Diffusion Anisotropy Evolution in Early Hyper-Acute Stroke

L. J. Lee[1,2], A. D. Harris[3,4], R. Frayne[1,2]

[1]Radiology and Clinical Neurosciences, University of Calgary, Calgary, Alberta, Canada, [2]Seaman Family MR Research Centre, Foothills Medical Centre, Calgary Health Region, Calgary, Alberta, Canada, [3]Biomedical Engineering, University of Calgary, Calgary, Alberta, Canada, [4]Electrical and Computer Engineering, University of Calgary, Calgary, Alberta, Canada

Introduction

Diffusion-sensitive MR imaging is commonly used to examine stroke and may be divided into two categories: (a) isotropic (or directionally independent) measures such as apparent diffusion coefficient (ADC) and (b) anisotropic (or directionally dependent) measures such as fractional anisotropy (FA). Previous studies have shown FA changes in the acute and sub-acute phases (>6 h from stroke onset).[1-3] However, a recent study found no consistent FA changes in the hyper-acute phase of stroke (<6 h from onset) [4] and no other studies have examined anisotropy exclusively in the hyper-acute phase. The purpose of this study was to further examine FA evolution in early hyper-acute stroke. Canine embolic stroke models were imaged repeatedly both before and after induction of stroke to monitor ADC and FA progression. Our hypothesis was that we would find no FA changes in hyper-acute stroke.

Methods

Embolic strokes were induced in three canines by autologous clot injection in to the internal carotid artery and serially imaged on a 3.0 T scanner (Signa; General Electric Healthcare, Waukesha, WI) for up to 4.5 h, including pre- and post- stroke imaging. This animal model had been previously developed and validated,[5] and we assume that once the clot is injected, a stroke occurs. Regions-of-interest (ROI) were placed on the ADC and FA maps in white and grey matter (WM, GM) in ischemic and contralateral normal tissue (4 regions per animal). Measurements on one animal were repeated 3 times by one observer, and then by two other observers. Coefficient-of-variation (COV) were calculated to assess intra- and inter-operator viability. To compare ADC and FA values, first, all pre-stroke data was pooled and all post-stroke data was pooled for each ROI, and *t*-tests compared values between the before stroke and after stroke induction. In attempt to remove the dynamic stage during the first hour of stroke when ADC values are changing rapidly, a second comparison was also performed. In the second comparison, the post-stroke data pool only included time points *greater* than 1 h after clot injection, and *t*-tests were performed to compare the pre-stroke and >1 h post-stroke data.

Results

For the ADC data, the maximum COV of intra-operator repetitions was 13.6% and the maximum COV of inter-operator repetitions was 14.4%. For the FA maps, the maximum COV for intra- and inter- operator repetitions were 21.5%, and 16.4%, respectively. The Figure shows typical time course results obtained in one dog: ADC changes but not FA changes were apparent after stroke onset (t = 0 min). In the contralateral normal tissue for both GM and WM there were no differences between the pre-stroke and post-stroke data. The Table summarizes the ROI data for the ischemic regions. Overall, statistically significant changes were seen in ADC measures in ischemic tissue for both post-stroke data pools but FA did not show significant changes in either analysis.

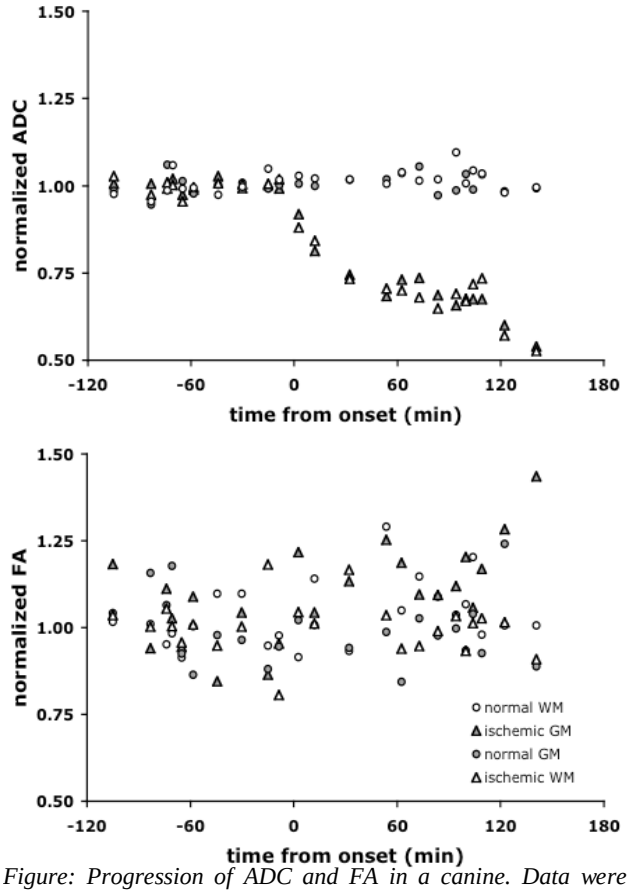

Figure: Progression of ADC and FA in a canine. Data were normalized to pre-stroke values. Clot was injected at t = 0 min.

Discussion and Conclusions

The ADC decrease is consistent with other studies of acute ischemic stroke, [1-4] and it is generally accepted that this indicates cytotoxic edema. As expected, no significant changes in FA of the ischemic tissue were found. This implies that changes in FA occur at the end of the hyper-acute phase, or in the early acute phase. This is consistent with the work of de Crespigny *et al*,[6] who observed no FA changes in a transient (mild) stroke model, but saw slight to significant FA increases in a permanent MCA occlusion (thus more severe) stroke model. We hypothesize that FA changes are related to the compromise of the blood brain barrier and other changes in cell tortuosity. If this is true, FA changes could be used to select patients for thrombolytic treatment.

Table. Pooled ADC and FA data of ischemic ROI before, after and greater than 1 h after stroke onset. p-*values are from the t-tests comparing pre- and post-stroke data.*

	White Matter			Grey Matter		
	pre-stroke	post-stroke	>1 h post- stroke	pre-stroke	post-stroke	>1 h post- stroke
ADC ($\mu m^2/s$)	635.343	492.662 p = 0.017	454.020 p = 0.016	649.549	474.43 p = 0.004	444.108 p = 0.002
FA	0.47	0.49 p =0.87	0.49 p = 0.92	0.35	0.36 p = 0.90	0.37 p = 0.88

References

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