A GENERIC PACKAGING TECHNIQUE USING FLUIDIC ISOLATION FOR LOW-DRIFT IMPLANTABLE PRESSURE SENSORS

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ABSTRACT

This paper reports on a generic packaging method for reducing drift in implantable pressure sensors. The described technique uses fluidic isolation by encasing the pressure sensor in a liquid-filled medical-grade polyurethane balloon; thus, isolating it from surrounding aqueous environment that is the major source of baseline drift. *In-vitro* tests using commercial micromachined piezoresistive pressure sensors show an average baseline drift of 0.006 cmH_2O/day (0.13 mmHg/month) for over 100 days of saline soak test, as compared to 0.101 cmH_2O/day (2.23 mmHg/month) for a non-fluidic-isolated one soaked for 18 days. To our knowledge, this is the lowest reported drift for an implantable pressure sensor.

KEYWORDS

Baseline-drift, Pressure Sensor, Implantable Sensor

INTRODUCTION

Pressure in various body organs, such as brain, heart, eyes, bladder, and gastrointestinal tract carries important diagnostic and prognostic information [1], [2]. Since the 1950s, researchers and clinicians have developed numerous implantable wireless sensors to monitor a variety of clinically relevant pressures [3]. The first implantable pressure sensing device was an FM-modulated RF oscillator coupled to a ferrite-based pressure sensor [4]. More recently, with advances in microelectromechanical system (MEMS) sensors, wireless communication, high-density energy sources, the implantable pressure sensing systems have become more sophisticated [5]–[8]. However, due to baseline and sensitivity drifts, accurate long-term pressure monitoring is difficult to attain. These drifts are typically due to the exposure of the sensor to the aqueous environment. This results in the absorption of water into various polymeric materials used in the sensor package, cause swelling and generation of stress that is subsequently transmitted to the sensing element. Other sources of drift include changes in mechanical properties of the sensing elements due to aging, variations in the pressure of the reference cavity, corrosion and changes in the elastic modulus of the diaphragm resulted from adsorption of biomolecules, cells, and other debris [9]. The current solution for sensor drift includes a periodic recalibration. However, this is not an ideal approach for implantable devices since it frequently requires invasive procedures. Other solutions reported by several group uses custom made devices based on careful package design [5], [10], [11] avoiding any polymeric material in the construction and packaging. This naturally results in high costs and in-house know-how, preventing the larger clinical and research communities from access to such systems. In this paper, we report a low cost and generic solution by isolating the sensor in an incompressible fluid-filled balloon. Performance of several fabricated prototypes were validated in aqueous environments.

PACKAGNE STRUCTURE AND DESIGN

Figure 1 shows a schematic view of the described sensor packaging method. The basic design of the implantable system can consist of the packaged pressure sensor and the main circuitry that handles signal and wireless communication. The two components are connected through a thin flexible cable. The advantage of such design is such that the sensor can be positioned near the pressure source, maintaining a small form factor, while the main circuitry can be implanted subcutaneously to increase the wireless link performance with moderate restrictions on size. In this paper, however, we focus on the sensor packaging. The combination of the packaging method with a readout and wireless interface can be found at our previous reports [12].

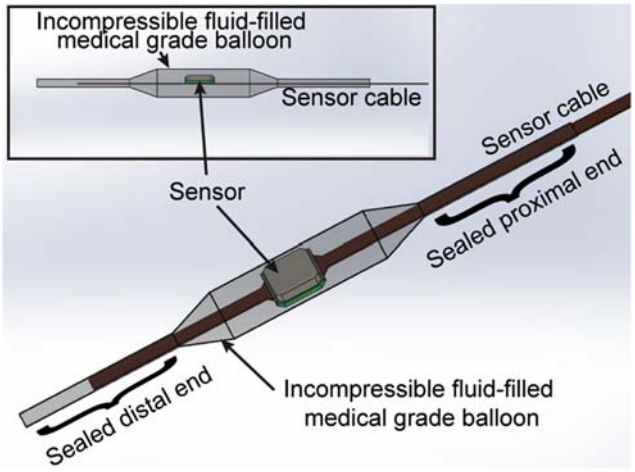

Figure 1: Schematic view of the pressure sensor package structure with fluidic isolation for baseline drift reduction.

The fluidic-isolation packaging technique for the low-drift implantable pressure sensor involves the encapsulation of the sensor along with the flexible interconnection cable in a medical-grade thin polyurethane balloon that is filled with a biocompatible incompressible liquid. The liquid must also be non-aqueous and non-polar to minimize its interaction with the pressure sensor and its polymeric packaging material

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(e.g. parylene coating and epoxy used to cover wire bonds). In our case, we used silicone oil which in biocompatible and fulfills these requirements. While the medical-grade balloon isolate the pressure sensor from environmental drift causing factors, it also transfers pressure information without sacrificing the sensitivity.

