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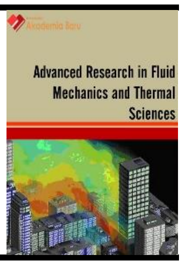

Impact of Excessive Volume of Cerebrospinal Fluid (CSF) Due to Abnormality Morphologies in Brain and Spinal Cord

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ABSTRACT

Cerebrospinal fluid is a colourless fluid produces in the brain in order to protect the brain from the serious injuries. Brain ventricle consist of several parts started from lateral ventricle, interventricular foramen, third ventricle, aqueduct of sylvius, fourth ventricles, lateral aperture and median aperture. Normally, normal person will produce the volume of cerebrospinal fluid approximately about 125 to 150 mL daily. However, volume of cerebrospinal fluid exceeded the daily production limit, causing instability in the human system that is called hydrocephalus condition. Thus, this study aims to understand the flow characteristic of cerebrospinal fluid for both normal and hydrocephalus conditions. Two different models of brain ventricle are modelled; normal and hydrocephalus conditions. Normal condition is analysed as a basis of comparison. Computational Fluid Dynamic (CFD) method is used to solve the complex problem in cerebrospinal fluid. Newtonian and incompressible flow are assumption parameters in modelling. Several fluid parameters namely pressure distribution, velocity distribution, wall shear stress and oscillatory shear index are investigated. The results show that high pressure region is recorded near to brain ventricle wall for hydrocephalus condition which significantly effects the stability of the body. Low velocity region and high flow recirculation are illustrated at the centre of brain ventricle. The high percentage of wall shear stress is demonstrated near to the brain ventricle wall and high oscillatory shear index is also illustrated at the centre of brain ventricle. In conclusion, hydrocephalus condition shows the abnormality of flow characteristic at brain ventricle which will manage to interfere the body stability control.

Keywords:
Cerebrospinal fluid; brain ventricles; production rate; parameter; CFD (computational fluid dynamics); hydrocephalus

1. Introduction

Cerebrospinal Fluid (CSF) is formed within the ventricles by small, delicate tufts of specialized tissue called the choroid plexus. Beginning in the lateral ventricles, CSF flows through two

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passageways into the third ventricle. From the third ventricle it flows down a long, narrow passageway (the aqueduct of Sylvius) into the fourth ventricle [1].

From the fourth ventricle it passes through three small openings (foramina) into the subarachnoid space surrounding the brain and spinal cord. CSF is absorbed through blood vessels over the surface of the brain back into the bloodstream. Some absorption also occurs through the lymphatic system. Once in the bloodstream, it is carried away and filtered by our kidneys and liver in the same way as are our other body fluids [2]. The properties of CSF are illustrated in Table 1. CSF has a Young modulus of tissue within 2100 N/m^2 and 500 N/m^2, fluid density within 1004 to 1007 kg/m^3, fluid viscosity of 10^{-3} Pa, spring elasticity of 8 N/m, brain dampening of 0.35 X 10^{-3} Ns/m, Ependyma density of 1000 kg/m^3, and Reabsorption constant of 1.067 10^{-11} m^3/Pas.

For the production of CSF, the average person produces nearly 500 millilitres (ml) of CSF every 24 hours [3]. Human usually have around 150 ml of CSF present in the system. If human brain produces 500 ml and only have 150 ml present, this means by human producing 3 times more than we need. Under the normal conditions, there is a delicate balance between the amount of CSF that is produced and the rate at which it absorbed. Hydrocephalus occurs when this balance is disrupted [4].

There are several functions of CSF in our brain and spinal cord as shown in Figure 1. The CSF is a core feature of the central nervous system because it provides a medium through which neurotransmitters can diffuse. This must occur for synapse to function. Below explain the functions of the cerebrospinal fluid.

i. Clearing waste: The individual cells use nutrients and excrete waste products; the CSF diffuses these compounds to and from the blood to maintain a proper balance and mitigate toxicity [6].
ii. Buoyancy of the brain: On average, the adults brain weight about 1.36078 kg (3lbs). So, the CSF keeps the brain from crushing blood flow to the deep brain structures by keeping it afloat [7].
iii. Protection of our brain: The CSF provides some protection to our cortex from the skull itself. Violent motions of the head can cause the brain to collide with the skull's also provides some dampering resistance to these forces [8].

