

An *in vivo* MEMS sensor system for percutaneous measurement of urinary bladder*

Ingelin Clausen, Lars Geir W. Tvedt, Are Hellandsvik, Dag Kristian W. Rognlien, and Thomas Glott

Abstract— An *in vivo* sensor system for direct measurement of pressure in the human urinary bladder is developed. The core component in the system is a small-sized and highly sensitive piezoresistive MEMS pressure sensor element integrated in a sensor catheter. The sensor catheter is wired to an external module for biasing, sampling, conversion and storage of sensor measurements. Our solution provides a target sensor placed directly into the urinary bladder and a reference sensor placed outside the bladder wall through a suprapubic and minimally invasive technique. Physiological recordings through natural filling and emptying cycles of the bladder are achievable. The case report from the first 17-hours investigation in a patient is presented in this paper. It reveals that the procedure was successful and no complications occurred. The patient expressed good experience during the participation. A functionality test shows that the percutaneous pressure sensor system responds immediately to external pressure stimuli.

I. INTRODUCTION

Measurement of pressure is highly important in clinical practice and medical research. Pressure in the circulatory system, intraocular, urinary bladder, muscle compartments, joints (e.g., knee and hip), and brain are only some examples of pressures routinely measured. Three types of pressure recording systems are regularly applied in the clinic. These include water perfused or air filled catheter systems and micro tip catheters. Water perfused and air filled catheter systems are vulnerable to movements, bending of the catheter, and delayed pressure transmission [1]. Until recently, the size of the micro tip catheters were relatively large and for multiple use. Sudden shifts or gradual drifts in baseline pressure were reported. These alterations are clinically relevant and may affect patient management [2,3]. The medical community, therefore, wants improved technology providing measurements that are more reliable. Likewise, technology offering the possibility for new clinical procedures and for continuously monitoring organ functions for longer times are desired. Small-sized and lightweight Micro Electro Mechanical Systems (MEMS) may represent a solution to these needs [4-6].

We have developed a sensor system for direct measurements of pressures in the human urinary bladder. Examination of the urinary bladder's capacity to store, contract and expel urine is evaluated for diagnosis of various disorders, including urinary stress incontinence, stroke, spinal cord injury, urethral obstruction, and overactive bladder. Bladder pressure measurements (cystometry) helps the medical experts to determine appropriate treatment. The conventional

cystometry protocol involves the insertion of one or two catheters through the urethra into the bladder [5]. The bladder pressure is transmitted through a water or air column, and measured at the distal end of the catheter with external transducers, as illustrated in Fig. 1. This method is known to be associated with inherent artefacts caused by sensory irritation from the catheter in the urethra [6]. An important part of the diagnostic procedure is to measure the urinary bladder pressure during a filling and drainage cycle. The urinary bladder is then filled with saline using an infusion pump. Fast distension of the bladder implies non-physiological measurements. In addition to being vulnerable to movements, bending of the catheter, and delayed pressure transmission, the existing method provides instantaneous measurements only.

Our solution allows for placement of the sensing part directly into the urinary bladder through a minimally invasive suprapubic technique (Fig. 2). With this method, there is no obstruction or irritation of the urethra. Long-term and high-quality recordings through several natural urinary bladder

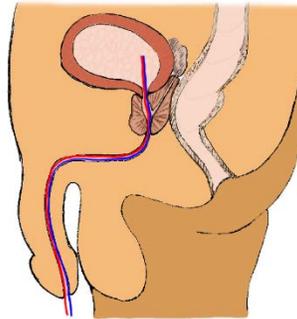


Fig. 1 Conventional method for cystometry (illustrated by the red and blue line).

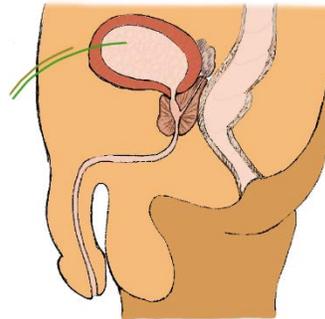


Fig. 2 Minimally invasive suprapubic technique for cystometry (illustrated by the green lines).

