Tina Memo No. 2015-003
Internal.

# A Review of Electrical Equivalence Models for the Evaluation of Intracranial Pulsatility.

W. Hartley.

Last updated[1]
16 / 3 / 2015


Imaging Science and Biomedical Engineering Division,
Medical School, University of Manchester,
Stopford Building, Oxford Road,
Manchester, M13 9PT.

[1]Supervisors: A.Jackson, N.A.Thacker.

# A Review of Electrical Equivalence Models for the Evaluation of Intracranial Pulsatility.

Wayne Hartley. 16/03/2015

## Abstract

*Arterial blood entering the rigid skull is pulsatile. The brain requires a homeostatic environment, and a number of disease processes are now being linked to excessive pulsatility in the brain. Given this fact there must be some mechanism in normal brains for diverting the pulsatility away from the brain, providing a smooth flow of blood. Any such system would be constrained by the Monro-Kellie doctrine, which tells us that the sum of volumes entering the rigid skull must equal the sum of volumes exiting the rigid skull for all instances of time. A further constraint exists whereby the normal brain is considered to be of constant volume. Consequently, the sum of the blood and cerebrospinal fluid (CSF) volumes in the skull is constant at any given time. Since the venous outflow does not exactly match the arterial inflow at all times, this must be compensated for by bulk movement of CSF from the skull. The production and absorption mechanisms of CSF are far too slow to be responsible for this. Fortunately there exists a compliant spinal subarachnoid space which is able to accommodate the superfluous CSF, during systole, and return it during diastole. It may be possible for the exact nature of the intracranial fluid dynamics to be described quantitatively via modelling with an equivalent electrical circuit. In this document we describe the relevant biological structures and discuss this possibility.*

## The Anatomy of the Ventricular System

The ventricular system (Fig.1) consists of four ventricles; two lateral ventricles, between and below which sits the third ventricle, which is connected by the cerebral aqueduct to the fourth ventricle [1].

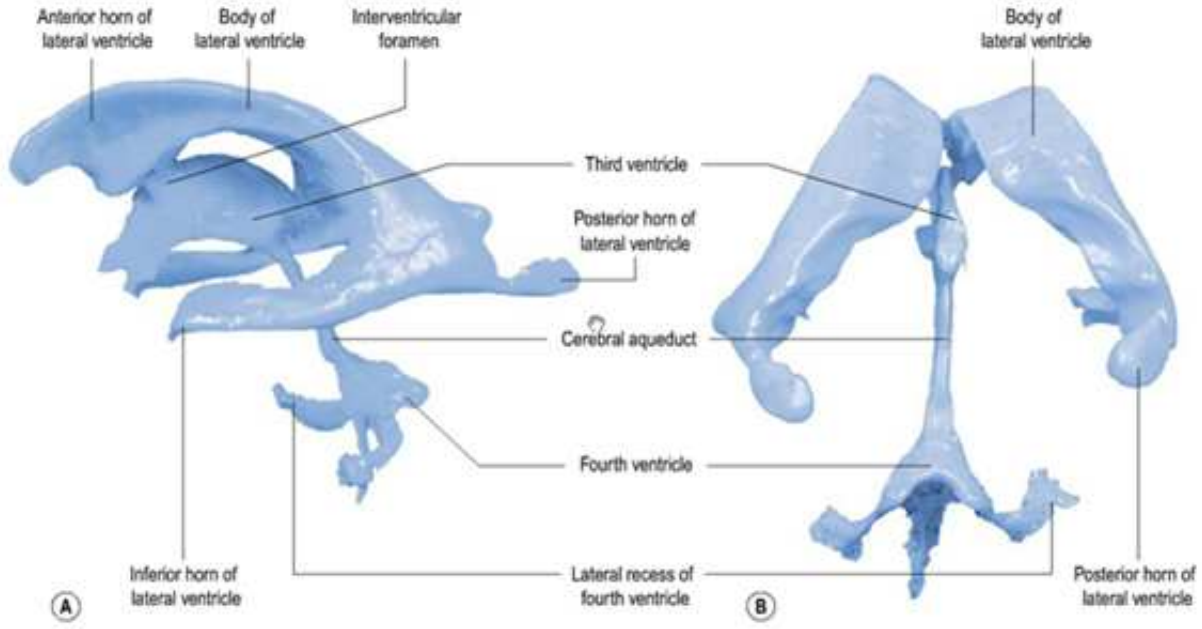


Figure 1: *A) Anterior view of the ventricular system B) Posterior view of the ventricular system.*

Each of the lateral ventricles sits in one of the cerebral hemispheres such that they become mirror images of one another. They form a shape that approximates the letter C, but with a tail, as if it was to be joined up to a previous letter. They are virtually independent, but a connection exists between them, known as the interventricular foramen, which also connects the lateral ventricles to the third ventricle. The third ventricle is thin in one dimension so as to slot in between the two cerebral hemispheres, but has a relatively large area in the other two dimensions. A tubular structure with diameter approximately equal to the thickness of the

third ventricle, known as the cerebral aqueduct links the third and fourth ventricles. The fourth ventricle then widens out, followed by a thinning, creating a diamond-like shape. The fourth ventricle has three openings; two lateral (foramen of Luschka), and one median (foramen of Magendie), which connect the ventricular system to the subarachnoid space. The subarachnoid space is the space between the pia matter and the arachnoid matter, which are connected, and separated by pillar-like structures known as trabeculae. The trabeculae would not be able to maintain this separation if it wasn't for the fact that this space is filled with CSF. The CSF is produced by the choroid plexus throughout the ventricular system, with the majority being formed in the lateral ventricles. CSF flows from the lateral ventricles, through the third ventricle, cerebral aqueduct, and fourth ventricle, into the subarachnoid space, where it is absorbed. It is thought that the principal absorption mechanism is thorough the arachnoid villi in the superior sagittal sinus. Creation and absorption of CSF is in equilibrium such that approximately 150ml of CSF is present in the cerebrospinal system at any given time.

