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Intravoxel incoherent motion diffusion-weighted imaging in stroke patients: initial clinical experience

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AIM: To evaluate the feasibility of using intravoxel incoherent motion (IVIM) to measure diffusion and perfusion parameter variations in stroke.

MATERIALS AND METHODS: Thirty-eight stroke patients were enrolled in the study. IVIM imaging was performed using 15 b-values from 0 to 1000 s/mm^2. Arterial spin labelling (ASL) magnetic resonance perfusion was also undertaken. Relations between the IVIM parameters (including apparent diffusion coefficient [ADC], diffusion coefficient D_{slow} [D], pseudo-diffusion coefficient D_{fast} [D*], fractional perfusion-related volume [f]) and fD* (the multiplication of the first two parameters) and the ASL-derived parameter, cerebral blood flow (CBF), were analysed using paired *t*-tests. Comparisons of all the parameters between lesions and contralateral normal regions, as well as between acute and subacute groups were analysed using Student's *t*-test.

RESULTS: There were positive correlations between f and CBF as well as fD* and CBF (r=0.472 and 0.653). Quantitative analysis showed a significant decrease in ADC, D, D*, f, fD*, and CBF of the lesions compared with the contralateral side, in which the decrease of fD* (68.6%) was highest. The values of ADC, f, and fD* increased in the subacute period group compared with the acute period group.

CONCLUSIONS: IVIM analysis allowed separation of perfusion contribution from true diffusion and thus provided an evaluation of the perfusion and diffusion variations during stroke, which might further elucidate the mechanisms of ischaemic stroke.

Introduction

Diffusion and perfusion imaging have multiple applications in patients with cerebrovascular diseases, especially for early detection of ischaemic stroke.[1,2] Obtaining images related to both perfusion and diffusion from one single intravoxel incoherent motion (IVIM) measurement is particularly attractive. In 1988, Le Bihan *et al.*[4] defined IVIM as the microscopic translational motions that occur in each image voxel during a magnetic resonance imaging (MRI) acquisition.[3,4] In biological tissues, motion includes molecular diffusion of water and microcirculation of blood in the capillary network. The diffusion coefficient, D_{slow} (D), is the true diffusion coefficient. The pseudo-diffusion coefficient, D_{fast} (D*), is related to blood speed and length of artery. The fractional perfusion-related volume (f) describes the

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percentage of incoherent signal arising from the vascular compartment over the total incoherent signal.[4,5] As reported, apparent diffusion coefficient (ADC) variations are caused by the fast diffusion component rather than by the slow diffusion component.[6,7] Recently, promising results to measure perfusion using the IVIM technique have been achieved in various diseases of different body organs. Research on the separation of perfusion and diffusion measurements using the IVIM technique in human brain disorders are relatively few. Further, a theoretical relationship between IVIM perfusion parameters f, D*, fD* (the multiplication of the first two parameters) and dynamic susceptibility contrast (DSC) perfusion parameters has been derived, for example, in gliomas.[8] IVIM modelling may also be applied in stroke imaging, as the method is not associated with a radiation burden or the external application of a paramagnetic contrast agent to estimate the perfusion-related parameters.[5]

The aim of the present study was to evaluate the feasibility of IVIM perfusion measurements with currently available imaging systems in stroke patients by comparing the IVIM parameters and the arterial spin labelling (ASL) magnetic resonance perfusion-derived cerebral blood flow (CBF) values and to study the variations of IVIM parameters during the process of stroke.

Materials and methods

This study was approved by the Ethics Committee at Tongji Hospital, Wuhan China. Informed consent was obtained from each patient. Images were collected from February 2013 to August 2014 in patients presenting with symptoms of hemispheric stroke at different stages. Eighty patients were initially considered for the study. Forty-two patients were excluded because of motion artefacts (13 patients), haemorrhagic transformation (four patients), infratentorial lesions (nine patients), and small lesions <0.5 cm in minimal diameter (16 patients). The final study population consisted of 38 cases (31 hypoperfusion and seven hyper-perfusion, 26 males, 12 females, mean age 55 years, age range 23–74 years).

