Contribution of Susceptibility-Weighted Imaging to Acute Stroke Assessment

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Background—Susceptibility-weighted (SW) MRI provides insight into the pathophysiology of acute stroke. We report on the use of SW imaging (SWI) sequences in clinical practice and highlight the future applications.

Summary of Review—SWI exploits the magnetic susceptibility effects generated by local inhomogeneities of the magnetic field. The paramagnetic properties of deoxyhemoglobin support signal changes related to acute hemorrhage and the intravascular spontaneous blood oxygen level dependent (BOLD) effect. SWI allows the early detection of acute hemorrhage within 6 hours after symptom onset. SWI may also identify previous microbleeds in acute ischemia; however, the impact of these findings on thrombolytic therapy safety has not been definitely established. The diagnosis of arterial occlusion is usually performed by magnetic resonance angiography. SWI allows intravascular clot detection at the acute stage.

Substantial experimental data suggest that spontaneous BOLD contrast may improve tissue viability assessment. The ratio of oxyhemoglobin to deoxyhemoglobin, measured by MRI in the capillary and venous compartments, reflects the oxygen extraction fraction (OEF) and the cerebral metabolic rate of oxygen. The combination of magnetic resonance (MR)-measured OEF and cerebral blood flow, via perfusion studies, may provide information about tissue viability.

Conclusions—SWI offers a spectrum of current clinical applications and may improve our knowledge of the pathophysiology of acute stroke.

Key Words: hemorrhage ■ ischemia ■ stroke, acute ■ magnetic resonance imaging

The advent of new MRI techniques has improved acute stroke diagnosis.1 Diffusion- and perfusion-weighted sequences and magnetic resonance angiography (MRA) provide data on the pathophysiology of ischemia and may contribute to therapeutic decisions.2 Susceptibility-weighted imaging (SWI) also adds information about acute stroke.3–6 In clinical practice, SWI enables the detection of acute hemorrhage5–10 and intravascular clots.11,12 SWI sequences also have the potential to assess tissue viability.13–15 In this article, we review clinical and imaging data about the use of SWI sequences (perfusion-weighted imaging [PWI] excepted) in current clinical practice and highlight the future applications of this method.

Basic Principles of SW Contrast
SWI exploits the magnetic susceptibility artifacts generated by local inhomogeneities of the magnetic field. The application of a magnetic field to a biological component generates an induced field characteristic of the specific tissue. The induced magnetization depends on the applied magnetic field and on the magnetic susceptibility of molecules. Because of the presence of unpaired electrons, deoxyhemoglobin is a paramagnetic substance that produces a local nonuniform magnetic field, resulting in rapid dephasing of proton spins in SWI sequences.16–18

This property accounts for the blood oxygen level dependent (BOLD) effect.19 Signal modification depends on the amount and magnetic properties of molecules and on the structure of tissues and lesions. Magnetic susceptibility variations are higher at the interface of 2 regions, owing to the generation of an intrinsic gradient, which is proportional to the difference in the magnetic susceptibility of the 2 adjoining structures.17 Signal changes are also dependent on the delay between symptom onset and scanning and other factors including hematocrit, deoxyhemoglobin concentration, red blood cell integrity, clot structure (fibrin and serum contents),20,21 molecular diffusion,22 pH,23 temperature, field strength,24 voxel size, previous contrast material use, blood flow, and vessel orientation.17,18

When interpreting SW images, care must be taken to avoid susceptibility artifacts generated by air–bone interfaces.18 Moreover, artifacts may obscure the evaluation of vascular structures close to the skull base.11

Imaging Protocols
Although a variety of MRI sequences can be used for SWI, SWI is mainly based on the high resolution method.25 Conventional gradient echo (GRE) images are extremely sensitive to magnetic field inhomogeneities because the
signal is generated by the reversal of the readout gradient alone without an accompanying 180° phase reversal pulse. Therefore, any magnetic field gradients that may be present will not be compensated for, and thus will attenuate the signal. The radiofrequency excitation pulse is operator-selectable and is generally less than the 90° flip angle of the spin-echo (SE) pulse sequence. Optimal SWI relies on a judicious echo delay and flip angle choice. Typical parameters for a conventional T2*-weighted gradient echo sequence are as follows: repetition time (TR), 600 to 800 ms; echo time (TE), 30 to 50 ms; and flip angle, 10° to 30°. These GRE-type and SE-type echo-planar imaging sequences are sensitive to susceptibility effects. These sequences are characterized by short acquisition times and have been applied to the detection of hemorrhagic lesions and clots. These shorter acquisition times result in fewer movement artifacts and shorter therapeutic delay (Figure 1).

