Biomed Microdevices (2009) 11:259–264
DOI 10.1007/s10544-008-9232-1

Development of a fully implantable wireless pressure monitoring system

Robert Tan · Timothy McClure · C. K. Lin · David Jea · Foad Dabiri · Tammara Massey · Majid Sarrafzadeh · Mani Srivastava · C. D. Montemagno · Peter Schulam · Jacob Schmidt

Published online: 3 October 2008

Abstract A fully implantable wireless pressure sensor system was developed to monitor bladder pressures *in vivo*. The system comprises a small commercial pressure die connected via catheter to amplifying electronics, a microcontroller, wireless transmitter, battery, and a personal digital assistant (PDA) or computer to receive the wireless data. The sensor is fully implantable and transmits pressure data once every second with a pressure detection range of 1.5 psi gauge and a resolution of 0.02 psi. In vitro calibration measurements of the device showed a high degree of linearity and excellent temporal response. The implanted device performed continuously *in vivo* in several porcine studies lasting over 3 days. This system can be adapted for other pressure readings, as well as other vital sign measurements; it represents the first step in developing a ubiquitous sensing platform for telemedicine and remote patient monitoring.

R. Tan · C. K. Lin · J. Schmidt (✉)
Department of Bioengineering, University of California,
Los Angeles, CA 90095, USA
e-mail: schmidt@seas.ucla.edu

T. McClure · P. Schulam
Department of Urology, University of California,
Los Angeles, CA 90095, USA

D. Jea · M. Srivastava
Department of Electrical Engineering, University of California,
Los Angeles, CA 90095, USA

F. Dabiri · T. Massey · M. Sarrafzadeh
Department of Computer Science, University of California,
Los Angeles, CA 90095, USA

C. D. Montemagno
College of Engineering, University of Cincinnati,
Cincinnati, OH 45221, USA

Keywords MEMS · Pressure sensor · Implantable · Patient monitoring · Telemetry · Telemedicine · Bladder · Wireless

1 Introduction

There has been significant interest in the medical community in telemedicine and remote patient monitoring at home and in the hospital (Field and Grigsby 2002). Current patient monitoring instrumentation and practices can be cumbersome and restrictive. For example, in the intensive care unit, blood pressure monitoring can be monitored continuously with an arterial line. This is a catheter that is placed in the artery, and an external transducer detects the pressure. The limitations of this are that the accuracy is highly variable, and the patient is often sedated to prevent him from injuring himself from movement. On the other hand, in standard floor care, while completely non-invasive and burden-free to the patient, standard blood pressure measurements with a cuff are non-continuous point measurements typically taken every 2–12 h. The development of critical vital signs between measurements could be missed. Currently, there is no device which provides clinicians with continuous monitoring of vital signs without being extremely invasive and/or cumbersome.

A device capable of continuous and real time measurement and monitoring without significantly reducing the patient's comfort or restricting his movement would fill the gaps in performance and comfort between intensive and standard care. A simple and cost effective solution is to utilize implantable microsystems utilizing wireless telemetry. Wireless telemetry frees the patient from being tethered to large hospital monitors and can participate in a hospital sensor network, which could increase monitoring efficiency

by minimizing staff work load, increasing the amount of data obtained, and streamlining its storage and processing. Micromachined pressure sensors are readily available and have been explored for use in blood pressure measurement, either in intravascular systems or implantable pressure cuffs (Chaer et al. 2006; Najafi and Ludomirsky 2004; Potkay 2008; Schlierf et al. 2007; Schnakenberg et al. 2003; Walton and Krum 2005; Ziaie et al. 2001). Sensors are also being developed for sensing intraocular pressure, intracranial and spinal pressure, and orthopedic stresses (Chiang et al. 2007; Eggers et al. 2000; Leonardi et al. 2003; Meir et al. 2008; Tofighi et al. 2006; Walter et al. 2000; Yoon et al. 2004). In urology, a field in which the etiology of disease is often times secondary to abnormalities in pressure, there have only been a few pressure sensors that been developed for this purpose, but to our knowledge, none have been tested successfully in vivo (Coosemans and Puers 2005; Siwapornsathain et al. 2002). The diagnosis and management of urologic diseases could benefit from these sensors.

