

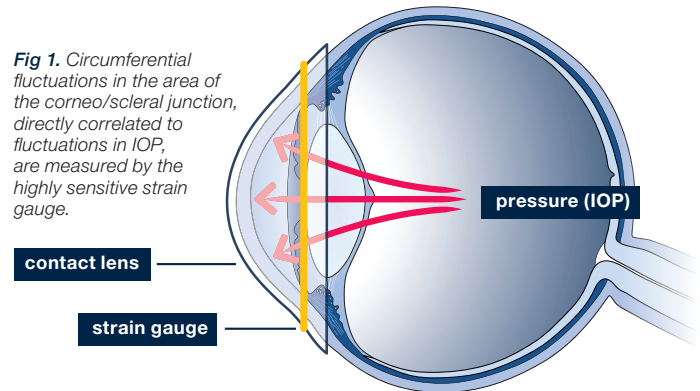
Principles and rationale for the SENSIMED Triggerfish® Sensor device.

The Unmet Need

The desire to measure, monitor and control intraocular pressure (IOP) levels over a 24 hour period in patients suffering from glaucoma is, at present, expensive, problematic and inevitably leads to compromises. In essence, the effectiveness of the patient's therapy is determined retrospectively, however, the visual damage which indicates therapeutic failure is irreversible and sadly all too common. The current gold standard for measuring IOP, Goldmann Applanation Tonometry (GAT), is a technology more than 50 years of age. Its major drawback is the fact that it only provides a snapshot of IOP at a given moment and is normally used during office hours by ophthalmologists. GAT can provide multiple static snapshots of IOP during a 24-hour period but even this is cumbersome and relatively unphysiological since it requires the patient to be upright and awake. Current best practice for obtaining circadian profiles involves an overnight stay in a hospital or sleep laboratory, which induces substantial artifacts as well as the inconvenience of awakening the patient periodically only to obtain an approximation of the real IOP pattern.

The importance of the circadian nature of IOP fluctuation is gathering wide acceptance and a method of non invasive, continuous, monitoring under normal conditions of activities and posture, including normal sleep, could reveal important unseen information regarding the characteristics of 24hour IOP in each individual patient. The unmet need is the ability to effectively identify danger signs and assess effectiveness of treatment to prevent irreversible visual damage.

Fig 1. Circumferential fluctuations in the area of the corneo/scleral junction, directly correlated to fluctuations in IOP, are measured by the highly sensitive strain gauge.



Principles of the SENSIMED Triggerfish®

The SENSIMED Triggerfish® Sensor device developed by SENSIMED AG is a contact lens capable of recording qualitative IOP profiles over a 24 hour period in patients with suspect or established glaucoma. The monitoring takes place while patients follow their routine activities. A strain gauge embedded in a soft silicone contact lens detects circumferential changes in the area of the corneo-scleral junction. This information is then transmitted to a recorder via wireless telemetry. As IOP increases, the circumference of the cornea increases and the strain gauge in the lens detects the change (Fig 1).

The relationship between these changes and IOP changes has been validated in vitro by Leonardi et al¹. The following figures demonstrate the relationship between the output of the Sensor and manometrically measured IOP in an enucleated pig eye model both in simulation of ocular pulsation (Fig 2) and in slow stepwise ramping of IOP (Fig 3).

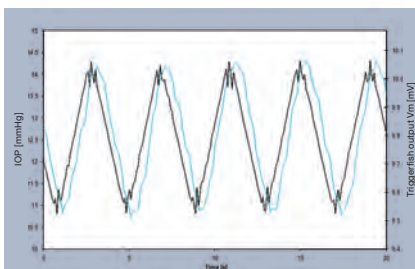


Fig 2. Recording of IOP variations and the Triggerfish output signal (mV) during dynamic IOP variations in the enucleated pig eye simulating a typical ocular pulse amplitude of 3 mmHg centred at 12.5 mmHg. The Triggerfish follows IOP variation well. (Black line, IOP; blue line, mV).

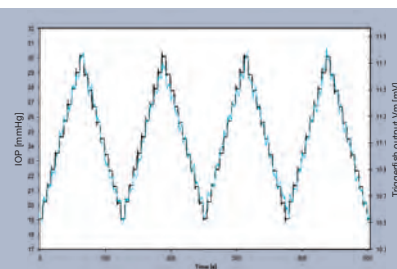


Fig 3. Recording of IOP and the contact lens sensor Triggerfish output signal (mV) during static IOP variations of 1 mmHg, between 20 and 30 mmHg. The Triggerfish shows high linearity and reproducibility. (Black line, IOP; blue line, mV).

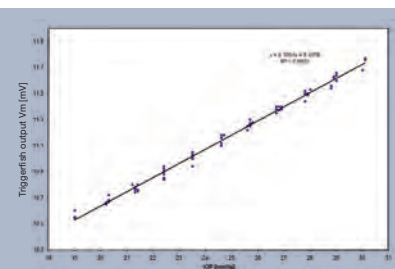


Fig 4. In static mode (Triggerfish median value of each 1 mmHg step shown in Fig. 3), the output signal of the Triggerfish (mV) has a highly linear behaviour (linear regression coefficient (R^2) = 0.9935) and a reproducibility of ± 0.2 mmHg (95% confidence interval).

