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Journal of Biomechanics 41 (2008) 2263–2271

JOURNAL OF BIOMECHANICS

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Biomechanical modelling of normal pressure hydrocephalus

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Accepted 11 April 2008

Abstract

This study investigates the mechanics of normal pressure hydrocephalus (NPH) growth using a computational approach. We created a generic 3-D brain mesh of a healthy human brain and modelled the brain parenchyma as single phase and biphasic continuum. In our model, hyperelastic constitutive law and finite deformation theory described deformations within the brain parenchyma. We used a value of 155.77 Pa for the shear modulus (μ) of the brain parenchyma. Additionally, in our model, contact boundary definitions constrained the brain outer surface inside the skull. We used transmantle pressure difference to load the model. Fully nonlinear, implicit finite element procedures in the time domain were used to obtain the deformations of the ventricles and the brain. To the best of our knowledge, this was the first 3-D, fully nonlinear model investigating NPH growth mechanics. Clinicians generally accept that at most 1 mm of Hg transmantle pressure difference (133.416 Pa) is associated with the condition of NPH. Our computations showed that transmantle pressure difference of 1 mm of Hg (133.416 Pa) did not produce NPH for either single phase or biphasic model of the brain parenchyma. A minimum transmantle pressure difference of 1.764 mm of Hg (235.44 Pa) was required to produce the clinical condition of NPH. This suggested that the hypothesis of a purely mechanical basis for NPH growth needs to be revised. We also showed that under equal transmantle pressure difference load, there were no significant differences between the computed ventricular volumes for biphasic and incompressible/nearly incompressible single phase model of the brain parenchyma. As a result, there was no major advantage gained by using a biphasic model for the brain parenchyma. We propose that for modelling NPH, nearly incompressible single phase model of the brain parenchyma was adequate. Single phase treatment of the brain parenchyma simplified the mathematical description of the NPH model and resulted in significant reduction of computational time.

Keywords: Normal pressure hydrocephalus; Brain; Biomechanics

1. Introduction

Diagnosis of normal pressure hydrocephalus (NPH) is a reoccurring problem faced by clinicians due to the overlap of symptoms and diagnostic findings between NPH and other neurodegenerative diseases (e.g. Alzheimer's). Hakim and Adams (1965) and Adams et al. (1965) were the first to identify the clinical condition of NPH. Cerebrospinal fluid (CSF) hydrodynamics approach (Czosnyka et al., 2004; Linninger et al., 2005) and analysing intracranial pressure (ICP) waves (Shulman and Marmarou, 1968; Marmarou et al., 1978; Czosnyka and Pickard, 2004) enhanced the diagnosis of NPH but offered limited understanding of NPH growth mechanics.

In previous attempts to understand NPH biomechanics, most authors (Nagashima et al., 1987; Tada et al., 1990; Péna et al., 1999; Taylor and Miller, 2004) used 2-D models of the brain anatomy. Kaczmarek et al. (1997) assumed the brain to be cylindrical. Majority of the studies (Nagashima et al., 1987; Tada et al., 1990; Péna et al., 1999), used infinitesimal deformation theory to compute brain parenchyma deformations. Notable exceptions were Kaczmarek et al. (1997) and Taylor and Miller (2004), who used finite deformation theory to model the deformations in the brain parenchyma. In previous works, linear elastic constitutive law was used to approximate the brain parenchyma material properties (Nagashima et al., 1987; Tada et al., 1990; Kaczmarek et al., 1997; Péna et al., 1999;

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0021-9290/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jbiomech.2008.04.014

Taylor and Miller, 2004). Several studies considered the brain continuum as biphasic (solid phase: brain parenchyma; fluid phase: cerebrospinal fluid) and used coupled pore fluid diffusion and stress analysis to compute deformations of the brain parenchyma and ventricles (Nagashima et al., 1987; Tada et al., 1990; Kaczmarek et al., 1997; Péna et al., 1999; Taylor and Miller, 2004). To model the skull–brain interaction, the outer surface of the brain was fixed to the skull (Nagashima et al., 1987; Tada et al., 1990; Kaczmarek et al., 1997; Péna et al., 1999; Taylor and Miller, 2004). Additionally, for intra-operative image registration of brain deformation during neurosurgery, prior work used infinitesimal deformation theory and linear elastic constitutive law for the brain parenchyma as well as coupled pore fluid diffusion and stress analysis (Miga et al., 1999, 2000; Paulsen et al., 1999; Platenik et al., 2002; Lunn et al., 2006).

