First Steps toward Noninvasive Intraocular Pressure Monitoring with a Sensing Contact Lens

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Purpose. To present a novel and minimally invasive approach to intraocular pressure (IOP) monitoring based on a sensing contact lens.

Methods. The key element of this measurement method is a soft contact lens with an embedded microfabricated strain gauge allowing the measurement of changes in corneal curvature correlated to variations in IOP. A prototype of this sensing contact lens was adapted and tested on enucleated porcine eyes. To verify the measurement principle of the device, the posterior chamber of the pig eyes was cannulated and connected to a syringe pump and a pressure sensor for precise control of IOP. The measurements of the contact lens were then compared to the ones from the pressure sensor, while pressure variations were induced through the cannula.

Results. Enucleated porcine eyes were stimulated with increasing and decreasing ramps of IOP. Measurements from the sensing contact lens and from the pressure sensor showed very good correlation, proving the high potential of this new measurement principle. In this study, a typical signal from the sensing contact lens obtained during the experiments is presented and discussed.

Conclusions. The sensing contact lens shows the potential for continuously monitoring IOP in enucleated porcine eyes. The ultimate step will be the validation of the system and the reproducibility of results in humans. The device is placed in the same way as a corrective contact lens, no anesthesia is required, and vision remains almost unimpaired. This device would allow minimally invasive IOP monitoring over prolonged periods, regardless of the patient's position and activity, thus opening up new diagnostic and therapeutic methods for the management of glaucoma. (*Invest Ophthalmol Vis Sci.* 2004;45:3113–3117) DOI:10.1167/iovs.04-0015

Although researchers and clinicians in the field recognize the need for continuous monitoring of patients with glaucoma, no method is yet available. This has been highlighted by a survey sent in July 2002 to 207 Swiss ophthalmologists (one third of all Swiss ophthalmologists, with an answering rate of 43%), which has shown that the need for an improved diagnostic tool capable of continuously monitoring IOP is considered necessary or at least useful by 89% of them. In particular, IOP monitoring would give a great improvement in managing glaucoma and in testing drugs that could lower IOP. According to the World Health Organization, glaucoma afflicts 70 million people worldwide. This widespread disease is characterized by a gradual and irreversible loss of peripheral visual field due to optic nerve cupping.

Today, applanation tonometry, most often performed with the Goldmann applanation tonometer, has become the standard procedure for measuring IOP. The Goldmann method was considered the most accurate and precise by 99% of the ophthalmologists who answered the survey. However, its weaknesses include a hygiene problem caused by the necessity for head of the tonometer to be in direct contact with the anesthetized cornea. Furthermore, the patient's collaboration is required (he or she has to visit the ophthalmologist's office), and during measurements, some aqueous humor may be displaced. Finally, while it can measure the present IOP, applanation tonometry cannot monitor variations over time, which is the most important limitation. In fact, the only way to obtain data on the behavior of the IOP, to improve diagnosis and management of glaucoma, is to repeat measurements many times per day, which provides only a rough estimation and is a very cumbersome procedure for the patients, who have to stay at the ophthalmologist's office or come back many times in a day. Detailed knowledge of the behavior of IOP in patients with glaucoma is of paramount importance, as increased IOP and wide diurnal IOP variations are considered major risk factors for the progression of glaucoma.[1–3] A recent study has shown that 24-hour IOP monitoring results in a change in clinical management of glaucoma in 79.3% of patients.[4]

Because standard clinic follow-up evaluations fail to identify peaks and IOP variations, many attempts to find a practical and portable solution for monitoring IOP have been made without success. Maurice[5] was the first in 1957 to create a recording tonometer. This device was a heavy metallic structure fixed to the head of the patient that continuously indented a portion of the cornea. Needless to say, the instrument was not portable and not comfortable at all. Collins[6] in 1966 proposed a clever pressure sensor functioning wirelessly by means of a coupled magnetic field. An IOP change induced a shift of the resonance frequency. Unfortunately, to monitor IOP, this device had to be surgically implanted into the eye, which greatly limited its application. In 1967, Gillman and Greene[7] proposed the first noninvasive method of monitoring IOP. Their system was nothing more than a soft contact lens, in which they embedded a strain gauge. It was positioned over the meridional angle of the corneoscleral junction to measure angular changes due to IOP. The major drawback of their invention was that, to detect changes in the meridional angle, the contact lens had to be molded as an exact copy of the eye shape. Such a contact lens had to be custom-made for each patient, leading to a very expensive sensing system, which was probably the main reason that the project was abandoned. Couvillon et al.[8] in 1976 tried to applanate a 5-mm circular portion of the sclera continuously, with a pressure transducer held in a hydrogel ring. Their system was based on the well-known principle of applanation tonometry: A ring positioned on the sclera allowed

