Sodium and Diffusion MRI as Biomarkers of Initial Tumor Response to Therapy in Rodents

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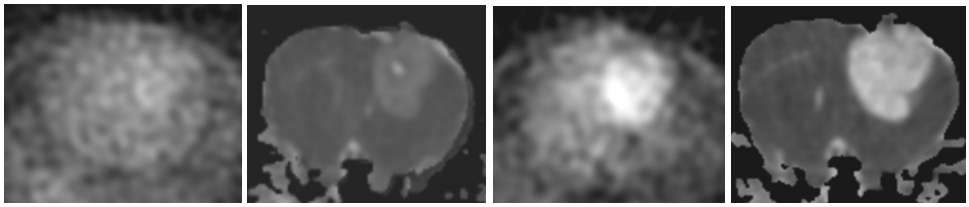
Background: The finding that, during therapy, tumors' sodium content correlates with corresponding alterations of water diffusion is attracting keen attention in the efforts to understand and further develop surrogate MRI biomarkers for tumor therapy. It is especially noteworthy that changes in both sodium and diffusion take place in the first days after therapy. Both types of imaging are able to detect a heterogeneity of tumor response and have potential to predict future individual tumor responses.

Methods: Rat 9L gliosarcoma cells were implanted intra-cranially or subcutaneously in male Fisher 344 rats (weight ~ 120 g). In ~14 days after tumor implantation, animals were subjected to a single ip BCNU chemotherapy with two different doses (13 & 26 mg/kg). Each 2-3 days, tumor growth, together with 3D sodium MRI and diffusion map were detected following the treatments. The previous experiments were performed using 9.4T MRI scanner and the latest results were acquired using 21T magnet.

Results: The overview of sodium/diffusion MRI studies of rodent glioma and 9L subcutaneous tumors will be discussed, including the latest data acquired using the ultra high magnetic field of 21.1T available at NHMFL. Representative MR images of sodium and diffusion map acquired before and seven days after BCNU therapy (26 mg/kg) demonstrate dramatic increases in tumor sodium and ADC. At 21T, a unique sodium resolution of 1μL was attained (Fig. 1).



A B C D

Fig. 1. *In vivo* sodium and diffusion map MRI of rat glioma before (A, B) and 7 days after BCNU chemotherapy (C, D), respectively, for the same animal and slice position.

Conclusions: Sodium MRI and proton diffusion exhibit early and strong correlated responses in rodent models during tumor treatments equally in brain and subcutaneous tumors. Both methods revealed a decreased response if therapy doses were decreased or if tumor acquired an additional resistance. The ultra high field experiments at 21T allowed a record high resolution for sodium and demonstrate a unique sensitivity of sodium MRI to tumor therapy. These two imaging modalities can be valuable biomarkers for individual evaluation of in vivo therapeutic cellular changes and for developing new drugs for tumor therapy.

Keywords: MRI, tumor, biomarker

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