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A novel method to investigate bladder wall behavior by acceleration and pressure sensing

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ABSTRACT

Bladder dysfunctions form a continuously growing problem as the ageing population in our society is steadily increasing. However, scientific knowledge about the fundamental principles underlying bladder diseases is still lacking. Conventional cystometry-based methods for assessing bladder function are quite limited in their scope. In this paper, a novel device is introduced to research the bladder. An exploratory device was designed for measuring bladder wall contractions in rats using accelerometers. Later, a fully implantable system was created to extend the measurements to larger animal models. The battery-powered implant provides a wireless readout of multiple sensors with synchronous visualization. An intelligent algorithm is used to optimize the power consumption and to extend the autonomy after implantation, yielding a useable measurement time of 16 continuous days and several months of standby-time.

1. Introduction

The number of people suffering from bladder dysfunctions is estimated to be well into the hundreds of millions worldwide [1]. Diseases affecting the sensation of urgency include overactive bladder syndrome, urinary incontinence and lower urinary tract symptoms, the exact functionalities of which are still poorly understood by modern medicine.

Traditional methods of assessing bladder function are based on intraluminal pressure measurements through a catheter, urine flow and volume measurements, and in some cases electromyography (EMG) of the sphincter muscle [2,3]. These methods are quite limited in their scope, as they provide only a summation of whole bladder activity and no localized bladder information. As such, they are mostly useful as a diagnostic tool rather than for providing new medical insights into the bladder. Moreover, the catheter and EMG leads, which are connected to an external measurement system, are a discomfort to the patient and also limit measurement duration to no more than several voids.

The hypothesis of autonomous bladder function, described in [4,5], suggests the bladder senses its volume and pressure, which is linked to the patient's feeling of urgency, by using localized contractions. Those theorized bladder wall movements might occur prior to voiding, as well as during voiding. Moreover, these local contractions may as well occur at random time intervals, unrelated to the emptying of the bladder. In fact, the autonomous function of the bladder is increased in absence of central nervous system efferent inhibition. This insight is promising for patients that experienced spinal trauma and suffer from urinary incontinence.

To obtain a better understanding of the fundamental bladder mechanics, a new method for assessing bladder functionality is explored in this paper. In a first study, an exploratory device for acute in vivo measurement of acceleration of the bladder wall of rats is proposed. The acceleration results are compared to conventional catheter pressure measurements and the design of the system, along with a measurement during voiding, is discussed in Section 2. Using the findings from the first phase, a fully implantable system is developed which monitors bladder wall accelerations and pressure and is described in Section 3. The implant has sensors placed in several localized spots, to compare localized bladder wall movements in different positions of the bladder. The system is fully implantable for several months while being unobtrusive for the patient. This novel approach will provide physicians with

Abbreviations: EMG, electromyography; PCB, printed circuit board; USB, universal serial bus; I2C, inter-integrated circuit; IPHFO, intraluminal pressure high frequency oscillations; UART, universal asynchronous receiver-transmitter; P_{ves}, vesical pressure; P_{det}, detrusor pressure.

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valuable new information about the inner operation of the bladder, the conditions that cause bladder dysfunctions and the possible relation between bladder muscle contractions and the sensation of urgency.

2. Exploratory study of physiological measurements of the bladder

This section discusses the methodology used to facilitate exploratory investigations of physiological functionality of the bladder: the placement of an accelerometer on the bladder of a rat.

2.1. Description of the device

In order to perform in vivo measurements of bladder functionality, a selection of sensors needs to be made according to the following specifications listed. The selected devices must inherently be biocompatible or at least permit a biocompatible packaging. The physical dimensions of the sensors need to be as small as possible, preferably smaller than $5 \times 5 \times 2$ mm. The power consumption during measurement as well as in idle state should be minimized to allow a long operating time of the battery (at least several days of autonomy). The sampling frequency is at least twice the bandwidth of the measured signal. However, given the novelty of these measurements, the bladder signals and their bandwidth are unknown. Therefore, inspiration to set the specifications needs to be sought with previous experience, signals from other medical fields and expert medical opinion. As shown in a smooth muscle experiment [6], a good estimate for the highest frequency components contributing to smooth muscle movements is in the order of 50–100 Hz. Therefore, the assumption is made that the bladder does not exhibit movements with frequency components more than 100 Hz. The range of inertial measurements from bladder contractions is expected not to exceed ± 2 g. The resolution required is unknown and should thus be as high as possible. The pressure difference of the bladder between its empty and filled state, as measured with intraluminal catheters, is 300 mbar. A resolution of 0.1 mbar is sufficient to measure any pressure variations in classical cystometry. Although the use of an EMG system has been shown to provide interesting results concerning bladder contractions [7] and can be made implantable, the choice was made to limit the system to inertial and pressure measurements in order to avoid biocompatibility as well as noise problems.

