Characterization of Brain Tumours with Spin-Spin Relaxation: Preliminary Investigations Reveal Unique T2 Distribution Profiles

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BACKGROUND

Prolonged spin-spin relaxation time in tumour tissue has been observed since some of the earliest NMR investigations of brain[1]. Over the last 3 decades numerous studies have sought to characterize tumour morphology and malignancy using quantitative assessment of T_2, although attempts to categorize and differentiate tumours have had limited success. Despite some evidence that meningiomas have a shorter T_2 than astrocytomas[2], and that glioblastomas show a single T_2 component if they consist mainly of solid tissue[3], but exhibit two T_2 components if they are a solid/necrotic mixture[3, 4], the majority of studies conclude that, because of significant overlap of T_2 (and T_1) in various tumour types, specific and histological characterization of brain tumours does not seem feasible based upon relaxation measures alone[2, 3, 5-11]. However, previous work must be interpreted with caution as relaxation data were typically acquired using a variety of multiple echo sequences with a range of echoes (2, 4, 6, 8, 16, 20, 24, 30, 32), varying and sometimes lengthy echo spacing (9, 18, 22, 25, 28, 30, 34ms) and T_2 decay curves were fit almost always with mono or occasionally biexponential analysis. Accurate T_2 determination begins with the collection of high fidelity T_2 decay curves with a sufficiently long echo train and appropriate echo spacing to encompass the T_2 window to be characterized[12]. Furthermore, careful analysis of the T_2 decay curve is fundamental for accurate characterization of all T_2 components contributing to the relaxation decay. When dealing with pathological tissue it is particularly important that no apriori assumptions are made about the number of contributing exponential components as changes in morphology may lead to additional T_2 components not present in healthy tissue. Two recent studies examining a rat glioblastoma model where such a non-apriori approach was employed for T_2 decay curve analysis found some tumours exhibited bi-exponential behaviour[13, 14], however differentiation between tumour types was not examined. Our current case study proposes to better define the distribution of T_2 components in vivo in 3 different types of human brain tumours (glioblastoma, oligodendroglioma and meningioma). In particular, we use a multi-echo sequence with a greater number of echoes and a longer acquisition window than previously used (48 echoes, data collection out to 1120ms) with no apriori assumptions about the number of exponential components contributing to the T_2 decay. Our ultimate aim is to better characterize tumours on the basis of their T_2 distribution profile.

METHODS

Subjects: Three subjects with brain tumours were examined: **Case 1** – 53 year old female with a large left frontal giant cell **glioblastoma** (grade IV astrocytoma) (~60cm^3); **Case 2** – 38 year old male with a right temporal lobe low grade **oligodendroglioma** (~30cm^3); **Case 3** – 81 year old male with a right benign **meningioma** (~1.5cm^3). **MRI Experiments:** MR experiments were conducted on a 1.5T GE Echo Speed scanner operating at 5.7 software level. Localizers, proton density and T_2 images were followed by a 48 echo modified Carr-Purcell-Meiboom-Gill (CPMG) sequence with variable TR, consisting of a 90° slice selective pulse followed by 48 rectangular composite 180° pulses flanked by slice-selective crusher gradient pulses for elimination of stimulated echoes[15]. For the CPMG T_2 relaxation measurement, a single transverse slice was acquired (TR = 2120-3800ms, TE = first 32 echoes @ 10ms, last 16 echoes @ 50ms, 5 mm thick, 256×128, 4 averages). A post Gd-DTPA T_1-weighted spin echo series was also collected. **Data Analysis:** T_2 relaxation decay curves for every voxel in the image were decomposed into an unspecified number of exponentials using a regularized non-negative least squares algorithm with 120 input relaxation times spaced logarithmically from 10ms to 2s[16, 17]. Results were displayed as a T_2 distribution plot of component amplitude as a function of T_2 for various regions of interest (ROI) including tumour and its enhancing periphery, edema, normal appearing white matter (NAWM) and maps of geometric mean T_2 were created. Healthy control data from white matter is shown as a reference.

RESULTS

T_2 was increased in tumour relative to NAWM (Fig. 1D). Each tumour showed a different T_2 distribution profile (Fig. 1E).

Case 1 (glioblastoma) showed broad T_2 peaks which were heterogeneous throughout the tumour. The edema ROI showed a large peak at T_2~243ms, which is longer than the enhancing periphery (dashed line).

Case 2 (oligodendroglioma) exhibited 2 consistent peaks (a narrow peak at 300-400ms, ~96% of the signal; and a shorter T_2 peak at ~20ms, 4% of the signal).

Case 3 (meningioma) showed two consistent T_2 components (one at ~120ms, 89% of signal; the second at ~490ms, 11% of signal). The edema ROI showed a large peak at T_2~238ms.

