



Neuro

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MR spectroscopy of 2HG and glycine in gliomas

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We will present proton MR spectroscopy (MRS) of 2-hydroxyglutarate (2HG) and glycine in gliomas. The clinical utility of 2HG MRS and our translation/dissemination of 2HG MRS will be briefly discussed. Following demonstration of an MRS method tailored for co-detection of 2HG and glycine, MRS data from 35 glioma patients will be presented. Glycine and 2HG concentrations as measured by MRS was correlated with post-gadolinium MRI, tumor cell proliferation rate (MIB-1 labeling index), expression of mitochondrial serine hydroxymethyltransferase (SHMT2) and glycine decarboxylase (GLDC) enzymes, and patient overall survival. Elevated glycine was strongly associated with presence of post-contrast enhancement, indicating association of high glycine with more rapidly proliferative disease. Glycine concentration was positively correlated with MIB-1, and levels higher than 2.5 mM showed significant association with shorter patient survival, irrespective of isocitrate dehydrogenase mutational status. 2HG concentration did not correlate with MIB-1 index. A high glycine/2HG concentration ratio, > 2.5 , was strongly associated with shorter survival ($p < 0.0001$). GLDC and SHMT2 expression were detectable in all tumors, with glycine concentration demonstrating an inverse correlation with GLDC. Our data suggest that aggressive gliomas reprogram glycine-mediated one-carbon metabolism to meet the biosynthetic demands for rapid cell proliferation. MRS evaluation of 2HG and glycine provides noninvasive metabolic imaging biomarkers that are predictive of tumor progression and clinical outcome.

Keywords: Glycine, 2-Hydroxyglutarate, 1H MRS, Gliomas, Cell proliferation, Overall survival