Hydrocephalus is characterized by the accumulation of excess cerebrospinal fluid (CSF) within the brain. Hydrocephalus affects individuals of all ages, especially newborn infants and older adults. Hydrocephalus is most commonly treated by surgically implanting a cerebral shunt, which is essentially a mechanical valve and tube that drains excess CSF from the ventricles to other body spaces such as the peritoneal cavity. Despite high failure rates, shunt design has changed little since these shunts were first used in the 1950s, mostly via valve designs intended to improve the fluid drainage characteristics. Advances have included the addition of antisiphon devices to reduce overdrainage, valves with externally adjustable pressure set points, and valves that regulate the flow rate rather than pressure. Valves are typically designed with static conditions in mind, but the dynamics of ICP and the CSF system can have unforeseen impacts on valve behavior (Supplementary Fig. S1). Electronic (i.e., smart) shunts are also being developed to address failure modes and allow sophisticated control of intracranial pressure (ICP). These smart shunts are designed to sense and maintain ICP within acceptable levels through a control algorithm that needs to respond appropriately to fast and slow ICP changes while saving power for long-term battery operation. Dynamic testing systems play an essential role in the testing and development of conventional mechanical shunts and emerging smart shunts.
Shunt drainage is affected by dynamic conditions such as posture changes and fluctuations induced by exercise, patient movement, and complex physiological cycles in CSF production and cerebral blood flow. For example, ICP constantly oscillates because of the influence of respiratory, cardiac, and other endogenous pressure waves in the brain. Oscillating ICP produces a pumping effect in many differential pressure valves that leads to an increase in the amount of drained CSF.9,15 This effect may be exacerbated by strenuous exercise and other circumstances with elevated respiratory and heart rates. Lundberg B waves, which produce high-amplitude fluctuations in cerebral blood flow (and consequently ICP) because of alternating dilation and constriction of the cerebral vascular bed,12–15,23 are another example of this phenomenon. The pumping effects driven by these fluctuations cause overdrainage, which leads to a gradual drop in ICP that presents as morning headaches.

Several benchtop rigs have been designed over the years to test shunts. Aschoff et al.3 documented setups designed to test the resistance and pressure-dependent flow rates of shunt valves and used physical changes in the system to model physiological conditions such as sinusoidal waves, impulse waves, and siphoning. Czosnyka et al.15 built a rig with an electronic pulse-pressure generator for producing ICP waves, and they tested for the effects of siphoning, reflux, and impulse waves on shunt behavior. Elixmann et al.19,27 designed a benchtop representation of the CSF system with a physical model of brain compliance that was based on a sponge in a fluid compartment. On the other hand, many completely virtual models of ICP and CSF dynamics have been developed, including the 6-compartment model proposed by Ko et al.,26 but these dynamics are excluded from typical shunt-testing systems.

Shunt-testing systems that use physical models require the hardware to be changed to simulate different physiological conditions (e.g., brain tissue compliance) and, thus, do not allow for the “on-the-fly” changes needed to simulate the physiological changes that would occur in real time within a patient (e.g., instantaneous variations in brain compliance with changing ICP). Our ultimate goal is to transcend these limitations by creating a smart system that is capable of actively responding to shunt performance under real-time patient scenarios (e.g., minute-to-minute variations in physiology in response to movements and posture changes) and using shunt responses to generate a new set of simulated testing conditions. Here, we present an essential step toward this goal by developing a flexible hardware-software interface that allows common dynamic conditions to be manipulated arbitrarily from a computer without changes to the hardware itself. Figure 1 shows the conceptual framework for a shunt-testing system based on a virtual model. At any instant, a shunt is subject to an applied ICP at the inlet and either abdominal or siphoning pressure at the outlet, and the flow through the shunt is measured. By creating a cycle with a virtual model, the measured drainage rate could be used to calculate a new condition based on a patient brain model or patient scenario (e.g., when the patient stands up) with the new condition being physically applied to the shunt, and so on. Here, we present a framework that is configured to test shunts affected by respiratory and cardiac ICP waves (with tunable frequencies and amplitudes), ICP amplitude elevations that occur with low brain compliance, posture-dependent ICP changes, impulse waves, noise, abdominal pressure effects, and siphoning.

