Understanding the recuded ADC in stroke lesions using repeated measurements with different diffusion times

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Introduction

Diffusion MRI is a well known method for visualisation of acute and subacute ischaemic stroke lesions. However, the underlying mechanisms of the image contrast and of the reduced apparent diffusion coefficient (*ADC*) are still under debate. Influx of water into the intracellular space [1], an increased tortuosity in the extracellular space [2], shrinking of neurons [3] and reduced cytoplasmic streaming [4] have been suggested as possible explanations. Recently, water exchange has been shown to be observable in subacute stroke lesions using diffusion MRI measurements with high *b*-values and a varied diffusion time (T_D) [5]. The aim of this study was to further investigate the origin of the reduction of *ADC* in stroke lesions by determining the signal-versus-*b* curve for different diffusion times (T_D) in stroke patients.

Theory

Signal-versus-*b* curves from measurements with different diffusion times can be analysed with a modified Kärger model, implemented in various forms in [5-7]. Here, a two compartment Kärger model was used, including one apparently freely diffusing extracellular component, described by ADC_e and a signal fraction f_e, and one restricted intracellular component, described by a signal fraction f_i and a maximal root-mean-square displacement rms_i. Exchange between the components was described by the intracellular exchange time τ_i.

Method

In this ongoing project, two patients were scanned on day three and day ten after their stroke, using a Philips 3T Achieva scanner. Signal-versus-*b* curves were obtained using 16 different *b*-values, with b_{max} = 9000 s/mm^2 in six non-collinear diffusion encoding directions, using a pulsed gradient spin echo (SE) sequence with diffusion times T_D = 30/60 ms, diffusion encoding duration δ = 21 ms, TR = 2000 ms, TE = 109 ms. To investigate possible differences in compartmental relaxation times, a pulsed gradient stimulated echo (STE) sequence was employed for T_D = 60 ms, with TE = 109 ms and TM = 36 ms, and with otherwise identical settings as in the SE-measurement. Regions of interest (ROIs) were placed in the lesion, in areas of grey matter (GM) and white matter (WM), see Fig 1. Geometrically averaged signal-versus-*b* curves were calculated and the two-compartment Kärger model was fitted to the obtained data, when all signal values exceeded three times the noise standard deviation.

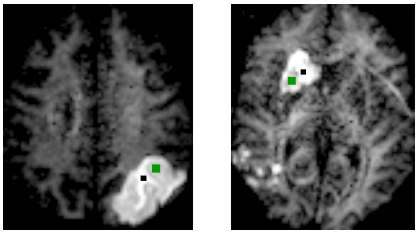

Figure 1. ROI-positions in a geometrically averaged diffusion-weighted image (b = 5000 s/mm^2) for patient 1 (left) and patient 2 (right). WM ROIs are black and GM ROIs green.

Results

In patient 1, the stroke lesion was located in the parietal peripheral WM and GM. In patient 2, the lesion comprised the anterior putamen, pallidum and internal capsule and the caudate nucleus.

Table 1. Model-parameters from the fitting with ADC_e in μm^2/ms, rms_i in μm and of τ in ms. D3 and D10 represent measurements three and ten days after the stroke onset.

	Pat 1		Pat 2	
	D3	D10	D3	D10
GM				
f_i	74%	N/A	47%	34%
ADC_e	1.6	N/A	1.1	1.2
rms_i	2.4	N/A	2.4	2.1
τ	18	N/A	21	25
WM				
f_i	79%	40%	73%	50%
ADC_e	1.0	1.1	1.0	0.5
rms_i	1.6	2.0	1.7	0.9
τ_i	160	100	41	100

Exchange was observed in GM as a decreased signal intensity for prolonged T_D (Fig 2a). However, the second measurement in patient 1 showed a high *ADC* and the noise floor was reached at *b* = 3500 s/mm^2. Model fitting revealed an exchange time of around 20 ms (Table 1).

In WM, the results were contradictory; a small increase in the signal intensity was observed for prolonged T_D in patient 1, whereas a small decrease was observed for patient 2 (Fig. 2b). This was also seen in the model fitting, where τ_i was generally longer for patient 1.

The STE measurements showed a lower signal intensity for high *b*-values, as compared to the SE measurements (Fig. 2c), even though the diffusion encoding parameters were identical.

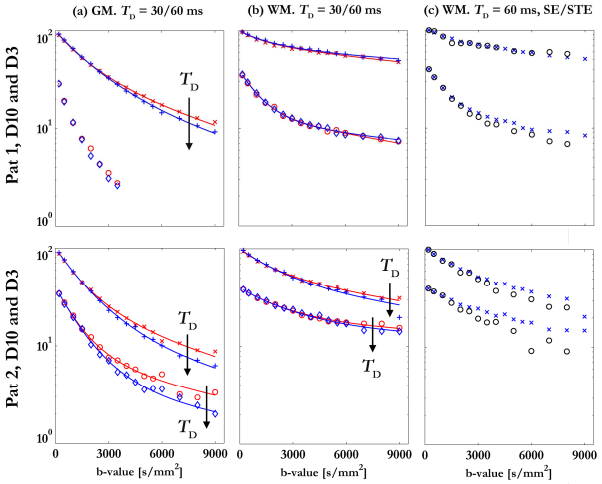

Figure 2. Normalised signal-versus-b curves, where the upper curve pair was measured three days (D3) after onset of stroke and the lower pair ten days (D10) after the onset. For the SE measurements (a and b), red/blue corresponds to T_D = 30/60 ms, and solid lines to the model fit. The STE-measurement in (c) is represented by black circle.

(a) For GM, a decreasing signal intensity for prolonged T_D was observed for high b-values in three out of four cases. (b) For WM, the signal intensity decreased for prolonged T_D for patient 2, but showed a tendency to increase for patient 1. (c) WM signal-versus-b curves obtained by the SE and the STE measurements, showing a lower signal intensity at high b-values for the STE measurement.

Discussion and conclusion

Using SE measurements where only T_D differed between the measurements, this study independently verified the presence of a water exchange in sub-acute stroke lesions, first observed by Lätt *et al.* [5]. In addition, the measurements at day 10 showed a decrease of the intracellular signal fraction, as compared to the measurements day 3 (Table 1, cf. D3 and D10), that can be interpreted as gradual cell destruction.

Indication of restricted diffusion, i.e. a tendency of increased signal intensity for prolonged T_D, was observed in WM for one of the two patients (Fig 2b). The differences between the WM signal curves of the different patients, can be due to lesion heterogeneity [8]. Also, the WM involved in the lesions is histologically different.

The STE measurement revealed indications of different compartmental relaxation times in WM (Fig. 2c), that is, a lower signal intensity at high *b*-values for the STE-measurement as compared to the SE-measurement (where only the mixing time, TM, and TE varied between the measurements). This was not observed for GM (data not shown), likely because the exchange time was shorter than the relaxation time.

In conclusion, we verified the existence of water exchange in stroke lesions using SE measurements where only the diffusion time was varied. Moreover, we showed effects of compartment specific relaxation rates in WM stroke lesions.

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