### Diagnosis of Intracerebral Hemorrhage Within the First Hours of Stroke

Intracerebral hemorrhage (ICH) is one of the most feared complications of acute ischemic stroke therapy. Computed tomography (CT) is considered the gold standard for imaging of brain hemorrhage. In the late 1980s, MRI emerged as a promising tool for the detection of acute ICH. Early signal changes in SWI are attributed to deoxyhemoglobin formation. On the basis of experimental data, this process occurs immediately after extravasation. The hyperacute hematoma appears as an isointense to hyperintense center with a hypointense periphery (deoxyhemoglobin) (Figure 1); signal changes progress from the periphery toward the center of the hematoma. T2*-weighted imaging was able to detect signal loss in a series of 6 patients with intracerebral hemorrhage imaged between 2.5 and 5 hours from symptom onset. The earliest clinical detection of hemorrhage has been reported within the 2.5 hour time window as early as 23 minutes from symptom onset. The ability of T2*-weighted gradient-echo imaging to detect ICH within 6 hours of symptom onset has been confirmed by a prospective, blinded, randomized trial involving 124 patients: 62 patients with ICH and 62 controls. The authors measured sensitivity, specificity, accuracy, and positive and negative predictive values of a multisequence MRI protocol compared with CT. Three experienced readers identified ICH with 100% sensitivity and 100% accuracy. In contrast to CT scan, the ability of SWI to detect recurrent hemorrhage has not been assessed. Fluid-attenuated inversion recovery (FLAIR) imaging has been advocated for the detection of acute subarachnoid hemorrhage; however, FLAIR hyperintensity within the subarachnoid space can be artifactual and is not specific for subarachnoid hemorrhage. SWI can also detect subarachnoid hemorrhage; however, definitive evidence of the sensitivity of SWI in this setting is still lacking.

### Identification of Microbleeds

The presence of previous microbleeds (Figure 2) may increase the risk of hemorrhage after thrombolysis or the use of other antithrombotic drugs. Small deposits of hemosiderin are found in 12% to 20% of MRI-examined stroke patients. Hypointense spots on T2*-weighted gradient echo MR have been considered microbleeds. Visualization of microbleeds is dependent on the scan sequence, field...
strength, and echo-planar or nonecho-planar imaging. A recent study suggests that stroke patients with a small number of microbleeds on pretreatment MRI could be treated safely with thrombolysis. Conversely, multiple microbleeds may signal a diffuse hemorrhage-prone vasculopathy. Larger prospective studies are needed to address the predictive value of the detection of microbleeds with regard to the risk of thrombolytic-induced ICH.

Detection of Spontaneous Hemorrhagic Transformation Earlier Than CT
SWI may also detect spontaneous hemorrhagic transformation of ischemic stroke earlier than CT scans. A recent observation supports this hypothesis (Figure 3). Determination of spontaneous hemorrhagic transformation before thrombolytic therapy may decrease the rate of symptomatic hemorrhage.

Early Detection of Post-Thrombolytic Hemorrhagic Transformation
Ultra-early hemorrhage (0 to 3 hours) following intravenous thrombolysis appears to be uncommon. Shortly after intra-arterial thrombolysis, the detection of mild ICH with conventional CT imaging may be limited because of the presence of angiographic contrast extravasation. The implications of SWI for decision making, with regard to the use of antithrombotic therapy, is important in this setting as demonstrated by Greer et al. On the basis of these studies, CT for exclusion of hemorrhage may be omitted in centers that use MRI as the primary assessment method for acute stroke patients.

Intra-Arterial Clot Detection
The demonstration and location of arterial occlusion may have prognostic and therapeutic implications in acute stroke patients (Figure 4). The rate of occlusion detected by MRA was 80% in a series of patients explored at a mean delay of 3.3 hours following symptom onset. The demonstration of persistent arterial occlusion may be mandatory when thrombolytic therapy is considered beyond the 3-hour time window. Flacke et al described the middle cerebral artery (MCA) magnetic susceptibility sign as a signal loss along the course of the artery at susceptibility-based perfusion MRI. These susceptibility changes can be attributed to the high deoxyhemoglobin content of fresh clots. This sign was correlated with the hyperdense MCA sign at plain CT scan and with clinical status at presentation. Chalela et al also briefly reported on the hypointense MCA sign at GRE imaging. However, clots limited to the intracranial internal carotid artery may be overlooked because of susceptibility artifacts generated by the paranasal sinuses and the skull base. A potential benefit of SWI may be the detection of distally located clots, which may be missed by MRA (Figure 5).

Diagnosis of Cerebral Venous Thrombosis
MR venography has surpassed conventional angiography as the imaging modality used to establish the diagnosis of cerebral venous thrombosis. However, pitfalls may occur as the nonvisualization of a transverse sinus may be caused by hypoplasia rather than acute occlusion. Alterations in blood flow and hemoglobin degradation products in thrombosed veins may produce signal changes on MR T1- and T2-weighted images. However, conventional sequences are relatively insensitive in the acute phase because the clot signal may be similar to normal flow. Three-dimensional acquisition following gadolinium administration and diffusion-weighted imaging (DWI) can increase the sensitivity of MRI. T2*-weighted GRE sequences allow the
detection of intravenous clots. The clot is directly visualized as an area of hypointensity in the affected vein or sinus or both (Figure 6). SWI may also detect associated hemorrhagic venous infarcts. SWI may be even more useful for the diagnosis of isolated cortical venous thrombosis, which is sometimes difficult to diagnose (Figure 7).

