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Influence of fluid-attenuated inversion-recovery on stroke apparent diffusion coefficient measurements and its clinical application

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ABSTRACT

Background and purpose: The application of a fluid-attenuated inversion-recovery pulse with a conventional diffusion-weighted MRI sequence (FLAIR DWI) decreases the partial volume effects from cerebrospinal fluid on apparent diffusion coefficient (ADC) measurements. For this reason, FLAIR DWI may be more useful in the evaluation of ischemic stroke, but few studies have looked at the effect of FLAIR on ADC measurements in this setting. This study quantitatively compares FLAIR DWI and conventional DWI in ischemic stroke of varying ages to assess the potential advantages of this technique.
Methods: We respectively analyzed 139 DWI studies in patients with ischemic stroke with and without FLAIR at varying time points ranging from hyperacute to chronic. ADC values were measured in each lesion, as well as in the contralateral normal side. Comparisons were made between the ADC values obtained from the DWI sequences with and without FLAIR for both the lesion and the normal contralateral side.
Results: The ADC measurements within the ischemic lesion were very similar on FLAIR DWI and conventional DWI for lesions less than 14 days old ($p > 0.05$), but were significantly decreased on FLAIR DWI for lesions between 15 and 30 days old and in lesions >31 days old (chronic stage) ($p < 0.01$). The contralateral ADC values were all significantly decreased on the FLAIR DWI sequence compared with conventional DWI ($p < 0.01$).
Conclusions: The application of an inversion pulse does not significantly affect the ADC values for early stage ischemic stroke (less than 14 days from symptom onset), but results in a more accurate relative ADC measurement by reducing the cerebrospinal fluid partial volume effects of the normal contralateral side. In addition, combined with the conventional DWI, FLAIR DWI may be helpful in determining the age of ischemic lesions.

1. Introduction

Diffusion-weighted imaging (DWI) is a powerful MR technique, which provides a noninvasive method of detecting changes in tissue microarchitecture in vivo, including quantitative analysis of brain diffusivity, which allows for detection of hyperacute and acute ischemic stroke [1,2]. There has been a divergence of opinion on the use of apparent diffusion coefficient (ADC) values to distinguish reversible from irreversible ischemic brain damage, and on its role in monitoring therapeutic effects and outcome prediction [3–9]. ADC values in the cerebrospinal fluid (CSF) are approximately three times as high as values in normal brain tissue. Partial volume effects from CSF in the cerebral sulci and ventricles could result in an overestimation of the ADC values by about 15–30% [10]. This was thought to be the cause of most differences between the ADC thresholds for distinguishing reversibly and irreversibly damaged ischemic brain parenchyma reported in some studies [6–8].

Kwong et al. [11] first suggested the use of an inversion pulse with a conventional DWI sequence to minimize partial volume effects from CSF that result in falsely elevated ADC values. This technique was further refined by Falconer and Narayana [12] and was applied to diffusion-tensor imaging [13]. Subsequent studies have used the technique for diffusion imaging of the aging brain [14], multiple sclerosis [15] and stroke [16–20]. Several studies have confirmed that these CSF-suppressed ADC measurements result in more accurate ADC values than conventional DWI in the cortical and periventricular regions. The ADC values in structures less susceptible to CSF partial volume effects, such as the centrum

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semiovale, are essentially the same with or without the addition of FLAIR to the DWI sequence [21]. In clinical practice, Bykowski et al. showed that use of FLAIR DWI increased the accuracy of ADC values in distinguishing viable from nonviable tissue in acute ischemic stroke [18].

ADC values obtained on sequences using inversion pulses have been shown to be different from those obtained using the conventional technique [16–20]. Studies regarding the influence of the inversion pulse on absolute ADC values in ischemic tissue are scarce, and only a few reports involving the hyperacute stage of ischemic stroke have been published [10,18]. The purpose of this investigation was to utilize the FLAIR DWI method in a large number of stroke patients at varying time points from the hyperacute to chronic stage to evaluate its influence on ADC measurements during the evolution of ischemic brain lesions, and to assess the potential use of this technique to estimate lesion age and the underlying pathophysiological changes.

2. Materials and methods

2.1. Patient characteristics

Patients were enrolled from March 2004 to March 2006. All patients presented to the emergency department and were evaluated by the stroke neurology team. Only patients who met the following inclusion criteria were included in the study: (1) unequivocal clinical diagnosis of stroke with persistent neurologic deficits and time of onset determined by using medical history. Patients with multiple ischemic episodes prior to MRI or acute progressive cerebral infarction were not included in the study; (2) a unilateral nonhemorrhagic ischemic stroke with no additional nonischemic intracranial pathology (e.g. abscess, brain tumor) on head CT or brain MRI; (3) infarct >2 cm in diameter (greatest dimension) and present on at least three contiguous, 6-mm-thick, axial slices to obtain high accuracy for quantitative measurements and to avoid partial volume effects; (4) a lesion visible on both imaging techniques; (5) no treatment with neuroprotective or thrombolytic agents before the MRI scan. Patients treated with anticoagulation or antiplatelet therapy were not excluded. (6) No notable asymmetric head tilting or motion artifacts. The ethics committee at our institution reviewed and approved our protocol, and written informed consent was obtained from all patients or authorized representatives.

