Introduction
The SENSIMED Triggerfish® developed by Sensimed AG is a contact lens-based device capable of recording qualitative circadian pressure related profiles over the full 24 hour period under physiological conditions in glaucoma patients at risk of progression. A strain gauge embedded in a soft silicone contact lens (Sensor) captures spontaneous circumferential changes at the corneoscleral area. The data is transmitted to a portable recorder via wireless telemetry.

Method and Findings
In a recent study¹, published in Archives of Ophthalmology, Mansouri et al. at the Hamilton Glaucoma Center, University of California, San Diego report that 24 hour profiles obtained with the SENSIMED Triggerfish® have fair to good reproducibility in the short-term. As part of a FDA-trial, the investigators evaluated safety, tolerability, and pattern reproducibility of the device. Forty patients with suspected or established glaucoma underwent two ambulatory 24 hour sessions at a 1 week interval.

Safety
To assess safety, this study used a stringent definition of adverse events, defining them as any change in ocular parameters from baseline. The most common adverse events were conjunctival hyperemia (80%) and “blurred vision” (82%). These adverse events were anticipated: the former due to the fact that most patients with glaucoma suffer from some form of ocular surface disease and have never worn a contact lens before; the latter mostly due to the orthokeratologic effect of the (intended) tight fit of the Sensor. Importantly, the vast majority of adverse events were classified as mild and the mean resolution time was less than 24 hours following the Sensor removal. The authors attributed the improved safety profile of the second-generation Sensor compared to a previous report² to the availability of 3 base curves for better ocular fit.

Tolerability
Tolerability of the repeated wear was assessed using the Visual Analogue Scale³, a 100-mm horizontal line on which patients draw a mark reflecting their comfort level. With values of less than 30 mm for both sessions, tolerability of the Sensor was considered good, with a non-statistically significant tendency for better comfort at the second visit.
Reproducibility
IOP is a highly dynamic parameter influenced by intrinsic and extrinsic factors. Therefore the evaluation of measurement reproducibility is necessary to distinguish measurement variability from physiologic changes. To assess the degree of similarity of individual patient patterns between the 2 sessions (Figure 1), pairwise Pearson correlation was computed between parallel time points in both sessions. Despite the uncontrolled ambulatory nature of this study, the authors reported an overall correlation of 0.59, which indicates fair to good reproducibility. This study is the first to assess the short-term reproducibility of pressure patterns throughout the full 24 hour cycle, including undisturbed sleep. There was higher agreement between specific periods of interest, such as the transition from wakefulness to the first 2 hours of sleep, with a correlation of 0.71. In comparison, Realini et al. had previously investigated the diurnal GAT measurement repeatability in glaucoma patients. Using intraclass correlation coefficients, they found correlations ranging from 0.45 to 0.71 at different time points between the two visits. The fact that IOP measurements were assessed during 12 hours and not the entire 24 hour period may have limited the conclusions of their investigation.

Summary
This study shows that the SENSIMED Triggerfish® is a safe and well-tolerated device for 24 hour recording of ocular dimensional changes in patients with suspect and established glaucoma. It further demonstrates that 24 hour profile have fair to good reproducibility in the short term. These results suggest that 24 hour individual profile obtained in “real-life” situations have the potential to assist clinical decision-making.

Figure 1: Example of an individual profile reproducibility with the SENSIMED Triggerfish® in a 60 year old male glaucoma suspect undergoing treatment with a once-daily prostaglandin eye drop. Two sessions at a one week interval are superimposed using the integrated software package.

REFERENCES
Technical white paper
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 non-invasive of continuous monitoring under normal conditions of activities and posture, including normal sleep, could reveal important unseen information regarding the characteristics of ocular dimensional changes over 24 hours 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.

Principles of the SENSIMED Triggerfish®
The SENSIMED Triggerfish® Sensor device developed by Sensimed AG is a contact lens capable of recording qualitative profiles over a 24 hour period in patients with 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 at the corneoscleral area (Fig 1). This information is then transmitted to a recorder via a wireless telemetry system.

The relationship between these changes has been validated in vitro by Leonardi et al. 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).

The SENSIMED Triggerfish® in Use
In the clinical setting, the SENSIMED Triggerfish® provides qualitative information on the behavior of the individual patient’s profile. Below is a typical 24 hour SENSIMED Triggerfish® profile as seen with the viewing software. The Sensor records for 30 seconds 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
REFERENCES


Conclusion

The SENSIMED Triggerfish® is a highly sensitive, non invasive system that records the ocular dimensional changes at the corneoscleral area over 24 hours. It has the potential to provide a way of personalizing treatment in glaucoma patients based on individual profiles. Its principles of measurement have been validated in both in vitro and in vivo studies and the device continues to be studied in clinical trials throughout the world.