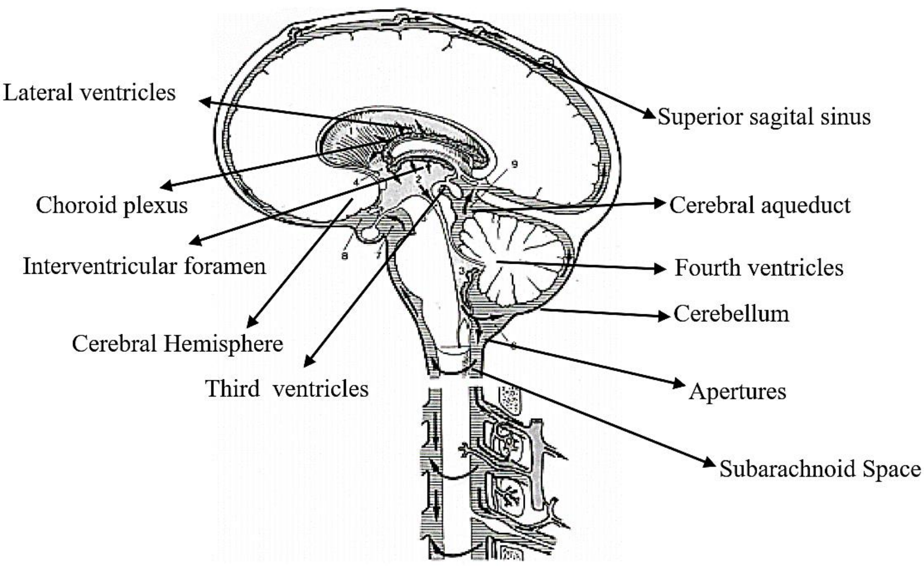

Fig. 1. Cerebrospinal fluid flow in human ventricles system [5]

The central nervous system commonly divided into major structural units, consisting of major physical subdivisions of the brain. The neuroscientists divide the central nervous system into the brain and spinal cord and further divide the brain into regions readily seen by the simplest of dissections. Based on research that has demonstrated that these large spatial elements are derived from independent structures in the developing brain, these subdivisions are well accepted. Human brain is divided into *hindbrain*, *midbrain*, and *forebrain* [9].

Table 1
Properties table for CSF [10]

Property	Value
The measured young modulus of the tissue	2100 N/m^2 3500 N/m^2
Fluid Density, ρ_f	1004-1007 kg/m^3
Fluid viscosity, μ	10^{-3} Pa second
Spring elasticity, k_e	8N/m (normal)
Brain dampening, k_d	0.35×10^{-3} (N second)/m
Ependyma density, ρ_w	1000kg/m^3
Reabsorption constant, κ	1.067×10^{-11} m^3/(Pa second)

The brain and spinal cord are under the central nervous system (CNS). The basic cell in the nervous system is a neuron which is made up of a dendrite, an axon and a cell body. The function of the neuron is for neurotransmission. The function of the brain is to be the control centre of the nervous system. There are three protective membranes/meninges [11].

In the parietal lobes, each lateral ventricle is connected to the third ventricle by channels called interventricular foramina [12]. Lateral ventricle communicates with the third ventricle by foramen of monro (FOM). The third ventricle is a cavity situated below the lateral ventricles between two parts of the thalamus and then it goes through with the fourth ventricles through a canal [13].

1.1 CSF Secretion and Volume

It is estimated to be about 150 ml in adults; distributed about 125 ml in cranial and spinal subarachnoid spaces and 25 ml in the ventricles, but with marked interindividual variations [8]. Abnormally narrow ventricles, described as ‘‘slit ventricles’’, are observed in complex disorders of CSF circulation. Slit ventricles associated with cerebral oedema in patients with a CSF hydrocephalus corresponds to an increased intracranial fluid volume. It is difficult to distinguish from cerebral atrophy, in which passive expansion of CSF spaces compensates for the reduction of brain volume [14]. This is the purposed for active secretion and the absorption of cerebrospinal fluid by the full entire cerebrospinal circulation system. It ignores of the mixing of CSF which is its substantiated by the motile cilia [15].

CSF secretion in adults varies between 400 to 600 ml per day and it depends on the subject and the method used to study CSF secretion [16]. CSF is produced by the choroid plexuses of the lateral ventricles (right and left ventricles), the third and fourth ventricles Choroidal cells present microvilli at their apical pole and are interconnected by tight junctions with a variable distribution according to the site on the ventricular wall [17].

Basically, cerebrospinal fluid is mainly composed by 99% of water with the remaining of 1% that are accounted by proteins, glucose, neurotransmitters and ions [18] Pathology with varies in cerebrospinal fluid characteristics is listed such as the surface tension of cerebrospinal fluid, the concentration of each of proteins and the total viscosity of the cerebrospinal fluid.

The side apical of the epithelium are covered by the microvilli that are beat with motion of the cerebrospinal fluid while the side of basolateral is packed with folds and creases which is increase the cell surface are, it is making it more suited for the absorption [19]. If it compared to the plasma, cerebrospinal fluid contains the higher concentration of sodium chloride, calcium, magnesium and lower concentrations of potassium [20] as shown in Table 2.

