

Noninvasive acoustic intracranial pressure measurement through the eye

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Abstract

Fluid pressure increase in the brain, contained in the skull, is a serious medical condition that can be life threatening. Intracranial pressure changes can be detected noninvasively using acoustic stimulation and analysis. The brain and eye are coupled resonant systems that will respond in a predictable fashion to brain pressure increases, given the constraints of the bioboundary (skull) conditions. Changes in acoustic damping in the eye co-vary with changes in cerebrospinal fluid or intracranial pressure. Feasibility of this approach is demonstrated in a preliminary study of five patients.

Keywords: eye/brain acoustics, intracranial pressure, noninvasive monitoring.

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Noninvasive intracranial pressure (ICP) measurements could potentially improve clinical outcomes; hence, ICP noninvasive monitoring could be a vital tool in the management of patients¹. Elevated or increased ICP is a serious complication that can result from various neurologic conditions such as head trauma, intracranial hemorrhage, and embolic stroke, alterations in cerebrospinal fluid (CSF) production or absorption, infections, and tumors^{1,2}. Patients with increased ICP are among the most challenging patients to care for in a critical care setting. Initiating rapid and effective treatment to protect a patient from a devastating outcome depends on aggressive and thorough clinical assessment. Owing to the damaging biochemical processes that activate within minutes to hours of injury, proper and rapid detection and treatment of a traumatic brain injury is critical in preventing further damage or death³.

ICP is carefully regulated by homeostatic mechanisms; however, in certain neuropathologies, ICP may become dangerously elevated and poses the risk of death. Support of cerebral perfusion pressure is a mainstay of care but can result in morbidity and mortality with the use of osmotic diuretics or in hyperventilation without guidance of the actual pressure in patients who are acutely hypovolemic. Such strategies may ultimately lead to exacerbated hemorrhaging and poor neurologic outcomes and, possibly, death without pressure monitoring. ICP measurement currently requires opening or placement of one of several pressure sensors within the cranium. Specifically, four invasive approaches to ICP monitoring exist: ventriculostomy, subarachnoid screw, subdural catheter, and intraparenchymal fiberoptic-tipped catheter. Ventriculostomy is a frequent choice⁴.

To date, no practical way of noninvasively monitoring ICP has surfaced. This is a serious problem, as the invasive monitoring procedures carry a risk of complications and infection and cannot be performed before the patient arrives at the hospital and usually not until the patient is admitted to an intensive care unit (ICU) and a neurosurgeon is present. Because of these limitations, the optimal window of opportunity for effective invasive ICP monitoring may be lost in many circumstances. Two noninvasive windows to assessing brain pressure are the ear and the eye, as the acoustic impedance of the CSF, brain, eye, and ear are essentially the same⁵. The eye is more accessible for direct placement of a noninvasive sensor to detect changes, but eye pressure and ICP correlations are disputed⁶⁻¹². Ear monitoring is also possible, as changes in ICP are known to change the perilymphatic fluid pressure via the cochlear aqueduct¹³⁻¹⁶, but this method has not yet been made clinically feasible. One difficulty is the effects of middle-ear mechanics in ICP measurements. The middle ear acts as a damper spring, which complicates sensitivity measures of tympanic displacement. Nonetheless, there is cause for optimism in its use, particularly in the case of increased ICP and pulsatile tinnitus¹⁷.

The ear produces sounds, termed *otoacoustic emissions* (OAEs). OAEs are recorded with a probe microphone in the ear canal and are generated by the outer hair cells (OHCs) in the inner ear; the sounds have been shown to decrease in amplitude with increased ICP pressure¹⁸ on the order of 2–4 dB SPL and independent of respiration confounding¹⁹. Nonetheless the OAE approach has not been widely implemented.

Although previous attempts have been made to acoustically measure ICP in animals and the validity of the concept has been demonstrated, application of the approaches used in these attempts has not been practical in humans. Semmlow and Fisher²⁰ observed the response of the head to low-level audiofrequency vibrations correlated with ICP elevation in young dogs. Stevanovic et al.²¹ demonstrated the basic concept of our method in sheep by artificially elevating ICP and monitoring the acoustic signal. However, although their method did not require surgery within the skull cavity, it did require implantation of screws in the skull, making it invasive.