*Research supported by Norwegian Research Council through the FORNY2020 program (project no 244494).

I Clausen, L.G.W. Tvedt, A. Hellandsvik and D.K.W. Rognlien are all with SINTEF Digital, NO-0314 Oslo, Norway (corresponding author to provide phone: +47 92650372; e-mail: ingelin.clausen@sintef.no).

T. Glott is with Sunnaas Rehabilitation Hospital, Nesodden, Norway (e-mail: thomas.glott@sunnaas.no).

filling and emptying cycles are therefore achievable. The system is intended to produce maximum 24-hours recordings.

In this paper, we present for the first time clinical overnight investigations in a patient applying the new percutaneous pressure sensor system.

II. MATERIALS AND METHODS

A. The Percutaneous Pressure Sensor System

The core component in the percutaneous pressure sensor system is a small-sized and highly sensitive piezoresistive MEMS pressure sensor element. The sensor element (Fig. 3) is especially designed for *in vivo* applications. The design, fabrication process, and performance is previously described, so are results from tests of biocompatibility, the ability to withstand temperatures typical for sterilization processes, and of performance in true body fluids [7,8]. The sensor element is integrated in a tube with an outer diameter of only 1.2 mm. The sensor tube is wired to an external electronic Sensor Data Logger (SDL) (Fig. 4).

The SDL provides bias voltage to the sensor element and performs A/D conversion of the sensor signal. The SDL is controlled by a central processing unit (CPU), has a microSD card storage, and is powered by battery or over USB. The USB connection is primarily used for interfacing the SDL to a laptop. The software running on the SDL sends the measurements to the laptop and simultaneously store them on the microSD card. The laptop is mainly used when starting a recording to ensure that the system is functional and that valid data are collected.

The SDL is designed to fulfil the requirements for safety of medical electrical equipment described in IEC/EN 60601-1

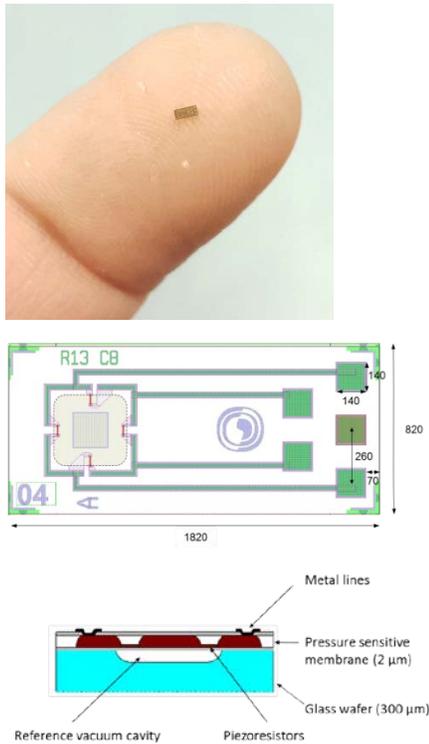


Fig. 3 Photo (top) and schematics of the top view (middle) and cross section (bottom) of the Si-glass sensor element (not to scale).

[9]. The SDL has two independent safety barriers, as shown in Fig. 5. One is a calibrated fuse that will detect small increases in sensor current and shut off the sensor bias if the current rises above a threshold. The second barrier is a current limiter that set an upper limit on how much power can be dissipated inside the body should the first barrier fail. Both barriers will prevent electrical discharge in the human body far below levels that represent any danger or discomfort. According to [9], the leakage current in the patient must not exceed 0.01 milliamperes under normal condition, while for single fault condition it must not go beyond 0.05 milliamperes. For our solution, the threshold for the single fault condition is set by the first protection mechanism to 0.037 milliamperes.

The SDL enclosure is small enough to be carried in a belt. The size of the SDL is 5 cm x 10 cm x 3 cm, and the weight is 200 gram, including batteries.