Table 2
Range for CSF composition in human body for normal adult [18]

Determination	Normal adult references range	
	Conventional unit	SI Units
Albumin	15-30mg/dL	150-300mg/L
Cell count (white blood cells)	0-5 cells/cu mm	0-5$\times 10^6$/L
Chloride	120-130mEq/L	120-130mmol/L
Glucose	50-75mg/dL, 50%-80% of blood glucose value	2.75-4.13 mmol/L
Glutamine	6-15mg/dL	0.41-1mmol/L
IgG	<5mg	<50mg/L
Lactic Acid	4.5-28.8 mg/dL	0.5-3.2mmol/L
Lactate dehydrogenase	$\frac{1}{10}$ that of serum level	Activity of fraction: 0.1 of serum
Protein	15-45mg/dL	150-450mg/L

1.2 In Silico Analysis in Human Brain Ventricles

There are a few studies conducting in silico modelling in human brain ventricles based on computational fluid dynamic (CFD) associated with the fluid solid interaction (FSI). These studies imposed pulsatile CSF flow in human brain modelling in order to determine the flow characteristic in CSF morphologies [18]. The results showed that the maximum pressure around 1.8 Pa, the displacement was 9m and the velocity was 10mm/s [19].

Chiari *et al.,* reported that modelling on CSF flow in dynamics motion for normal and the subarachnoid space during exertion. 3D flow modelling was performed using CFD method. The geometry was discretized into hexahedral mesh with suitable number of nodes about 0.15mm to 1.25mm. In the other hand, the subarachnoid space, spinal cord and the tonsils were assumed to be a rigid and immobility model boundary representing natural flow condition. The velocity profiles were specified at the model boundaries [20-21].

2. Methodology
2.1 The Geometry of Brain Ventricle

The simplified model of brain ventricle was reconstructed from CT scan images data as illustrated in Figure 2. Figure 2(a) shows the brain ventricular model from front view while Figure 2(b) illustrates the 3-dimensional view of vestibular model from the right side. The vestibular system model was sorted into certain segmentation layer and reconstructed using computer aided design (CAD) software.

The CSF was produced from small components called choroid plexus. Then, the fluid filled the lateral ventricles, interventricular foramen, third ventricle, aqueduct of sylvius (cerebral aqueduct), fourth ventricle, lateral aperture and median aperture.

(a) (b)

Fig. 2. The geometry of brain ventricles (a) front view and (b) right side view

2.2 Governing Equations and Parameter Assumptions

ANSYS CFX 19.2 software (Canonsburg,PA,USA) was used for the simulation. The solver using a vertex centered finite volume method governing equations on a spatially rectangular computational mesh designed in the Cartesian coordinate system with the planes orthogonal to its axes and refined locally at the solid and fluid interface. Additional refining was done for specified cerebrospinal regions, at the brain ventricle surfaces during calculation. The time derivatives are approximated with an implicit second-order accurate in both space and time. Steady state condition is run in order to achieve the convergence for all results. Both velocity inlet and pressure outlet are computed to solve the continuity and Navier-Stokes equations. Hence, the physical laws describing the problem of brain ventricle is the conservation of mass and the conservation of momentum. The flow is governed by the following incompressible Navier-Stokes equation.

$$\frac{\partial p}{\partial t} + \vec{\nabla} \cdot \left(\rho \vec{V}\right) = 0 \tag{1}$$

$$\frac{\partial \rho \vec{V}}{\partial t} + \vec{\nabla} \cdot \left(\rho \vec{V} \cdot \vec{V}\right) = -\vec{\nabla} \rho + \vec{\nabla} \cdot \left(\vec{\vec{\tau}}_{ij}\right) \tag{2}$$

where ρ is the fluid density, P is the static pressure and $\vec{V}$ is the velocity vector.

The solver solves the governing equations with the finite volume method on a spatially rectangular computational mesh designed in the Cartesian coordinate system with the planes orthogonal to its axes and refined locally at the solid and fluid interface.

2.3 Discretization/Meshing

Spatial discretization or meshing divides the geometries into a number of discrete volumetric elements or cells. The temporal discretization divides the solution into discrete time steps. There are various shapes of grids and the meshing used in this study was tetrahedron as illustrated in Figure 3. Then, the boundary zone was also set for the inlet, outlet, wall and the fluid zone in the mesh editor.

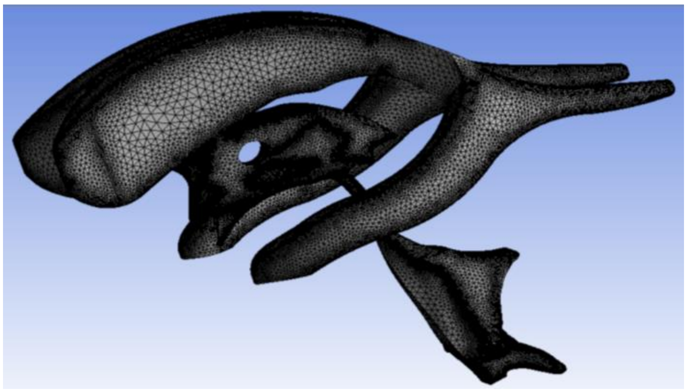

Fig. 3. Mesh generated in tetrahedron shapes for brain ventricles model

2.4 Boundary Conditions

Boundary conditions specified for the flow domain are summarized in Table 3. In this study, the flow was treated as incompressible flow and the inlet and outlet for the CSF flow were at the lateral ventricles and fourth ventricle, respectively. Velocity was set as the inlet boundary and pressure was set as the outlet boundary. The velocity of normal condition was 0.00443 m/s whilst the velocity of hydrocephalus was double of the normal condition at 0.00769m/s. The properties of CSF were assumed as density of 1007 kg/m^3, viscosity of 1x10^{-3} Pa second and temperature was set at 310.15 K.

