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REVIEW ARTICLE

# Medical implants based on microsystems

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**Abstract**
The fast development of CMOS technologies to smaller dimensions led to very high integration densities with complex circuitry on very small chip areas. In 2006 Intel fabricated the first products in a 65 nm technology. The cointegration of microsensors or actuators together with the very low power consumption of the CMOS circuitry is very well suited for use in implanted systems. Applications like intracranial or intraocular pressure measurements have become possible. This review presents an overview over actual applications and developments of sensor/actuator-based microsystems for medical implants. It concentrates on the technical part of these investigations. It will mainly review work on systems measuring pressure in blood vessels and on systems for ophthalmic applications.

**Keywords:** microelectronic implants, ophthalmic implants, intravascular pressure monitoring, retina implant, retinitis pigmentosa, transponder

(Some figures in this article are in colour only in the electronic version)

## 1. Introduction

Nowadays, a lot of microelectronic systems are used in implantable devices. The most frequently used device is the cardiac pacemaker that is implanted nearly 600 000 times worldwide, followed by defibrillators [1]. Beside these well-known devices, a lot of new ones have been developed and established over the last few decades.

Since about 1980 cochlear implants have been used to partially restore hearing of deaf people. Herein an external signal processor translates the incoming sound into coded electrical information. These 'codes' are transmitted through the skin via magnetic coupling to a surgically implanted device directly under the skin. According to the information in the 'codes' implanted electrodes in the cochlea stimulate the auditory nerve fibres to send information to the brain where it is interpreted as meaningful sound. According to the Food and Drug Administration 2002 data, approximately 59 000 people worldwide have received cochlear implants. In the United States, about 13 000 adults and nearly 10 000 children have already received these devices [2].

In 1997 a deep brain stimulator (DBS) for suppressing the tremor of Parkinson patients was approved by the FDA for use in the United States using sophisticated technology (e.g. magnetic resonance imaging) to locate the exact area in the brain causing tremors. A tip of a very thin wire can be inserted exactly into this area. The wire then runs up through a small hole in the skull and under the scalp down to a device implanted under the collarbone. The device, called a deep brain stimulator, sends electrical pulses to stimulate this special brain area in such a way that the tremor gets suppressed. The patient has full control of the device so that he can turn the DBS on when needed and turn it off, e.g. during sleep cycles [3]. Over 2000 people with Parkinson's disease in the United States have already got such brain stimulator systems implanted.

More recently, sensor functions have been added to implantable systems. For example, due to the small dimension of new sensor devices, it got possible to integrate a CMOS camera chip into a system wirelessly monitoring the small intestine [4]. This system can be used to partly replace standard colonoscopy.

Beside this there are a lot of activities in the field of implantable devices and sensors world wide. Demonstrators have been presented for intelligent orthopaedic implants [5–7],

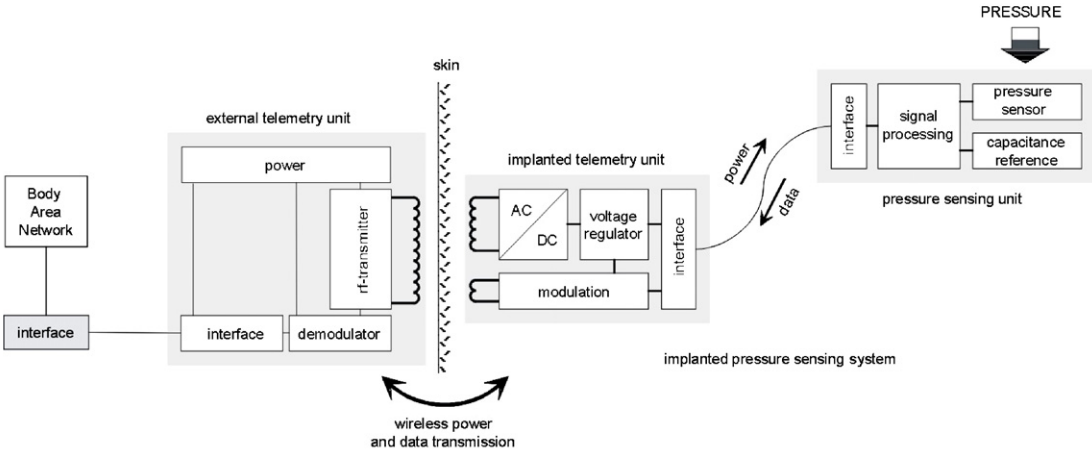



**Figure 1.** The ITES concept (by courtesy of T Eggers, Campus Microtechnology GmbH, Bremen, Germany, 2005).

for measuring bladder pressure [8] or cranial pressure [9–12]. It is not possible to give an overview of all the work done in this field up to now. Therefore, this review will concentrate on systems for measuring pressure in blood vessels and systems for ophthalmic applications.

## 2. Invasive measurement of blood pressure

Body temperature and pressure are the most frequently used parameters in medical diagnoses and therapy. The technical concept of measuring pressure by implants is often based on inductive energy and data transmission through the skin to an external monitoring and data logging unit. The required energy can be extracted from the magnetic field, and the data transmission is performed by a load modulation method. By this there is no need for an active power source in the implant. This means an increased lifetime of the implant and a reduction of size. The disadvantage of this transmission method is the short operating distance of a few millimetres to several centimetres due to the power consumption of the implant, the transmission frequency and the absorption in the tissue and organs.

