Diffusion-Weighted MRI in Acute Subcortical Infarction

Michael B. Singer, MD; June Chong, MD; Dongfeng Lu, PhD; Wouter J. Schonewille, MD; Stanley Tuhrim, MD; Scott W. Atlas, MD

Background and Purpose—Conventional imaging lacks sensitivity and specificity for the detection of early subcortical cerebral infarction. The purposes of our study were (1) to determine the accuracy of diffusion-weighted (DW) MRI for early subcortical infarction and (2) to determine the efficacy of DW MRI for differentiating acute from nonacute subcortical infarctions when conventional MR demonstrates multiple infarctions.

Methods—Thirty-nine patients with clinically diagnosed acute subcortical infarction and 17 control subjects were imaged with both conventional and DW MRI from 7 hours to 4 days (mean, 2.0 days) after onset of symptoms. All images were read blinded to specific clinical findings. In all cases, the precise neuroanatomic locations of lesions were noted. These lesions were subsequently correlated by an experienced stroke neurologist to determine whether their locations correlated to the patients’ symptoms.

Results—The accuracy of DW MRI for acute subcortical infarction was 94.6%. In 4 of 39 cases, the acute infarction was not detected on conventional MRI. In 24 of 39 cases, conventional MRI showed the acute lesion as well as multiple other subcortical lesions. In each of these 24 cases, the DW MRI showed a single lesion to be acute, and in all 24 cases, that lesion corresponded to the patients’ acute symptoms.

Conclusions—DW MRI has very high accuracy for acute subcortical infarction and can differentiate acute from nonacute lesions. These data have significant implications in guiding patient management and patient selection for clinical trials.

Key Words: cerebral infarction ■ diagnostic imaging ■ magnetic resonance imaging ■ stroke, acute

Subcortical infarctions constitute approximately 25% of all ischemic events and form an important subgroup of stroke patients. It is generally recognized that conventional imaging lacks sensitivity for the detection of very early cerebral infarction. Moreover, in the case of subcortical infarction specifically, it is often impossible to distinguish acute from nonacute lesions on conventional spin-echo or FSE MRI. Both of these issues are important for appropriate patient management, particularly in the era of acute stroke treatment. Preliminary studies have suggested that DW MR may have high sensitivity for early cerebral infarction. The purpose of our study was twofold: (1) to determine the accuracy of DW MR for early subcortical infarction and (2) to determine the efficacy of DW MR for differentiating acute from nonacute subcortical infarctions when conventional MR demonstrates multiple subcortical infarctions.

Subjects and Methods
Thirty-nine adult patients with a clinical diagnosis of acute subcortical infarction were imaged with both conventional FSE and DW MR with a 1.5-T MR scanner modified with hardware for echo-planar imaging (GE Signa Horizon Echospeed). All images were obtained during the same imaging session and at the same slice locations in all cases; 5-mm-thick sections with 2.5-mm interisoc age gaps and a 24-cm field of view were used for all scans. Proton density–weighted FSE used TR 2000 ms, effective TE 30 ms, number of excitations 2, 192×256 matrix, echo train length 4 (acquisition time≈2:32); T2-weighted FSE used TR 3600 ms, effective TE 95 ms, 192×256 matrix, echo train length 8, number of excitations 1 (acquisition time≈1:41). Multislice single-shot spin–echo diffusion echo-planar imaging (Δ=31 ms, Δ=36.6 ms, TR/TE=10 000/99 ms) was performed with diffusion sensitivity b≈1000 s/mm². The diffusion gradients were applied sequentially in three orthogonal directions to generate three sets of axial DW MR images. The acquisition time for DW images equaled 25 seconds. Interpretations were made with the use of all three sets of DW images.

Time interval of imaging relative to onset of ictus ranged from 7 hours to 4 days (mean, 48.1 hours or 2.0 days). Of these 39 patients, 6 were imaged less than or equal to 12 hours after onset of clinical symptoms, 3 were imaged 12 to 24 hours after symptom onset, 12 were imaged 24 to 48 hours after onset of symptoms, and 18 were imaged 48 to 96 hours after onset of symptoms.

The DW and FSE MR images were read by an experienced neuroradiologist blinded to specific clinical findings except for the history of “rule out acute infarction.” Included in the blinded readings as controls were 17 other patients with nonfocal neurological symptoms who were also scanned with both FSE and DW MR with the use of the identical protocol.