Table 3
Boundary conditions setup for normal condition and hydrocephalus condition [10]

Internal Cell	Type of fluid that is cerebrospinal fluid
Internal face	Internal pressure
Wall	Symmetry, the periodic ,axis of XYZ and pressure.
Inlet and outlet	Both inlet and outlet part, mass flow rate ,velocity and the pressure
Inlet Velocity	0.00443 m/s (Normal) / 0.00769 m/s (Hydrochepalus)
Inlet Pressure	490 Pa (Normal) / 2889 Pa (Hydrochepalus)
Fluid density	1007 kg / m^3
Fluid viscosity	1×10^{-3} Pa Seconds
Temperature	310.15 Kelvin / 37C°

3. Results and Discussion
3.1 Grid independence study

Grid independence test was performed by using the distribution of velocity to analyse the suitability of the meshing model and to estimate the numerical error in the brain ventricles simulation that been included the normalised relative error. Figure 4 shows the velocity distribution in the brain ventricle model for CSF flow inlet from the lateral ventricles to the outlet of the lateral aperture and median aperture for various element sizes. Details for the meshing element and node are summarized in Table 4. From Figure 4, it can be observed that the velocity trends are similar for Meshing 4 (5mm, 851,402 elements) and Meshing 5 (6mm, 754,034 elements).

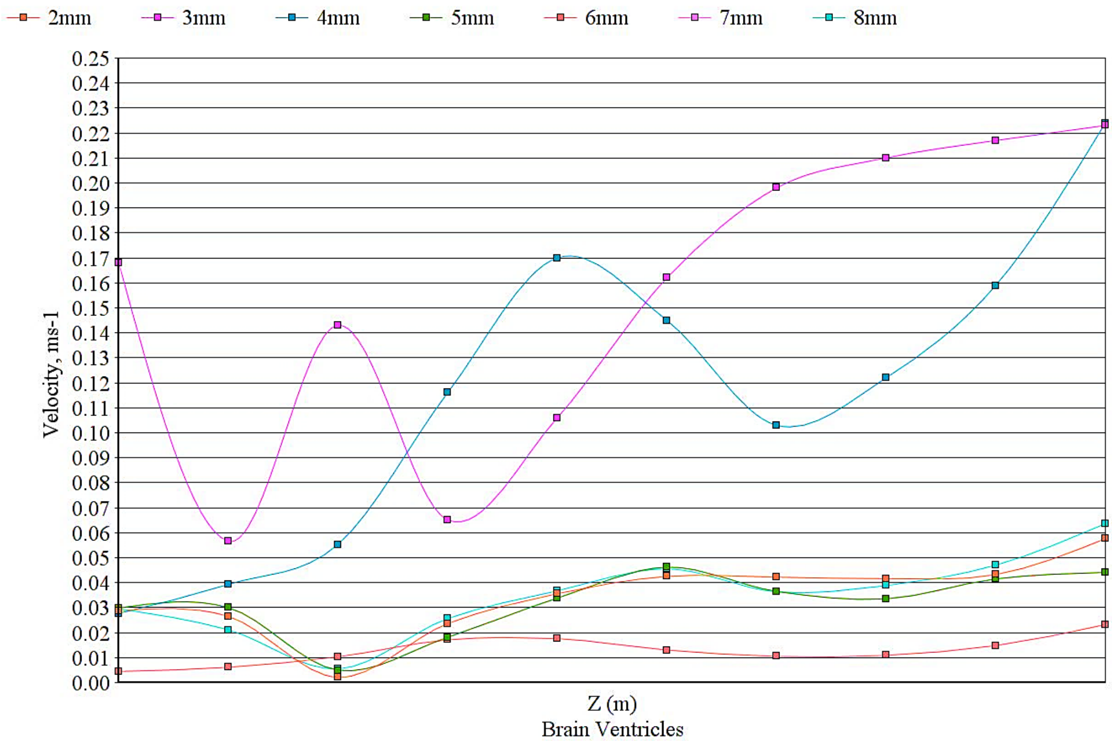

Fig. 4. Velocity distributions in the brain ventricles

Table 4
The number of meshing elements and nodes for different element sizes

Meshing	Element Size	Element	Nodes	Orthogonal Quality
1	2mm	9715348	1854291	0.15487
2	3mm	7662636	1466366	0.14571
3	4mm	6136959	1178387	0.15486
4	5mm	5095805	981477	0.14644
5	6mm	4408774	851402	0.1486
6	7mm	3894226	754034	0.15277
7	8mm	3494335	678005	0.15513

It was found that the suitable number of nodes were within 754k to 851k with element size of 6mm. Thus, a mesh with 851,000 elements was used in this simulation.

