WIRELESS INTRA-OCULAR PRESSURE MONITORING SYSTEM INTEGRATED INTO AN ARTIFICIAL LENS

T. Eggers (1), J. Draeger (2), K. Hille (3), C. Marschner (4), P. Stegmaier (5), J. Binder, R. Laur (4)

(1) Campus Micro Technologies GmbH, Universitätsallee 29, D-28359 Bremen, Germany,
Tel.: +49 421 2020-783, Fax:+49 421 2020-700, E-Mail: torsten.eggers@campus-micro-technologies.de
(2) University Hospital Hamburg Eppendorf (Ophthalmology), Germany
(3) University Hospital Homburg, Saarland
(4) University of Bremen, FB1, Microsystem Center Bremen, Kufsteiner Str., 28359 Bremen, Germany
(5) ETH Zurich, Switzerland, Germany

Abstract **– This paper reports the concept and first results of a hybrid integrated telemetric pressure measuring system for continuous monitoring of the intra-ocular pressure. The system is designed for glaucoma differential diagnosis and follow up. The measuring system is highly miniaturized using advanced flip-chip mounting technology to fulfil the spatial requirements of integration into the fringe of an intra-ocular lens without the necessity of a monolithically integrated sensor. The surface micro-machined pressure sensor is used in an integrated hybrid circuit comprising the sensor itself and a dedicated read-out circuit in standard CMOS technology. First experimental results of the system will be presented. The concept of the telemetric data transmission, mounting and assembly, the coating and EMC problem will be discussed briefly**.

I. INTRODUCTION

The glaucoma disease is the main cause for blindness in the industrialized world. An indicator for a patient who is going to suffer from glaucoma disease is an increased intra-ocular pressure (IOP). The increased pressure damages the delicate neuronal structures due to reduced perfusion pressure and therefore reduced supply with cytoplasma. Back in 1966 Sampaolesi et al [1] showed that the intra-ocular pressure is not constant during the day. Especially at night and in the early morning hours steep pressure peaks up to 70 mmHg of relative pressure can occur. It is therefore essential to continuously monitor the IOP to provide reliable pressure data even during the patient's sleeping phase. With conventional tonometry ophthalmologists have only access to discrete data which have been gathered often scattered across a day. Despite of early work in that field [2] and great efforts in the past [3], [4] so far no continuous measuring system is available on the market, neither in clinical research nor in regular glaucoma prevention.

In view of a statistical 11% coincidence of cataract (germ. "Grauer Star") and glaucoma (germ. "Grüner Star") [5] it is advisable to integrate a telemetric measuring system into an intra-ocular lens (IOL) and apply it during cataract surgery where today the human lens is replaced by an artificial one. This will ensure continuous control and early detection of critical IOP and will ultimately lead to reduced rates of blindness in the glaucoma patients by supplementing the ophthalmologist in their ambulant control measurement of IOP.

II. SYSTEM DESIGN

The basic system design has been developed for a different medical application in the German joint research project "Implantable Telemetric Endosystem (ITES)"[6], [7].

The technical concept of ITES (Fig. 1) is based on the inductive telemetric transmission of energy to an implant and transmission of data through the skin to an external monitoring and data logging unit by a passive absorption modulation method.

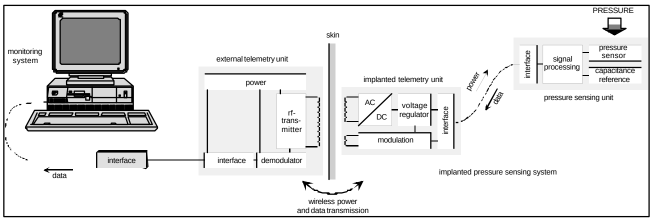

Fig. 1 ITES system concept

This eliminates the need for an active power source (e.g. battery) in the implant. The lifetime of the implant does no longer depend on the lifetime of a battery and the risk of pollution due to the battery is avoided. The disadvantage of this transmission method is the short operating distance of a few millimeters which is a direct result of the near-field effect of magnetic induction which decreases with distance r as r^3.

