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Demonstration that a new flow sensor can operate in the clinical range for cerebrospinal fluid flow

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ABSTRACT

A flow sensor has been fabricated and tested that is capable of measuring the slow flow characteristic of the cerebrospinal fluid in the range from less than 4 mL/h to above 100 mL/h. This sensor is suitable for long-term implantation because it uses a wireless external spectrometer to measure passive subcutaneous components. The sensors are pressure-sensitive capacitors, in the range of 5 pF with an air gap at atmospheric pressure. Each capacitor is in series with an inductor to provide a resonant frequency that varies with flow rate. At constant flow, the system is steady with drift <0.3 mL/h over a month. At variable flow rate, $\dot{\boldsymbol{V}}$, the resonant frequency, $\mathbf{f}_0$, which is in the 200–400 MHz range, follows a second order polynomial with respect to $\dot{\boldsymbol{V}}$. For this sensor system the uncertainty in measuring $\mathbf{f}_0$ is 30 kHz which corresponds to a sensitivity in measuring flow of $\Delta\dot{\boldsymbol{V}} = 0.6$ mL/hr. Pressures up to 20 cm H_2O relative to ambient pressure were also measured. An implantable twin capacitor system is proposed that can measure flow, which is fully compensated for all hydrostatic pressures. For twin capacitors, other sources of systematic variation within clinical range, such as temperature and ambient pressure, are smaller than our sensitivity and we delineate a calibration method that should maintain clinically useful accuracy over long times.

1. Introduction

A common, useful treatment for patients with head trauma and hydrocephalus is the placement of a shunt to drain excess cerebrospinal fluid (CSF) and reduce the intracranial pressure (ICP), thereby reducing brain damage [1–3]. Many commercially available shunt systems use a valve to regulate the flow. These valves are controlled by changes in pressure, but generally do not provide the ICP to the caregiver. There are variations in performance reported amongst the commercially available shunts with pressure control systems [4]. It might seem that the ICP is the most important parameter since the ICP is directly related to cell damage. Incorporation of a pressure sensor into the shunt apparatus would be valuable as a monitor of the operation of the shunt and the health of the patient if the pressure sensor reading can be related to ICP. However, there are situations where there is an occlusion upstream from where a pressure sensor can be located along the shunt, which could lead to a false reading of CSF pressure that is not related to ICP and a possible danger to the patient. A method to measure flow and pressure of CSF along its path within the shunt would provide an unambiguous way to monitor ICP, the performance of the shunt, and possibly predict shunt failure before the patient's ICP has been compromised. It would also be an important step towards realization of a "smart shunt" [5].

Measurement of flow and pressure are needed because approximately 50–70% of patients report shunt malfunction within 1 year after initial placement and then at a rate of 5% per year [6]. Among the malfunctions reported for shunts, blockage is the most common. Important studies indicate that the deployment of shunts

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Table 1
Pressure sensor and flow sensor measurement requirements.

Parameter	
Pressure	0–50 ± 0.1 cm H_2O (0–500 ± 1 Pa)
Flow Rate	0–100 ± 4 mL/h

Table 2
Comparison of composition of CSF and blood serum [11].

Component	CSF	Serum
Water content (%)	99	93
Protein (mg/dL)	35	7000
Glucose (mg/dL)	60	90
Na^+ (mEq/L)	138	138
K^+ (mEq/L)	2.8	4.5
Ca^{2+} (mEq/L)	2.1	4.8
Mg^{2+} (mEq/L)	0.3	1.7
Cl^- (mEq/L)	119	102
pH	7.33	7.41

has overall been successful, but shunt failures due to mechanical malfunction and blockage are more common than experts desire [1,2,7–10]. Table 1 lists the requirements of a pressure/flow-rate sensor to be useful as a monitor of shunt effectiveness while providing an indication of ICP.

We report the development of a wireless sensor that could potentially be used to enhance the functionality of ventriculoperitoneal shunts. It measures both pressure and flow to monitor ICP and provide early warning of a shunt failure. The system employs a pair of capacitors made using micro-electro-mechanical systems (MEMS) technology with flexible membranes used as fluid pressure sensors that are inline with the flow. The flow rate through a path with known flow resistance is calculated from the difference in pressure. Wiring inductors to the capacitive sensors forms resonant circuits. The device is designed for subcutaneous implantation as part of a smart shunt system. They provide the CSF flow rate and pressure. Tests here indicate that the device is sensitive enough to allow the detection of the approach to shunt occlusion and to monitor the efficacy of treatments. This type of device may allow the physician to check for failure of CSF flow without surgery and make an informed and quick decision about further diagnosis and treatment.

