

CSF Physiology and its Relationship to Intracranial Pressure

Target audience: Physicians and scientists interested in implementing CSF flow protocols into their clinical or research practice, in particular those interested in quantitative methods for accurately quantifying CSF flow in hydrocephalus, Chiari and other patients.

Background: The intracranial compartment is a very unique biomechanical environment, due to both its enclosure within a closed container, i.e. the skull, and the tight control of protein/solute transport maintained by the blood brain barrier [1]. This environment dictates the need for the proper maintenance of intracranial pressure (ICP) and fluid flow in order to preserve fluid balance and transport. In this respect, cerebrospinal fluid (CSF) plays a number of important roles within the brain, particularly in the brain fluid homeostasis, the delivery of nutrients to brain tissue and the removal of cell metabolism waste products. All of these functions are critically dependent on the proper flow of CSF from its sites of production, mainly within the ventricular system, to the absorption sites, primarily via the arachnoid villi and the nasal lymphatics.

While this bulk flow of CSF through the intracranial system is important for maintaining normal pressure, flow and CSF turn-over, there is another component to the flow which is unique to intracranial fluid dynamics. Approximately once a second, shortly following cardiac systole, a pulse of arterial blood enters the cranium. While pulsatile arterial blood flow exists everywhere in the body, this pulse is quickly dissipated as it is transmitted down the vascular tree. By the time the pulse reaches the capillary bed, it has been completely dissipated, resulting in smooth capillary and venous flow; this is facilitated by the transfer of the pulse wave into the surrounding compliant tissue. Because of the unique biomechanical environment of the cranium, however, dissipation of the arterial pulse wave is more complex. In this case, the pulse wave is transferred into the fluids surrounding the incoming arteries, i.e. the CSF within the subarachnoid spaces [2]. Part of the pulse wave reaches the deeper tissue and is transferred into the brain tissue, ultimately being transmitted into the CSF-filled ventricles and subarachnoid spaces. In turn, the CSF dissipates the pulse wave by transmitting it either into the venous system, or into the compliant subarachnoid spaces of the spine, where the pulse waves are transmitted into the surrounding tissues. While it has yet to be determined if this component of CSF flow has important physiological effects on overall CSF turn-over and drainage, the pulsatile motion of CSF within the brain has the effect of enhancing fluid mixing within the CSF spaces [3], and the rapid transport of tracer out of the CSF compartments are difficult to explain based on bulk drainage alone [4].

Methods and results: CSF flow can be measured accurately in vivo, primarily at the cerebral aqueduct and the craniocervical junction, using low velocity sensitivity cine phase contrast sequences [5-8]. We will discuss the techniques used for quantification of bulk and pulsatile CSF flow, as well as the potential issues related to sequence parameters, analysis software and appropriate outcome measures which can affect comparisons of CSF flow measurements across sites and between MRI vendors. We will also address the issues which need to be considered in applying phase contrast sequences for measuring bulk CSF flow rates, where flow velocities are much lower with an increased potential for errors [9, 10]. These techniques have been particularly important in hydrocephalus and Chiari malformations, because of the affect of these disorders on fluid balance in the brain. We will review the findings of studies using

CSF flow measures, both as a diagnostic tool as well as for prediction of outcome from surgical interventions. Other MRI techniques capable of visualizing CSF motion, such as spatial labeling sequences, will also be discussed as potential adjuncts for providing additional functional information about the normal and pathological CSF flow patterns within the ventricles and subarachnoid spaces [11].

In addition to the importance of CSF pulsatility in disorders involving fluid imbalance in the brain, intracranial compliance has more recently been shown to be another important parameter, as a direct consequence of the closed intracranial environment. Compliance is the change in pressure of a system for a given change in volume, and reflects the ability of the brain to respond to changes in fluid balance, such as might occur in acute hydrocephalus or during a shunt failure. We will review the methods for measuring intracranial compliance in vivo; cine phase contrast techniques (which will be reviewed more extensively in the talk by Dr. Alperin in this session) can provide a global measure of compliance [12, 13], whereas MR Elastography can offer whole brain, localized measures of changes in brain tissue stiffness [14-16].

