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Initial Investigative Report

On

NORMAL PRESSURE HYDROCEPHALUS

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Summary

An initial attempt was made to understand the mechanics of growth of Normal Pressure Hydrocephalus (NPH) using a computational biomechanical model. Person specific brain geometry for a healthy human brain was obtained from MRI scans and a brain mesh was created. The brain was treated as a single phase continuum. Non-linear material models for the brain tissue were used. Parametric transmantle pressure was applied to produce the condition of NPH. The deformations of the ventricles and brain were obtained using fully non-linear, explicit Finite Element procedures in time domain for incompressible, slightly compressible and compressible brain. The results indicated significant differences between transmantle pressure measured experimentally during NPH and that required for producing NPH in our simulations.

Keywords: Normal Pressure Hydrocephalus, Brain, Biomechanics

Objectives

The following objectives are desired from the initial report:

a) Understand the perception of CSF pressure, intracranial pressure (ICP) and transmantle pressure as used by clinical practitioners.
b) Determine if the brain be treated as single or bi-phasic continuum to model NPH.
c) Co-relate our initial results (transmantle pressure applied to produce hydrocephalus) with experimental data available with Dr. Czosnyka.
d) Invite comments from Dr. Czosnyka, Dr. Mehta and Dr. Knuckey on our work.

Definitions

CSF pressure: The pressure in Cerebrospinal Fluid (CSF) as measured by lumbar puncture (spine) or directly in ventricles.

Intracranial Pressure (ICP): The pressure exerted by the CSF in the ventricles on the brain tissue.

Transmantle Pressure: The pressure difference between the ventricular and the brain outer surface.

1. Introduction

In their seminal work published in 1965, the condition of Normal Pressure Hydrocephalus (NPH) was recognised by Hakim **[1]** and Adams et al. **[2]**. The authors in their work described a condition of dilation and increase in ventricular size with normal Cerebrospinal Fluid (CSF) pressure as recorded by performing a spinal puncture. The patients presented a triad of clinical symptoms. Diagnostic tools indicated dilated lateral ventricles and/or third and fourth ventricles.

Though the condition of NPH is well recognised, in current clinical practice, positive differentiation between NPH and other neurodegenerative disorders is a well known problem faced recurrently by clinicians. This is due to the fact that there is an overlap of clinical symptoms and similarity of diagnostic findings with other neurodegenerative disorders (e.g. Alzheimer's etc, leading to atrophy of brain) and could lead to faulty diagnosis between them. Further more, the treatment for these disorders are different. Incorrect diagnosis of these disorders would be a major disservice to patients. Moreover, as the symptoms of NPH are similar to presenile and senile dementia, recognising and treatment of NPH could also bring "cure" to people misdiagnosed with conditions similar to dementia.

Engineers have approached the problem of diagnosing NPH from the point of view of CSF hydrodynamics **[3, 4, 5, 6, 7, 8, 9, 10, 11, 12 and 13]**. We propose to model the biomechanics of NPH to study the progression of this disorder. It is hoped that our research work would lead to creation of additional inputs for the neurosurgeons/neurologists, which could work as a tool to give the neurosurgeons/neurologists a better chance in differentiating NPH from other neurodegenerative disorders.

2. Biomechanical Model

2.1 Physical Model

Brain: Though the time scale of flow of CSF in brain is of the order of disease (NPH) progression, the brain was considered as a single phase continuum for our initial work. This was done because we are interested in understanding the perception of CSF pressure and intracranial pressure (ICP) as used by clinical practitioners, debate use of single or bi-phasic continuum for brain tissue and also to reduce complications in the computational model.

Recently, Miller and Chinzei **[14, 15]** have proposed a hyper-viscoelastic constitutive model for the brain tissue. This model is described using the following formulae:

$$W = \frac{2}{\alpha^2}\int_0^t [\mu(t-\tau)\frac{d}{d\tau}(\lambda_1^\alpha + \lambda_2^\alpha + \lambda_3^\alpha - 3)]d\tau \quad (1)$$

$$\mu = \mu_0[1 - \sum_{k=1}^{n} g_k(1 - e^{-t/\tau_k}) \quad (2)$$

where W is the potential function, λ_i are the principal stretches, μ_0 is the instantaneous shear modulus in undeformed state, τ_k are the characteristic times, g_k are the relaxation coefficients and α is the material coefficient which can assume any real value without any restrictions.

