ISSN: 0975-766X
CODEN: IJPTFI
Available Online through
www.ijptonline.com
Research Article

BRAIN TUMOUR AND CEREBRO SPINAL FLUID DYNAMICS

***R. Jagannathan[1] and Shanbkar[2]**
[1]Dept.of. Biomedical Engg, Bharath University, Chennai, Tamilnadu, India.
[2] SRM University, Chennai , Tamilnadu, India.
Email: jaganpatho@yahoo.co.in

Received on 02-09-2013 *Accepted on 24-09-2013*

Abstract

The project aims at understanding the flow dynamics of the cerebrospinal fluid flowing through the tumor affected region and sub-arachnoids space through computational fluid dynamics. This methodology is proposed by using MIMICS software in combinational analysis with ANSYS. This study will be useful to differentiate cancer affected brain from normal brain and can help for surgery planning and other possible chemotherapeutic drug delivery.

Keywords: Brain tumor, CSF, CFD.

Introduction

Brain Tumour

A brain tumor is a group of abnormal cells that grows in or around the brain. Tumors can directly destroy healthy brain cells. They can also indirectly damage healthy cells by crowding other parts of the brain and causing inflammation, brain swelling and pressure within the skull. Brain tumours are either malignant or benign. A malignant tumor, also called brain cancer, grows rapidly and often invades or crowds healthy areas of the brain. Benign brain tumours do not contain cancer cells. They look normal under a microscope and are usually slow growing. Brain tumors fall into two different categories., viz primary or metastatic. Primary brain tumours begin within the brain. A metastatic tumour is formed when cancer cells located elsewhere in the body break away and travel to the brain. For this reason, metastatic brain tumors are almost always malignant, while primary brain tumors may be benign or malignant.

Types of Brain Tumour: Mainly there are three types of classification, The most common types of brain tumors include the following:

Gliomas: The most common type of primary brain tumor is a glioma. Gliomas begin from glial cells, which are the supportive tissue of the brain.

Astrocytomas: Astrocytomas are glial cell tumors that are derived from connective tissue cells called astrocytes. These cells can be found anywhere in the brain or spinal cord.

Cerebro Spinal Fluid

Cerebrospinal fluid is a modified tissue fluid present in the cerebral ventricles, spinal canal and subarachnoid spaces thus bathing the entire nervous system. It acts as a "cushion" or buffer for the cortex, providing a basic mechanical and immunological protection to the brain inside the skull .It is produced in the choroid plexus**.**

CSF is formed at a rate of approximately 500ml/day, which is about three times the volume of fluid in the entire nervous system. Two- third or more of this fluid originates as a secretion from choroids plexus in the fourth ventricle, mainly in the two lateral ventricles. The CSF contains approximately 0.3% plasma proteins, or approximately 15 to 40 mg/dL, depending on sampling site. CSF pressure ranges from 80 to 100 mmH_2O (780–980 Pa or 4.4–7.3 mmHg) in newborns, and < 200 mmH_20 (1.94 kPa) in normal children and adults, with most variations due to coughing or internal compression of jugular veins in the neck

Flow of CSF

Cerebro spinal fluid passes out of the fourth ventricle through three small openings, two lateral foramen of Luschka and a midline foramen of Magendie, entering the cisterna magna, a large fluid space that lies behind the medulla and beneath the cerebellum. The cisterna magna is continuous with the subarachnoid space that surrounds the entire brain and the spinal cord. Almost all CSF then flows upwards from the cisterna magna through the subarachnoid space surrounding the cerebrum. From here the fluid flows into multiple arachnoid villi that project into large sagittal venous sinus and other venous sinuses of the cerebrum. Finally, the fluid empties into the venous blood into the surface of the villi.

Hydrocephalus and Increased Intra Cranial Pressure (ICP)

Presence of tumor in the lateral ventricle and in around the brain tissue affects the flow of CSF which leads to hydrocephalus and Increased Intra Cranial Pressure. Hydrocephalus is of two types**[1]**

(a) Non-communicating - caused by block in the acqueduct of Sylvius, resulting from atresia before birth in many babies or from a tumour at any age.As fluid is formed by the choroid plexus the volume of three ventricles increases greatly [2]. This flattens the brain into a thin shell against the skull. In new born babies the increased pressure also causes the whole head to swell because the skull bone still have not fused.

