A Smart Catheter System for Minimally Invasive Brain Monitoring

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Keywords: Smart Catheter, TBI, Real-Time Monitoring, Pressure, Temperature.

Abstract: This paper demonstrates a smart catheter system with intracranial pressure (ICP) and temperature sensing capability which is designed for real-time monitoring in traumatic brain injury (TBI) therapy. It uses a single flexible catheter with a 1 mm (3 Fr) diameter that integrates electrodes and sophisticated silicon chip on flexible substrates, enabling multimodality monitoring of physiological signals. A micro-electro-mechanical-system (MEMS) catheter pressure sensor is mounted on the distal end. It can be used for detecting both pressure and temperature by different switch configurations, which minimizes the size of catheter and reduces the cost. The interconnects (signalling conductors) are printed on a bio-compatible flexible substrate, and the sensor is interfaced with an embedded electronic system at the far-end. The electronic system consists of analog front end with analog-to-digital converter (ADC), a microcontroller, and data interface to the hospital infrastructure with a graphical user interface (GUI). The overall smart catheter system achieves a pressure sensing root mean square error (RMSE) of ±1.5 mmHg measured from 20 mmHg to 300 mmHg above 1 atm and a temperature sensing RMSE of ±0.08 ºC measured from 32 ºC to 42 ºC. The sampling rate can be up to 10S/s. The *in vivo* performance is demonstrated in laboratory animals.

1 INTRODUCTION

Traumatic brain injury (TBI) is a type of acquired brain injury, occurs when a sudden force traumatically injures the brain. The main causes include falls, traffic accidents, and violence. TBI is one of the major causes of death and disability in patients from ages 1 to 44 years. TBI results in 1.4 million reported injuries and 52000 deaths each year in the United States (Faul, 2010). Secondary neurological damage, a variety of events that take place in the ensuing hours and days following the primary injury, contribute substantially to the worse damage caused by primary injury and accounts for the greatest number of TBI deaths occurring in hospitals. Raised intracranial pressure (ICP) is a common factor in secondary injury. The causes of raised ICP include swelling or a mass effect from a lesion such as subdural hematoma. When the ICP rises, the cerebral perfusion pressure (CPP) decreased, resulting in ischemia or even brain death. Therefore, a precise monitoring of the ICP is very important for minimizing secondary ischemic injury in TBI. In addition, the brain of neurosurgical patients with severe traumatic brain injury is extremely sensitive and vulnerable to small temperature variations, thus fever is considered a secondary injury to the brain (Mrozek, 2012). Hence, continuous monitoring of intracranial temperature is also highly recommended.

The intraventricular catheter is the most accurate pressure monitoring method, in which catheters are inserted into the lateral ventricle through a hole drilled on the skull (MedlinePlus, 2014). Current TBI care unit uses separate catheters for monitoring multiple signals, which are collected by external electronic system through separate cables for signal processing and real-time data display (Stiefel, 2005). However, a big burr hole is needed to accommodate multiple catheters, which is susceptible to infection and complications. Therefore a smart catheter system providing ICP and temperature monitoring capability with single catheter insertion is highly desirable to minimize incision.

Thanks to the steady and considerable effort directed towards the development of sensor fabrication technology, some pressure sensors for biomedical applications have been reported. They

Bao D., Zou Z., Huan Y., Zhai C., Bagaian T., Tenhunen H., Källbäck B. and Zheng L..
A Smart Catheter System for Minimally Invasive Brain Monitoring.
DOI: 10.5220/0005285501980203
In *Proceedings of the International Conference on Biomedical Electronics and Devices* (BIODEVICES-2015), pages 198-203
ISBN: 978-989-758-071-0

usually fall into two categories, pressure sensor on solid substrate and on flexible substrate. Pressure sensors manufactured using MEMS technology, typically provide increased reliability and higher precision. However, they are often expensive and fabricated on rigid substrates (Wahab, 2008). Meanwhile, electronics on flexible substrates is considered as an alternative approach that enables low-cost manufacturing of thin, flexible, light devices. The revolutionary technologies have enabled displays, sensors (Pritchard, 2008), antennas on flexible substrates. Flexible pressure sensor is highly non-linear; thus careful, frequent calibration may be necessary. However, it provides a promising solution for chip-system integration (Xie, 2012). In this work, a heterogeneous system which seamlessly integrates MEMS sensor with flexible printed circuit board (PCB) is employed to develop a low cost catheter. A piezoresistive MEMS pressure sensor is employed in proposed system.