A total of 139 diffusion MR studies from 78 patients (25 women, 53 men) ranging in age from 32 to 81 years old (mean age was 58.84 ± 11.83 years old) were included in the analysis. Twenty-five patients were studied more than once (15 patients were studied 2–3 times, and 10 patients were studied 4–6 times). The time from symptom onset to imaging ranged from 2.2 h to 236 days. This time was determined by interviewing all patients and available family members at the time of scanning. Onset time was designated as the time the patient was last known to be without the new deficit. If a patient awoke with a new deficit, the time the patient went to bed or was last seen without the deficit was taken as stroke onset time. All patients were stratified into nine groups based on time from stroke onset: less than 6 h ($N = 12$), 7–12 h ($N = 14$), 13–24 h ($N = 12$), day 2 ($N = 12$), days 3–4 ($N = 11$), days 5–7 ($N = 15$), days 8–14 ($N = 17$), days 15–30 ($N = 19$), and 31 days or more ($N = 27$).

2.2. DW imaging

The majority of the MRI studies ($n = 117$) were performed on a 3.0 T MR scanner (Signa; GE Medical Systems, Milwaukee, WI) with gradient strengths of 40 mT/m. All imaging was acquired with a standard 4-channel head coil. FLAIR DWI was performed by using a spin-echo single-shot echo-planar sequence with the following parameters: 10,000 ms/102 ms/2250 ms (TR/TE/TI), field of view = 22 cm, bandwidth = 100 kHz, and matrix of 128×128. The diffusion gradients were applied along the *x*-, *y*-, and *z*-axes, with a *b*-value of 0 and 1000 s/mm^2. A total of 16 axial slices (6 mm thick with a 2 mm gap between slices) were acquired through the whole brain with a scan time of 40 s. Conventional DWI was acquired with the same parameters as the FLAIR DWI, except for the parameters of TR and TE (8000 ms/102 ms), with an acquisition time of 24 s. The remaining studies ($n = 22$) were performed at 1.5 T MR scanner (Signa; GE Medical Systems, Milwaukee, WI). FLAIR DW images were acquired with the same parameters as the 3.0 T MR except for the TI, which was 2200 ms with an acquisition time of 60 s. Conventional DWI was acquired with the same parameters as the FLAIR DWI, except for the parameters of TR and TE (7000 ms/96.5 ms), with an acquisition time of 40 s. DWI and FLAIR DWI were performed in each patient in a randomized order.

2.3. Data analysis

The acquired FLAIR DWI and conventional DWI images were transferred to a separate workstation (Advantage Windows Workstation; GE Medical Systems), and ADC maps were calculated using commercial software (FuncTool; GE Medical Systems). The mean ADC values were calculated on conventional DWI and FLAIR DWI (ADC_{CON} and ADC_{FLAIR}) sequences within the ischemic lesions at all time points. The mean ADC_{CON} was obtained by drawing a region of interest (ROI) around the entire ischemic lesion on the DW image at a slice level containing the ischemic core by an experienced neuroradiologist. For acute lesions, the ROI was drawn on the isotropic image with $b = 1000$ s/mm^2. The ROI measurements obtained at later stages were based on findings on the $b = 0$ EPI T2-weighted image because the infarct was more conspicuous than on the DW image. The neuroradiologist reviewing the images was informed of the expected anatomic location of the lesion based on each patient's medical records to ensure that the lesion chosen was the one that corresponded to the neurologic deficit. For all patients who had more than one exam included in this study, the neuroradiologist reviewed these studies in chronologic order. For any subsequent exams following the initial study, the lesion ROI was placed in the same anatomic location as it was on the first exam. When multiple acute lesions were seen in the same hemisphere, the largest one was selected. The ADC value was measured in the contralateral normal brain parenchyma by placing an ROI in an area that was nearly the same size and location as the chosen ischemic region, and an attempt was made to ensure this ROI contained the same proportions of grey and white matter. These regions were confirmed by a second neuroradiologist. The selected ROIs were then transferred to the same region in the corresponding slice on the ADC map to obtain the mean ADC values. The corresponding ADC_{FLAIR} in both the lesions and corresponding contralateral sides were obtained in a similar way. To avoid the differences in ROI placement between two sequences, conventional DW images and FLAIR DW images for a given patient were consecutively analyzed to ensure similar ROI placement, shape and size between each sequence. Relative ADC was also calculated as a ratio of the ADC value within the ROI in the ischemic lesion to the ADC value in the ROI in a corresponding location in the normal contralateral hemisphere.

2.4. Statistical analysis

All statistical analyses were performed using a commercially available SPSS release 10.0 software package (SPSS, Chicago, IL, USA). The results are presented as the mean ± SD. The comparison between the ADC values obtained from conventional DWI and FLAIR DWI in the ischemic lesions and the contralateral control