6th International Conference on Computational and Mathematical Biomedical Engineering - CMBE2019
10–12 June 2019, Japan
P. Nithiarasu, M. Ohta, M. Oshima (Eds.)

FINITE ELEMENT POROELASTIC MODELLING OF BRAIN OEDEMA FORMATION AFTER ISCHAEMIC STROKE REPERFUSION

Mohd Jamil Mohamed Mokhtarudin[1], Aina Najwa Nadzri[1], and Stephen J. Payne[2]

[1]Faculty of Mechanical Engineering, Universiti Malaysia Pahang, 26600 Pekan, Pahang, Malaysia,
mohdjamil@ump.edu.my,ainanadzri2696@gmail.com

[2]Institute of Biomedical Engineering, Department of Engineering Science, Old Road Campus Research Building, University of Oxford, Headington, OX3 7DQ, Oxford, UK,
stephen.payne@keble.ox.ac.uk

SUMMARY

One of the risks of ischaemic stroke reperfusion treatment is the formation of brain oedema. This is usually observed clinically by the formation of herniation, which if not treated, it may disrupt brain functionality. In this paper, a mathematical model of brain oedema formation after stroke has been developed and simulated on an ideal 3D brain geometry with different infarct sizes and locations, to see their effects on brain herniation. The brain tissue displacement and pressure are then analyzed. It is found that those infarcts with large sizes and located nearer to the brain ventricle cause severe brain herniation.

Key words: *brain tissue swelling, ischaemic stroke, poroelastic theory, finite element modelling*

1 INTRODUCTION

Brain oedema or tissue swelling can occur as a result of ischaemic stroke reperfusion. A prolonged ischaemia may result in blood-brain barrier (BBB) breakdown. Upon reperfusion, either naturally or through medication and surgery, BBB damage may become irreparable [1] and may increase its permeability. When BBB permeability increases, the capillary filtration of molecules and ions from reperfused blood into the interstitial space increases the osmotic pressure difference, resulting in water movement into the brain tissue, a condition called vasogenic oedema or brain tissue swelling [2].

Brain tissue swelling can usually be observed by the formation of cerebral herniation and by the increase of intracranial pressure (ICP). Brain herniation can be observed using medical imaging modalities such as CT scan and MRI. This is usually seen by the movement of the brain midline structures, for example the ventricles. Various quantitative methods to measure brain herniation after stroke have been developed, which could be used for stroke pronostic [3]. Meanwhile, the ICP measurement is invasive and is seldomly performed on ischaemic stroke patients. However, research on non-invasive ICP measurements is still on-going [4].

The formation of brain tissue swelling during ischaemia-reperfusion has been modelled by [5] using poroelastic theory and capillary filtration model. In this model, the interstitial water pressure is coupled with the brain tissue displacement, to demonstrate the effect of capillary filtration on brain tissue swelling or oedema. Here, the model is solved in an ideal 3D brain geometry to simulate the effect of brain tissue swelling for different ischaemic stroke infarct sizes and locations towards brain herniation and pressure.

2 METHODOLOGY

2.1 Poroelastic model

We assumed that the brain tissue as an isotropic poroelastic material, which consists of a solid matrix permeated by interstitial fluid and the swelling occurs at a very small strain. The stress balance in the tissue is given by:

$$\nabla \cdot \sigma_{ij} - \alpha_w \nabla P_w = 0 \tag{1}$$

where σ_{ij} is the total stress of the tissue, P_w is the interstitial fluid pressure, and α_w is the Biot parameter for water. The total tissue stress is linearly related to the strain, ϵ_{ij} by:

$$\sigma_{ij} = \mathbb{C}\epsilon_{ij} \tag{2}$$

where $\mathbb{C}$ is the stiffness tensor. Then, the rate of change of the interstitial fluid is given by the conservation of mass relationship:

$$\frac{1}{Q_w}\dot{P}_w - \nabla \cdot w - \dot{S}_{b\to w} = 0 \tag{3}$$

where Q_w is the relative compressibility of water and w is the relative interstitial fluid velocity, which can be further related to P_w by Darcy's law:

$$w = -\kappa_w \nabla P_w \tag{4}$$

Here, κ_w is the interstitial fluid permeability in the porous tissue. Meanwhile, the term $\dot{S}_{b\to w}$ is the net of water flow into the brain tissue through capillary filtration, given by:

$$\dot{S}_{b\to w} = L_{b\to w} f(P_b - P_w - \sigma\Pi_b) \tag{5}$$

where $L_{b\to w}$ is hydraulic permeability constant of the capillary. P_b is the baseline blood pressure, σ is the reflection coefficient, and Π_b is the osmotic pressure in the capillary. Lastly, the term f represents the ratio of capillaries that remain open after the swelling process. A more detail explanation of these equations and the parameters value can be found in [5].