**Methods**

The goal of the hardware was to apply desired pressures to the inlet and outlet of the shunt and measure the resulting flow rate. Dynamic pressures were classified as 1) long-timescale changes (e.g., patient position, drainage responses) that were applied by the pressure/vacuum sources and 2) short-timescale changes (e.g., noise, impulses, pulsations) that were applied by the speakers. The testing rig in Fig. 2 consisted of 2 tanks representing the cephalic and abdominal spaces. Each tank consisted of a closed Plexiglas cylinder fitted with a speaker on the top (Dayton Audio DA115–8 4 Aluminum Cone Woofer),...
which was used to produce oscillations and other short timescale disturbances. Inlet pressure (i.e., ICP) and outlet pressure (i.e., abdominal) were defined as the air pressures above the water in each cylinder and were measured using electronic pressure sensors (HCLA series; SensorTech).

The average ICP levels were controlled in the tanks using electronic airflow regulators for low-pressure applications (Kelly Pneumatics, Inc.). These regulators (which were fitted with internal pressure sensors) were connected to house air and vacuum sources and used to set and maintain the desired baseline ICP. The response time of the regulators was tuned to prevent them from reacting to short-timescale transients, ensuring that regulator control did not interfere with the simulating ICP waves, noise, and impulse spikes within the tanks. A level switch (Omega Engineering LVK-91) was fitted to the abdominal tank to monitor its water level, and a peristaltic pump was used to pump water (i.e., a mock CSF) from the abdominal to the cephalic tank to counteract shunt drainage and maintain constant water levels in the tanks. When testing the shunts, a flow sensor (Sensirion ASL 1600) was added to the distal catheter to measure the flow rate through the shunt. Each tank was fitted with a port to allow connection to the shunt tubing.

All electronic devices were connected to a National Instruments USB-6259 Data Acquisition System for controlling the system and receiving data. The data acquisition system was controlled from a computer using National Instruments LabVIEW Software. A LabVIEW control panel was programmed to adjust the pressure set point in both tanks through the regulators and record the pressure in both tanks. A control loop connecting the pump and level switch was set up to maintain the tank water level (Supplementary Fig. S2). When the water in the abdominal tank rose to the switch point (because of shunt drainage), the level switch would activate the pump. Speakers were used to simulate short timescale ICP spikes, as well as the longer timescale oscillations from the respiratory, cardiac, and C waves. Speaker controls were used to adjust the frequency and amplitude of the ICP waves. The simulation results were recorded in LabVIEW, written to an Microsoft Excel file, and plotted. The flow sensor was operated independently of LabVIEW using Sensirion measurement software.

A shunt-testing experiment was performed using the simulation system by connecting a Strata valve shunt to the system. The valve was obtained for research purposes after it was opened for a planned surgery but not used. Before initiating the experiment, the valve was first rid of air bubbles, and a finite pressure (i.e., ICP) was applied to the cephalic tank. Flow through the distal shunt catheter was measured and recorded using the electronic flow sensor, and fluid was recycled into the cephalic tank from the abdominal tank using the peristaltic pump. ICP and CSF flow measurements through the experiment’s time course were jointly plotted in Microsoft Excel. The experiment involved a single run of measurements under 2 conditions: oscillating ICP and nonoscillating ICP.

Results

To demonstrate the system, we focused on 5 dynamic conditions: 1) basal ICP oscillations (respiratory, cardiac, and C waves); 2) short-timescale disturbances (rapid, transient, and irregular spikes); 3) ICP amplitude dependence on baseline pressure; 4) posture-dependent ICP changes; and 5) abdominal pressure and shunt-siphoning effects. The ICP parameters reported in the literature (Table 1) were used to define the test conditions.