Criteria for the diagnosis of acute subcortical infarction on DW MR included the following: (1) focal high intensity, based on prior literature; (2) a location in the basal ganglia, deep and/or subcortical white matter, or brain stem; (3) a location or configuration not thought to represent normal anisotropy of diffusion; and (4) a location or configuration not thought to represent a magnetic susceptibility...
artifact (ie, typically seen near interfaces between brain and air-filled paranasal sinuses). The lesion did not necessarily have to be present on more than one of the three single-axis DW images to be interpreted as an infarction (ie, obscuration of stroke-related hyperintensity situated within normal internal capsule hyperintense signal on one diffusion axis might be eliminated by changing the direction of diffusion sensitivity, making these anisotropic effects less problematic). In all cases, the precise neuroanatomic locations of such lesions were noted. These lesions were subsequently correlated in consultation with an experienced stroke neurologist, who had personally examined the patients before the MRI study, to determine whether the locations of high intensity on DW MR correlated to all or part of the patients’ symptoms. On FSE images, all focal hyperintense abnormalities in deep and subcortical neuroanatomic locations were noted.

Results

Thirty-seven of the 39 patients with the clinical diagnosis of acute subcortical infarction had focal areas of high intensity on DW MR that correlated with all or part of the patients’ clinical symptoms. Of the two patients with acute subcortical infarction and negative DW MRI, one was imaged within 34 hours and the other within 72 hours of ictus. In 1 of the 17 control patients, an acute focal subcortical infarction was identified on DW MRI. Overall, the sensitivity of DW MR for acute subcortical infarction was 94.9%, specificity was 94.1%, positive predictive value was 97.4%, and negative predictive value was 88.9%. The accuracy of DW MRI for acute subcortical infarction was 94.6% (Table).

In 4 of 39 cases, the acute infarction (ie, the hyperintense lesion on DW MR) was not detected on FSE images. Two of these were imaged in less than 12 hours after onset of symptoms. In 24 of 39 cases, FSE images showed the acute lesion as well as multiple other subcortical lesions that were indistinguishable from each other. In each of these 24 cases, the DW MR showed a single lesion to be acute, and in all 24 cases, that lesion corresponded to the patients’ acute symptoms (Figure). In these 24 cases, 11 were imaged within 48 hours and 14 were imaged between 56 and 96 hours.

In 1 case DW MR demonstrated additional acute lesions that did not correlate with clinically apparent deficits but were subsequently shown to be clinically relevant and likely due to an acute ischemic insult.

Discussion

DW MRI is a technique that is exquisitely sensitive to the net translational movement of water molecules. When placed into a strong magnetic field gradient, translational movement of water protons results in a phase shift that can be detected as relative signal loss compared with regions of reduced water motion. Preliminary studies using DW MRI have indicated that early infarction is demonstrated as regional high signal intensity compared with background tissue. This relative hyperintensity presumably reflects restriction of tissue water movement in the area of infarction, although the precise pathophysiological events underlying the change in water diffusion are unclear. It is thought that the loss of normal homeostasis and cell membrane function within ischemic cells leads to increased cell membrane permeability. The secondary shift of water from the extracellular space, where diffusion is nearly unrestricted, to the intracellular compartment, where there is apparently a more restricted environment for water

Summary of Results: DW MRI for Acute Subcortical Infarction in 39 Patients

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<td>Accuracy</td>
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movement, is postulated by many investigators as the cellular event correlating to the change on MRI.\textsuperscript{5-9}

