Nuclear magnetic resonance (NMR) has been recognized for well over 40 years. Although the first successful in vivo NMR experiments date back to 1946–1948, it was not until the 1970s that the first experiments involving NMR spectroscopy and imaging of living systems were reported in the literature. Since that time the clinical application of NMR has experienced exponential growth. Because of this rapid pace of development and the concurrent increase in hospital-based NMR facilities, it is timely to review the application of NMR to the diagnosis and investigation of cerebrovascular disease.

Nuclear Magnetic Resonance

Detailed physics of the NMR experiment are beyond the scope of this review. However, the parameters used to determine contrast in magnetic resonance imaging and the basics of NMR spectroscopy are briefly described.

Magnetic Resonance Imaging (MRI)

There are three parameters that determine contrast in NMR imaging: nuclear density, $\rho$, and two intrinsic NMR parameters called $T_1$ and $T_2$. $T_1$ and $T_2$ are relaxation time constants that can have characteristic values for various tissues. By exploiting certain timing aspects of the pulse sequence (a collection of radio frequency [RF] pulses delivered in a specifically timed sequence) used in obtaining an image, one can enhance the relative contribution of $\rho$, $T_1$, and $T_2$ contrast. The time delays in the RF pulse sequence, which are adjusted to produce variable contrast, are called TR (time-to-repetition) and TE (time-to-echo). TR is related to the speed with which the entire pulse sequence is delivered, usually on the order of seconds, and TE is related to the time between the individual RF pulses within the RF pulse sequence, usually on the order of milliseconds. $T_1$, $T_2$, and $\rho$ image contrast are produced as follows:

$T_1$ contrast. The faster the pulse sequence is delivered (i.e., the shorter the TR), the more $T_1$ contrast will be apparent in the image, and conversely, the slower the pulse sequence is delivered (i.e., the longer the TR), the less $T_1$ contrast. (It is assumed that in $T_1$ contrast images TE is kept as short as possible to avoid any contribution from $T_2$.)

$T_2$ contrast. The longer the TE (i.e., the longer the time between individual RF pulses in the sequence, not the rate at which the entire pulse sequence is delivered), the more $T_2$ contrast will be apparent in the image. Short TEs result in little $T_2$ contrast. (Here it is assumed that in $T_2$ contrast images TR is kept reasonably long to avoid any contribution from $T_1$.)

$\rho$ contrast. Nuclear density contrast, $\rho$, is obtained by minimizing $T_1$ and $T_2$ effects with the use of a short TE and a long TR.

MR images are not pure $\rho$ images or pure $T_1$ or $T_2$ images but rather $\rho$ or $T_1$ or $T_2$ “weighted” images. For practical reasons, however, images which accentuate either $\rho$, $T_1$, or $T_2$ are simply referred to as $\rho$ images, $T_1$ images, and $T_2$ images, respectively.

From the discussion above, it is obvious that it is possible to obtain a full spectrum of $\rho$, $T_1$, and $T_2$ contrast in any one image. Indeed, this is the basis for the extreme versatility in soft tissue contrast seen in MRI. $T_1$ contrast is also dependent on the field strength of the magnet that is used to obtain the image, and in general, the higher the field strength, the more difficult it can be to generate $T_1$ contrast. However, this factor has not been very limiting in practice.

Magnetic Resonance Spectroscopy (MRS)

The RF signals received from the nuclei can be processed and displayed as a spectrum, which usually comprises several peaks representing the individual groups of nuclei that make up the various molecules contained in the sample. For instance, if we collect a spectrum of the phosphorus-containing compounds in human brain, we can see at least seven readily identifiable peaks: phosphocreatine, inorganic phosphate, phosphodiesters, phospho-
Ischemic Cerebrovascular Disease

Measurements are made of relative magnitude and position, width, shape, and time-dependent appearance of the peaks. Mobility, structure/conformation, local environment (pH, metal ion binding), kinetics and relative concentrations, compartmentalization, and transport, flow, and diffusion can be inferred from these measurements.

