Impedance Changes Indicate Proximal Ventriculoperitoneal Shunt Obstruction In-Vitro

Sukhraaj Basati, Kevin Tangen, Ying Hsu, Hanna Lin, David Frim, and Andreas Linninger

Abstract—Extracranial CSF shunt obstruction is one of the most important problems in hydrocephalus patient management. Despite ongoing research into better shunt design, robust and reliable detection of shunt malfunction remains elusive. The authors present a novel method of correlating degree of tissue ingrowth into ventricular CSF drainage catheters with internal electrical impedance. The impedance based sensor is able to continuously monitor shunt patency using intraluminal electrodes. Prototype obstruction sensors were fabricated for in-vitro analysis of cellular ingrowth into a shunt under static and dynamic flow conditions. Primary astrocyte cell lines and C6 glioma cells were allowed to proliferate up to 7 days within a shunt catheter and the impedance waveform was observed. During cell ingrowth a significant change in the peak-to-peak voltage signal as well as the root-mean-square voltage level was observed, allowing the impedance sensor to potentially anticipate shunt malfunction long before it affects fluid drainage. Finite element modeling was employed to demonstrate that the electrical signal used to monitor tissue ingrowth is contained inside the catheter lumen and does not endanger tissue surrounding the shunt. These results may herald the development of “next generation” shunt technology that allows prediction of malfunction before it affects patient outcome.

Index Terms—CSF, Hydrocephalus, Impedance sensor, Shunt failure, Shunt obstruction, Ventriculoperitoneal shunt.

I. INTRODUCTION

Cerebrospinal fluid (CSF) shunts and shunting procedures are the most effective management strategy for many types of hydrocephalus. However, ventriculoperitoneal shunt failure is still common. Following initial shunt insertion, the failure rate by one year post-implantation is still between 15 and 40% [1]. The primary reason for shunt failure is obstruction followed by under-drainage. In a randomized evaluation of treatment efficacy, shunt obstruction was found to be the main reason for shunt revision, accounting for 31% of total surgeries [2]. These observations imply that improved monitoring for shunt obstruction will improve patient outcome. In addition, such monitoring will likely enhance our understanding of the progression of cell invasion into shunting catheters.

Extracranial ventricular shunt systems consist of a ventricular catheter which is connected to a valve that regulates CSF flow into a distal catheter that diverts the CSF to an extracranial resorption site. Shunt obstruction can occur anywhere in the system, but most often occurs at the proximal inlet ports of the ventricular catheters. These ports are invaded by choroid plexus tissue, free floating endothelial cells, or are encapsulated by gliotic scar [3]-[4]. Protein aggregation and buildup has also been implicated in impaired shunt function. Investigations to understand the relationship between port hole size and cellular ingrowth have found ingrowth of astrocytes and macrophages occurs through small diameter holes [5]. These observations have improved our understanding of catheter port occlusion, but have not produced a system for monitoring shunt status or determination of the location of a shunt obstruction.

In the present study, we describe a promising method to monitor proximal shunt obstruction by detecting intraluminal impedance changes caused by cellular ingrowth or other obstruction. We are concerned with the proximal shunt area because proximal ingrowth, as measured near the shunt ports, may be the primary reason for distal obstruction [6]. Over time, migration of cells, proteins, and tissue to distal sites may prevent proper fluid drainage—causing distal obstruction typically seen in older patients. The proximal obstruction technique in this paper observes dynamic alterations to the spatial extent of an induced electric field caused by cells invading the shunt ports. The electrical impedance ratio of CSF and brain tissue is a factor of 12; therefore the large impedance difference allows for the distinction of spaces occupied by CSF and brain cells [7]. We have previously developed an impedance-based volume sensor [8]-[9] and here we demonstrate the impedance principle for detecting whether the proximal shunt region is clear or obstructed.

Previous studies on electrical cell-substrate impedance sensing (ECIS) show impedance changes due to cell growth of E. coli in suspensions of equal concentration [10]-[11]. Other work has demonstrated the effectiveness of impedance measurements to detect the locomotion and growth of live cells in solution [12]-[14]. The electrode-solution interface impedance was found to be inversely proportional to the electrode area and its magnitude is frequency dependent. Therefore the impedance waveform change correlates with the degree of density at the interface. The present study investigates whether the principle governing ECIS is also effective for detecting shunt invasion by live cells, long before fluid drainage through the shunt is diminished.

Copyright (c) 2013 IEEE. Personal use of this material is permitted. However, permission to use this material for any other purposes must be obtained from the IEEE by sending an email to pubs-permissions@ieee.org.
II. METHODOLOGY

A. Shunt Fabrication

Catheters with novel obstruction sensors were microfabricated with biocompatible materials. Figure 1A illustrates a schematic of the sensor integrated with a ventriculoperitoneal shunt. Sensor electrodes were made using platinum-iridium ring cylinders (0.7mm OD) welded with a resistive spot welder to platinum-iridium wire. Electrodes were concentrically placed within a silicone tube for CSF drainage shown in Figure 1B. The wire/ring electrodes were bonded to the inner lumen of silicone catheter using silicone adhesive. Once the silicone adhesive has cured, the polyimide shunt was removed from the sensor. The leads were soldered to a nano-connector (Omnetics, MN) for connection with the instrumentation. An instrumentation diagram of the shunt obstruction sensor system is shown in Figure 1C.

B. Sensor Instrumentation

The instrumentation to provide the sinusoidal signal and power the sensor was constructed as follows. A Howland current source driven by a low frequency (4kHz) sine wave voltage applies an excitatory signal of 10µA to the electrodes. The signal across the electrodes passes to an instrumentation amplifier with high input impedance (AD620, Analog Devices) and is recorded using an oscilloscope for analysis.

C. Ingrowth in Cell Culture

A catheter with prototype sensors was placed inside 100x15 mm polystyrene petri dishes (Fisher Scientific) shown schematically in Figure 2. To test the robust nature of the fabrication process, eight prototype sensors were developed to compare measurement accuracy. Sensor measurements were taken in fluids with high (artificial CSF and 5M NaCl aq) and low (air) electrical conductivities to assess performance under varying environments.

Different types of mechanical obstruction, such as lumen blockage by paraffin wax, bovine species coagulated blood, and collagen protein aggregates were used to test the null hypothesis that mechanical blockage will not induce an impedance change relative to aCSF. Four repetitions were performed to assess the reliability of each prototype sensor.

To test sensor measurements with various concentrations of cell suspension (n=6), the catheter lumen was filled with L929 mouse fibroblast cells suspended in growth medium ranging from 50,000 to 10^6 cells/0.1 cm^3. Analysis of measured values tested the null hypothesis that manually loaded cell densities do not change impedance measurements compared to aCSF. Our alternate hypothesis was that a significant difference in impedance between different manually loaded cell densities and aCSF was observable.

A time dependent experiment for simulated cellular ingrowth into a shunt was also conducted. Two different cell types were used to emulate cellular obstruction and choroid ingrowth. Primary rat astrocytes, embryonic day 19 (E19), and C6 glioma cell lines were cultured separately in an

Figure 1. Schematic of obstruction sensor embedded with existing shunt devices depicted in frame A. Frame B is a fabricated sensor prototype with open ports and the placement of shunt obstruction electrodes inside the catheter. Frame C shows the basic instrumentation design of impedance based shunt obstruction detection.

Figure 2. Experimental setup for static flow in vitro experiments. Sensor prototypes were placed in a dish, two different cell lines were allowed to grow within the shunt lumen, and impedance measurements were obtained.