Apparent Diffusion Coefficient and Fractional Anisotropy may predict newly diagnosed low-grade glioma subtypes

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Introduction: The pure low-grade astroctyoma (AC) and oligodendroglioma (OD) glioma subtypes are known to have different prognosis and response to treatment. Oligodendrogliomas tend to have longer latent period to malignant progression and tend to be more responsive to chemotherapy[1]. Currently phenotyping is performed through biopsy, which is risky as it is a surgical procedure. It is also prone to sampling error due to glioma heterogeneity. Non-invasive methods of subtyping low-grade gliomas are very important for prognostics and stratifying patients for treatment. Prior studies have reported that an Apparent Diffusion Coefficient (ADC) histogram analysis may aid in subtyping low-grade gliomas[2]. The goal of this study was to retrospectively analyze the ADC and FA values for pure oligodendrogliomas and astrocytomas subtypes and confirm trends and findings from previous studies.

Methods: We scanned a total of 38 newly diagnosed brain tumor glioma patients, consisting of 23 oligodendroglioma patients and 15 astrocytoma patients on a 1.5T GE Signa Echospeed scanner (GE Healthcare Technologies). The MRI protocol included post-gadolinium (Gd) T1-weighted image, axial T2-weighted images, and either a three directional axial diffusion imaging with (TR/TE= 1000/110ms), voxel size = 1.4×1.4×5mm, b=1000 or a 6 directional axial diffusion imaging with (TR/TE= 1000/108ms), voxel size = 1.7×1.7×3mm, b=1000. Diffusion images were analyzed using in-house software to calculate the apparent diffusion coefficient (ADC) and if 6 directional data the fractional anisotropy (FA). The ADC and FA maps were normalized by normal appearing white matter (NAWM) to generate nADC and nFA maps. A semi-automated segmentation method was used to define the T2 hyperintense region (T2All) from the T2 weighted image. Table 1 shows the number of 3 directional data and 6 directional data for each subtype. The ADC values from 3 vs. 6 directional data sets were compared using a Wilcoxon signed-rank test of the median ADC values using 14 patients with both 3 and 6 directional data. A Mann-Whitney rank-sum test was performed on oligodendroglioma and astrocytoma median, 25th and 75th percentile ADC, nADC, FA and nFA values.

Low Grade Subtype	3 dir DWI	6 dir DTI	Total
Oligodendroglioma	8	15	23
Astrocytoma	8	7	15

Table 1. Number of diffusion data sets per subtype, separated into 3 direction diffusion weighted imaging or 6 directional diffusion tensor imaging.

Results and Discussion: The Wilcoxon signed-rank test of the 3 directional and 6 directional ADC values showed no significant difference for the median (p=0.91259), 25th (p=0.4631) or 75th (p=0.2958) percentile ADC values within the T2ALL. Therefore, the 3 and 6 directional data sets were analyzed together. The median, 25th and 75th percentile were calculated for ADC and FA values. The median ADC and FA values for NAWM and T2ALL regions are shown in Table 2.

Low Grade Subtype	ADC		nADC	FA		nFA
	NAWM	T2ALL	T2ALL	NAWM	T2ALL	T2ALL
Oligodendroglioma	760± 147	1181 ± 265	1.57 ± 0.34	436 ± 136	196 ± 96	0.48 ± 0.21
Astrocytoma	767 ± 122	1476 ± 281	1.97 ± 0.36	369 ± 128	115 ± 75	0.32 ± 0.19
p-value	0.9523	0.000004*	0.000003*	0.751	0.0165**	0.0004*

Table 2. Descriptive statistics of the ADC and FA median values within NAWM and T2ALL for the OD and OA subtypes.
*=p<0.01, **=p<0.02

The median nADC OD values were significantly smaller than the median nADC AC values, as shown in Figure 1a. This also held true for the 25th and 75th percentile nADC values showing significant difference between OD and AC with p-values of 0.00006 and 0.00003 respectively. The median nFA OD values were significantly larger than the median FA AC values, as shown in Figure 1b. Significant difference between OD and AC could also be found for nFA 25th and 75th percentile with p-values of 0.0006 and 0.001 respectively. Therefore, plotting nFA versus nADC values shows a more distinct separation of OD and AC than nADC or nFA separately, see Figure 1c.

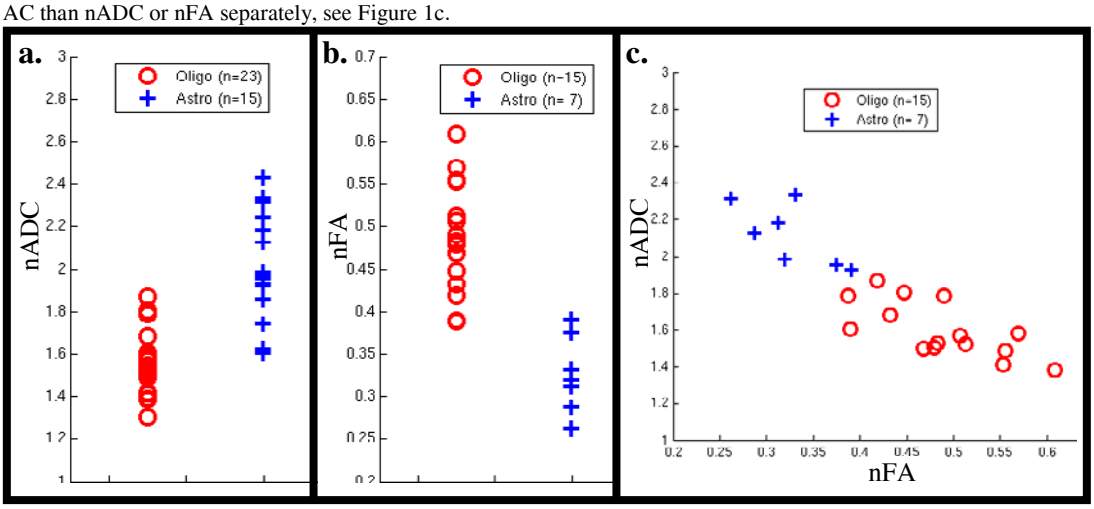

Figure 1.
(a.) Corresponding median nADC for oligodendroglioma and astrocytoma patients, showing a significant difference between the medians.
(b.) Corresponding median nFA also showing a significant difference between the medians.
(c.) Plot of nFA and nADC showing a separation between oligodendrogliomas and astrocytomas.

Conclusions: A previous study suggests a trend towards significant differences in ADC values for newly diagnosed low grade oligodendroglioma and astrocytoma subtypes. This study suggests a significant difference between not only nADC, but also nFA. Therefore, utilizing both nADC and nFA from diffusion tensor imaging could be utilized as a non-invasive biomarker for subtyping low grades.

References: [1] Kitange GJ et al. Anticancer Ther. 2001; 1: 595–605. [2] Tozer DJ et al. NMR in Biomedicine. In Press.

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