Constants for the brain tissue constitutive model as proposed by Miller and Chinzei **[14]** are given in Table 1.

Table 1: Material constants for the constitutive model of the brain tissue

Instantaneous Response	μ_0=842 Pa	
	Characteristic Time	Relaxation Coefficients
k=1	τ_1=0.5 sec	g_1= 0.450
k=2	τ_2=50 sec	g_2= 0.365

The values for material constants given in Table 1 are valid for relatively high strain rates such as those encountered during surgical intervention. During hydrocephalic growth, the brain is loaded extremely slowly as the development of NPH takes place over a few days. Hence, limiting case of the relaxation function **[16]** given in Equation (2) is considered and is given by:

$$\lim_{t\to\infty} \sum_{k=1}^{n} g_k(1 - e^{-t/\tau_k}) = \sum_{k=1}^{n} g_k \tag{3}$$

For the limiting case, the brain tissue becomes hyperelastic in nature. The relaxed hyperelastic shear modulus is given by modified form of equation (2):

$$\mu_\infty = \mu_0[1 - \sum_{k=1}^{n} g_k] \tag{4}$$

Using n=2 and values given in Table 1, the relaxed hyperelastic shear modulus is:

$$\mu_\infty = 155.77 \text{ Pa} \tag{5}$$

This relaxed hyperelastic shear modulus is significantly lower than that proposed by Miller and Chinzei **[14]**. This translates to "softer" brain and was used for simulation purposes.

To explore the issue of treatment of brain as a single or bi-phasic continuum to model NPH growth, the brain was modelled as:

1) Incompressible
2) Slightly compressible
3) Compressible

For incompressible and slightly compressible cases, constitutive model as proposed by Miller and Chinzei **[14]** (generalisation of Ogden Rubber **[17]**) with Poisson's ratio (υ) of 0.499 and 0.490 respectively was used. For compressible case, constitutive model for compressible rubber (Blatz and Ko **[18]**) and υ of 0.463 was used. It is important to point out that for all cases relaxed hyperelastic shear modulus as given by Equation 5 was used. For clarity the material properties are summarised in Table 2.

Table 2: Material properties for incompressible, slightly compressible and compressible brain

Case	υ	μ_∞ (Pa)	E_∞ (Pa)	K_∞ (Pa)	Constitutive Model
Incompressible	0.499	155.77	466.99	77833.07	Ogden Rubber
Slightly Compressible	0.490	155.77	464.19	7736.5	Ogden Rubber
Compressible	0.463	155.77	455.78	2053.08	Blatz- Ko rubber

Loading: To produce NPH, the brain was loaded by transmantle pressure (P_{trans}) as shown in Figure 1 for all simulations. Normal CSF pressure (145 mm of H_2O **[19]**) acted on the brain outer surface (P_{outer}) for all cases while the pressure acting on the ventricular surface (P_{vent}) increased parametrically. The pressure loading applied for producing NPH is summarised in Table 3.