The output readings from the sensor catheter is in millivolt. The output voltage characteristics is unique for each sensor catheter, depending e.g. on the assembly process. Each sensor catheter is therefore characterized under controlled pressure and temperature to set up the output characteristics curve. We use a combined pressure controller and calibrator (Druck DPI 515) to apply controlled pressure inside a nitrogen-filled pressure chamber submerged in a temperature-controlled water bath (Haake DL30-V15/B).

Before use, each sensor catheter is also sterilized in a hydrogen peroxide gas plasma process and packed in a Tyvek® flat pouch. The sensor catheter is for single use.

B. The Clinical Investigation

The results presented here was part of a larger clinical investigation of the percutaneous pressure sensor system. The clinical investigation followed the good clinical practice according to ISO14155 [10]. A notification was sent to the Norwegian Directorate of Health (the national competent authority in Norway) before the initiation of the investigation. Before commencing the investigation, it was clarified that the Directorate of Health did not have any objections (13/9677). In addition, approval from the Regional Committees for Medical and Health Research Ethics, Region South in Norway was obtained (2013/1604). Furthermore, informed consent from the patient was obtained before study inclusion.

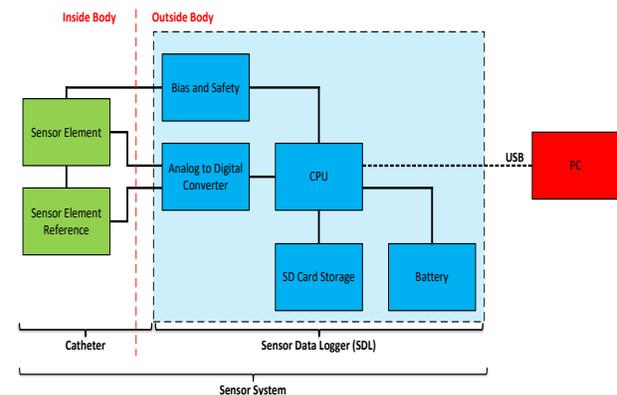


Fig. 4 Overview of the Sensor Data Logger (SDL).

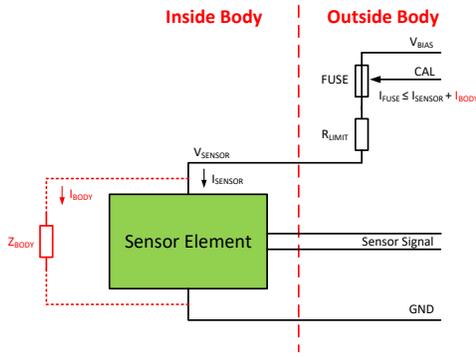


Fig. 5 Overview of the bias and safety function of the SDL.

The patient was a 27-year old male with a chronic complete spinal cord injury (SCI) admitted for cystometry at Sunnaas Rehabilitation Hospital's urodynamic laboratory. The patient had a clinical indication for cystometry. He was examined with conventional technique with catheters inserted through the urethra (Fig. 1). The conventional cystometry was the basis for the routine clinical assessment. In addition, the patient was examined with suprapubic technique using the percutaneous pressure sensor system with a 17 hours recording (Fig. 2). The patient was also assessed with urine samples before and after the procedure. The patient-reported outcome was assessed with a questionnaire.

Placement of the sensor was done in the urodynamic laboratory at Sunnaas Rehabilitation Hospital using sterile equipment and procedures. The procedure followed the International Continence Society's (ICS) *Standardization of Ambulatory Urodynamic Monitoring* [5].

Two sensor catheters were inserted through the skin in the lower part of the abdomen, one inside the bladder (intravesical target sensor) and another outside the bladder wall (prevesical reference sensor) (Fig. 6). The intravesical catheter was inserted ultrasound guided into the bladder. Correct placement was verified by aspiration of urine. The reference sensor was inserted in the prevesical space using the same technique. The sensor catheters were then secured with adhesive dressings to the patient, before connected to the SDL. The continuous signals from the two sensor catheters were thus sampled simultaneously.

