. In the third case, more conventional two-dimensional slices were obtained with a 1.5 t superconducting magnet (Teslacon, Technicare). Images were obtained 5 months before death; postmortem scans were not obtained. The brain was sectioned to match the two-dimensional NMRI planes as closely as possible.

Results

Chronic Infarction with Wallerian Degeneration

Case 1. Three days before death, a 59-year-old man was admitted with lethargy and fever and was found to have a left lower lobe pneumonia. Four years previously, the patient had developed a mild right hemiparesis and expressive aphasia; at that time, CT (Figure 1) showed areas of low attenuation in both the left frontal white matter as well as the deep right parietal temporal region, consistent with infarction. On neurologic examination at the time of his current admission, he was lethargic and disoriented. He intermittently followed commands; he responded to his name and to questions with head nod and short single phrases containing paraphasic errors. Handgrip was strong, and he was able to lift both legs off the bed. He was hyperreflexic throughout, with bilateral Babinski responses and positive grasp reflexes. The patient succumbed to a ruptured mycotic aneurysm of the left renal artery.

At autopsy, a right hemisphere lesion (Figure 2) was observed consisting of a chronic infarct associated with extensive Wallerian degeneration of the white matter adjacent to the cavitory lesions. Similar findings, with cavitory gliosis and secondary degeneration of the white matter, were also associated with the old infarct in the deep left frontal region.

Postmortem IR and spin-echo images (Figure 3, left and right) showed areas of prolonged T1 and T2, respectively, in the right parietotemporal region as well as in the region of the left frontal white matter. These areas of prolonged T1 and T2 corresponded to the areas of chronic infarction as well as to the areas of Wallerian degeneration documented pathologically. Qualitatively and quantitatively, the areas of chronic infarction had more prolonged T1 and T2 relaxation times than those of Wallerian degeneration (Table 1).

This case of pathologically proven Wallerian degeneration surrounding chronic infarcts, examined post mortem by NMRI, had characteristics similar to those in a case of obvious Wallerian degeneration in a 15-year-old right frontoparietal infarct imaged ante mortem (Figure 4, top and bottom). Atrophy of the right peduncle noted by CT to be consistent with Wallerian degeneration was noted on the transverse spin-echo image (Figure 4, top); the coronal image (Figure 4, bottom) showed prolonged T2 in the region of infarction with Wallerian degeneration extending both caudally to the cerebral peduncle as well as across the corpus callosum. Therefore, even when imaging with our first-generation prototype equipment, the correlation of the extent and location of chronic infarction with that of actual pathology is excellent. In addition,
surrounding areas of Wallerian degeneration can be identified as having T1 and T2 relaxation times somewhat less prolonged than chronic infarction, but more prolonged than normal brain.

**Intracerebral Hematoma, Hemorrhagic Infarction, Acute Bland Infarction**

Case 2. Ten days before death, a 48-year-old man was found writhing on the floor, complaining of severe headaches. On arrival at the hospital, he was agitated and did not know where he was. Although his speech was fluent, he was difficult to engage in conversation. His strength and sensation were normal, but he had bilateral upgoing toes. X-ray CT (Figure 5, a and b) showed he had clot in both Sylvian fissures, both insular cisterns, and in the basal frontal interhemispheric fissure extending into both frontal lobes. Based on this CT scan, the development of subsequent severe symptomatic vasospasm in the stem of both middle cerebral arteries, the proximal upper division of both middle cerebral arteries, and in the anterior communicating artery complex could be predicted. Eight days later, the patient became comatose with bilateral decerebrate posturing. He improved with volume expansion, regaining purposeful movements of the right arm and leg, but continued to have decerebrate posturing of the left arm and leg. He remained stuporous. This new deterioration was presumed to be secondary to the development of bilateral symptomatic cerebral vasospasm in both middle cerebral arteries. CT at that time (not shown) showed a new infarct in the right basal ganglia. On Day 9, one day before death, the patient

**Figure 2.** Left: Modified horizontal ("CT-plane") hemisection of the right hemisphere from Case 1 showed an old infarct and surrounding white matter degeneration. Right: The same hemisection showing the old infarct outlined by the solid black line with adjacent white matter degeneration outlined by black dots. (Luxol fast blue–hematoxylin and eosin stain, no magnification).
suffered transtentorial herniation with loss of brainstem reflexes. A CT scan done at that time (Figure 5, d open arrows) showed bilateral low density areas in the medial occipital lobes (posterior cerebral artery territory) consistent with recent infarction, as well as the previously mentioned right basal ganglia infarct (Figure 5d, closed arrow) and low absorption in both frontal and left parietal and occipital lobes.

