Noninvasive intracranial compliance and pressure based on dynamic magnetic resonance imaging of blood flow and cerebrospinal fluid flow: review of principles, implementation, and other noninvasive approaches

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Current techniques for intracranial pressure (ICP) measurement are invasive. All require a surgical procedure for placement of a pressure probe in the central nervous system and, as such, are associated with risk and morbidity. These considerations have driven investigators to develop noninvasive techniques for pressure estimation. A recently developed magnetic resonance (MR) imaging–based method to measure intracranial compliance and pressure is described. In this method the small changes in intracranial volume and ICP that occur naturally with each cardiac cycle are considered. The pressure change during the cardiac cycle is derived from the cerebrospinal fluid (CSF) pressure gradient waveform calculated from the CSF velocities. The intracranial volume change is determined by the instantaneous differences between arterial blood inflow, venous blood outflow, and CSF volumetric flow rates into and out of the cranial vault. Elastance (the inverse of compliance) is derived from the ratio of the measured pressure and volume changes. A mean ICP value is then derived based on a linear relationship that exists between intracranial elastance and ICP. The method has been validated in baboons, flow phantoms, and computer simulations. To date studies in humans demonstrate good measurement reproducibility and reliability. Several other noninvasive approaches for ICP measurement, mostly nonimaging based, are also reviewed. Magnetic resonance imaging–based ICP measurement may prove valuable in the diagnosis and serial evaluation of patients with a variety of disorders associated with alterations in ICP.

KEY WORDS • intracranial pressure • intracranial elastance • motion-sensitive magnetic resonance imaging • cerebrospinal fluid flow dynamics • total cerebral blood flow

Accurate assessment of ICP is critical to the evaluation and management of patients with a variety of neurological disease processes. Accepted techniques for ICP measurement are invasive, require a surgical procedure for placement, and as such are associated with potential morbidity. Placement of intraparenchymal and subdural catheters allows for pressure monitoring; intraventricular catheters provide the additional benefit of therapeutic CSF drainage.

Although invasive continuous ICP monitoring may be appropriate in certain settings, the indications for and advisability of such monitoring in other patient populations are less clear, even when knowledge of ICP might play a role in guiding therapy. In fact, there remain insufficient data to support the use of invasive pressure monitoring as a treatment standard for patients with elevated ICP. One reason for this is that there are no quantitative guidelines regarding treatment thresholds for elevated ICP. The results of studies have consistently demonstrated that elevated ICP (> 20 mm Hg) portends a poor outcome. Brainstem herniation, however, also has been reported following mild elevations of ICP. This apparent discrepancy both emphasizes the regional nature of invasive monitoring and implies that pressure alone may not adequately account for pathophysiology. A reliable noninvasive technique for estimation of global intracranial compliance and pressure might facilitate establishment of guidelines for invasive monitoring.

Because current techniques for ICP monitoring are invasive, one also must consider the potential morbidity associated with placement and maintenance of such devices. Common complications associated with ventriculostomy (the most accurate of the available modalities) include hemorrhage, infection, seizures, obstruction, and device malfunction. According to studies by Mayhall, et al., and Paramore and Turner, the risk of bacterial colonization increases significantly after 5 days. The mean rate of colonization for ventriculostomies is 5% (range 0–9.5%). The overall incidence of hematoma is 1.4%. Malfunction or obstruction occurs at a rate of 6 to 16%. Seizures and/or

Abbreviations used in this paper: CFP = cochlear fluid pressure; CSF = cerebrospinal fluid; GCS = Glasgow Coma Scale; ICP = intracranial pressure, ICVC = intracranial volume change; MR = magnetic resonance; TCD = transcranial Doppler.
motor deficits also may result from invasive monitor placement. Furthermore, probe “drift” may compromise the reliability of measurements over time. Thus, the potential for complication, although modest, is not insignificant when considered in the context of the primary ICP-altering disease process.

**REVIEW OF OTHER APPROACHES FOR NONINVASIVE ICP MEASUREMENTS**

Noninvasive techniques for the measurement of ICP were reported as early as 1966 in newborns and infants. Because these techniques rely on an open fontanelle, they are not applicable in older children and adults. Others have proposed indirect approaches based on acoustic or dielectric properties of the cranial compartment. National Aeronautics and Space Administration researchers have used an ultrasonic transducer to obtain a measurement of dielectric properties of the cranial compartment. They found a correlation labeled through the brain parenchyma to detect changes in ICP. The distance between the lateral temporal walls of the cranium was determined by the transit time of an acoustic wave reflected from the bone-soft tissue interface. A small increase in distance with increasing pressure was found, providing evidence that the cranium is not absolutely rigid and that the volume of the intracranial space can change. Limitations of the technique are the absence of a direct relationship between distance and pressure and the fact that the propagation of the acoustic wave varies between brain tissue and the CSF. Ragauskas, et al., used the dispersion of the acoustic signal that traveled through the brain parenchyma to detect changes in the cerebral blood volume. They found a correlation between ICP recording and an acoustic signal, which was assumed to reflect the dynamic changes in the blood volume along the acoustic pathway.