Due to four-fold increase in ventricular volume during NPH, large strain and finite deformations occur in the brain parenchyma. Hence, to model NPH growth, use of linear elastic constitutive law (Nagashima et al., 1987; Tada et al., 1990; Kaczmarek et al., 1997; Péna et al., 1999; Taylor and Miller, 2004) and infinitesimal deformation theory (Nagashima et al., 1987; Tada et al., 1990; Péna et al., 1999) for the brain parenchyma was unsound. NPH computational model should include nonlinear constitutive law (e.g. hyperelastic) and finite deformation formulations (Bathe, 1996) for brain parenchyma. Following Wittek et al. (2007b), the simplified skull–brain interaction (Nagashima et al., 1987; Tada et al., 1990; Kaczmarek et al., 1997; Péna et al., 1999; Taylor and Miller, 2004) needed to be updated and appropriate boundary conditions between the skull and the brain needed inclusion.

For valid biomechanical modelling of NPH, as well as intra-operative image registration during neurosurgery, we require realistic 3-D model of the brain anatomy, appropriate mathematical model describing the deformations in the brain parenchyma and inclusion of suitable boundary conditions between the skull and the brain. In our present work, we overcame the limitations of the previous studies listed above by using a fully nonlinear (geometric, constitutive and boundary) 3-D model of the brain parenchyma. The nonlinear boundary condition in our model was the contact between the skull and the brain outer surface. We loaded both single phase and biphasic model of the brain parenchyma with transmantle pressure difference and investigated the suggestion that no more than 1 mm of Hg transmantle pressure difference (Penn et al., 2005; Czosnyka, 2006) is associated with NPH. The model we present in the following sections is not intended to accurately represent the brain in various aspects of its behaviour. Our goal is much more modest: we formulate our models to investigate the relationship between pressures, volumes and displacements within the brain in a reliable and efficient way.

2. Biomechanical model

2.1. Brain mesh

Fig. 1 shows the brain mesh for a normal human brain. We modified person specific brain mesh (Wittek et al., 2007b) using Hypermesh (Altair Engineering, USA) preprocessing software and created a generic mesh of a human brain. The brain and ventricular volume in our brain mesh were consistent with values reported by Matsumae et al. (1996) for a normal human brain (Table 1).

As the brain is approximately symmetrical, we used half of the brain in our simulations. Thus, ventricular volume in our model of a normal human was 14 cm^3 and NPH developed when the ventricular volume increased from 14 cm^3 to more than 58 cm^3 (Table 1).

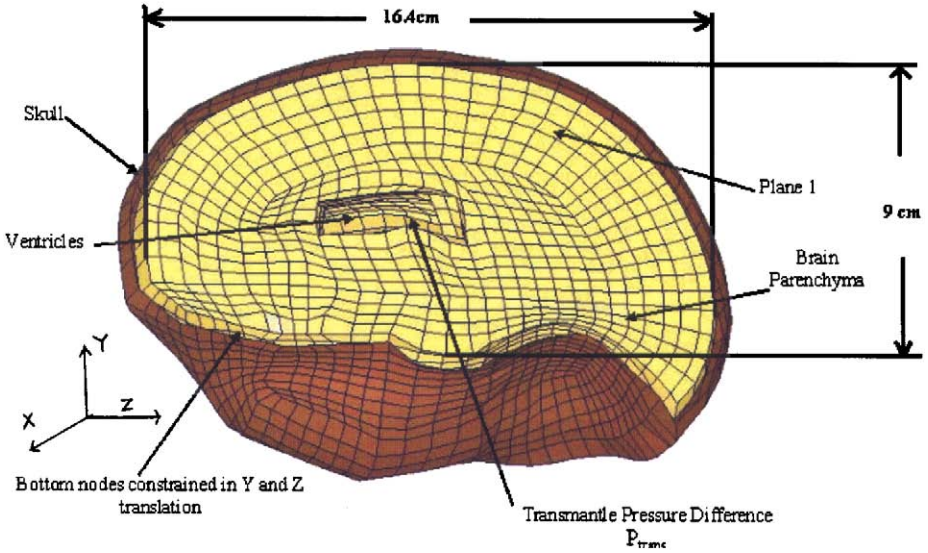

Fig. 1. Brain geometry, pressure loading and applied boundary conditions for the brain.