FABRICATION

Figure 2 depicts the fabrication procedure for the generic fluidic-isolation sensor packaging technique. The packaging can be used with any conventional diaphragm-based pressure sensors. In our case, we used a commercial piezoresistive pressure sensor (Measurement specialties, MS5637-02BA03), Figure 2a. The dimensions of the pressure sensor is 3 x 3 x 0.9 mm^3, small enough to be adapt for many medical applications. Figure 2b illustrates the pressure sensor being mounted and connected to the main circuitry via a custom-made polyimide flexible cable. The sensor and cable are then coated with Parylene-C for passivation. It is important to design the cable to have a certain length at both the distal and the proximal ends for full encapsulation by the balloon. The medical-grade balloon (Vention Medical, 06001000CA) in then inserted to encase the sensor and flexible cable, Figure 2c. The overall size of the balloon used in our experiments was 10-mm length, 6-mm diameter, and 2.5-mm proximal/distal diameter. The balloon wall thickness was 30 μm, thin enough to transfer the pressure without degrading the sensitivity and reliability.

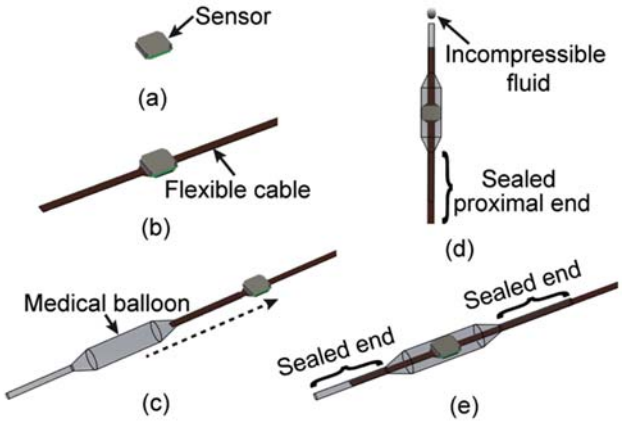

Figure 2: Packaging procedure starts with (a) pressure sensor (b) mounted on a flex-cable, (c) encapsulated with medical grades balloon and sealed at proximal end, (d) filled with incompressible fluid, (e) the balloon sealed at the distal-end.

The next step involves sealing the proximal end of the balloon (cable side) using a UV-curable acrylated urethane adhesive (Loctite, 3105 cured under a UV lamp, 100mW/cm^2, for 5 minutes). The UV-curable adhesives offer a tight leak-proof sealing on polyurethane medical-grade balloons [13]. While the sensor and cable are hold upright, an incompressible fluid such as silicone oil (Sigma-Aldrich, Dow Corning 200 fluid) is filled from the distal end, follow by dispensing a small amount of UV-curable adhesive, Figure 2d. Since the density of UV-curable adhesive is less than silicone oil, it forms a thin layer on the top, Figure 2e. Figure 3 shows the prototype of a fabricated device using the generic fluid-isolation sensor packaging technique.

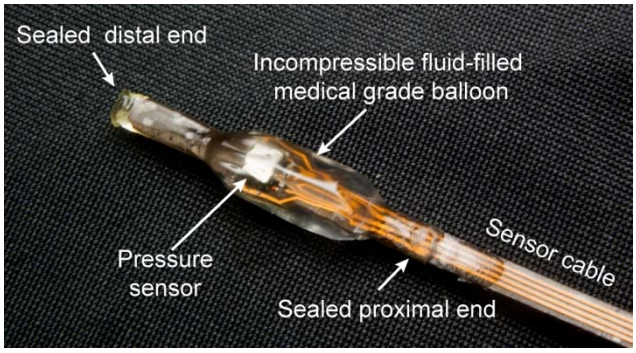

Figure 3: Optical photograph of a packaged sensor.

EXPERIMENTAL RESULTS

The packaged pressure sensor was evaluated *in vitro* by comparing its readouts with: 1) another similar sensor without the liquid-filled balloon (i.e., parylene-coated sensor in direct contact to saline, Figure 2b) called un-packaged from here on, and 2: a standard reference pressure sensor, called reference from here on. Figure 4 illustrates the validation experimental setup. The packaged sensor was placed in a pressure chamber that was filled with saline solution. The pressure chamber was then connected to a syringe pump and a commercial in-line pressure gauge (reference) (Omega DPG4000).

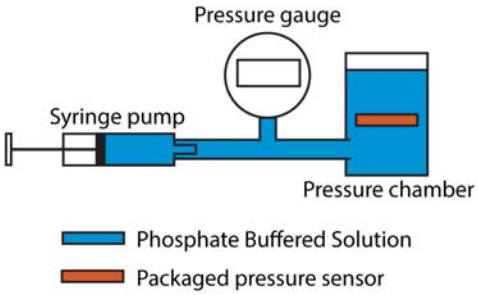

Figure 4: Pressure sensor experiment setup; a syringe pump applied various pressures that is simultaneously monitored by the in-line commercial pressure gauge.

Figure 5a shows the pressure measurements for the packaged and reference sensors (calibration test). As can be seen, the packaged sensor output matches with the reference in both pressure level and response time. Figure 5b shows concurrent agreements of pressure measurements for two

systems, indicating a strong correlation of linear regression ($R^2 = 0.98$, slope of 1.06 ± 0.01).

