CMBES/SCGB

2016 CMBEC39 Conference
Calgary AB
May 24–27, 2016

MULTICOMPONENT T2 ANALYSIS OF GLIOBLASTOMA IN A MOUSE MODEL

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INTRODUCTION

MRI (Magnetic Resonance Imaging) is the standard imaging method for brain tumors and current MRI methods are not very sensitive to the extent of tissue heterogeneity in the tumor. This lack of sensitivity can make it difficult to detect tumor variability as well as response to treatment. Soft tissue contrast in MRI is obtained from the distribution of hydrogen protons from water-filled biological tissues. T2, the spin-spin relaxation time, is affected by the water environment and will increase with edema and specific changes in cell type. Hence, unique T2 times reveal distinctive tissue characteristics [1].

To date, T2 analysis of tumors has largely used monoexponential fitting. However, this method is not sensitive to the multicomponent nature of tissues within a voxel. Therefore, multiexponential T2 analysis can allow for superior differentiation between tissues within the mouse gliobastoma [1,2]. We will use novel visualization software to determine how the multicomponent T2 can improve our sensitivity to specific tumor microenvironments. A study showing proof of principle was published using SCID mice implanted with patient-derived brain tumor initiating cells (BTICs) [1]. This study will use human derived glioblastoma cells in mice models to examine whether T2 can be used to detect treatment response.

METHODS

Previously, a study was established using anesthetized NOD-SCID mice (with invasive gliomas and controls). The mice were imaged on a 9.4 Tesla scanner using a modified Carr-Purcell-Meiboom-Gill sequence. A novel in-house software program was developed to analyze and visualize the multiecho T2 decay from axial brain slices [1]. This study was able to visualize regional heterogeneity and quantify specific tumour regions (i.e. boundaries).

The proposed study will also use a mouse model of NOD-SCID mice implanted with BTICs (patient derived brain tumour initiating cells). Mice will be imaged using the same 9.4T Bruker MRI sequences using a 35mm volume coil. The mice will be imaged on day 28 after tumor implantation. 28 days are the tumor is implanted, the mice will also be given a combination treatment of Temozolomide (TMZ) and Niacin. After 8 days of treatment the mice will again be reimaged using the same sequences. There will be control mice that are not given treatment and the rest will be given treatment. The T2 maps that will be acquired from the MRI will be analyzed using the in-house developed software as mentioned before. The software will be used to visualize the multicomponent nature of tumor cells and the T2 changes will be evident. A difference within the tumor regions is expected. The T2 maps should show tissue heterogeneity changing as the tumor cells respond to the treatment. At the end of the study, the mice will be sacrificed to perform histology in order to specifically compare tumor volumes to the T2 analysis results conducted using MRI.

RESULTS

Distinguishing between tissues is possible from T2 properties of mouse brain tissues in the scanned slices. Quantitative T2 analysis shows subtle differences from the T2 ranges of interest; these ranges are usually undetermined using the traditional ROI based approach [1]. T2

properties of all the brain tissue regions can be studied using this approach. The longer T2 times correspond to the respective anatomical areas within the tumour region. These subtle differences were not easily identified using the traditional ROI based approach. In addition, using the histology of brain tumors, the relationship between voxel-based T2 ranges and values and water microcompartment alterations within the regions can be studied.

CONCLUSIONS

Quantitative T2 MRI analysis has been used to analyze several neurological conditions i.e. tumour and multiple sclerosis [1]. Changes in the tissue environment result in an increase in free water, which in turn increases the T2 relaxation time. In conventional MRI, long T2 times have been observed in regions with increased water and blood volume [1].

Previously, T2 relaxation time distribution maps have been created to differentiate between glioblastoma and metastatic brain tumors in patients [3]. By producing a quantitative T2 map in adjunction to the multiexponential T2 analysis conducted, one can show the varying T2 distributions in the same mouse gliobastoma. The structural changes within the tumour regions were identitifed in relation to the T2 variations. These results will be used in the proposed study to allow for a clearer distinction of tumor margins and to provide a sensitive metric of treatment response.