Table 1
Brain and ventricular volumes for normal and NPH affected brain (adapted from Matsumae et al. (1996))

Case	Brain volume (cm^3)	Ventricular volume (cm^3)
Normal brain	1188 ± 104	27 ± 10
NPH	1163 ± 129	116 ± 42

2.2. Brain parenchyma material parameters

We modified a hyper-viscoelastic constitutive law proposed by Miller and Chinzei (2002) that includes stress–strain rate dependency (Miller and Chinzei, 1997, 2002) and nonlinear stress–strain behaviour of the brain parenchyma, to account for a very long time of NPH development. NPH typically develops over 4 days (Nagashima et al., 1987). Hence, load application on the brain was slow compared to a surgical intervention and therefore the strain rate dependency of the hyper-viscoelastic constitutive law (Miller and Chinzei, 2002) could be excluded (Taylor and Miller, 2004). Hence, we used hyperelastic (Ogden, 1984) constitutive model for the brain parenchyma:

$$W = \frac{2\mu}{\alpha^2}(\lambda_1^\alpha + \lambda_2^\alpha + \lambda_3^\alpha - 3) + \frac{1}{D_1}(J^{el} - 1)^2. \quad (1)$$

where W is the potential function; λ_i's are the principal stretches, μ is the relaxed shear modulus, α is the material coefficient which can assume any real value without any restrictions; J^{el} is the elastic volume ratio and D_1 is the material coefficient related to the initial bulk modulus (K_0). The values of μ and α were 155.77 Pa (Taylor and Miller, 2004) and -4.7 (Miller and Chinzei, 2002), respectively. We considered the brain parenchyma to be homogenous and isotropic for our simulations (Ozawa et al., 2001; Miller et al., 2005).

In our approach, the properties of the modelled tissue are effectively averaged over characteristic length scale—in our case approximately 1 cm (see e.g. Miller and Chinzei, 1997, 2002). The constitutive model of the tissue (Eq. (1)) contains contributions of all constituents of brain tissue, including the contribution of blood vessels, in the sense of volumetric averaging with the characteristic scale of approximately $1\,cm^3$. These modelling issues were explained in our earlier publications (e.g. Miller, 1998; Miller and Chinzei, 1997, 2002; Miller et al., 2000; Taylor and Miller, 2004).

2.2.1. Biphasic model of brain parenchyma

In previous NPH growth studies, authors (Hakim, 1971; Nagashima et al., 1987; Kaczmarek et al., 1997; Péna et al., 1999; Taylor and Miller, 2004) treated the brain as a sponge like structure which consisted of a solid matrix of neurons and neuroglia with extracellular space (voids) between them filled with CSF. The brain parenchyma was biphasic due to presence of neurons and neuroglia (solid or porous phase) and CSF (fluid phase) at each point in the continuum. Following the above previous studies and Miller (1998), we performed coupled pore fluid diffusion and stress analysis (Biot, 1941) to study the interaction between the CSF (fluid phase) and brain parenchyma (solid or porous phase) when loaded by transmantle pressure difference.

In our model, we used Poisson's ratio (υ) of 0.35 (Nagashima et al., 1987; Kaczmarek et al., 1997; Péna et al., 1999; Miller et al., 2005) for the solid phase (brain parenchyma), with relaxed hyperelastic material properties ($\mu = 155.77$ Pa; Section 2.2). The initial void ratio of the brain parenchyma was 0.2 (Nagashima et al., 1987; Sykova, 2004) with permeability of 1.59×10^{-7} m/s (Kaczmarek et al., 1997). The brain parenchyma was fully saturated with CSF. The fluid phase (CSF) was incompressible, non-viscous with mechanical properties of water. Darcy's law (Bowen, 1976) modelled the flow of CSF within the brain parenchyma.

2.2.2. Single phase model of brain parenchyma

To investigate the effect of brain parenchyma compressibility on the transmantle pressure difference in single phase model, we modelled the brain parenchyma as incompressible (Miller, 2001; Miller and Chinzei, 1997, 2002), nearly incompressible and compressible by varying Poisson's ratio (υ). We used hyperelastic constitutive law (Ogden, 1984) with Poisson's ratio (υ) of 0.5, 0.49 and 0.35 (Kaczmarek et al., 1997; Miller et al., 2005) and relaxed hyperelastic shear modulus (Section 2.2). The material properties of the brain parenchyma for different Poisson's ratio (υ) are summarised in Table 2.