2.2 Ideal brain geometry

The model is implemented on a semi-spherical ideal brain geometry with a hollow semi-spherical ventricle in the middle, as proposed by [6] as shown in 1 below. Here, the skull and the ventricle radius is 80 mm and 24 mm, respectively. The non-infarct or normal tissue region is set to have $\dot{S}_{b\to w} = 0$ representing no capillary filtration occurrence. The location and size from the ventricle of the infarct are varied from 0 mm to 14 mm, to investigate these effects on the ventricle movement. All geometries are meshed using 10-node tetrahedral elements and the number of elements are in between 17,000 to 47,000, with the infarct has finer mesh then the other region.

2.3 Numerical procedure

The skull, R_S is assumed to have a fixed pressure at baseline ICP, $\bar{P}$ and a tissue displacement, u of zero. Meanwhile, the ventricle R_V is allowed to move freely due to the force applied from the swollen tissue, as follows:

$$\sigma_{ij}(R_V, t) \cdot \mathbf{n} = -\bar{P}\mathbf{n} \tag{6}$$

The brain tissue is assumed to have initial displacement and pressure fixed at zero and ICP, respectively. The simulation is solved using a standard solver in COMSOL Multiphysics 5.3a.

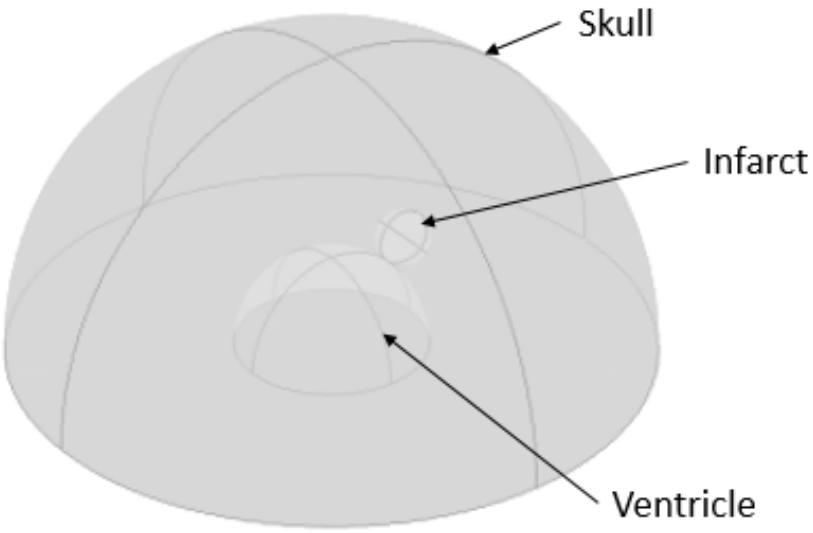

Figure 1: Ideal brain geometry as proposed by [3].

3 RESULTS AND CONCLUSION

The simulations are ran to see the effects of brain tissue swelling after 3 hours from stroke onset. Figure 2 shows the pressure and displacement for the infarct radii 7 mm, 14 mm, and 21 mm located 0 mm from the ventricle. Here, the label 0mm/7mm (which is used throughout the paper) indicates the results for the infarct radius 7 mm located 0 mm from the ventricle. From 2, the ventricle is slightly moved. The ventricle will move significantly if the swelling time is longer, as predicted by the simulation [8] on a real patient geometry. Other than the infarct size and location, the brain tissue mechanical properties [7] also affect the brain tissue swelling, subsequently result in the ventricle movement.

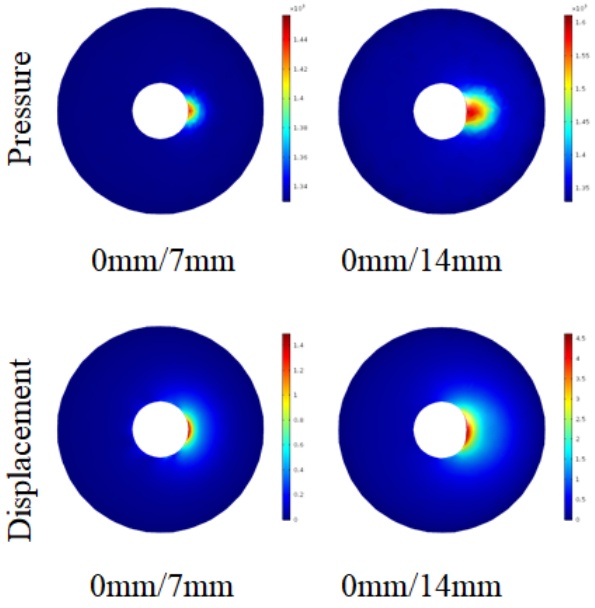

Figure 2: Pressure and displacement distributions for a slice of the brain located 10 mm from the bottom.

