Apparent Diffusion Coefficient Thresholds and Diffusion Lesion Volume in Acute Stroke

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Background: Apparent diffusion coefficient (ADC) thresholds are used to determine acute stroke lesion volume, but the reliability of this approach and comparability to the volume of the magnetic resonance diffusion-weighted imaging (MR-DWI) hyperintense lesion is unclear. *Methods:* We prospectively recruited and clinically assessed patients who had experienced acute ischemic stroke and performed DWI less than 24 hours and at 3 to 7 days after stroke. We compared the volume of the manually outlined DW hyperintense lesion (reference standard) with lesion volumes derived from 3 commonly used ADC thresholds: $.55 \times 10^{-3}/mm^2/second^{-1}$, $.65 \times 10^{-3}/mm^2/second^{-1}$, and $.75 \times 10^{-3}/mm^2/second^{-1}$, with and without "editing" of erroneous tissue. We compared the volumes obtained by reference standard, "raw," and "edited" thresholds. *Results:* Among 33 representative patients, the acute DWI lesion volume was 15,284 mm^3; the median unedited/edited ADC volumes were 52,972/2786 mm^3, 92,707/6,987 mm^3, and 227,681/unmeasureable mm^3 ($.55 \times 10^{-3}/mm^2/second^{-1}$, $.65 \times 10^{-3}/mm^2/second^{-1}$, and $.75 \times 10^{-3}/mm^2/second^{-1}$ thresholds, respectively). Subacute lesions gave similar differences. These differences between edited and unedited diffusion-weighted imaging and ADC volumes were statistically significant. *Conclusions:* Threshold-derived ADC volumes require substantial manual editing to avoid over- or underestimating the visible DWI lesion and should be used with caution. **Key Words:** Stroke—apparent diffusion coefficient—magnetic resonance imaging—threshold.

Magnetic resonance diffusion-weighted imaging (MR-DWI) shows acute ischemic lesions very soon after stroke. These can be quantified by tracing around the visible hyperintense DWI lesion to measure the volume.[1] This is time consuming. Automated techniques could facilitate quantification of stroke lesion volume in research and clinical practice.[2] One method is to "threshold" the apparent diffusion coefficient (ADC) map, using a percentage of normal[3] or an absolute[4,5-7] ADC value, and record the resulting volume. The relationship between the DWI visible lesion volume and the ADC-thresholded volume, and which threshold

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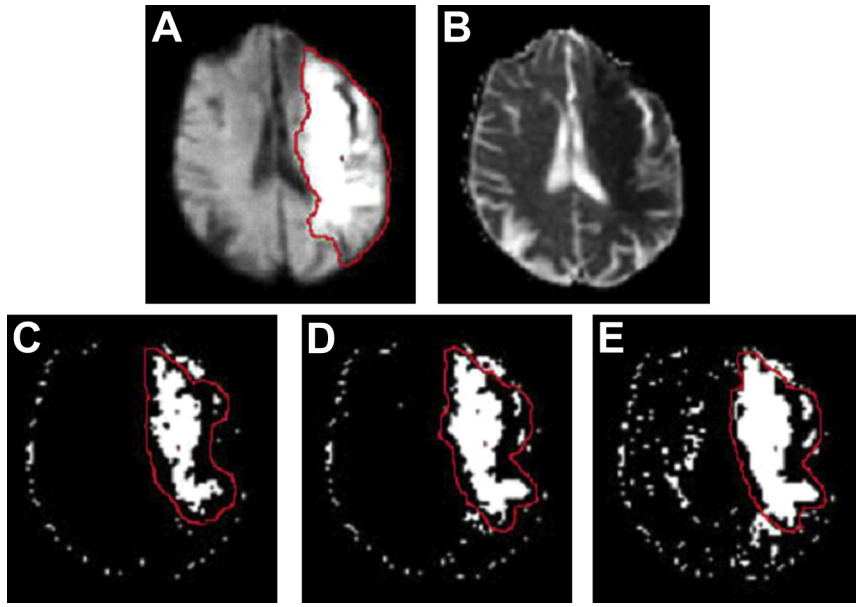