MRI in Stroke

Ischemic Cerebrovascular Disease

Experimental studies have demonstrated that ischemic changes due to stroke can be detected on MRI within the first 4 hours of the ictus and as early as 1 hour.9-11 In the early stages of ischemia, the increased accumulation of tissue water results in prolongation of both T1 and T2. In early ischemia these effects are best appreciated with T1 images, in which the ischemic region appears as high signal intensity. Later in the ischemic process the infarct is better appreciated with low (relative) signal intensity produced from T1 images (T1 prolongation effect). With time an infarct will appear as a low signal (dark) region on T1 images and as a high signal (bright) on T2 images.10 The appearance of infarcted tissue in the subacute stage can be appreciated on both MRI and CT. One advantage of MRI, however, is its superior image resolution, which allows for the identification of relatively smaller regions of infarct (including “lacunar” type stroke) missed by CT.11-14 Additionally, in the subacute to chronic stages (beyond the edema stage and before cavitation starts to appear), CT images of the stroke might appear isodense with surrounding tissue (pseudonormalization effect), whereas with MRI a rim of hyperintensity on T1 images can frequently be seen surrounding a darker zone (the actual infarct).11 This may reflect either persistent ischemia (penumbra) or Wallerian degeneration15 and may have future therapeutic implications. In the chronic stage the cavity formed will have an appearance similar to that of cerebrospinal fluid (CSF) in a closed space, that is, hypointense (dark) region on T1 images and hyperintense (bright) on T2 images. Another advantage of MRI over CT is better resolution in the posterior fossa so that brainstem infarcts missed on CT can be readily detected by MRI.

CT abnormalities in patients with transient ischemic attacks (TIA) have been found with variable frequency ranging from 0-20%.16-18 MRI is abnormal in up to 80% of patients with TIA.13,14 This wide variation reflects the lack of correlation between the “ischemic” lesion on CT or MRI and the clinical picture, as well as the broad definition of TIA used (deficit lasting less than 24 hours). Subclassifying TIA as completed infarcts with transient symptoms (CITS)16,17 versus true transient ischemic episodes, in which the deficit generally lasts less than 1-3 hours,19 might result in less variability in the incidence of abnormalities seen on MRI. MRI may thus aid in providing a more exact diagnosis for future natural history and treatment studies of lacunar infarction or small vessel disease.

There is a surprising lack of MRI-neuropathological data on stroke.15 Dewitt and colleagues have correlated both ischemic and hemorrhagic cerebrovascular disease with gross and histopathological examination. More studies of this type on high-field (1.5 T) magnets are needed.

Intracerebral Hemorrhage

A detailed description of the evolution of a blood clot and its MR image characteristics has been covered in several recent publications.20-22 A much simplified schema will be presented here. Acutely, red blood cells (RBC) are hemoconcentrated and form deoxyhemoglobin which results in hypointense regions on T1 images. In the subacute stage, as methemoglobin starts forming around the fourth to seventh day and proceeding centripetally, hyperintense signals initially appear on T1 images and later on T2 images (Figure 1). This observation is believed to be related to the lag of RBC lysis behind methemoglobin formation. Therefore, the bright signal initially seen on T1 images because of the methemoglobin T1 shortening effect will not be complete in the center of the hemorrhage until the deoxyhemoglobin is completely replaced with lysis of centrally located RBC. At the same time, two peripheral zones are delineated on T2 images: a more medial hemosiderin hypointense rim (dark zone) and a more peripheral hyperintense signal (bright zone), reflecting edema formation.