Perspectives

Assessment of Brain Tissue Viability in Acute Ischemic Stroke

The determination of cerebral hemodynamic status and tissue viability is crucial for therapeutic applications in acute ischemic stroke. In the acute phase of ischemia, DWI and PWI have the potential to define hypoperfused areas with a potential risk for infarction. It remains debatable to what extent these methods may allow the distinction between reversible and irreversible ischemia. Experimental data suggest that endogeneous BOLD contrast analysis may improve tissue viability assessment. The ratio of oxyhemoglobin to deoxyhemoglobin, measured by MRI in the capillary and venous compartments, reflects the oxygen extraction fraction (OEF) and the cerebral metabolic rate of oxygen (CMRO). A decrease in signal intensity in gradient-recalled echo-planar T2*-weighted MRI was reported to take place shortly after the vascular occlusion. In a rat focal stroke model, areas of susceptibility-related signal intensity extended beyond that of decreased diffusion. Tamura et al demonstrated susceptibility changes in the affected hemisphere in acute ischemic stroke patients and suggested that there was a relation to “misery” perfusion. The OEF-related signal changes are detected in the early minutes of ischemia and during moderate hypoperfusion in penumbra-like tissue. The OEF obtained using MRI is in good agreement with values reported in the positron emission tomography literature. The combination of MR-measured OEF and cerebral blood flow is possible. Lee and colleagues demonstrated the feasibility of obtaining oxygen metabolic maps in conjunction with diffusion and perfusion MRI during the acute stage. Although a growing interest supports these methods, further validation is required to use these techniques in the assessment of acute metabolic and hemodynamic abnormalities. The use of gradient-echo MRI to assess brain tissue viability in acute stroke is still fraught with difficulty. A major problem is that signal intensity in SWI does not only depend on oxygenation, but will also vary with other factors including brain iron and water content, edema, and gliosis.

Imaging of Leptomeningeal Collateral Circulation

Another source of signal loss along the course of vessels may be the low oxygen arterial saturation associated with slow flow distally to an arterial occlusion. The outcome of tissue at risk for necrosis depends on the presence of an efficient collateral blood flow. To date, the assessment of leptomeningeal collateral circulation in acute stroke remains poorly documented by MRI and mainly relies on the analysis of perfusion sequences and vascular enhancement following contrast injection. Roussel et al reported on

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Figure 5. A 64-year-old man presenting with aphasia and right hemiplegia of sudden onset 3 hours before MRI. A, 3-dimensional time-of-flight MRA; asymmetry of insular arterial branches, less visible on the left side (arrow). B, T2*-weighted gradient-echo image; hypointense left insular clot (arrow).

Figure 6. Left transverse sinus thrombosis (arrows). A, T2*-weighted gradient echo image; hypointense clot. B, frontal projection of the 2-dimensional time-of-flight MR venography following contrast injection.

Figure 7. Isolated left cortical vein thrombosis; tubular hypointensity at T2*-weighted gradient-echo image.
the identification of collaterally perfused areas following focal cerebral ischemia by comparison of gradient echo and DWI findings. Liebeschid et al recently reported on the visibility of intravascular deoxygenation changes (at T2*-weighted GRE imaging) within small arteries ipsilateral to MCA occlusion in acute stroke patients. This finding could represent the visualization of efficient leptomeningeal collaterals because patients exhibiting this sign had smaller infarct volumes at baseline. This hypothesis may require further validation. Methods that look at arteries or veins are hampered by small vessel size compared with MRI pixel size. Additional perfusion studies may improve the understanding of this finding.

Prediction of Hemorrhagic Transformation
SWI is able to detect changes in cerebral venous blood oxygenation. A signal drop within cerebral veins is expected in severe acute ischemia. The predictive value of the abnormal visibility of transcerebral veins at SWI for further hemorrhagic transformation has been reported in acute stroke patients treated by intravenous thrombolysis. In a preliminary study, most patients who later presented with intraparenchymal type 2 hematomas (according to the European Cooperative Acute Stroke Study I [ECASS] classification) had evident susceptibility changes along the course of white matter veins. This sign was correlated both with severe baseline clinical status and severe impaired hemodynamic status at presentation. Although the small sample size of this study did not allow assessment of the positive or negative predictive values of this finding, it may have potential implications for the selection of patients for thrombolytic therapy.

Conclusions
In current clinical practice, SWI provides relevant information about stroke mechanisms and should be added to MRI stroke protocols. Moreover, this method has potential applications in the near future.

References
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