Gross pathology (Figure 6A) showed a large hematoma in the basal frontal interhemispheric fissure extending into both medial frontal lobes. Clot was also noted in the stem of both Sylvian fissures, both Sylvian cisterns, and both insular cisterns. A ruptured anterior communicating artery berry aneurysm was documented as the cause of the SAH. Both cerebral hemispheres in the entire territory of the middle and anterior cerebral arteries appeared edematous. A bland infarct was noted in the right putamen (Figure 7A), which microscopically appeared recent with no evidence of hemorrhage (not shown). Hemorrhagic infarction (Figure 8 left) was noted in the right superior and midoccipital lobe and the left inferior and midoccipital lobe, which were soft and friable. There was cerebellar tonsillar herniation bilaterally. Microscopically (Figure 8 center), the extensive, recent hemorrhagic infarctions in both occipital lobes contained focal polymorphonuclear leukocyte infiltration, suggesting a duration of 24-48 hours.

IR NMRI (Figure 6B) showed the 10-day-old hematomas to have short T1 relaxation times. The spin-echo study (Figure 6C) revealed the areas of clot to have prolonged T2 relaxation times. The right putaminal infarct (Figure 7B) as well as the right and left occipital hemorrhagic infarcts (Figures 7B and 8 right) had prolonged T1 relaxation times on IR NMRI. The spin-echo study (Figure 7C) showed the corresponding areas to have prolonged T2 relaxation times.

Quantitatively, the areas of 10-day-old clot had T1 relaxation times slightly shorter than those of white matter and mildly prolonged T2 relaxation times between those of white and gray matter (Table 2). The hemorrhagic infarct noted pathologically, but not by x-ray CT, had T1 and T2 times that were prolonged, but less so than those of acute bland infarction.

This SAH from a ruptured anterior communicating artery aneurysm had clot in the basal cisterns extending into both frontal lobes that allowed the prediction of subsequent severe symptomatic vasospasm leading to acute infarction and edema in both the middle and anterior cerebral territories. Death ensued as a result of transtentorial herniation with compression of both posterior cerebral arteries and hemorrhagic infarction developing in both medial occipital lobes before death. There was excellent correlation between NMRI demonstration of the extent and location of acute bland and hemorrhagic infarct and that seen by gross pathology. In this example, T1 and T2 relaxation times were more prolonged in acute bland than acute hemorrhagic infarct; clotted blood, whether subarachnoid or intracerebral, had shortened T1 and prolonged T2 relaxation times. With our first-generation prototype images, clot appeared less distinct than noted by CT or gross pathologic examination.

Subcortical Arteriosclerotic Encephalopathy (Binswanger's Disease)

Case 3. This 65-year-old man with well controlled hypertension had a 10-year history of progressive neurologic deterioration consisting of abulia, dementia, rigidity, ataxia, and bilateral upgoing toes. He had had a 10-year-old right posterior cerebral artery territory occipital infarct, which resulted in left homonous hemianopia, and an old left cerebellar infarction.

CT scan obtained 6 months before death (Figure 9 left) showed periventricular areas of decreased x-ray...
Table 2. Quantitative Data from Case 2

<table>
<thead>
<tr>
<th></th>
<th>T1</th>
<th>T2</th>
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<tbody>
<tr>
<td>Acute hemorrhagic infarct</td>
<td>367±3</td>
<td>155±25</td>
</tr>
<tr>
<td>Acute bland infarction</td>
<td>386±4</td>
<td>163±33</td>
</tr>
<tr>
<td>Hematoma (10 days)</td>
<td>261±11</td>
<td>133±16</td>
</tr>
<tr>
<td>Gray matter</td>
<td>328±4</td>
<td>148±23</td>
</tr>
<tr>
<td>White matter</td>
<td>285±4</td>
<td>108±15</td>
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</table>

Values are mean ± SD milliseconds.

attenuation and the old right occipital and left cerebellar infarcts. IR two-dimensional, 8-mm thick slices obtained with 0.6 t superconducting imagers (Technicorp) (Figure 9 center) showed regions of prolonged T1 times involving the periventricular white matter. The spin–echo study (Figures 9 right and 10 top) showed corresponding regions of prolonged T2 times but also more extensively involved the entire white matter. The most prominent areas of involvement seemed to cap the lateral ventricles. The spin–echo study more strikingly demonstrated the abnormal white matter.

Table 1. Quantitative Data from Case 1

<table>
<thead>
<tr>
<th></th>
<th>T1</th>
<th>T2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic infarction</td>
<td>465±12</td>
<td>195±34</td>
</tr>
<tr>
<td>Wallerian degeneration</td>
<td>399±6</td>
<td>166±27</td>
</tr>
<tr>
<td>Gray matter</td>
<td>333±10</td>
<td>148±23</td>
</tr>
<tr>
<td>White matter</td>
<td>283±4</td>
<td>124±9</td>
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Values are mean ± SD milliseconds.