Functioning of the system was first monitored when the SDL was connected via the USB to a laptop. Correct recording was verified by the patient coughing and by tapping or pressing the abdomen (Fig. 7). The SDL was then disconnected from the laptop, and measurements were thereafter recorded on the SD card. After sensor placement and control of the system functionality, the patient returned to the ward. The patient returned to the urodynamic lab after 17 hours for removal of the sensor system due to other activities planned during the admission.

III. RESULTS

Both sensor catheters were successfully inserted in the patient during a ten minutes procedure (Fig. 6). We observed immediate response in sensor signal through a series of



Fig. 6 Two sensor catheters inserted through the skin.

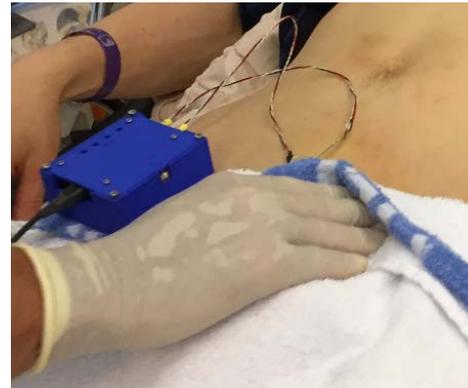


Fig. 7 Test of the sensor system functionality by pressing the abdomen.

external applied abdominal pressures (pressing and tapping) during the system functionality test. The voltage output signals from the two sensor catheters followed each other closely, as shown in (Fig. 8).

The sensor catheters were inserted in the patient for a total of 17 hours. The patient did not experience any complications during this period. Test of urine samples after removal of the sensor catheters confirmed that no infection or bleeding had

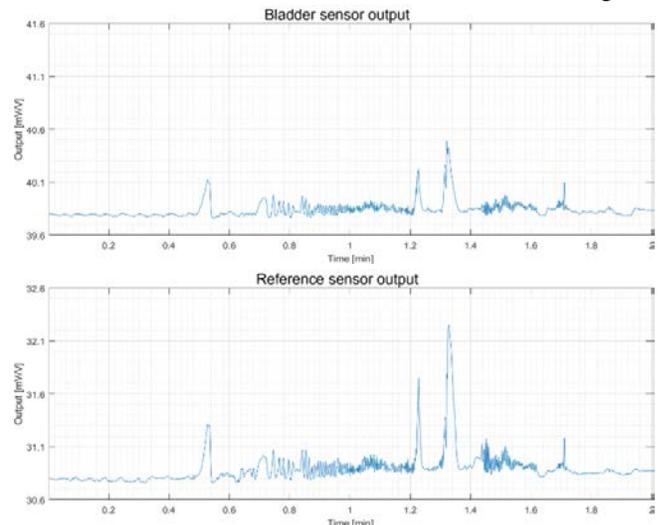


Fig. 8 Results from the functionality test. The bladder catheter (above) and the reference catheter (below) follow each other, i.e. both records the same "external" events. The output signal is in mV/V.

occurred. The patient also expressed good experience while taking part in the investigation.

IV. DISCUSSION

This report is part of a larger ongoing study to quantify the safety and feasibility of suprapubic application of a new MEMS percutaneous pressure sensor system. We report, for the first time, this technique applied in a human. Our initial experience is that the technique is both safe, feasible and satisfactory for the patient for a 17-hours duration. The case report also shows promising measurement results.

As shown in Fig. 8, the two sensor catheters respond simultaneously to the external applied pressure. However, the signal level differs. This is due to a different output characteristics curve for the two sensor catheters, i.e. the two catheters have a slightly different sensitivity and offset.

The sensor signal is presented as nominal voltage (mV/V) and not as pressure. Calculation of absolute pressure values for this case was not possible due to technical problems during characterization. We can therefore not relate the sensor output signal directly to the real bladder pressure. However, based on experience with comparable sensor catheters from the same batch, the value lies between 1000 – 1100 mbar absolute pressure.