Direct measures of skull vibration in humans, bypassing the windows of the eye and ear, have been attempted, but with limited success because it is technically complicated and is not a promising clinical alternative chiefly due to intrasubject variability²²⁻²⁴. A variation is the interpretation of temporal events in a phase loop approach,²⁵ but the approach has not been reduced to medical practice. Herein a much simpler system, based on resonance and pressure-induced stiffness, which has clinical viability, is introduced²⁶.

METHODS

Subjects

The subject population was drawn from patients presenting at the Virginia Commonwealth Health Systems' Emergency Department and the Neuroscience Intensive Care Unit with a diagnosis of acute intracranial hemorrhage from trauma or other causes considered to be a risk for elevated ICP. A total of five patients were enrolled in this institutional review board–approved study over a 6-month period. According to the inclusion criteria, subjects had to have documented evidence of intracranial injury on computed axial tomography, be comatose (Glasgow Coma Score of ≤ 8), and be mechanically ventilated. Patients meeting these criteria are usually considered candidates for invasive ICP monitoring. All five patients with ventriculostomy catheters already placed for monitoring of ICP as a part of care for brain trauma or intracranial hemorrhage from other causes were selected randomly. Although there was no control group, one of the five selected subjects who had a normal ICP of 2 mm Hg served as a reference.

Data Acquisition

Single-session recordings were made, but subjects

were followed for a period of a few hours. ICP in the subjects was not manipulated; instead, natural variations were monitored as possible. Data from the five subjects' eye vibratory responses to head vibration, reflecting the acoustic transmission from the brain to the eye with elevated ICP, were analyzed. The acoustic eye recording technique itself offered no more than minimal risk.

Comparison measurements were made with the implanted pressure-monitoring device and the eye acoustic technique. The analysis consisted of a comparison of the ICP measurements obtained through the invasive monitor to the pressures calculated from the changes in the acoustic spectrum. The reliability of the data was explored through two comparisons: (1) within subjects, with repeated measurements of pressure, and (2) between subjects. Within subjects, the measure of interest will be the standard deviation of the slopes of the equations used to calculate pressure from the acoustic changes. This measure yielded an estimate of the variability of the calculated pressures within a given subject for a given pressure. This was possible only on one subject because of ICU access limitations. Between subjects, the average slope of the equations was compared in the same way, to determine the intersubject variability. As no clinical data on the technique currently exist, the researchers assumed that a small sample size of five patients would allow for determining feasibility with an estimated detection of a 2-mm Hg difference between invasive and noninvasive measurements with a power of 90%. Table 1 summarizes the ICPs in the five subjects.

Table 1. Intracranial Pressure Obtained by Invasive Monitoring in Five Subjects at Time of Study, Calibrated to the Ocular Response.

Subject	Invasive Monitoring Method	ICP (mm Hg)
HB	Ventriculostomy	7
GC	Ventriculostomy	11
GJ	Ventriculostomy	15
BP	Ventriculostomy	18
RR	Ventriculostomy	20

The Acoustic Monitoring System

The sensor assembly for acoustic monitoring consists of two piezoelectric transducers attached with adhesive. The transducers were connected to the acoustic monitoring system with wires. The sensors were sterilized with a commercial sterilant. The acoustic monitoring system consists of signal generation, signal reception, and analysis components. Signals (broadband noise with energy to 100 kHz) were generated and analyzed by a Hewlett Packard 3561A Dynamic Signal Analyzer (Agilent Technologies, Inc. Santa Clara CA). The noise was amplified and sent to a custom-designed piezoelectric transducer (pass band from 2–50 kHz). Signals were received from an

accelerometer (model ACH-01, Measurement Specialties Inc. Hampton VA) on the closed eyelid and were spectrum analyzed. The ICP correlate was signal intensity, calculated from spectrum values based on changes in the amplitude at particular resonances (Figure 1). Stevanovic et al.²¹ have used a similar method to calculate ICP based on acoustic measurements in sheep. The present approach capitalizes on the acoustic resonant properties of the eye, a globe that can be modeled accurately as a sphere. Sixty percent of the globe is bounded by bone, representing a high impedance interface. Calculations of resonant frequencies are in the ultrasonic range from ~31–41 kHz based on the small radius of the eye (~0.75 mm) and the speed of sound in brain (146,000 m/s).

