Repeatability of Apparent Diffusion Coefficient and Fractional Anisotropy in Patients with Recurrent Glioblastoma Multiforme

M. J. Paldino[1], D. Phadke[2], A. DesJardins[2], J. Vredenburgh[2], H. Friedman[2], and D. P. Barboriak[1]

[1]Radiology, Duke University Medical Center, Durham, NC, United States, [2]Duke University Medical Center, Durham, NC, United States

Background/Purpose:

Diffusion tensor magnetic resonance imaging (DTI) has been used to monitor changes in the microscopic tissue environment within tumors as a means of assessing early response to chemotherapy. However, the reproducibility of measurements derived from DTI in patients with neoplastic disease has not been widely studied. The purpose of this study is to quantify the repeatability of apparent diffusion coefficient (ADC) and fractional anisotropy (FA) within regions of contrast enhancement and FLAIR signal abnormality in patients with recurrent high grade glioma.

Materials and Methods:

Institutional Review Board approval and informed consent were obtained for this HIPAA compliant study. 16 patients (10 men, 6 women; age range 38-62 years) with recurrent Grade IV astrocytoma underwent serial 1.5T MR imaging on the same magnet. Scanning was performed at two time points within a 72 hour period without interval intervention or therapy. Sequences obtained included: (a) Axial single-shot echo planar DTI (TR/TE (ms): 6000/100; flip angle: 90 degrees; matrix: 128 x 128, voxel: 1.72 x 1.72 x 5mm), (b) Sagittal contrast-enhanced 3D SPGR (TR/TE (ms): 8.6/4.1; Flip angle: 20 degrees; matrix: 256 x 256, voxel: 1mm isotropic), and (c) Sagittal 3D FLAIR (TR/TE/IR (ms): 6000/353/2200; flip angle: 180 degrees; matrix: 256 x 216, voxel: 1mm isotropic). For DTI, a total of 13 image sets were acquired: one without diffusion weighting and twelve with non-collinear diffusion-weighting gradients and a *b* value of 1000 sec/mm^2. For each patient, ADC and FA maps from each time point were aligned to both the contrast-enhanced SPGR and FLAIR image volumes obtained on day 1 using a rigid body normalized mutual information algorithm. Volumes of tumor-related contrast-enhancement (TRE) and FLAIR signal abnormality (FSA) were defined using a semi-automated image segmentation technique. Mean ADC and FA within the TRE and FSA volumes were calculated for each time point (see example, Figure 1). In each region, the following statistics were calculated for both ADC and FA: within patient standard deviation, mean coefficient of variation, route mean square (RMS) coefficient of variation, intra-class correlation coefficient (ICC), and regression coefficient. A coefficient of repeatability and 95% confidence interval for change were also calculated as described by Bland and Altman (Bland and Altman, 1999. *Stat Meth Medical Res*, 8: 135-60).

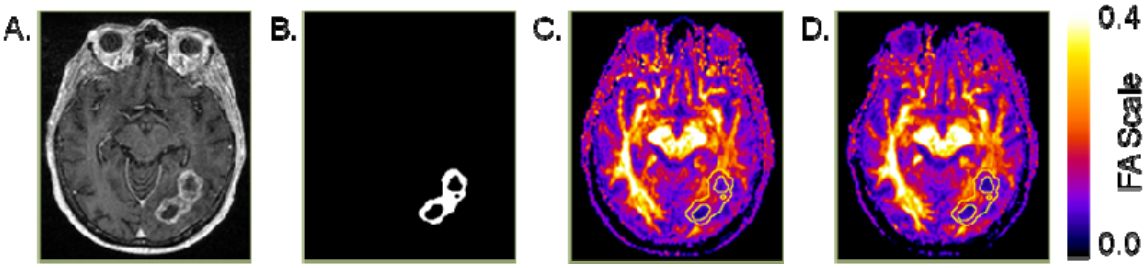

Figure 1. Contrast-enhanced T1-weighted SPGR image (A) demonstrating left temporoparietal glioblastoma multiforme was segmented to isolate tumor-related enhancement (TRE; B). In this example, mean fractional anisotropy (FA) was calculated within TRE on days 1 (C) and 3 (D).

Results:

Statistical analysis of the repeatability of ADC and FA within regions of TRE and FSA is presented in Table 1.

	TRE		FSA	
	ADC	FA	ADC	FA
Mean	1.34 x 10^{-3}	0.127	1.34 x 10^{-3}	0.158
Mean difference	0.0079 x 10^{-3}	0.00011	0.0102 x 10^{-3}	0.00019
Within subject standard deviation	0.038 x 10^{-3}	0.0059	0.026 x 10^{-3}	0.0047
Mean CoV (%)	2.0	3.3	1.3	2.3
Route mean square CoV (%)	2.7	5.0	1.9	3.1
Intra-class correlation coefficient	0.792	0.795	0.917	0.890
Regression Coefficient	0.947*	0.947*	0.979*	0.972*
Repeatability Coefficient	0.104 x 10^{-3}	0.016	0.071 x 10^{-3}	0.013
95% CI change (%)	7.4	13.9	5.2	8.7

Table 1: Repeatability analysis of apparent diffusion coefficient (ADC) and fractional anisotropy (FA) within regions of tumor-related enhancement (TRE) and FLAIR signal abnormality (FSA). Unless specified, ADC is listed in units of mm^2S^{-1}. CoV: coefficient of variability. CI: confidence interval. Asterisk (*): $p < 0.0001$.

Conclusion:

For an individual patient, changes after therapy greater than the repeatability coefficient are unlikely to be related to intra-method variability in the measurement of ADC and FA. These data provide a context with which to interpret changes in diffusion parameters that occur after treatment. They also serve as a preliminary step toward a broader understanding of the reproducibility of diffusion-weighted MR imaging.