Differentiation of Low-Grade Glioma Subtypes Using Mutiparametric MR Data

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Introduction: Oligodendroglioma (OD), astrocytoma (AC), and oligoastrocytoma (OA) are the three histologic subtypes of low-grade glioma (LGG). The planning of therapy and prognosis of LGG depend on tumor subtype. Currently, the diagnosis and subtyping of LGG rely on histopathologic examination. The accuracy of tissue biopsy is limited by the sampling error that is introduced by the heterogeneity of gliomas and surgical accessibility. Noninvasive MR imaging methods have been proposed for achieving better assessment of LGG. The maximum relative cerebral blood volume (rCBV) from perfusion imaging[1] and apparent diffusion coefficient (ADC) histogram[2] or both ADC and fractional anisotropy from diffusion-weighted imaging[3] have been reported to be useful in LGG subtype classification. Because the consideration of a single imaging modality may have limited sensitivity and specificity in determination of tumor type, we hypothesized that combined imaging information consisting of structural, metabolic, and physiologic properties from multimodality imaging is more useful in classifying these lesions. The purpose of this study was to determine whether the differentiation of LGG would be improved by combining information from diffusion, perfusion, and proton MR spectroscopic imaging (MRSI).

Methods: Forty five newly diagnosed low-grade (grade II) glioma patients (17 OD, 11 AC, and 17 OA) underwent MRSI, diffusion, and perfusion imaging at a 1.5T GE scanner (GE Medical Systems, Milwaukee, WI). 3D MRSI data were acquired using PRESS volume selection with TR/TE=1000/144, voxel size=1cm^3, and phase encoding array=12/16×8×8. The acquisition of diffusion imaging included either three gradient directions (TR/TE=1000/110, voxel size=1.4×1.4×5mm, and b=1000) or six gradient directions (TR/TE=1000/110, voxel size=1.7×1.7×3mm, and b=1000). The perfusion imaging consisted of the injection of a bolus of 0.1 mmol/kg body weight of gadopentetate dimeglumine (Gd-DTPA) contrast agent at a rate of 5 mL/s. A series of 60 T2*-weighted gradient-echo, echo-planar images were acquired during the first pass of the contrast agent bolus injection, with a TR/TE of 1000-1250/54 ms, 35° flip angle, FOV of 26 × 26 cm^2, 128 × 128 acquisition matrix, and 3-6 mm slice thickness. Metabolite intensities of Choline, NAA, and Creatine, ADC map, and rCBV were generated using in-house software. Region of interest (ROIs) were defined for T2 hyperintense region (T2ALL) and normal appearing white matter (NAWM) from T2 flare image. The median, 25th, and 75th percentile of signal intensities of ADC and rCBV and the median intensity of Choline, NAA, and Creatine were calculated within T2ALL and NAWM. All parameters in T2ALL were normalized by NAWM to generate normalized counterparts. Statistical analysis was performed using SPSS (SPSS, Chicago, IL). Analysis of covariance (ANCOVA) was used to determine differences between groups. Discriminant analysis was performed to determine MR parameters that better differentiated subtypes of LGG.

Results and Discussion: Table 1 shows median ADC and 25th percentile rCBV values, which were the most statistically significant variables between groups among measured median, 25th, and 75th percentile level, and median metabolite intensity from Choline, NAA, and Creatine. ***OD vs. AC*** OD showed lower median ADC ($p<0.001$) and higher 25th percentile rCBV ($p=0.002$) than AC. There was no significant difference on metabolite levels between the groups. Using median ADC and 25th percentile rCBV as predictors, discriminant analysis showed that 67.9% of the cases were correctly classified when considering only 25th percentile rCBV, 85.7% when considering only median ADC, and 92.9% when considering both median ADC and 25th percentile rCBV (Figure 1a). ***OD vs. OA*** OD showed lower median ADC ($p<0.001$) and higher median Choline ($p=0.017$) than OA. Discriminant analysis including both median ADC and Choline produced the best classification between OD and OA with 94.1% of cases being correctly classified (Figure 1b). The accuracy was 70.6% for Choline and 85.3% for median ADC when they were used as predictor individually. Although there was a significant difference on 25th percentile rCBV ($p=0.031$) as well, it did not improve the classification accuracy. The present results suggest that median ADC may be the most distinctive marker between OD and both AC/OA. 25 percentile rCBV and Choline were the second most important parameter in distinguishing OD from AC and OD from OA, respectively. Although a similar analysis was performed for distinguishing AC and OA, and for separating all three groups, the similarity of values between AC and OA limited the reliability of the method. The highest accuracy for classification between AC and OA was 78.1% (predictor: 25th percentile rCBV) and among all three groups was 71.6% (predictors: 25th percentile rCBV, median ADC and Choline). Because OA consists of tumors with varying degrees of astrocytic and oligodendrocytic components, further genotypic and survival analysis are needed to verify the resemblance of OA to AC observed in this study.