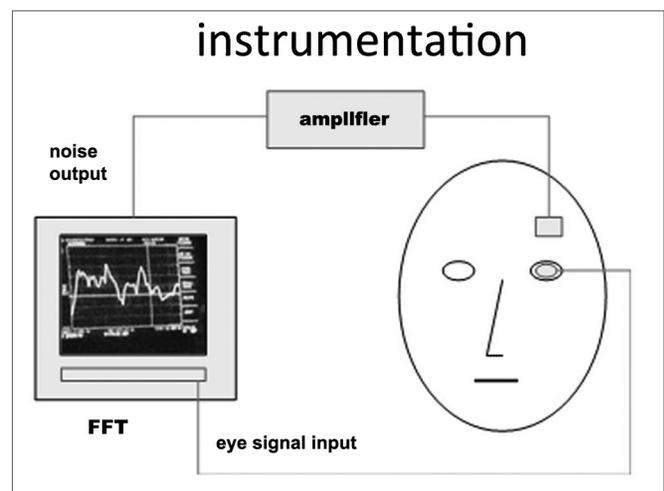


Figure 1. Block diagram of the instrumentation. The fast Fourier transform (FFT) generates the noise delivered to the sensor on the forehead and also analyzes the signal recorded from the accelerometer on the eyelid.

The acoustic response of the eye reflects the coupled influence of the brain/skull resonance system: The eye and brain have similar tissue densities²⁷ and, as a result, constitute a natural acoustic filtering system (pass chiefly 30+ kHz) that results in a narrow band of energy conducive to a clinical approach. Coincidentally resonance frequencies (of the eye and higher) between ~40 and 100 kHz were reported to be well defined and repeatable.^{28,29}

RESULTS

Increased ICP altered the acoustic response of the eye in a reliable and consistent fashion. With elevated pressures, the amplitude of frequencies in the region of the eye resonance decreased on the order of 11 dB. It was not possible to systematically compare the effects of changed pressures within individuals because of time limitations in the ICU, but comparing the effects between individuals was robust and significant ($p > .001$). Two representative

individual eye plots are presented in Figure 2. Eye resonance was expected to be in the frequency range of 32–42 kHz by modeling.⁵ Note that the amplitudes in the eye resonance range were the greatest overall, and the difference between the two curves is approximately 11 dB near eye resonance. The curve associated with the higher ICP yielded the lowest relative intensity (baseline of about -100 dB volts [dBV]). Attenuation was expressed in relative decibel volts because the mass of the head was not measured, though the intensity of the noise was constant for each subject; thus, the noise input to each head could differ. The highest ICP was set at -100 dB, and the lower ICP spectrum was automatically scaled to determine relative attenuation between the two spectra. Repeated measures were obtained only twice under the ICU conditions.

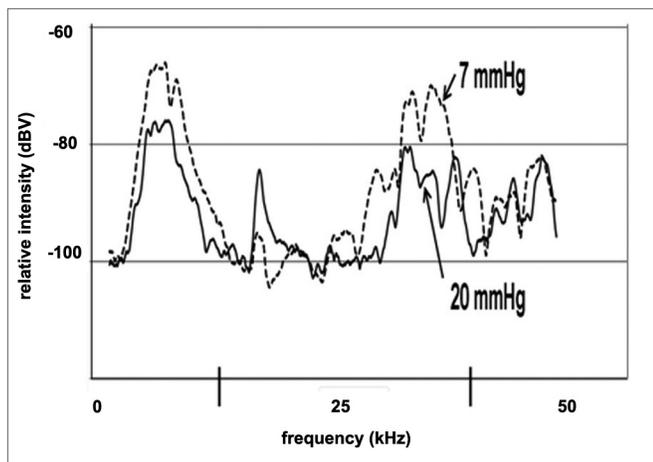


Figure 2. The eye recording from two individuals with intracranial pressures of 7 mm Hg and 22 mm Hg is depicted. The response amplitude is maximal for each subject in the frequency region around eye resonance (30–40 kHz). The higher intracranial pressure is approximately 11 dB lower in amplitude.