Previous studies have noted that DW MRI demonstrates acute infarctions that are not detectable by conventional T2-weighted MRI.\textsuperscript{2,5} Our data indicate that isolated symptomatic acute subcortical infarction can be detected with a very high degree of accuracy and can be readily differentiated from subacute and chronic infarctions in the basal ganglia and subcortical white matter with the use of DW MRI (Figure). (It should be noted that it is difficult to estimate the actual number of nonstroke cases likely to be evaluated in the clinical context described in this study. The actual accuracy and positive and negative predictive values of a diagnostic test will vary with the prevalence of the disease in the population studied and may be quite different depending on the circumstances in which the test is applied. However, the high sensitivity and specificity demonstrated are stable properties, and the values reported are likely to be generally applicable.)\textsuperscript{10} Regardless of the exact explanation of the cause of the signal alteration, this important advance in MRI compensates for two major limitations in brain imaging that had yet to be solved: (1) a lack of sensitivity for very early cerebral infarction and (2) an inability to clearly distinguish new from old lesions. We have also demonstrated that the use of single-axis orthogonal DW MRI, without off-line postprocessing and without quantitative apparent diffusion coefficient maps, is highly accurate for these lesions. Extremely high accuracy in our blinded reader study was noted despite the theoretical problems of diffusion anisotropy, in which high intensity can be present due to the inherent anatomic orientation of fiber bundles, as in the subcortical white matter, relative to the direction of diffusion sensitivity.\textsuperscript{2,11} In suspected infarctions in or near the internal capsule specifically, where diffusion anisotropy is high, it might even be postulated that separating directional sensitivity to diffusion could be advantageous. While we concur with the notion expressed by Ulug et al\textsuperscript{12} that quantitative apparent diffusion coefficient maps may be useful in research protocols in which quantitation may be useful, our data contradict the contention\textsuperscript{13} that apparent diffusion coefficient maps, requiring imaging with multiple diffusion sensitivities and subsequent image processing, are necessary for clinical stroke imaging.

Our study design did not lend itself to answer potentially important questions about DW MRI interpretation. For instance, because our blinded reader viewed all three single-axis DW images as a set, we cannot test the hypothesis that only a single direction of diffusion sensitivity may be adequate to diagnose these lesions. Similarly, we cannot determine how many or what percentage of infarctions were detectable by using only one or only two directions of diffusion sensitivity. Moreover, we cannot answer questions about which single diffusion direction is the most important direction to which this type of imaging should be sensitive for the highest yield. We also recognize that we may have increased the yield by presenting the reader with all three images with diffusion sensitivity at each slice location as a set, simply because the reader had three chances to detect a lesion. These limitations and questions represent interesting studies that should be performed in the future.

Our data also demonstrate that abnormal foci in the subcortical gray and white matter can be identified on DW MRI in regions that do not correspond to clinically apparent neurological deficits. It is possible that these are false-positive findings that do not represent cerebral lesions, but it is more likely that these are acute infarctions that fail to produce recognized symptoms ("silent" infarctions). Indeed, silent infarctions are reportedly present on CT scans of between 10% and 30% of patients with cerebrovascular disease and are usually small, subcortical lesions.\textsuperscript{14,15} It is therefore not unlikely that the foci of hyperintensity on DW MRI (ie, restricted diffusion) without clinical correlation do indeed represent infarctions.

The recent development of thrombolytic and neuroprotective agents has further raised the significance of accurate detection of acute infarction to new levels, since the real possibility of early intervention to limit the extent of damage from the ischemic event exists. However, since the therapy is not without significant risk, it is important to distinguish patients who have evidence of new ischemic damage from those who have (re)emergence of signs and symptoms from preexisting lesions, perhaps due to unrelated intercurrent infections or metabolic derangement. Because it is precisely those patients with small subcortical infarctions who are most likely to have multiple lesions, many of which may be silent, DW MRI appears to hold important promise for aiding the clinician in making distinctions that are difficult on clinical grounds alone. Since most acute interventional trials are currently limited to patients who can be treated within 6 hours of symptom onset, it remains to be demonstrated that our findings can be extended to that time window. However, previous work suggests that DW abnormalities appear very shortly after the onset of ischemia.\textsuperscript{2,4}

The technique of DW MRI is readily performed in patients who cannot otherwise cooperate for conventional MRI, since in the echo-planar implementation image acquisition occurs in subsecond time frames, making this technique particularly attractive as an option in very ill patients. Moreover, the accurate diagnosis of acute infarction by such a rapid imaging method is also appropriate for subjects entering therapeutic trials, where time is of the essence in patient management and triage. It is as yet uncertain whether DW MRI offers a method for distinguishing patients who have reversible (or at least potentially treatable) lesions from those who do not.

**Conclusion**

DW MR, without the use of quantitative diffusion coefficient maps, has very high sensitivity, specificity, and accuracy for acute subcortical infarction and can differentiate acute from nonacute lesions. DW MR can also reveal additional "acute lesions" in these patients, which either represent additional clinically silent acute infarctions or represent false-positive findings. These data have significant implications in guiding patient management and patient selection for clinical trials.

**References**


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