Table 1. Diffusion, perfusion, and MRSI parameters within T2ALL and NAWM for each subtype

Parameter	ROI	OD	AC	OA
Median ADC	T2ALL*	1.56±0.14	2.08±0.28	1.88±0.18
	NAWM	759.94±24.94	755.81±20.22	763.81±22.42
25th percentile rCBV	T2ALL	1.05±0.40	0.61±0.17	0.80±0.20
	NAWM	1.01±0.01	1.03±0.08	1.01± 0.01
Median Choline	T2ALL	1.37±0.49	1.22±0.53	1.05±0.19
	NAWM	15.57±2.18	10.84±4.78	15.07±3.65
Median Creatine	T2ALL	0.98±0.23	0.85±0.30	0.86±0.13
	NAWM	13.58±1.34	9.41±4.40	12.41±2.64
Median NAA	T2ALL	0.55±0.20	0.43±0.11	0.50±0.19
	NAWM	31.17±4.38	20.79±10.45	27.27±5.98

* Values within T2ALL were normalized to NAWM.

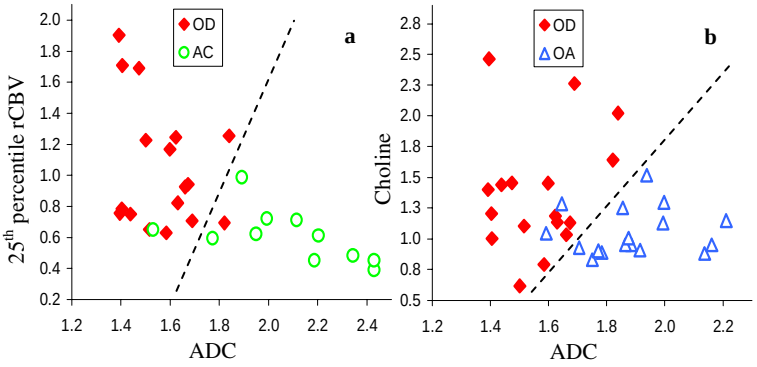

Figure 1. (a) Median ADC versus 25th percentile rCBV. The dashed line is the discrimination function L=4.3×median ADC-0.752×25th percentile rCBV-6.942 that differentiates OD from AC. (b) Median ADC versus median Choline. The dashed line is the discrimination function L=5.795×median ADC-1.339×median Choline-8.383 that differentiates OD from OA.

Conclusions: Multiparametric MR data from MRSI, diffusion, and perfusion imaging discriminate OD from OA and OD from AC among LGG subtypes. Unlike previous studies, in which only perfusion[1] or diffusion[2,3] data were used, this study suggests that better classification accuracy could be achieved by using parameters from mutimodality MR imaging. This method may provide a more objective and reproducible noninvasive method for the differentiation of LGG subtype, augmenting the current approaches to histopathologic diagnosis and contributing to therapy planning for patients with LGG.

References: 1. Cha S AJNR. 2005; 26: 266-273.
2. Tozer DJ et al. NMR Biomed. 2007; 20: 49-57.
3. Khayal IS et al. Proc. ISMRM, 15th Annual Meeting, Berlin, Germany 2007, p.838

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