Phantom Model of Physiologic Intracranial Pressure and Cerebrospinal Fluid Dynamics

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Abstract—We describe herein a novel life-size phantom model of the intracranial cavity and its validation. The cerebrospinal fluid (CSF) domains including ventricular, cysternal and subarachnoid spaces were derived via magnetic resonance imaging (MRI). Brain mechanical properties and cranio-spinal compliance were set based on published data. Both bulk and pulsatile physiologic CSF flow were modeled.

Model validation was carried out by comparisons of flow and pressure measurements in the phantom with published in vivo data of healthy subjects. Physiologic intracranial pressure (ICP) with 10 mmHg mean and 0.4 mmHg peak pulse amplitude was recorded in the ventricles. Peak CSF flow rates of 0.2 ml/s and 2 ml/s were measured in the cerebral aqueduct and subarachnoid space (SAS), respectively.

The phantom constitutes a first-of-its-kind approach to modeling physiologic intracranial dynamics in vitro. Herein, we describe the phantom design and manufacturing, definition and implementation of its operating parameters, as well as the validation of the modeled dynamics.

Index Terms—anatomical model, compliance, subarachnoid space, ventricular system

I. INTRODUCTION

The cerebrospinal fluid (CSF) contributes to the homeostasis of the central nervous system (CNS). Within the intracranial cavity, CSF is confined in the ventricular and subarachnoid spaces (SAS) pressurized with respect to atmospheric reference. CSF supports the brain by buoyancy, protects it from impact, transports nutrients as well as neuroendocrine substances, and removes metabolic waste products.

Alteration in CSF dynamics relates to several disorders. Hydrocephalus and syringomyelia, for example, have been linked to disturbances in CSF bulk flow as well as pulsation [1-3]. However, the specifics of these relations are not yet understood.

Models of intracranial dynamics can improve the understanding of CNS patho-physics. Both lumped parameter and computational fluid dynamics (CFD) models have been used to characterize dynamics within the CSF spaces [4-11], as well as in major intracranial arteries [12, 13]. The lumped parameter approach is particularly well suited for a global, empirical description of intracranial dynamics [9-11]. Corresponding model parameters such as CSF outflow resistance and pressure-volume index have become standards in the clinical practice during the last decade [14]. In contrast, CFD models can be employed to access spatially resolved flow information that cannot be obtained through measurement [15, 16].

However, neither lumped parameter nor CFD models of the intracranial cavity have proven to be optimal for the development of medical devices that alter intracranial dynamics. For example, CSF shunts used to treat hydrocephalus are tested experimentally according to the ISO 7197 standard to assess hydraulic resistance [17]. To analyze the full dynamic behavior of a specific shunt rather than just measuring hydraulic resistance, animal models have to be employed. However, besides ethical concerns, these are expensive, especially when larger animals such as dogs, goats or monkeys are used, whose intracranial dynamics are closer to those of humans compared to those of mice, rats or rabbits.

In vitro phantoms represent a fourth model type that may aid in the investigation of CNS pathophysiology. Both anatomically detailed and simplified phantoms have been used to validate MRI sequences [18-20], computational models of brain mechanics [21] as well as CSF flow in the third ventricle [22]. In brain injury research, phantom models have been employed to study tissue response to impact [23, 24]. To our knowledge, only one phantom model of fluid and pressure dynamics in the spinal CSF space has been reported; it was employed to gain understanding of syringomyelia [25, 26].