Figure 4. The transverse spin–echo image from a patient with an old right frontoparietal infarct (top) shows atrophy of the right cerebral peduncle (reception time, TR = 2000 msec; echo time, TE = 30 msec). On the coronal spin–echo image (bottom), a bright region representing prolonged T2 is seen in the right frontoparietal region, with tracts of prolonged T2 extending down to the cerebral peduncle as well as across the corpus collosum (arrows) (TR = 2000 msec, TE = 60 msec).

Figure 5. Computed tomography (CT) scan of Case 2 done within 24 hours of onset of symptoms (a and b) demonstrates extensive subarachnoid hemorrhage extending intracerebrally in the left frontal area (b, arrow). CT scan performed 1 day before death shown with higher cuts (c and d) shows a new area of decreased attenuation in the right basal ganglia (closed arrow), and low density regions in the occipital lobes bilaterally (open arrows). (Both a and b correspond to levels similar to that shown in Figure 6; c and d correspond roughly to the level in Figure 7.)
FIGURE 6. A: Modified horizontal gross section (Case 2) shows hematoma in the interhemispheric fissure extending into the right frontal lobe and the left Sylvian fissure. B: Inversion recovery (IR) image shows the corresponding regions to be bright, representing short T1 relaxation times (arrows). C: Spin-echo image shows the areas of clot (arrows) to decay away slowly, representing prolonged T2 relaxation time (Carr-Purcell-Meiboom-Gill spin-echo, CPMG SE, study with repetition time, TR = 1 sec; echo time, TE = 183 msec).

Pathologically (Figure 10 bottom), there was diffuse discoloration of the white matter with a granular appearance; there were multiple lacunes throughout the basal ganglia and brainstem in addition to the large right occipital and left cerebellar infarcts. Microscopically, there was patchy, irregular, more or less complete loss of central white matter; small vessels down to arteriolar size were abnormal, with an extreme degree of dense hyalinosis and foamy macrophage infiltration (Figure 11). The pathologic picture was felt to correspond with previous descriptions of subcortical arteriosclerotic encephalopathy, so-calledBinswanger's disease.16,17

This case offers one explanation for the subcortical and periventricular areas of prolonged T2 relaxation times noted on spin-echo T2-weighted images in many patients. Certainly many patients who clinically would not be suspected of having such extensive subcortical
leukoencephalopathy would not have such extensive white matter relaxation time prolongation.

**Discussion**

Early clinical applications of three-dimensional proton (1H) NMRI have dealt with determining the T1 and T2 relaxation characteristics of various clinical conditions where the areas of abnormal NMRI signal characteristics have been compared with the clinical picture or with the findings on CT scan. We have presented here 3 cases correlating the NMR characteristics with the neuropathologic findings, the first 2 cases being imaged post mortem and the third, ante mortem.

Although there have been several reports of NMRI findings in various clinical stroke syndromes,\(^1\) only 1 pathologic study of both acute (3 days) and chronic (10 years) embolic infarction has been described.\(^1\) In that case and in our cases, both acute and chronic thrombotic or embolic infarction is represented as an area of prolonged T1 and T2 relaxation times in a particular vascular distribution. However, in our first case, the areas of prolonged T1 and T2 presumed to be chronic infarction actually corresponded not only to the areas of chronic infarction, but also to contiguous areas of Wallerian degeneration. Qualitatively, on the spin-echo study, the area of chronic infarction appeared to have a more prolonged T2 relaxation time than the surrounding region of Wallerian degeneration. A halo of T2 prolongation has been noted previously around chronic infarcts;\(^8\) it has been proposed that this could represent "blood flow alterations," "hypometabolism," or the ischemic penumbra. In our case, we have pathologically documented it to correspond with Wallerian degeneration. This is in agreement with the in
Coronal spin-echo images from Case 3 (top) show that the most involved areas of prolonged T2 times seem to cap the lateral ventricles (repetition time, TR = 2000 msec; echo time, TE = 60 msec). Coronal gross pathologic sections (bottom) demonstrate the discoloration of the white matter in the corresponding areas (arrows).

In the second case, we show that a 10-day-old hematoma, which was demonstrated by pathologic examination to be a subarachnoid clot extending intrahemispherically, had a very short T1 relaxation time, slightly shorter than that of white matter, and a mildly prolonged T2, greater than that of white matter, but slightly less than that of gray. This is in keeping with...
the findings of short T1 and long T2 noted in intracerebral hematoma in the literature. Acute hematomas, on the other hand, have been found to have short T1 and T2 relaxation times. It is still uncertain when the transition from short to long T2 occurs. Sipponen et al. noted a qualitative change in the image of an acute hematoma at about 3 days. The transition point may be variable, depending not only on the age of the hematoma, but also on other factors (e.g., hematocrit, hemoglobin content of the blood, initial volume of blood in the tissue, amount of tissue injury, presence of edema).

