# CLASSIFICATION OF DIFFERENT BRAIN TUMOR GRADES USING MAGNETIC RESONANCE SPECTROSCOPY

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**Introduction:** Proton ($^1$H) magnetic resonance spectroscopy (MRS) adds complementary information in the diagnosis of brain tumors before surgery (1,2). Single voxel $^1$H MRS has been applied to investigate the distinct metabolic features of brain tumors (3,4). During the past two decades, MRS studies have shown that common features of tumors relative to normal brain are i) an elevated choline (Cho) to creatine (Cr) ratio, ii) a reduced *N*-acetylaspartate (NAA) to Cr ratio, and iii) an increased lactate to Cr ratio (5,6). The ability to discriminate among major types of primary brain tumors is critical in formulating a precise and effective treatment plan. The purpose of this prospective study was to differentiate tumor from contralateral healthy tissue using metabolite ratios and also to determine their relationship to tumor grade using single voxel magnetic resonance spectroscopic technique.

**Methods**: We studied 47 adult patients with intracranial gliomas between November 2009 and Sep 2010. These patients were divided into three groups: grade II (n=7), grade III (n=13) and grade IV (n=27). The mean age and standard deviation (Mean±SD) of the patients with grade II, grade III and grade IV were 46.8±15.4 (range 30-75 years), 45.7±11.7 (range 32-69 years) and 57.4±10.2 (range 41-87 years), respectively. This research protocol was approved by the Institutional Review Board, and all subjects gave written informed consent. All patients underwent MRI and proton MRS on a 3T MRI/MRS scanner (Trio-Tim, Siemens Medical Systems, Erlangen, Germany). The following parameters were used for one dimensional (1D) MRS: TR/TE=2s/30ms, 2x2x2cm$^3$ voxel, 128 averages. The voxel was placed in the tumor and contralateral normal appearing brain. The 12 channel "receive" brain coil was used for the MR study. LC-model algorithm was used for metabolites quantitation. We did logistic regression analysis and consequent receiver operating characteristic (ROC) curve analyses to calculate the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), area under curve (AUC), and accuracy for classifying tumor grade.

**Results**: Figure 1 shows statistically significant metabolite differences in patients with tumors grade II, III and IV. LC-model algorithm quantified the following metabolites: NAA, Cr, Cho, aspartate (Asp), glucose (Glc), glutamine (Gln), glutamate (Glu), glutathione (GSH), myo-inositol (mI), lactate (Lac), N-acetylaspartate glutamate (NAAG), phophoethanolamine (PE), scylloinositol (Scy) and glycerophophocholine (GPC). Out of these metabolites, the estimation of 5-6 metabolites showed less than or equal to 20% Cramer-Rao lower bound (CRLB) indicating acceptable reliability of metabolite estimations. We found that within tumor grades, statistically significant changes were observed for the ratios of tNAA, NAA and Glx between the grades II & III and II &IV. Also between grades III & IV, the Glu and Glx ratios were statistically significant. ROC curve enabled differentiation of significant metabolite ratios between grades II &III, III&IV and IV&II. Among the grades II&III and II&IV, the accuracy values of NAA, tNAA, Glx were around 73 and 84% & 81 and 85%. For the grades III&IV, the accuracy of Glu and Glx values were around 78 and 85%. On combining tNAA and Glx between the grades II&IV the accuracy increased to 93%. We also observed a statistically significant increase in GPC and total Cho (tCho) and decrease in NAA and total NAA (tNAA) in tumor patients in all grades compared to contralateral healthy side. The mean and standard deviation (SD) ratios of GPC, NAA, tNAA and tCho with respect to creatine in the contralateral and tumor sides of the grade II were: 0.240±0.058, 0.416±0.090, 1.278±0.412, 1.091±0.044, 1.317±0.429, 0.889±0.456, 0.251±0.060 and 0.417±0.089. Similarly for grade III, the metabolites ratios were: 0.273±0.059, 0.521±0.290, 1.110±0.353, 0.483±0.231, 1.301±0.374, 0.602±0.278, 0.304±0.088, 0.646±0.491. For grade IV, the metabolites ratios were: 0.241±0.044, 0.398±0.164, 1.144±0.234, 0.645±0.248, 1.302±0.249, 0.766±0.280, 0.241±0.043, 0.490±0.179.

**Discussion** Affected MR regions had consistently lower NAA than in normal-appearing tissue, which is consistent with the theory that NAA is found primarily in neurons, and that tumor and necrotic and reactive tissues all demonstrate an abnormally low neuronal cell density (7). Our results confirmed previous reports (3-5) that high-grade tumors that are highly cellularized and have high proliferative potential evidenced by increased tCho levels compared to contralateral, normal-appearing brain. Our results are consistent with prior work showing that Cho resonance though to be most prominent in regions with high neoplastic cellular density, (8) increases with tumor grade.

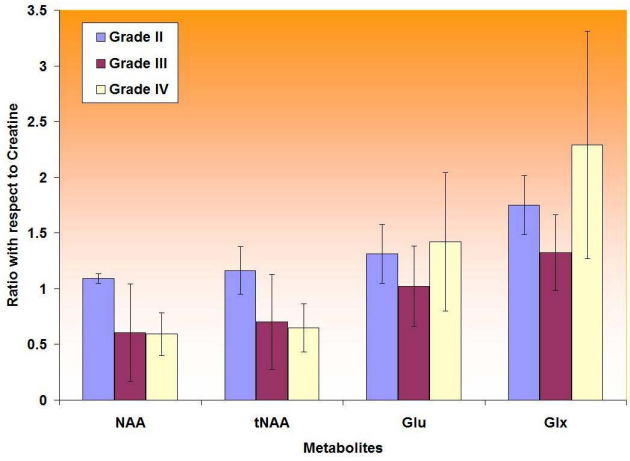


***Table 1. Significant metabolites of patients with grade II, III and IV in tumor sides (All metabolites: p value <0.05)***

**Conclusion:** Our findings indicate that MR spectroscopy may be helpful in discriminating high from low grade gliomas when including the tNAA and Glx ratios.

**References:**

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