Respiratory, Cardiac, and C Waves

Slow- to medium-timescale waves of ICP typically manifest as respiratory, cardiac, and nonpathological slow waves, the most important of which are C waves. Respiratory waves are caused by the breathing cycle and affect ICP by changing intrathoracic pressure and, consequently, systemic venous return and blood pressure.
Cardiac ICP waves have a much higher frequency that corresponds to the heart rate. Each systolic contraction leads to an increase in arterial pressure that produces a transient ICP increase.\(^4,26\) C waves, on the other hand, are low-frequency oscillations that are an intrinsic property of ICP with causes that are not yet fully understood.\(^23\) Figure 3 shows simulated respiratory, cardiac, and C waves. In our system, ICP waves were specified by their virtual frequency and amplitude, and the resulting combined waveform was used to drive the speakers.

### Rapid, Transient, and Irregular Spikes in ICP

ICP can also be altered by spikes in pressure caused by activities such as exercise, coughing, sneezing, and Valsalva maneuvers. Brimioulle et al.\(^5\) measured ICP spikes in physiotherapy patients who were asked to perform hip adduction exercises, and Coté et al.\(^10\) simulated the ICP impulse response associated with random transient events such as coughing and sneezing. In our system, short-timescale, high-amplitude changes were produced in the tanks using the speakers (Fig. 4). The amplitude, frequency, and duty cycle can be adjusted to modify the strength, rate, and duration of each ICP spike to model different types of exercises, as well as coughing, sneezing, and Valsalva.

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Parameter Description</th>
<th>Magnitude</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sakka et al., 2011</td>
<td>Normal ICP (recumbent)</td>
<td>15 cm H(_2)O</td>
</tr>
<tr>
<td>Chapman et al., 1990; Foltz et al., 1994</td>
<td>Normal ICP (upright)</td>
<td>~6.6–0 cm H(_2)O</td>
</tr>
<tr>
<td>Juul et al., 2000</td>
<td>Hypertension threshold</td>
<td>26–32.5 cm H(_2)O</td>
</tr>
<tr>
<td>Lemaire et al., 2002</td>
<td>C-wave amplitude range</td>
<td>0–27.2 cm H(_2)O</td>
</tr>
<tr>
<td>Dunn, 2002</td>
<td>C-wave frequency range</td>
<td>4–8 waves/min</td>
</tr>
<tr>
<td>Czosnyka et al., 2004</td>
<td>Respiratory amplitude</td>
<td>&lt;1 cm H(_2)O</td>
</tr>
<tr>
<td>Daley et al., 1982</td>
<td>Cardiac amplitude</td>
<td>0.78–9.36 cm H(_2)O</td>
</tr>
</tbody>
</table>

![Figure 3](image-url)
Effect of Baseline ICP on the Amplitudes of the Waves of All Timescales

As ICP increases, brain compliance and the ability to maintain a constant net intracranial volume decrease.34 This mechanism eventually leads to an exponential increase in ICP with relatively small changes in intracranial volume.40 This phenomenon is also observed with ICP waves: as baseline ICP increases, the corresponding decrease in brain compliance leads to higher wave amplitudes than what is observed under physiologically normal ICP.15,40 Figure 5 shows the comparison of amplitude dependence on baseline ICP as presented by Keong et al.24 with those simulated in our physical system. As baseline ICP increases, the amplitudes of the simulated respiratory, cardiac, and C waves also increase. Increases in amplitude were simulated through control of the voltage output to the speaker. ICP baseline was established at the set point by the pressure regulators, and the amplitude of the voltage output to the speaker was increased to simulate the larger magnitude due to reduced compliance.

Posture-Dependent CSF Drainage

Switching from the recumbent position to the upright position leads to a decrease in ICP.23,24,33 This is caused by a reduced venous return and pooling of blood in the lower extremities. The decrease is gradually compensated for by endogenous blood pressure control mechanisms and CSF production by the choroid plexus, which leads to progressive ventricular filling. Figure 6 shows a comparison of data from the literature with the simulated conditions in our system. Figure 6A from Chapman et al.8 demonstrates a decrease in ICP with an increase in the angle of posture from the horizontal. Figure 6B shows an initial decrease in ICP when sitting upright that eventually increases because of the filling phase,31 and Fig. 6C demonstrates this effect in our physical system. Posture-dependent drainage was simulated by tuning the starting and ending ICP baseline values and the timing of ICP recovery in the upright state due to compensatory mechanisms such as filling. Both normal and pathological conditions are demonstrated.