Phantom models of the intracranial space have the potential to reduce, refine and to a smaller extent replace animal models for the testing of shunts and other neurosurgical devices. An important step towards such application is the replication of healthy state intracranial dynamics. We present herein a first-of-its-kind phantom model of the intracranial cavity that can reproduce physiologic cerebrospinal fluid and pressure dynamics. We report on the phantom design, development and validation with in vivo data described in the literature, showing that this modeling approach can contribute to the understanding of intracranial dynamics.
II. MATERIAL AND METHODS

A. CSF and Ventricular System

We formed a ventricular system in a silicone brain using the following approach: A three-dimensional reconstruction of MRI data acquired on a 27 year old healthy male volunteer [5] provided the anatomical reference to design the ventricular domain of the phantom. The ventricular system was simplified to obtain a sagittal symmetry suitable for casting: The lateral ventricles were merged to a single ventricle representation using computer aided design (CAD) software (NX 7.5, Siemens PLM Software, Plano, TX, USA); the foramina of Monro were unified into a single connector to the third ventricle; the foramina of Luschka and Magendie were also merged into a single channel. A negative of this simplified ventricular domain was manufactured in two sagittal symmetric halves by 3D printing on an Eden350V photopolymer printer (Objet Geometries Inc., Billerica, MA, USA).

After obtaining a positive of the ventricle space (see Section II.B), a 2 mm inner diameter silicone tube was inserted into the cerebral aqueduct to avoid its deformation during the phantom construction. For simulation of CSF production in the ventricles [27], an access port was established at the top of the ventricular system. The same access port was also used for the initial filling of the CSF space. Two access points for pressure sensing were established at the top and bottom of the cerebral aqueduct. The adapted ventricular system is shown in Fig. 1, and the effects of the simplifications are discussed in Section IV.

B. Brain and Skull

A life-sized silicone brain was made using Sylgard 527, A&B Dielectric Silicone Gel (Dow Corning, Midland, MI, USA). Previous investigations have shown this material to have similar mechanical behavior as brain under static deformation [21] and dynamic loading up to 10 Hz [28]. The silicone was cast around each of the two ventricle negative halves. After curing, the negatives were removed and the left and right brain parts were glued together with the same silicone. A thin layer of a standard casting silicone (Ecoflex, Smooth-on Inc., Pennsylvania, USA) was applied onto the ventricle walls to prevent adhesion when collapsed.

The completed brain was placed in a plastic human skull model (3B Scientific, Hamburg, Germany) of which the upper part had been removed (Fig. 1).

C. Cisterns and Subarachnoid Space

CSF bulk flow originates in the ventricles, continues to the cisterns at the base of the skull, and reaches the spinal and cortical SAS where it is to a large part reabsorbed into venous blood. The SAS microstructure influences CSF dynamics [15]. The effect of the microstructure can be spatially averaged and expressed through its hydraulic resistance, which is related to permeability. Subarachnoid space permeability has been reported to range in the orders $10^{-8}$-10$^{-7}$ m$^2$ [15]. We used a homogenous pillar structure between parallel plates (Fig. 2) to account for the hydraulic resistance of the SAS. In such a structure, the permeability k is a function of the pillar radius r and the void fraction $\varepsilon$ of the representative unit cell [29]:

$$\frac{k}{r^2} = \frac{\pi \varepsilon (1 - \sqrt{1 - \varepsilon})^2}{24 (1 - \varepsilon)^{3/2}}$$

and

$$\varepsilon = \frac{V_{\text{fluid}}}{V_{\text{tot}}} = \frac{L^2 - \pi r^2}{L^2}$$

where L is the center-to-center distance between two neighboring representative unit cells. We chose a configuration with $r=0.5$mm and $L=1.5$mm, with a resulting permeability value of $1.7 \times 10^{-9}$ m$^2$ according to (1) and (2). This pillar configuration was manufactured by 3D printing (Eden350V, Objet Geometries Inc.) and placed in a PMMA case outside the phantom brain to represent its SAS with 123.7 mL volume according to in vivo MRI data [6, 15] (Fig. 2). The SAS compartment is connected to the ventricular space via a cylindrical cavity of 24 mL volume representing the cysternal space (Fig. 1). This modular approach allows for an uncomplicated change of the SAS resistance to address the effects of pathologic conditions, such as hemorrhage, that can lead to SAS obstruction.

With exception of the SAS representation and compliance modules (see Section II.D), all intracranial elements including skull, silicone brain, cistern and ventricular lumen are enclosed in a water filled, hermetically sealed PMMA box (Fig. 4). The water replicates the buoyancy effect on the brain observed in vivo and serves as a transmission medium for the pressure pulses from the pulsatile pump (Section II.E) to the intracranial compartments, simulating the effects of arterial pulsation.