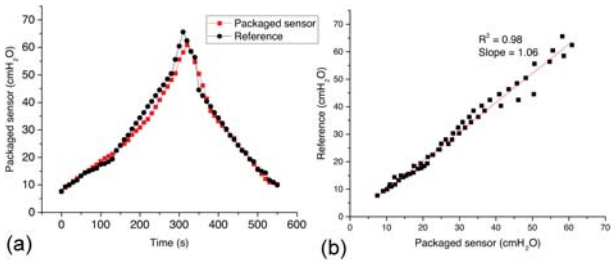

Figure 5: (a) Pressure measurements comparing the packaged and reference sensors, (b) Linear regression showing pressure measured by the balloon-packaged sensor and the reference sensor.

After validation/calibration tests, long-term baseline drift was investigated. The packaged pressure sensor was soaked in saline solution at room temperature (measuring daily atmospheric pressure changes) and its output was compared against the reference sensor. For control group, an unpackaged pressure sensor (Figure 2b) was prepared and soaked in saline. The packaged and unpackaged sensors were monitored for 100 days and 18 days, respectively. The baseline pressure measurement of packaged and unpackaged sensors compared to the reference is shown in Figure 6.

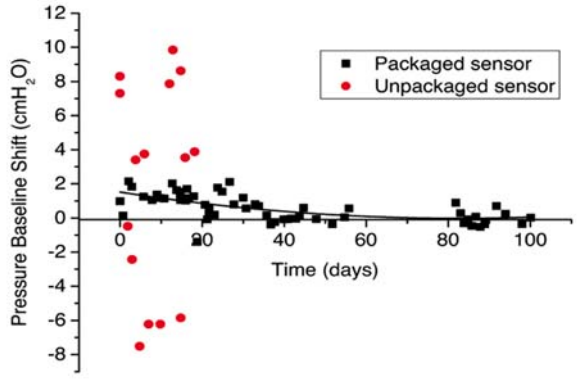

Figure 6: Long-term baseline stability of the packaged sensor using fluidic-isolation technique and the unpackaged sensor

The baseline drift of the packaged pressure sensor showed a slight fluctuation (maximum of 2 cmH_2O) during its first 30 days; however, it remained very stable for the remaining time period. The extrapolated baseline drift of the packaged sensor was 0.006 cmH_2O/day (or 0.13 mmHg/month). The unpackaged sensor showed significant baseline drift even in the short investigation period (18 days); extrapolated baseline drift was 0.101 cmH_2O/day (or 2.23 mmHg/month).

We also performed statistical analysis to show the agreement between the packaged sensors as compared to the reference using the Bland-Altman method, Figure 7. This method finds the relationship between the new technique and a gold standard that measure the same parameter using graphical techniques and simple calculations [14]. A zero difference in pressure between the packaged and the reference sensor indicate absolutely no baseline drift. The results show a negligible drift between the packaged and the reference sensor over time; remaining within -0.58 cmH_2O for 100 days, Figure 7a. The major baseline drift of the unpackaged sensor was also evaluated using the Bland-Altman method. The baseline of unpackaged sensor shifted by a maximum of -2.93 cmH_2O after 18 days, Figure 7b.

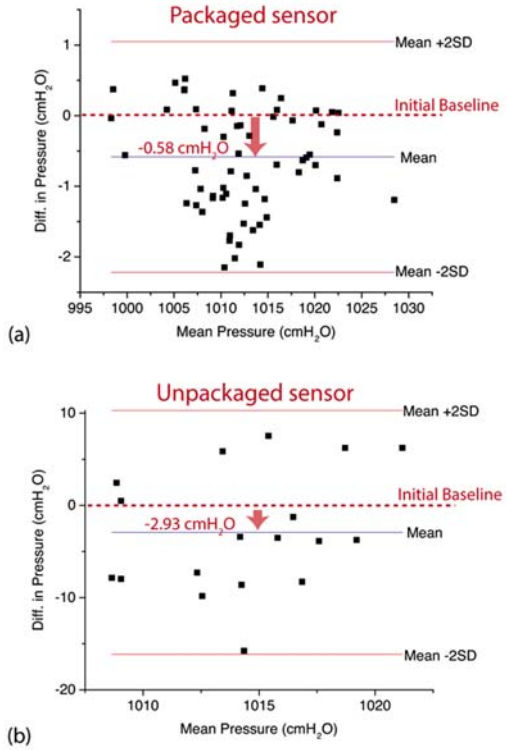

Figure 7: Comparison of two measurement methods analyzed using Bland-Altman limit of agreement. The pressure difference is compared as a function of mean pressure

CONCLUSIONS

In conclusion, we demonstrated a generic packaging technique that leads to an extremely low baseline drift for implantable pressure sensors. After validation experiments, long-term baseline drift was investigated for 100 days. Overall baseline drift was 0.006 cmH_2O/day (0.13 mmHg/month), while the control un-packaged sensors showed a drift of 0.101 cmH_2O/day (2.23 mmHg/month). The statistical analysis, linear regression and Bland-Altman agreement test, confirmed such low baseline drifts.

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