Pathological conditions were modeled with higher than...
normal upright and recumbent ICPs, higher maximum upright pressure, and a faster than normal rise in filling pressure, the latter two of which are characteristics of reduced brain compliance.

Abdominal Effects and Shunt Siphoning

Intraabdominal pressures (IAPs) can affect shunt function, and IAP simulations can be a useful way of testing shunt reflux. In our system, the IAP effects are tested by changing the set point pressure in the abdominal/peritoneal tank that is connected to the shunt outlet. To test reflux, a high positive pressure is applied inside the tank, and the magnitude and direction of the flow through the shunt is measured in response to these changes in order to assess the degree of reflux.

Shunt-Testing Experiments

The Medtronic Strata valve was first tested with basal ICP oscillations (respiratory and cardiac cycles) and then spikes. The results of our testing are shown in Fig. 7. To test for this phenomenon, the average measured ICP and flow through the shunt with oscillating pressure is compared with the same parameters when basal oscillations (respiratory, cardiac, and C waves) are absent. The mean ICPs in both scenarios were tuned to be virtually the same value: 13.6 ± 0.1 cm H$_2$O without oscillations and 13.8 ±
0.8 cm H₂O with oscillations. Interestingly, the flow rates, as measured by the flow sensor, were significantly different for these 2 scenarios. A rate of 462 ± 6 μl/minute was measured without oscillations, while a rate of 494 ± 15 μl/minute was measured with basal oscillations.

**Discussion**

An important limitation regarding the ICP parameters provided in Table 1 is that they are primarily obtained from experimental measurements made in adults and therefore may or may not be representative of a pediatric population. Adding to this limitation is the paucity of information in the literature on certain characteristics of intrinsic ICP waves (e.g., C-wave amplitude and frequency), with the sources listed here being among the very few that provide concrete values for these parameters (the values for pediatric patients are even more scarce). Nevertheless, our goal was to design a flexible test bed that would appropriately accommodate and adapt to a variety of physiological parameters. As such, the parameters that we provide here merely serve illustrative purposes meant to demonstrate the test bed’s working capability.

With respect to simulating respiratory, cardiac, and C waves, we wanted to make sure that our system can incorporate a good deal of physiological variability in our simulations. To this end, the frequency and amplitude of the respiratory and cardiac waves were made tunable through LabVIEW’s front-panel controls (Supplementary Figs. S2 and S3) to virtually model variations in the heart rate, breathing rate, and blood pressure that can then be physically simulated by the testing hardware. Testing shunts through simulations of physiological variations within the CSF system, which we have demonstrated in our setup, will play an important role in achieving the following treatment goals: 1) optimized shunt function to suit each patient’s personalized needs, and 2) flexible and adaptable shunt responses that are well suited to intrapatient physiological variability.

With regard to simulating spikes in ICP, the amplitudes of these spikes will be lower in a patient with a properly functioning shunt (as opposed to a patient without a shunt) because of compensation by shunt drainage. In addition, it is important to simulate fast-timescale changes in ICP in order to enable the optimization of shunts and prevent overdrainage. Simulation of fast-timescale changes will be

![Fig. 6. Posture-dependent changes in ICP. A: The literature results demonstrating ICP levels at the sine of various angles of depression or elevation, with a drop in ICP associated with the transition to upright posture. Reproduced with permission from Chapman PH, Cosman ER, Arnold MA: The relationship between ventricular fluid pressure and body position in normal subjects and subjects with shunts: a telemetric study. Neurosurgery 26:181–189, 1990. B: ICP shift produced in a patient with aqueductal occlusion by switching from lying down to sitting up. After sitting up, the initial ICP drop is followed by a slow rise due to ventricular filling. Reproduced with permission from Magnaes B: J Neurosurg 44:687–697, 1976. C: Data from the simulation system illustrating position-dependent ICP changes under normal and pathological conditions. In patients with aqueductal occlusion, baseline ICP is elevated and the rate of ICP increase is higher during the filling phase of the upright position. To align the time of the transition points for all traces, a portion of the steady-state trace in the upright position is not shown for 3 of the 4 traces. Figure is available in color online only.](image-url)
especially important in testing smart shunts, which must be programmed to appropriately interpret discrete pressure measurements (e.g., a measurement made during a short spike should not be interpreted as high ICP that requires drainage).

