

## Magnetic Resonance Spectroscopy identifies Endothelial Growth Factor Receptor amplification in high-grade gliomas.

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**Background:** Endothelial Growth Factor Receptor (EGFR) amplification in high-grade glioma is associated with unfavorable prognosis (1). After the uptake of glutamate into astrocytes it is converted to glutamine by glutamine synthetase (GS). EGF increases GS activity in astrocytes (2). Magnetic Resonance Spectroscopy (MRS) is able to detect in vivo different metabolites in brain tumors. With a short echo time also small metabolites, like glutamine, can be identified (3).

**Aim:** to improve non-invasive characterization of gliomas by MRS.

**Materials and Methods:** From 2007 to 2009 we collected 76 biopsies from 35 patients with a high grade glioma. In all patients a preoperative proton MRS scan (3D multivoxel, TE 30ms, semi-LASER sequence) was performed at a 3 Tesla MR scanner. In 31 patients the EGFR status was determined by Multiplex Ligation-dependent Probe Amplification (MLPA) (1). Tumors were divided into two groups based on normal and low level gain versus (high copy) amplification, and in two groups based on presence or absence of EGFRvIII.

**Results:** The concentration of glutamine was significantly correlated with EGFR copy number (Mann Whitney U,  $p < 0,001$ ) and with the presence of EGFRvIII (Mann Whitney U,  $p = 0,014$ ). Glutamine concentrations in tumors with normal or low level gain of EGFR were between 1.6 – 3,7 mM (comparable with normal brain concentrations reported in literature (4). With a sensitivity and specificity of 100% a threshold of 4 mM was found for the presence of EGFR amplification. Similarly, glutamine concentrations in tumors with EGFR variant III were significantly higher than in those lacking EGFRvIII (threshold 4.7 mM, sensitivity 100%, specificity 87%).

**Conclusions:** Glutamine concentration in high-grade gliomas as detected by MRS is significantly correlated with EGFR status of these tumors. In vivo proton MRS of gliomas may thus be a promising tool for non-invasive detection of particular molecular features in gliomas, either at first diagnosis or during follow-up of patients suffering from these neoplasms.

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