For the most part, wireless implantable pressure sensor development has focused on devices powered by radio frequency (RF) induction, which enables indefinite implantation and operation without the need for subsequent surgeries to exchange batteries. Also, the total device volume is minimized, as the battery is typically the largest component. Several groups have developed and tested devices that detect dynamic blood pressure in the femoral artery or aorta of animal models (Najafi and Ludomirsky 2004; Schlierf et al. 2007). Two systems are commercially available: the Savacor HeartPod and CardioMEMS Endosure for implantation in the left atrium and aortic aneurysm, respectively (CardioMEMS 2007; Chaer et al. 2006; Walton and Krum 2005). However the transmission range is often limited to centimeters (Najafi and Ludomirsky 2004; Schlierf et al. 2007) and the sensor can only transmit data when it is exposed to RF energy. This often limits the measurements to discrete points in time or tethers the patient to an antenna at all times for continuous measurements (CardioMEMS 2007; Walton and Krum 2005).

Here we present a different approach to monitor ambulatory pressures, which consists of a micromachined pressure die, amplifying electronics, microcontroller, wireless transmitter, and battery, that is implanted into the body and communicates with a personal digital assistant (PDA) or computer. Because the RF energy involved does not need to power the device, the frequency can be chosen to maximize transmission range. Therefore, the PDA or computer can be located relatively far away, and the patient is free to move around without fear of losing data. Monitoring can be done during normal activity levels of the patient as opposed to being bedridden and immobile as is currently required.

2 Methods and materials

The pressure sensing platform is divided into three parts: the pressure sensing catheter lead, the sensor node (Fig. 1), and the PDA or computer receiver. The fabrication of each of these parts is discussed below:

2.1 Catheter lead

The catheter lead houses the pressure sensor and connects it to the sensor node (Fig. 2). It consists of a piezoresistive pressure sensor (Silicon Microstructures 5108) measuring 0.65×0.65 mm affixed onto a ceramic printed circuit board (PCB) with UV epoxy (Masterbond UV10). The die was chosen for its size, sensing range, and precision, with a sensitivity of 1.6 mV/psi/V. The strain gauges on the die are configured in a temperature-compensated Wheatstone bridge. The chip was then wirebonded (West Bond 7402C) to contact pads on the substrate board. Four individually insulated platinum–iridium (Pt–Ir) wires threaded through a 7.5 French (2.5 mm) catheter were soldered to leads on the board connected to the contact pads. UV epoxy was applied over all contact and solder pads on the substrate board and chip and cured for 8 min to prevent any of the Pt–Ir wires or wirebonds from breaking contact. A gold cap with four wedge-shaped holes cut out of the side was affixed with UV epoxy onto the PCB over the pressure die to protect the chip. The four Pt–Ir wires were wound around a high-tensile insulating polyester core and threaded through tygon tubing. This assembly was threaded through silicone tubing prior to soldering.

For packaging, 44.5 μm-thick cellophane film (3M) was wrapped around the substrate board and gold cap. The film was sealed with 5 min epoxy (Devcon). Once cured, the tip of the catheter lead was compression-molded in medical-grade polydimethylsiloxane (PDMS) silicone (Nusil Med4011), which is FDA-approved for short term implan-

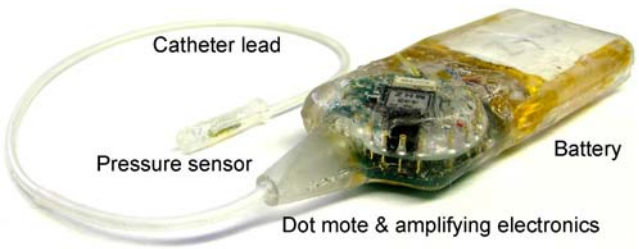

Fig. 1 The implanted device after fully being fully packaged. The pressure sensor is housed at the end of a 7.5 French catheter, which is implanted directly into the bladder or peritoneal cavity. The other end of the catheter is connected into the sensor node, which consists of the dot mote (microcontroller and wireless transmitter), the amplifying electronics, and battery. The device is wrapped in LDPE film and molded in medical-grade PDMS