2.3. Brain model loading

We used transmantle pressure difference (P_{trans}) applied on the ventricular surface (Fig. 1), to load both single and biphasic models. There was no pressure acting on the outer surface of the brain. It is widely believed that at most 1 mm of Hg (133.416) Pa transmantle pressure difference is associated with the clinical condition of NPH (Penn et al., 2005; Czosnyka, 2006). Accordingly, we first applied a transmantle pressure difference (P_{trans1}) of 1 mm of Hg (133.416 Pa) on both single and biphasic models to verify this view. Since this transmantle pressure difference (P_{trans1}) did not produce NPH, we increased it to P_{trans2},

Table 2
Material properties for incompressible, nearly incompressible and compressible brain (E_∞ and K_∞ are calculated from standard formulae, μ_∞ is taken from Section 2.2)

Case	υ	μ_∞ (Pa)	E_∞ (Pa)	K_∞ (Pa)
Incompressible	0.5	155.77	467.31	–
Nearly incompressible	0.49	155.77	464.19	7736.5
Compressible	0.35	155.77	420.58	467.31

Table 3
Loading applied to single and biphasic model of brain parenchyma

Model	Load Case	
	Load Case 1: (P_{trans1})	Load Case 2: (P_{trans2})
Single phase	1 mm of Hg (133.416 Pa)	Pressure required to produce NPH
Biphasic	1 mm of Hg (133.416 Pa)	Pressure required to produce NPH

which produced NPH. The two load cases are summarised in Table 3.

2.3.1. Biphasic model of brain parenchyma

Even though material strain rate effects were absent due to the use of the hyperelastic constitutive law for the brain parenchyma, rate effects due to the relative motion between the solid (brain parenchyma) and liquid (CSF) phases were present. The time period of pressure load application was important. We applied the transmantle pressure difference (P_{trans}) over a period of 4 days (Nagashima et al., 1987).

2.3.2. Single phase model of brain parenchyma

As we used hyperelastic constitutive law for the brain parenchyma, material strain rate effects were absent and the pressure load application time for static solution of the single phase model was unimportant. The time period of transmantle pressure difference (P_{trans}) application was arbitrarily taken to be 10 s.

For both, single and biphasic model of the brain parenchyma, we applied the transmantle pressure difference (P_{trans}) using a 3–4–5 polynomial (Waldron and Kinzel, 1999). This polynomial ensured vanishing derivatives at the beginning and end of the loading, minimising possible dynamic effects.

2.4. Brain model boundary conditions

Due to approximate symmetry of the brain about the mid-sagittal axis, we used half of the brain in our simulations. Nodes on Plane 1 (Fig. 1) had symmetric boundary conditions in the YZ plane (no motion allowed for X translation) applied to them. As the brain was resting in the skull, we constrained all the nodes at the bottom of the brain in Y and Z translation (Fig. 1). At the top of the brain, we accounted for sub-arachnoid's space by introducing a 3 mm gap between the brain outer surface and the skull. To constrain the nodes on the outer surface of the brain within the skull, we used a frictionless, finite sliding, node-to-surface penalty contact between the brain and the skull (ABAQUS/Standard, 2004). This follows previous studies by Miller et al. (2000); and Wittek et al. (2007a, b). The contact boundary condition is nonlinear because an iterative method would be required to establish whether the brain is in contact with the skull or not even if the rest of the model were linear (i.e. infinitesimal deformation and liner material properties). For modelling brain deformations, boundary conditions are one of the main sources of nonlinearity. The other sources of nonlinearity are finite deformations and nonlinear material properties.

2.4.1. Biphasic model of brain parenchyma

In addition to the above, boundary conditions for the pore pressure variable needed to be defined for the biphasic model. We set the pore pressure on the ventricular surface equal to the transmantle pressure difference (P_{trans1} or P_{trans2}) and on the outer surface of the brain to be 0 Pa.

2.5. Computational model

2.5.1. Biphasic model of brain parenchyma

We used 5858 porohyperelastic type C3D20P (20-node brick, pore pressure) (ABAQUS/Standard, 2004) and 89 type C3D10 (10-node quadratic tetrahedron) (ABAQUS/Standard, 2004) elements for the biphasic model. In order to accurately represent the complex brain geometry, tetrahedral elements completed the mesh in places where the quality of the hexahedral elements was poor.

2.5.2. Single phase model of brain parenchyma

Incompressible/nearly incompressible brain parenchyma model consisted of 5858 type C3D20H (20-node quadratic brick, hybrid) (ABAQUS/Standard, 2004) and 89 type C3D10H (10-node quadratic tetrahedron, hybrid) (ABAQUS/Standard, 2004) elements. 5858 type C3D20 (20-node quadratic brick) (ABAQUS/Standard, 2004) and 89 type C3D10 (10-node quadratic tetrahedron) (ABAQUS/Standard, 2004) elements constituted the compressible brain parenchyma model. As with the biphasic model, in order to accurately represent the complex brain geometry, tetrahedral elements completed the mesh in places where the quality of the hexahedral elements was poor. Elements of type C3D20H and C3D10H do not exhibit volumetric locking and therefore can be confidently used for an incompressible/nearly incompressible continuum (e.g. brain).