The temperature can be detected by a separate sensor (Li, 2012). However, it is limited in applications required more sensors because of the small size of catheter. In (Chan, 2013), a temperature sensor circuit which consists of a portional to absolute temperature (PTAT) voltage generator, a bandgap voltage generator, and a V_{BE} amplifier is integrated. Nevertheless it is non-contact sensor. Thermistors are very low cost and available in a wide variety of packages. However, the resistive change is relatively small. Therefore, an amplification circuit is necessary to ensure the output signal quality.

In this paper, a 1 mm (3 Fr) diameter smart catheter, inserted with flexible PCB, is proposed to sense the ICP and temperature signal for detection of any anomaly in the patient. A piezoresistive MEMS pressure sensor is utilized to provide accurate pressure measurement within the very small spaces and harsh environments of the catheter. The sensor can also be used for detecting temperature by switch configurations, which minimizes the catheter size. The sensor signals are fed into an external electronic system by flexible PCB. An instrumentation amplifier in electronic system provides the required amplification of the sensed signal and the temperature sensing output can be used to compensate pressure sensor error caused by temperature variations. The electronic system reads out signal and quantizes it with an integrated ADC.

Therefore, not only physiological parameters can be shown directly in real time *in vivo*, but also reduce the effects and complications caused by surgery. To demonstrate the proof of concept, a smart catheter system is implemented and measured in laboratory animals.

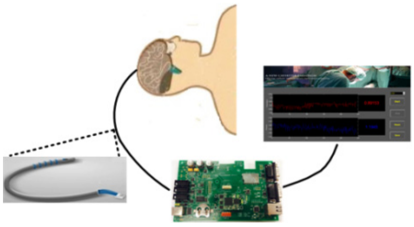

Figure 1: Smart catheter system for continuous ICP and temperature measurement.

The remainder of this paper is organized as follows. The proposed smart catheter system is described in Section 2. The catheter and electronic system are elaborated in Section 3 and 4 respectively. The system characterization is discussed in Section 5 with conclusions given in Section 6.

2 SYSTEM DESCRIPTION

The objective is to develop a catheter for invasive measurement of ICP and temperature and to show that it can be produced at a low enough cost and be integrated in current hospital procedures and infrastructure. Due to the small size of mini-invasive catheter, the proposed system adopts flexible PCB for transmission such that the pre-mount sensor information can be collected outside of the body using an external electronic device. Fig. 1 illustrates the whole system. The system is composed by four major components: a catheter with pre-mount sensors and electrodes, a sensor interface and measurement logic, a microcontroller and a computer with GUI. The proposed mini-invasive catheter measures pressure and temperature *in vivo* and sends the signal to the analog signal conditioning circuitry through flexible PCB. The output signals of sensors are collected by an analog interface of instrumentation amplifier, which is followed by a microcontroller-based socket board comprised an integrated ADC and a RS-232 serial port interfacing to the computer. The computer will process the data received from external electronic devices to display the situation of the patient. The calibration algorithm will also run on the computer. Then the corresponding pressure and temperature can be calculated based on the measured voltage after calibration.

3 HETEROGENEOUS INTEGRATION CATHETER

To measure physiological parameters, such as tissue pressure and temperature, sensors should be incorporated in the catheter. Moreover, a single catheter provides multiple signal sensing capability is highly desirable to minimize wound. In this work, Prefab technology from CathPrint AB is adopted (CathPrint AB, 2014) (Kallback, 2009). The Prefab is inserted into a lumen of the customer's extrusion which is prepared with holes for electrodes and pre-mounted sensors. It enables an uncomplicated solution for connecting electrodes, sensors inside body to external electronic and data analyzing system.

In general the catheters are long (in the order of one meter) and thin (between 0.3 and 3 mm) (Kallback, 2009). Therefore, a thin but long PCB (e.g. 2 meters with 350 um diameter) is the basis for catheter manufacturing as illustrated in Fig. 2 (CathPrint AB, 2014).

In this Prefab technology, sensors are mounted on the flexible board, having contact with the surrounding substance through an access hole in the catheter for measurement use as shown in Fig. 3. The bond pads on the flexible PCB are connected to respective bond pads on the sensors by bonding wires. In this work, a MEMS pressure sensor is integrated to demonstrate the potential applications as shown in Fig. 3 (CathPrint AB, 2014). This heterogeneous integration catheter combines flexible substrates based technology and silicon based electronics which takes advantages from both technologies. Thus the proposed heterogeneous integration approach provides a promising solution for mini-invasive applications. Electrodes can also be integrated in the catheter, which are in contact with the liquid surrounding the device for invasive applications, such as blood oxygen detection. The electrodes are placed outside the tube, and they are connected to an inner catheter via a conductive plug as shown in Fig. 4 (CathPrint AB, 2014). Therefore it is convenient to connect the electrodes to an electronic system at the far-end.

