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, phosphodiester, phospho-
Ischemic Cerebrovascular Disease

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

MRI in Stroke

Ischemic Cerebrovascular Disease

Experimental studies have demonstrated that isch-
emic changes due to stroke can be detected on MRI
within the first 4 hours of the ictus and as early as 1
hour. In the early stages of ischemia, the in-
creased 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 inten-
sity 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. The appearance of
infarcted tissue in the subacute stage can be appre-
ciated 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. 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). This may reflect either persistent isch-
emia (penumbra) or Wallerian degeneration and
may have future therapeutic implications. In the
chronic stage the cavity formed will have an appear-
ance similar to that of cerebrospinal fluid (CSF) in a
closed space, that is, hypointense (dark) on T₁
images and hyperintense (bright) on T₂ images.
Another advantage of MRI over CT is better resolu-
tion in the posterior fossa so that brainstem infarcts
missed on CT can be readily detected by MRI.

CT abnormalities in patients with transient isch-
emic attacks (TIA) have been found with variable
frequency ranging from 0–20%. MRI is abnor-
mal in up to 80% of patients with TIA. 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
TIAs as completed infarcts with transient symp-
toms (CITS) versus true transient ischemic epi-
sodes, in which the deficit generally lasts less than
1–3 hours, 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 lacu-
nar infarction or small vessel disease.

There is a surprising lack of MRI-neuropatho-
logical data on stroke. Dewitt and colleagues have
correlated both ischemic and hemorrhagic cere-
brovascular disease with gross and histopathologi-
cal 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. A much
simplified schema will be presented here. Acutely,
red blood cells (RBC) are hemoconcentrated and
form deoxyhemoglobin which results in hypoin-
tense regions on T₁ images. In the subacute stage,
as methemoglobin starts forming around the fourth
to seventh day and proceeding centripetally, hyper-
intense 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
dehemoglobin is completely replaced with lysis of
centrally located RBC. At the same time, two
peripheral zones are delineated on T₁ 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 vari-
able 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 prolone-
gation 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) sur-
rounding 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 hem-
orrhagic 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 sinus29 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 thomboosed 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 $T_1$ and $T_2$ 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 anatomic data in patients with cerebrovascular disease.

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