Conclusions: Bulk and pulsatile CSF flow are altered in diseases such as hydrocephalus and Chiari malformation, and are critically tied to alterations in intracranial pressure. At the end of this talk, participants will have an increased understanding of the changes in CSF flow seen in these diseases, how they relate to changes in intracranial pressure and how to implement the sequence and analysis techniques needed for accurate CSF flow quantification.

References

1. Fenstermacher, J.D., *Volume regulation of the central nervous system*, in *Edema*, N.C. Staub and A.E. Taylor, Editors. 1984, Raven Press: New York, NY. p. 383-404.
2. Wagshul, M.E., P.K. Eide, and J.R. Madsen, *The pulsating brain: A review of experimental and clinical studies of intracranial pulsatility*. *Fluids Barriers CNS*, 2011. **8**(1): p. 5.
3. Vladojevic, A., M. Klarica, and M. Bulat, *Dynamics of distribution of 3H-inulin between the cerebrospinal fluid compartments*. *Brain Res*, 2009. **1248**: p. 127-35.
4. Rennels, M.L., O.R. Blaumanis, and P.A. Grady, *Rapid solute transport throughout the brain via paravascular fluid pathways*. *Adv Neurol*, 1990. **52**: p. 431-9.
5. Enzmann, D.R. and N.J. Pelc, *Normal flow patterns of intracranial and spinal cerebrospinal fluid defined with phase-contrast cine MR imaging*. *Radiology*, 1991. **178**(2): p. 467-74.
6. Bradley, W.G., Jr., et al., *Normal-pressure hydrocephalus: evaluation with cerebrospinal fluid flow measurements at MR imaging*. *Radiology*, 1996. **198**(2): p. 523-9.
7. Luetmer, P.H., et al., *Measurement of cerebrospinal fluid flow at the cerebral aqueduct by use of phase-contrast magnetic resonance imaging: technique validation and utility in diagnosing idiopathic normal pressure hydrocephalus*. *Neurosurgery*, 2002. **50**(3): p. 534-43; discussion 543-4.
8. Wagshul, M.E., et al., *Amplitude and phase of cerebrospinal fluid pulsations: experimental studies and review of the literature*. *J Neurosurg*, 2006. **104**(5): p. 810-9.
9. Bateman, G.A. and K.M. Brown, *The measurement of CSF flow through the aqueduct in normal and hydrocephalic children: from where does it come, to where does it go?* *Childs Nerv Syst*, 2012. **28**(1): p. 55-63.
10. Gideon, P., et al., *Cerebrospinal fluid flow and production in patients with normal pressure hydrocephalus studied by MRI*. *Neuroradiology*, 1994. **36**(3): p. 210-5.
11. Yamada, S., et al., *Visualization of cerebrospinal fluid movement with spin labeling at MR imaging: preliminary results in normal and pathophysiologic conditions*. *Radiology*, 2008. **249**(2): p. 644-52.
12. Alperin, N.J., et al., *MR-Intracranial pressure (ICP): a method to measure intracranial elastance and pressure noninvasively by means of MR imaging: baboon and human study*. *Radiology*, 2000. **217**(3): p. 877-85.
13. Glick, R.P., et al., *Early experience from the application of a noninvasive magnetic resonance imaging-based measurement of intracranial pressure in hydrocephalus*. *Neurosurgery*, 2006. **59**(5): p. 1052-60; discussion 1060-1.
14. Mariappan, Y.K., K.J. Glaser, and R.L. Ehman, *Magnetic resonance elastography: a review*. *Clin Anat*, 2010. **23**(5): p. 497-511.

15. Freimann, F.B., et al., *Alteration of brain viscoelasticity after shunt treatment in normal pressure hydrocephalus*. *Neuroradiology*, 2011.
16. Streitberger, K.J., et al., *In vivo viscoelastic properties of the brain in normal pressure hydrocephalus*. *NMR Biomed*, 2011. **24**(4): p. 385–392.