To enables the possibility of producing flexible catheters with a diameter that is as small as 0.35 mm, the flexible circuit board is then rolled up to form an extremely narrow tube, which is done by feeding the flexible PCB through a funnel as illustrated in Fig. 5 (CathPrint AB, 2014) (Kallback, 2009). The inner space of catheter-to-be is filled with glue that holds the catheter in a tube shape after the process. The resulting flexible catheter features a

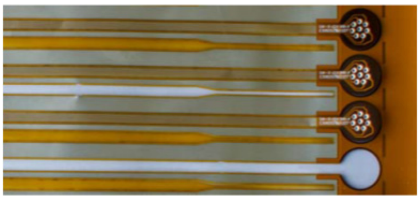

Figure 2: Thin flexible PCBs for catheter (CathPrint AB, 2014).

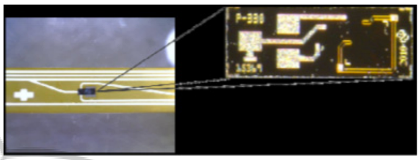

Figure 3: Pressure sensor mounted on the flexible board (CathPrint AB, 2014).

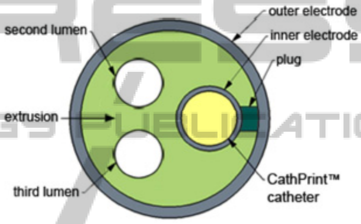

Figure 4: CathPrint integrated catheter with electrodes outside (CathPrint AB, 2014).

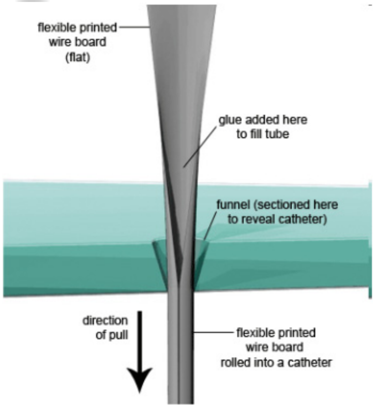

Figure 5: The flexible PCB is pulled through a funnel producing a catheter (CathPrint AB, 2014).

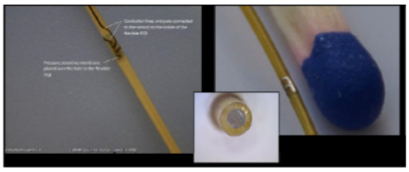

Figure 6: A miniature solid catheter with sensor inside and electrode outside (CathPrint AB, 2014).

diameter ranging from 0.33 to 1 mm and a maximum length of approximately 1.5 meters. This technique significantly reduces the fabrication process, and decreases the cost as well as the catheter size. The proposed method for manufacturing catheters transforms the flat circuit board into a solid catheter which carries the sensor inside the flexible PCB and has the electrodes outside as shown in Fig. 6 (CathPrint AB, 2014).

4 ELECTRONIC SYSTEM

4.1 Pressure and Temperature Sensor

A switch regulator on socket board will regulate 3.3 V, which provides the power supply for the analog interface and sensors. The pressure sensor employed is P330 silicon MEMS pressure die, which is from GE Measurement & Control. Its equivalent circuit is illustrated in Fig. 7. A stable 3.3 V power supply is applied between VDD and GND. In pressure sensor mode, two 3.3 KΩ external resistors are utilized to form a half bridge. When a change in pressure causes the sensor to deflect, a corresponding change in resistance is induced. Then the differential output voltage on Vo+ and Vo- will also be changed by the pressure. As the input range of ADC on socket board is from 0 to 2 V with 14-bit effective number of bits (ENOB), 1 LSB will be presented as 122.1 μV. While the sensitivity of sensor in proposed system is about 8.6 $\mu V / V / mmHg$. Therefore the pressure sensing resolution of this system is nearly $122.1/8.6/3.3 = 4.3$ mmHg at 3.3 V power supply. This is because the changes in strain and resistance are extremely small. To improve the overall resolution, in proposed sensor interface, an instrumentation amplifier (IA), INA155 from Texas Instruments, is used to amplify the changes in resistance as shown in Fig. 7. INA155 is a CMOS instrumentation amplifier (IA) with rail-to-rail output. The gain can adjusted to any value between 10 and 50 by connecting a resistor R_G between the gain pins according to the following equation (Texas Instruments, 2014):

$$Gain = 10 + 400k\Omega / (10k\Omega + R_G) \qquad (1)$$

And the output voltage of IA is (Texas Instruments, 2014)

$$V_O = (V_{IN}^{+} - V_{IN}^{-}) \bullet Gain + V_{REF} \qquad (2)$$

Where V_{IN}^{+} and V_{IN}^{-} are the input voltages and V_{REF} is the reference voltage.