The first implants based on this concept were presented for measuring intraocular pressure [13]. An implantable low power integrated pressure sensor system for minimal invasive telemetric patient monitoring was developed in the German project ‘Implantable Telemetric Endosystem’ (ITES) [14, 15]. Figure 1 shows the system concept.

The system consists of an external telemetry unit and an implantable pressure sensing system. The implantable part is divided into a telemetry unit for receiving energy and transferring the pressure data via a load modulation and a pressure sensing unit.

### *2.1. Intravascular pressure measurement*

The knowledge of permanent measured intravascular signals opens new diagnostical and therapeutical possibilities in monitoring, e.g. the blood pressure, temperature in hypertension disease or the pulse rate for detection of arrhythmia. In order to measure the pressure in blood vessels, two different approaches have been developed.

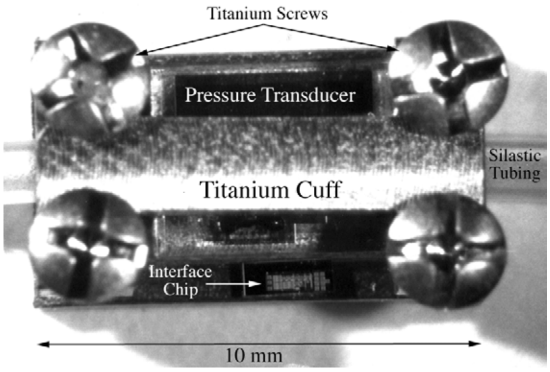



**Figure 2.** Photo of a blood vessel pressure measurement by means of a titanium cuff [17] (by courtesy of Professor Babak Ziaie, School of Electrical and Computer Engineering, Purdue University, USA).

One approach is based on an integrated pressure sensor system that forms a cuff wound around the blood vessel. Pressure changes are measured by micromachined pressure sensors [16–18]. This can be seen in figure 2 [17]. Zacheja *et al* used acceleration sensors integrated into a cuff to measure the intravascular flow [19].

The second approach is based on the ITES concept. Here, the implantable system measures directly in the vessel. Clasbrummel *et al* used an implantable system consisting of two parts. The first part is a small pressure sensor with read-out electronics that is placed directly into the vessel. The second part contains the electronics, which is placed directly under the skin, capable of receiving telemetrically the needed energy and transferring data. A microcable connects the sensor and transponder part [15, 20]. In another approach, the complete system is placed into the vessel [21, 22]. Figure 3 shows a silicone capsule which can be placed via a catheter into a branching of a blood vessel of the lower part of the artery system, where it is of no danger to the patients [22].

To ensure that the capsule stays in position within the branching of the vessel, three self-expanding levers serve as a locking mechanism. The capsule dimension without the three levers is 2 mm in diameter and 30 mm in length.

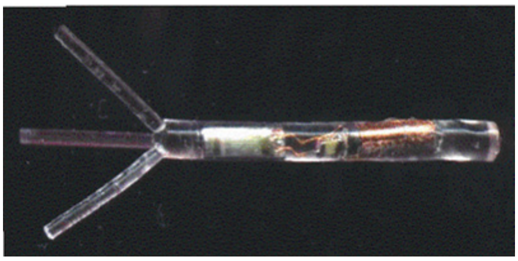


**Figure 3.** Silicone capsule with an integrated pressure sensor transponder.

A telemetric sensor chip (figure 4(*b*)) and a ferrite coil (figure 4(*a*)) are integrated in the capsule. The sensor chip uses a surface micromachined capacitive pressure sensor [23, 24] that consists of an array of single circular pressure sensitive elements and of reference elements switched in parallel. Such elements consist of vertical capacitors which are formed by a fixed electrode in the substrate and a movable membrane made of polycrystalline silicon above, as shown in figure 5. The height of the cavity beneath the membrane is less than 1 $\mu$m.

The implemented reference elements are identical to the pressure sensitive elements except for an additional oxide layer on top [25]. By variation of the membrane diameter, nearly any desired pressure range can be realized.

Surface micromachining techniques can be implemented in a standard CMOS process which enables the integration of a sensor with the read-out electronics on the same chip. The realized chip, which is shown in figure 4(*b*), was designed for measuring in the pressure range of 0.5 bar to 1.5 bar. Beside the described pressure sensor and an additional temperature sensor, the chip contains read-out and calibration electronics, a microcontroller based digital unit and an RF-transponder front end [21]. The chip covers an area of $1.5 \times 5.4$ mm$^2$ and is fabricated in a 1.2 $\mu$m *n*-well CMOS technology. Temperature and pressure values measured inside the capsule will be transferred wirelessly to an external hand-held unit using 13.56 MHz transponder technology. Preliminary measurements were carried out in a silicone model of a human vessel system. Figure 6 shows the output signal of the pressure measured in the vessel system with respect to time. Due to the frequency of 13.56 MHz, the vessel has to be very close to the reading coil ($\leqslant$3 cm). Using 133 kHz distances up to 12 cm can be reached with a reduced data rate.

