Biomechanical modelling of normal pressure hydrocephalus: Advancing understanding of white matter damage

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I. INTRODUCTION

Mechanical loading can damage axons, but studying this relationship in human is challenging due to limited data on loading or injury. Normal pressure hydrocephalus (NPH) is a neurological condition marked by the enlargement of ventricles and associated white matter damage [1], providing an opportunity for investigating the relationship between mechanical loads and axonal injury. Finite element (FE) modelling is a promising approach for predicting brain loading in NPH. However, previous NPH FE brain models lack details of brain anatomy and ventricular expansion accuracy due to applying pressure on the lining of ventricles [2-4]. This study presents a novel FE model of NPH, which addresses these shortcomings, and uses it to predict imaging characteristics of NPH. This model will be used in future to investigate the relationship between biomechanical loads and axonal injury, advancing our understanding of axonal injury biomechanics.

II. METHODS

Image processing

Average brain templates were created for 30 healthy controls (HC, aged 62-82) and 22 NPH patients (age 54-85) using advanced normalization tools (ANTs) on T1 images (Fig. 1). All four ventricles were manually segmented using 3D Slicer. The ventricles of HC-template were registered to NPH-template using a combination of non-linear ANTs, NiBabel library, NiftyMITK software, and an in-house code.

FE modelling

An FE model of the HC-template was created using an in-house pipeline, providing an accurate anatomical geometry for ventricles [5]. The HC/NPH registration results were used to define displacement boundary conditions on ventricle's surface nodes, enabling a more accurate simulation of ventricular expansion compared to using pressure differences. Importantly, these displacements were derived from the ventricular boundaries, where image registration is most reliable. In contrast, in homogeneous brain regions like deep white matter, registration accuracy diminishes, making FE modelling essential for predicting tissue deformations. A quasi-static loading condition was assumed due to the long-term progression of NPH. LS-Dyna's explicit solver was used, but parameters influencing kinetic energy, such as total simulation time, were adjusted, ensuring kinetic energy remained below 5% of internal energy.

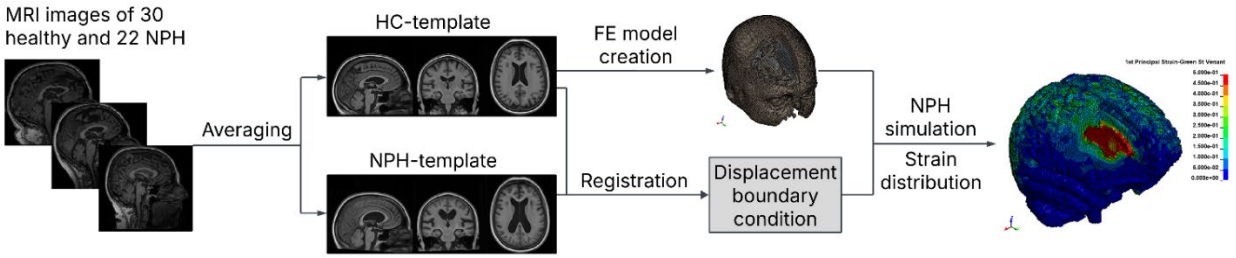

Figure 1. The overall process of FE model development.

III. INITIAL FINDINGS

The FE brain model predicted key NPH imaging biomarkers. It predicted a 20.5% increase in Evan's Index, which

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is defined as the ratio of the maximal width of the frontal horns of the lateral ventricles to the maximum inner skull diameter, in good agreement with the MRI-based measurement of 20.4%. The inter-hemispheric distance in the posterior region is reduced in NPH patients by 75.6%, and the model predicted a 70.8% reduction (Fig. 2A). In NPH patients, the thickness of the Septum Pellucidum (SP) is reduced by an average value of 26.3% (Fig. 2B), which is predicted well by the brain model with an average 26.5% predicted reduction. The model predicted maximum principal strains of up to 0.5 in NPH, with larger strain concentrated in periventricular white matter.

