Postmortem Relaxometry Study in the Rat Brain

A. J. Fagan[1], B. Condon[1,2], J. M. Mullin[1], D. M. Hadley[2], I. M. Macrae[1]

[1]Wellcome Surgical Institute, University of Glasgow, Glasgow, United Kingdom, [2]Institute of Neurological Sciences, Glasgow, United Kingdom

Introduction

The surgical dissection of the postmortem corpse (autopsy) is a vital investigative tool in forensic investigations, medical training / audit, epidemiology and medico-legal issues. However, there has been a marked decline in autopsy rates over the past decade. Factors contributing to this decrease include ambivalence toward the procedure by pathologists and clinicians, risks of innoculation from infected patients, issues related to patient / family consent, and restrictions placed by religious doctrines. The emergence of rapid, high resolution radiological imaging techniques such as X-ray computed tomography (CT) and MRI offer an alternative method of non-invasively assessing the cause of death in situations where an autopsy is not possible. However, while the former is perhaps optimal for assessing bony structures, the soft tissue contrast afforded by MRI is required to distinguish subtle tissue lesions postmortem. To date, postmortem studies in humans have predominately involved formalin-fixed tissue, in particular focussing on imaging issues related to maintaining gray / white matter conspicuity following the fixing process [1]. However, some examples involving non-fixed tissue have recently been published. These include an investigation of tissue decomposition via ^{1}H spectroscopy with a view to determining the postmortem interval [2]; forensic investigations in which MRI was used to differentiate and classify the grade of damage following gunshot injury [3] and subcutaneous fatty tissue trauma [4]; and the use of MRI as an alternative to conventional autopsy [5-7]. To optimise the image contrast obtainable in such postmortem imaging studies, a knowledge of the tissue relaxation properties and their evolution in the postmortem period is vital. The work described herein aims to quantify changes in T_1 and T_2 relaxation rates *in situ* in a postmortem rat model with a view to optimising image acquisition parameters. It is also important as a first step in attempting to establish how long after death MR-based findings may be valid.

Experimental

Three adult male Sprague-Dawley rats (bodyweights approximately 260 g) were anaesthetised and maintained with 1-2 % halothane in 7:3 N_2O/O_2. The rats were subsequently sacrificed by a halothane overdose of approximately 5 %, with the ventilator turned off after the physiologically monitored respiration terminated, after which they were allowed to equilibrate to room temperature. MR imaging experiments were carried out using a 7 T Bruker BioSpec 70/30 system (Bruker, Germany) using a 200 mm inner-diameter actively shielded gradient set (400 mT/m maximum gradient) with a 152 mm birdcage volume resonator. T_2 imaging was carried out before and 48 hours after death using a RARE sequence (TR/TE = 5000/72 ms, RARE factor 16, 117 µm in-plane resolution, 0.5 mm slice thickness). Relaxation measurements were carried out before death, 10 minutes after death and at frequent intervals up to 46 hours postmortem. T_1 measurements were performed in an inversion recovery experiment using a segmented FISP readout sequence, in which 8 lines of *k*-space were acquired per time interval (in-plane resolution = 312 µm, slice thickness = 2 mm, acquisition time = 22 minutes). T_2 measurements were carried out using a multi-spin multi-echo technique, producing the same resolution as the T_1 measurements with an acquisition time of 15 minutes. T_1 and T_2 measurements were validated using calibrated Eurospin agar-based gel phantoms, while parameter fitting was carried out using the Bruker ParaVision software using regions of interest placed over the corpus callosum and caudate for measurements of the white and gray matter respectively.

Results and Discussion

T_2 images of the brain at the level of the striatum, acquired before and 48 hours after death are presented in Figure 1. By 48 hours postmortem, some degree of brain swelling within the confines of the skull is evident, together with the loss of gray / white matter differentiation and a decrease in visibility of the ventricles. Figure 2 illustrates the changes in the measured T_1 and T_2 values postmortem for white and gray matter in one rat – similar results were measured for the other two rats. Contrary to expectations, both values were found to decrease with time, indicating a potential change of compartment of water molecules (extra- to intra-cellular, leading to an increase in viscosity and consequent decrease in the measured T_1 and T_2 values). The changing magnetic state of blood, as O_2 is released from haemoglobin molecules in the decomposing blood, may also contribute to the observed effects. The differentiation between the measured T_2 values for grey and white matter increased progressively postmortem, while the corresponding differentiation of the T_1 values peaked between 10-20 hours, with a decrease observed thereafter.

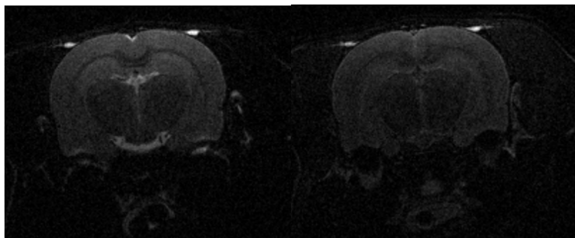

Figure 1 *T_2 images before (left) and 48 hours after death (right)*

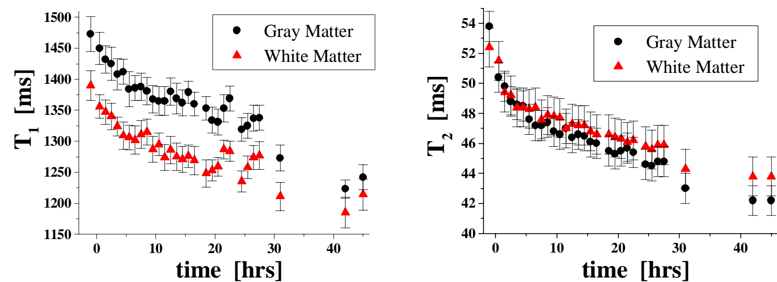

Figure 2 *T_1 and T_2 relaxation rates as a function of time postmortem*

Conclusions

The measured T_1 and T_2 values of both the white and gray matter were found to decrease significantly postmortem (by 7 % and 13 % respectively at 10 hours postmortem for white matter), indicating that imaging parameters need to be modified in order to maintain optimal contrast between these tissues. The relaxation changes in brain pathology are also of interest and are currently being investigated. Further studies are required to determine the applications and limitations of postmortem MRI, and also to delineate normal from abnormal postmortem changes. It is felt that the use of animal models greatly simplifies this task, not least in obtaining adequate sample numbers for such studies, but also since this approach allows for the comparison of changes in tissue differentiation pre- and postmortem.

References

[1] Pfefferbaum A. *et al.*, *NeuroImage* 21 (2004) 1585-1595. [2] Ith M. *et al.*, *MRM* 48 (2002) 915-920. [3] Thali M.J. *et al.*, *Forensic Sci. Int.* 138 (2003) 8-16. [4] Yen K. *et al.*, *J. Forensic Sci.* 49(4) (2004) 799-806. [5] Bisset R.A. *et al.*, *Brit. Med. J.* 324 (2002) 1423-1424. [6] Patriquin L. *et al.*, *J. Magn. Reson. Imaging* 13 (2001) 277-287. [7] Ezawa H. *et al.*, *Pathol. Int.* 53 (2003) 865-873.

Acknowledgements

This work was supported by an RDG grant from SHEFC, UK.