Russegger and Ennemoser described an approach based on measurements of the dielectric property of the cranium. A high frequency alternating voltage (1–1.5 MHz) was applied via electrodes attached to the head. The goal was to measure changes in the filling state and composition of the intracranial space as reflected by changes in the dielectric property. They reported a high correlation with invasively measured ICP for 20 patients with intracranial space-occupying lesions.

Communication of the CSF space through the inner ear has provided the basis for further attempts to measure ICP. The ICP wave is transmitted through the cochlear aqueduct and middle ear, toward the tympanic membrane. Intracranial pressure is recorded using a cerebral and CFP analyzer to measure fluid pressures in the inner ear. The analyzer stimulates a muscle in the middle part of the ear by introducing an ultrasonographic signal through an earpiece. This technique has been evaluated in several applications. In one study, the technique for tympanic membrane displacement demonstrated no increase in ICP in individuals with acute mountain sickness. Reid, et al., investigated the relationship between CFP measured indirectly by tympanic membrane displacement and mean ICP, as determined by direct measurement in 58 patients (age 5–77 years). The authors reported a positive correlation in young patients with hydrocephalus and benign intracranial hypertension. The relationship, however, did not hold under conditions in which the stapedial reflex was absent or the cochlear aqueduct was not patent. Other groups have also reported flaws in the CFP technique. The authors of one study conducted in eight children with shunt-treated hydrocephalus questioned the reliability of the technique. Phillips and Marchbanks studied the effects of posture and age on the transmission of CSF pressure changes to the cochlear fluid in 32 patients (16 in the 19–32-year-old group and 16 in the 40–63-year-old group). They reported smaller changes in the measured tympanic membrane displacement in the older group during posture changes compared with those in the younger group.

The eye has also been investigated as a window for noninvasive ICP measurement. Because the optic nerve is surrounded by a dural sheath filled with CSF, pressure in the retina vein is influenced by ICP. It is assumed that high ICP is associated with collapse of the retinal vein. On this basis, Motschmann, et al., used ophthalmodynamometry for assessment of ICP. Ophthalmodynamometry is performed by exerting pressure on the sclera by using a spring plunger while observing the vessels through an ophthalmoscope. The pressure is gradually increased until the central retinal vein just starts to pulsate. Evaluation in 31 patients demonstrated a strong linear correlation with the invasively measured ICP value (r = 0.968). The ophthalmodynamometry technique, however, can be hazardous when performed in comatose patients and those with high myopia. Quantitative pupillometry has also been reported recently as a reliable and safe method to identify patients with ICP greater than 20 mm Hg. This technique takes advantage of the fact that there is a relationship between high ICP and a reduction in pupillary constriction velocity, which in turn can be measured accurately with the aid of a special instrument.

Other investigators have considered noninvasively measured physiological parameters as markers of increased ICP. Hassler, et al., found changes in TCD arterial waveforms in 71 patients with known intracranial hypertension and subsequent brain death. Transcranial Doppler ultrasonography has also been used to demonstrate a correlation between increased ICP and a rise in the Goesling Pulsatility Index, although great variability exists in the Pulsatility Index for normal individuals. Schmidt, et al., measured middle cerebral artery flow velocity and used a systems-based approach to predict relative increases in ICP waveforms noninvasively. Schoser, et al., demonstrated, over a certain range, a linear relationship between mean ICP and maximum venous blood flow velocity in the straight sinus or basal vein of Rosenthal. Shakhnovich, et al., measured flow velocity in the straight sinus during a body tilt test to differentiate normal from increased ICP states. Systolic flow velocity and the amplitude of pulsation were usually higher in patients than in healthy volunteers in a horizontal position. These TCD-based blood velocity measurements are evidence of the strong coupling between intracranial hemodynamics and hydrodynamics (that is, blood flow and ICP). It is not clear, however, whether they can be used as a reliable estimate of ICP because of a lack of a theoretical basis or physiological principles relating them directly to ICP values.
NEUROPHYSIOLOGY BASIS OF THE MR IMAGING–BASED METHOD FOR ELASTANCE AND PRESSURE MEASUREMENT

