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MRS study of human glioma-initiating cells grown in the brain of nude mice

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Abstract:
Purpose: Proton spectra of gliomas at lower magnetic fields show only few resolved spectral lines, thus limiting the number of metabolites, which can be quantified in gliomas in vivo. The aim of the study was to use human glioma cell xenografts (3), which mimic tumour cell infiltration in humans, for studying the effect of tumour development on metabolite concentrations of the mouse brain and for obtaining the metabolic profile of the glioma at 14 T.
Materials and Methods: Human glioma cells were injected into the striatum of three nude mice. These mice were examined before and on days 7 to 35 after the cell injection on a 14.1 Tesla Varian animal scanner. The protocol consists of T_2-weighted axial imaging followed by short echo-time localized proton MR spectroscopy from a volume of interest located at the injection site and symmetrically in the contralateral hemisphere. Finally, a series of T_1-weighted images were measured after intraperitoneal administration of the Gd(DTPA) contrast agent.
Results: Tumours near injection sites appeared on both T_2- and post-contrast T_1-weighted MR images on days 28 or 35 (Fig. 1). Proton spectra from the injected hemisphere before detecting solid tumours (days 7 to 21) showed about 15% decrease in concentration of NAA, a 30% decrease in glucose (Glc), a 30% increase in lactate (Lac) but no change in choline (PCho+GPC). The spectrum of a solid tumour visible on MRI on day 35 revealed dramatic changes of many metabolites: huge peaks of lipids, a 3- to 5-fold decrease in NAA, Cr and glutamine(Gln)+glutamate(Glu), and a 2- to 4-fold increase in choline and glycine (Gly) (Fig. 2).
Discussion and Conclusion: The changes in the metabolite concentrations at the injection site of the tumour cells are in an excellent agreement with metabolic changes observed in regions of tumour infiltration in patients (A. Stadlbauer et al., Invest Radiol. 2007;42:218-23). Thus, the nude-mice model seems to be suitable for studying tumour infiltration, which is important in therapy management and surgical planning. These initial results clearly show that concentrations of a number of metabolites can be detected in brain tissue prior to overt tumour formation.

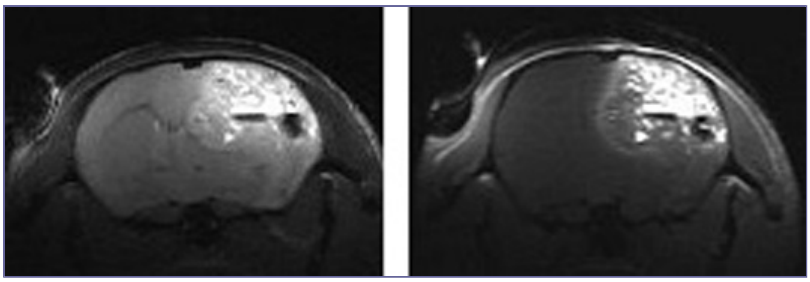

Fig. 1. T_2- (left) and post-contrast T_1-weighted (right) MR images of the mouse brain acquired on day 35 at 14.1T.

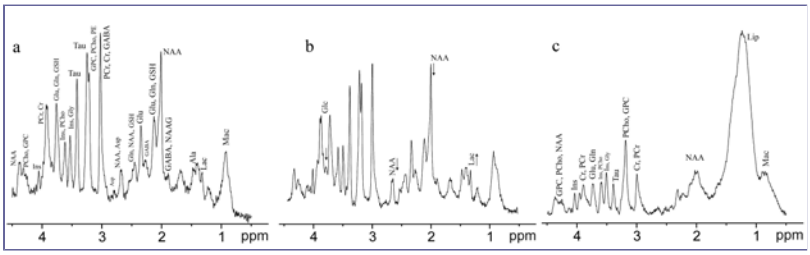

Fig. 2. Proton spectra acquired from the injection site before the injection (**a**), on day 21 (**b**) and on day 35 (**c**).

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Topic (Complete): 210 Animal models - Brain Pathologies
Presentation Preference (Complete): Oral preferred
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