A similar picture is presented in Figure 3, in which the eye resonance associated with an ICP of 20 is approximately 11 dB lower than that associated with an ICP of 7. Additionally, the frequencies on either side of resonance are also attenuated, as previously indicated (see Figure 2). Although this study lacked a normal control group, one individual was available with a normal ICP of 2 mm Hg and served as a reference. When that eye recording was compared with an individual with a moderate ICP pressure of 15, the eye resonance frequency range was again approximately 11 dB lower for the subject with elevated pressure (Figure 4). Thus, the picture emerges of a damped acoustic response of the eye of nearly 11 dB, prominent at resonance, which reflects moderately elevated ICP.

The test-retest reliability was very good, as exemplified in two recordings from the same individual (Figure 5). The eye resonance was prominent and repeatable, as was the response in other frequency ranges, presumably

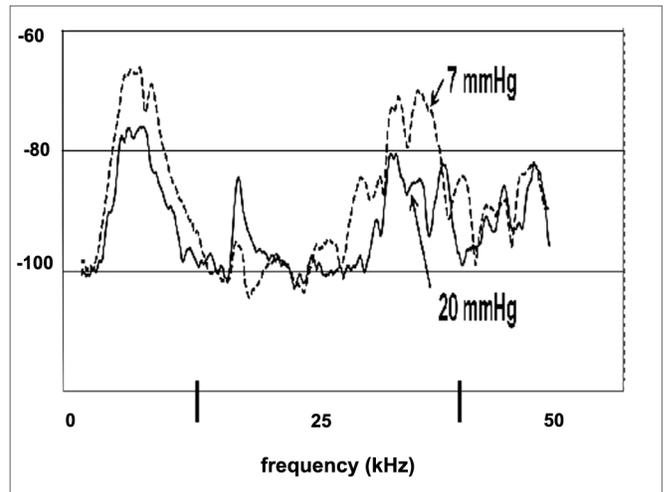


Figure 3. Two eye recordings showing the effect of brain pressure. The more intense intracranial pressure (20 mm Hg) results in an attenuation of the eye response by approximately 11 dB. Maximal response is in the region of eye resonance.

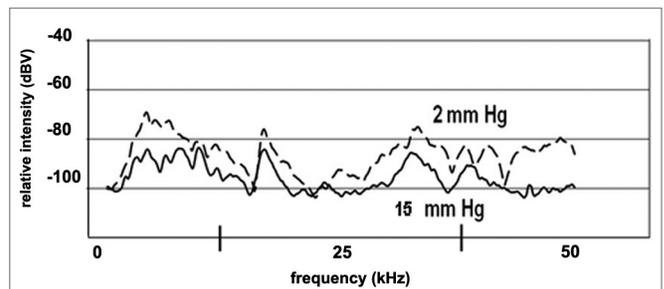


Figure 4. Eye recording in a subject with an intracranial pressure of 15 mm Hg as compared with that of a subject who, at the time of recording, had a normal intracranial pressure is depicted.

reflecting resonant contributions of the brain and skull. The amplitude reductions, with elevated ICP, over the pressures recorded from the five subjects, are presented in Table 2. When both pressures were low, the difference in intensity in the eye resonant range was 4.7 dB. When the pressures were moderately elevated, the differences ranged from 9.2 to 13 dB (see Table 2). When three discrete frequencies (36, 38, and 40 kHz) in the eye resonance range were measured in all five subjects and plotted as the log of the maximum ICP – maximal normal ICP, an encouraging trend of linear slopes was observed. This finding is not a substitute for a larger subject pool, which is necessary, but suggests feasibility of the eye recording approach (Figure 6). Assuming linearity, as is suggested in Figure 6, these data provide the first principle acoustic calibration at the transducer for the pressurized brain/eye response that has medical utility.