The SENSIMED Triggerfish® in Use

In the clinical setting, the SENSIMED Triggerfish® provides qualitative information on the behavior of the IOP in individual patients. Below is a typical 24 hour Triggerfish curve as seen with the viewing software. The Sensor records for 30 seconds at 10Hz at 5 minute intervals during the 24 hour period. Each “burst” provides 300 data points. The software then filters out the high amplitude eye blinks in each burst and plots the median of these data points as a single point on the curve. Each point on the curve represents a burst 5 minutes apart which taken together make up the 24 hour profile. The detailed view of any burst can be visualized in a zoom window beneath the main curve. It is notable that the system has a sufficient level of sensitivity to show the ocular pulsation, clearly visible in bursts recorded during sleep in the absence of blinking (Fig. 5).

The curve appears to be unique for each patient and provides several pieces of important information.

1. The time of day or night when a peak is registered under physiological conditions. i.e. during normal activities or asleep with eyes closed and in supine/sleep body position.
2. How long the peak lasts and its rate of ascent/descent.
3. Efficacy of treatment on the timing, extent and duration of IOP peaks and fluctuations by comparing successive monitoring sessions.

Therefore, because glaucoma in each patient is different we can have individualized “signature” profiles to enable

individualized patient treatment and monitoring of treatment effectiveness. Just how influential this data could be is still to be determined via clinical studies. It could give vital indications of unseen peaks in IOP e.g. in the progressing patient, and allow the physician to modify treatment options to maximize their efficacy⁴.

Note: The vertical axis of the curve is in “Arbitrary Units (AU)” and not in mmHg.

Conclusion

The SENSIMED Triggerfish® is a highly sensitive, non invasive system for monitoring IOP over a 24 hour period. It has the potential to provide a way of personalizing treatment in glaucoma patients based on individual patterns in IOP. Its principles of measurement have been validated in both in vitro^{1,2} and in vivo^{3,4} studies and the device continues to be studied in clinical trials throughout the world.

References

1. Matteo Leonardi, Elie M. Pitchon, Arnaud Bertsch, Philippe Renaud and Andre Mermoud: *Wireless contact lens sensor for intraocular pressure monitoring: assessment on enucleated pig eyes. Acta Ophthalmol. 2009: 87: 433–437.*
2. J. Hjortdal and P.K. Jensen, “In vitro measurement of corneal strain, thickness, and curvature using digital image processing”, *Acta Ophthalmologica Scandinavia, 73, 5-11 (1995).*
3. A. K. C. Lam and W. A. Douthwaite, “The effect of an artificially elevated intraocular pressure on the central corneal curvature”, *Ophthal. Physiol. Opt., 17, 18-24 (1997).*
4. Mansouri K, Shaarawy T. *Continuous intraocular pressure monitoring with a wireless ocular telemetry sensor: initial clinical experience in patients with open angle glaucoma. Br J Ophthalmol 2011 Jan 7.*

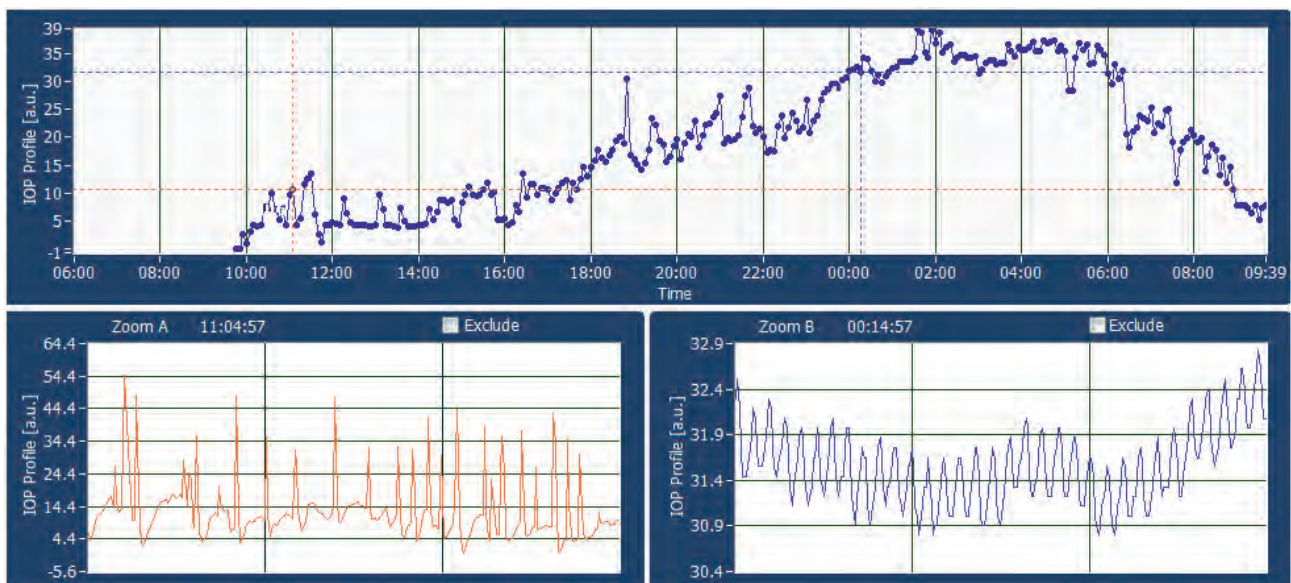


Fig 5. The SENSIMED Triggerfish 24 hour IOP curve as seen on the viewing software which allows each point on the curve to be individually investigated by a zoom function. Eye blinks at 11:04 appear as high amplitude spikes in zoom A (red, bottom left). Zoom B (blue, bottom right) shows the measurements of a burst on the curve at 00:14 corresponding to ocular pulsation during sleep.