In the chronic state a well-demarcated bright signal is seen from the whole clot on T1 image and T2 image as methemoglobin fills both the periphery and center of the hematoma. The hypointense rim of hemosiderin is well formed at this stage, and variable edema (bright signal) is well demarcated on T2 images. The hyperintensity of the hematoma may persist for as long as a year or more. Subsequently, the hematoma is replaced by CSF, and T1 prolongation effects appear. Therefore, the image of an old clot of more than 1 year of age would appear hypointense on T1 images and hyperintense on T2 images with a hypointense rim (hemosiderin) surrounding the cavity. The rim of hypointensity of hemosiderin is useful in differentiating ischemic infarct from intracerebral hemorrhage of more than 1 year of age since in the former no hemosiderin signal is appreciated. An exception would be hemorrhagic infarcts which after 1 year can have the same MR signal characteristics as intracerebral hemorrhage. At this stage MRI is more useful than CT for detecting small brainstem hemorrhage which can be missed on CT because of bone artifact. A recently developed technique using gradient echo pulse sequences (beyond the scope of this review)
FIGURE 1. Acute to subacute intraparenchymal hematoma in the right occipital lobe. (Left) T1-weighted axial MRI (TR=600 msec, TE=30 msec) demonstrating the isointense lesion of hemorrhage (deoxyhemoglobin) (arrow) surrounded by the hyperintense rim of methemoglobin (arrow head). Blood forming a CSF-blood layer is seen as a hypointense signal (deoxyhemoglobin effect) in the left lateral ventricle (open arrow). (Right) T2-weighted axial MRI (TR=2800 msec, TE=90 msec) demonstrating a central region of hypointensity (deoxyhemoglobin) (short arrow) surrounded by the hyperintense peripheral rim of methemoglobin (arrow head) and the most peripheral, less hyperintense zone of edema (long arrow). The hypointense signal from the contralateral ventricle represents deoxyhemoglobin (open arrow) within the CSF. (Reprinted through courtesy of Suresh Patel, MD, Division of Neuroradiology, Department of Radiology, Henry Ford Hospital, Detroit, MI)

has been shown to improve the specificity in the diagnosis of intracerebral hemorrhage.24

Subarachnoid Hemorrhage

Contrary to initial in vitro studies, which indicated that acute subarachnoid hemorrhage might be missed on MRI,25 acute hemorrhage can be detected with pulse sequences that are intermediate in contrast characteristics (i.e., mixed T1-T2 images) so that CSF is isointense with brain parenchyma.26 With such pulse sequences (TE=80 msec, TR=2200 msec), using a 0.15-T magnet (low-field), the blood-stained CSF causes a marked shortening of T1 and a slight shortening of T2, resulting in a hyperintense signal that contrasts with the isointense signal of normal CSF. In the subacute stage, methemoglobin formation (as in intracerebral hemorrhage) will cause marked shortening of T1 and prolongation of T2 giving the bright signal of blood-stained CSF on both T1 and T2 images. In addition, MRI could prove superior to CT in demonstrating the cause of hemorrhage. In a recent study no aneurysm was demonstrated by CT in 25 of 30 cases, whereas in 14 of these cases, MRI detected aneurysms in various locations.26 MRI also appears superior to CT in demonstrating small posterior inferior cerebellar artery aneurysms that are often missed on CT when only trace hemorrhage into the CSF occurs.

Subdural and Epidural Hematoma

The evolution of the blood clot in both subdural and epidural hematoma is similar to that of intracerebral hemorrhage as described previously (Table 1). Epidural hematoma can be differentiated from subdural hematoma by the MR appearance of the fibrous dura mater.27 With intermediate magnetic field strength the fibrous dura mater, which has an even lower signal characteristic than the hematoma on T2 images (TE=60 msec, TR=2000 msec), will appear darker than the underlying or overlying lesion (subdural versus epidural, respectively). If a higher field strength is used, the appearance of both acute subdural and epidural hematoma is the same because dural demarcation is lost. In the subacute stage the high signal of the hematoma is clearly demarcated from the low signal of the dura regardless of field strength.

Cerebral Venous Thrombosis

CT reveals direct signs (delta sign, cord sign) of cerebral venous thrombosis in only 33% of cases.28 MRI may be more sensitive, possibly replacing angiography in confirming the clinical suspicion of venous sinus thrombosis. Sagittal MR images will show not only the actual thrombosed superior sagittal sinus but also the extent of the thrombus and the degree of recanalization, which may have future therapeutic implications. Acutely, the expected “flow void” signal of the sinus (hypointensity) on T1 images is lost because it appears bright; T2 images will reveal a low signal relating to the deoxyhemoglobin effect. Subacutely, the intraluminal clot evolves in a pattern similar to that of
intracerebral hemorrhage. In the chronic phase recanalized vessels will result in reappearance of the dark flow void signal on $T_1$ images. Indirect signs of thrombosis (intracerebral hemorrhage and diffuse edema with slit ventricles) do not differ in characteristics whether they are associated with cerebral venous thrombosis or other conditions.