The MR imaging–based method integrates human neurophysiology and fluid dynamics principles with dynamic MR imaging techniques to measure elastance and ICP. It utilizes the fact that in the physiological range, the relationship between ICP and volume is monoexponential: when the volume of the intracranial space increases, the pressure inside increases exponentially. A consequence of this relationship is that at a low pressure the elastance (defined as the change in pressure for a unit change in volume) is small, whereas at a high pressure (larger volume) the elastance is large. This is illustrated in Fig. 1 where \( dP \) is the change in pressure and \( dV \) is a unit change in volume during the cardiac cycle. The elastance (that is, the derivative of the exponential pressure–volume curve) is also a monoexponential function of volume. It follows that because elastance and pressure are both exponential functions of volume, elastance is a linear function of ICP.

The monoexponential relationship between ICP and intracranial volume was described by Ryder, et al., and was confirmed in subsequent studies. The pressure–volume relationship, however, could not be determined from a direct measurement of the volume of the intracranial space; there was no in vivo means of measuring that volume. Instead, based on results obtained in animals and in patients, it was inferred from the linear relationship between elastance and pressure. The elastance is measured with a volume–pressure response test. In this test, shown in Fig. 2, the total intracranial volume is rapidly increased by injecting a known amount of fluid into the ventricles. The elastance is then derived from the ratio of the resultant pressure change \( (Q_2-Q_1) \) to the amount of injected volume, \( \Delta V \).

Similarly, the MR imaging–based ICP method assessment provides a measure of elastance from the ratio of pressure and volume changes that occur naturally with each cardiac cycle. Intracranial pressure is then derived through the linear relationship between elastance and pressure. The small volume change that occurs naturally with each cardiac cycle is analogous to the injected volume used in the volume–pressure response test. Volume and pressure changes occur because of the pulsatile nature of blood flow. During systole, more volume flows into the cranial vault (arterial inflow exceeds venous and CSF outflows), whereas during diastole the outflow is larger. The MR imaging method measures the pulsatile arterial, venous, and CSF flows into and out from the cranial vault. The small (on the order of 1 ml) volume change is derived from the instantaneous differences between inflow and outflow at different time points in the cardiac cycle. The pressure change is calculated based on the CSF flow by using fluid dynamics principles.

The proportionality factor between elastance and pressure, the elastance coefficient constant, was estimated by Szewczykowski, et al., from the slope of the linear relationship between ICP change over the cardiac cycle and mean ICP. Intracranial pressure was manipulated by a continuous injection of fluid into the CSF space. The ICVC during the cardiac cycle was not measured but rather was assumed to vary randomly around the same value for all patients. A relatively small variability in the standard deviation in the measured slopes was found \( 0.329 \pm 0.084 \) [standard deviation]). It is possible that even less variability in the elastance coefficient constant would have been found if the actual value of ICVC had been measured for each patient. It is unknown to what extent the elastance coefficient is affected by disease. An open cranial vault or variation in the elasticity of the dura mater might alter this value.

IMPLEMENTATION OF THE MR IMAGING–BASED METHOD

Intracranial Volume Change During the Cardiac Cycle

The focus of our early work was the characterization of CSF flow dynamics during the cardiac cycle. Although it was well documented that the CSF pulsatility is related to the pulsatility of blood flow, the relationships among the arterial, venous, and CSF flow dynamics have not been determined. A flow-volume-pressure craniospinal model was proposed and was used to explain and quantify the relationship between arterial inflow, venous outflow, and CSF flow between the cranium and the spinal canal. This model, shown in Fig. 3, includes intracranial and spinal canal compartments, as well as the following inputs and outputs: arterial inflow, venous outflow, and CSF oscillatory flow between the cranium and the spinal canal. A change in the volume of the intracranial space at each time point in the cardiac cycle can be measured from the difference between inflows and outflows as long as blood, CSF, and brain tissue are incompressible. The Monro–Kellie doctrine makes this assumption. The doctrine, however, also assumes that the volume of the intracranial space is constant. Today, we know that a small periodic change in the intracranial volume occurs with each cycle.
cardiac cycle (sensitive ultrasonographic methods measure changes in the distance between the lateral temporal walls of the cranium during the cardiac cycle). The mean intracranial volume, however, averaged over a cardiac cycle at steady state, is constant. The MR imaging method measures the small ICVC during the cardiac cycle at steady state, based on the above-described craniospinal flow-volume-pressure model.

