Exploration of multi-exponential decomposition of T2 decay in gliomas and its implications on targeting for radiotherapy

K. Wachowicz[1,2], and B. G. Fallone[2,3]

[1]Medical Physics, Department of Oncology, University of Alberta, Edmonton, Alberta, Canada, [2]Medical Physics, Cross Cancer Institute, Alberta Health Services, Edmonton, Alberta, Canada, [3]Departments of Physics and Oncology, University of Alberta, Edmonton, Alberta, Canada

Introduction: MR imaging of brain tumours for radiotherapy purposes is heavily reliant on the use of simple weightings from relaxation processes inherent to tissue. As a complement to contrast-enhanced T1, one of the primary contrast mechanisms used by radiation oncologists to identify regions of the brain to be dosed by radiation is T2 weighting, where all the contrast of the image is generated by an acquisition at a single echo time. Where tissues can be assumed to undergo transverse relaxation in a purely mono-exponential sense, this kind of T2-weighted image would offer a fairly complete picture of the contrast that can be generated by T2 decay. However, in the case where water diffusion between various tissue microstructures is limited (at least over the timeframe of an MRI echo time) T2 decay will not in general play out in a mono-exponential manner. In such a circumstance, the distillation of transverse relaxation contrast into an image derived at a single echo time will represent a limited portion of the contrast potential of this particular relaxation mechanism.

It has been known for some time that nerve tissue, including peripheral nerves and white matter in the central nervous system, can exhibit multi-exponential decay. Water within the myelin sheathing has been well-attributed to a short-lived decay on the order of 10-30 ms.[1] Other microanatomical structures such as the extracellular matrix and axonal space have been seen as separate components in peripheral nerve with T2 times of roughly 100 and 200 ms.[2,3] However, in normal white matter all structures apart from the myelin water have been generally seen as a single decay component on the order of 100 ms. It is the hypothesis of this work that under the presence of edema and tumour infiltration the different microstructures may be affected in disparate ways, resulting in unique T2 distributions that can help distinguish different heterogeneous tumour regions that are all presently seen as brightened regions on a conventional T2-weighted image. The use of sequences that can extract this decay distribution on a pixel by pixel basis would add to a radiation oncologist's ability to contour regions to be given more dose, and other regions, such as edematous tissue with no evidence of tumour infiltration to be dosed less or not at all. This could lead to better tumour control and fewer side-effects to the patient. Additional benefit from the use of this technique can be obtained by taking advantage of its quantitative nature. Oncologists could potentially use this information to define a threshold in T2 decay (above normal tissue and below CSF). This threshold could be used to assist in the contouring of abnormalities, potentially removing some subjectivity from the process. Finally, quantitative assessment of long-term change in tumour development and response to therapy could be achieved.

Methods: Data from four patients with high grade gliomas were scanned prior to radiotherapy and six months following. A 3D spoiled multiple spin echo sequence was used to obtain multi-echo data sets. Thirty-two echoes were acquired and 4 lines of k-space were acquired for each echo. Four cm of coverage was achieved in the foot-head direction with a native resolution of 4 mm per slice, and an in-plane resolution of 2 mm. Data were reconstructed to an isotropic 2 mm resolution. Each inter-echo spacing was roughly 9.3 ms and a TR of 1200 ms was implemented. A longitudinal recovery pulse was used after the acquisition of the last echo to partially compensate for the relatively short TR. All data was acquired using a 3T Philips whole-body scanner.

Each anatomic slice was manually contoured to include only brain tissue. The signal decay across the 32 echoes for each pixel was processed to decompose the decay pattern into its exponential components. A non-negative least-squares algorithm was used for this decomposition. In this process, the decay curve was compared to a basis set of 120 mono-exponential decays ranging from 1 to 4000 ms, logarithmically spaced. Discounting the short-lived component attributed to myelin-water and the long-lived component seen through partial volume effects from CSF, the T2 decay time of normal brain tissue was seen to be limited to a single exponential decay. Measurements over the region of the tumour were taken to assess the range of fitted exponential components following decomposition. An extended range of components is indicative of multi-exponential behaviour which could hopefully be taken advantage of in future investigations. The decay distribution from each pixel within the tumour region of interest, and a similar region on the contralateral side was assessed between the decay time of 50 and 400 ms. A standard deviation from each of these distribution subsets was calculated and used for comparison between the tumour and non-tumour regions.

