TECHNICAL NOTE

Higher Prevalence of Cortical Lesions Observed in Patients with Acute Stroke Using High-Resolution Diffusion-Weighted Imaging

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SUMMARY: Ischemic lesion conspicuity on routine diffusion-weighted imaging (DWI, 30 seconds) was compared with an improved sequence (high-resolution DWI [DWI-HR], 256 seconds) having increased spatial resolution and signal to noise and decreased eddy current artifact in 42 patients with acute ischemic stroke. Total lesion volumes were similar; however, twice as many lesions were identified on DWI-HR, predominately in cortical gray matter. Modest improvements to imaging resulted in increased conspicuity, potentially affecting diagnosis, suspected pathogenic mechanism, and therapeutic decision.

Although the sensitivity and specificity of diffusion-weighted imaging (DWI) for the detection of acute ischemic stroke exceeds 90%,[1,2] false-negative DWI is not uncommon,[3,4] and protocols used in routine clinical practice remain plagued by limited spatial resolution, low signal-to-noise ratio (SNR), and artifacts. We hypothesized that modest improvements in image quality would result in a significant increase in lesion conspicuity.

Description of the Technique

MR imaging studies were performed on a 1.5T clinical MR imaging unit (General Electric Medical Systems, Milwaukee, Wis) using a neurovascular array (In Vivo, Orlando, Fla). DWI was acquired using a spin-echo single-shot echo-planar imaging (SS-EPI) sequence with the following parameters: repetition time (TR)/echo time (TE), 7000/72.8 ms; field of view (FOV), 220 × 220 mm; matrix, 128 × 128; $b =$ (0,1000) along 3 orthogonal directions. Coverage of the brain was accomplished with 20 contiguous sections for a voxel size of 20 mm^3 (1.7 × 1.7 × 7 mm), and a total acquisition time of 30 seconds. High-resolution DWI (DWI-HR) was acquired using an SS-EPI sequence with the following parameters; TR/TE, 10250/72.5 ms; FOV, 220 × 220 mm; matrix, 128 × 128. A second refocusing pulse, a pan option in our commercial sequence (release 11.x), was added for reduction of eddy current-induced distortion.[5] Acquisition was done with 4 images acquired at $b = 0$ and 19 images at $b = 1000$ in 6 gradient directions (acquisition followed a tetrahedronal encoding scheme with the following gradient directions: [0, 1, 1], [−1, 0, 1], [0, 1, 1], [1, 1, 0], [0, 1, −1], and [−1, 1, 0]). Gradient strength (100%) was applied simultaneously along 2 axes affecting a factor of 2 gain in $|b|$ and allowing for a shorter TE. Total brain coverage was accomplished with 40 sections for a voxel size of 10 mm^3 (1.7 × 1.7 × 3.5 mm) and a total acquisition time of 256 seconds.

This was a retrospective study of patients admitted to the National Institutes of Health Suburban Hospital Stroke Service. The inclusion criteria were consent to participate in an institutional review board-approved natural history protocol, have both DWI and DWI-HR in the same imaging examination within the first 24 hours of symptom onset, and have a final clinical diagnosis of acute ischemic stroke. DWI always preceded DWI-HR in the scanning protocol, with a median and average latency time between both sequences of 3 and 4 minutes, respectively. Symptom onset was defined as the time the patient was last seen to be normal.

Lesion segmentation was performed on trace-weighted images using an automated level-set algorithm and a 3D morphometric analysis,[6] by 2 experienced readers (research fellow in neurology and clinical trialist) blinded to patient identifiers and to DWI to DWI-HR pairing. Lesions were identified as hyperintense regions by either reader and were verified for acuity using corresponding apparent diffusion coefficient maps and fluid-attenuated inversion recovery imaging. The resulting volumes of interest were saved for each patient and reader then transformed in a common space for analysis. SNR and contrast-to-noise ratio (CNR) were measured for each sequence using method 2 of the National Electrical Manufacturers Association standard.[7]

SPSS for Windows (version 13; SPSS, Chicago, Ill) was used for statistical analysis. A value of 2-tailed $P < .05$ was considered significant. Total lesion volume and average volume per lesion were compared between DWI and DWI-HR using a paired Student t test. Lesion count between both techniques was compared using the Wilcoxon rank-paired test. Inter-reader agreement was assessed using the interclass correlation coefficient.