Imaging Measurements of CSF Flow, Total CBF, and ICVC

Cerebrospinal fluid and blood volumetric flow rates into and out of the cranial vault are measured using a well-established MR imaging motion-sensitive technique, velocity-encoded phase-contrast MR imaging. This method has been shown to provide highly accurate (within 2.8%) volumetric flow rate measurements in nonsteady (pulsatile) flow. The dynamic phase-contrast MR imaging technique provides a series of images (velocity maps) with values of picture elements proportional to the velocity value at that location. The phase-contrast MR imaging method is based on the principle that the resonance frequency of nuclei is proportional to the magnetic field strength. Therefore, the phase of a proton can be modulated by application of magnetic field gradient. Moving protons, such as those in the blood, will experience different field strength than static protons during application of a magnetic field gradient. This can be translated to a net phase change proportional to the proton’s velocity.

Examples of phase-contrast MR images of CSF and blood flow obtained in a healthy volunteer are shown in Figs. 4 and 5, respectively. The oscillatory CSF flow between the cranial and the spinal compartments is visualized on images acquired in a transverse anatomical orientation through the upper cervical spinal canal. Figure 4a depicts outflow (white pixels) during the systolic phase and Fig. 4b depicts inflow (black pixels) during the diastolic phase. A blood flow image is shown in Fig. 5b. The total volumetric arterial flow rate—that is, CBF—is calculated directly from the sum of the volumetric flow through the four vessels carrying blood to the brain (internal carotid and vertebral arteries) during one cardiac cycle. An example of the calculated flow waveforms for CSF, total arterial inflow, and venous outflow is shown in Fig. 6.

The rate of the time-varying ICVC (net transcranial volumetric flow rate) is obtained by subtracting outflow rates from inflow rates at each time point. The volume change (Δ of volume from a given reference point) is then obtained by integrating net transcranial volumetric flow rate waveform with respect to time. An example of the ICVC waveform during one cardiac cycle obtained for the same healthy volunteer is shown in Fig. 7. Magnetic resonance imaging measurements in a flow phantom performed to assess the inherent performance of the ICVC values demonstrated measurement reproducibility and accuracy within approximately 5%.
Calculation and Validation of ICP Change During Cardiac Cycle

Urchuk and Plewes\(^{13}\) reported a method for measuring pressure gradients of pulsatile flow in tubes from MR imaging–documented velocities. They found agreement between MR imaging–derived measurements of pulsatile pressure gradients and direct pressure measurements obtained in a phantom. The method of calculating the pulsatile pressure gradients is based on the Navier–Stokes equation. In our laboratory we have adapted this method to calculate CSF pulsatile pressure gradients in the upper cervical spine.\(^{1,5}\) The assumptions of a rigid chamber and incompressible fluid are justified in the case of CSF flow in the cervical spinal canal. Computational fluid dynamic simulations were used to demonstrate that the change in pressure is directly related to change in the pressure gradient.\(^{14}\) The relationship between pressure changes and pressure gradient changes has been further studied and verified at multiple ICP values in two baboons by comparing the MR imaging–derived pressure gradients and the invasively measured pulse pressure.\(^{5}\)

Evolution of the MR Imaging–Based ICP Measurements in Humans

The method was validated in five patients in whom an external ventricular drain was in place at the time of the MR imaging study, allowing for direct comparison of MR imaging–derived and invasively measured ICP values. A large number of MR imaging measurements were acquired in humans (healthy volunteers and patients) for whom no invasive ICP measurements were available. The mean ICP value measured by the external ventricular drain catheter was compared with the elastance measurement.

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**Fig. 4.** Phase-contrast MR images of CSF flow in the spinal canal. The pixel values in these images are proportional to velocities in a direction perpendicular to the image plane. a: Cerebrospinal fluid flow during systole. b: Cerebrospinal fluid flow during diastole. Gray denotes static tissue; white, outward flow (from the cranium to the spinal canal); and black, inward flow.