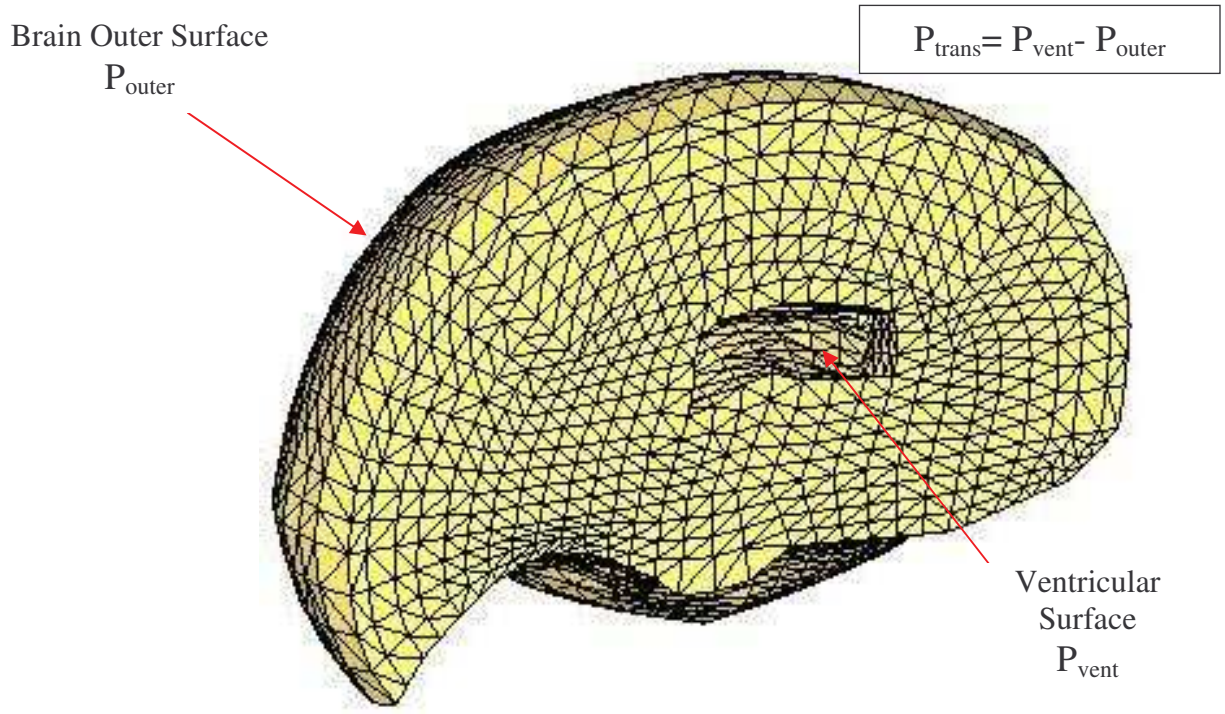

Figure 1: Pressure loading of Brain

Table 3: Pressure loading for producing NPH

Case	P_{vent} (mm of H_2O)	P_{outer} (mm of H_2O)	$P_{trans}= P_{vent} - P_{outer}$ (mm of H_2O)
Incompressible	205	145	60
Slightly Compressible	180	145	35
Compressible	170	145	25

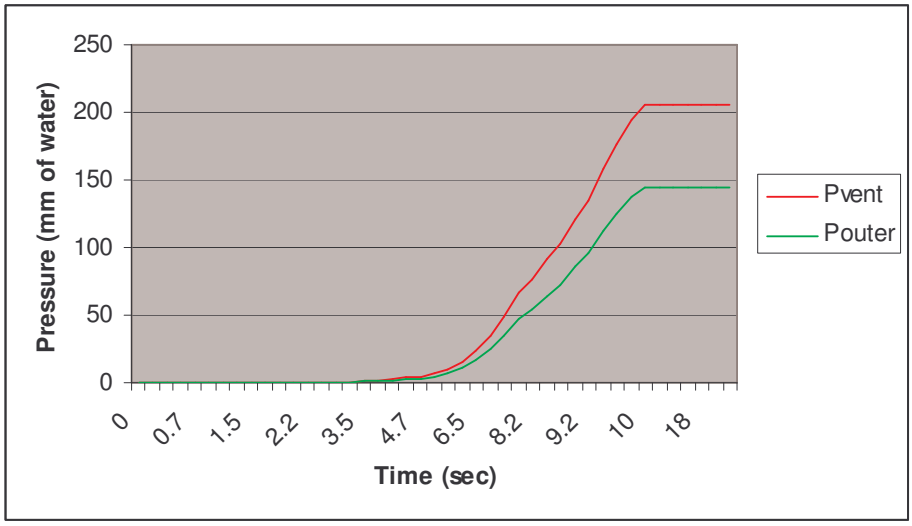

Figure 2: Applied Pressure Loading Profile

P_{outer} and P_{vent} were gradually applied over a period of 10 secs using a 3-4-5 curve profile as shown in Figure 2. After initial 10 secs the pressures were held constant for further 10 secs to ensure convergence of solution for our simulations.