Because of the exclusion of a cable link no barometric pressure is available at the point of measurement. Therefore it is mandatory to measure the absolute pressure. In order to obtain the medically important relative pressure, the barometric pressure outside the body is measured separately and subtracted.

One of the main targets of the development was the minimization of power consumption in order to maximize the operating distance. Due to the nature of the application a strong demand is put on the maximum admissible size of all the components needed for the implant. These requirements could be met by the use of miniaturized capacitive surface micro-machined pressure sensors.

A. Capacitive Pressure Sensor

A capacitive absolute pressure sensor (Fig. 2) fabricated in an eight mask MOS-type process flow was developed. The total sensor capacitance $C_x = C_0 + \Delta C(p)$ comprises the pressure dependent contribution $\Delta C(p)$ and an offset capacitance C_0. An additional reference capacitance C_0, which is independent of pressure p, is integrated on the sensor chip. This capacitance is used for compensation of the offset capacitance and its technology induced variations by a subtraction scheme by the read-out circuitry.

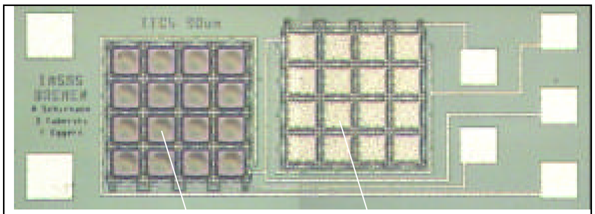

Fig. 2 MOS (Metal-Oxide-Semiconductor) process based surface micro-machined pressure sensor (0.8 mm x 2 mm)

In telemetric operation no barometric pressure is available at the point of measurement. Therefore the sensor is designed for measuring the absolute pressure. Technologically, this is achieved by sealing the micro-cavity below the pressure sensitive membrane under low pressure conditions: a reference pressure inside the micro-cavity of well below 100 Pa is easily accomplished by LPCVD (low pressure chemical vapor deposition) sealing with LTO (low temperature oxide).

As a side effect, this process step ensures a low temperature dependency of < 200 ppm/°C because the small amount of trapped gas does not cause a variation of the reference pressure due to temperature induced expansion. An additional temperature dependency is introduced by the minor difference of the mechanical construction of sensor and reference element, but this effect can be neglected. Therefore no additional temperature measurement for compensation is needed for the small medical temperature range of approx. 35°C – 40°C.

B. Read-out circuitry

The read-out circuitry (Fig. 3) features a micro-power differential SC-relaxation-oscillator based on [8]. The current consumption is less than 85 µA at a supply voltage of 3.5 V. The simple read-out structure has a 10 bit resolution in a $\Delta C \approx 500$ fF measurement range. The converter produces a quasi-digital PWM output dT

$$dT(C_X) = \frac{\Delta T}{T} = \frac{T_1 - T_2}{T_1 + T_2} = \frac{C_X - C_0}{C_r} = \frac{\Delta C}{C_r} \qquad (1)$$

with T_1 = low time ("0") and T_2 = high time ("1") of the PWM output signal.

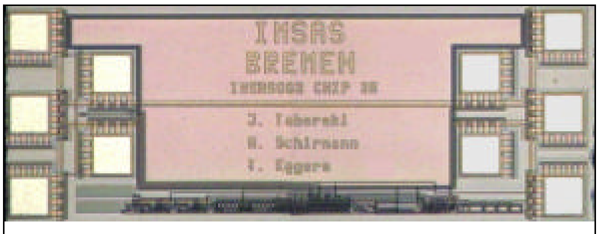

Fig. 3 0.7 µm CMOS signal pre-processing SC relaxation oscillator (ΔC to PWM converter) ASIC (0.8 mm x 2 mm).

