

## Quantification and differentiation of periventricular white matter injury in post-hemorrhagic hydrocephalus using diffusion basis spectrum imaging

Albert Isaacs<sup>1</sup>, James (Pat) McAllister<sup>3</sup>, Leandro Castaneyra-Ruiz<sup>3</sup>, Diego Morales<sup>3</sup>, Harri Merisaari<sup>4</sup>, Tsen-Hsuan Lin<sup>4</sup>, Travis Crevecoeur<sup>5</sup>, Joel Brown<sup>3</sup>, Alexis Hartmann<sup>3</sup>, Jennifer Strahle<sup>3</sup>, Sheng-Kwei Song<sup>4</sup>, David Limbrick<sup>3</sup>

1 Department of Biology and Biomedical Sciences, Washington University in St. Louis, St. Louis, MO. USA

2 Department of Clinical Neurosciences, University of Calgary, Calgary, Alberta, Canada

3 Department of Neurosurgery, Washington University School of Medicine, St. Louis, MO. USA

4 Department of Radiology, Washington University School of Medicine, St. Louis, MO. USA 5. Washington University School of Medicine, St. Louis, St. Louis, MO. USA

albert.isaacs@wustl.edu

### Background

Periventricular white matter (PVWM) disruption is a dominant pathology in post-hemorrhagic hydrocephalus (PHH), and accounts for long-term morbidity. Diffusion Tensor Imaging (DTI), which is frequently used to assess PVWM integrity, is unable to differentiate complex cellular pathologies such as edema, inflammation and axonal loss. We used Diffusion Basis Spectrum Imaging (DBSI), which has been validated to be more effective for assessing complex WM pathologies in multiple sclerosis, spinal cord injury and brain tumors to address the PVWM pathology associated with PHH.

### Materials and Methods

PHH was induced in 20-day-old ferrets by intraventricular injection of autologous blood (n=7). Controls (n=6) received intraventricular PBS. At about 50-days-old, brains were fixed in 4% PFA and scanned ex vivo in a Varian® 4.7T MRI for T2W, multi-echo, spin-echo, and diffusion weighted sequences in 99 directions. Regions of Interest and voxel intensities for corpus callosum (CC), anterior (ALIC) and posterior (PLIC) limbs of the internal capsule were statistically analyzed using R package v3.4.1. Immunohistochemistry was done to assess PVWM.

### Results

The PHH group had a 68% ( $p<0.005$ ) proportional increase in hindered fraction: 120% ( $p<0.005$ ) and 51% ( $p<0.005$ ) in the CC and ALIC, respectively. CC and ALIC demonstrated proportionally decreased fiber density by 7% ( $p<0.05$ ) and 10% ( $p<0.05$ ), respectively. ALIC demonstrated axonal injury with decreased axial diffusivity of 8% ( $p<0.05$ ). While similar trends were observed in the PLIC, none were statistically significant. Immunohistochemistry demonstrated significantly higher PVWM damage in PHH.

### Conclusions

DBSI demonstrated marked edema, neuroinflammation, axonal injury and axonal loss in the PVWM of the PHH cohort. DBSI is a versatile tool for differentiating and quantifying the different components of WM disruption, and can be used as a novel non-invasive biomarker for PVWM integrity in PHH.