DISCUSSION

These data from a preliminary sample of five patients with implanted ventriculostomy catheters suggests

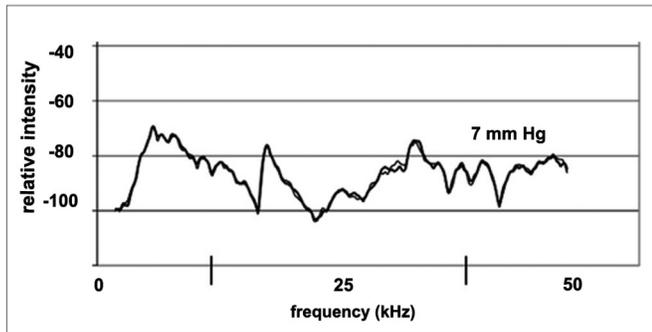


Figure 5. The repeatability of the recording in one subject is presented. The recordings were approximately 30 minutes apart. Sensors were not removed and replaced.

Table 2. Difference in Intracranial Pressure Values Between Selected Subjects.

ICP	Δ dB
7-11	-4.7*
7-15	-9.2*
7-20	-11.3*
11-15	-10.3*
11-18	-13*
11-20	-12.9*

*Significant at the $p > .001$ level.

Note: For all moderately elevated pressures, the difference is ~ 11 dB.

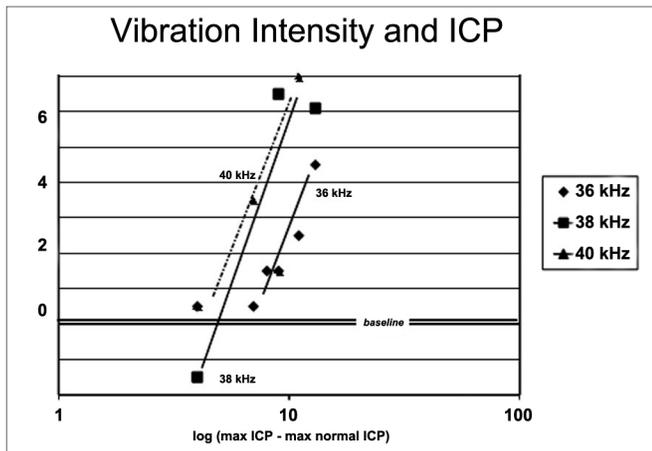


Figure 6. Intensity of the eye recording at three frequencies around resonance plotted as a log function of the maximum for each subject – the maximum recorded that was considered clinically normal. Trend line suggests a reasonable degree of linearity in the eye response for just five subjects.

a relationship between vibration intensity measured on the eye and elevated ICP. Although the sample was small, a clear trend was evident. The metric used was the intensity difference in the frequency range between ~ 30 and 50 kHz, presumably reflecting the acoustic properties of the eye and brain under conditions of various ICPs as measured noninvasively and calibrated invasively. The eye, especially

at resonance, has acoustic properties that reflect an internalized, pressurized brain. These properties are reduced amplitude at resonance and reduced amplitudes in the frequency regions above and below resonance. The eye acoustic effect is a classic example of a damped response due to pressurization resulting in increased stiffness. The concept that the brain and eye share the same pressure is poorly supported¹², but equivalent pressures are not necessary if it can be demonstrated that the eye reflects the acoustic properties of brain pressurization. How the eye is affected by brain pressure—by the direct pathway via the optic nerve or by brain vibration communicated to the eye via the skull (or both)—is not known. However, the direct pathway is favored in that the tissue densities (acoustic impedances) are essentially the same^{5,27}. Although both pathways have utility, small sensor movements on the skin of the skull can result in ± 5 dB changes due to positioning which approximate some of the effects of ICP changes, limiting its clinical application^{23,24}. The brain/skull complex exhibits a set of complex resonances and antiresonances in response to a wide band noise, and it is possible that other frequency ranges may be of value in devising the algorithm equating ICP to decibels of attenuation on the eye, as needed for widespread use of this technique. The acoustic features of fluid damping are stable over recording sessions, encouraging additional studies.