For both biphasic and single phase models, the skull model consisted of 1006 type R3D4 (four-node, bilinear quadrilateral, three-dimensional rigid) (ABAQUS/Standard, 2004) elements.

2.6. Finite element solver

We used ABAQUS-Standard nonlinear implicit finite element code (ABAQUS/Standard, 2004) to obtain the

solution for the NPH biomechanical model. The code accounts for constitutive, geometric (finite deformation) and contact nonlinearities. The STATIC (ABAQUS/Standard, 2004) procedure was used to solve single phase model and the SOILS (ABAQUS/Standard, 2004) procedure for the biphasic model. Wu et al. (1998) validated the use of the SOILS procedure in ABAQUS for hydrated biphasic tissues. In the SOILS procedure, permeability of the porous medium is a function of saturation and void ratio. For the biphasic model, the brain parenchyma (porous medium) is fully saturated with CSF. The permeability of the porous medium (brain parenchyma) is deformation and void ratio dependent (ABAQUS/Standard, 2004).

3. Results

3.1. Ventricular volume

Load Case 1. Transmantle pressure difference (P_{trans1}) equivalent to 1 mm of Hg (133.416 Pa).

3.1.1. Biphasic model of brain parenchyma

Ventricular volume computed when $P_{trans1} = 133.416$ Pa loaded the biphasic model of brain parenchyma was 36.6 cm^3. P_{trans1} load did not produce NPH.

3.1.2. Single phase model of brain parenchyma

Ventricular volume for incompressible, nearly incompressible and compressible brain parenchyma (Section 2.2, single phase model of brain parenchyma) under P_{trans1} load is given in Table 4. As can be seen from Table 4, the level of brain tissue compressibility has limited influence on the ventricular volumes produced. Also, P_{trans1} failed to produce the condition of NPH.

Ventricular volumes summarised in Table 4 above are similar to the ventricular volume obtained for biphasic model of the brain parenchyma under P_{trans1} load.

Load Case 2. Transmantle pressure difference (P_{trans2}) required for clinically producing the condition of NPH.

3.1.3. Biphasic model of brain parenchyma

As $P_{trans1} = 133.416$ Pa failed to produce the condition of NPH (Table 4), we used a higher transmantle pressure difference (P_{trans2}) to load the brain parenchyma. For the biphasic case, due to excessive distortion in a few elements of the complicated brain mesh (quality of these elements could not be improved due to complicated brain geometry), our solution failed to converge under transmantle pressure difference load higher than 1.69 mm of Hg (226.27 Pa).

Since the biphasic brain parenchyma is fully saturated with CSF in its undrained condition, we can consider it to be incompressible or nearly incompressible continuum. Therefore, to compare the results, we used the same transmantle pressure difference ($P_{trans2} = 1.69$ mm of Hg = 226.27 Pa) to load incompressible (Poisson's ratio $\upsilon = 0.5$) and nearly incompressible single phase (Poisson's ratio $\upsilon = 0.49$) brain parenchyma. The ventricular volumes produced under this load for incompressible and nearly incompressible single phase and biphasic brain parenchyma are given in Table 5. It can be seen clearly from the results that a transmantle pressure difference (P_{trans2}) higher than 1.69 mm of Hg would be required to produce NPH for the biphasic model.

3.1.4. Single phase model of brain parenchyma

P_{trans1} did not produce NPH for the single phase model (Table 4). We then increased the transmantle pressure difference from P_{trans1} to P_{trans2} to produce NPH (Table 6). Table 6 clearly shows that for all cases, transmantle pressure difference higher than 1 mm of Hg (133.416 Pa) was required to produce NPH.

3.2. Periventricular lucency

In a healthy human brain, tightly packed ependymal cells line the ventricular cavity (Standring, 2004). This

Table 4
Ventricular volume when transmantle pressure difference (P_{trans1}) equivalent to 1 mm of Hg (133.416 Pa) is applied to single phase brain parenchyma

Case	Poisson's ratio (υ)	Ventricular volume (cm^3)
Incompressible	0.5	34.8
Nearly incompressible	0.49	35.1
Compressible	0.35	37.3

NPH develops when ventricular volume increased from 14 to 58 cm^3.