Medical studies have shown that continuous monitoring of haemodynamic parameters in the right ventricle provides

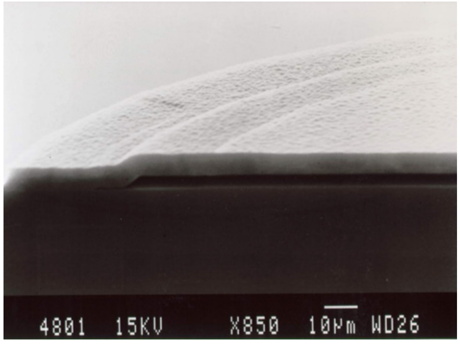



**Figure 5.** Electron micrograph of the surface micromachined capacitive pressure sensor (by courtesy of FhG IMS, Duisburg, Germany, 2006).

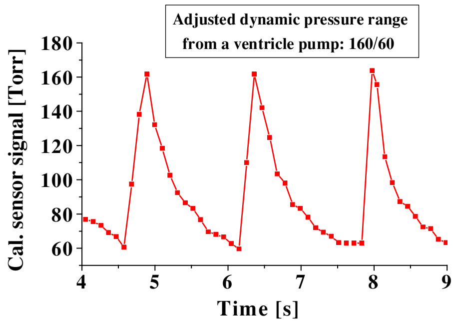
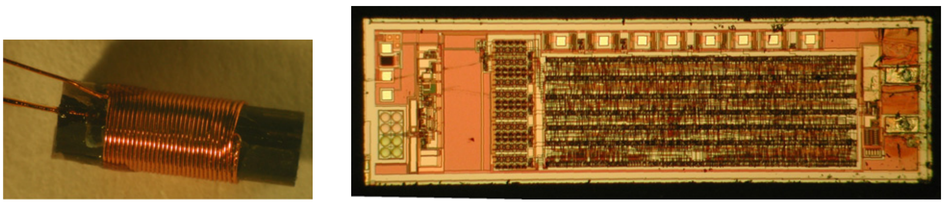



**Figure 6.** Wirelessly transmitted sensor output signals from the transponder capsule placed inside a silicone circulatory model. A dynamic pressure range of 160 Torr/60 Torr was delivered from a ventricle pump.

important information for optimization of pacemaker algorithms [28]. Medtronic introduced a system for measuring pressure in the right ventricle [26]. The implantable haemodynamic monitor (Chronicle, Medtronic Inc., Minneapolis, USA) consists of an electronic memory device and a transvenous lead carrying the pressure sensor [28]. The device is implanted similar to a pacemaker system with the memory device positioned subcutaneously beneath the left clavicle. The lead is inserted via the left subclavian vein into the right ventricular outflow tract. Information regarding the heart rate and multiple pressure-related haemodynamic parameters, including right ventricular systolic and diastolic pressure, the maximum positive rate of right ventricular pressure development (d$P$/d$t$) [27] and an estimation of the pulmonary artery diastolic pressure, is collected from the



(*a*) (*b*)

**Figure 4.** (*a*) Photo of the coil. (*b*) Photo of the integrated pressure sensor chip (by courtesy of FhG IMS, Duisburg, Germany, 2006).

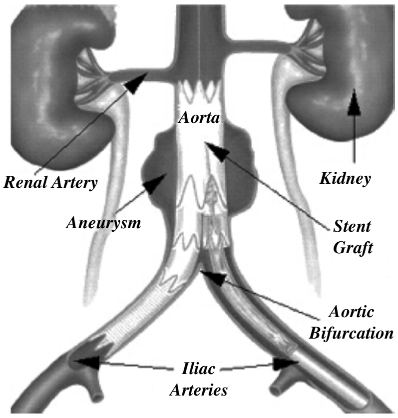



**Figure 7.** Schematic view of an aortic aneurysm with stent.

device. As the pressure sensor measures absolute pressure, all haemodynamic data need to be corrected for barometric pressure. Each patient carries an external pressure reference (Model 2805, Medtronic Inc.) which measures and stores the barometric pressure once every minute.

### *2.2. Wireless pressure sensing of abdominal aortic aneurysms*

The increasing incidence of cardiovascular diseases including aneurysms makes the treatment of abdominal aortic aneurysms (AAA) important. To treat AAA, endovascular, keyhole surgery has been established over the last few years. Herein, a foldable prosthesis (stent) is inserted through an inguinal incision in order to eliminate the aneurism (compare figure 7). A recent FDA analysis estimated that the aneurysm-related death rate after repair is 0.4% per year. Incomplete exclusion of the aneurysm sac or endoleak is among the most common complications and results in ongoing perfusion and pressurization of the sac [30]. Such leakages can be detected using different approaches. CardioMEMS (Atlanta/USA) [31, 32] uses a telemetric pressure sensor developed by the group of Mark Allen (Georgia Institute of Technology). This system is based on a micromechanical pressure sensor. The

