CSF FLOW IN CHIARI MALFORMATION AND SYRINGOMYELIA

1 Elizabeth C Clarke, 2David F Fletcher, 3Marcus Stoodley and 4Lynne E Bilston
1Kolling Institute of Medical Research, University of Sydney, Sydney, Australia,
2School of Chemical and Biomolecular Engineering, University of Sydney, Sydney, Australia
3Australian School of Advanced Medicine, Macquarie University, Sydney, Australia
4Neuroscience Research Australia, University of New South Wales, Sydney, Australia;
email: Elizabeth.clarke@sydney.edu.au

SUMMARY
The aim of this project is to determine if there are changes in the timing of cerebrospinal fluid (CSF) flow relative to the cardiac cycle in patients with Chiari Malformation Type I, and whether this relates to syringomyelia development. Preliminary results from MRI flow studies of the CSF and computational fluid dynamics models suggest moderate changes in CSF velocity and pressure profiles in Chiari malformation versus normal control participants.

INTRODUCTION
Chiari malformation (Type I) is a congenital abnormality of the skull and hindbrain, characterized by herniation of the cerebellar tonsils through the foramen magnum into the spinal canal. Up to two thirds of affected patients also develop cysts within the spinal cord (syringomyelia), however the cause of syringomyelia in association with Chiari malformation is not clear.

It has been demonstrated that such syrinxes are enlargements of the central canal (the normal CSF channel in the spinal cord), but the source of syrinx fluid and the forces driving fluid into syrinxes remain unknown. We have previously demonstrated that fluid flows from the spinal subarachnoid space into the cord and central canal via peri-vascular spaces, and that this flow is dependent on arterial pulsations [1]. In simulations we have also demonstrated that phase differences between the pressure wave transmitted to the subarachnoid space (a result of brain expansion during systole) and the arterial pulse wave in vessels entering the spinal cord has the potential to substantially affect flow along the peri-arterial spaces into the cord.

Our hypothesis is that Chiari malformations result in a phase difference and/or pulse shape difference between the pulse wave in the penetrating arteries of the spinal cord and subarachnoid space pressure pulse that could result in enhanced fluid flow from the subarachnoid space into the cord, potentially enlarging a syrinx. Cerebellar tonsil movement and CSF flow have been examined in patients with Chiari malformation, but this has not been related to arterial pulses in the cord or a potential phase decoupling.

The aim of this project was to use MRI to measure CSF flow in patients with Chiari malformation and syringomyelia, and to use these data in computational modeling to determine whether phase or pulse shape differences between the cardiac and sub-arachnoid space pressure waves exist.

METHODS
Participants were 8 healthy subjects (aged 24-59 years) and 7 patients with clinically diagnosed Chiari malformation type I (3 with syringomyelia aged 42-58 years; 4 without Syringomyelia aged 27-60 years). The UNSW human ethics committee approved all methods.

Participants volunteered for an MRI scan that consisted of a 3D Sagittal T1 isotropic (0.94mm) scan of the head and neck and four cardiac-gated cine phase-contrast scans at the following levels with planes aligned perpendicular to the CSF flow; 5mm above the base of the cerebellar tonsils, the foramen magnum, mid-vertebral C2 and mid-vertebral C5. The temporal resolution of the cine scans was 30 cardiac phases.

CSF velocities and flow rates were calculated from the cine MRI scans using the freely available analysis software Segment [2]. This analysis was performed for the total CSF area, and additionally using 10 control points (2mm diameter) spaced evenly around the CSF for the C2 and C5 levels. The magnitude and timing of the annulus and point-cloud velocity data were compared for Chiari malformation and normal control participants using t-tests.

The 3D T1 image sets and tonsil-level flow data were used for a subset of participants to develop subject-specific computational fluid dynamics (CFD) models in ANSYS-CFX. Model validation involved comparison between model-predicted CSF velocities and MRI-measured CSF velocities at 10 control points spaced around the sub-arachnoid space for each of the C2 and C5 levels. The models were used to compare phase and shape of the pressure pulse for Chiari malformation and normal control models.
RESULTS AND DISCUSSION
From the MRI quantitative flow data, the peak velocity was significantly lower (p=0.02) and occurred significantly earlier (p=0.05) for the Chiari malformation group (C5 level). Other levels showed qualitative differences in velocity profiles between Chiari malformation and control participants, however these differences were not significant. This may be because of the relatively low numbers used for the current analysis (data collection is ongoing).

Preliminary results from the CFD models showed that while peak pressure in Chiari malformation was more than double that of control participants, there was only a small phase shift of the pressure wave (~7% of the period) in Chiari malformation versus normal control participants. From our previous simulations, this phase shift would appear to cause only a moderate change in flow along the peri-arterial spaces into the cord and spinal canal, however further analysis of the model outputs is ongoing.

CONCLUSIONS
Preliminary quantitative flow and CFD modeling analyses suggest that there are differences in pressure and velocity profiles between Chiari malformation and control subjects. Shifts in phase and shape of CSF flow are believed to be implicated in development of Syringomyelia in relation to Chiari malformation.

ACKNOWLEDGEMENTS
This study has been supported by funding from the Column of Hope Foundation. LEB is supported by an NHMRC senior research fellowship. ECC is supported by an NHMRC training fellowship.

REFERENCES