Variability in ADC and FA Measurements in Acute Ischemic Stroke

M. Govindaraj[1], A. D. Harris[2,3], R. Frayne[2,4]

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

Introduction

Diffusion tensor imaging (DTI) to characterizes diffusion of water in tissues with parameters such as the apparent diffusion coefficient (ADC) and fractional anisotropy (FA) is becoming increasingly used to examine ischemic stroke.[1,2] However, to understand these parameters in stroke, an understanding and quantification of the variability measurements required. Here, we evaluate the intra- and inter-operator variability when quantifying ADC and FA using region-of-interest (ROI) analyses in acute stroke. From these data, we estimate the minimum detectable difference (MDD) for ADC and FA measures in grey and white matter (GM and WM, respectively).

Methods:

DTI data (TR/TE =9000 /80.7; FOV = 24 cm × 24 cm; 192 × 192 acquisition matrix, 1 signal average, b = 1000 s mm^{-2}) were examined from 10 acute stroke (< 24 h from onset) patients with moderate-to-large diffusion lesions (*i.e.*, infarcted tissue) on the acute diffusion-weighted image. ROIs were placed in infarcted and normal regions in both GM and WM (total: 4 regions). Infarcted tissue was determined from the diffusion-weighted image. GM and WM were delineated from the T2-weighted acquisitions. Two ROI types (elliptical and free-hand polygon) were evaluated. Four observers were instructed which map (FA or ADC) and which ROI type to examine for each analysis. Analysis periods were separated by at least one day and repeated three times by each observer, with each ROI type-map combination being separated by at least a week. Analysis of variance (ANOVA) examined the effects of observer, repetition, patient, ROI type and tissue and *F*-tests examined the variability of ROI type. Inter- and intra- operator variability and MDD was assessed based on the ANOVA method described by Eliasziw *et al*.[3] For all statistical analyses $p = 0.05$

Results

In the initial ANOVAs, observer, repetition and tissue had significant effects on ADC values, and observer, patient, tissue type and the observer-patient interaction had significant effects on FA values. In the follow-up ANOVAs tissue types were separated and patient effects were removed. For ADC, observer remained significant, except in normal WM and repetition remained significant in normal GM. In FA, the follow-up ANOVA showed observer as the only significant factor in all tissue types. The *F*-tests did not detect any variability differences between the two ROI types on ADC or FA in pooled or individual tissues types. When determining inter- and intra- rater variability for ADC, patient was always a significant factor of variability, and observer, trial and patient-observer interactions were significant in infarcted tissues and normal GM. While determining FA inter- and intra- observer variability, patient, observer and the patient-observer interaction were always significant factors of variability, and trial was significant in normal WM. The average, MDD and inter- and intra- coefficients of reliability (ρ_{inter} and ρ_{intra}, respectively) are summarized for each tissue in the Table.

Table 1. Mean MDD and coefficients of reliability for ADC and FA in acute ischemic stroke.

	ADC (× 10^{-3} mm^{2}s^{-1} for Mean and MDD)				FA			
	Mean (SD)	MDD	ρ_{inter}	ρ_{intra}	Mean (SD)	MDD	ρ_{inter}	ρ_{intra}
Pooled	0.492 (0.173)	0.474			0.351 (0.149)	0.41		
Normal WM	0.577 (0.074)	0.160	0.56	0.63	0.482 (0.982)	0.19	0.39	0.68
Normal GM	0.683 (0.112)	0.212	0.21	0.73	0.220 (0.053)	0.10	0.06	0.75
Infarcted WM	0.303 (0.070)	0.129	0.49	0.74	0.478 (0.085)	0.18	0.41	0.63
Infarcted GM	0.406 (0.102)	0.210	0.29	0.65	0.225 (0.054)	0.09	0.37	0.78

Discussion

For ADC and FA, we quantified the MDD and the variability of ROI measurements. With an acute stroke DTI protocol, we confirm the ability to detect ADC changes; however, the MDD is larger than the expected FA changes. This may explain the discrepancy between Harris *et al,* [1] in not detecting significant FA changes while Sorenson *et al*,[2] did find significant FA changes in acute stroke.

The expected finding that tissue type significantly affects ADC and FA measurement was seen in the initial ANOVA, as it is generally accepted that ADC is significantly reduced in acute stroke and FA in WM is higher than GM.[1,2] Additionally, it was shown that FA is different between patients, which was interpreted as the ROI location (*i.e.*, more specific than WM or GM) significantly affects FA measurements. This is not surprising considering the range of FA values that can occur in WM. The effect of observer in all three ANOVA analyses was attributed to the intrinsic difficulty to define ROIs in pure WM and GM in the cortex. Using the reliability characterizations suggested in Ref 3, for ADC, ρ_{inter} is considered "moderate" in WM and "fair" in GM. For FA, ρ_{inter} is "fair" in normal WM and infarcted GM, "slight" in normal GM and "moderate" in infarcted WM. For both ADC and FA ρ_{intra} was "substantial" for all tissues. This infers that drawing ROIs is subject to a relatively high degree of inter-rater variability; however, intra-observer variability is relatively low. Future ADC and FA ROI analyses may benefit in terms of observer variability by using observer consensus to place ROIs. The major limitation of this study is the use of ANOVA on FA data, as FA is not normally distributed.[4] However, non-parameteric tests do no have the same statistical power or capabilities, especially when examining multiple factors and interactions, thus using parametric tests may be an acceptable alternative.

References: [1] Harris *et al.*, *J Magn Reson Imaging* 2004; 20: 193-200. [2] Sorenson *et al.*, *Radiology* 1999; 212: 782-792. [3] Eliasziw M, *et al*., *Phys Ther* 1994; 74: 777–788. [4] Pajevic S and Basser PJ. *J Magn Reson* 2003; 161: 1-14