3.2 Pressure Distributions
3.2.1 Pressure distribution for normal condition

Figure 5 shows the CSF pressure contour for brain ventricles during normal condition. From Figure 5, it can be observed that the maximum pressure is located at the lateral ventricles and the area of the third ventricle. The maximum pressure 519.04 Pa while the prediction area for minimum pressure occured at lateral aperture and median aperture for 92.17 Pa to 53.37 Pa.

Fig. 5. Brain ventricle pressure contour for normal condition

3.2.2 Pressure distribution for Hydrocephalus condition

Figure 6 shows the pressure distribution for the hydrocephalus condition. From Figure 6, it can be observed that the highest-pressure area occurred at the lateral ventricles. Some parts of the lateral ventricles contributed approximately 2890.65 Pa. The lowest pressure was demonstrated at the fourth ventricle to the lateral aperture and median aperture, which is the outlet for the CSF to the spinal cord. The pressure was recorded to be about 94.80 Pa to 320.818 Pa. In comparison, the pressure distribution between normal condition and hydrocephalus condition is observed to be different especially near to third ventricle.

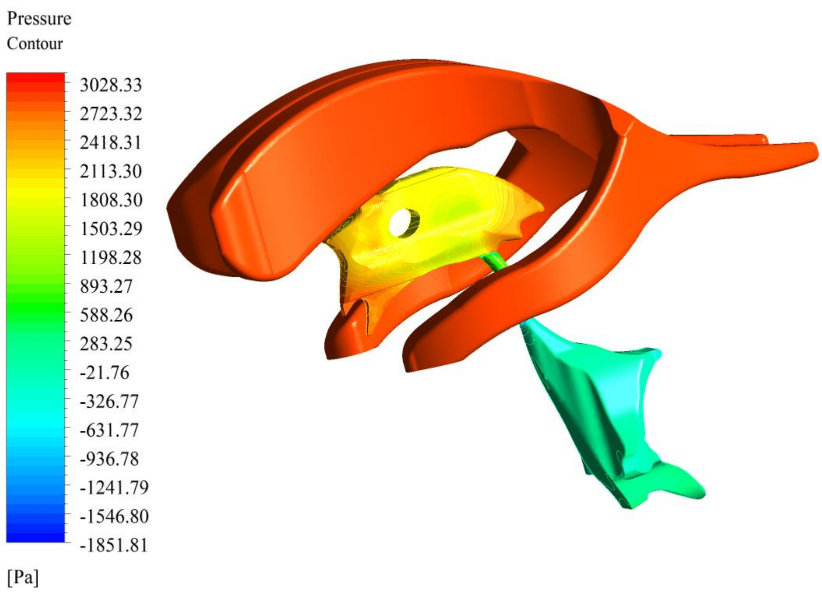

Fig. 6. Brain ventricle pressure contour for hydrocephalus condition

3.3 Wall Shear Stress

Wall shear stress (WSS) is a tangential force generated by the friction by fluid flow in the system. Generally, wall shear stress will increase as the CSF velocity increases. In this study, the value of the WSS was collected for each case simulated for normal condition and hydrocephalus condition.

3.3.1 WSS distribution for normal condition

Figure 7 shows the WSS distribution at brain ventricle for normal condition. The result indicates that the WSS distribution appeared to be similar for the whole brain ventricle model. However, a slightly different distribution can be observed near to interventricular foreman and aqueduct of sylvius. The highest value of WSS was illustrated at the aqueduct of sylvius which contributed approximately 11.5031 Pa and at 9.08056 Pa respectively. The lowest WSS was depicted at the lateral ventricle that contributed about 3.5867 Pa due to the effect of complex geometry of the brain ventricle.