1.1. Physiological fluid flow sensors

In a healthy individual, the volume of cerebrospinal fluid (CSF) is approximately 140 mL. This volume of fluid is continuously absorbed by the body. It is formed at a rate of 0.35 mL/min [11]. This results in a flow rate of approximately 21 mL/h in a healthy individual. For comparison, blood flows through a person's aorta at about 576,000 mL/h [12]. In order to measure the extremely slow flow rate of CSF, a highly sensitive device must be designed.

Although derived from blood, CSF has a different composition. The differences are listed in Table 2. As can be seen, CSF is mostly water with smaller ions contained in it. Unlike blood, this makes it a very clear. Blood also contains coagulating agents, which CSF lacks. This makes it slightly easier to measure since there is no danger of CSF forming a clot that would inhibit its proper flow.

There are various flow sensor technologies that have been applied to physiological fluids. Blood flow has been measured for intraoperative and laboratory use using various methods. Transit time, electromagnetic and Doppler methods have been used including implantable systems [13]. CSF poses challenges in extending their applicability to meet the requirements listed in Table 1 while incorporating the flow measurement into an existing transpalpebral shunt system. Two methods that have been used previously are transit-time and calorimetric flow sensors [14,15].

The transit-time method uses a pair of ultrasonic transducers to launch and record an ultrasonic wave along the path of the flowing fluid [13]. The transit-time of the wave to the recorder is a function of the fluid velocity and can be determined by the phase difference between the launched and recorded waves. Drost et al. [14] have adapted this technique to a wireless CSF flow sensor that can be incorporated into a shunt system. In tests with sheep it was able to measure flow rates in the range of 0–130 mL/h. The major error in the measurement method was in the positioning of the external reader, which was inductively coupled to the sensor. However, this error was reduced to ~1 mL/h by correcting for the amplitude variation in the signal. The signal could be detected within 9 mm of the sensor, which makes it suitable for subcutaneous implantation near the shunt valve mechanism.

The calorimetric method for measuring blood flow was first suggested by Rein in 1928 [16]. The principle is to apply heat locally to a flowing fluid and measure the temperature downstream [17]. The rate of cooling of the fluid is a function of the flow rate. Bork et al. [15] have adapted this method to CSF flow for use in a shunt system. They were able to obtain an accuracy of ±10% in the range of 2–40 mL/h for artificial CSF in vitro. This system uses a telemetry recording system with an inductively coupled reader that is relatively insensitive to positioning once the reader is in close enough proximity.

Both the transit-time and calorimetric flow sensors may be adapted to shunt systems but will not provide a measure of ICP, which would be a direct indication of the condition of the patient as a function of the CSF flow parameters. A solution might be to use a separate ICP monitor along with the flow sensor. However, a less complicated solution would be to incorporate the ICP measurement with the flow sensor. The flow sensor that we propose uses two pressure sensors to derive the CSF flow rate. The absolute pressure measurement from these sensors is related to ICP while the difference in pressure between the two sensors is related to the flow rate. There is a clear advantage to deriving CSF flow rate in the shunt and ICP from a single implantable device with only one reader. The challenge was to design a compact pressure sensor that could be designed and fabricated to work in the range needed for CSF pressure measurements. A MEMS based capacitive pressure sensor provides a solution that meets the requirements

1.2. Capacitive pressure sensors

Capacitive pressure sensors have been in use for decades. For instance, Akar et al. [18] fabricated a pressure sensor consisting of a 6 μm-thin silicon diaphragm and a metal electrode supported on a glass substrate. The capacitor was wired to a gold-electroplated planar inductor coil on the same substrate, which facilitated external detection of the capacitance using mutual induction. Chang et al. [19] performed tests on three types of capacitive pressure sensors. The group successfully fabricated these sensors by using lamination processing with Kapton polyimide, stainless steel, and titanium films as diaphragms on a stainless steel shim stock substrate. They demonstrated the integration of readout circuitry on the substrate. Recently scientists developed a useful and effective, miniaturized, flexible capacitive pressure sensor with polydimethylsiloxane (PDMS) as the dielectric for plantar pressure measurement in biomechanical systems [20]. The good scale and flexibility of the sensor allows this configuration to be adapted as shoe-integrated sensor system for long-distance data collection for gait analysis.

Miniaturization using MEMS technology has opened up new biomedical applications of capacitive sensors. For instance, Ha et al. [21] developed a prototype flexible MEMS capacitive pressure sensor with a sensing area of 500 × 500 μm^2 for implantation in the