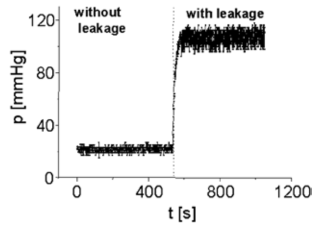
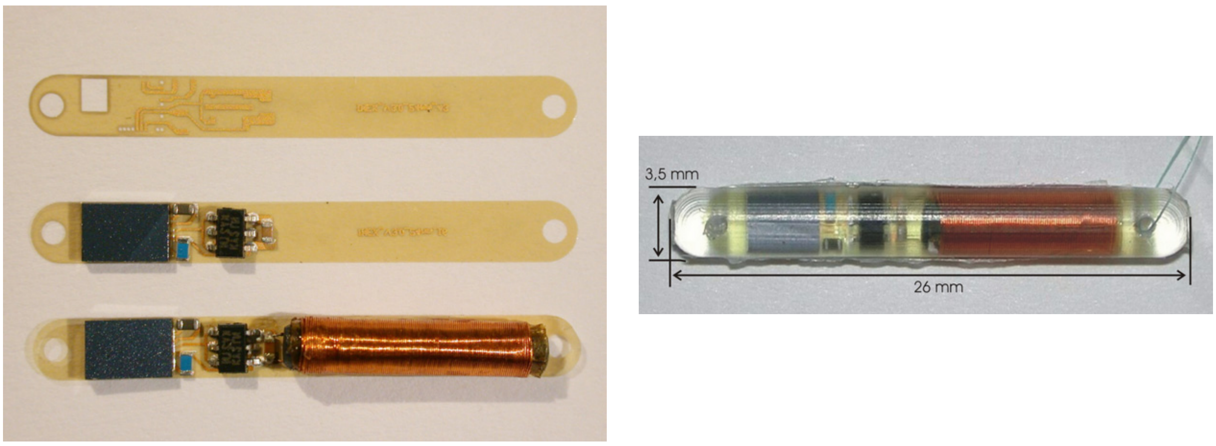



**Figure 9.** Measuring curve from the AAA model.

pressure is measured by capacitance variations which lead to changes of the resonant frequency of a *LC*-resonant circuit that can be detected. A second approach, followed by Remon Medical Technologies (Caesaria Industrial Park/Israel) [33], is based on surface acoustic waves (SAW) to transmit pressure signals out of the human body. Both methods have in common that they use analogue signal transmissions.

Schlierf *et al* recently presented a pressure monitoring system integrated in a small capsule that can be implanted in the human body [34]. The new monitoring system can be used to measure the pressure in abdominal aorta aneurisms and to digitally transmit the data out of the human body. The system achieves the needed transmission range of at least 8–10 cm and can be used with standard catheters of an inner diameter of 4 mm (12 French). The pressure monitoring system consists of a reader station with a PC-controlled plotting unit and an implantable capsule. This capsule comprises a sensor-ASIC, which includes a capacitive absolute pressure sensor with an inductive telemetry unit as well as necessary passive components. The required energy is transmitted by an inductive link from an outer reader station at a frequency of 133 kHz. The complete capsule consists of a micro flex-tape with a hybrid-integrated capacitive pressure sensor ASIC, two protecting Zener diodes and a resonant circuit with a tunable ferrite coil. The assembly steps of the flex-tape and all other parts are illustrated in figure 8(*a*). In a first step the implant is moulded in biocompatible silicone, forming the shape of the capsule in the process. Second, a Parylene-C layer approximately 5 $\mu$m thick is deposited. This second




(*a*) (*b*)

**Figure 8.** (*a*) Assembly steps of the AAA leakage control system. (*b*) Encapsulated system.

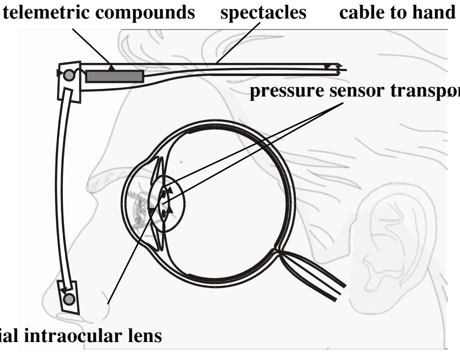



**Figure 10.** Schematic presentation of a system for measuring the intraocular pressure continuously.

**Figure 12.** Soft artificial lens with a micro coil and transponder chip.

**Table 1.** Technical data of the integrated sensor chip.

| | |
|---|---|
| Supply voltage | 3 V |
| Current consumption | <70 $\mu$A |
| RF carrier | 13.56 MHz |
| Operating pressure | 0.5–1.5 bar |
| Die area | 6.75 $mm^2$ |

layer produces the needed stiffness, so that the capsule can be pushed through a catheter. Figure 8(*b*) shows the implantable capsule. The system was tested in an artificial model of an AAA model. Figure 9 shows that this system is very well suited to detect leaks.

## 3. Ophthalmic implants

### *3.1. Microsystem for measuring intraocular pressure*

The disease glaucoma is the main cause of blindness in the industrialized world. Glaucoma patients suffer from increased intraocular pressure. The increased pressure damages the delicate neuronal structures due to reduced perfusion pressure and therefore reduced nutrient supply. Measurements of the intraocular pressure are usually performed as single measurements at only one certain time of the day. Rarely glaucoma patients are hospitalized to measure intraocular pressure more often. However, the resulting intraocular pressure 'profile' consists of a maximum of 5–10 data points a day and is obtained under the artificial conditions of hospitalization. Already in 1968, Sampaolesi *et al* [36] showed that the intraocular pressure is not constant during the day. Especially at night and in the early morning hours, steep pressure peaks up to 70 mm Hg of relative pressure can occur while the normal intraocular pressure is below 22 mm Hg. For more frequent intraocular pressure measurements, an intraocular implant for continuous measurements of intraocular pressure has many advantages and implies new perspectives in the therapy of glaucoma. Collins [37] suggested an implantable intraocular pressure sensor. Bäcklund and coworkers [38] also suggested a system which could be integrated into an artificial intraocular lens. Puers *et al* developed electrodeposited copper inductors for intraocular pressure telemetry [45]. The pressure is measured by changes of the resonant frequency of a *LC*-resonant circuit that can be detected. A fully integrated concept [35, 39, 40] is shown in figure 10.