## Arterial inflow and Venous Outflow

The blood flow into the brain can be split into posterior and anterior components. The anterior component is fed by the internal carotid arteries, and as such is known as the internal carotid system. The posterior component is fed by the vertebral arteries, which combines to create the basilar artery, and as such is known as the vertebrobasilar system. Both systems supply structures other than the brain, but these are not of present concern. What is of concern is the fact that the vast majority of the arterial network lies within the subarachnoid space between the pia matter, and the arachnoid matter. This subarachnoid CSF provides a means of transferring pressure from the blood vessels to the CSF and vice-versa.

The carotid arteries rise through each side of the neck, lateral to the trachea, giving rise to the carotid pulse, and enter the skull through the middle fossa. Once in the skull, the internal carotid follows a series of bends known as the carotid syphon whose function, it seems, is to reduce pulsatility and pressure to some degree before supplying the brain. Each internal carotid artery then splits into two: the anterior carotid artery, and the middle carotid artery. The anterior carotid arteries travel along the great lateral fissure, with one on either side of the falx cerebri, feeding the inside portion of the frontal lobes of the corresponding cerebral hemisphere. Should one side be obstructed in some way, there exists a communicating artery, which can facilitate a limited compensation mechanism. The middle carotid arteries branch out over the cerebral hemispheres, feeding the outer portions of the frontal, parietal, and temporal lobes.

The vertebral arteries (fig.2) rise through the spinal column, and enter the skull through the foramen magnum. The vertebral arties give rise to the posterior inferior cerebellar arteries, feeding the lower part of the cerebellum. The vertebral arteries then fuse together, forming a single basilar artery. This gives rise to the anterior inferior cerebellar arteries and the superior cerebellar arteries. The basilar artery also supplies the medulla, pons, and midbrain directly. The basilar artery finally branches out forming the posterior cerebral arteries which feed the occipital lobe, as well as part of the temporal lobe. The posterior cerebral arteries also branch out to form the posterior communicating arteries, which connect to the ends of the middle cerebral, and internal carotid arteries. The size of these communicating arteries varies greatly between individuals. The communication between the carotid system, and vertebrobasilar system is limited the size of the communicating arteries.

The circle of Willis (fig.2) is formed at the termination of the internal carotid and vertebrobasilar systems in order to connect these through communicating arteries. The principal being that the pressure at each entrance should be approximately equal following perfusion. A reduction in flow to one of the entrances would cause a reduction in pressure here. This would allow flow out of that entrance which would supply areas which failed to sufficiently perfuse. In fact the circle of Willis is commonly incompletely formed.

The brain is drained by deep veins and superficial veins. The deep veins penetrate the brain and drain from within, whereas the superficial veins spread across the surface of the brain in the subarachnoid space. All of the veins drain into dural venous sinuses, which are formed where the two, normally fused dura matter layers, open up to form channels for venous drainage. The largest of the dural venous sinuses is the superior sagittal sinus, into which the superior cerebral veins empty. The dural venous sinuses are interconnected, and eventually drain into the jugular vein in order to release the blood from the skull. Dura matter is extremely tough, and as such the sinuses are protected from the flow dynamics within the intracranial system. Some of the sinuses such as the superior sagittal sinus (fig.3) are connected to the intracranial pressure system through arachnoid villi which have thin membranes, and penetrate into the sinus.

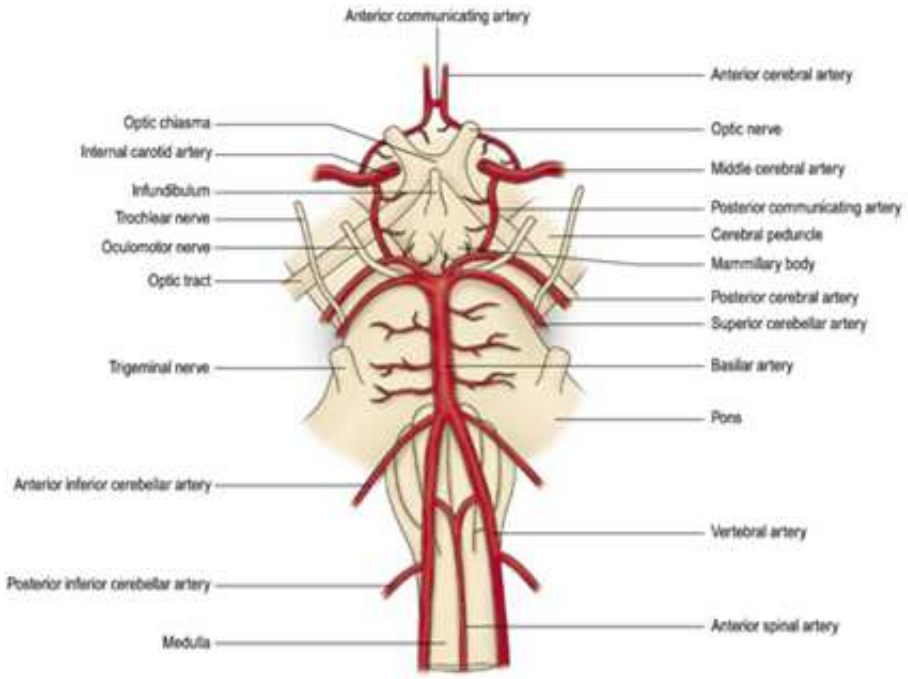


Figure 2: *The vertebrobasilar network and circle of Willis.*

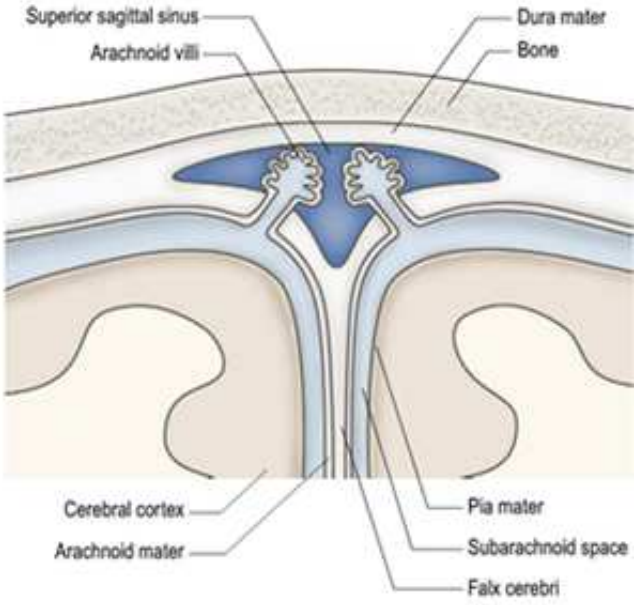


Figure 3: *Slice perpendicular to the superior sagittal sinus showing the arachnoid villi responsible for the communication of pressure with the subarachnoid space.*

