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Investigating cerebral oedema using poroelasticity

John C. Vardakis [a], Dean Chou [b], Brett J. Tully [c], Chang C. Hung [d,e], Tsong H. Lee [d], Po-Hsiang Tsui [f,g], Yiannis Ventikos [a,*]

[a] Department of Mechanical Engineering, University College London, Torrington Place, London WC1E 7JE, UK
[b] Institute of Biomedical Engineering & Department of Engineering Science, University of Oxford, Oxford OX1 3PJ, UK
[c] First Light Fusion Ltd., Begbroke Science Park, Begbroke, Oxfordshire OX5 1PF, UK
[d] Stroke Center and Department of Neurology, Chang Gung Memorial Hospital, Linkou Medical Center and College of Medicine, Taoyuan, Taiwan
[e] Department of Electrical Engineering, College of Engineering, Chang Gung University, Taoyuan, Taiwan
[f] Department of Medical Imaging and Radiological Sciences, College of Medicine, Chang Gung University, Taoyuan, Taiwan
[g] Medical Imaging Research Center, Institute for Radiological Research, Chang Gung University and Chang Gung Memorial Hospital, Taoyuan, Taiwan

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ABSTRACT

Cerebral oedema can be classified as the tangible swelling produced by expansion of the interstitial fluid volume. Hydrocephalus can be succinctly described as the abnormal accumulation of cerebrospinal fluid (CSF) within the brain which ultimately leads to oedema within specific sites of parenchymal tissue. Using hydrocephalus as a test bed, one is able to account for the necessary mechanisms involved in the interaction between oedema formation and cerebral fluid production, transport and drainage. The current state of knowledge about integrative cerebral dynamics and transport phenomena indicates that poroelastic theory may provide a suitable framework to better understand various diseases. In this work, Multiple-Network Poroelastic Theory (MPET) is used to develop a novel spatio-temporal model of fluid regulation and tissue displacement within the various scales of the cerebral environment. The model is applied through two formats, a one-dimensional finite difference – Computational Fluid Dynamics (CFD) coupling framework, as well as a two-dimensional Finite Element Method (FEM) formulation. These are used to investigate the role of endoscopic fourth ventriculostomy in alleviating oedema formation due to fourth ventricle outlet obstruction (1D coupled model) in addition to observing the capability of the FEM template in capturing important characteristics allied to oedema formation, like for instance in the periventricular region (2D model).

1. Introduction

1.1. Hydrocephalus

Hydrocephalus (HCP) can be defined as the abnormal accumulation of CSF within the brain [1,7]. A balance between production and reabsorption exists, and it attempts to maintain the CSF pressure within a fairly narrow range of intracranial pressure (ICP) values [8]. HCP itself is not a singular pathological entity, but instead, a consequence of a variety of congenital and acquired disorders present within the central nervous system (CNS) [9]. HCP is classified with regards to whether the point of CSF obstruction or discreet lesion lies within the ventricular system (obstructive) and obstructs the flow before it enters the subarachnoid space (SAS) [10], or not (communicating). Normal Pressure Hydrocephalus (NPH) is a form of HCP that possesses no radiographically identifiable flow obstruction, however, there is evidence of craniomegaly and ventriculomegaly taking place [11,12].

1.2. Cerebral oedema

Cerebral oedema refers to swelling produced by expansion of the interstitial fluid volume (or an increase in water content above the normal level of brain water content) and is a common response to primary brain insult [13,14]. Cerebral oedema is usually classified into the major subtypes: cytotoxic, vasogenic, interstitial or combined [13–16]. Most brain injuries however involve a combination of these subtypes, making overall classification difficult. Interstitial oedema is considered a consequence of impaired CSF outflow (as in obstructive HCP), leading to increased intraventricular pressure and a compromised ependymal lining. Subsequently, an increase in transependymal CSF flow migration into the parenchyma and the periventricular regions take place. Osmotherapy is a well-known (albeit

* Corresponding author. Tel.: +44 20 7679 7068/3908.
E-mail address: y.ventikos@ucl.ac.uk (Y. Ventikos).

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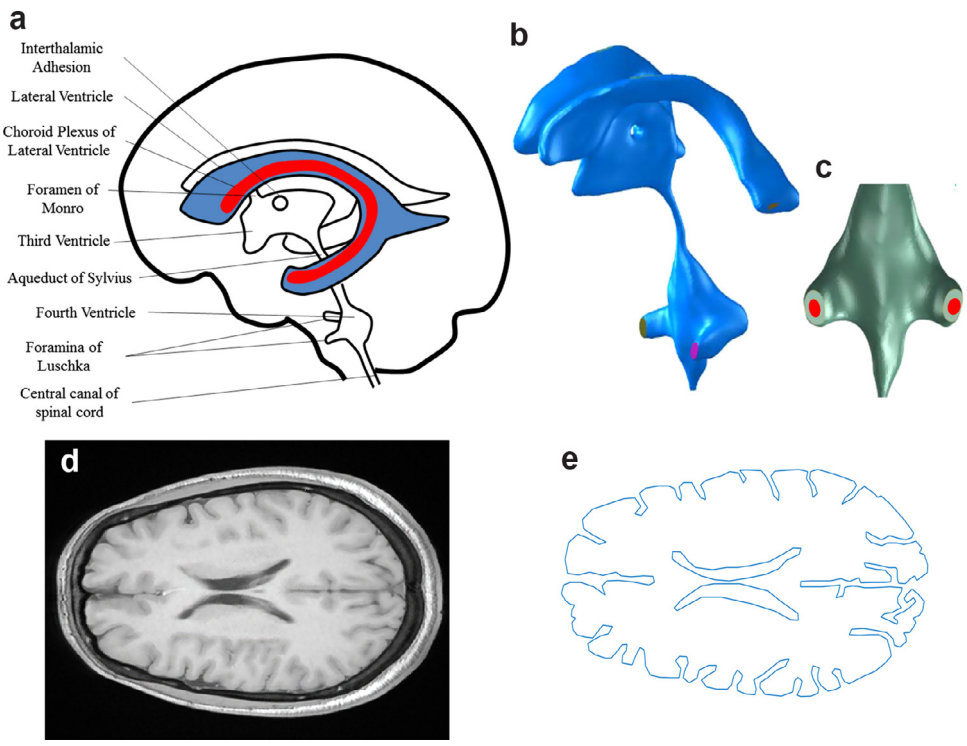