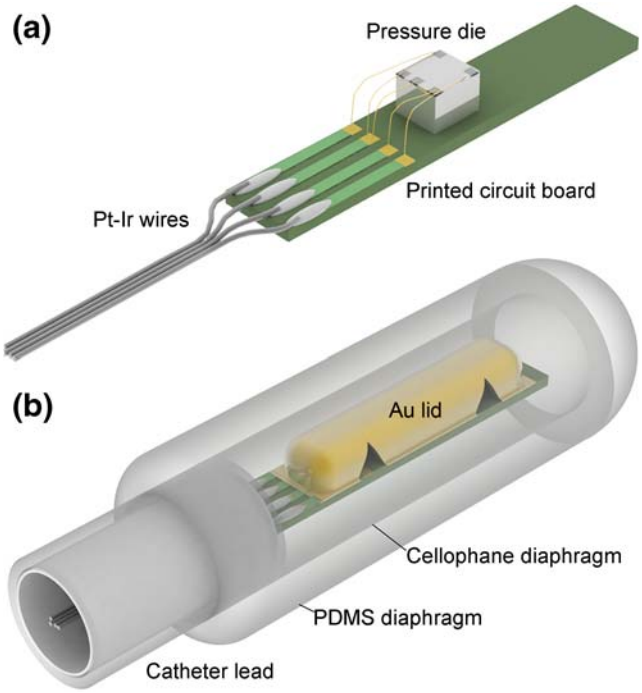

Fig. 2 Artist's rendition of catheter lead tip. (**a**) Shows the lead tip unpackaged. A commercial pressure die is affixed and wirebonded onto a PCB substrate. Four Pt–Ir wires fed through the catheter are soldered onto the PCB. (**b**) Depicts the lead after packaging. A gold lid covers and protects the chip and wirebonds. Cellophane is wrapped around the lead; PDMS is molded around it to make it biocompatible

tation (Nusil 2008). The PDMS was mixed in a 10:1 elastomer base to curing agent ratio and degassed under vacuum. Once in the mold, the PDMS was allowed to cure for ~24 h at room temperature. The final diameter of the molded tip of the catheter lead measured about 12 French (4 mm).

2.2 Sensor node

The sensor node consists of three components: amplifying electronics, microcontroller and wireless transmitter, and the battery. The free end of the catheter lead is soldered onto a custom-designed circuit board. On this circuit board are a quad micro-power, single supply operational amplifier (Texas Instruments TLV2764), a 2.5 V voltage regulator chip (Analog Devices REF192), and a single pole, double-throw (SPDT) magnetic reed switch to turn the device on and off (Hamlin) (Lin 2007). The voltage regulator chip sets the supply voltage powering the device and other electronics to 2.5 V to prevent any variations in signal from the pressure die due to variations in battery voltage. The operational amplifiers were configured to null any offset from the sensor bridge and amplify the bridge voltage by a factor of 300. The physiologically-relevant pressure measurement range was 1.5 psi gauge pressure, and with the device sensitivity, supply voltage, and amplification, the device output was 1.2 V/psi and 1.8 V for the physiological pressure range.

The output of the amplifying circuit was connected to the microcontroller and wireless transmitter (Mica2Dot (Crossbow MPR510CA), hereafter referred to as the dot mote), which transmits at 433 MHz. We programmed the microcontroller to acquire and transmit data while maximizing battery life in three ways: first, the microcontroller pulses the sensor for only 30 μs each measurement cycle, after which the entire device goes into sleep mode. Second, the measurements are taken only once per second. Finally, since the greatest power draw comes from transmission, the sampled data is stored locally on the dot mote and is transmitted every 30 measurements (Lin et al. 2007). These techniques reduce the energy consumption from 3 mJ per measurement to 625 μJ (Lin 2007; Lin et al. 2007). The battery used is a 3.7 V, 850 mAH lithium-polymer battery (Batteries America). The device was observed to have a lifetime of 387,300 measurements or >4 days at this sampling rate before the battery voltage dropped below the supply voltage of the device.

Once fully fabricated, the sensor node was wrapped in 25 μm-thick low density polyethylene (LDPE, Plastic Sheeting Supply) and compression-molded in PDMS. Afterwards, the device was dipped into PDMS for a second silicone layer to plug any holes in the first PDMS layer. During and after the packaging process, the battery cannot be charged or replaced, so neodymium magnets were stacked on top of the mold to activate the magnetic switch and turn off the device while it cured for 24 h.

2.3 Wireless communication

The dot mote communicates with a complementary receiver station (Crossbow MIB510CA), which is connected to a computer. The dot mote sends data in a hex format that includes a timestamp, a unique ID tag, the remaining battery voltage, and the amplified pressure data. LabVIEW (National Instruments) was programmed to read and convert the data packets, which are stored in a text file and graphed in real time.