Ideally, the difference in pressure between the two sensor catheters should cancel to zero for all other incidents than those related to bladder contraction. The patient did not experience any such contraction during the observation period. The reason why the two signals did not zero each other perfectly, although bladder contraction did not occur, was partly due to the signal presentation in voltage, as explained above. Another reason was placement of the sensor catheters. The bladder sensor catheter was located a certain distance below the reference sensor catheter. Extra pressure was therefore added on the bladder sensor caused by the weight of the tissue (water). This extra pressure corresponds to approximately 4 millibar. The sensor system was designed to have a measurement uncertainty within ± 1 millibar, and we know from extensive pre-testing that this resolution can be achieved (unpublished data). We therefore expect the pressure detected by the bladder sensor catheter to be higher than the one from the reference. More measurements are needed to gain experience with effects on sensor signal caused by the procedure and by *in vivo* operation.

V. CONCLUSION

A percutaneous MEMS pressure sensor system for *in vivo* measurements was clinically tested on a patient admitted for cystometry. A target sensor was placed inside the urinary bladder and a reference sensor was placed outside the bladder wall, through a minimally invasive suprapubic technique. Bladder pressure was recorded using a purpose-built sensor data logger. The case report from the first 17-hours investigation showed good promise in terms of safety and feasibility, and from the subjective experience of the patient taking part. Some technical adjustments to the measurement system is needed to relate the measured sensor voltage to actual pressure, and to zero out non-relative components between the target and the reference sensor.

REFERENCES

- [1] Lose, G.; Griffiths, D.; Hosker, G.; Kulseng-Hanssen, S.; Perucchini, D.; Schafer, W.; Thind, P.; Versi, E. "Standardisation of urethral pressure measurement: Report from the standardisation sub-committee of the international continence society". *Neurourology and Urodynamics* **2002**, *21*, 258-260.
- [2] Eide, P.K. "Comparison of simultaneous continuous intracranial pressure (icp) signals from a Codman and a Camino ICP sensor". *Medical Engineering & Physics* **2006**, *28*, 542-549.
- [3] Eide, P.K.; Bakken, A. "The baseline pressure of intracranial pressure (ICP) sensors can be altered by electrostatic discharges". *Biomedical Engineering Online* **2011**, *10*.
- [4] Clausen, I.; Glott, T. "Development of clinically relevant implantable pressure sensors: Perspectives and challenges". *Sensors* **2014**, *14*, 17686-17702.
- [5] Barkam, S.; Saraf, S.; Seal, S. Fabricated micro-nano devices for in vivo and in vitro biomedical applications. *Wiley Interdisciplinary Reviews-Nanomedicine and Nanobiotechnology* **2013**, *5*, 544-568.
- [6] Meng, E.; Sheybani, R. Insight: Implantable medical devices. *Lab on a Chip* **2014**, *14*, 3233-3240.
- [5] Abrams, P. *Incontinence*. 4th ed.; Health Publications Ltd: 2009.
- [6] Thyberg, M.; Ertzgaard, P.; Hakansson, L.; Spangberg, A.; Granerus, G. "Obstructive effect of a closed 12F urethral catheter during the emptying phase of cystometry in patients with a spinal reflex bladder". *Paraplegia* **1995**, *33*, 40-45.
- [7] Clausen, I.; Moe, S.; Tvedt, L.G.; Vogl, A.H.; Wang, D.T. "A miniaturized pressure sensor with inherent biofouling protection designed for in vivo applications", 33rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society, Boston, MA USA, 2011; IEEE: Boston, MA USA, pp 1880-1883.
- [8] Clausen, I.; Tvedt, L.G.W.; Moe, S.; Vogl, A. "The effect of true human synovial fluid on the functionality of an in vivo pressure sensor element", Sensors, 2013 IEEE, 3-6 Nov. 2013, 2013; pp 1755-1758.
- [9] IEC_60601-1. "Medical electrical equipment- part 1: General requirements for basic safety and essential performance". **2005**.
- [10] ISO14155. "Clinical investigation of medical devices for human subjects - good clinical practice". 2011.