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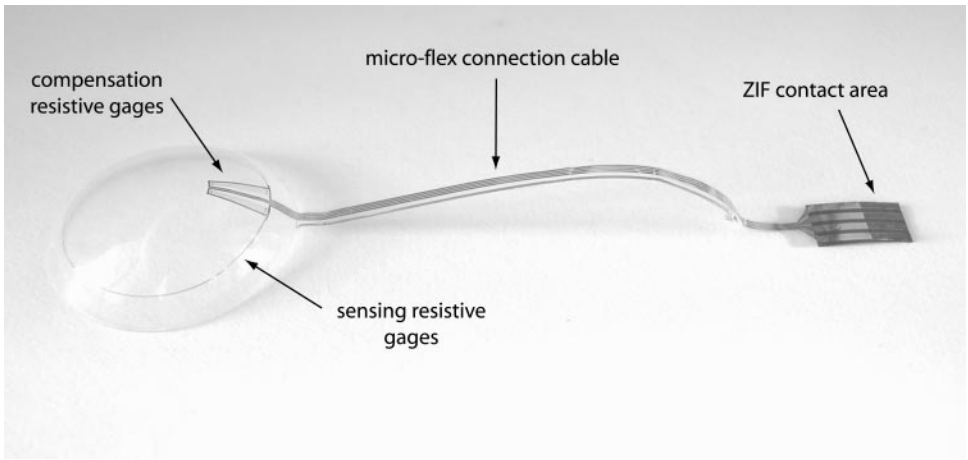

FIGURE 1. The sensing contact lens. Shown is the location of the active gauges, which are placed circumferentially for sensing changes in the corneal curvature due to IOP, and the passive gauges for thermal compensation, which are placed radially, where no strain should be measured. The gauges are made of thin metallic film patterned by surface micromachining on a polyimide microflex substrate, which is then embedded into the silicone soft contact lens.

monitoring of the IOP without interfering with vision. Many other researchers tried in different noninvasive ways to fix a device on the surface of the eye with the intent of applanating a portion of the cornea or sclera. These attempts included an applanating suction cup by Nissen[9] (1977), a haptic contact lens by Cooper et al.[10] (1979), a scleral buckle by Wolbarsh et al.[11] (1980), and a contact lens tonometer by Lee[12] (1988), which was presented only as a theoretical design. Because none of these devices could accurately monitor the IOP, none was commercialized. Then Svedbergh et al.[13] in 1992, with improved surgical capability, revisited the idea of implanting a pressure transducer into the eye. They targeted patients with cataract who already needed surgery to replace the intraocular lens. In fact, their invention incorporates a pressure transducer functioning wirelessly by passive telemetry in the haptics of an intraocular lens. They were not able to bring a product on the market, but other teams are currently trying to develop a commercial product based on this principle.[14–16] It is intended that this approach will remain limited to patients needing intraocular surgery (e.g., cataract surgery).

With this in mind, we present a novel approach to IOP measurement, which would permit minimally invasive continuous monitoring over prolonged periods, regardless of the patient's position and activities. The key element of this innovative measurement method is a soft contact lens with an embedded microfabricated strain gauge that allows the measurement of changes in cornea curvature correlated to IOP.[17] The purpose of this study was to verify the measurement principle of this device under simplified physiological conditions, which for the purpose of the study are limited to a physiological interface between the eye and the lens, as the principle is to measure corneal deformation due to IOP. In the discussion, the influence of all other physiological parameter such as eye movements, lid pressure, and blinking are presented. The sensing contact lens has been tested on an eye-simulating device consisting of a small balloon, and the results showed that the sensor is sensitive enough to detect changes in corneal curvature that are correlated to IOP.[18]

MATERIALS AND METHODS

Sensing Contact Lens Tonometer

Our method of indirect online monitoring of the IOP is to detect spherical deformations of the eyeball (changes in cornea curvature) due to variations in IOP. The rationale of this approach is based on the fact that, according to the results of an in vivo study[19] and an in vitro study[20] about the correlation between IOP and corneal curvature in humans, an IOP change of 1 mm Hg causes a change of central corneal radius of curvature of approximately 3 μm (over a typical radius of 7.8 mm). To measure the change, we designed a soft contact lens with an embedded microfabricated strain gauge inserted in a Wheatstone bridge configuration, with two sensing resistive gauges (double sensitivity) and two compensation resistive gauges (thermal compensation). Figure 1 shows this soft contact lens with the location of the gauges.