Fig. 1. CSF containing cavities, image-based reconstruction of the ventricular morphology and MRI slice used to create the 2D region of interest. (a) CSF circulates through the four brain ventricles and in the subarachnoid space surrounding the brain and spinal cord. A sizeable proportion is produced in the choroid plexus of the lateral, third and fourth ventricle regions. A schematic depiction of the *C* shaped choroid plexus is shown for the left lateral ventricle. (b) The final ventricular geometry used for the 1D-3D coupled simulations. (c) Location and approximate size of outlet (red oval) created to mimic EFV at the bilateral Foramina of Luschka, situated on the fourth ventricle. (d) MRI slice used to create the parenchymal region in addition to extracting the ventricles. (e) Outline of the parenchymal region that was discretized for the 2D FEM simulations.

controversial) non-invasive treatment of oedema [16]. Aquaporins (AQPs) are widely considered as key players in the resolution of oedema, owing to their regionally distinct distribution [15,17,18]. More specifically, AQP4 is believed to evoke an interrelation between cerebral oedema and neuroinflammation [17,19]. The recently coined glymphatic system and its regulation is also considered to have a potentially active role in developing key therapies for oedema. Thrane et al. [20] for instance, suggest that vasogenic oedema is representative of prolonged increase of glymphatic fluid influx that assists in paravascular leukocyte and cytokine delivery. In this work, interstitial oedema is investigated, as this type of oedema is borne out of ventriculomegaly, and targets the periventricular region. In addition, a simple relationship that allows for small variations of permeability in the MPET model which account for the swelling characteristics induced by AQP4 (see Eq. (5)) is also included within the MPET framework.

1.3. Endoscopic ventriculostomy for alleviating oedema and hydrocephalic symptoms

Many recommend that endoscopic third ventriculostomy (ETV) be suggested as a first-line treatment to all patients that require management of HCP [21–27]. ETV involves passing an endoscope into either lateral ventricle (see Fig. 1a) via a burr hole in the frontal region. The enlarged third ventricle will have its thin floor stretched due to HCP, and it will resemble a translucent membrane. The floor is perforated and enlarged via various means such as a balloon catheter, Grotenhuis perforation [28] or Decq forceps [29], thus creating an artificial opening into the basal subarachnoid spaces. Ultimately, this is a natural way of draining excess CSF. Similarly to ETV, endoscopic fourth ventriculostomy (EFV) involves puncturing and dilating the occluded membranes due to atresia of the foramina of the fourth ventricle. EFV may prove to be a sound alternative treatment (as ETV is considered the preferred option for various types of Fourth Ventricular Outlet Obstruction (FVOO) [30] and sequestrated or trapped fourth ventricle [23]) in cases where ETV cannot be considered.

1.4. Pertinent models of oedema using small-strain poroelasticity

Nagashima et al. [31–34] modeled vasogenic brain oedema, using the finite element method. The authors in the aforementioned work [31] used a set of parameter values and boundary conditions that do not coincide with the most recent literature, notably the use of a Poisson's ratio (of 0.47), and Young's modulus (in the work presented here, a value of around 584 Pa [35] is used). Peña et al. investigated the biomechanics of acute obstructive HCP and periventricular lucency (PVL) through the use of a two-dimensional biphasic poroelastic model solved using the FEM [36]. Further references to work on existing models of the CSF compartment are given in a previous publication by the same authors [3]. A thorough and recent review on the mechanics of the brain is also given by Goriely et al. [16].

2. Methods

2.1. Geometry

Imaging was performed on a 1.5T GE Signa system (Waukesha, WI, USA) and a T2 weighted imaging sequence was used for obtaining the brain anatomy data of a male volunteer in his 60s. The acquired voxels were manually segmented for the ventricular system using Amira (Mercury Computer Systems, San Diego, CA, USA) and the raw segmented geometry from this process was converted to a Stereo Lithography (STL) file. In order to preserve key anatomical features, smoothing of the STL file was executed using Blender (The Blender Foundation, www.blender.org), as it provides the option of locally smoothing parts of a mesh, in addition to its global smoothing capabilities. Alternating between local and global smoothing was required in order to keep the angle between faces within expected limits. The