The system is based on an artificial intraocular lens containing a microsystem for measuring the intraocular

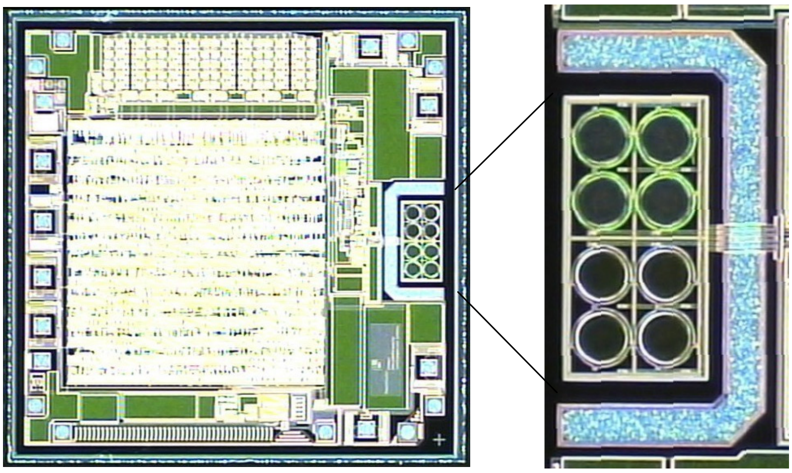


**Figure 11.** Photograph of the integrated pressure transponder chip.

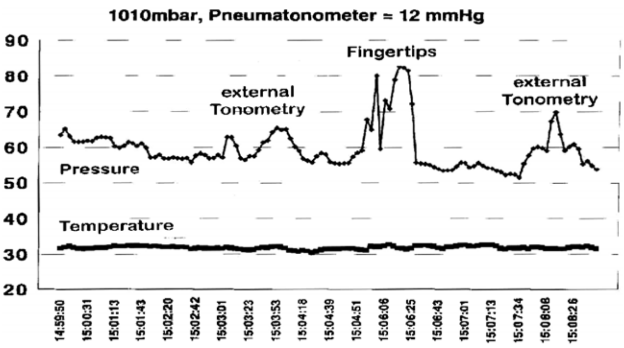



**Figure 13.** Measurement curve from a system implanted into a rabbit eye.

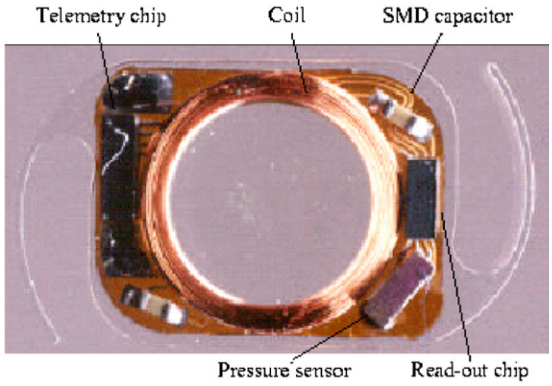



**Figure 14.** Intraocular lens with hybrid components [35] (by courtesy of T Eggers, Campus Microtechnology GmbH, Bremen, Germany, 2005).

pressure. The implant consists of only two parts, a micro coil and an integrated pressure sensor chip (figure 11) [41, 44]. Besides analogue circuits for the sensor read-out, there are circuits for A/D conversion and digital circuitry for a telemetric data transfer plus an EEPROM for storing sensor and device specific data, integrated in the chip. Technical data of the pressure sensor chip can be derived from table 1.

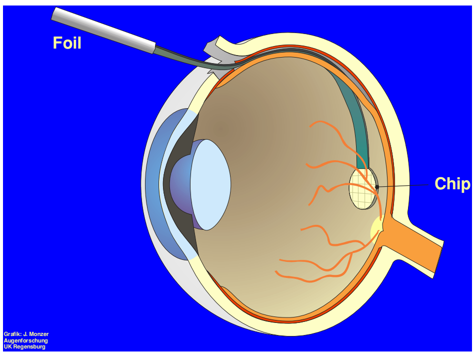
The used micro coil is fabricated by microelectroplating gold onto a flexible polyimide foil [42]. The sensor chip and the micro coil are assembled into an artificial soft lens made from silicone (figure 12) and cover the haptic area of the lens. Together with this soft material, the implant is foldable so that the already established standard surgery techniques can be carried out. At the moment, the outer diameter of the lens is about 10 mm. The pressure is transferred to the sensitive membranes directly by the silicone.

The integrated system has no battery, but it is powered by an external high frequency field. Energy and data transmission are carried out using the active inductively coupled communication method. Pressure data are transferred to the outer system digitally by switching an additional load to the system. The load can be sensed by the outer system. The external RF transmission components will be integrated into spectacles. Transmission matching and data storage are arranged in a hand-held unit which can be connected to a PC. In this configuration, it is possible to measure the intraocular pressure continuously over a long period of time (figure 13) [43].