There are five major physical forces acting on a contact lens applied to the eye.[21] The atmospheric pressure (P_0) envelopes the free anterior and peripheral surfaces of the lens tears; the hydrostatic pressure (P_1) is the pressure of the precorneal tear film and acts against the lens as water acts against the wall of a dam—P_1 is supported by P_0 at its free surface; the force of gravity (p) is the lens weight; the lid force (F_{lid}) is the force developed by the lid during a blink; and the surface tension forces ($F\sigma$) represent the cohesive forces between the molecules of tears at an interface, such as the interface between air and tears or between tears and lens (Fig. 2). Their interplay, in different positions of the eye and lens, under various conditions, determine the fit of the lens. In normal conditions (proper fitting), the lens has both pre- and post-tear films, which let the contact lens slide on the corneal surface and find a stable balanced position (which is normally slightly eccentric) after each blink. Under these conditions, a soft contact lens bends and follows corneal deformations, behaving like a partial spherical shell subjected to a uniform edge moment, and has only circumferential strain.[22] For this reason, the sensing resistive gauges in the device are designed to have a circular arc shape around the center, placed over a circumference of 11.5 mm diameter, which is the average of the

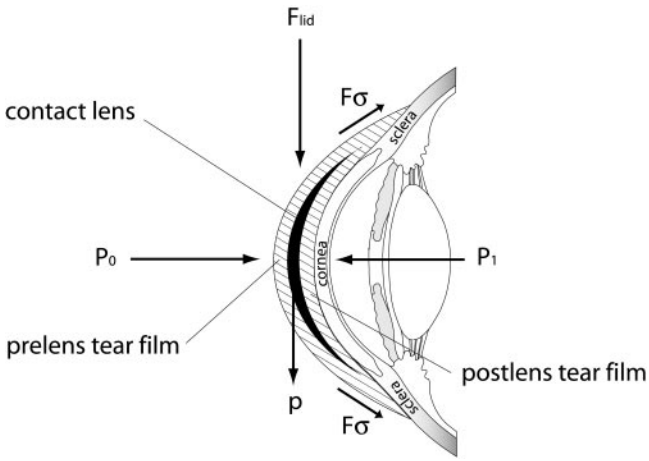

FIGURE 2. The five major physical forces acting on a contact lens: P_0, atmospheric pressure; P_1, hydrostatic pressure of the postlens tear film; $F\sigma$, surface tension of the prelens tear film; p, lens weight; and F_{lid}, lid force.

corneoscleral junction position, where we believe changes in IOP induce maximum corneal deformation. (The structure of the eye and studies on the distensibility of the cornea and the sclera suggest that this area varies more with change in IOP than any other.) The compensation-resistive gauges, used only for thermal compensation, are placed radially, where no strain should be measured.

The sensing contact lens is stimulated by a typical DC current (I_o) of 100 μA, and it gives an output voltage *Vm* proportional to strain and therefore to the IOP variations.[18]

Design and Fabrication

The sensor embedded in the soft contact lens is built around a thin microfabricated platinum-titanium (200 nm Pt/20 nm Ti) strain gauge. The gauge is sandwiched between two layers of polyimide (PI 2611; Dupont, Wilmington, DE), which is an insulating, protecting, and flexible carrier material. PI[23] is an excellent material for biomedical applications and offers advantages over other polymers, such as its excellent chemical and thermal stability, low water uptake, and good biocompatibility.[24] Furthermore, PI is widely used in integrated circuit manufacturing and therefore is suitable for mass production. The total thickness of the sensor is approximately 6 μm and is embedded in a silicone (MED-6015; NuSil Technology, Carpinteria, CA) soft contact lens by a cast-molding technique. In the first step, the sensor is positioned in the mold and the outer shape of the lens is polymerized. Then, silicone is added and polymerized to form the inner shape. Silicone is hydrophobic, and to render the surface of the contact lens hydrophilic and thus achieve proper fitting conditions (with a pre- and post-tear film), the contact lens surface was treated with oxygen plasma. Finally, a 3-cm microflex connection cable was designed (which is covered by a protective silicone layer) as well as a contact area for a zero insertion force (ZIF) connection (Fig. 1), to be able to handle the sensor and easily connect it to the electronics for measurements.

