



2010 ESICM ECCRN Awards Project report

Name: Virginia Newcombe

Project title: Pathophysiological changes in perilesional tissue post traumatic brain injury: insights from high resolution diffusion tensor imaging.

Award: ESICM ECCRN Levi-Montalcini Biomedical Sciences Award

Project start date: Aug 2011

Project end date: ongoing – aiming to complete all recruitment by Aug 2012

Final report

Interim report

Investigators are asked to supply the following information:

Before final publication: advancement of the study (number of patients or animals included so far) and references of abstract published. This information will be made public. A brief summary of your findings is needed for internal files.

After final publication, a summary of the data, which will be available to the members on website and references of the final paper (and derived manuscripts, whenever apply)

Project overview:

Please provide a short overview of the project performed using the funds provided by the ESICM

Traumatic brain injury (TBI) is often exacerbated by secondary events that lead to secondary brain injury, and represent potentially modifiable cause of mortality and morbidity post TBI. Such secondary injury results from activation of an auto-destructive cascade of metabolic, immunological and biochemical changes that ultimately result in irreversible cell damage or death. Clinical therapy aims to prevent or minimise the burden of secondary injury, but demonstration of the benefit of individual interventions is difficult, and is hampered by clinical heterogeneity and the fact that most outcome measures are assessed months after the intervention, and may hence be confounded by multiple factors.

Few clinical trials have demonstrated efficacy in improving the clinical outcome of such patients, perhaps because the translation from experimental therapies to clinical trials has been undertaken without adequate refinement of the interventions tested (Janowitz and Menon). One potential means of improving such translation is to characterise tissue at risk using early imaging studies, and define markers of injury progression in these tissue compartments. The modulation of such injury progression could then provide an imaging biomarker of intervention efficacy in the clinical setting. In principle, this approach proposes that, like the ischemic penumbra in stroke, there may be a “traumatic penumbra”¹ of at risk-tissue following TBI, which may be rescued by effective therapy. However, this area(s) is difficult to localise, since injury in TBI does not conform to vascular



territories or anatomical boundaries. The only exception to this is pericontusional tissue, which is often absorbed into the contusion core over time.

Diffusion tensor MR imaging (DTI) may provide better characterisation of such pathophysiology and allow contusion growth to be used as an imaging biomarker of treatment efficacy in early drug development. This technique characterizes the diffusion of water molecules in tissue environments, which is influenced by the microstructural organization of tissues and their constituent cells, and can provide unique insights into pathophysiology, particularly in white matter.

This study aims to use high resolution diffusion tensor imaging (DTI) to better characterise pathology in pericontusional tissue, and its temporal evolution to help inform the development of imaging biomarkers of acute pathophysiology, tissue fate, and intervention success.

Results:

Please provide a summary of the results obtained, incl. number of patients/animals included (if applicable)

1) Sequence development and implementation

The first part of the project has involved scanning controls to design a bespoke high resolution DTI sequence in collaboration with Dr Marta Correia (MR physicist, MRC Cognition and Brain Sciences Unit). This sequence, with 1.4mm isotropic resolution, has been successfully implemented on a 3 Tesla Siemens Verio MR Scanner.

In order to obtain adequate signal-to-noise with such small voxel size without making the scan time too long for intensive care patients to tolerate we are using a 32 channel head coil. As this head coil is much smaller than the usual 12 channel coil used clinically a plastic mould has been made by the medical engineering department to ensure recruited patients, who usually have intracranial monitoring in place, will fit with no compromise to their monitoring equipment prior to being moved to the scanning table.

The sequence has been optimised in a series of healthy volunteer studies, and has been implemented as part of our MR dataset for TBI; the technical challenges of coil size have meant that we have only recently been in a position to recruit patients in serial studies, and now have our first patient successfully imaged at three time points within the first 2 weeks of injury (see Figure 1). Now the entire protocol is in place we aim to have recruitment completed in time to submit an abstract to the next ESICM congress.

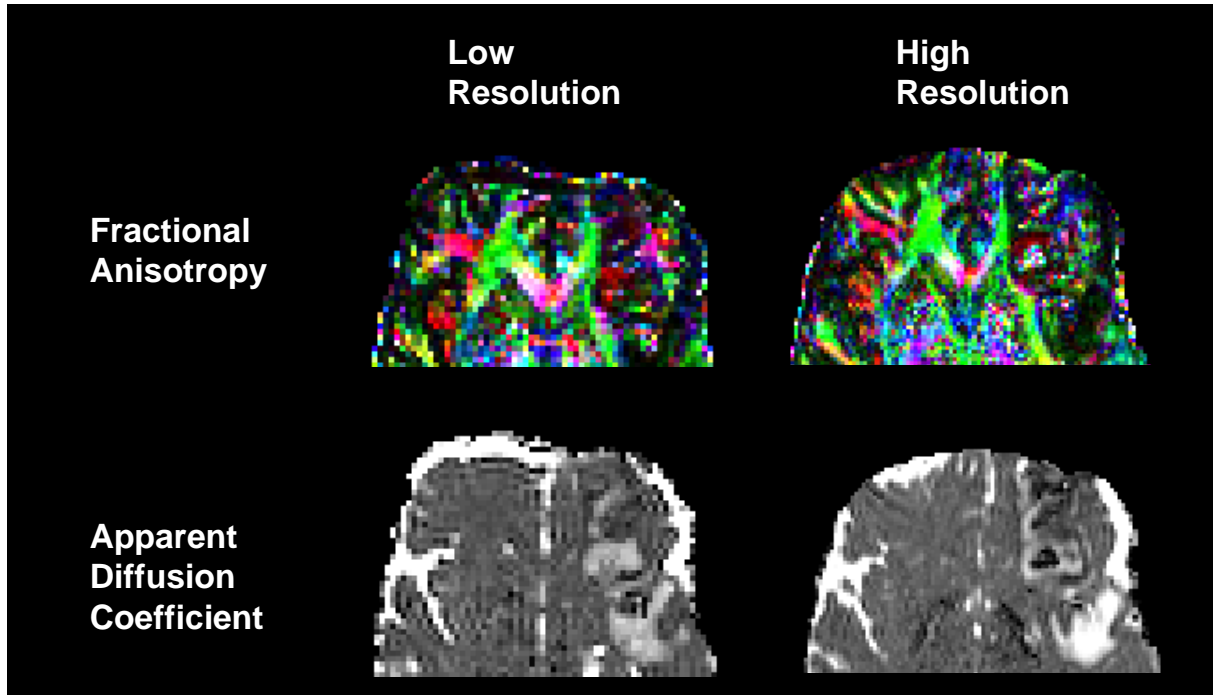


Figure 1: Comparison of the usual clinical (2mm isotropic) and the high resolution (1.4mm isotropic) diffusion tensor imaging in a patient imaged within 24 hours of injury. The fractional anisotropy map show greater detail about white matter on the high resolution map. The pericontusional area of cytotoxic oedema (dark rim on the periphery of the contusion) can clearly be seen better on the higher resolution apparent diffusion coefficient map.

Budget justification:

Please provide a detailed overview of how the money awarded to you was spent

32 channel head coil model approximately €350

Control scanning for sequence development and for comparison with patient data: approximately €5000

Patient scanning: approximately €14650

Abstract submitted to the ESICM Annual Congress: We aim to submit an abstract for the next congress.

Abstracts submitted to other congresses: We feel that the ESICM Annual Congress will be the most appropriate forum for the results as so would aim to submit there first. If appropriate we may submit to other congresses with the most likely one being the International Society of Magnetic Resonance Medicine.