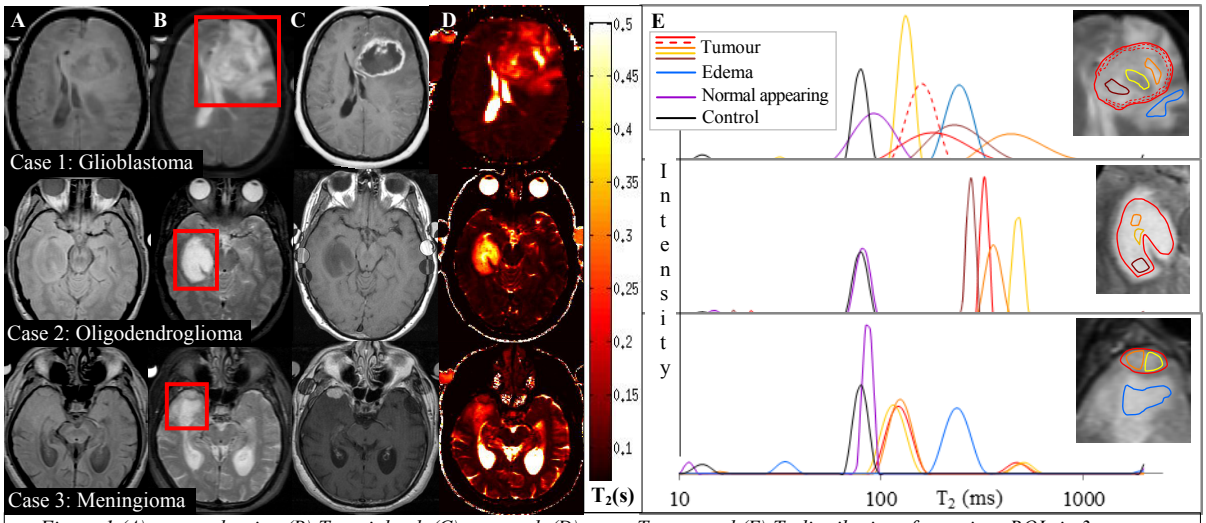

Figure 1 (A) proton density, (B) T_2-weighted, (C) post-gad, (D) mean T_2 map and (E) T_2 distributions for various ROIs in 3 tumours

DISCUSSION/CONCLUSION

Tumours have complex and unique compartmentalization characteristics arising from changes in morphology and increased cellularity. For intra-axial tumours, (glioblastoma and oligodendroglioma) the typically observed short T_2 (myelin water) signal in healthy white matter is markedly reduced by the excessive intracellular water of the tumour replacing the myelin water. In the glioblastoma, the heterogeneity of the T_2 distribution profiles is consistent with the histopathological heterogeneity of glioblastomas. Not only is the signal from edema in white matter prolonged, tumours are themselves edematous (containing excessive extracellular water) which may in part explain some of the longer T_2 peaks within the tumour. For the extra-axial tumour (meningioma), the largest T_2 component is shorter than both intra-axial tumours and is similar in size and location to the signal normally associated with intra/extracellular water in healthy brain tissue. This observation is consistent with the typical meningioma morphology of very little extracellular space and joined cell processes of adjacent cells by numerous junctions on their cell membranes. The T_2 peak from the meningioma associated edema is distinct from the tumour T_2 profile. Based on the above observations of the largest T_2 component, it may be that shorter times arise from intracellular water, while longer times are associated with extracellular water. Consequently, increases in extracellular water from vasogenic edema lead to prolongation of that T_2 component. We conclude that multi-echo T_2 relaxation may be useful in evaluating different classes of brain tumours and further study with a larger sample size is warranted.

Acknowledgements: Subjects, MRI technologists, neuropathologists & surgeons, MS Society of Canada. **References: 1.** Parrish, Science, 1974. **2.** Kjaer, Acta Radiol, 1991. **3.** Naruse, MRM, 1986. **4.** Martin-Landrove, Conf Proc IEEE Eng Med Biol Soc, 2007. **5.** Chatel, J Neurooncol, 1986. **6.** Ngo, MRI, 1985. 7. Rinck, Radiology, 1985. **8.** Just, MRI, 1988. **9.** Wilmes, JMRI, 1993. **10.** Eis, MRM, 1995. **11.** Hoehn-Berlage, MRI, 1992. **12.** Whittall, MRM, 1999. **13.** Dortch, NMR Biomed, 2009. **14.** Ali, ISMRM 2009 #3163. **15.** Laule, MRI, 2007. **16.** Whittall, JMR, 1989. **17.** Bjarnason, JMR, 2010.