31P and 1H spectroscopic imaging of recurrent malignant gliomas

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Introduction

Changes in the concentrations of choline compounds have been implicated in both cell proliferation and death processes. In vitro ^{1}H HR-MAS in biopsies of human malignant gliomas (1) revealed a dominant contribution of phosphocholine (PCho) whereas increased glycerophosphocholine (GPC) and phosphocholine (PCho) were increased under therapy-induced programmed cell death in rat brain glioma (2). In vivo proton decoupled ^{31}P and ^{1}H MRS was already used to quantify markers of membrane synthesis and breakdown in pediatric patients with untreated tumors (3). Here we present data from combined ^{1}H and ^{31}P MRSI which was employed to investigate human recurrent malignant gliomas in order to provide in vivo analysis of membrane metabolism and neuronal brain damage (tNAA).

Methods

Nine patients with recurrent malignant gliomas were included in the study. MRSI was performed on a 3 Tesla whole body system (Magnetom Trio, Siemens Medical AG, Erlangen, Germany) with a double tuned ^{1}H/ ^{31}P volume head coil (Rapid Biomedical, Würzburg, Germany). For ^{1}H MRSI (TR 1500 ms, TE 30 ms, 24 x 24 matrix extrapolated to 32 x 32, 240 x 240 mm^2 FOV, 15 mm slice thickness) a transversal slice was positioned to cover a maximum of tumor tissue. For ^{31}P spectroscopy, a 3D MRSI slab aligned to the 1H MRS slice was used (60° pulse, TR 2000 ms, TE 2.3 ms, 10 acquisitions,10 x 10 x 8 matrix extrapolated to 20 x 20 x 16, 300 x 300 x 200 mm^3 FOV, WALTZ4 proton decoupling). Data were sampled from voxels within the tumor and, as control, from the respective area in the contralateral hemisphere. For each selected voxel, spectra were analysed with jMRUI for ^{31}P data or LCModel for ^{1}H data. Signal intensities were corrected for T1 and T2 relaxations and averaged over the target region. ^{31}P data were quantified as intravoxel metabolite ratios with inorganic-phosphate/phophocreatine (Pi/PCr) measuring energy metabolism, PCho/GPC and phosphoethanolamine/glycerophosphoethanolamine (PEth/GPE) measuring membrane metabolism. Significant differences between tumor and control tissue were established using Student's t-test on ratios .

Results

Results for 31P and 1H metabolites are shown in Fig. 1. As expected, NAA is significantly reduced in tumor tissue, while the decrease for total creatine was not significant. It should be noted that the median for the TMA compounds (mainly choline compounds) is not much changed compared to controls. This is in agreement with literature and reflects the large inhomogeneities within the group of glioblastomas, representing a mixture of proliferating and necrotic tissue. In contrast to total choline, phosphorylated components in the membrane metabolism showed clear changes indicating a shift to proliferating cell fractions. While the increase in the phosphocholine/glycerophosphocholine ratio in tumor tissue did not reach significance (p=0.07) the respective ratio for the ethanolamine compound was clearly significant (p=0.02). Further, the significant increase in the inorganic-phosphate/phosphocreatine ratio hints to limited energy supply within the tumor.

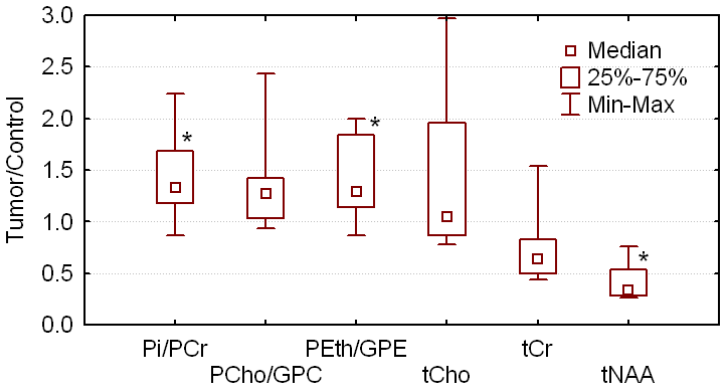

Fig. 2: Tumor metabolite ratios (^{31}P) or concentrations (^{1}H) normalized to their respective values in healthy (control) tissue. Significant deviations (p=0.05) are marked by *.

Discussion

^{31}P-MRSI gives valuable information on tumor membrane metabolism. Using an imaging technique provides data from control tissue which can be used as an internal reference. As expected the malignant tissue exhibits an increased ratio of PCho/GPC and PEth/GPE.

References

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