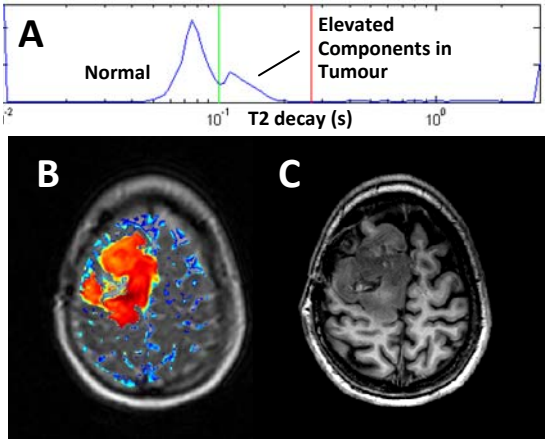

Figure 1. A. T2 decay distribution over one axial slice. Note the distinction between elevated T2 components found in the tumour region and the normal grey/white matter decay components below. **B**. Map of the decay components (total sum) present in the region defined between green and red boundaries. **C**. T1 weighted image of the same anatomic section.

Results and Discussion: The most basic usefulness of this technique is demonstrated in Figure 1, where the displayed map overlay is derived from one particular region of the decay distribution in which normal tissue is rarely found to have any components. This method easily segments regions of abnormality and may assist the oncologist not only in terms of ease and speed of contouring, but also through increased inter-operator consistency. A second useful derivative of this T2 distribution analysis is the quantitative tracking of decay rate over time. Changes in quantitative T2 have already been investigated in an animal model for use as a marker for response to radiotherapy.[4] The tracking of these quantitative changes could also be of benefit in a longer-term follow up regime for early detection of recurrence. An example of this technique is shown in Figure 2, where the change in the mean T2 time between pre and post radiotherapy was calculated (on the non-myelin tissue component). It has long been known that the presence of tumour will cause an overall elevation in T2 decay, but this work was aimed at determining if that elevation was simply a result of a longer-lived mono-exponential decay, or rather, a more complex distribution of decay components that could one day be used towards classification of tumour regions and the identification of tumour response to therapy. The standard deviation measurements as described in the Methods section did not reveal a global increase in multi-exponential behaviour over the tumour region. However, there were often small localized tumour regions that appeared to have a broader distribution of components. Future work will be aimed at determining if there is a consistent nature to these distributions. For this task to proceed successfully, great care will be required to ensure proper spoiling of coherences not following the spin echo pathway. The decomposition algorithm is very sensitive to loss of precision along the measured signal decay, and small deviations to the echo amplitudes due to stimulated echoes (which were seen to some extent in the acquired data) will compromise the ability of the algorithm to correctly identify decay components as separate when situated near each other in the distribution.

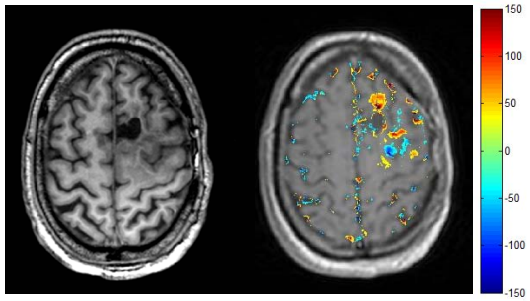

Figure 2. T1-weighted image and corresponding proton density image with overlay. Overlay represents change in non-myelin tissue water T2 from pre-radiotherapy to 6 months post. Displayed colour units are in ms.

Acknowledgments: The authors acknowledge Philips Medical Systems for helpful technical advice and support.

References: 1. MacKay et al, MRM 1994 31:673. 2. Vasilescu et al, Experientia 1977 34:1443. 3. Wachowicz et al, MRM 2002 47:239. 4. Larocque et al, Phys Med Biol 2010 55:1381.