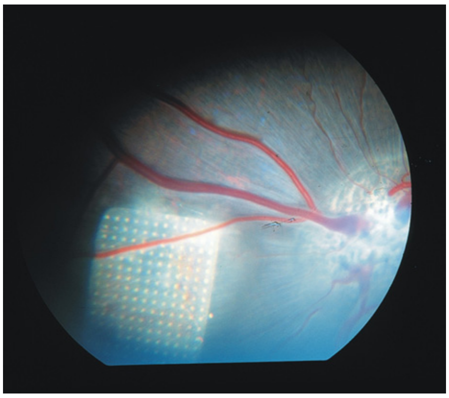
A similar system was introduced by Eggers *et al* [46]. The system is based on a pressure sensor chip, a sensor-readout chip, a telemetry chip, discrete coil and additional smd parts. The capacitive absolute pressure sensor is fabricated in surface micromachining, similar to the one described in [25]. The read-out circuitry has a current consumption of less than 85 $\mu$A at a supply voltage of 3.5 V. The telemetry chip has implemented the 128 bit ISO RF-ID standard with a 125 kHz transmission frequency. Figure 14 shows the assembled system.

### 3.2. Retinal implants

According to the World Health Organization in 1997 [47] more than 8 million people were legally blind from retinal degeneration, mostly caused by macular degeneration and retinitis pigmentosa. In patients suffering from retinitis pigmentosa the photo receptors, the rods and cones of the retina, degenerate within several years starting from the outer region of the retina. In this way, the field of sight becomes smaller and smaller resulting in total blindness. As with cochlea implants, the idea is to restore loss of body functions




(*a*)



(*b*)

**Figure 15.** (*a*) Schematic view of the subretinal approach. (*b*) View through the ganglion cell layer on to a subretinal implant (by courtesy of the Retinal Implant AG, Reutlingen, Germany, 2006).

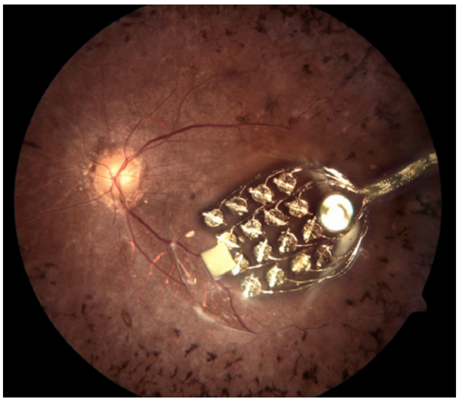


**Figure 16.** Photo of an epiretinal stimulation array placed onto the retina [74]. Photograph by Jessica Dougall, Copyright 2005, Doheny Eye Institute and Second Sight Medial Prodcuts, Inc. All rights reserved.

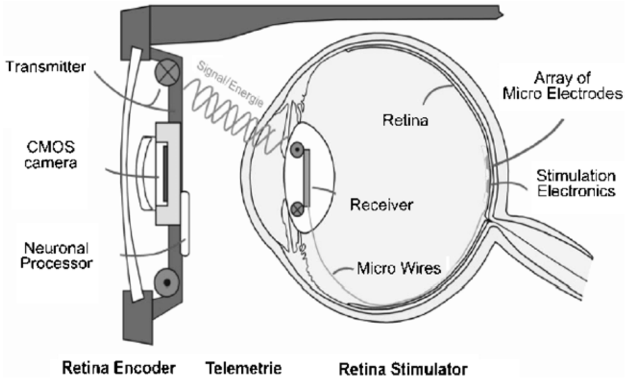


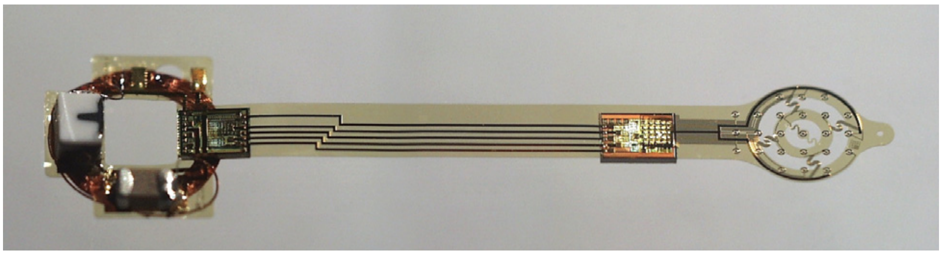

**Figure 17.** System concept of a visual prosthesis for epiretinal stimulation.

with the help of an electrical device. There have been several attempts to restore vision by coupling electrodes directly to the visual cortex of blind people [48–51]. A Belgian group is working on the stimulation of the optical nerve by means of a cuff electrode surrounding it [52–55].