Fig. 1. The cranial domain of the phantom. A silicone brain is contained in a plastic human skull. The lumen of the simplified ventricular system is shown as superimposition of the CAD model.
Compliance C of the cranio-spinal system is defined as the change of its volume V in response to a variation in its pressure P:

\[ C = \frac{dV}{dP} \] (3)

Compliance can be measured by infusion testing [30]. The physiologic pressure-volume relation from which compliance can be derived follows approximately

\[ ICP = P_0e^{KV} + P_1 \] (4)

where \( P_0 \) is the resting ICP level prior to infusion and K is the brain elastance coefficient. K has been reported to range between 0.0886 and 0.177 ml/mmHg in healthy humans [14], with a corresponding physiological compliance between 0.56 and 1.13 ml/mmHg for undisturbed ventricular volume and healthy resting pressure of \( P_1 = 10 \text{ mmHg} \).

Two compliance boxes filled with water and air are used to reproduce physiologic compliance values. Their overall design is based on the assumption of ideal gas behavior with adiabatic compression and expansion according to

\[ PV^{1.4} = \text{const} \] (5)

The boxes were calibrated experimentally to yield overall compliance of 1 ml/mmHg at the phantom’s operating conditions. They connect to the cisternal and SAS compartments, respectively. The former represents spinal compliance (35% of the overall compliance), and the latter cranial compliance [31, 32].

While compliance follows an exponential trend during infusions tests, it can be considered constant under physiologic conditions [30]: Cranial blood volume changes during the cardiac cycle are two orders of magnitude smaller than volumes injected during infusion [33].

E. Actuation System

Both bulk and pulsatile CSF flow can be reproduced by the phantom. Deionized water at room temperature is used to represent CSF [34]. A peristaltic pump (Peristaltic Pump 66 & 77, Harvard Apparatus, Massachusetts, USA) imposes CSF production in the ventricles and absorption in the cortical subarachnoid space. CSF bulk flow was set to 0.35 ml/min (500ml/day) at both production and absorption sites to model healthy conditions. A programmable pump (CompuFlow 1000MR, Shelley Medical Imaging Technologies, Ontario, Canada) is used to pressurize the water surrounding the cranial compartment in the PMMA box, as well as the CSF space, transiently with 1 Hz. This induces CSF and ICP pulsation similar to healthy in vivo conditions (Table I). The pulsatile pump is controlled through a LabVIEW interface (National Instruments, Texas, USA). Two fine-regulating valves (Serto AG, Aadorf, Switzerland) divide the pump output into two parts: The first induces transient changes in ventricular CSF volume through ventricular wall displacement, while the second displaces CSF in the SAS compartment.

F. Acquisition System

Pressure and flow are monitored at selected locations in the phantom. Intracranial pressure is recorded in the ventricles, cisterns and SAS. Following the gold standard for clinical ICP monitoring, microtip pressure transducers and a corresponding control unit are used to acquire ICP (Microsensor™ and ICP Express™, Codman&Shurtleff, Raynham, MA, USA). Measured data are transferred to a datalogger (Beckhoff Automation GmbH, Verl, Germany), processed in LabVIEW and recorded on a desktop computer. Pressure sensors (Series
41X, Keller AG, Winterthur, Switzerland) are connected to the access points of the cerebral aqueduct (Fig. 1). A coriolis flow transducer (Cubemass, Endress+Hauser Metso AG, Reinach, Switzerland) is used to measure oscillatory flow rates between the pulsatile pump and the SAS.

III. RESULTS

The results given in here demonstrate the validation of the phantom model with physiologic in vivo literature data on intracranial dynamics. Concretely, mean ICP, pulsatile ICP amplitude as well as CSF flow rates in the aqueduct and the cortical SAS were analyzed.