Experimental Setup and Procedure

In an initial assay of this sensing contact lens, juvenile porcine eyes were chosen (from approximately 45-kg pigs) because their dimension (approximately 23-mm diameter) is close to that of human eyes. After enucleation, the eyes were kept humid in a small jar for transportation (<5 hours) and then placed in an eye-holder plate with the cornea facing upward for experiments (Fig. 3). The eyes was cannulated with a butterfly 23-gauge needle placed into the posterior chamber and connected with a silicone tube to a bag filled with normal saline (0.9% NaCl) and to a syringe pump (PSD2; Hamilton, Reno, NV) to induce controlled IOP pressure variations. A pressure sensor (PR-15/8735.22-0.1; Keller, Basingstoke, UK) inserted in the silicone tube and close to the eye, allowed the online visualization of the real IOP to be compared with the signal from the sensing contact lens.

The experiments were performed at room temperature (21 ± 1°C). The sensing contact lens was placed on the enucleated eyes, taking care that a pre- and post-tear film was maintained during experiments by adding some drops of saline solution (proper fitting conditions). An initial pressure was preset by the height of the solution in the saline bag. The saline bag was then excluded from the liquid circuit by turning the stopcock, so that during experiments, IOP was gently controlled by a precise 50-μL syringe with a programmed syringe pump set of injections and ejections from the preset starting point. Signals from the pressure sensor and from the sensing contact lens were stored in a computer and processed by a dedicated program for online visualization or postanalysis (measuring period of 10 points/sec). The graph of the IOP changes recorded by the pressure sensor was compared to the changes recorded by the sensing contact lens.

Results

Six enucleated eyes were stimulated by applying ramps of increasing and decreasing IOP. In all cases, the sensing contact lens voltage followed the IOP variations very well. Because the fitting of the lens was not optimized for a porcine eye (the base curve and size of the contact lens used were those of a normal disposable soft contact lens and not specifically adapted for the porcine eye: 0.1 mm thick, 14.2 mm diameter, and a base curve of 8.6 mm) and because the sizes of the eyes were significantly different from one to the other (from juvenile pigs of different growth), the sensitivity calibration of the measurement varied from eye to eye. This means that, for each new juvenile porcine eye, two calibration points were needed to set the correspondence to the IOP. To show the capability of this sensing contact lens for monitoring IOP under simplified physiological conditions, only one curve is presented and discussed in detail. The enucleated eye was stimulated with increasing and decreasing ramps of IOP ranging from an absolute pressure of 17 to 29 mm Hg, measured with a handheld tonometer (TonoPen; Mentor, Norwell, OH) at the end of the recording. (The pressure sensor used to measure the IOP is a relative sensor that had to be calibrated with an absolute measurement, and to do it, and considering our setup, a portable tonometer was the best choice.) Figure 4 shows a 4-minute recording from the pressure sensor and the output signal *Vm* of the sensing contact lens, while IOP pressure cycles were induced by the syringe. As shown, the sensing contact lens followed the IOP measurements recorded from the pressure sensor well. To highlight the linear behavior of the sensing contact lens, Figure 5 shows the static calibration graph of the device. In this case, the output signal *Vm* of the sensing contact lens had an experimental fitted sensitivity of 8.37 μV/mm Hg.