Results

A total of 42 patients [20 men (mean age, 75; range, 42–94)] were included. The median time between time of symptom onset and first scan was 5 hours and 21 minutes (mean, 8:06; range, 0:47–23:29). No patients were excluded for inability to complete the imaging examination, and image quality was adequate in all.

The anteroposterior translational shift, a typical effect of residual eddy currents occurring between the different diffusion gradient directions, was significantly decreased by the addition of a second refocusing pulse as shown in Fig 2. This resulted in a decrease in the blurring of small lesions particularly those located on the cortex. The average SNR in conventional DWI was 29.7 (range, 23.9–37) compared with 35.6 (range, 27.7–43.2) on DWI-HR ($P < .01$) representing an increase of SNR by 20%. The average CNR was 10.7 (range, 8–17) on DWI compared with an average of 14.8 (range, 12.6–20.6) on DWI-HR ($P < .01$), increasing the CNR by 42%.

A total of 129 discrete lesions was identified on DWI and 253 lesions on DWI-HR for an average of 3.07 lesions per

Received February 28, 2006; accepted after revision April 25.

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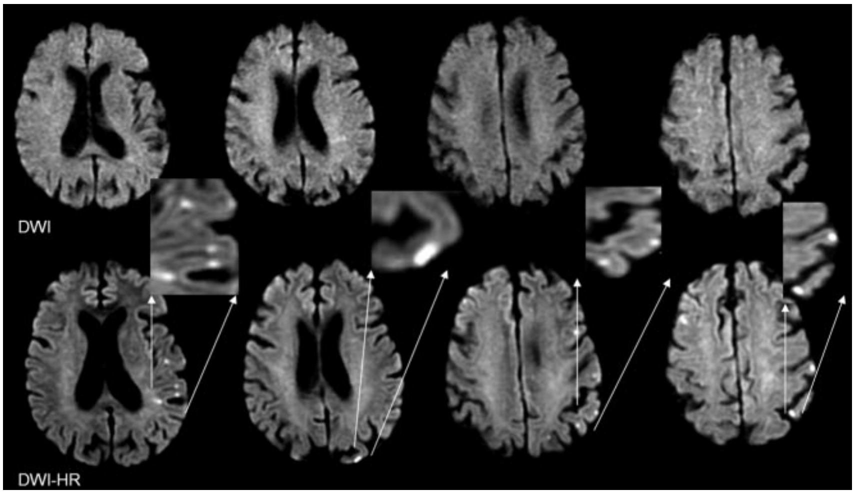

Fig 1. Cortical ischemic lesions identified by high resolution diffusion-weighted imaging (*bottom*), missed by conventional DWI (*top*). Note in the magnifications, the location of the lesions mainly along the cortical gray ribbon.

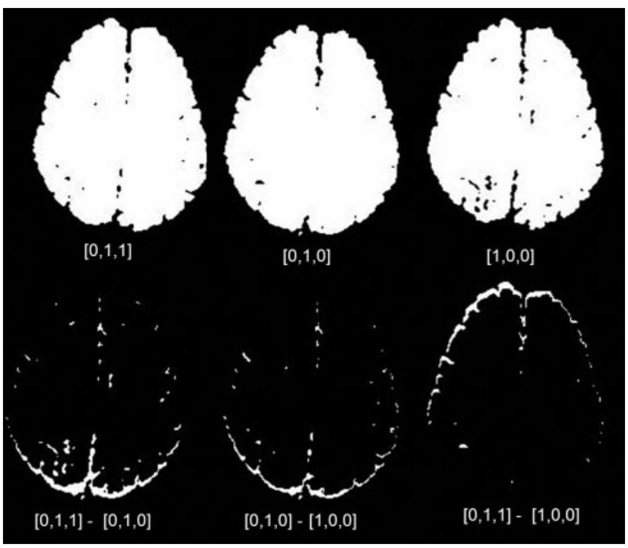

Fig 2. Thresholded binary images resulting from source diffusion-weighted images (DWI) in 2 gradient directions at the *top left* and *center*, and from source high-resolution diffusion-weighted images (DWI-HR) at the *bottom left* and *center*. Note the greater anteroposterior shift on the image resulting from the DWI source images subtraction at the *top right* compared with the one resulting from the dual-echo corrected DWI-HR source images at the bottom left.

patient on DWI and 6.04 on DWI-HR ($P < .001$) (Table 1). Seven lesions unique to DWI were identified in 5 patients, whereas 134 lesions unique to DWI-HR were identified in 23 patients; these lesions were nearly 3 times more prevalent in the cortex than in other brain structures, as illustrated in Fig 1.