Meanwhile, figure 3 shows the variation of maximum pressure and displacement against time for all infarct sizes and locations. From the maximum pressure, it can be seen that the infarcts located 0 mm from the ventricle have the highest pressure. However, the infarct radius 7 mm has the highest pressure of all infarct variations. This shows that brain oedema reaches steady value quicker in smaller infarct compared to bigger one as proven in [5]. If the simulations were run for a longer time, the maximum pressure for larger infarcts is expected to reach a higher steady-state value.

On the other hand, the maximum displacement is higher for infarct radius 21 mm, followed by 14 mm and 7 mm. This is as expected because larger infarct will produce bigger swelling, as also predicted in [8]. It should be noted here that both maximum pressure and displacement do not reach steady-state value within the 3 hours simulation time. The study on ischaemic stroke patients found that brain tissue continues to swell after 6 to 24 hours after stroke onset [9]. This model has the potential to be used to predict brain oedema progression of ischaemic stroke patient upon reperfusion if suitable boundary conditions and parameter values are used.

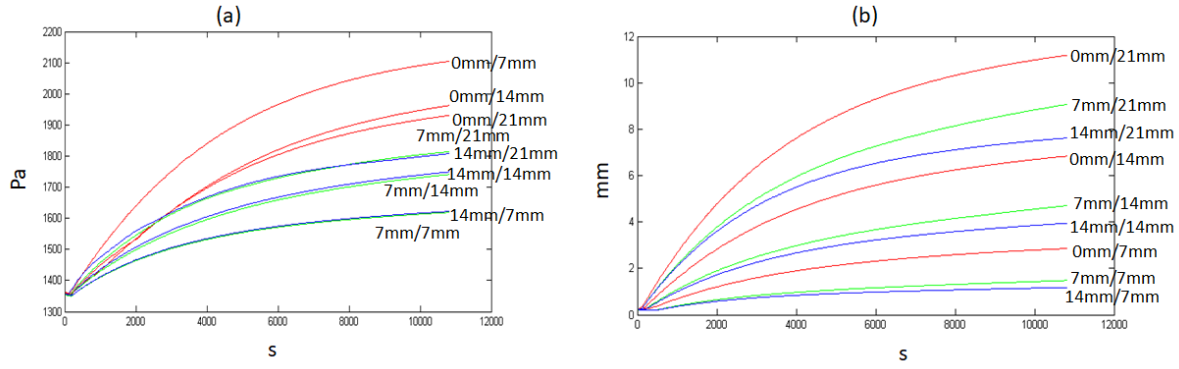

Figure 3: Maximum pressure (a) and maximum displacement (b) for various infarct sizes and locations.

4 ACKNOWLEDGEMENT

This research is funded by UMP RDU1703310, RDU1803120, and FRGS RDU190132 research grants.

REFERENCES

[1] Y. Yang and G. A. Rosenberg. Blood-brain barrier breakdown in acute and chronic cerebrovascular disease. *Stroke*, 42:3323–3328, 2011.

[2] A. W. Unterberg, J. Stover, B. Kress, and K. L. Kiening. Edema and brain trauma. *Neuroscience*, 129, pp:1021–1029, 2004.

[3] N. Paletta, L. Maali, A. Zahran, et. al. A simplified quantitative method to measure brain shifts in patients with middle cerebral artery stroke. *Journal of Neuroimaging*, 28:61-63, 2018.

[4] C. Robba, D. Cardim, T. Tajsic, et. al. Ultrasound non-invasive measurement of intracranial pressure in neurointensive care: A prospective observational study. *PLoS Medicine*, 14(7): 1–16, 2017.

[5] M. J. Mohamed Mokhtarudin, and S. J. Payne. Mathematical model of the effect of ischemia-reperfusion on brain capillary collapse and tissue swelling. *Mathematical Biosciences*, 263:111–112, 2015.

[6] S. Hakim, J. G. Venegas, and J. D. Burton. The physics of the cranial cavity, hydrocephalus, and normal pressure hydrocephalus: Mechanical interpretation and mathematical model. *Surgical Neurology*, 5:187–210, 1976.

[7] M. J. Mohamed Mokhtarudin, A. Shabudin, S. J. Payne. Effects of brain tissue mechanical and fluid transport properties during ischaemic brain oedema: A poroelastic finite element analysis. In *2018 IEEE-EMBS Conference on Biomedical Engineering and Sciences (IECBES)*, 1–6, IEEE, 2018.

[8] M. J. Mohamed Mokhtarudin. Mathematical modelling of cerebral ischaemia-reperfusion injury. *Doctoral dissertation. University of Oxford*, 2016.

[9] A. E. Baird, et al. Transmural coupling of fluid flow in microcirculatory network and interstitium in tumors. *Microvascular research*, 53, 128-141, 1997.