## Monro-Kellie

In 1783 Alexander Monro reasoned that because the brain is essentially incompressible, and is encased in a rigid skull, so that the rate at which additional volume entering the skull must be compensated by an exit of volume at an equal rate [2]. He stated that the sum of bloodflow in and any volume produced by the blood vessels, is equal to the bloodflow out. He continued to convey the fact that this does not negate features such as pulsatility. This of course presupposed that blood is incompressible at pressures within the skull.

Roughly 40 years later during a double autopsy George Kellie found 3-4 ounces of fluid outside of the blood vessels in the skull [3]. He assumed that this was the cause of death. His colleague, Mr Cheyne was convinced that the

brain must have lost a mass equal to this volume following from the hypothesis put forward by Monro. Having inferred a time period for this process of a few hours, Kellie reasoned that losing this amount of brain volume in such a short time is unrealistic, hypothesising that instead, the volume of blood within the skull must have reduced by this amount. Although based on an incorrect assumption, and not actually adding anything to the original hypothesis, which did in fact, state that the outflow must be equal to the sum of all contributions of inflow, this hypothesis became widely recognised as the Monro-Kellie doctrine.

Blood is delivered to the rigid skull in a pulsatile nature, and as such it must follow the Monro-Kellie doctrine, that the outflow of blood must be pulsatile in the same way. In doing so the flow characteristics of the jugular vein must differ to the other veins in the body which exhibit continuous flow. This pulsatile nature has indeed been observed in the jugular vein.

If the arteries were continuous with the veins this would be trivial, but there is a brain between them to feed, and to drain. This is done through a network of capillaries of varying length, and path direction. For such a network to transfer the pulsatile profile from the arteries to the veins perfectly, with no phase shift, would be unlikely in itself. Furthermore, the relative perfusion to different areas of the brain is known to differ according to the metabolic demand for a given task. Combining these factors, with the fact that increased pulsatility in the brain has been linked with a number of pathologies, it becomes obvious that the inflow matching the outflow must be achieved in some other way.

## Dissipation of the Arterial Pulse

In his 1925 lecture on The third circulation and its channels Harvey Cushing accredited Francois Magendie with having pioneered research pertaining to the understanding of CSF and the role it plays in the intracranial system [4]. In this lecture he presents a circulatory diagram (fig.4) which demonstrates a flow, being driven by the inflow of the arteries, which circulates the ventricle system, the spinal subarachnoid space, and the cranial subarachnoid space, and adds drive to the venous outflow. It is the compliant spinal subarachnoid space that accounts for the fact that arterial flow is greater than venous flow during systole, with the opposite being true during diastole [5]. This diagram still holds true, but the theory has been refined through additional observations, and the creation of quantitative models. It is now believed that the arterial inflow is pulsatile, and that during systole, an inflow resistance at the surface of the brain facilitates the swelling of the arteries which expand into previously occupied by the CSF. This forces a displacement of the CSF which principally leaves the rigid skull to enter the compliant spinal subarachnoid space. A portion of the displaced CSF also compresses superficial veins, and expands the arachnoid villi. It has also been suggested that compliance discontinuities can result in a partial reflection of the pressure wave, and that this may help reduce the pulsatility entering the brain [6].

## How to study intracranial Pulsatility

Forming an understanding of intracranial pressure dynamics is thought to be of such importance that it has led the use of highly invasive data collection modalities such as the use of implantable pressure sensors [7]. The use of such modalities introduces considerable risks, and they lack the temporal resolution to accurately assess the pressure dynamics over a cardiac cycle. For these reasons non-invasive modalities such as ultrasound and magnetic resonance imaging (MRI) are understandably preferable, even though they measure flow rather than pressure. MRI has become the modality of choice due to the fact that ultrasound techniques are presently too insensitive to provide a useful clinical tool, as well as the fact that data collection is considerably operator dependent, and PET involves the administration of ionising radiation [8] [9].

The major compromise with MRI is image quality against scan time. When imaging a large volume, acquiring thin slices, using small fields of view are impractical. Further to this, the move to higher field strengths has provided a number of additional artefact problems to arise, as well as the requirement of energy absorption and tissue heating having to be taken into account [10] [11]. For these reasons it is useful to examine small volumes which may infer information about the whole intracranial system. Techniques such as angiography using phase contrast MRI (PC-MRI) have enabled the direct measurement of the flow, and hence the corresponding pulsatility of that flow [12]. This is achieved by applying a gradient pulse to a selected slice, followed by its exact negative. The effect of these pulses are additive, and as such the phase of a given volume of known tissue following this is relative to the velocity, with the two gradients cancelling for stationary tissues. In order to obtain a set of velocities, these gradients must be set such that the magnitude of the phase shift due to the maximum velocity to be measured cannot exceed pi, since a velocity corresponding to a phase shift of 3/2 would be indistinguishable from a velocity in the opposite direction of pi/2, or of a velocity in the same direction corresponding to a phase shift of 5pi/2. If