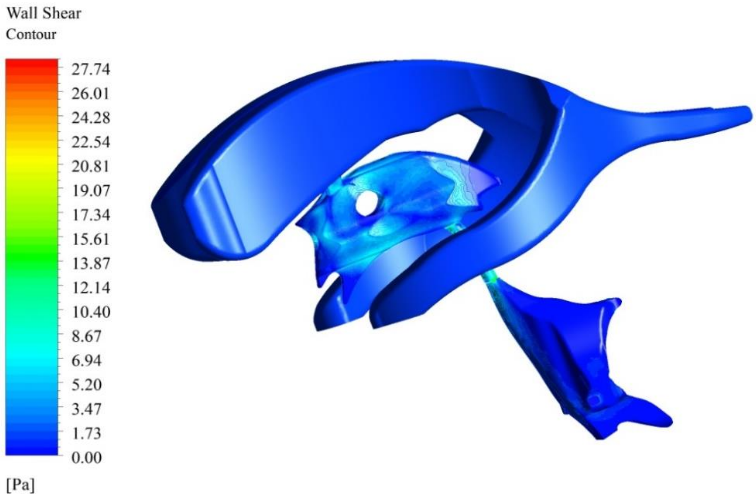

Fig. 7. Wall shear stress distribution at brain ventricle for normal condition

3.3.2 WSS distribution for hydrochepalus condition

Figure 8 shows the wall shear stress distribution at brain ventricle for hydrochepalus condition. The highest wall shear stress value was depicted at the third ventricle that contributed approximately 38.1665 Pa. High activities or flow recirculation was also demonstrated near to the third ventricle.

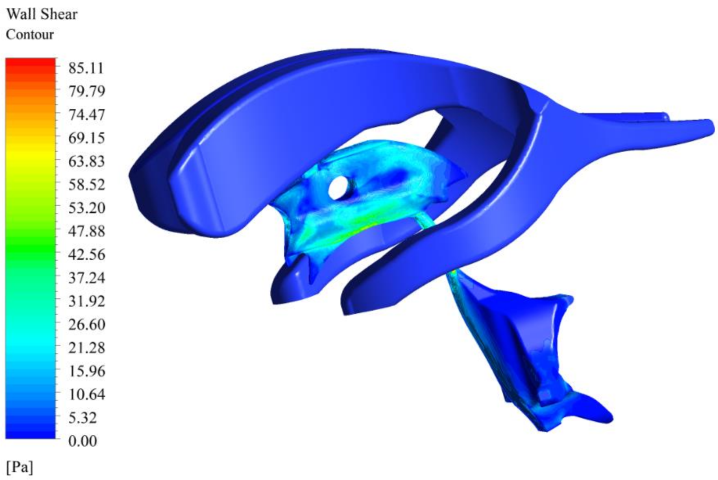

Fig. 8. Wall shear stress distribution at brain ventricle for hydrocephalus condition

3.4 Pressure Profile for Normal and Hydrocephalus Conditions

Figure 9 shows the pressure distribution at different locations in brain ventricular system. Seven different locations which include lateral ventricle, interventricular foreman, third ventricle, aqueduct of sylvius, fourth ventricle, lateral ventricle and median aperture, were investigated. For the normal condition, the highest pressure occured at the lateral ventricle that contributed approximately about 518.35 Pa whilst the lowest pressure occured at the lateral aperture at 15.0035 Pa. For the hydrocephalus condition, the highest pressure occured at the lateral ventricle that contributed about 2890.65 Pa even though the pressure dropped at the third ventricle and the lateral aperture were approximately 1166.84 Pa and 124.098 Pa, respectively.