Phase contrast MRI is used routinely to measure CSF flow in the aqueduct of Sylvius and the cervical spinal SAS, yielding in healthy subjects amplitudes of up to 0.3 ml/s and 1.18 to 3.97 ml/s, respectively [33, 35, 36]. In the phantom, the operating parameters described in Section II.E were adjusted to obtain flow rates within the above range in the corresponding sections, i.e. in the aqueduct and the entrance to SAS compartment.

ICP is not measured routinely in healthy subjects due to the invasive nature of the procedure, but data have been reported for animals as well as for humans. Physiologic mean ICP has been shown to be of the order of 10 mmHg [37], but there is no agreement on the range of ICP pulsation amplitude that can be considered healthy: Only few quantitative measurements of amplitudes have been published with peak values of the order of 0.1 mmHg in cats [38] and of approximately 4 mmHg in patients with neurologic disorders [39].

Concurrent measurements of flow rates and ICP are not carried out routinely on patients because standard ICP monitoring equipment is incompatible with MRI scanners. In
the phantom, on the other hand, such measurements are possible: We recorded simultaneously pulsatile ICP and CSF flows in the cerebral aqueduct and the SAS. An overview of the operating parameters used to reproduce physiologic ICP and CSF flow patterns is given in Table I.

Table I

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
<th>Phantom Values</th>
<th>Physiologic Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \Phi )</td>
<td>CSF bulk flow</td>
<td>0.35 ml/min</td>
<td>0.27-0.45 [14]</td>
</tr>
<tr>
<td>( C_{sv} )</td>
<td>Total compliance,</td>
<td>1 ml/mmHg</td>
<td>0.56-1.12 [14]</td>
</tr>
<tr>
<td>( k )</td>
<td>SAS permeability</td>
<td>1.7 ( 10^{-8} ) m(^2)</td>
<td>9.05 ( 10^{-8} )</td>
</tr>
<tr>
<td>( \omega )</td>
<td>Basal heart rate</td>
<td>60 bpm</td>
<td>50-100 [40, 41]</td>
</tr>
<tr>
<td>( A\text{\textsubscript{ventricles}} )</td>
<td>Amplitude of ventricular pulse</td>
<td>0.2 ml/s</td>
<td>(&lt;0.3 ) [33, 35, 36]</td>
</tr>
<tr>
<td>( A\text{\textsubscript{SAS}} )</td>
<td>Amplitude of SAS pulse</td>
<td>2 ml/s</td>
<td>1.18-3.97 [33, 36]</td>
</tr>
<tr>
<td>( V\text{\textsubscript{ventricles}} )</td>
<td>Volume of ventricles</td>
<td>29.6 ml</td>
<td>17.6-34 [42]</td>
</tr>
<tr>
<td>( V_c )</td>
<td>Intracranial CSF Volume</td>
<td>177.3 ml</td>
<td>143.1-246.3 [42]</td>
</tr>
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</table>

List of operating parameters used to define the phantom working condition for the healthy state. Values reported in the literature, which define the physiologic range for a healthy subject, are also reported.

Fig. 5 shows intraventricular pressure recording in the phantom over several cardiac cycles, demonstrating the stability of the setup. A mean physiologic ICP of 10 mmHg was reproduced and pulsations with approximately 0.4 mmHg amplitude were observed. Both are in agreement with values reported in the literature for in vivo healthy conditions [37-39].

Transient ICP and corresponding CSF flow rate curves of one representative cardiac cycle are shown in Fig. 6. CSF oscillations showed peaks of 0.2 ml/s in the aqueduct and 2 ml/s in the SAS, thus matching in vivo values [33, 35, 36]. This was achieved with the proper choice of the pulsatile pump output and fine regulating valve settings as described in Section II.E.

To analyze the effect of change in CSF pulsation origin, the entire pulsatile pump output was applied to the brain surface, resulting in ventricular pulsation without contribution from the SAS. This reduced ICP amplitude from 0.4 mmHg to 0.15 mmHg, where the latter value corresponds to the expected peak aqueductal pressure drop [43]. Physiologic ICP amplitude of 0.4 mmHg was restored when CSF pulsation originated again in both the ventricles and the SAS.