In our simulation for testing the effect of baseline ICP on the amplitudes of ICP oscillations, one particular limitation we encountered was the inability to increase the speakers’ displacement indefinitely. At a certain baseline air pressure in the tank (i.e., baseline ICP), the opposing force was too large for the speaker, thereby limiting the amplitude of the speaker’s pressure waves. However, this did not detract from our ability to reliably test a working shunt because unless the shunt has severely malfunctioned or been completely obstructed, excessively high ICPs have a low chance of occurrence. Thus, the system was able to produce the magnitude of pressure oscillations expected for a typical range of ICP.

When it comes to testing patient positioning on CSF dynamics, the effects of patient posture on the shunts need to be tested because of the importance of siphoning and overdrainage in shunt design. This simulation can also be used to test the response times of the smart shunts to orthostatic ICP changes and can ultimately facilitate the selection of the control parameters that lead to optimal drainage control and power draw in smart shunts. Furthermore, siphoning by shunts is a major cause of overdrainage in the upright position. Siphoning pressure, which is directly proportional to the distance between the ventricles and the peritoneal cavity, is high in both pediatric and adult patients (although much higher in adults). Both physiologically and in our model, elevated IAP contributes to a positive outlet pressure that can lead to reflux, while siphoning acts as a vacuum that can lead to overdrainage. Oscillatory wave components can also be imposed on these pressures through our virtual model.

In showing a differential flow rate across valves with identical mean ICPs under oscillating and non-oscillating conditions, the results of the shunt testing experiment effectively demonstrate a pumping effect with net fluid loss at a given baseline pressure when oscillations are present. This phenomenon is observed because oscillations in ICP lead to increased shunt drainage over time compared with what was observed at baseline ICP, leading to the conclusion that the 1-way valve of the shunt becomes a pump under oscillating pressures.

**Conclusions**

Our main purpose here was to establish a proof-of-concept system to allow virtual models of ICP and CSF dynamics to be integrated into shunt-testing procedures. By simulating a variety of physiological variations in ICP and using simulations to test shunt drainage, we have
demonstrated that our testing framework can be used as a foundation upon which more complex virtual models can be constructed to test for more sophisticated performance factors.

A useful implementation of this system would incorporate an automated feedback model to bridge the physical and virtual systems. We envision this as an interaction in which the physical model receives continuous inlet (i.e., ICP) and outlet (i.e., IAP or siphoning) pressures as inputs and the measured volume of drained CSF is fed back to the virtual model, which is programmed to generate a new set of instantaneous inputs (see Fig. 2). The virtual model can be expressed as any algorithm that the researcher would like to simulate, including the dynamics of the CSF system and patient scenarios. This type of approach is useful for modeling changes in brain compliance and intracranial volume (ICV(t)) and their relationship to ICP changes. Unlike physical compliance models, a dynamic feedback scheme allows for modeling compliance as a time-dependent relationship between ΔICP (input) and ΔICV(t) (output) based on the brain compliance models that represent different patient populations and scenarios.

For testing smart shunts, the figure of merit (FOM) is a quantitative assessment of electronic shunt performance and power consumption that is calculated using algorithms that can be incorporated into the testing system. FOM algorithms can be run alongside the electronic simulations of the testing system in order to assess the smart shunt’s response to various physiological ICP fluctuations. As such, FOMs are a potentially useful way to model the quantitative relationship between power consumption and physiological conditions and will perhaps help establish an optimal balance between efficiency and efficacy in smart shunts.

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Disclosures
Drs. Browd and Lutz report that they own stock in Aqueduct Neurosciences Inc. and Aqueduct Critical Care Inc.

Author Contributions
Conception and design: Lutz. Acquisition of data: Venkataraman. Analysis and interpretation of data: Venkataraman. Drafting the article: Venkataraman. Critically revising the article: Lutz, Browd. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Lutz. Administrative/technical/material support: Browd. Study supervision: Lutz.

Supplemental Information
Online-Only Content
Supplemental material is available with the online version of the article.

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