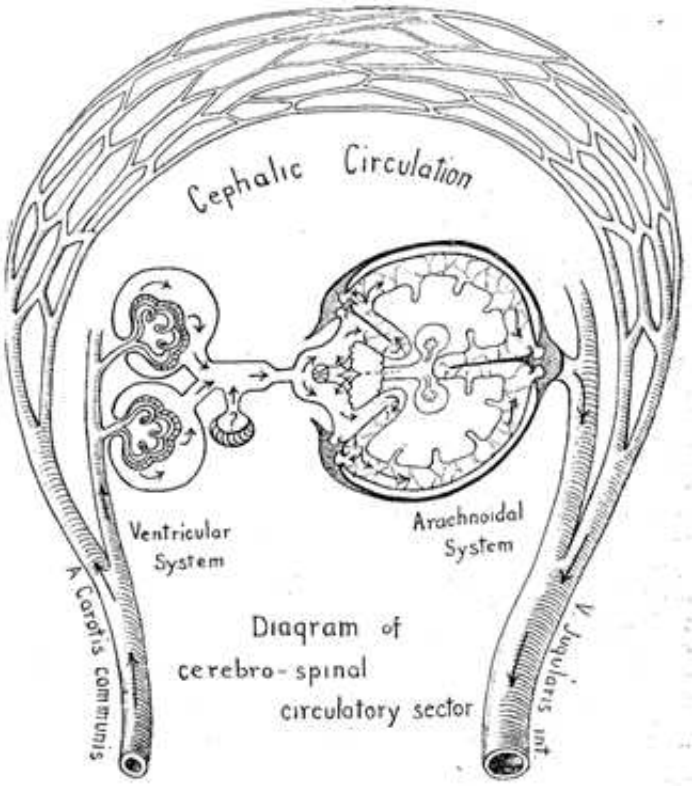


Figure 4: *Early diagram of the interaction between bloodflow and CSF.*

a complete mono-directionality is present the range of phase shifts allowable doubles. This maximum allowable velocity is known as the encoding velocity (Venc). A larger Venc corresponds to an increase in the noise associated with velocity measurements, so setting it arbitrarily large in order to ensure all possible velocities fall below Venc would reduce the reliability of the measurements [13]. For this reason, preliminary experiments and/or consultation of literature should be used to obtain a reasonable estimate of the maximum expected velocity of the vessel of interest before finalising this parameter. Slow moving fluids should, where practicable, be assessed separately from fast moving fluids. Phase shift is related to the magnetic susceptibility of the tissue being imaged, and as such understanding the composition of the fluids involved is crucial.

In order to reduce the noise when assessing rapid flows, the use of a Venc corresponding to a lower velocity than the maximum to be measured is often used. This would inevitably lead to a dataset where phases are superimposed on one another. Such a dataset is referred to as being phase wrapped, and it is theoretically possible to separate the superimposed velocities through phase unwrapping techniques. Such techniques require assumptions to be made, and research is ongoing to optimise phase unwrapping. Many of these require additional data to be acquired, thereby increasing scan time.

Phase contrast angiography (PCA) can be done in 2D or 4D, with 4D having the advantage of providing a dataset of the whole intracranial flow system that can later be analysed offline. 2D enables velocity encoding to be optimised for each vessel giving a better signal to noise ratio for slow moving fluids [14] [9]. 2D and 4D data generally correspond, with agreement being strongest when the heart rate varies the least due to the difference in scan times [15].

As a general rule a 32 channel head coil is used, and 32 acquisitions per heart beat are acquired in order to adequately describe the shape of pulse waves, but some authors opt to use more acquisitions for those with slower heart rates [16] [17] [18]. Unfortunately this technique is limited by the spatial resolution of the scanner, with many reporting accurate descriptions of the flow to be limited to vessels with a diameter greater than 2mm [19].

CSF is driven by the arterial inflow, with the relative peak positions and morphology of the waves being related to compliance and resistance. An accurate representation of the waveform cannot be acquired in one sweep, and as such a gating procedure is required in order that the correct point in the cardiac cycle is imaged every time. Combining such a gating system with PC-MRI gives an acquisition method known as CINE-MRI. Gating is usually done through the use of an electrocardiogram (ECG) using probes attached to the chest, but more distal

measurements such as finger plethysmography have been used. The gating can be done retrospectively, where data is acquired continuously, then later sorted into the correct time point in the cardiac cycle for both methods of gating. This method leads to heart rate averaging, and as such can lead to a smoothing effect. Prospective gating, where the signal triggers the acquisition is also possible with ECG, but not with plethysmography due to the time delay associated with this. Prospective gating is unable to account for heart rate variability, and once the acquisitions are started, they occur at equal time points until another heart beat resets the acquisition. The consequences of this are that shorter heartbeats can lead to a lower number of acquisitions being acquired, and longer heartbeats can lead to dead time towards the end of the cycle where no acquisitions are acquired, leaving this section invisible. It becomes clear that the time points in each of these would not correspond to the same sections of the cardiac cycle, and combining them would inevitably be problematic.

Describing flow dynamics at any point over a given time period would be made simpler and more reliable by increasing the temporal resolution. In practice, obtaining an image with a reasonable signal to noise ratio requires a finite imaging time, leading to a trade-off between temporal resolution and scan time. The temporal resolution must be high enough for the data to be useful, without the volunteer having to be still within the scanner for an unreasonable amount of time. Advancements in MRI technology, particularly the parallel imaging techniques designed for use with 3T scanners, have dramatically reduced the scan times required to achieve PC-MRI data with acceptable signal to noise ratio [20] [21]. This means that greater spatial and temporal resolutions can be achieved for a given scan time. The two main parallel imaging techniques used are generalised auto-calibrating partially parallel acquisition (GRAPPA), and sensitivity encoded MRI (SENSE) with the former calculating the missing data points in the frequency domain, and the latter calculating them in the image domain. Echo times should be optimised to reduce or eliminate flow artefacts [22] [23]. The plane of acquisition should always be perpendicular to the direction of flow in order that it may be accurately assessed.

The data acquisition methods described above may allow for an approximate qualitative description of intracranial flow dynamics to be inferred. To gain a full understanding of intracranial flow (and corresponding pressure) dynamics, a quantitative model must be formed. The present literature indicates that such models can be split into two types; fluid dynamics, and electrical equivalence [24] [25] [26] [27] [28]. The motivation behind the fluid dynamics models is clear  were looking at the dynamics of a system containing fluids. Unfortunately the number of variables in three dimensional space, with limited information makes this complex. Pitfalls include the creation of overly complex models, which can never be implemented clinically, or the creation of incorrectly simplified models. The motivation behind the construction of electrical equivalence models is varied; the behaviours of the intracranial fluids strictly analogous to an alternating current circuit, the analysis is much simpler, parameter fitting is practically testable, and the effect of alterations within the system become more intuitive, thereby providing an effective learning tool. Both types of models have been created to describe the whole, or part of the intracranial flow system, and have helped gain insight into a number of pathologies. Unfortunately, a definitive model is yet to be presented.