Considering the future use of such a device for monitoring IOP in humans and considering that the noise in the output

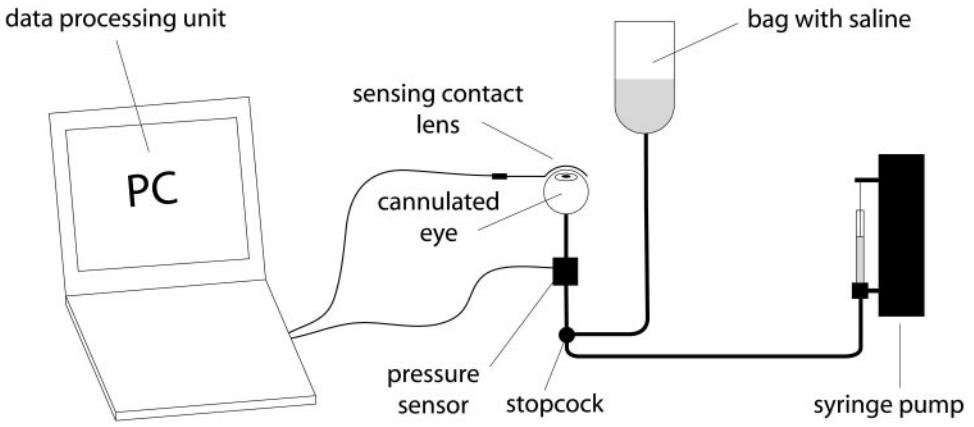

Figure 3. Setup for measuring IOP in an enucleated porcine eye with the sensing contact lens. The eye is cannulated with a butterfly 23-gauge needle placed in the posterior chamber and connected with a silicone tube to a bag filled with normal saline (0.9% NaCl) and to a syringe pump, to induce controlled variations in IOP. A pressure sensor inserted in the silicone tube and close to the eye allows the online visualization of the real IOP to be compared with the signal from the sensing contact lens. Data from the sensing contact lens and the pressure sensor are recorded and displayed by the data-processing unit.

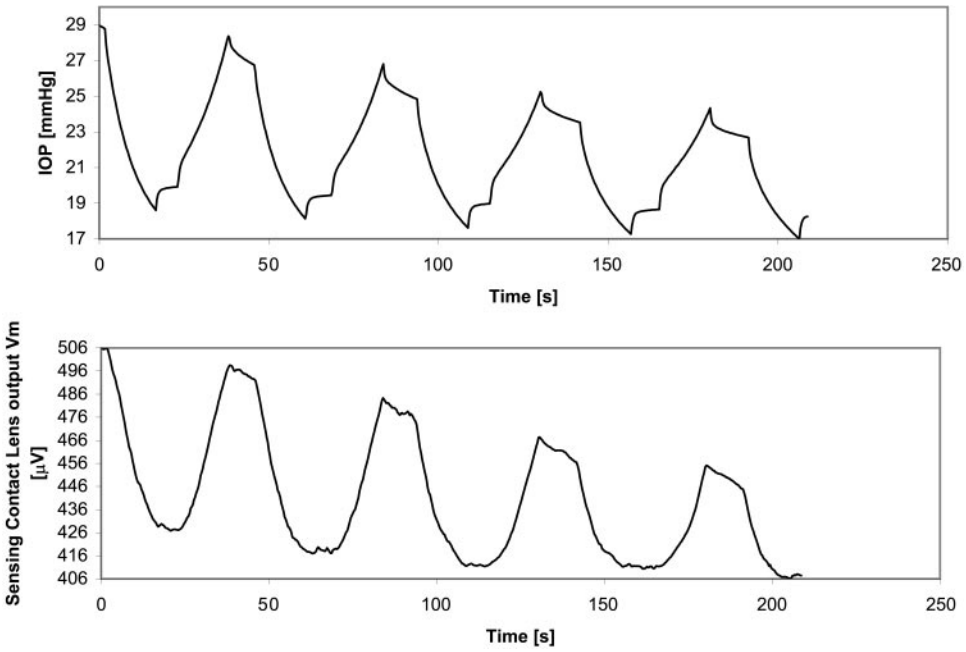

FIGURE 4. Record of the IOP and the sensing contact lens output signal *Vm* during liquid injection–ejection cycles. The sensing contact lens followed the pressure sensor well and showed the potential for continuously monitoring IOP in enucleated porcine eyes.

signal can be reduced to ± 1 μV, it is expected that our device will be capable of monitoring IOP variations in humans of <0.5 mm Hg. In fact, as previously reported in the introduction, an IOP change of 1 mm Hg causes a change in central corneal radius of curvature of approximately 3 μm, which corresponds to a theoretical output signal *Vm* of the sensing contact lens of approximately 50 μV (calculated from the response of the sensing contact lens to a 3-μm curvature deformation), which would be a much higher sensitivity than that obtained in the porcine juvenile eyes. Because the changes in cornea curvature due to variations in IOP are very small and linear,[18] we expect also that our device will be able to measure IOP up to 100 mm Hg.