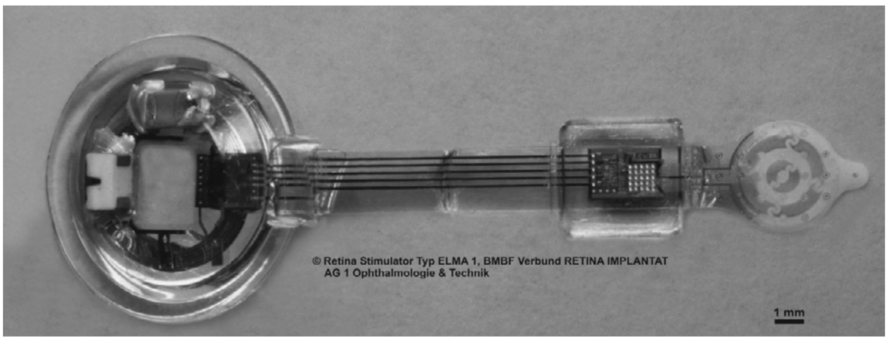
Another approach is to electrically stimulate the retinal neurons. This approach seems to be more favourable [60, 61, 63]. Studies have found that about 30% of retinal ganglion cells of retinitis pigmentosa patients are still working even after several years of blindness. It has been shown that electrical stimulation of ganglion cells inside the eye at the inner surface of the retina yields visual sensations [55, 66, 68, 69]. Therefore, bypassing the degenerated photoreceptors by electrical stimulation of retinal ganglion cells seems to be possible. A system comparable to a cochlea implant based on this concept seems to be feasible [76].

There are two different concepts for the stimulation of retinal nerve cells that are studied by several groups in different countries. In the subretinal approach, an implant with stimulation electrodes is placed behind the retinal nerve cells at the place where the cones and rods are located. In the epiretinal approach, an array of stimulation electrodes is brought inside the eye in contact with the ganglion cell layer. In this review, we want to concentrate on these two concepts.

*3.2.1. Subretinal approach.* Chow and colleagues [57–62] in Chicago and the Zrenner group [63–66] in Tübingen, Germany are developing subretinal implants. There are also groups in Japan, Australia and Korea working on that subject. Recently, the MIT group around Wyatt and Rizzo changed from the epiretinal approach to the subretinal approach [84]. The first approach for a subretinal device was proposed by Chow [59]. This implant is based on a microelectrode array powered by



(*a*)




(*b*)

**Figure 18.** Photograph of a retina implant system of the first generation: (*a*) not encapsulated, (*b*) encapsulated.

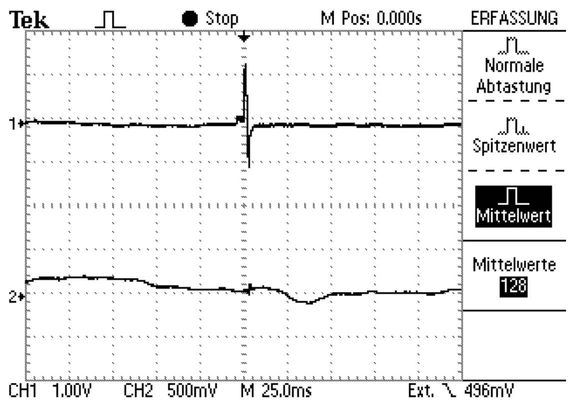



**Figure 19.** Cortical recording after electrical stimulation of retinal ganglion cells by a telemetric system [80] (by courtesy of Dr Laube, Eye Clinic University Essen, Germany (2005)).

about 3500 microscopic solar cells. The idea of this approach is to generate photo currents by light stimulation which are capable of altering the membrane potential of overlying neurons and thereby activate the visual system. Because of the small area, the current generated is too small to evoke nerve potentials. Therefore, this system has to be supported by additional circuitry and external powering. In the subretinal approach of Zrenner, a thin plate carrying several hundreds of photodiodes together with stimulation electrodes arranged in arrays is placed subretinally (compare figures 15(*a*) and (*b*)). The electrodes are made from gold or titanium nitride. The photodiodes directly replace the damaged photo receptors. The picture of a visible object on the retina is converted to stimulation pulses to the neurons of the retina and by this using the neural network of the retina.

*3.2.2. Epiretinal approach.* Epiretinal implants are investigated by a German EPIRET consortium [66–68, 76, 78–82], the German company Intelligent Implant Technologies Ltd[1], Second Sight[2], Humayun [71–73] and Rizzo [70, 74, 75].

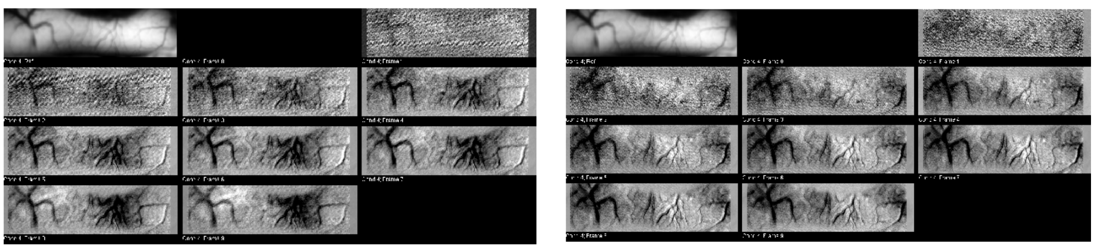
In the epiretinal approaches, the visual information is recorded by a camera. From this data stimulation patterns are calculated for the stimulation of retinal ganglion cells via electrodes of an implant. Energy and information are transferred via transponder techniques to an implant. Second Sight and partners introduced a system based on a cochlea implant [74, 85]. The implanted electronics is mounted to the outer side of the sclera. From there a cable is brought through the sclera into the eye. The cable connects a four-by-four stimulation electrode array that is put onto the retina (figure 16).

