In vivo Intraocular Pressure Monitoring using Implantable Optomechanical Sensor

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Abstract: We have successfully demonstrated the remote optical readout of intraocular pressure (IOP) from nanodot-enhanced micromachined IOP sensors implanted in *ex-vivo* and *in-vivo* rabbit eyes at a distance of 12 cm using the Zeiss SL-30 slit lamp, a standard ophthalmic scope widely used by clinicians. This detection distance of 12 cm has not been accomplished by other technical approaches such as inductor- or capacitor-coupling method. We achieved this result by (1) designing optomechanical IOP sensors with a noticeably high signal-to-noise ratio; and (2) incorporating a novel robust detection algorithm, which includes a highly precise opto-mechanical model. This model allows us to remove the background noise and instantaneously map the sensor's optical signal to a corresponding IOP value. We believe that this achievement -- a clinically significant readout distance accomplished using a well established ophthalmic clinical scope -- makes our IOP system a more clinically viable choice.

Summary

Glaucoma is a leading cause of irreversible blindness with 60 million cases worldwide. Because accurate, reliable, and most of all continuous monitoring of IOP in glaucoma patients has proven to be very crucial in large scale studies recently sponsored by National Institute of Health, the use of implantable IOP sensors is very attractive for optimal management. However, previously reported IOP sensors suffer from a major technical challenge: their readout distance is limited to 0.6-3 cm while the sizes of IOP sensors range between 3-11 mm, too large for minimally invasive procedure [1-3].

In our sensor, a change in IOP alters the deflection of the flexible membrane that forms the optical cavity of the sensor, and this change is remotely detected by exciting the sensor with a white light source and observing the resonance shift in the reflected spectrum (Fig.1a). To maximize the sensor's readout distance while maintaining its sub-1mm size, we have 1) included a very large active sensing area embedded with nanodot arrays to enhance the resonance and to match the slit lamp beam; (2) set the cavity height to 5~10 μm to track multiple spectral features for improved accuracy; (3) suppressed the background noises by growing silicon grass (black silicon) in the surrounding area as an anti-reflection (AR) coating; (4) avoided using Parylene membrane with hysteresis and chose mechanically more robust silicon-nitride membranes (Fig.1 b and c); and (5) incorporated a novel extrema-matching algorithm with a much improved opto-mechanical model to read out IOP values in real time. In addition, we have also slightly modified the slit lamp to use as a readout system.

The fabricated sensor is shown in Fig.1(d, e, f), with the black silicon coating the region surrounding the enlarged sensing area. Figs.2 and 3 show the accuracy of our optomechanical model and the robust performance of the extrema-matching technique: one can observe excellent matching between theoretical predictions and experimental measurements, and the pressure mapping is highly linear and accurate. For *ex-vivo* testing, the fabricated sensor was embedded onto a flexible PVC strip and inserted into an enucleated rabbit eye through an incision of 2 mm. The PVC strip stabilized the sensor position (Fig. 4), and in a systematic testing (18-gauge needle with a hydrostatic pressure controller, ± 0.1-mmHg accuracy), the sensor successfully read out IOPs between 3 and 40 mmHg (Fig. 5). The consistent results were produced at 12-cm readout distance when measured using a clinically used slit lamp integrated with a CCD and the spectrometer (Fig.6). Similar experiements were performed in living rabbits and obtained accurate IOP measurements for short and long term periods.

[1] P. J. Chen, et al., "Microfabricated implantable parylene-based wireless passive intraocular pressure sensors," JMEMS, vol. 17, no. 6, pp. 1342–1351 (2008).

[2] N. Xue, et al., "A SU-8-based microfabricated implantable inductively coupled passive RF wireless intraocular pressure sensor," JMEMS, vol. 21, no. 6, pp. 1338–1346 (2012).

[3] Melki, Samir, et al. "An implantable intraocular pressure transducer: initial safety outcomes." JAMA ophthalmology, 132(10), pp. 1221-1225 (2014).

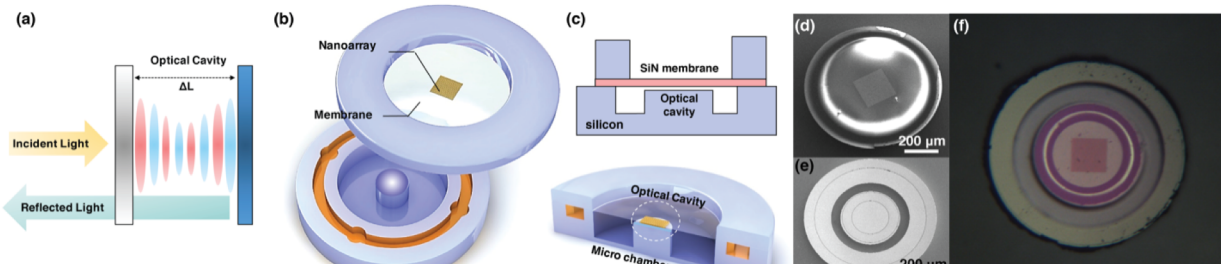

Figure 1. Illustration of micromachined IOP sensor: (a) Schematic of an equivalent optical resonance cavity; (b,c) Illustration of micro-machined optical resonance cavity sensor; (d,e) SEM images of fabricated device before assembly; and (f) photo of newly designed and fabricated sensor with enlarged optical active area and AR coated surrounding area.