Table 5
Ventricular volume produced when transmantle pressure difference (Load Case 2 (P_{trans2}) = 226.27 Pa = 1.69 mm of Hg) is applied to incompressible/nearly incompressible single and biphasic model

Case	Poisson's ratio (υ) for solid phase	Load Case 2: P_{trans2}	Ventricular volume (cm^3)
Biphasic	0.35	1.69 mm of Hg (226.27 Pa)	49.57
Incompressible	0.5	1.69 mm of Hg (226.27 Pa)	51.64
Nearly incompressible	0.49	1.69 mm of Hg (226.27 Pa)	52.56

NPH developed when ventricular volume increased from 14 to 58 cm^3.

limits the extracellular space, keeping permeability of brain parenchyma low and results in minimal CSF diffusion into the brain parenchyma. As the region of brain parenchyma around the ventricular surface stretches under pressure load (P_{trans1} or P_{trans2}), it may disrupt the brain parenchyma. This resulted in an increase of void ratio (Fig. 2) and permeability (Section 2.6), which suggested swelling of extracellular space. The pressure gradient between ventricles and sub arachnoid's space, combined with increased extracellular space (Fig. 2) and permeability (Section 2.6, finite element solver), facilitated increased seepage of CSF through the brain parenchyma (Fig. 3). As a result, CSF accumulated in the extracellular space around the ventricular surface thereby promoting brain oedema. Mori et al. (1980) observed the brain oedema as periventricular lucency in CT scans of NPH affected patients. Our interpretation of modelling results is consistent with Péna et al. (1999) and Taylor and Miller (2004). Biphasic brain parenchyma model explains the phenomenon of periventricular lucency. The same cannot be explained by single phase model of the parenchyma.

Table 6
Transmantle pressure difference (Load Case 2: P_{trans2}) required to produce NPH in single phase brain parenchyma model

Case	Poisson's ratio (υ)	Load Case 2: P_{trans2}
Incompressible	0.5	2.059 mm of Hg (274.68 Pa)
Nearly incompressible	0.49	1.985 mm of Hg (264.87 Pa)
Compressible	0.35	1.764 mm of Hg (235.44 Pa)

NPH developed when ventricular volume increased from 14 to 58 cm^3.

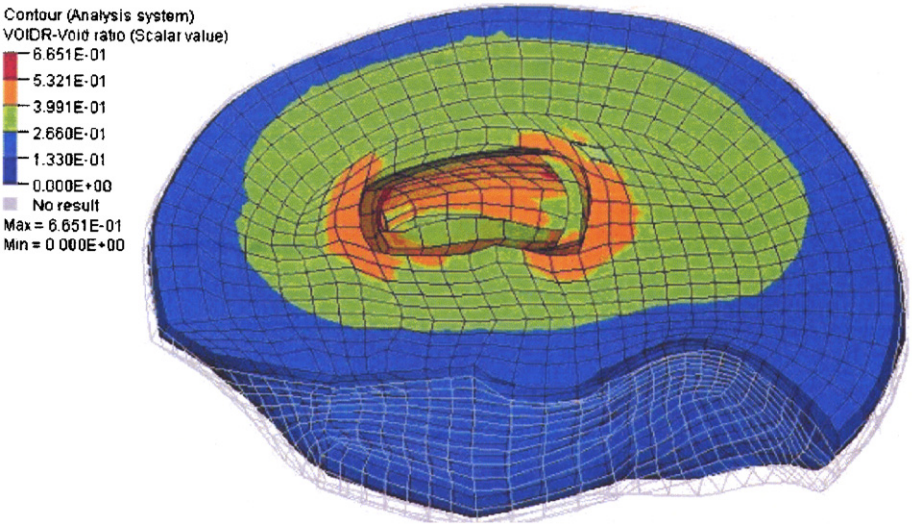

Fig. 2. Void ratio distribution for biphasic model [loading pressure: 1 mm of Hg (133.416 Pa)].

