The First Sodium and Diffusion MRI during Chemotherapy of Rodent Glioma at 21T

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Introduction

In-vivo MRI biomarkers for tumor therapy are needed for the development of effective drugs and for individualized therapies. Sodium and proton diffusion demonstrate a strong potential for assessing therapeutic changes inside tumors and predicting outcomes of the therapy. For the first time, experiments of this type were performed using a record high magnet of 21T. The experiments also demonstrate the NHMFL new capability to perform MRI in vivo studies using large rodents.

Experimental

Male Fisher 344 rats with 9L glioma were subjects for the MRI study when their tumor size reached ~150µl (n=8). Tumor treatments were performed using chemotherapeutic agent 1,3 bis(2-chloroethyl)-1-nitrosurea (BCNU) as single IP injections (26.6 mg/kg). Animals in the control group (n=4) remained untreated. The MR imaging was performed using UWB900 magnet with proton frequency at 900 MHz and sodium at 237 MHz. New RF probes were specifically developed for in vivo MRI of large rodents. Three-D sodium images were acquired by a back-projection GE pulse sequence with TE/TR = 1 ms/100 ms, matrix 42x32x32, FOV 42 mm and acquisition time of 30 min. Proton diffusion mapping was performed by a DW SE pulse sequence with b1=100 s/mm² and b2=1000 s/mm², 15 axial slices, FOV 30x30 mm, slice thickness 0.7 mm, TR/TE = 3750/36 ms. All animal experiments were conducted according to the protocol approved by the Florida State University ACUC.

Results and Discussion

Immediately before therapy, sodium content in the brain tumor was ~ 80 mM, while in the normal part of the brain it was ~50 mM. Diffusion in the tumor was also elevated (~ 1.2 *10⁻³ mm²/s) relative to a normal part of the brain (~0.7*10⁻³ mm²/s). Within four days after the BCNU chemotherapy, high resolution sodium images and diffusion maps revealed dramatic increases in both tumor sodium content up to ~120 mM and tumor diffusion up to ~1.7 *10⁻³ mm²/s. Non-treated tumors showed a slow increase of sodium content over time. To exclude any possible partial volume effect, all sodium MR imaging scans were performed with an ultra high resolution of 1 µL which is possible only at 21T.

Fig. 1. In vivo chemotherapeutic response in rodent glioma detected by sodium (A, B) and diffusion MRI (C, D) after injection of BCNU (26.6 mg/kg). The first tumor responses to chemotherapy can be easily seen already in four days by increased intensity of sodium and diffusion throughout tumors (B, D).

Conclusions

Sodium MRI and proton diffusion demonstrate a strong correlation with the effects of therapy. Both the high field sensitivity and the capability of the simultaneous use of two imaging modalities for rodent glioma are valuable tools in evaluating new cancer drugs and for developing and testing new biomarkers to predict the outcome of tumor treatment.

Acknowledgements

Authors thank project consultants Profs. T.L. Chenevert, B.D. Ross and A. Rehemtulla from University of Michigan, Ann Arbor for their valuable insights. The study was supported by NIH grant R21 CA119177 (PI V.D. Schepkin). MRI imaging program at NHMFL is supported by Cooperative Agreement (DMR-0084173) and the State of Florida.