(b) Communicating - caused by block of fluid flow in subarachnoid space around the basal regions of brain or blockage of arachnoids villi themselves **[4].** Fluid therefore collects both inside the ventricles and outside the brain **[3].** In infants the swelling of head occurs and in older age group the brain is damaged**.** Intracranial pressure (ICP) is the pressure inside the skull and thus in the brain tissue and cerebrospinal fluid (CSF)**[5]**

Cerebro Spinal Fluid Analyis

Presence of brain tumour changes the flow patterns of CSF and thus increase in the intracranial pressure is observed. By analyzing the flow patterns of CSF in normal and abnormal brain, neurosurgeon would be able to understand and to plan the possible surgical treatment. MRI of brain tumour and healthy image was obtained and the CSF flow space was segmented and meshed in MIMICS. Pressure and velocity analysis was performed using Computational Fluid Dynamics (ANSYS). The results were compared.

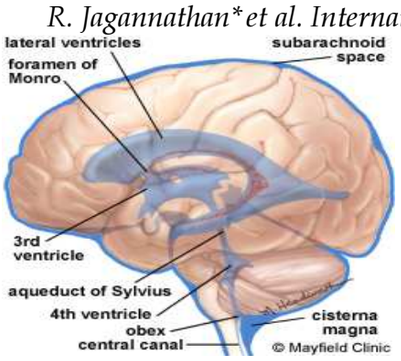

Fig 1- CSF Flow

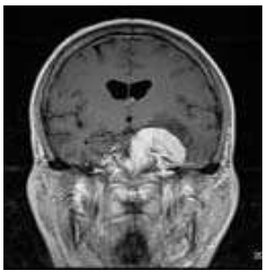

Fig -2 MRI of Brain Tumor

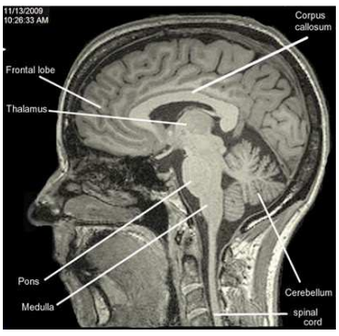

Fig 3- CSF Flow

Materials and Methods

Materials

MRI image of the 72 years old individual's with a history of tumor at the ventricle and another MRI image of healthy individual was obtained from Aarthi Scan(slice thickness =1mm, 0.5mm) **[6],[7],[8].**

Methods

Mimics

MMICS (Materialise's Interactive Medical Image Control System) is the Materialise's software for processing medical images and creating three-dimensional (3D) design and modeling **[9], [10].** Mimics generate and modify surface 3D models from stacked medical images of Computed Tomography (CT) through image segmentation done in the STL file **[11],** A stack of images can be loaded into the software, Mimics consists of images in the XYplane (axial images). Mimics then calculates and creates images in the XZ (coronal) and YZ (sagittal) direction **[12], [13].**

Steps Involved

1. The given MRI data of Brain which has tumor was imported into mimics software.
2. The imported image is viewed in three planes (Axial, coronal, saggital).

3. Using a tool '*THRESHOLDING*' in the segmentation tool bar the mask value for required region of brain is selected by setting minimum and maximum pixel values.
4. The selected region of brain is visible in appropriate color.
5. Using a tool **'***MULTIPLE SLICE EDIT* ***(2D)'*** in the segmentation tool bar the brain tissue is separated from the skull by deleting the contacts between brain tissue and skull at each and every slice.
6. Now using ***'REGION GROWING'*** tool in the segmentation tool bar the separated brain tissue is selected and showed in different color.
7. Then using ***'CALCULATE 3D'*** tool in the segmentation tool bar the 3D model of the separated brain tissue is created and showed in 3D plane of the mimics.

Using the same steps above mentioned brain tumor is segmented and 3D model of brain tumor was created and its dimensions were measured.

Ansys

Analysis can be done in Ansys software. After the fixation ofsuitable implant to the fracture location in mimics, its is necessary to import the data into ansys for further analysis. Different load conditions have to be given to the implant to identify the stability of the implant. The steps to be followed in ANSYS are given below

- Pre-processor :- Generating the model and Creation of geometry.
- Selecting the types of analysis.
- Applying the material properties of bones of hand.
- Boundary conditions applied.
- Load (Applying)
- Mesh.
- Solution stage (whether the datas given as input is right or not).
- Post-process [Boundary Condition, Load].
- Check output [Pressure, Velocity]

Results and Discussion

Here from Mimics software the segmented Brain tumor was recon struted in 3D was displayed.