Boundary Conditions: To reduce computational costs, half of the brain was simulated. Nodes on Plane 1 (Figure 3) have symmetric boundary conditions in the YZ plane (no motion allowed for X translation and Y-Z rotation). As the brain is resting in the skull, all nodes on the bottom of the brain were constrained in Y and Z translation (Figure 3).

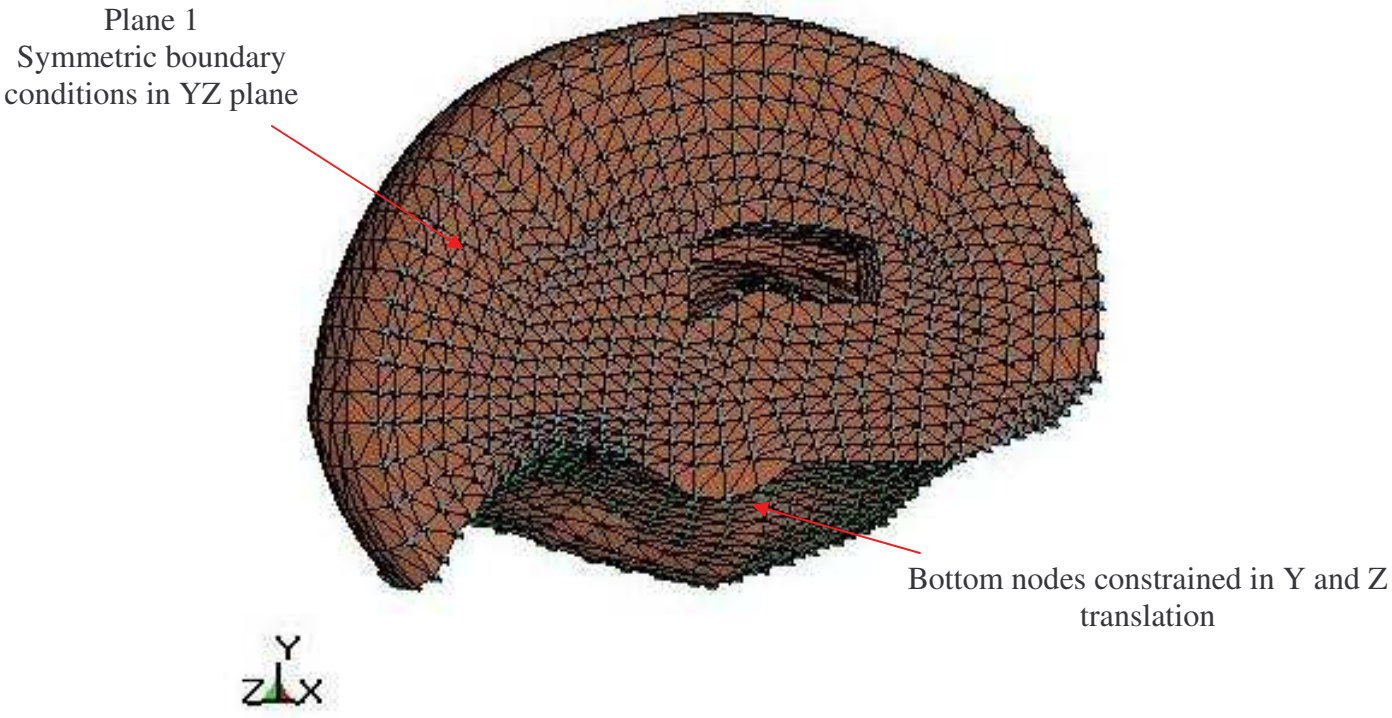

Figure 3: Applied Boundary Conditions

2.2 Computational Model

Finite element solver: The model was computed using LS-DYNA (Livermore Software Corporation, Livermore California, USA) non-linear finite element code. This code uses explicit time integration and accounts for both the constitutive and geometric (i.e. finite deformation formulations are used) nonlinearities.