To investigate the phantom’s flexibility in reproducing potential pathologic conditions by alterations of its operating parameters, we set the cranial compliance to zero. Fig. 7 shows ICP measurements under physiologic conditions compared to ones made with out cranial compliance. More than a factor of two increase in ICP pulse amplitude was observed in the pathologic case.

IV. DISCUSSIONS

The phantom described herein represents a novel approach for the modeling of intracranial dynamics. Based on MRI data and the results of detailed CFD simulations, a model of the intracranial space including brain, ventricular and subarachnoid spaces was realized that allows for the reproduction and monitoring of bulk and pulsatile CSF flows.
as well as ICP dynamics. The phantom was validated by comparison to physiologic CSF flow and pressure values reported in the literature.

The phantom features a set of operating parameters whose physiologic values cannot be readily obtained in vivo. Specifically, these are the output wave form of the pulsatile pump and the division of this output for actuation in the ventricular and subarachnoid CSF spaces. In vivo, the expansion and contraction of blood vessels propels CSF either directly or through transient brain tissue motion. As this complex interaction has not been fully quantified to date, our approach of directly displacing the ventricle walls and SAS volume is justified. More importantly, by treating the pulsatile pump output and the output division ratio as variables, we have obtained indication that in vivo CSF oscillation is likely the result of transient changes in both SAS and ventricular volume of similar magnitude, rather than the result of a single compartment volume variation. In the phantom, the relative contribution is 2:3 in favor of the subarachnoid space.

While in its current state the phantom has not been validated for the reproduction of pathologic conditions, we have nevertheless simulated a hypothetical disorder in which cranial compliance was reduced. This was done to demonstrate that the phantom’s operating parameters can be easily adapted to study pathologic intracranial dynamics.

As all models, the phantom at hand is a simplified representation of the very complex real system. In particular, simplifications were introduced to handle the anatomic complexity of the intracranial space. The cerebral vasculature and its contribution to intracranial dynamics were included implicitly in the volume variation of the ventricular and SAS compartments. As a consequence, local effects of blood flow are not taken into account. Similarly, the simplification of the ventricular and subarachnoid spaces precludes the acquisition of local flow information. The phantom nevertheless produces realistic pressure dynamics within the modeled CSF spaces: The aqueduct of Sylvius and SAS are responsible for the main CSF pressure drop under physiologic conditions [6, 15, 43], and both of these compartments are accurately modeled in our setup. Due to the short length of the foramina of Monro, Luschka and Magendie, and the large cross-section of the lateral ventricles, their simplified representations have negligible impact on global pressure dynamics and flow rates.

While the bandwidth of physiologic intracranial dynamics is limited to a few Hertz, taking into account only their first harmonic at 1 Hz as done here constitutes nevertheless a clear simplification. As a result, the shape of the measured flow profiles does not fully match those obtained on healthy subjects, even though amplitudes, mean flow rates and stroke volumes do. Reproducing in vivo flow profiles in detail would require a more sophisticated actuation system with a bandwidth of at least 10 Hz. This would introduce a large new set of variables to be calibrated, while providing only very limited added value.

The phantom is operated in an air-conditioned room at 22 °C rather than at body temperature of 37 °C. Consequently, the density and viscosity of the working fluid (water) are higher than that of in vivo CSF [34]. This results in an overestimation of peak pressure gradients of the order of 10%. For applications that require a more accurate representation of CSF, active heating of the setup could be implemented, or a different working fluid could be used.

The phantom features constant compliance, which represents a valid assumption for healthy conditions. Under pathologic conditions, however, cranio-spinal compliance variations may become important. To study these, the employed constant compliance elements can be replaced by exponential compliance modules as reported in [44].

ACKNOWLEDGMENT

We would like to thank Salim Kassem and Dr. Martin Pfeiderer from Research and Development at Codman&Shurtleff for kindly providing the Microsensor™ pressure transducers and the ICP Express™ control unit.

REFERENCES

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