In a study of intracranial hematomas by high-field NMRI, (1.5 T) Gomori et al. outlined changes seen over time. They observed 3 characteristic intensity patterns: 1) a central hypointensity on T2-weighted images in the acute stage, 2) a change to hyperintensity initially on the T1- and then on T2-weighted images that extends from the hematoma periphery inward in the subacute stage (1 week-1 month), and 3) a rim of parenchymal hypointensity on the T2-weighted images in the brain immediately adjacent to the hematoma in the subacute and chronic stages. These patterns, the central hypointensity and the parenchymal rim of hypointensity seen on T2-weighted images, occur only on images obtained at high magnetic fields. It was proposed that intact hypoxic red blood cells with high deoxyhemoglobin concentrations are responsible for the central hypointensity, and that hemosiderin is the likely paramagnetic relaxant causing the parenchymal rim of hypointensity.

Studies of NMRI in SAH have produced varying results. In one study, which included 2 patients with SAH, no visible abnormalities were seen on the IR studies, while in both cases the CT clearly showed subarachnoid blood; in 1 of the 2 cases, a spin–echo image revealed a bright signal in the region of blood seen on CT, indicating a prolonged T2. In another study in which there was subarachnoid extension of blood from an intracerebral hemorrhage, the area of subarachnoid blood appeared bright on the IR images, representing a short T1. These differing results may be due to differences in the thickness of the subarachnoid clot and the mixture of clot and CSF in the subarachnoid space. If the presence of subarachnoid clot as opposed to unclotted blood is important in predicting the development of symptomatic vasospasm, then NMRI may differentiate between the two and become diagnostically superior to CT in cases of ruptured saccular aneurysm.

The NMRI characteristics of hemorrhagic infarction have been noted in previous studies to be the same as those of hematoma (i.e., short T1 and long T2 relaxation times). These results for hemorrhagic infarction were likely obtained because patients were chosen for study on the basis of noncontrast x-ray CT showing a region of high attenuation consistent with blood, most likely representing hematoma rather than hemorrhagic tissue. In Case 2, the CT showed no increased attenuation suggestive of hemorrhage. On NMRI both the acute, bland infarct as well as the hemorrhagic infarct appeared qualitatively the same on IR (dark) and spin–echo (bright) studies. Had no pathologic examination been performed, it would appear that neither contained blood since clot has different NMRI characteristics. Once the difference in these lesions was verified pathologically, their relaxation time characteristics could be examined quantitatively (Table 2). In the acute hemorrhagic infarct, T1 was prolonged, but less so than in acute bland infarction; T2 was also prolonged, also slightly less than in acute bland infarction. Although we present here only 1 case, this case does suggest that on NMRI, hemorrhagic infarction may be quantitatively different from chronic bland infarction. With the ability to quantify NMRI to more precise gray scales, the technique may be more sensitive than x-ray in detecting hemorrhagic infarction.

There has been much recent interest in the finding of areas of prolonged T2 relaxation time in the periventricular white matter noted on spin–echo NMRI. In Case 3, the pathologic picture was consistent with previous descriptions of subcortical arteriosclerotic encephalopathy orBinswanger’s disease. The periventricular changes noted on NMRI were secondary to leukomalacia and arteriolar hyalinosis. However, this NMRI abnormality has been seen in normal patients as well as in patients with other neurologic diseases. Further NMRI–pathoanatomic correlation is needed to evaluate periventricular NMRI changes.

In summary: With pathologic correlation of NMRI in chronic infarction, we found that the halo of T2 prolongation seen surrounding chronic infarcts actually represented Wallerian degeneration. Acute bland and hemorrhagic infarction had the same qualitative NMRI appearance, but differed slightly with quantitative measurements, the hemorrhagic infarction having quantitative characteristics suggestive of hemorrhage. A 10-day-old subarachnoid clot had short T1 and long T2 relaxation times as would be expected in hematoma. And lastly, the marked prolongation of T2 relaxation times in the periventricular white matter of a patient who clinically appeared to haveBinswanger’s disease (subcortical arteriosclerotic encephalopathy) was pathologically documented to be consistent with that diagnosis.

With the rapid changes occurring in the NMR scanning equipment and the pulse sequences being used, neuropsychological correlation remains the sorely needed standard to clarify the processes underlying T1 and T2 changes.

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