Dynamics of brains proteins in CSF

The dynamics of brain-derived proteins have been investigated (Reiber, 2011)with reference to the CSF flow rate as reflected by CSF / serum album in concentration quotients. Three different groups can be discriminated: proteins from neurons or glial cells which enter CSF primarily in the ventricular and cisternal space. Their concentration decreases between normal ventricular and lumbar CSF in contrast to blood proteins, and in the case of pathologically decreased CSF flow rate, the concentration in lumbar CSF remains constant.

Brain proteins with primarily leptonmen ingeal origin (e.g. b –trace protein and cystatin C) show an increasing concentration (11-fold for beta trace protein) between normal ventricular and lumbar CSF and, in the case of pathologically decreased CSF flow rate, a linearly increasing concentration in lumbar CSF. The characterization of the ventricular to-lumbar concentration gradient in addition to the CSF –to-blood gradient can yield important information about the source of the protein and the influence of pathophysiological processes **[14].**

The empirical results for brain proteins **[15, 16]** buttress the general reliability of the molecular flux/CSF flow theory as a physiologically correct, biophysically derived concept for the evaluation of brain derived proteins, blood-dervied proteins or proteins with mixed sources in brain, leptomeninges or blood. In particular, the reference to the albumin quotient as a measure of CSF flow rate is important for evaluating and understanding protein concentrations and their change in CSF in health and disease in CSF points to possible metabolic interference **[17, 18].**

This basic information about CSF dynamics including the ventricular /lumbar and CSF /blood gradients also helps to determine whether the absolute concentration (e.g. NSE, S-100, tau protein) or the CSF /serum concentration quotient of a brain protein (e.g. sICAM should be used for most sensitive evaluation.

Disease related data patterns in CSF

Patterns of disease related immune response

The unambiguous value of immunoglobulin patterns for differential diagnosis of neurological diseases has greatly improved the general relevance of CSF analysis compared to earlier reports of single analyte parameters **[22].** It is in particular, the IgA and IgM analyses combined with IgG that have improved the clinical relevance.

Clinical specificity and sensitivity of single data patterns are also critically dependent on the time of puncture during the course of the disease. The onset of clinical symptoms varies from very rapid in bacterial meningitis or a few days for viral meningitis to a delay of 2-3 weeks for subacute tuberculous meningitis **[19, 20].** In conditions such as brain abscess the diagnostic sensitivity varies with the distance of the pathological process from CSF space. The specificity of immunoglobulin patterns increases with the number of complementary data available. In the case of b-trace protein in bacteril morungitis , the Q Alb – independent reduction is seen and this points to a particular influence of the menigeal reaction **[21].** This differential diagnostic context provides discriminative power to the patterns of CSF data sets in general and in particular to the immunoglobulin class response.

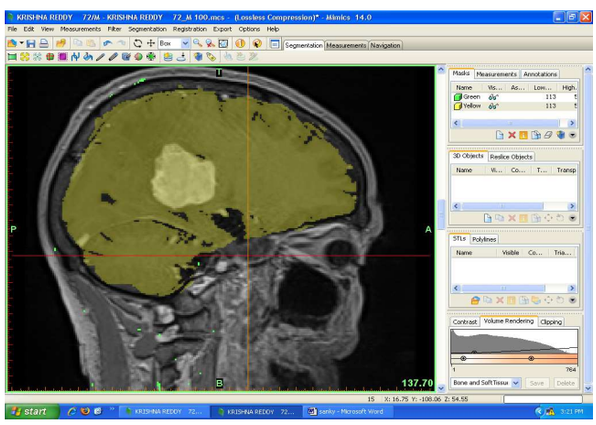

Fig 4: Thresholding and Region Growing.