Total lesion volume per patient was 7040 ± 2010 mm^3 on DWI and 7052 ± 1950 mm^3 on DWI-HR ($P = .95$), for an average of 3600 ± 1300 mm^3 and 2800 ± 1200 mm^3 on DWI and DWI-HR, respectively ($P < .001$). The average volume per lesion of lesions unique to DWI was 134.41 ± 88.23 mm^3 and 70.50 ± 16.90 mm^3 of those unique to DWI-HR ($P = .65$).

A total of 16 (37%) patients had a single lesion, and 8 (19%) patients had more than 5 lesions on DWI, whereas 12 (28%) patients had a single lesion, and more than 19 (42%) patients had more than 5 lesions on DWI-HR. Eight (19%) patients with a single lesion on DWI had multiple lesions on DWI-HR.

Inter-reader reliability was excellent for lesion volumes in both DWI-HR and DWI (0.98 [range, 0.92–0.99]) and 0.96 [range, 0.93, −0.98]), respectively. Interclass correlation for lesion count was higher for DWI-HR 0.92 (range, 0.85–0.96) compared with DWI of 0.77 (range, 0.59−0.87).

Discussion

Time constraints on imaging in critically ill stroke patients have limited the DWI used in routine practice to minimum trace-weighted images calculated from 3 orthogonal directions. Although clinicians are reluctant to extend the protocol without clear benefit, our results indicate that modest improvements to the present DWI protocol can provide substantially more information, which may alter patient management.

DWI-HR resulted not only in increased lesion conspicuity but also in a dramatic increase in the number of cortical ischemic lesions as shown in Fig 1. Such lesions were present on DWI-HR and absent on DWI in more than half of the patients studied. Moreover, a change in lesion pattern was observed, with more patients having multiple lesions on DWI-HR. Lesion pattern has been shown to be linked to clinical outcome[8] as well as to lesion recurrence, potentially pointing to a stroke prone state,[8,9] which could prompt more vigorous preventive measures.

Our study showed no patients with a negative DWI and positive corresponding DWI-HR; a follow-up study, however, is under way, including both patients with ischemic stroke and patients with transient ischemic attack to explore a potential increased sensitivity for negative DWI. Moreover, understanding the relationship of these cortical lesions to the vascu-

Discrete lesions identified on diffusion-weighted MR imaging (DWI) and high-resolution DWI (DWI-HR)

	DWI	DWI-HR	*P* Value
Signal-to-noise ratio, mean (range)	29.7 (23.9–37)	35.6 (27.7–43.2)	<.01
Contrast-to-noise ratio, mean (range)	10.7 (8–17)	14.8 (12.6–20.6)	<.01
Total no. of lesions	129	253	<.001
Average no. of lesions	3.07	6.04	<.001
No. of unique lesions	7	123	<.001
Total lesion volume (mm^3)	7040 ± 2010	7052 ± 1950	.95
Average volume per lesion (mm^3)	3600 ± 1300	2800 ± 1200	<.001
Average volume per lesion of unique lesions (mm^3)	134.41 ± 88.23	70.50 ± 16.90	.65
No. of patients with a single lesions, *n* (%)	16 (37%)	12 (28%)	n/a
Number of patients with greater than 5 lesions, *n* (%)	8 (19%)	19 (42%)	n/a

Note:—DWI-HR was acquired following a tetrahedronal encoding scheme with the following gradient directions: (0, 1, 1), (−1, 0, 1), (0, 1, 1), (1, 1, 0), (0, 1, −1), (−1, 1, 0). 100% gradient strength was applied simultaneously along 2 axes affecting a factor of 2 gain in |b|, and allowing for a shorter echo time.

lar territories affected, and thus potentially to the stroke etiology, was beyond the scope of this study; however, it is being addressed in a follow-up study.

Both signal intensity averaging to increase SNR and decreased section thickness to decrease partial volume averaging, improved CNR, and contributed to the increased conspicuity of small lesions; however, the most dramatic improvement was probably realized through use of a dual-echo technique.[5] Alternative techniques to the EPI readout may provide a similar advantage, yet remain esoteric and have not received widespread clinical use.[10,11]

In conclusion, modest improvements in spatial resolution, increased signal intensity-to-noise ratio, and eddy current distortion reduction, resulted in significant improvement in lesion conspicuity. Lesions revealed by the improved imaging could result in a change in observed lesion pattern, presumed underlying pathogenic mechanisms,[12] diagnosis, and treatment strategy.

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