The sampling rate is approximately 100 samples per second. A reference capacitance C_r = 600 fF defining the maximum measurement range ΔC of the sensor capacitance and the SC-integrator feedback capacitance $C_F \geq 2^b \times C_r$ (b = required resolution in bit) are integrated on the signal preprocessing ASIC. The serial PWM signal is transmitted to a telemetry ASIC [8].

C. Telemetry chip

The telemetry chip (Fig. 4) provides a data reduction scheme for the sensor PWM output signal by means of two 12-bit counters, data encoding by Manchester-coding, laser burned identification code, generation of the 128-bit ISO protocol and the passive data modulation functionality. It is based on the telemetry device [9] developed in the framework of the ITES project.

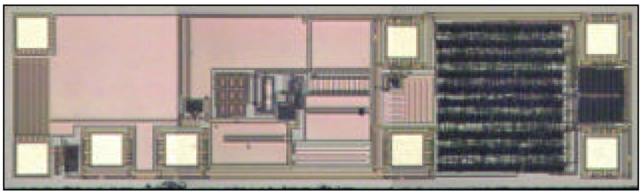

Fig. 4 0.7 µm CMOS telemetry ASIC (0.9 mm x 2.9 mm) following 128-bit ISO RF-ID standard with 125 kHz transmission frequency

It provides a rectified and stabilized 3.5 V voltage for power supply and 125 kHz clocking for the switched capacitor (SC) read-out circuit extracted from the carrier frequency of the external transmitter. At this stage of development, the telemetry ASIC is connected to a single discrete coil with several hundred windings made of 31 µm thin wire.

The whole system is powered by the 125 kHz transcutanous telemetry link. The data are transmitted by passive absorption modulation recently suggested by other researchers [10],[11] and frequently used in radio frequency identification (RF-ID) applications, e.g. in smart-cards.

The flat air coil inductance L is approx. L = 850 µH. A capacitance C of

$$C = \frac{1}{L(2p \cdot f_r)^2} = \frac{1}{850mH(2p \cdot 125kHz)^2} \approx 1.9nF \qquad (2)$$

is therefore needed to obtain a resonance frequency f_r of 125 kHz. This capacitance is too large being reasonably integrated on-chip and is therefore realized as an external multi-layer ceramic SMD component in the smallest available package (0.5 mm x 1.0 mm).

D. Mounting & assembly, coating

At the moment all components are mounted on a 100 µm thin standard FR4 substrate using flip-chip technology with single chip bumping and mounting. The substrate is going to by replaced by a 50 µm flexible polyimide carrier.

The multi-chip-module (MCM) fits into the fringe of a modified standard IOL made from poly-methyl-meta-acrylate (PMMA). The complete measurement module can be coated with a bi-layer stack: a first thin layer acting as a protection against moisture and a second flexible bio-compatible layer. The coating does not significantly affect the mechanical sensitivity of the sensor membrane and ensures the longevity of the implant. After the coating the MCM is mounted into the modified PMMA IOL (Fig. 5).

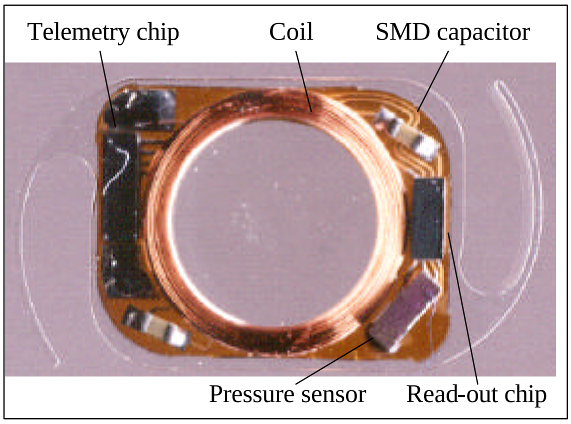

Fig. 5 Top view of flip-chip mounted MCM measurement module (6.5 mm x 9 mm) integrated into an IOL (optical part in the middle)

E. Complete measuring system

The electrical power for the implant is provided by an external coil integrated into the frame of eyeglasses or into an eye patch at night. The data are recorded by an external transceiver device, which also identifies the implant and performs calibration functions for the offset.