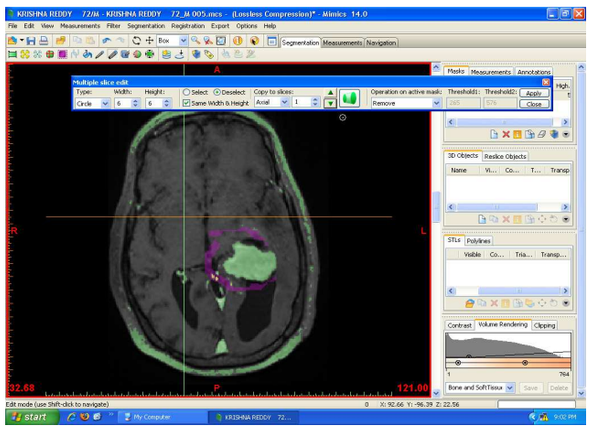

Fig 5: Edit masking

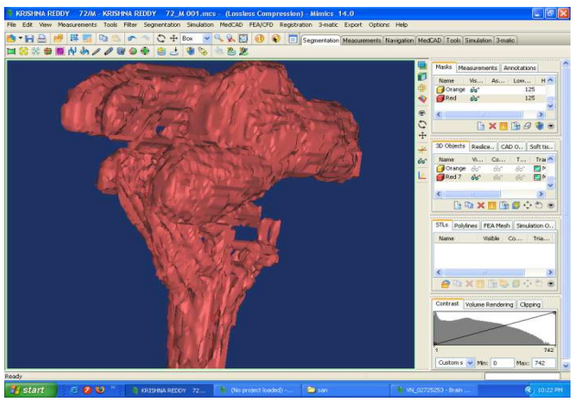

Fig6-3D view of segmented Brain Tumor.

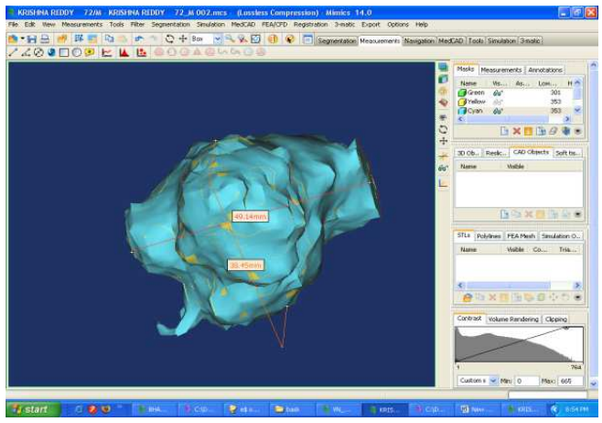

Fig 7: 3D view of segmented CSF flow path (Ventricle).

The segmentation of CSF flow path was done using Mimics software and its flow analysis performed using Ansys Fluent.

Summary and Conclusion

CSF proteins from brain cells

Proteins in CSF which originate from brain cells, like neurons or glial cells, which enter CSF primarily in the ventricular and cistenal spaces show the same dynamic.

- Their concentration is decreasing between normal ventricular and lumbar CSF and
- Their concentration does not vary with pathologically decreasing CSF flow rate, i.e. in cases of a so-called blood – CSF barrier dys-fusnction for blood –derived proteins.
- The first observation, the decreasing rostro caudal gradient, is easily explained by a net diffusion of neuronal and glial proteins from inside /out of CSF on the way downstream. This is due to the inversion of the tissue to CSF concentration gradients CSF spaces. This decreasing concentration of brain –derived proteins is opposite to the steady (non-linear) increase of the concentrations along the rostro-caudal flow way of blood derived proteins in normal CSF.
- The second observation, that protein concentrations in lumbar CSF do not change with decreasing CSF flow rate, i.e., increasing Q_{Alb} be explained by derivation from laws of diffusion and CSF flow. The dynamic of brain proteins fit as a particular linear case into the molecular flux/CSF flow theory. With decreasing CSF flow rate, i.e., reduced

CSF volume turnover, the ventricular CSF concentration is increasing linearly but with increasing CSF concentration there is downstream a larger concentrating gradient for a larger molecular flux inside/out. Both effects compensate each other quantitatively, what keeps the lumbar CSF concentration constant.

CSF proteins from meningeal cells

Proteins like B-trace protein or cystatin C, which originate primarily from leptomeningeal cells, show:

- An increasing concentration between normal ventricular and lumbar CSF.
- A linearly increasing concentration in CSF in case of pathologically decreasing CSF flow rate.
- A particular modification is observed in in-flammatory meningeal processes.

The rostro – caudal increase of B-trace protein and cystatin C concentration under normal conditions are easily understood as a steady release of protein into CSF along its flow path, due to a local outside /in concentration gradient at the border with the subarachnoid space. The B-trace protein concentration is increasing. This larger concentration in lumbar CSF has consequences for the dynamics of B-trace protein in the case of a pathologically reduced CSF flow rate.

The second observation, the linear increase of B-trace protein concentration in lumbar CSF in case of pathologically decreasing CSF flow rate, can be important also from a theoretical point of view. This linear increase, e.g. of B-trace protein or cystatin C concentration, is different from the non-linear hyperbolic function for blood derived proteins in CSF.