**Vascular Malformations and Developmental Anomalies of the Cerebral Vasculature**

Vascular malformations, which may present as intracerebral or subarachnoid hemorrhage, are categorized as follows:

1. Occult vascular malformations, including thrombosed arteriovenous malformations, cavernous angiomas, capillary telangiectasia, and venous angioma. MR is more sensitive than CT and is the modality of choice for detecting and characterizing these malformations. They appear as mixed signal intensity on both $T_1$ and $T_2$ images. Unique areas of signal void are present that represent calcification, hemosiderin, or both.

2. Arteriovenous malformations. The entangled, dilated vessels appear as serpiginous and punctate regions of signal void because of rapid flow and turbulence. Previous hemorrhage, cysts, and calcification may be evident.

3. Aneurysms are diagnosed by the location, morphology, and mixed signal intensities in a concentric lamellar arrangement. Flow void (high velocity signal loss) within the lumen, or increased signal intensity on $T_2$ images associated with thrombus (methemoglobin), or both may be detected within all or part of the aneurysm. In giant aneurysms (>2.5 cm diameter), complex signal intensities result from a combination of flowing blood, turbulence, organizing thrombus, calcification, and hemosiderin deposition.

**MR Spectroscopy**

Studies of clinical stroke with MRS are limited. Metabolic abnormalities detected by MRS (reduced phosphocreatine and ATP, increased inorganic phosphate, elevated lactate, and acidosis) in ischemic brain may precede structural alterations detected by CT or MRI. The metabolic data obtained by MR spectroscopy may eventually lead to biochemical markers of clinical stroke prognosis and response to therapy since serial studies can be easily performed. Other applications of NMR technology that are being developed include the ability to measure cerebral blood flow, oxygen utilization, and glucose metabolism. This information will undoubtedly be important to clinicians who manage patients with cerebrovascular disease and will emphasize the need to treat stroke patients as soon as possible to minimize the extent of ischemic damage seen on MRI.

**Summary**

MRI is becoming the imaging modality of choice in patients with ischemic cerebrovascular disease although CT is still the test of choice to exclude acute hemorrhagic stroke. We have briefly reviewed characteristic features of ischemic and hemorrhagic cerebrovascular disease as well as vascular anomalies as seen on MRI. In time MRS should provide useful noninvasive metabolic data to complement the anatomical data in patients with cerebrovascular disease.

**References**


**TABLE 1. Optimum MRI Contrast in Cerebrovascular Disease**

<table>
<thead>
<tr>
<th></th>
<th>Acute (0–3 days)</th>
<th>Subacute (4–14 days)</th>
<th>Chronic (2 weeks–1 year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic stroke</td>
<td>$T_2$</td>
<td>$T_1$ and $T_2$</td>
<td>$T_1$ and $T_2$</td>
</tr>
<tr>
<td>ICH/SDH/EDH</td>
<td>$T_1$</td>
<td>$T_1$ and $T_2$</td>
<td>$T_1$ and $T_2$*</td>
</tr>
<tr>
<td>SAH</td>
<td>Mixed $T_1$ and $T_2$</td>
<td>$T_1$ and $T_2$</td>
<td>$T_1$ and $T_2$*</td>
</tr>
<tr>
<td>CVT (sinus appearance with associated clot)</td>
<td>$T_1$ and $T_2$$^\dagger$</td>
<td>$T_1$ and $T_2$</td>
<td>$T_2$ and $T_2$‡</td>
</tr>
</tbody>
</table>

ICH, intracerebral hemorrhage; SDH, subdural hematoma; EDH, epidural hematoma; SAH, subarachnoid hemorrhage; CVT, cerebral venous thrombosis.

*Progressive loss of signal after 1 year on $T_1$ image.

†Disappearance of the flow void signal on $T_1$ image.

‡Reappearance of flow void signal on $T_1$ and $T_2$ image.

KEY WORDS: cerebrovascular disorders • magnetic resonance imaging • nuclear magnetic resonance

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