2.4 In vitro tests

Once fabrication of each catheter lead was completed, the lead alone was tested and characterized by placing it in a sealed pressure chamber (Binks). It was electrically connected to wires threaded through the lid of the pressure chamber. The lead was externally powered (Agilent E3630A) and the output voltage was read by a high precision multimeter (Keithley 2000). The pressure was held constant at atmospheric pressure for 30 min while the

device output and pressure readings from an NIST-calibrated pressure gauge (Omega DPG5600B-30A) were recorded every 5 min. The chamber was connected to a cylinder of compressed nitrogen through a pressure regulator and the pressure was raised in 1.0 or 1.5 psi increments and held for 30 min. For the first 10 min, pressure and voltage readings were taken every minute and every 5 min for the following 20 min. At the conclusion of the calibration, the pressure vessel was vented back to atmospheric pressure and voltage and pressure were read every minute for 10 min and every 5 min for the following 20 min. The calibration was performed three times for each lead to test the effects of the environment on the lead and its packaging. It was tested in air first as a control, and then the tip of the lead was placed in a beaker of water inside the chamber. It was left submerged for 4 days when it was tested again. If the output magnitude and temporal response stayed consistent after the fourth day, it was paired with a sensor node.

After a sensor node was paired to a catheter lead, the entire device was tested again before packaging. The lead was placed in water within the sealed pressure vessel. The sensor node was connected to the lead outside the pressure chamber and powered either by the battery or DC power source. The LabVIEW program ran on the computer and stored the wireless pressure data. The pressure was incrementally stepped up from 0–1.5 psi to test the required pressure range and held at each step for 5 min with pressure readings taken every 2 min. To test the resolution of the device, the incremental pressure changes were 0.02 psi from 0–0.1 psi and 0.1 psi for 0.1–1.5 psi. At the conclusion of each test, a calibration curve was generated that related the voltage recorded on the computer to the pressure inside the chamber.

Another test of the packaged device was performed by submerging it in a 2.5 gal bucket of dyed water and left to transmit data until the battery drained out. Afterwards, the data was analyzed to look for any signs of short circuits, characterize any sensor drift, and quantify the full lifetime of the device. The packaging was later removed to look for any signs of water leakage.

2.5 In vivo tests

Adult female swine were used for in vivo testing as approved by UCLA Medical Center IRB #2004-185-11. One device was implanted into the bladder and another was placed inside the peritoneal cavity as a reference. The tips of the catheter leads were placed in those spaces while the sensor nodes were placed in a subcutaneous pocket. Following surgery, the pigs were kept in a holding pen in a vivarium while the computer and radio receiver were set up outside the pen to collect the data. At this point, the pigs were fully conscious and ambulatory. After 2–4 days, the pigs were sacrificed and the devices were explanted. A brief necropsy was performed to look for tissue inflammation or any immune response to the silicone packaging. The devices were later inspected for any damage, leaking, or any other failure points if necessary.

3 Results & discussion

3.1 In vitro tests

Testing of the fully assembled lead and sensor node showed a rapid and linear response (1.34 psi/V) of the sensor (Fig. 3). When the device was disassembled and reassembled following the initial tests, the offset was observed to change slightly. Once the device was fully packaged and ready to be implanted, this change was compensated by comparing the calculated pressure from the calibration curve and the actual pressure from a pressure gauge and adjusting the offset value on the calibration curve.