Brain: The brain geometry for the model was taken from a set of magnetic resonance images (MRI) of healthy human brain obtained by Department of Surgery, Brigham and Women's Hospital (Harvard Medical School, Boston, Massachusetts, USA). MRI images were processed using SLICER software (http://slicer.org) to obtain the brain cross-sections. From the sections, 3-D finite element mesh of the brain consisting of 26000 (approximate) linear average 1 point nodal pressure tetrahedron (4 node solid elements) elements **[20]** was built using Hypermesh (Altair Engineering, USA) pre-processing software (Figure 2 and 3). Linear average 1 point nodal pressure tetrahedrons **[20]** are suitable for explicit non-linear computation of incompressible/nearly incompressible continua (e.g. brain) as they do not exhibit volumetric locking.

3. Result

The volume of the brain and ventricular space for healthy brain used in our simulations were consistent with those present in the literature **[21]**. The brain and ventricular volume for healthy and NPH cases are adapted from Matsumae et al **[21]** and given in Table 4.

Table 4: Brain and ventricular volumes for healthy and NPH cases (adapted from Matsumae et. al. **[21]**])

Case	Brain Volume (cubic cm)	Ventricular Volume (cubic cm)
Healthy Brain	1188 ± 104	27 ± 10
NPH	1163 ± 129	116 ± 42

As the simulations were carried out for half of the brain, NPH was deemed to have developed when the ventricular volume increased from 15 cm^3 to more than 58 cm^3.

The results for the simulations are presented for all three cases in Table 5. It is important to point out that for all simulations relaxed hyperelastic material properties for brain (Table 2) were used. The brain and ventricular volumes presented in the following discussions are for half of the brain.

Incompressible Brain: 60 mm of H_2O (4.4 mm of Hg) transmantle pressure was required to produce NPH. The ventricular volume increased from 15 cm^3 in healthy brain to 60 cm^3 for NPH condition. The brain volume decreased due to applied pressure by 1.7% and is consistent with observations by Matsumae et al **[21]**. This suggests that even though the brain volume decreases slightly, the brain tends to bulge outwards.

Slightly Compressible Brain: Much lower transmantle pressure of 25 mm of H_2O (2.5 mm of Hg) was required to produce NPH. The brain volume decreases by 15% to 481 cm^3 whereas the

ventricular volume increased to 60 cm^3. The decrease in brain volume is significantly different from observations by Matsumae et al **[21]**.

Table 5: Brain and ventricular volumes for NPH from simulations

Case	Brain Volume (cubic cm)	Ventricular Volume (cubic cm)	$P_{trans} = P_{vent} - P_{outer}$ (mm of H_2O)
Healthy Brain	566	15	-
Incompressible	556	60	60
Slightly Compressible	481	60	35
Compressible	479	59	25

Compressible Brain: Only 25 mm of H_2O (1.8 mm of Hg) was required to reach NPH condition. The brain volume decreases by 15.3%. This decrease in brain volume is significantly different from observations by Matsumae et al **[21]**.

4. Discussion

The results of the simulations presented in Section 3 leads us to the following conclusions:

a) A minimum transmantle pressure of 25 mm of H_2O (compressible brain) was required to produce NPH whereas maximum transmantle pressure of 60 mm of H_2O was required for incompressible brain. These values (at both ends of spectrum) were significantly higher than the values measured by Dr. Czosnyka (around 1mm of Hg) **[22]**.
b) Simulations carried out for all cases (incompressible, slightly compressible and compressible brain) suggested using a bi-phasic approach to model NPH growth. In this approach the brain tissue will be treated as a bi-phasic continuum (solid brain mass with CSF fluid filling voids in brain mass). In layman's term, the brain will be treated as a sponge, with fluid filling the voids in the solid mass. This would make the brain squeezable without affecting its incompressible nature.

5. Conclusion

An initial attempt was made to understand the growth mechanics of NPH. Person specific brain geometry for healthy brain was obtained from a set of MRI scans and brain mesh was created. The brain was treated as incompressible, slightly compressible and compressible in nature. Parametric transmantle pressure was applied to load the brain. The results indicated significant differences between transmantle pressure measured experimentally during NPH and that required for producing NPH in our simulations. This significant difference needs to be understood and explained. Moreover, there is little understanding about the mechanics of growth of NPH. In the future, we would like to fill in this gap in knowledge by our research.

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