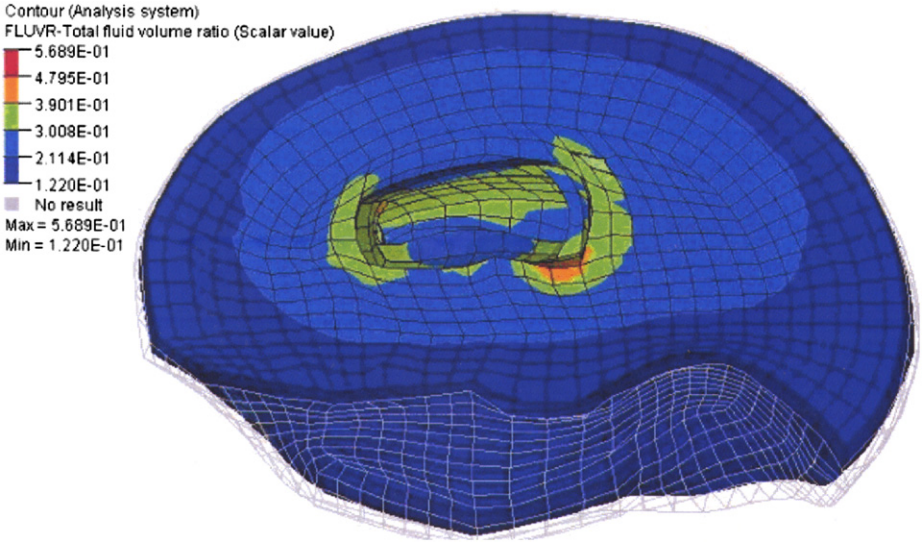

Fig. 3. Total fluid volume ratio distribution for biphasic model [loading pressure: 1 mm of Hg (133.416 Pa)].

4. Discussions and conclusions

In undrained condition, the biphasic brain parenchyma is fully saturated with CSF. Therefore, we can consider it to be incompressible or nearly incompressible continuum. Hence, we compared the ventricular volume obtained for the biphasic model with that for incompressible/nearly incompressible single phase model, under 1 mm of Hg (133.416 Pa) transmantle pressure difference (P_{trans1}) load. The ventricular volume for biphasic brain parenchyma (36.6 cm^3) was 5.1% and 4.2% higher compared to incompressible ($\upsilon = 0.5$) and the nearly incompressible ($\upsilon = 0.49$) single phase model of the brain parenchyma, respectively (Table 4). For biphasic and single phase incompressible/nearly incompressible model of the brain parenchyma, P_{trans1} load did not produce NPH (Section 2.1).

As P_{trans1} did not produce NPH in the biphasic model, we started to increase the transmantle pressure difference in an attempt to produce NPH. We could obtain the results only for transmantle pressure difference (P_{trans2}) of up to 226.27 Pa (1.69 mm of Hg) load. Under transmantle pressure difference higher than P_{trans2}, the biphasic model did not converge due to excessive distortions of some elements in the complicated brain mesh. This pressure load ($P_{trans2} = 226.27$ Pa $= 1.69$ mm of Hg) did not produce NPH for the biphasic model. As mentioned above, the biphasic brain parenchyma in its undrained condition is incompressible or nearly incompressible. Therefore, we applied the same transmantle pressure difference ($P_{trans2} = 226.27$ Pa $= 1.69$ mm of Hg) load to incompressible ($\upsilon = 0.5$) and nearly incompressible single phase model ($\upsilon = 0.49$) and compared the ventricular volume with that obtained for the biphasic model. For the incompressible ($\upsilon = 0.5$) and nearly incompressible ($\upsilon = 0.49$) single phase model, ventricular volume was 4.2% and 6% higher, respectively, when compared to the biphasic model (Table 5).

In the results presented above, it is clearly seen that there are no significant differences in computed ventricular volumes between biphasic and incompressible/nearly incompressible single phase model of the brain parenchyma under equal load. Hence, no major advantage would be gained by using a biphasic model for the brain parenchyma. We propose that for modelling NPH, single phase model of the brain parenchyma is adequate. The single phase model simplifies the mathematical description of the NPH model and results in significant reduction of computational time (483 min for the single phase incompressible model compared to 2921 min for the biphasic model on Pentium 4, 3.2 GHz, 2 GB RAM personal computer), while appropriately representing the brain constitutive properties for NPH investigation.

Under $P_{trans1} = 133.416$ Pa load applied to single phase brain model, ventricular volume was 7.18% and 6.3% higher for the compressible brain parenchyma ($\upsilon = 0.35$) compared to incompressible ($\upsilon = 0.5$) and the nearly incompressible brain parenchyma ($\upsilon = 0.49$) respectively (Table 4). Although the relaxed bulk modulus (K_∞) for the compressible parenchyma was significantly lower than incompressible and nearly incompressible cases (Table 2), brain compressibility exerted limited influence on the ventricular volumes produced. This could be explained by the inclusion of realistic boundary conditions which comprised of the sub arachnoid's space (3 mm gap between the brain outer surface and skull) and the skull–brain interaction modelled using contact boundary conditions (Miller et al., 2000; Wittek et al., 2007a, b). P_{trans1} load deformed the brain because the brain outer surface displaced outwards. The skull–brain contact included in our model checked the displacement of the brain outer surface and limited further movement after it displaced through a distance equal to sub arachnoid's space (3 mm). Therefore, even for low Poisson's ratio (υ) of 0.35 (Table 4), 1 mm of Hg (133.416 Pa) transmantle pressure difference failed to produce the clinical condition of NPH (Section 2.1).