A previous acoustic approach combined the measurements of skull vibrations with ultrasonic measurement of blood flow in the main optic artery^{28,29}. The optic nerve and its vascular bundle are exposed to ICP because the optic nerve and the nerve sheath have a sleeve of CSF that extends up to the globe. Using a mask over the eye that is capable of exerting pressure over the globe, it has been determined that pressure in the eye equals ICP when the retinal arterial pulsations stop. The technique is cumbersome nonetheless; the eye can reflect increased ICP via ultrasonography.³⁰ However, adding cerebral blood flow data to ICP does not improve patient outcomes³¹.

Yet another acoustic approach to monitoring ICP relies on the fact that the skull is synchronously displaced by pulsating blood volume produced by the cardiovascular system. Yost²⁵ observed that the phase of ultrasonic echoes reflects slight displacements in the skull with increased pressure. A linear relationship between ICP and skull displacement was found using an ultrasonic pulsed-phase locked-loop device to measure ICP waveforms. The focus was on the waveforms rather than pressure alone. The concept that the skull moves with the pulsing of the brain and that, with increased pressure, skull displacement can damp wave propagation in the brain and eye^{32,33} also supports the present findings.

Others have demonstrated relationships between intraocular pressure and ICP⁶⁻¹², but the general consensus is that no such correlation between the pressures exists.

Intraocular pressure measures were unable to accurately track changes in ICP in real time, with the limits of agreement being too wide for clinical use.

Elevated ICP will alter acoustic emissions from the cochlea in an animal model^{34,35}. The cochlea is connected to the CSF system via the cochlear aqueduct. The patent duct allows pressure equalization between the ventricles and the inner ear. Prior attempts to use impedance audiometry to measure ICP have met with mixed success^{14,17}, although acoustic emission appears more effective. Briefly, increased intracochlear pressure results in increased stiffness in the stapes in the middle ear, which, in turn, phase shifts the acoustic emissions (maximally around 2 kHz). Changes in ICP induced by head positioning (up, down) in rats have also been shown to increase the summing potential in the electrocochleogram³⁶. All these methods support a brain “window” approach^{14–16}, which forms the basis of the current approach.

The present data only suggest feasibility of this more simplified approach to ICP acoustic monitoring; an algorithm relating decibels of attenuation to ICP has yet to be developed. Two types of analysis for algorithm to be developed are envisioned based on the preliminary data using a neural network approach. Peaks in the acoustic response near resonance certainly could be identified, given some set range of variation, and the peak amplitude could be measured and compared to previous readings as well as the normal baseline. The alternative (or possibly complimentary) approach would be to quantify the area under the curve between the zero level and the peaks. Here, the variable to be correlated with ICP will be spatial. More subject data are needed for this step.

As a final note, the ICP resolution of this approach is not clear. Though it is premature to place much confidence in the outcomes of a mere five subjects, it seems that mild hyper-pressure is associated with an acoustic attenuation of approximately 5 dB, whereas moderate hyper-pressure is associated with approximately 10 dB of attenuation (Table 2). Even if this approach can only differentiate among mild, moderate, and high ICP, that information is clinically valuable, especially in determining whether ICP is static or changing.

SUMMARY

Acoustic coupling of the skull, brain, and eye have complex resonance frequencies that are transformed, in a predictable manner, with changes in ICP. Furthermore, these changes can be calibrated to acoustic equivalents of ICP at a scale allowing for diagnostic value. The overarching goal of this program is to develop technology that will assist in reducing the mortality and morbidity associated with brain injury by enhancing diagnostic and treatment capabilities.

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