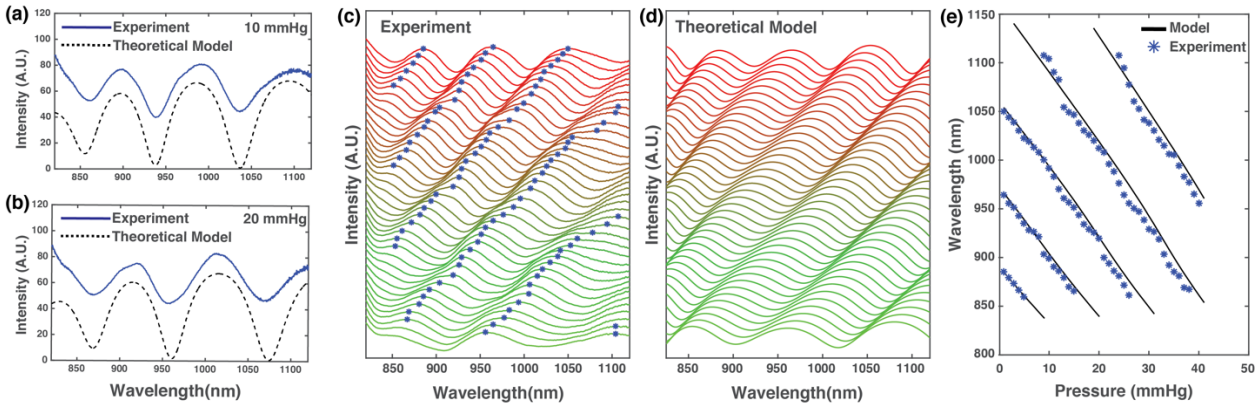

Figure 2. Testing in a pressure chamber (a) experimental optical spectrum obtained at 10mmHg. (b) experimental and theoretical optical spectrum at 20mmHg. (c) systematic peaks shift in respect to the pressure change from 1mmHg (top) to 40mmHg (bottom). (d) theoretical expectation for the peaks shift. (e) peak-shift comparison between experiment and theoretical model

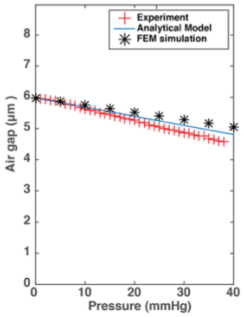

Figure 3. Experimental, analytical, and numerical air gap extraction

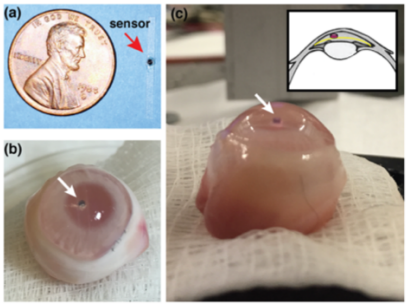

Figure 4. *ex-vivo* test platform (a) IOP sensor on a PVC strip (b) implanted device, top view (c) side view

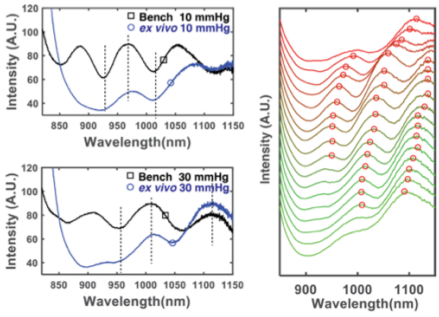

Figure 5. *ex-vivo* and the pressurized chamber spectra and the peaks shift for IOP between 3 and 40 mmHg

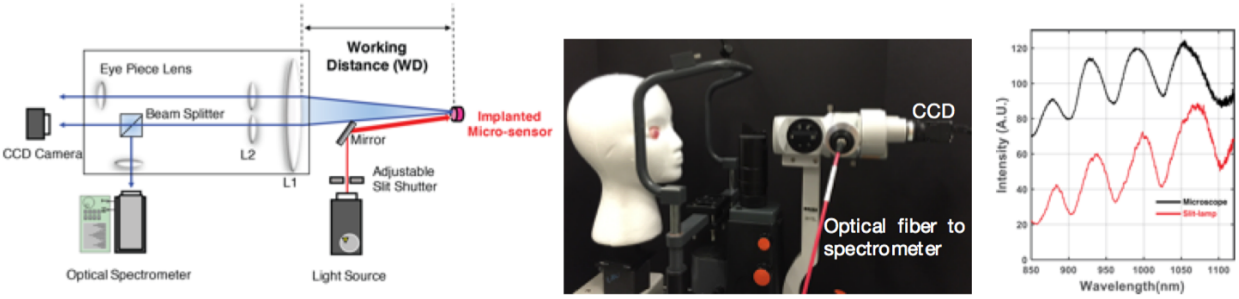

Figure 6. Schematic of remote monitoring of IOP using white-light source and implanted micro-sensor (left). Photos of the measurement schematic (center). Long distance measurement result (right); black-line indicates a reference measurement from typical microscope-based spectrometer (Mitutoyo 20x) and red line indicates a slit-lamp measurement (Zeiss SL-30).