**Fig. 5.** a: A blood vessel MR scout image revealing the location of the blood flow measurement (dashed line). b: A phase-contrast MR image of blood flow through the same location. Black pixels indicate arterial inflow and white pixels the venous outflow. R = right.
obtained by MR imaging. A linear relationship with a high correlation coefficient ($r^2 = 0.965$) was found. More than 110 MR imaging studies were performed in 21 volunteers (20 men, one woman; mean age 28 ± 8.7 years). Magnetic resonance imaging–derived ICP values ranged from 3.8 to 18.8 mm Hg; most measurements were between 8 and 10 mm Hg. Wide distribution of ICP values measured invasively in healthy individuals has been previously reported: from 2 to 16 mm Hg in one study and up to 18 mm Hg in another. These authors also noted that invasively measured ICP values were affected by the lumen size of the needle used. Lower values were measured using wider needles. Thus, it is reasonable to assume that the small volume of CSF that leaks from the intracranial space during these measurements could bias the reading toward lower ICP values. Distribution of ICP values measured invasively in 1033 healthy individuals and the distribution of the MR imaging–based derived measurements are shown in Fig. 8, respectively. Three of the 110 MR imaging–based measurements (two obtained in the same individual) were between 16 and 18.7 mm Hg, above the upper range found in the 1937 study. It is not possible, however, to determine whether this represents a normal variation of ICP, an MR imaging measurement error, or the true ICP value, because no invasive values are available for comparison. Based on the current view that ICP value of 20 mm Hg is a critical threshold for elevated ICP, no false-positive results were obtained using MR imaging. That 96% of the MR imaging measurements were between 4 and 16 mm Hg and no values were found above 20 mm Hg provide strong evidence for the method’s ability to identify normal ICP correctly (that is, a false-positive rate of 0%).

The distribution of MR imaging–derived total CBF measurements in the same individuals is shown in Fig. 9. It is interesting to note that the total CBF spans over a much narrower range relative to the ICP. It is known that the blood flow to the brain is highly regulated; a narrower distribution may reflect that degree of regulation.

DISCUSSION

A noninvasive method for measuring intracranial compliance and pressure that integrates principles of neurophysiology, fluid mechanics, and MR imaging measurements of blood and CSF flow has been presented. The MR imaging–based ICP technique offers two distinct advantages to traditional invasive monitoring. Although invasive pressure monitors provide for continuous tracking of ICP, this measurement is necessarily regional and subject to “compartmentalization.” Therefore, a measurement in one lobe may not accurately reflect the contralateral lobe pressure state. The MR imaging–based technique for measuring ICP, on the other hand, provides a global assessment of the ICP state in a system unperturbed by the iatrogenic disruption of the intracranial system, which necessarily occurs after placement of an invasive monitor.

The role of MR imaging–based ICP measurement may be different from that of the invasive technique. Whereas invasive monitoring provides continuous ICP measurements, the MR imaging study provides a single time point measurement. There are several clinical settings in which a “snapshot” of ICP may be beneficial. Management of cases involving blunt head trauma may be one area. Placement of an invasive monitor to track ICP continuously is recommended for patients with severe head injuries, defined as a GCS score of 3 to 8. The necessity of ICP monitoring in patients with intermediate GCS scores (9–12), and in particular those in whom admission computerized tomography scans reveal normal findings, has been the subject of debate. Ten to thirty percent of these patients will develop increased ICP over the first few days after injury. Invasive monitoring techniques are not routinely used in this population. At the same time, however, it is not clear which of these patients will progress to an increased pressure state. Likewise, in patients with diffuse axonal injury, a GCS score in the severe injury range may be present despite the appearance of normal ICP levels noted after placement of an invasive monitor. In these settings, noninvasive MR imaging–based ICP measurement would provide a means of objective assessment of the need for an invasive monitor without exposing the patient to potential morbidity.
Magnetic resonance imaging–based ICP measurement may also play an important role in diagnosis and serial evaluation of several chronic disorders potentially associated with changes in ICP. Such processes include hydrocephalus, pseudotumor cerebri, intracranial mass lesions, and toxic–metabolic encephalopathy (in which a depressed level of consciousness may or may not correspond to an increased ICP). Magnetic resonance imaging–based ICP measurement may prevent unnecessary invasive monitoring in an increased risk setting.

Single-time measurement of ICP may also be helpful in the evaluation of patients with possible ventriculoperitoneal shunt malfunction, particularly young children who present with nonspecific complaints and/or who are unable to communicate their symptoms. An MR imaging–based technique would limit exposure to harmful radiation from repeated computerized tomography scans and shunt series. Additionally an MR imaging–documented finding of normal ICP might prevent unnecessary shunt exploration.

If proven accurate and reliable, noninvasive MR imaging–based measurement of ICP may provide a valuable adjunct to the evaluation of patients with various causes of increased ICP. In the setting of traumatic brain injury, a finding of increased ICP may provide the physician with an early warning signal to adjust therapy. This tool may also prove valuable in cases in which external factors confound clinical evaluation (for example, drug intoxication), coma does not necessarily reflect an increased pressure state (that is, diffuse axonal injury); or coexisting medical problems make placement of an invasive monitor too dangerous (that is, bleeding disorders). In each case, noninvasive ICP measurement would enhance the array of currently available evaluation modalities, providing a novel adjunct to patient diagnosis and serial monitoring with limited expense and morbidity.

References