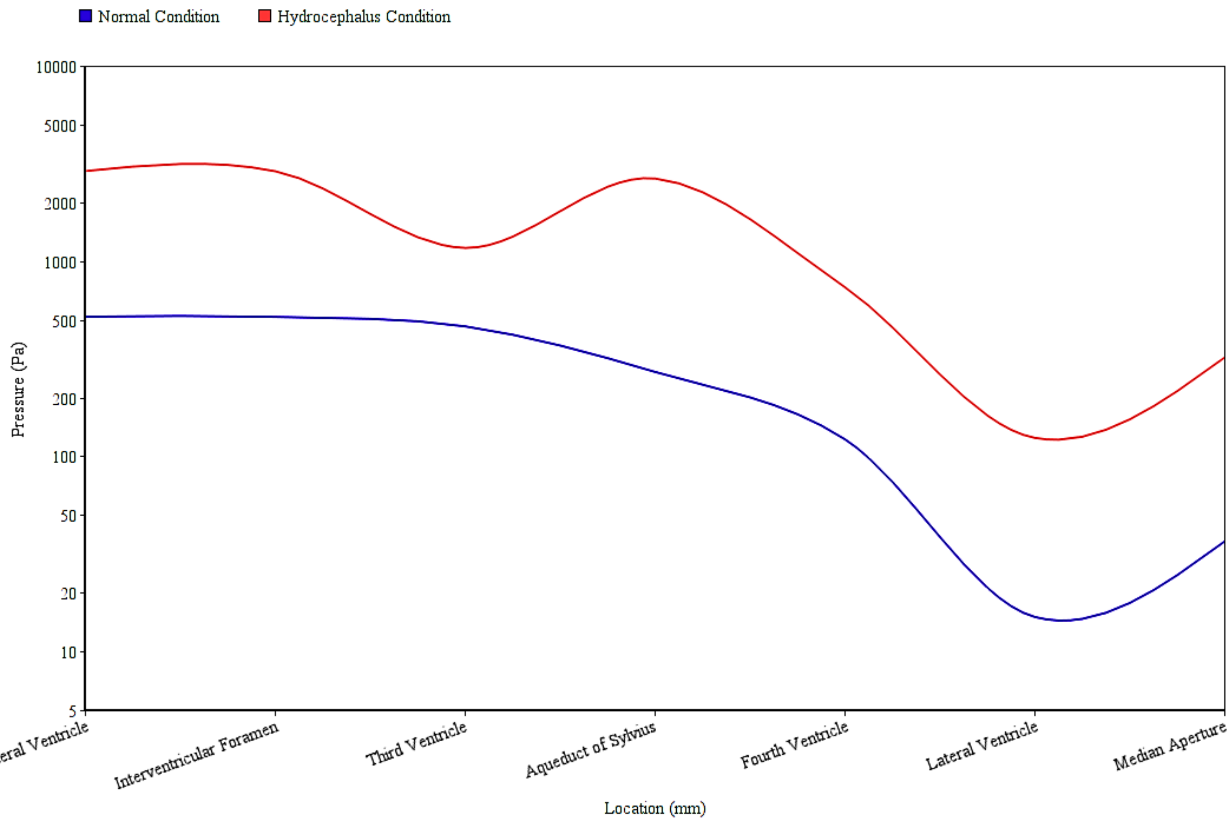

Fig. 9. Pressure distribution at different locations in brain ventricular system

3.5 Velocity Distribution for Normal and Hydrocephalus

Figure 10 shows the velocity profile at different locations in brain ventricle system. In this study, seven locations were identified. From observation, velocity was drastically increased starting from the lateral ventricle to the interventricular foramen and contributed about 0.00555036 m/s to 0.376896 m/s in normal condition. However, the velocity was slightly dropped from 0.679775 m/s to 0.0817163 m/s from the fourth ventricle to the lateral aperture. The different cross-sectional area for each component in brain ventricle system affects the velocity characteristic.