A miniature 3-axis accelerometer (Bosch Sensortec BMA280) is mounted at the end of a 25 cm long, flexible PCB. Besides this accelerometer, the optional functionality was added to monitor bladder pressure, so a digital pressure sensor (TE Connectivity MS5637) was added close to the accelerometer. The sensors are selected for their compact size and low power consumption. The accelerometer measures $2 \times 2 \times 0.95$ mm and consumes 130 μA in active mode. It is configured with range of ± 2 g, resolution of 14 bits and sampled at 500 Hz. The pressure sensor has dimensions of $3 \times 3 \times 0.9$ mm and an average current consumption of 150 μA during sampling. The pressure signal is sampled at the same frequency of 500 Hz, has a range of 0–2 bar and 24-bit resolution. The assembled device is depicted in Fig. 1.

A biocompatible packaging is necessary to protect the sensors from the body fluids, as well as to shield the organs from the electronics. The MS5637 is a barometric pressure sensor designed for operation in air and is covered by a metal cap to protect the electronics. However, since a mechanical coupling is needed between the pressure sensitive membrane under the protective cover and the bladder wall, the metal cap must be removed, exposing two silicon dies and the bondwires connecting them. Three packaging layers are used: (1) parylene-C with a thickness of 5 μm is applied by chemical vapor deposition and provides low water permeability, (2) a medical grade epoxy is used to mechanically reinforce the electrical connections of the sensors, as well as the dies and bondwires of the pressure sensor, taking special care not to cover the sensor membrane, and (3) the device is dip-coated in medical grade PDMS. The factory calibration of the pressure sensor is invalidated by the application of the packaging layers, so it needs to be recalibrated. The BMA280 acceleration sensor, however, is completely sealed and unaffected by the packaging, so the factory calibration and baseline drift correction remain valid.

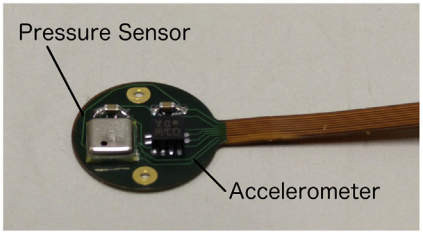

Fig. 1. The bladder wall measurement sensors, an accelerometer and pressure sensor mounted on a flexible PCB.

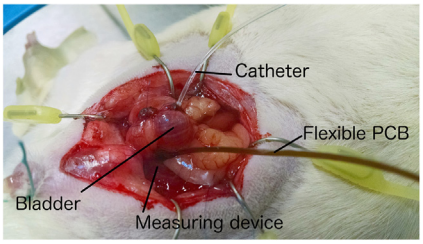

Fig. 2. Placement of an accelerometer on the bladder of a male rat, covered by abdominal tissue. A pressure catheter, used for filling the bladder, perforates the detrusor.

The flexible PCB is connected to a readout board that contains a microcontroller. The digital samples of the sensors are read out over a synchronous serial I2C interface and transmitted to a personal computer over USB. The readout board and acquisition software can simultaneously measure and plot two accelerometers and two pressure sensors.

2.2. Implantation procedure and measurement

All experimental procedures are performed in accordance with applicable institutional and national guidelines. The accelerometer is implanted in a male Sprague-Dawley rat. Under urethane anesthesia (1.3 g/kg s.c.), the bladder is exposed by laparotomy. Continuous saline infusion cystometry at 100 μL/min is performed through a flared-tip suprapubic catheter (PE-50, Intramedic) with luminal pressure registration (BIOPAC MP150). The catheter perforates the outer bladder muscle, called detrusor. The small size of the bladder prevents the use of the pressure sensor, so only the accelerometer is used. To prevent the accelerometer to move away from its position on the bladder muscle and to ensure an intimate connection of the sensor to the bladder wall, the tip of the PCB is clamped under a patch of abdominal tissue using stitches. The implanted device is depicted in Fig. 2.

A continuous measurement is carried out during the entire infusion, resulting in records of several voiding events. The conventional rise in pressure at the onset of each voiding event was clearly observed, as well as the aftercontraction. During the voiding itself, intraluminal pressure high frequency oscillations (IPHFO) are visible in the pressure signal, as described in [8]. The IPHFO, traditionally only described in the pressure signal, have a clear counterpart in the acceleration signal, as shown in Fig. 3. The accel-