The calibration data might be integrated into the implant itself at the next stage. The transceiver unit can either be used in stand-alone mode or optionally connected to standard communication equipment for relaying the data to clinical support centers.

F. Electromagnetic field compatibility

The system operates at a frequency of only 125 kHz. Therefore the absorption of the RF-field due to the electrically conductive liquid inside the eye can be neglected compared to higher frequency telemetry systems operating at 13.56 MHz, 27.12 MHz or even 433 MHz, because the wavelength is large compared to the distance to the receiver coil inside the implant.

According to [12], no known health hazards are associated with exposure to RF sources emitting fields too low to cause a significant temperature rise in tissue. Although some biological effects from low-level RF exposure were identified in that study, this item needs further studies.

III. MEASUREMENT RESULTS

The 10 bit resolved pressure values are externally filtered to reduce the phase noise of the used read-out oscillator structure (Fig. 6).

Offset variations of the individual measuring system (Fig. 7) due to remaining mismatch of the offset of pressure dependent capacitance and the offset compensation capacitance are calibrated externally prior to implantation to reach an accuracy of approx. ± 2 mmHg needed for exact IOP measurement and glaucoma detection.

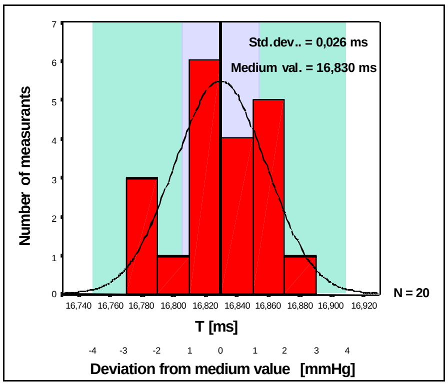

Fig. 6 Noise measurement of read-out circuitry output PWM period time $T = T_1 + T_2$ at static absolute pressure p = 850 mmHg

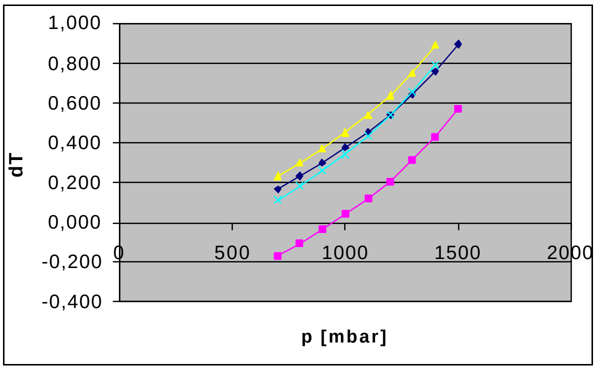

Fig. 7 Offset variation of four different digital pressure sensor pulse width modulated output signals $dT = (T_1 - T_2)/(T_1+T_2) = (C_X - C_0)/C_r$

The effective sample rate of the system is 30 samples per second due to the 128-bit frame ISO transmission protocol which uses 32 clock cycles for the transmission of each individual data bit. The noise level is reduced by external filtering (e.g. moving average over 10 samples). Despite of this filtering need the measurement system in its current state is able to resolve the IOP dynamically.

IV. CONCLUSIONS

The approach of a highly miniaturized hybrid system for measuring the IOP has shown a potential for successful commercialization. The resolution and accuracy requirements of the medical application could be met. On-chip storage of calibration data via the telemetry link following the packaging step and a higher degree of integration will be addressed in the coming product development cycle.

The system described in this paper is going to be subject to intensive clinical tests in the near future. The system is designed to be put in place during cataract surgery, in which the natural lens is replaced by an artificial one. Preferably this would be done in cases where a coincidence with glaucoma is already evident. This system provides the means for continuous control and early detection of critical IOP peaks. This will ultimately lead to reduced rates of blindness in the glaucoma patients by supplementing the ophthalmologist in their ambulant control measurements of IOP.

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