## Clinical Implications

Normal pressure Hydrocephalus (NPH) is a disease which generally effects women over 60, but occurs in elderly men too. The characteristic symptoms include dementia, confusion, urinary incontinence, and a shuffling gait. Traditional computed tomography (CT) imaging of NPH in the 1970s showed ventricular dilation, however insertion of pressure monitors revealed that the pressure is equal to that in the healthy ventricular system, giving rise to the name 'normal pressure hydrocephalus'. It was later realised that NPH patients showed an increase in pressure pulsatility the ventricular system. This is likely to be due to the passage of the systolic pulse wave from the peripheral arteries into the capillaries; a mechanism which is prevented in the healthy population. This led to the conclusion that hydrocephalus is caused by abnormal capillary pulsatility, which generates a transmantle pressure gradient across the brain between the ventricular system and the extracranial CSF space, and that this is causes dilation of the ventricular system.

More recently It has been concluded that these volume changes can be measured through the use of a surrogate measure of CSF volume change derived from studying the flow of CSF through he cerebral aqueduct. Since the CA lies between the forebrain and hindbrain, this represents the pulsatility volume of the forebrain fairly accurately. This measurement is simple to make using PCA, and studies have used it to demonstrate the increased pulsatility associated with NPH. Further to this, criteria have been developed for the diagnosis of NPH based entirely on the volume of CSF traversing the cerebral aqueduct over a cardiac cycle. Such criteria have proved useful given the fact that a procedure known as shunting has proved successful alleviating the symptoms of NPH almost completely in many patients, whilst having no effect whatsoever in others. Shunting is an invasive procedure whereby a tube is connected from the ventricles to the abdomen, forming a CSF drainage mechanism, thereby alleviating pressure

within the ventricles.

A number of studies have been carried out which attempt to understand why some patients did not respond. The conclusion reached from these is that NPH is a dynamic process which starts through increased capillary pulsatility due to small vessel disease. This causes secondary hydrocephalus due to the increased capillary pulsatility with associated decrease of cerebral blood flow through the capillaries and hypoperfusion. This in turn (possibly together with the pulsatility) leads to brain damage which is seen as areas of very high signal and gliosis in the white matter of the forebrain. When this stage is reached, the CSF pulse has dropped significantly, giving rise to the concept of 'burned out NPH', where the damage to the forebrain is so extensive that the pulsatility abnormality is no longer seen. This represents a stage where the damage is irreversible, rendering treatments such as shunting ineffective. It is clear that a method of accurately determining whether the patient has reached the burned out stage would be invaluable. Extensive research has led to the conclusion that abnormal intracranial pressure pulsatility is the best indicator of shunt success.

Idiopatic intracranial hypertension (IIH) AKA benign intracranial hypertension is a disease process which results in increased CSF pressure in a manner which may be indicative of a cerebral tumour, leading to this often being referred to as a pseudotumour. It is most commonly diagnosed in young obese women, and may be triggered by rapid weight gain. Characteristic symptoms include persistent headaches, vision abnormalities, pulsatile tinnitus, and nausea [29]. Cognitive function is unaffected by the disease, and it is not fatal, but the persistent headaches lead to a significant decrease in quality of life, and lack of treatment can lead to blindness.

The disease is not well defined, and is diagnosed by an increased CSF pressure in the absence of a known intracranial disease process, other than swelling of the optic disks. In fact a number of pathologies which were previously categorised as IIH are now better defined, thereby further restraining the diagnosis of IIH [30].

The symptoms can be relieved through the reduction of CSF pressure, through the diagnostic lumbar puncture leading to either an extremely short term or permanent relief of symptoms [31]. The disease ceases without treatment in a number of patients, whereas others require medical intervention. These factors indicate that a number of unknown disease processes may be defined under the umbrella term of IIH. IIH has been hypothesised to occur through one, or a combination of three mechanisms; brain swelling (increased interstitial fluid or cerebral blood volume), increased CSF production to absorption ratio, and increased resistance to the outflow of blood [32].

It has been noted that IIH patients display an increased arterial inflow and a degree of venous sinus stenosis [33]. An increase in one of these factors corresponds to a decrease in the other. There has been much debate regarding whether the stenosis is a primary cause of IIH, or a secondary effect, which further progresses the disease. The main arguments against it being a primary cause are the fact that a significant proportion of IIH patients display little or no measurable stenosis, and the fact that the pressure gradient across the transverse sinus (which is indicative of stenosis) has been reversed through the reduction of CSF pressure. It has been suggested that increased venous compliance leads to a feedback loop mechanism leading to increased arterial inflow, and eventually increased CSF pressure. Both cases provide motivation for research methodologies to include modelling which takes account of inflow, and the compliance and resistance to outflow. This indicates the requirement of the use of electrical equivalence models.

Many other neuropathologies such as Arnold-Chiari type I malformation, where the cerebellar tonsils herniate into the foramen magnum, have successfully been studied through intracranial fluid dynamics models [34].

## Electrical Equivalence Circuit Models

Given the fact that the brain is very sensitive with a high metabolic demand, it follows that the numerous pathologies would be related to a breakdown in the pressure dynamics, which facilitate a significant steady inflow of metabolites to the brain, and outflow of waste from it [9] [28] [33]. Such pathologies may present as a malfunction of a single component for which the other components are unable to compensate, or as a combination of a number of malfunctions within the intracranial system. For this reason it is crucial that the intracranial system as a whole is assessed when a neuropathology presents. Whilst it is not currently possible to directly measure intracranial pressure non-invasively, it is possible to measure flow. Flow and pressure are related, much like voltage and current. When we consider that the pressure dynamics within the brain are the point of importance, we are able to exploit the fact that pressure moves at the speed of sound, effectively leading to instantaneous transport throughout the skull. This leads to the possibility of the intracranial pressure network being modelled as an electrical circuit.