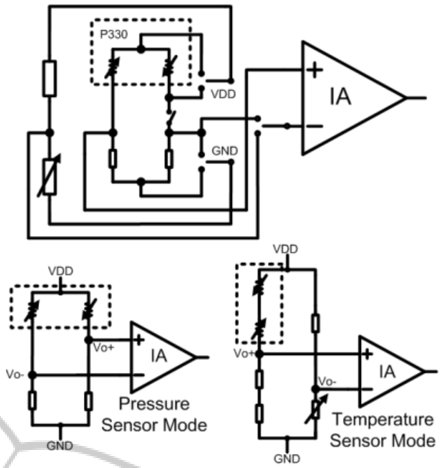

Figure 7: Schematic of the pressure/temperature sensor and interface circuit.

The pressure sensor in proposed system provides a differential output voltage nearly 40 mV at 1 atm. Therefore we set 0 mV to be V_{REF} which maximizes the swing range and 30 be the gain which take full advantage of ADC's input range. The system performance can be estimated using specifications. The intrinsic output voltage of IA at 1-atm pressure will be 1.2 V. If we set 20 to 300 mmHg above 1 atm to be measurement ranges, the sensor output range will be from 1.217 V to 1.455 V at 3.3 V power supply. Then the span of this system including proposed sensor interface and ADC is 1951 LSBs. The overall pressure sensing resolution is therefore nearly 0.14 mmHg. The resolution improvement is due to amplified resistance changes by INA155.

The resistance of resistors in pressure sensor decreases with increasing temperature. Therefore the pressure sensor can also be used for temperature measurement. However, the two resistors are sensitive to both pressure and temperature change. It is difficult to separate the two reasons for resistance change. Note that the 2 resistors in the half bridge sensor are both pressure sensitive but the resistances change in opposite directions. While these resistances also change with temperature but in the same direction. Hence, the series resistance of the 2 bridge resistors can be used for temperature measurement independent of pressure. In temperature sensor mode, the two resistors in P330 and the two external resistors compose a branch. Due to the small changes in resistance, an on-board reference voltage is also used in a differential configuration with INA155 providing the required amplification of the sensed signal. In proposed sensor interface, a simple voltage-divider with a resistor and a trimmer in series is employed for reference voltage. Moreover, the sensor has to be switched between pressure and temperature measurement. As shown in Fig. 7, three analog multiplexers and one analog switch are needed. The data amount to be transmitted is not heavy that many off-shelf products meet the mentioned requirements. A triple 2-channel CMOS analog multiplexers SN74LV4053A and an analog switch TS5A1066 from Texas Instruments are used in this system at 3.3 V VDD operation. The temperature coefficient of resistance (TCR) of sensor employed is 0.04 %/ºC, which can be used for estimating temperature sensing resolution. The two bridge resistances are assumed to be 3 KΩ in subsequent analysis. If 32-42 ºC is set to be measurement range and the differential output voltage of IA is 1 V at 32 ºC, the temperature sensor output range will be from 1 V to 1.099 V at 3.3 V power supply. Then the total range of this system is 811 LSBs. The temperature sensing resolution of system is about 0.012 ºC. However, non-ideal factors will result in apparent system performance degradation.

4.2 Data Recording and Analyzing System

The data recording is important when the proposed system is used for *in vivo* signal observing. The data recording and analyzing system including an analog interface PCB board, a socket board from Imsys Technologies AB and a computer. The micro-controller on socket board collects sensor data and outputs it to a RS-232 serial port. With a RS232-USB cable, the computer is allowed to connect serial port through USB ports. The computer receives and analyzes gathered data from socket board by programming software. Power is also supplied to the socket board from the USB interface of computer. The sensor will be switched between pressure and temperature measurement automatically by the socket board. The sampling rate of temperature or pressure sensing is 10S/s. A graphic user interface (GUI) that processes the signal sent by the mini-invasive system is installed on the computer. We can continuously display the pressure and temperature from the start point. The results will be displayed in either pressure or temperature chart. And the average values of the last 10 readings are shown in digital format at the right-hand side of the GUI. Calibration is executed with reference data to increase system resolution. And then we can calculate the original physiological parameters using the gathered digital codes. The main function of this program is to analyze and display all the data delivered by the socket board. It also records them into files for future statistics and analysis.