Image acquisition

Imaging was performed using a 3 T MRI system (GE Medical Systems, Discovery 750, Waukesha, WI, USA) with a 32-channel receiver head coil. The protocol included T1-weighted, T2-weighted, fluid-attenuated inversion recovery (FLAIR), IVIM imaging, and ASL. IVIM imaging was based on a diffusion-weighted spin-echo echo planar imaging (EPI) sequence, with 15 b-values (0, 20, 40, 80, 110, 140, 170, 200, 300, 400, 500, 600, 700, 800, 900, 1000 s/mm^2) in three orthogonal directions. Other parameters were as follows: 5 mm section thickness; 240 × 240 mm^2 field of view; 160 × 160 matrix size; 5200 ms repetition time (TR); minimum echo time (TE); 4 minutes 51 seconds acquisition time.

ASL was performed using a pseudocontinuous pulse sequence with the following parameters: 4787 ms TR; 14.6 ms TE; 1500 label time; 1525 ms post-label delay; 240 mm field of view; 4 minutes 38 seconds acquisition time. A total of 34 pairs of tagged and control images were obtained.

Image analysis

Parametric maps of the IVIM parameters, including the ADC, D, D*, f and fD* values, were obtained by fitting the IVIM bi-exponential model on the GE AW4.5. A two-step analytical method was implemented to avoid overfitting of the bi-exponential model by deriving D from a simplified mono-exponential function:

$$Sb = S0 \times \exp^{(-bD)}$$

using b-values >200 s/mm^2. The f and D* values were then estimated by non-linear regression for all b-values.

In the measurements, regions of interest (ROIs) in the ischaemic lesions were obtained on two axial sections with the largest area of infarction, and the results were averaged for subsequent analysis. The ROIs were then controlled by a neuroradiologist (Y.Y., 3 years of experience) and manually corrected if necessary. A ROI was then placed in the contralateral region. All ROIs were placed so that they included as little cerebrospinal fluid (CSF) or large vessels as possible.[1] To evaluate interobserver reproducibility, these ROIs were measured by another neuroradiologist (J.S., 5 years of experience). Values with f >0.3 and D* >0.05 were set to zero, because they are not physiological and are likely to result either from noise or from partial volume effects of the CSF.[9]

Statistical analysis

Relations between the IVIM parameters (including ADC, D, D*, f and fD*) and the ASL parameter (CBF) were analysed using paired two-tailed *t*-tests. Pearson's correlation coefficient was considered to be poor ($0 \leq r \leq 0.2$), weak ($0.2 < r \leq 0.4$), fair to good ($0.40 < r \leq 0.75$), or excellent ($0.75 < r$). Comparisons of all the parameters between lesions and contralateral normal regions as well as between acute and subacute groups were analysed using Student's *t*-test (SPSS version 18.0; SPSS, Chicago, IL, USA). Statistical significance was defined at $p<0.05$. The intraclass correlation coefficient was considered to be poor ($0 \leq ICC \leq 0.4$), weak ($0.4 < ICC \leq 0.75$), fair to good ($0.75 < ICC \leq 0.9$), or excellent ($0.9 < ICC$).

Results

Interobserver agreement in the quantitative analysis was evaluated as fair to good. The variation trends of f-values of the lesions were consistent with those of the ASL-CBF values compared to the normal regions under both hyper- and hypo-perfusion levels (Figs 1–2). The sample size of the hyper-perfusion patients was small, the results of hypo-perfusion patients (n=31) underwent both IVIM imaging with 15 b-values and ASL perfusion scanning were mainly discussed. Twenty-four of the 31 patients showed a mismatch of the area of f and ASL-CBF (f<CBF, n=23, f>CBF,