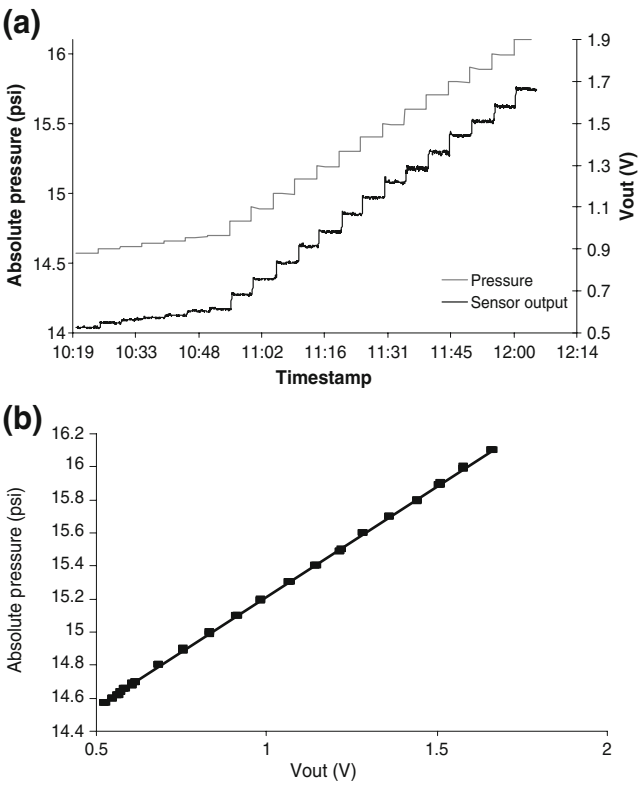

Fig. 3 Typical results of *in vitro* testing. (**a**) Is the temporal response of the measured voltage and the pressure input. Each small increment is 0.02 psi; each large increment is 0.1 psi. The pressure range is from 0–1.5 psi gauge. (**b**) There was high linearity between the measured voltage and the pressure. The equation of the best fit line is $P=1.3393\ V_{out}+13.873$ ($R^2=0.9998$)

While testing the integrity of the PDMS packaging, the device performed without malfunction until the battery drained for a lifetime of 107 h. The output voltage stayed constant for the initial 2.5 days with a variance of <0.0003. However, for the next 2 days, the voltage steadily decreased until the device ceased functioning. An inspection of the device once it had ceased functioning showed no liquid or gaseous water or water penetrated the PDMS layer and the data was free of short circuits.

3.2 In vivo test

When the pressure from the peritoneal sensor is subtracted from the pressure of the bladder sensor, the detrusor (bladder muscle) pressure is obtained. Therefore, any pressure change can be attributable from activities within the bladder or from other sources, such as abdominal contractions, peristalsis, movement, etc. Pressure changes of the detrusor possibly due to bladder contractions were observed (Fig. 4) during the animal studies. This data shows that the detrusor pressure stayed relatively constant as the bladder filled as the bladder wall is highly compliant. The pressure increased sharply followed by a sudden decrease in pressure, which is representative of a bladder void. Figure 4 is demonstrative of known pressure graphs of voiding.

The devices in this test transmitted data for more than 4 days in vivo until the batteries drained out. Furthermore, they were able to transmit data to the computer more than 20 ft away while implanted. Neither device showed signed of fluid leaks; however, the device implanted into the peritoneal cavity had a damaged catheter lead tip. In fact, the gold lid protecting the pressure die was flattened along the back half of the substrate board. Despite the damage, the chip remained functional throughout the test. Analysis of the data revealed the data obtained for the first 2.5 days had several urination events. The pressure data from the peritoneal cavity had many discontinuities: the baseline pressure suddenly jumped to a higher level before falling back down. This may be due to the sensor contacting various internal structures as the animal moves (Fig. 5). These discontinuities are not seen in the bladder trace possibly since the sensor was placed in a bag of fluid and thus would not encounter these phenomena. Towards the end of the study, the data became unreadable and was characterized by high loss of data packets and many sudden spikes. This may be due to a combination of a draining battery and the hostile environment for transmission as it was known that the radio receiver had difficulty picking up the wireless signals at the beginning of each *in vivo* study.

4 Conclusion

In summary, we have constructed a fully implantable wireless *in vivo* pressure sensor for use in short term urological studies and patient monitoring. *In vitro* testing demonstrates its quick temporal response and its high linearity. Through *in vivo* tests in the bladder and peritoneal cavity of porcine models, the pressure sensing system was able to successfully record medically relevant data, which contained physiological events like urination.

This platform can be expanded with additional sensing modalities, such as a thermistor for core temperature, platinum and silver electrodes for blood or tissue oxygen tension, and analysis of blood pressure to obtain heart rate if the lead was implanted into an artery. Further miniaturization of the catheter to a point such that it can fit inside a needle can eliminate the need for major surgery. While the electronics and wireless transmission unit were kept internally for this test because of fears of damage to it by

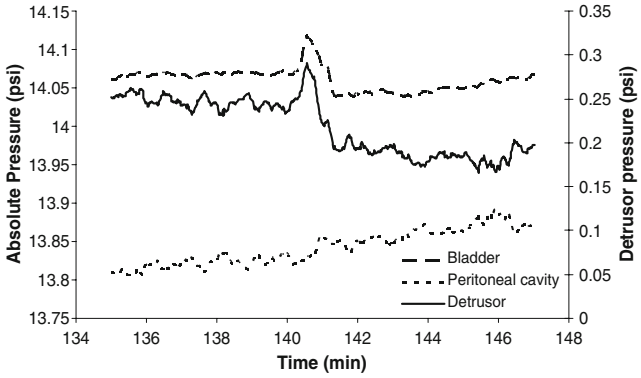

Fig. 4 The results of a urination event during an in vivo test. The peritoneal cavity pressure is subtracted from the bladder pressure to calculate the detrusor pressure