FIGURES AND TABLES

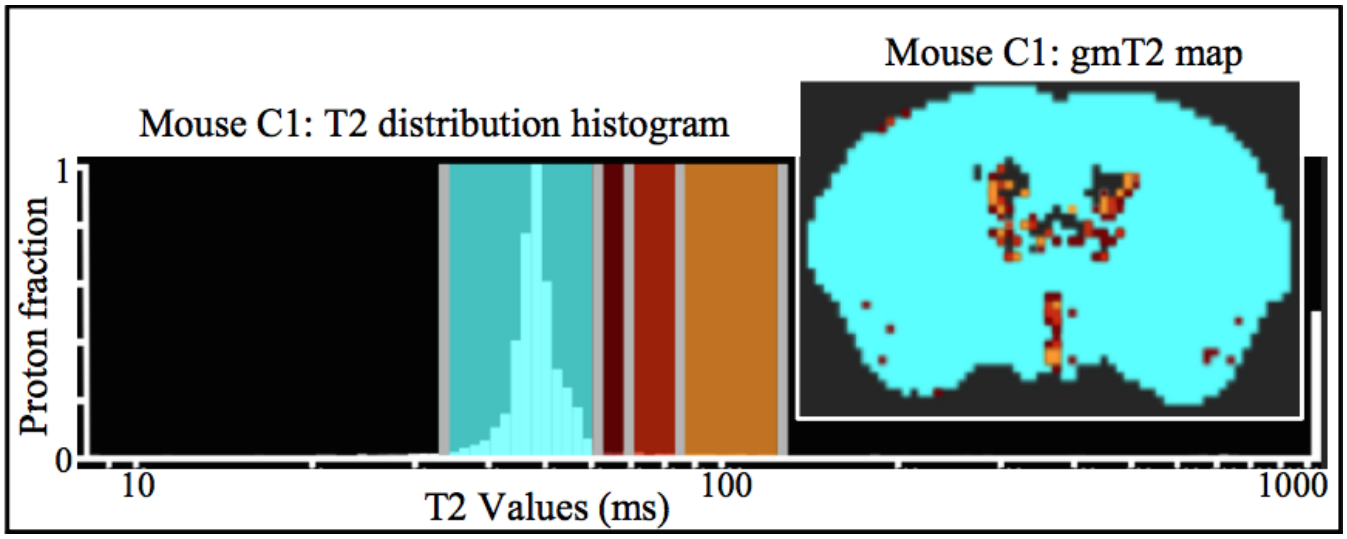

Figure 1: Control Mouse T2 Histogram and Corresponding T2 Map [Adapted from Reference 1]

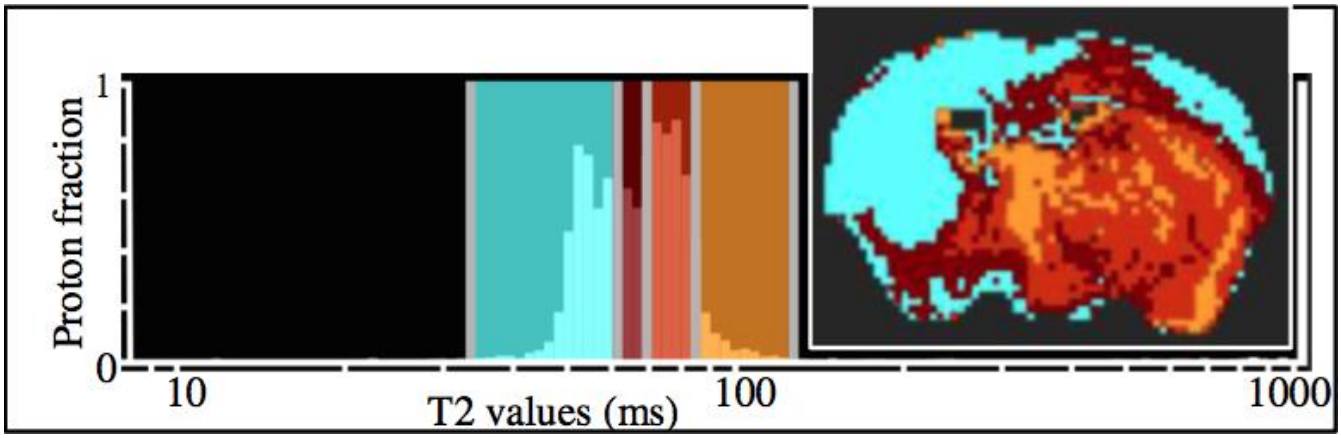

Figure 2: Glioma Mouse T2 Histogram and Corresponding T2 Map [Adapted from Reference 1]

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