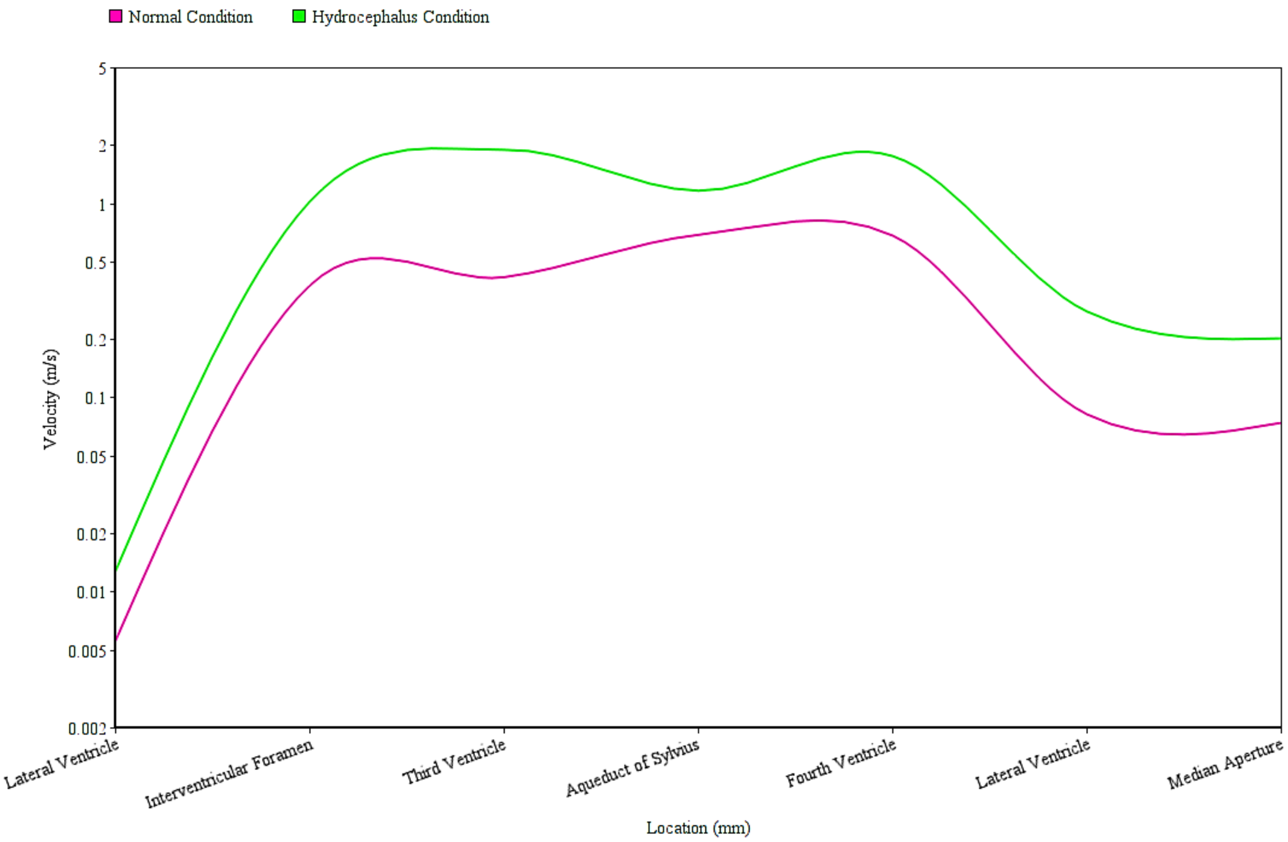

Fig. 10. Velocity profile at different locations in brain ventricle system

3.6 Wall Shear Stress Distribution for Normal and Hydrocephalus

Figure 11 shows the WSS profile at different locations in brain ventricle system. It can be observed that the range of wall shear stress was between 0.4 Pa to 12 Pa for the normal condition. However, the range of wall shear stress for hydrocephalus condition was approximately 3 Pa to 28 Pa.

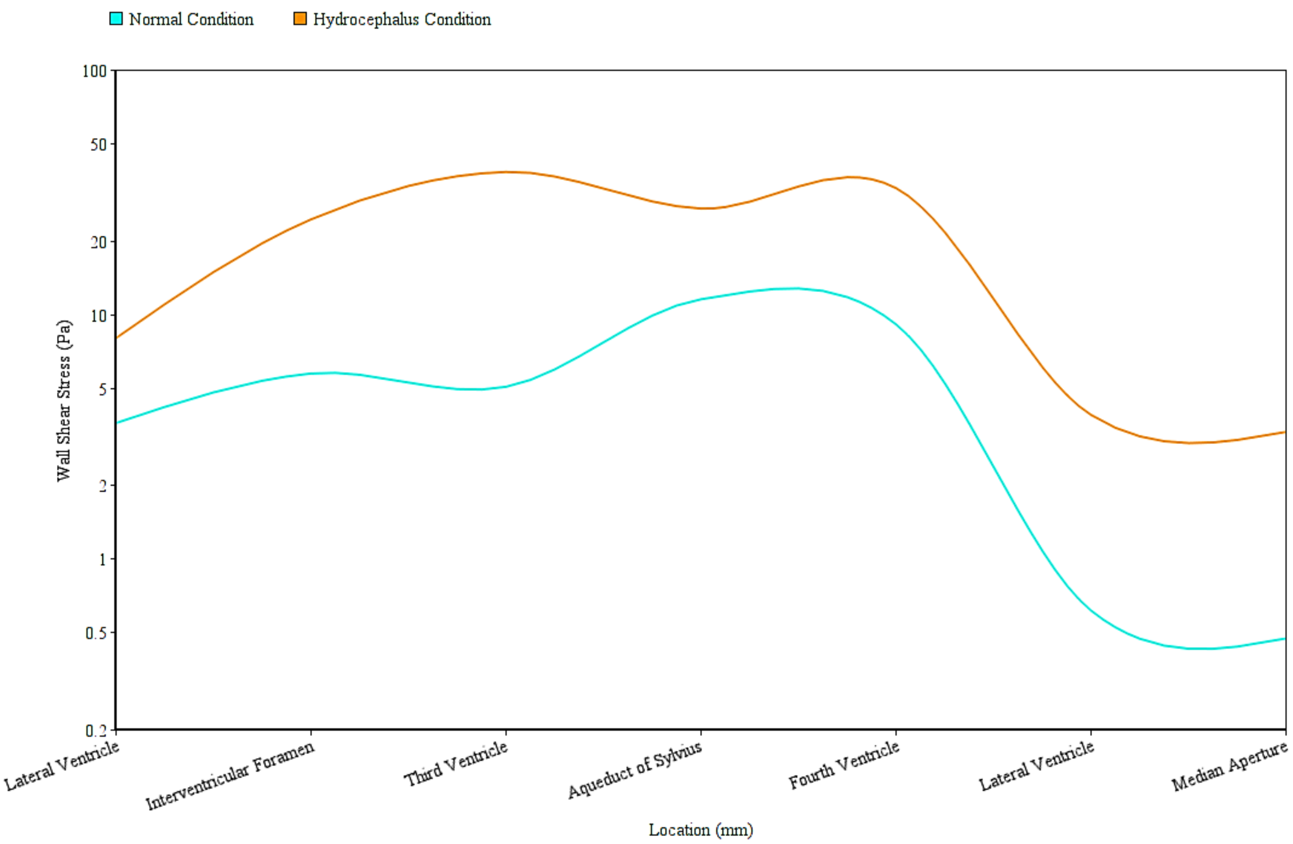

Fig. 11. Wall shear stress profile at different locations in brain ventricle system

4. Summary

In summary, the velocity of the flow increased due the changing of pressure and motion of the fluid. Shearing forces for the fluid cannot be resist when the fluid condition was at rest or moving but the fluid resistance action for shearing forces appeared when the fluid was in motion. The chaotic molecular motion took place when the fluid moving with the different value of velocities.

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