DISCUSSION

In this study, a new approach to IOP monitoring based on a sensing contact lens was tested on enucleated porcine eyes to verify this new measurement principle. In a previous study,[18] the device was tested on an eye-simulating device consisting of a small balloon. The ultimate validation step will be clinical human trials to validate the system and the reproducibility of results in humans.

The typical result presented in this article shows that the device was adequately sensitive and followed the IOP variations very well. The sensing contact lens would allow, for the first time, minimally invasive, continuous monitoring over prolonged periods, regardless of the patient's position and activities. As the system is placed in the same way as a corrective contact lens, no anesthesia is required, and patient vision remains almost unimpaired. Not only would this device facilitate the evaluation of new approaches to glaucoma therapy, it would also open up new possibilities in presurgical and outpatient follow-up, as well as the monitoring of new drug therapies.

As previously mentioned, the purpose of this study was to verify the measurement principle of this device under simplified physiological conditions, which in this case were limited to a physiological interface between the eye and the lens, as the principle of the lens is to measure corneal deformation due

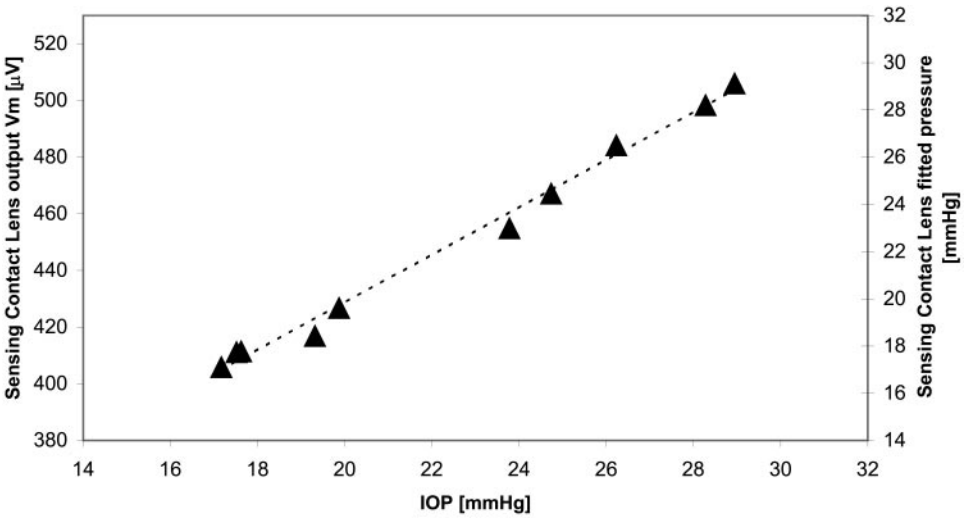

FIGURE 5. Static calibration graph. The output signal *Vm* of the sensing contact lens has an experimental fitted sensitivity of 8.37 μV/mm Hg, and it can be seen that it showed good linear fit. For linear regression, $R^2 = 0.992$.

to IOP. For a clinical trial in a living eye, all physiological parameters have to be considered. First of all, a much better interface and fitting condition with a good postlens tear film is expected in a living eye with an improvement of performance. Concerning the blinking of the eye and eyelid movements, those conditions should be easily filtered from the IOP signal, because they occur at a stable frequency and because they will create big and very short perturbation signals. There is also the question of movement of the lens, but we expect the contact lens to return to a fixed, balanced position after each eyelid blink or eye movement, as is the case with corrective soft contact lenses. Finally, other factors that could affect the precision of the sensing contact lens, such as corneal thickness or astigmatism, must be investigated, but we expect that, if there is a change in performance, it will be only in the sensitivity calibration of the lens and not in the linearity of the measurement. In this case, two calibration points would be needed to set the reference to the IOP.

The actual prototype of the sensing contact lens is connected to an external power and recording unit by wires (Fig. 1), which should not cause discomfort, because the microflex cable is very thin and covered by a silicone protective layer. We are currently also developing a telemetry chip and an antenna to be embedded in the contact lens for wireless power and data transfer.

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