Figure 1. *Acute time point images from 1 subject (same slice) on (A) diffusion-weighted imaging (DWI), (B) unthresholded apparent diffusion coefficient (ADC) map, (from left to right) thresholded ADC maps at (C) .55 × 10^{-3}/mm^2/second^{-1}, (D) .65 × 10^{-3}/mm^2/second^{-1}, and (E) .75 × 10^{-3}/mm^2/second^{-1}, respectively. Red line shows manual lesion outline of abnormal tissue in A and the manual edit to exclude tissue captured erroneously by ADC thresholds in C.*

to use, is unclear.[8] We compared lesion volumes calculated using commonly cited ADC thresholds with volumes determined by manually outlining the visible DWI lesion.

Methods

We prospectively recruited patients who had experienced acute stroke (>18 years old) and presented to a tertiary hospital and who could undergo magnetic resonance imaging (MRI) within 24 hours of symptom onset. We excluded patients with hemorrhagic stroke, coma, those unable to lie still for MRI, or those who had technical or clinical incompatibility with MRI. A trained stroke physician determined the National Institute of Health Stroke Score. The study was approved by the ethics committee (06/MRE00/119); all patients or their relatives gave consent.

We performed MR-DWI as soon as possible after admission and at 3 to 7 days on a GE Signa HDX 1.5T (GE Healthcare, Milwaukee, WI) scanner with self-shielding gradients (33 mT/m maximum) and quadrature head coil. The DWI sequence had echo time of 79.3 milleseconds, repetition time of 7.7 seconds; field of view of 256 × 256 mm, matrix of 128 × 128, 28 slices, thickness of 5 mm, gap of 0 mm, and diffusion sensitizing gradients with scalar b-values of 1000 seconds/mm^2 applied in 30 noncollinear directions.

The DWI image data were registered to the first baseline b = 0 image (FLIRT; FMRIB Centre, Oxford, UK), motion corrected, the background removed (BET; FMRIB Centre), the diffusion tensor calculated,[9] and directionally independent DWI maps calculated by averaging all b = 1000 DWI images. ADC maps were obtained from the average of the diagonal elements of the diffusion tensor.

A neuroradiologist, blind to all data, outlined the hyperintense lesion on DWI using Analyze (Mayo Foundation, Rochester, MN) and calculated the lesion volume (reference standard). ADC lesion volumes were determined with the ADC thresholds of .55 × 10^{-3}/ mm^2/second^{-1},[2,6] .65 × 10^{-3}/mm^2/second^{-1},[4,6] and .75 × 10^{-3}/mm^2/second^{-1},[5,7] (Fig 1). We first recorded the entire ("raw")

Table 1. *Median and range of ischemic stroke lesion volumes (mm^3) from acute and follow-up scans**

	Acute scann = 30 (mm^3)		Follow-up scann = 31 (mm^3)	
Lesion volume method	Median	Range	Median	Range
DWI reference standard	15,284	668-489,041	26,543	1,336-621,826
ADC .55 × 10^{-3}/mm^2/s^{-1} (raw)	52,972	37,828-335,443	51,135	32,748-257,045
ADC .55 × 10^{-3}/mm^2/s^{-1} (edited)	2786	0-294,908	1793	0-218,180
ADC .65 × 10^{-3}/mm^2/s^{-1} (raw)	92,707	59,221-416,285	97,998	59,994-393,645
ADC .65 × 10^{-3}/mm^2/s^{-1} (edited)	6,987	0-354,762	7805	0-335,496
ADC .75 × 10^{-3}/mm^2/s^{-1} (raw)	227,681	137,461-539,719	241,910	131,027-547,963

Abbreviations: ADC, apparent diffusion coefficient; DWI, diffusion-weighted imaging.

*Measured by manually tracing visibly hyperintense lesions seen by diffusion-weighted imaging (DWI) (reference standard), and using 3 different apparent diffusion coefficient (ADC) thresholds to create "raw" and "edited" lesion volumes. There is no edited value for ADC threshold .75 × 10^{-3}/mm^2/s^{-1} because it was not possible to determine the lesion edge from normal tissue.