The systems developed by the EPIRET team consist of an extraocular and an intraocular part (figure 17). The components of the extraocular part are a CMOS image sensor for acquisition of visual images, an artificial neural net that imitates the functions of different ganglion layers of the retina (retina encoder) and a transmitter. The visual images are transformed by the neural net into control signals for the stimulation electrodes [82]. These signals are finally transmitted into the interior of the eye together with the energy needed to supply the intraocular part. The EPIRET team uses only RF links while IIP uses RF for energy transfer and an optical link for data transfer. The intraocular part of the system consists of receiver circuitry where energy and data signals are separated, the clock signal is extracted and the data signals are decoded. These data are transferred via a micro cable to the stimulation unit. Integrated circuitry decodes the information from the serial data stream. From this information, the chosen electrode is selected and a stimulation current with a programmed pulse width and height is applied to the electrode. By this action potentials in the upper ganglion cell layer of the retina are evoked, causing a visual sensation.

Complete systems (see figure 18) were implanted into mini pigs and cats. Full telemetric functioning could be shown with several systems. Figure 19 shows cortical recording from a mini pig after telemetric stimulation of retinal ganglion cells. As expected, the response can be seen about 25 ms after stimulation. In figure 20, measurements of cortical activity of a cat during stimulation are given.

For this experiment the visual cortex was exposed. A red sensitive camera looks to the area of the visual cortex that corresponds to the area of the retina that is electrically stimulated. If the area of the visual cortex is active due to the stimulation of the retina, more oxygen is consumed. This results in a change in the red colour of the blood [79, 81, 83]. The next generation of implants has an integrated planar

[1] www.iip-tec.com.
[2] www.2-sight.com.



(*a*) (*b*)

**Figure 20.** (*a*) Optical imaging from the visual cortex of a cat during electrical stimulation of the corresponding regions on the retina. The black regions in the right part of the pictures show increased oxygen consumption in areas of the visual cortex that correspond to the stimulated areas of the retina [81]. (*b*) Control experiment without stimulation pulses [81].

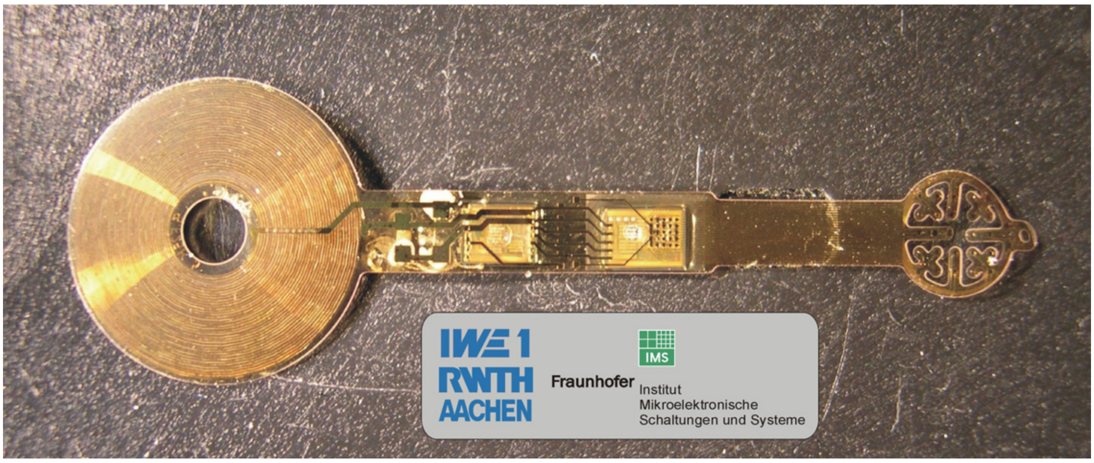



**Figure 21.** Second generation of the retina implant (uncapsulated).

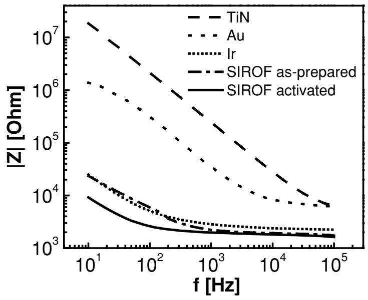



**Figure 22.** Impedance spectra of different electrode materials measured in Ringer solution.

micro coil which makes the system more compact (figure 21). In addition, three-dimensional electrodes were integrated to increase the coupling to the ganglion cells. These electrodes should have a high charge delivery capacity in order to achieve the best stimulation effect from the inserted energy. The electrodes were fabricated using microelectroplating of gold. The gold surfaces were then covered with noble metals like platinum or iridium. Experiments have shown that sputtering of iridium in an argon/oxygen plasma is a reliable method for production of iridium oxide films (SIROFs) [78]. It can yield reproducible thin iridium oxide layers, which are very stable but very sensitive to process parameters such as inert and reactive gas flow rates while sputtering. The SIROFs obtained possess a maximal charge delivery capacity of 98 mC $cm^{-2}$, which is higher than the values reported in the literature for other biocompatible materials such as Pt and TiN. In addition, these electrodes show the lowest impedance values (figure 22).

## 4. Conclusion and outlook

The presented examples show that MEMS technology is a powerful tool for realizing small and complex electronic implants. This technology will help to increase the functionality of existing systems significantly. New applications will be possible that nobody thought possible some years ago. These intelligent implants and prostheses will support the field of home care to a great part. In addition, wire-based or implantable microsystems with sensing and actuating functions will have a strong impact on clinical research.

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