The pressure pulsatility is thought to be almost entirely diverted around the brain through the CSF. The morphology and peak position relative to the arterial input are related to compliance. Electrical equivalence models

are often based on the fact that the arterial input has an approximately oscillatory nature, and the fact that flow, resistance, and compliance, all have identifiable analogies to electrical circuit parameters. This provides motivation for creating models using a sinusoidal input at around 1Hz, resistors, capacitors, and often inductors [18] [36].

One of the most prolific authors in the field of electrical equivalence modelling is Mauro Ursino. Motivated by the fact that existing models only described a single component of an interlinked system which he felt was insufficient, he presented his first electrical equivelance model [28]. This was an ambitious project, and attempted to include pulsatility, auto-regulation, and CSF production, which all operate on different timescales. The model was split into 4 sections (arteries, veins, CSF dynamics, and CSF production/absorption). He stated that the arterial compliance only becomes relevant at high ICP's, with an exponential relationship between ICP and pulse pressure amplitude. He noted that the venous pressure in the dural sinus is lower than the CSF pressure, but it is higher than the CSF pressure elsewhere indicating the requirement for two different resistances, and perhaps a third to account for venous bed collapse. In truth there is no CSF in the dural sinuses, but communication exists through the arachnoid villi. Further to this, the blood volume in the veins was noted as around two and a half times that in the arteries on average.

It later occurred to Ursino, that an overly complex model could never be implemented clinically, leading to the presentation of a simplified model [37]. This model describes a feedback loop system whereby negative feedback loops act to stabilise the pressure system from high amplitude pressures, and that positive feedback loops act to stabilise low pressure amplitudes through delayed amplification, which can act as a secondary source of periodic pressure variation. They state that CSF outflow resistance, elastance coefficient, and gain have all been linked to periodic pressure variability. For this reason they simplify the model in order to focus on these three factors, and their interactions. They propose that it would be most relevant to study these interactions where the combinations are stable, but that any further deviation would cause the spiral into instability. At this point the stability can be maintained, and given the correct treatment, possibly driven back towards normality. Unfortunately this simple model is unable to assess the pulsatility of pressure.

The electrical equivalence model proposed by Kim et al [25] makes use of the fact that the viscosity of flow paths gives rise to resistances, and the elastic barrier boundaries facilitating components analogous to capacitance. Upon the addition of a resistor, a capacitor value changed from being negligible, to being the largest capacitor in one model [38] [39]. This highlights the requirement for an accurate estimation of resistance and/or compliance to be acquired. This also acts to confirm the idea that overly complex models lack clinical applicability. This means that a model should be as simple as possible, whilst describing the flow system as fully as possible. The central idea behind the model is that following the pulsatile arterial input, the current will flow predominantly through the main rail, analogous blood flowing through the capillary network in the brain, and then out into the venous network. At the same time, the voltage pulsatility is diverted through the branches, analogous to the pressure being diverted through the CSF. It is important to note that the physical system drives an oscillation, about the mean of the pulsatile pressure, and as such, this simplistic analogy is justified. Further down the line the pressure can be transferred to the veins, which aids the ejection of the venous blood. Although retrospective gating was used in both studies, there appears to be an offset in the starting point of the graphs. Timings may be skewed depending on the type of gating trigger used, and it could be useful to keep half a beat ether side, so that the wave form can be manually or automatically adjusted to known form. Although simple, this model is able to assess pulsatility, which is has been demonstrated through its use in predicting the jugular waveform [25]. Further to this, it can calculate the pressure pulsatility in the brain relative to that at any other part of the intracranial system analogous to a point in the equivalent circuit. There are others who created similar models motivated by the analogy of the pulsatile nature with simple harmonic motion [27].

Ambakari et al [5] were able to construct a complex model using information on blood flow and CSF motion obtained through PC-MRI. They noted that other researchers had neglected the associated CSF kinetic energy influence on the brain. Their model was split into 5 sections, with three of these dedicated to CSF behaviour in different spaces, one to the blood inflow mechanism, and one to the blood outflow mechanism. They described the viscosity of CSF as being approximately equal to that of water. They noted that the venous cross section was greater than that of the arteries with a ratio of 7:3, which is agrees well with previous literature. They noted that venous flow is not equal to arterial flow in systole, or in diastole, but that the average volume in must equal the average volume out. Once again it is noted that pressure is transferred from the arterial pulse to the CSF, which transfers some of this energy into squeezing the blood out of the veins, and that some of the CSF is necessarily ejected to the spinal subarachnoid space. They seem to have entirely dismissed the fact that the brain exists in this model, which seems unreasonable. They used the standard sine wave input for electrical equivalence modelling. They admitted to scaling the venous outflow to match the average arterial inflow due to theoretical assumptions. The overall result was that the simulation results were not convincingly similar to the data, but there was sufficient agreement to demonstrate the potential of this being improved in further work. There are of course similarities of this model with others, but surprisingly, where others use resistances in series along the main line of blood flow,

here conductances are used in series, which have characteristics of resistances in parallel. Crucially, this model makes no attempt to understand the dampening of the pressure wave, but simply hopes to show the relationship between arterial inflow with two different CSF measurements, and the venous outflow. It must be concluded that this model provides an example of what can go wrong in electrical equivalence modelling by selecting the wrong simplifications, whilst keeping unnecessary complexities.

A review in 2011 demonstrated the fact that the question of how pulsatility is distributed in the skull has yet to be adequately answered, and is still an important one [19]. It was noted that that several studies show brain pressure as being constant throughout, unlike flow. The same can be said for other components of the intracranial system. They note the exponential relationship between ICP and pulsatile pressure wave amplitude, and that intracranial compliance gives a measure of the ratio between volume change and pressure change. It is known that a number of cerebral diseases lead to (or are caused by) changes in compliance of one or more components of the ICP network. As such it follows that non-invasive pressure measurements could play an invaluable role in the diagnosis of such conditions. They note that the overall cranial compliance can be split into 4 major components: brain tissue, arteries, veins, and spinal CSF.

