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

TECHNICAL NOTE

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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 mm³ (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 tetrahedral 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 mm³ (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

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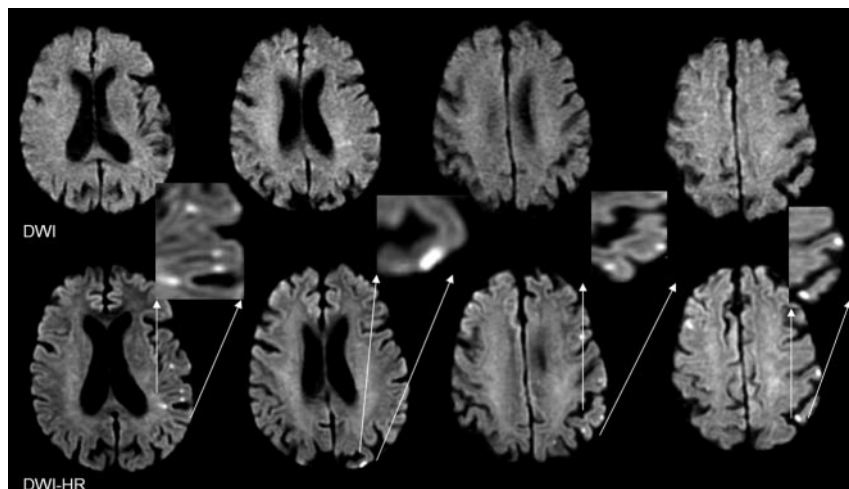


Fig 1. Cortical ischemic lesions identified by high resolution diffusion-weighted imaging (*bottom*), missed by conventional DWI (*top*). Note in the magnifications, the location of the lesions mainly along the cortical gray ribbon.

[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 improve-

ments 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 outcome⁸ 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-

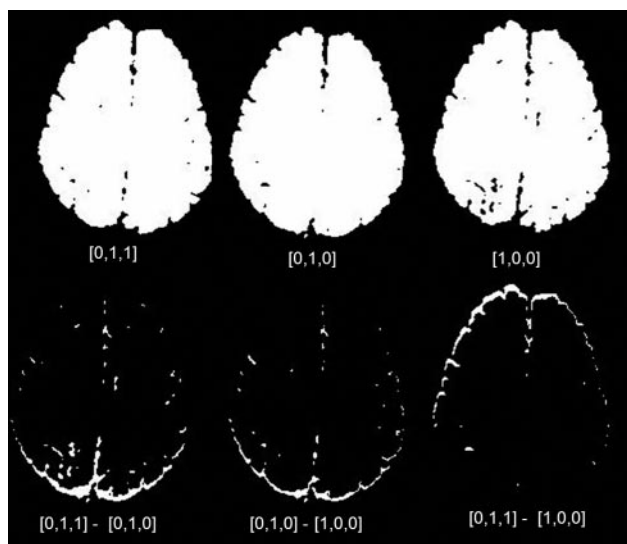


Fig 2. Thresholded binary images resulting from source diffusion-weighted images (DWI) in 2 gradient directions at the *top left* and *center*, and from source high-resolution diffusion-weighted images (DWI-HR) at the *bottom left* and *center*. Note the greater anteroposterior shift on the image resulting 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 $7040 \pm 2010 \text{ mm}^3$ on DWI and $7052 \pm 1950 \text{ mm}^3$ on DWI-HR ($P = .95$), for an average of $3600 \pm 1300 \text{ mm}^3$ and $2800 \pm 1200 \text{ mm}^3$ on DWI and DWI-HR, respectively ($P < .001$). The average volume per lesion of lesions unique to DWI was $134.41 \pm 88.23 \text{ mm}^3$ and $70.50 \pm 16.90 \text{ mm}^3$ 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

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

| | DWI | DWI-HR | <i>P</i> 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, <i>n</i> (%) | 16 (37%) | 12 (28%) | n/a |
| Number of patients with greater than 5 lesions, <i>n</i> (%) | 8 (19%) | 19 (42%) | n/a |

Note:—DWI-HR was acquired following a tetrahedral 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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