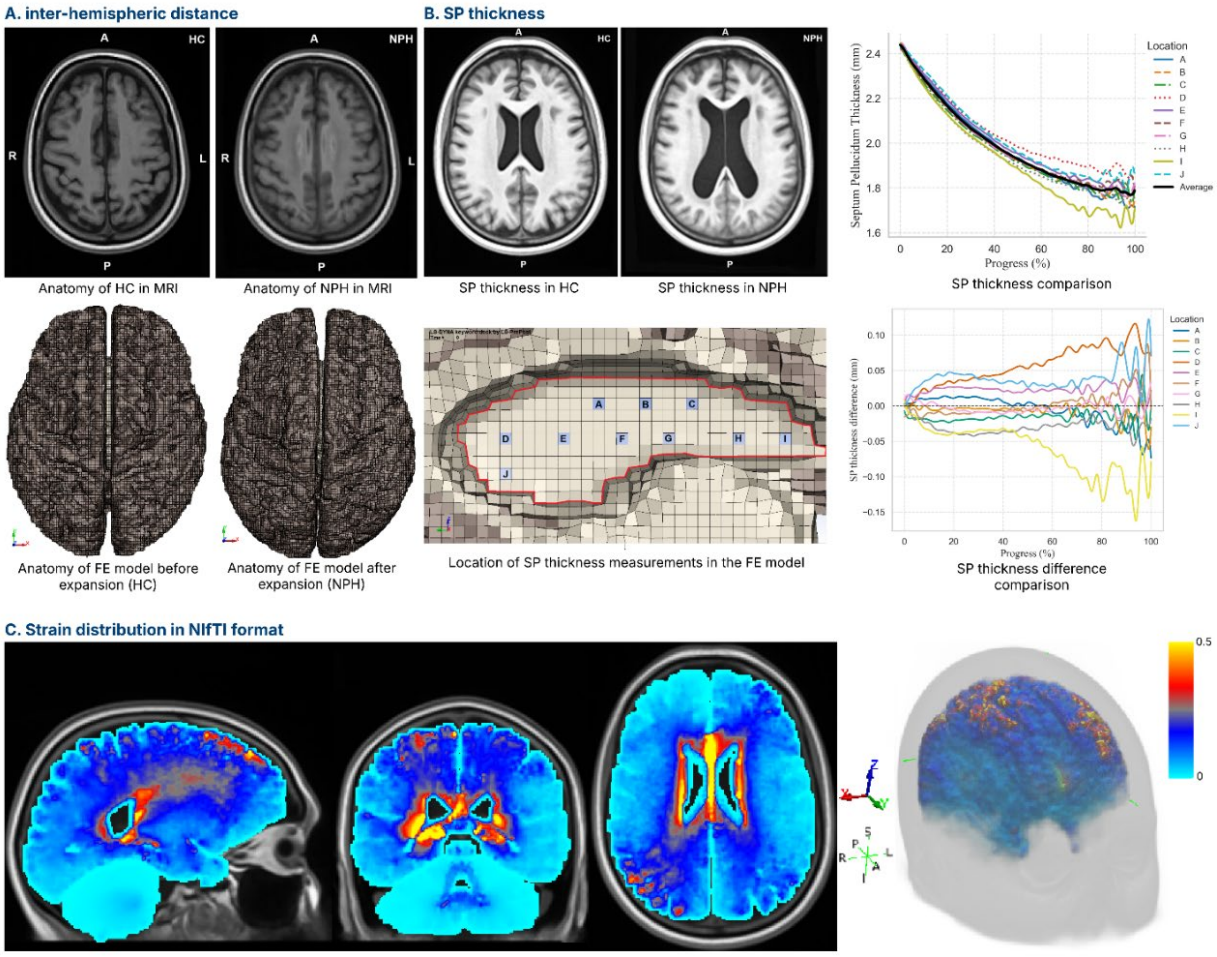

Figure 2. (A) MRI and model predicted decrease in the inter-hemispheric distance. (B) MRI and model predicted reduction in SP thickness, with a greater reduction in posterior regions. (C) Strain distribution in NPH brains.

IV. DISCUSSION

In this study, a new FE model of NPH has been developed to facilitate the exploration of the links between mechanical loading of axons and axonal injury in live human data. It incorporates the detailed anatomy of the brain and simulates loading by displacing the ventricular lining. This model predicts key imaging characteristics of NPH, showing its accuracy. The high consistency between the model predictions of brain morphology in NPH and MRI-based measurements suggests that mechanical loading plays an important role in the development of NPH. Additionally, it serves as a validation of the model predictions.

The FE model predicts strain concentration in the periventricular white matter, where imaging biomarkers of axonal injury have shown abnormalities in NPH patients, consistent with their symptoms. However, the FE model currently lacks a description of axonal anatomy. Future work will incorporate axonal anatomy into the brain model and use it to predict patterns of axonal injury observed in diffusion imaging. Another limitation of this study is that the brain model was developed for average images of NPH patients, while NPH patients show variations in ventricular expansion and outcome. Future work should develop patient-specific models. The NPH offers a novel opportunity to study the biomechanics of axonal injury in human.

V. REFERENCES

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