

## Imaging and Characterizing Brain Iron via MRI and Synchrotron X-ray Analysis: Implications for neurodegenerative disease research & MRI signal validation

J. Dobson (UF, Materials Sci. & Eng. / Keele University, ISTM); J.R. Forder (UF, Radiology & Biomed. Eng.); C. Batich (UF, Materials Sci. & Eng.); M. Davidson (UF, Materials Sci. & Eng.); S. Chandra (UF, Biomed. Eng.); A. Mikhaylova (UF, Materials Sci. & Eng.); J.F. Collingwood (UF, Materials Sci. & Eng. / Keele University, ISTM)

---

### Introduction

There are currently no reliable early diagnostic techniques for AD. We are investigating the potential for development of a non-invasive, MRI-based early detection technique. Our previous and on-going studies have been aimed at identifying and quantifying iron compounds associated with neurodegenerative disorders and their potential effects on disease progression as well as MR imaging [1-3]. Our aim is to identify, at high resolution, the specific iron compounds responsible for T2 shortening in the MR images. Using both MRI and synchrotron x-ray fluorescence, we are currently determining the compounds responsible for contrast in these images.

### Experimental

Iron standards were initially examined using the 750MHz Bruker NMR wide bore instrument in order to obtain T1 and T2 relaxation times for specific concentrations and particle forms. Imaging sequences were optimized on the 750MHz and 600 MHz Bruker NMR instruments, to quantify T1, T2 and T2\*. We have since switched to the 600MHz platform for the majority of the data collection. Data was also collected from autopsy AD brain tissue from the Human Brain Tissue Bank at the University of Florida. Images were collected from unfixed tissue samples using spin echo sequences for the T1 and T2 estimates, and gradient echo for the T2\* estimates, allowing for correlation with subsequent analysis by synchrotron techniques to identify specific iron compounds.

### Results and Discussion

Scan sequences on the 750 MHz and 600 MHz instruments were optimized using iron standards to determine tissue relaxation parameters (T1, T2 and T2\*) in autopsy brain tissue. Protocols were developed for the imaging of unfixed tissues at stable temperatures near freezing (~4°C). Following work with standards and test samples of brain tissue, hippocampal tissues from twelve Alzheimer's cases have been imaged (Fig. 1). Complete blocks of tissue were imaged at 250  $\mu\text{m}$  isotropic voxel resolution. Selected slices, designed to be correlated with the subsequent synchrotron sections, have been imaged at 60 x 60 x 80  $\mu\text{m}$  resolution. Synchrotron data acquisition and analysis are progressing, and correlation maps are being constructed for comparison with the MR relaxation maps.

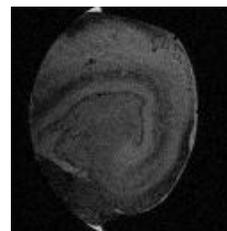


Fig. 1: Hippocampal AD tissue imaged at 600 MHz with GRE seq., FOV 8mm, 60 x 60 x 80  $\mu\text{m}$  voxels.

### Conclusions

We have been successful in developing protocols to obtain T1, T2, and T2\* in un-fixed autopsy tissue sections. Synchrotron data has been obtained from the tissues for a number of tissue sections. Our preliminary results enabled us to secure an NIH R21 grant to expand this research (see acknowledgements). A R01 will be submitted in June 2009.

### Acknowledgements

The authors wish to thank the NHMFL for supporting this research, and to the NIH (1R21NS060304-01), EPSRC and RCUK (UK) for additional funding. Thanks to staff at HBTB, UF and HBTR, Newcastle, UK, for providing tissue samples.

### References

- [1] Dobson, J., *et al*, Ann. NY Acad. Sci., 1012, 183-192 (2004); [2] Collingwood, JF., *et al.*, J. Alz. Dis., 7, 267-272 (2005); [3] Pardoe, H., *et al*, Phys. Med. Biol., **48**, 89-95 (2003).