Electrical equivalence models have also been used to understand changes in cerebral artery flow and resistances associated with posture change [40]. This was done with the motivation that such a model might help explain changes due to ageing and a number of pathologies more prevalent in older people. It was noted that the auto regulation system is widely understood throughout the majority of the body, but of course the intracranial system is known to alter things. A decrease in pressure upon standing is noted, and this is rectified inside a 20 second window. The model used is very simple, as would be expected when using an ultrasound technique since the sensitivity of such an acquisition method is low. The paper essentially highlights the requirement for a robust model which can be refined to assess different systems and pathologies. There seems to be some merit to the hypothesis that repeated postural changes over a period of time may have an adverse effect on the health of the ageing brain, but the study is far too limited to reach any conclusions.

None of the models use a full circuit as this would necessitate extending to the heart which would introduce unnecessary complexity. Some studies use only simulations, which are then compared to collected data [41]. Issues such as abnormal blood pressure would play a role in the intra-cranial pressure system. These models are intended to demonstrate the mechanisms by which pulsatile pressure differences to the brain are reduced, and should eventually extend to identify pathologies and track treatments.

# Discussion

Intracranial fluid dynamics have been a topic of much intrigue for centuries, with Alexander Monro hypothesising that a volume entering the skull must force an equivalent volume to exit the skull at the same rate. This was based on the skull being a rigid casing, with its contents being incompressible. By the late 19th century, a qualitative diagram was formed of the intracranial fluid dynamics, which has changed very little since. The fact that the rate of venous outflow, in general, does not match the rate arterial inflow has been explained generally by the existence of an opening which allows CSF to move between the rigid skull, and a compliant spinal subarachnoid space.

Advancement in technology has enabled research to move beyond the qualitative, and start to quantify the intracranial fluid dynamics. This has led to pressure pulsatility, which is related to flow pulsatility being implicated in many pathologies. Since pressure propagates at the speed of sound, this propagation can be thought of as instantaneous within the bounds of the skull [28]. This relationship has allowed the creation of models of intracranial pressure dynamics based on alternating current circuits operating at a frequency equal to the heart rate.

The basis of these is generally a resistive entry of blood from the arteries into the brain, causing systolic swelling of the arteries in the subarachnoid space, which must displace the CSF fluid previously occupying this space. This forces most of the CSF out of the skull, and into the compliant spinal subarachnoid space. Meanwhile some of the displaced CSF causes compression of the venous structure, both directly, and through the arachnoid villi. The pressure exerted by the arteries on the CSF reduces during diastole, and the movement is reversed.

The intracranial compliance system, which has been implicated in a number of pathologies, presents as differences in pressure waveform phase and morphology over the cardiac cycle. These features then help to create electrical equivalence models.

One of the principal aims of electrical equivalence models is to provide a means of non-invasively assessing the pressure at the centre of the brain. It is not unreasonable to expect to achieve this through the study of pulsatility since pressure pulsatility displays an exponential relationship with mean pressure.

In effect the parameters of pressure, compliance, and resistance can theoretically give us incredible insight into

cerebral pathologies, with electrical equivalence models representing the most promising method for assessing these. Unfortunately research in this area seems to have slowed dramatically over the last decade, with the most promising model being published in 2007 by Kim et al [25] This model seems to represent an effective starting point to study intracranial pressure dynamics. With improvements in MRI technology, the model must now be validated and refined where appropriate. The first refinement is motivated by the fact that the skull is believed to be split into two communicating pressure systems with separate arterial inputs, but a common venous drainage. This new study is motivated by understanding how brain tumours alter the compliance of the brain. CSF dynamics are said to be the driving force behind motion of the healthy brain [26]. Compliance is a factor in CSF dynamics, and it may be that the alteration of cerebral compliance is the factor that causes the change in CSF hydrodynamics which leads to a phenomenon known as coning, whereby the brain is effectively forced into the foramen magnum.

# References


[1] Crossman, Alan R., and David Neary. Neuroanatomy: an illustrated colour text. Elsevier Health Sciences, 2014.

[2] Monro, Alexander. "Observations on the Structure and Functions of the Nervous System." (1783).

[3] Kellie G. An account of the appearances observed in the dissection of two of three individuals presumed to have perished in the storm of the 3d, and whose bodies were discovered in the vicinity of Leith on the morning of the 4th, November 1821 : with some reflections on the pathology of the brain. Trans Medico-Chirurg Soc Edinb 1824;1;84-16

[4] Cushing, Harvey. "The third circulation and its channels." Lancet 2.Oct. 24 (1925): 851-857.

[5] Ambarki, Khalid, et al. "A new lumped-parameter model of cerebrospinal hydrodynamics during the cardiac cycle in healthy volunteers." Biomedical Engineering, IEEE Transactions on 54.3 (2007): 483-491.

[6] Mitchell, Gary F., et al. "Arterial stiffness, pressure and flow pulsatility and brain structure and function: the Age, Gene/Environment SusceptibilityReykjavik study." Brain 134.11 (2011): 3398-3407.

[7] Tain, Rong-Wen, and Noam Alperin. "Noninvasive intracranial compliance from MRI-based measurements of transcranial blood and CSF flows: indirect versus direct approach." Biomedical Engineering, IEEE Transactions on 56.3 (2009): 544-551.

[8] Bulte, Daniel P., et al. "Quantitative measurement of cerebral physiology using respiratory-calibrated MRI." Neuroimage 60.1 (2012): 582-591.

[9] Bammer, Roland, et al. "Timeresolved 3D quantitative flow MRI of the major intracranial vessels: Initial experience and comparative evaluation at 1.5 T and 3.0 T in combination with parallel imaging." Magnetic resonance in medicine 57.1 (2007): 127-140.

[10] Bernstein, Matt A., John Huston, and Heidi A. Ward. "Imaging artifacts at 3.0 T." Journal of Magnetic Resonance Imaging 24.4 (2006): 735-746.

[11] Soher, Brian J., Brian M. Dale, and Elmar M. Merkle. "A review of MR physics: 3T versus 1.5 T." Magnetic resonance imaging clinics of North America 15.3 (2007): 277-290.

[12] Stivaros, Stavros Michael, and Alan Jackson. "Changing concepts of cerebrospinal fluid hydrodynamics: role of phase-contrast magnetic resonance imaging and implications for cerebral microvascular disease." Neurotherapeutics 4.3 (2007): 511-522.