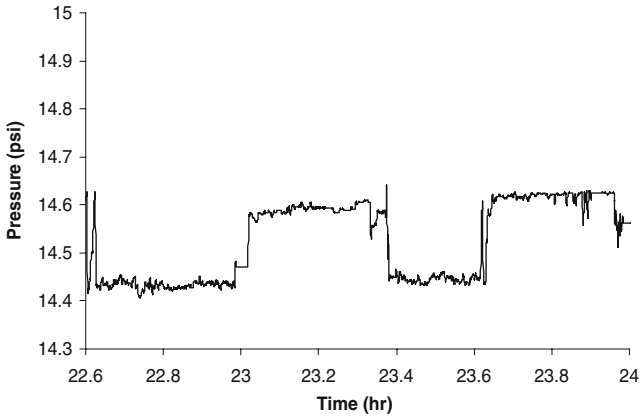

Fig. 5 Pressure measurements from the sensor located within the peritoneal cavity. The discontinuous changes in measured pressure may be a result of intermittent contact with abdominal organs in the mobile animal

the animal, for human applications, it may be more practical to keep it outside yet secured to the body. This would make deployment of a sensor platform like this more practical and ubiquitous within a hospital.

Acknowledgements The authors would like to thank Robert Schaeffer, Andy Chen, Tony Kennestrasi, Virgil Mancion, David Choi, Anthony Hernandez and Ed Chernoff of Medtronic for their support and expertise in this field. Also, Tim Canan, Neil Boroumand, Jason Poulos, Dan Garcia, Dr. Alberto Breda, Dr. Hyunwoo Bang helped on this project. The United States Army Telemedicine and Advanced Technology Research Center (TATRC) provided financial support.

References

M.E.M.S. Cardio, A. Endosure, AA Sensor (2007), http://www.cardiomems.com/content.asp?display=medical+mb&expand=ess. Accessed July 2, 2008

R.A. Chaer et al., J. Vasc. Surg. **44**, 6 (2006). doi:10.1016/j.jvs.2006.08.031

C.-C. Chiang et al., Sens. Actuators A Phys. 134 (2007)

J. Coosemans, R. Puers, Sens. Actuators A Phys. **123–124**, 155 (2005)

T. Eggers, et al., *Presented at the 1st Annual International, Conference On Microtechnologies in Medicine And Biology*. 2000. IEEE Lyon, France

M.J. Field, J. Grigsby, JAMA **288**, 4 (2002). doi:10.1001/jama.288.4.423

M. Leonardi, et al., in: *TRANSDUCERS*, 12th International Conference on Solid-State Sensors, Actuators and Microsystems, 2003, 2003

C.K. Lin, *The development of an implantable sensor network system for continuous measurement of obstructed renal pressures*, UCLA, 2007

C.K. Lin, et al., in *4th International Workshop on Wearable and Implantable Body Sensor Networks (BSN 2007)*, 2007

A. Meir et al., Proc. Inst. Mech. Eng. [H] **222**, H2 (2008)

N. Najafi, A. Ludomirsky, Biomed. Microdevices **6**, 1 (2004). doi:10.1023/B:BMMD.0000013367.30870.4e

Nusil, Med-4011 Product Profile (2008), http://www.nusil.com/library/products/MED-4011P.pdf. Accessed July 10 2008

J.A. Potkay, Biomed. Microdevices **10**, 3 (2008). doi:10.1007/s10544-007-9146-3

R. Schlierf et al., J. Micromech. Microeng. **17**, 7 (2007). doi:10.1088/0960-1317/17/7/S06

U. Schnakenberg et al., Sens. Actuators A Phys. **110**, 1–3 (2003)

E. Siwapornsathain, et al., in *2nd Annual International IEEE-EMBS Special Topic Conference on Microtechnologies in Medicine & Biology*, 2002

M.R. Tofighi et al., Electron. Lett. **42**, 3 (2006). doi:10.1049/el:20063658

P. Walter et al., Ophthalmic Res. **32**, 6 (2000). doi:10.1159/000055626

A.S. Walton, H. Krum, Heart, Lung & Circulation **14**, Suppl 2, (2005)

H.J. Yoon et al., Sens. Actuators A Phys. **110**, 1–3 (2004). doi:10.1016/j.sna.2003.10.047

B. Ziaie et al., Biomed. Microdevices **3**, 4 (2001). doi:10.1023/A:1012452613720