It seems beyond any doubt that CSF turnover is the crucial determinant for the concentration of its macromolecular components. The empirical data and their interpretations for clinical purposes refer to a mean turnover rate, which does not not need to take into account the local and temporal fluctuations, including to-and-fro motions of the CSF by cardiac cycles parkola et al 2001 or the circadian rhytms lecities can be very fast due to an aqueduct stenosis but, the absolute values of aqueductal velocities cannot be regarded as representative for the overall CSF turnover rate. This is a limitation of imaging techniques for a correlation with the disease –related change of the albumin quotient.

Acknowledgement

We would like to thank the faculty, Department of Biomedical Engineering Bharath University and, SRM University who extended their helping hand in bringing out my idea into reality. We sincerely thank MATERIALISE, Chennai for their timely help in designing the project.

References

1. Gibbs, P., Buckley, D., Blackb, S., and Horsman, A., .Tumour volume determination from MR images by morphological segmentation,.*Physics in Medicine and Biology* **41**, 2437.2446 (1996).
2. Schmidt, M., *Automatic brain tumor segmentation*, Master's thesis, Univ. of Alberta (2005).
3. Gering, D., *Recognizing Deviations from Normalcy for Brain Tumor Segmentation*, PhD thesis, MIT (2003).

4. Lee, C.-H., Schmidt, M., Murtha, A., Biaritz, A., Sander, J., and Greiner, R., .Segmenting brain tumors with conditional random_elds and support vector machines,. in [*Workshop on CVBIA at ICCV*], (2005).
5. Corso, J. J., Sharon, E., Dube, S., El-Saden, S., Sinha, U., and Yuille, A., .Ef_cient multilevel brain tumor segmentation with integrated bayesian model classi_cation, *Medical Imaging, IEEE Transactions on* **27**(5), 629.640 (2008).
6. Neculai, A., Ferenc, A. J., and Simon, K.W., .A validation framework for brain tumor segmentation,. *Academic Radiology* **14 (10)** (October 2007).
7. Cobzas, D., Birkbeck, N., Schmidt, M., and Jagersand, M., .3d variational brain tumor segmentation using a high dimensional feature set,. in [*MMBIA in conjunction with ICCV*], (2007).
8. Liu, J., Chelberg, D., Smith, C., and Chebrolu, H., .Distribution-based level set segmentation for brain mr images,. in [*BMVC07*], (2007).
9. Liu, J., Udupa, J., Odhner, D., Hackney, D., and Moonis, G., A system for brain tumor volume estimation via mr imaging andfuzzy connectedness.,. *Comput. Medical Imaging Graph.* **21**(9), 21.34 (2005).
10. Prastawa, M., Bullitt, E., Ho, S., and Gerig, G., .A brain tumor segmentation framework based on outlier detection.,. *Med ImageAnal* **8**, 275.283 (September 2004).
11. Chan, T. and Vese, L., .Active contours without edges,. *IEEE Trans. Image Processing* **10(2)**, 266.277 (2001).
12. Rousson, M., Brox, T., and Deriche, R., .Active unsupervised texture segmentation on a diffusion based feature space,. in [*CVPR*], (2003).
13. Cremers, D., Fluck, O., Rousson, M., and Aharon, S., .A probabilistic level set formulation for interactive organ segmentation, in[*Proc. of the SPIE Med. Imaging*], (2007).
14. http//www.radiologyinfo.org/en/photocat/gallery3.cfm
15. Reiber H. Flow rate of cerebrospinal fluid (CSF) a concept common to normal blood –CSF barrier function and to dys-function in neurological diseases. J. Neurol Sci 1994, 122: 189-203.
16. Reiber H. Biophysics of protein diffusion from blood into CSF the modulation by CSF flow rate. In Greenwood J. Begley D, Segal M, editor's new concepts of a blood –brain barrier. New York Plenum; 1995p. 219-27.
17. Parkkola R.K., Komu MES, Aanman TM, Alanen MS. Thomsen C, Cerebrospinal fluid flow in children with normal and dilated ventricles studied by MR imaging Acta Radiol 2001, 4233-8.
18. Reiber H. Dynamics of brain proteins in cerebrospinal fluid Clin Chim Acta, 2001, submitted.
19. Felgenhauer K. Laboratory diagnosis of neurological diseases. In Thomas L. eidotr, Clinical laboratory diagnostics – use and assessment of clinical laboratory results, Frankfurt TH Books. 1998,pp 1308-26.
20. Felgenhance K, Beucher W, editors, Labordiagnostik N eurologischer Erkrankungen, Stuttgart: Thiene, 1999.

Corresponding Author:

R. Jagannathan*,

Email: *jaganpatho@yahoo.co.in*