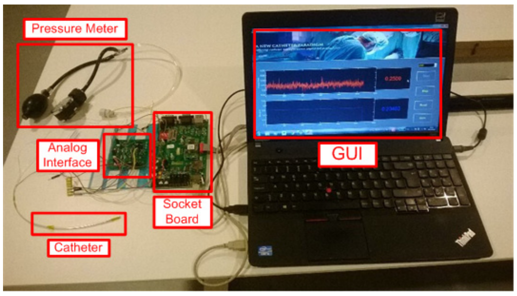

Figure 8: The measurement site of the propose system.

5 MEASUREMENT RESULTS

The measurement site of the system is illustrated in Fig. 8. A blood pressure meter based device is used to control the pressure of catheter. The device consists of an inflatable arm cuff, a manual gauge and a rubber bulb for pumping up the cuff. The internal pressure of the cuff hose with a catheter in it is controllable by the rubber bulb. The manual gauge can measure the pressure in the chamber to calibrate the proposed mini-invasive system with the overall pressure range from 20 mmHg to 300 mmHg above 1 atm. An incubator with thermostat is employed for temperature sensor measurement. A connector joining flexible PCB together is placed at the proximal end of catheter. The analog interface board connects to catheter by dupont lines. The socket board records sensor data and feeds the serial digital signal into the data recording and analyzing computer. The computer can process the digital codes by the program of the GUI.

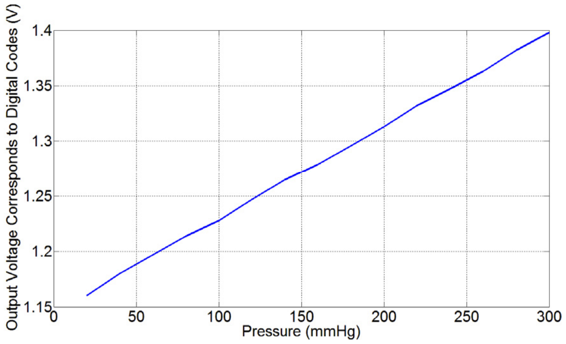

Figure 9: The linearity relative to pressure.

The linearity of the whole system for pressure measurement is shown in Fig. 9 indicating that the root mean square error (RMSE) is 1.43 mmHg. While the linearity of system for temperature sensing is shown in Fig. 10 indicating that the RMSE is 0.08 ºC. The catheter is also measured in laboratory animals as shown in Fig. 11. The results show the system works properly.

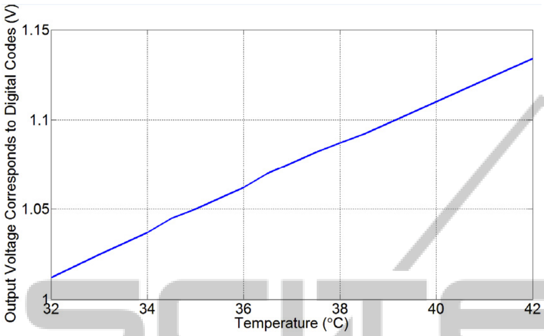

Figure 10: The linearity relative to temperature.

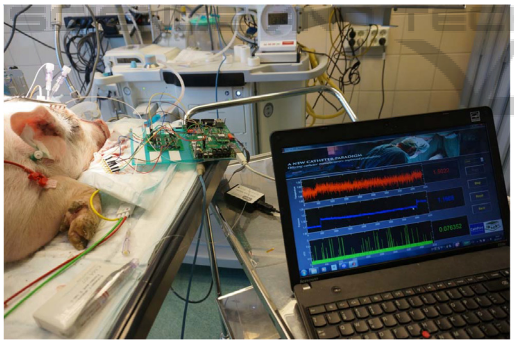

Figure 11: The animal experiment.

6 CONCLUSIONS

This paper proposed a smart catheter system to acquire the ICP and temperature signal for TBI measurement. A piezoresistive MEMS based pressure sensor is mounted on a 1 mm (3 Fr) diameter catheter to detect both pressure and temperature, which minimizes the required catheter space. Flexible PCB is inserted into the catheter for signal transmission. An electronic system records sensor signal and transmits the information to a computer. Measurements results show the system is able to sense the pressure in the range of 20-300 mmHg above 1 atm with RMSE of ±1.43 mmHg and the temperature in the range of 32-42 ºC with RMSE of ±0.08 ºC.

ACKNOWLEDGEMENTS

Dongxuan Bao thanks financial support from China Scholarship Council for study at KTH-Royal Institute of Technology. This work was supported in part by Vinnova (The Swedish Governmental Agency for Innovation Systems) through the Vinn Excellence centers program.

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