As P_{trans1} did not produce the condition of NPH, we loaded the model with higher transmantle pressure difference (P_{trans2}) which could produce NPH (Table 6). Incompressible and nearly incompressible models required 16.67% and 12.9% higher transmantle pressure difference, respectively, when compared to the compressible model. Brain compressibility had influence on the transmantle pressure difference required to produce NPH.

It can be seen from the results presented above, that we required a minimum transmantle pressure difference of 1.76 mm of Hg (235.44 Pa) to produce NPH for compressible ($\upsilon = 0.35$) single phase model of the brain parenchyma (Table 6). Based on transmantle pressure difference–ventricular volume plot shown in Fig. 4, it could be argued that the biphasic model would require a load higher than 1.76 mm of Hg (235.44 Pa) transmantle pressure difference to produce NPH. Penn et al. (2005) and Czosnyka (2006) have measured and reported that transmantle pressure difference (133.416 Pa) of unto 1 mm of Hg is associated with NPH. Despite using various constitutive models (single phase and biphasic) and varying Poisson's ratio (υ) to a value as low as 0.35, we could not produce NPH for 1 mm of Hg (133.416 Pa) transmantle pressure difference load.

The limitation of modelling and computer simulation work on brain biomechanics conducted to date, including this paper, is that vasculature is not explicitly included in the model. However, the computational model presented in this paper implicitly models the vasculature as the constitutive law of the brain parenchyma includes contribution of the blood vessels (Miller et al., 2000). The constitutive law used in our work (Miller and Chinzei, 2002) treats the brain parenchyma as a continuum and was developed by subjecting cylindrical samples of the brain parenchyma (the blood vessels were not removed from them) to tension and compression. This is a standard approach when attempting to identify *effective mechanical*

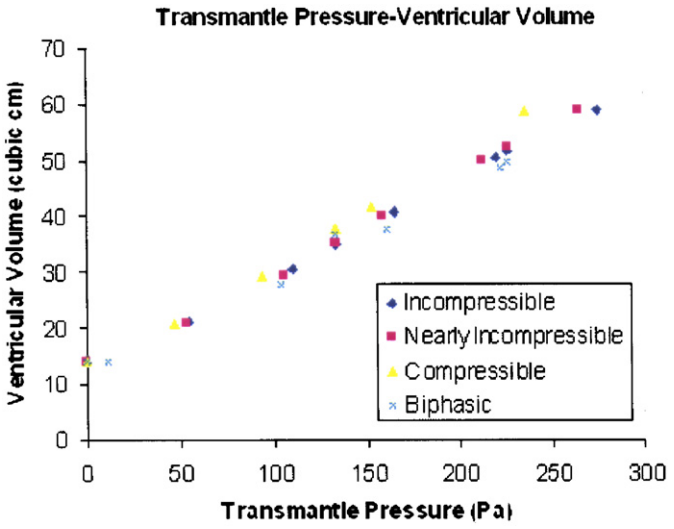

Fig. 4. Transmantle pressure difference vs. ventricular volume for single phase (incompressible, nearly incompressible and compressible) and biphasic brain model.

properties of complex materials (see e.g. Gemanovich and Dyskin, 1994). It is also worth noting that Gefen and Margulies (2004) showed experimentally that mechanical properties of perfused brain tissue were very similar to the properties measured *in vitro*.

In conclusion, our work showed that there is no significant advantage gained by treating the brain parenchyma as biphasic continuum for computing ventricular volume. To model NPH, we propose that the brain parenchyma be treated as nearly incompressible single phase continuum. The single phase model for the brain parenchyma simplifies the mathematical description of the NPH model and reduces the computational time.

According to our results, transmantle pressure difference of unto 1 mm of Hg (133.416 pa) is not sufficient to produce the condition of NPH. To the best of our knowledge, our work is the first conclusive demonstration of this using modelling and simulation techniques, adding strength to the previous, purely experimental studies (Penn et al., 2005). This suggests that the hypothesis of a purely mechanical basis for NPH growth needs to be revised.

Conflict of interest

I, Tonmoy Dutta-Roy on the behalf of all authors (Dr. Adam Wittek and Prof. Karol Miller) of the paper titled "Biomechanical modelling of normal pressure hydrocephalus" confirm that none of the authors have any conflict of interests with the review/publication process.

Acknowledgements

Financial support of the William and Marlene Schrader Trust in form of the William and Marlene Schrader Post-Graduate Scholarship for the first author is gratefully acknowledged. This research has also been funded by Australian Research Council (Grant nos. DP0343112 and DP0664534) and National Institute of Health (Grant no. R03 CA126466-01A1).

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