[13] Johnson, Kevin M., and Michael Markl. "Improved SNR in phase contrast velocimetry with fivepoint balanced flow encoding." Magnetic Resonance in Medicine 63.2 (2010): 349-355.

[14] Whlin, Anders. "Cerebral blood flow and intracranial pulsatility studied with MRI: measurement, physiological and pathophysiological aspects." (2012).

[15] Whlin, Anders, et al. "Measuring pulsatile flow in cerebral arteries using 4D phase-contrast MR imaging." American Journal of Neuroradiology 34.9 (2013): 1740-1745

[16] Linninger, Andreas A., et al. "Pulsatile cerebrospinal fluid dynamics in the human brain." Biomedical Engineering, IEEE Transactions on 52.4 (2005): 557-565

[17] ElSankari, Souraya, et al. "Concomitant analysis of arterial, venous, and CSF flows using phase-contrast MRI: a quantitative comparison between MS patients and healthy controls." Journal of Cerebral Blood Flow & Metabolism 33.9 (2013):1314-1321.

[18] Bhadelia, Rafeeque A., Andrew R. Bogdan, and Samuel M. Wolpert. "Analysis of cerebrospinal fluid flow waveforms with gated phase-contrast MR velocity measurements." American journal of neuroradiology 16.2 (1995): 389-400.

[19] Wagshul, Mark E., Per K. Eide, and Joseph R. Madsen. "The pulsating brain: a review of experimental and clinical studies of intracranial pulsatility." Fluids Barriers CNS 8.1 (2011): 5.

[20] Schmitz, Bernd L., et al. "Advantages and pitfalls in 3T MR brain imaging: a pictorial review." American journal of neuroradiology 26.9 (2005): 2229-2237.

[21] Alvarez-Linera, Juan. "3T MRI: advances in brain imaging." European journal of radiology 67.3 (2008): 415-426.

[22] Dietrich, Olaf, et al. "Influence of multichannel combination, parallel imaging and other reconstruction techniques on MRI noise characteristics." Magnetic resonance imaging 26.6 (2008): 754-762.

[23] Drangova, Maria, and Norbert J. Pelc. "Artifacts and signal loss due to flow in the presence of Bo inhomogeneity." Magnetic resonance in medicine 35.1 (1996): 126-130.

[24] Linninger, Andreas A., et al. "A mathematical model of blood, cerebrospinal fluid and brain dynamics." Journal of mathematical biology 59.6 (2009): 729-759.

[25] Kim, J., et al. "Prediction of the jugular venous waveform using a model of CSF dynamics." American journal of neuroradiology 28.5 (2007): 983-989.

[26] Nitz, W. R., et al. "Flow dynamics of cerebrospinal fluid: assessment with phase-contrast velocity MR imaging performed with retrospective cardiac gating." Radiology 183.2 (1992): 395-405.

[27] Egnor, Michael, Arthur Rosiello, and Lili Zheng. "A model of intracranial pulsations." Pediatric neurosurgery 35.6 (2001): 284-298.

[28] Ursino, Mauro. "A mathematical study of human intracranial hydrodynamics part 1the cerebrospinal fluid pulse pressure." Annals of biomedical engineering 16.4 (1988): 379-401

[29] Wall, Michael, and DONNA GEORGE. "Idiopathic intracranial hypertension a prospective study of 50 patients." Brain 114.1 (1991): 155-180.

[30] Skau, M., et al. "What is new about idiopathic intracranial hypertension? An updated review of mechanism and treatment." Cephalalgia 26.4 (2006): 384-399.

[31] Soler, D., et al. "Diagnosis and management of benign intracranial hypertension." Archives of disease in childhood 78.1 (1998): 89-94.

[32] Gideon, P., et al. "Assessment of CSF dynamics and venous flow in the superior sagittal sinus by MRI in idiopathic intracranial hypertension: a preliminary study." Neuroradiology 36.5 (1994): 350-354.

[33] Bateman, Grant A., Scott A. Stevens, and Jesse Stimpson. "A mathematical model of idiopathic intracranial hypertension incorporating increased arterial inflow and variable venous outflow collapsibility: clinical article." Journal of neurosurgery 110.3 (2009): 446-456.

[34] Alperin, Noam, Anusha Sivaramakrishnan, and Terry Lichtor. "Magnetic resonance imaging-based measurements of cerebrospinal fluid and blood flow as indicators of intracranial compliance in patients with Chiari malformation." Journal of neurosurgery 103.1 (2005): 46-52.

[35] Bateman, Grant A., et al. "The venous manifestations of pulse wave encephalopathy: windkessel dysfunction in normal aging and senile dementia." Neuroradiology 50.6 (2008): 491-497.

[36] Kumar, Y. Kiran, Sashi B. Mehta, and Manjunath Ramachandra. "Vessel Deformation Modeling-Cerebral Arteriovenous Malformation." Journal of Biomedical Engineering and Technology 2.2 (2014): 10-12.

[37] Ursino, Mauro, and Carlo Alberto Lodi. "A simple mathematical model of the interaction between intracranial pressure and cerebral hemodynamics." Journal of Applied Physiology 82.4 (1997): 1256-1269.

[38] Kim, J., et al. "A Simple Electrical Equivalence Model of Intracranial Cerebrospinal Fluid Pulsatility: Design and Validation in Healthy Normals." Proceedings of MIUA. 2006.

[39] Kim, J., et al. Empirical Validation of Cerebrospinal Fluid Pulsatility Model. No. 2004-011. Tina Memo, 2004.

[40] Olufsen, Mette S., Ali Nadim, and Lewis A. Lipsitz. "Dynamics of cerebral blood flow regulation explained using a lumped parameter model." American Journal of Physiology-Regulatory, Integrative and Comparative Physiology 282.2 (2002): R611-R622.

[41] Takemae, Tadashi, et al. "A simulation study of intracranial pressure increment using an electrical circuit model of cerebral circulation." Biomedical Engineering, IEEE Transactions on 12 (1987): 958-962.

[42] Wall, Michael. "Idiopathic intracranial hypertension." Neurologic clinics 28.3 (2010): 593-617.