Fig 2. Recording of IOP variations and the Sensor’s 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 Sensor follows IOP variation well. (Black line, IOP; blue line, mV).

Fig 3. Recording of IOP and the Sensor’s output signal (mV) during static IOP variations steps of 1 mmHg. It shows a high linearity and reproducibility. (Black line, IOP; blue line, mV).

Fig 4. In static mode (median value of each 1 mmHg step shown in Fig. 3), the output signal of the Sensor (mV) has a highly linear behaviour (linear regression coefficient (R²) = 0.9935) and a reproducibility of ± 0.2 mmHg (95% confidence interval).

Fig 5. The SENSIMED Triggerfish® 24 hour profile as seen on the software which allows each point on the curve to be individually investigated by a zoom function. Eye blinks can be seen in details during 30 seconds in the zoom A window while ocular pulsation during sleep are shown in the zoom B.

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, asleep with eyes closed and in supine/sleep body position.
2. How long the peak lasts and its rate of ascent/descent.
3. Treatment impact on the patient’s profile by comparing two successive 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.
Technical white paper
The “hyper” oxygen permeability characteristics (Dk/t) of the SENSIMED Triggerfish® Sensor.

Background
Continuous IOP monitoring presents special challenges from a technological standpoint. It still remains an important and unmet clinical need. The SENSIMED Triggerfish® Sensor is designed to capture ocular dimensional changes utilizing a technological breakthrough in miniature electronics incorporated in an extended wear silicone contact lens. This novel approach makes it possible to record changes over a 24 hour period. Circumferential dimensional changes at the corneoscleral area are detected and the information is transmitted to a recorder via a wireless telemetry system. Since diurnal and nocturnal variations can be important in prescribing effective treatment for glaucoma patients, comparisons of day time and night time recordings are of particular interest. It is therefore vital to use a lens material which will facilitate a successful recording session for up to 24 hours without compromising the oxygenation of the cornea and patient comfort.

Materials and Characteristics
The material chosen was pure silicone with an oxygen plasma surface treatment to create a highly hydrophilic interface between the Sensor and all tissues in contact.

The oxygen permeability coefficient of a material is normally measured in Dk units \((10^{-11} \text{ cm}^3 \text{ O}_2 \text{ x cm}/\text{cm}^2 \text{ x s x hPa})\). This value (expressed as Dk) when divided by the thickness of a sample i.e. the lens, provides the specific Dk/t value for the lens in question. The pure silicone used has an exceptionally high Dk of 292 units and the harmonic mean thickness of the Sensor (t) is 325μm.

Therefore, the Dk/t for the lens is **119 Dk/t units** which is consistent with, or greatly exceeds recommended performance to avoid corneal hypoxia in extended wear with mainstream ocular correction lenses\(^1\).

An accepted classification for comparing the oxygen permeability of different contact lenses is the Benjamin Classification which proposed low, medium, high, super and hyper categories\(^1\). Using this classification the SENSIMED Triggerfish® Sensor qualifies for **HYPER oxygen transmissibility**.
Conclusion

The SENSIMED Triggerfish® Sensor provides a level of oxygen permeability equal to or greater than the recommended boundaries of extended wear to avoid corneal hypoxia. This means the cornea is as protected as possible from metabolic stress during the monitoring period. In addition, surface treatment of the pure silicone lens with oxygen plasma makes this diagnostic sensor equally safe and comfortable.

REFERENCES

Technical white paper
Rationale for single use of the SENSIMED Triggerfish® Sensor.

Introduction
The SENSIMED Triggerfish® Sensor device developed by Sensimed AG is a contact lens capable of capturing spontaneous circumferential changes at the corneoscleral area over a 24 hour period. A strain gauge embedded in a soft silicone contact lens is highly sensitive and permits practitioners and patient not to influence the spontaneous eye behaviour. The device relies on the finest precision manufacturing and cutting edge technology. The Sensor, supplied in a pre-packed sterile delivery unit, has been designated as a single use device by the manufacturer.

Rationale
Due to the very nature of the Sensor and its specific design, for patient safety the lens is made of silicone, which is highly permeable to oxygen. The Dk/t (oxygen permeability) measurement for the Sensor is 119 Dk/t. Although this property is highly desirable, the natural silicone material itself is hydrophobic. It is therefore necessary to treat the surface of the Sensor with oxygen plasma which creates a highly hydrophilic environment at the lens/cornea interface providing maximum patient safety and comfort. However, this treatment does not survive the first use of the device and thereafter reverts to a hydrophobic surface incompatible with clinical use (Fig 1). Therefore, never re-sterilize and never reuse. This can lead to an unacceptable level of both adherence to the cornea and discomfort for the patient, jeopardizing compliance and safety.

In addition, after the recording session, normal and recommended removal of the Sensor necessitates a more robust approach to handling and distorts the lens and the components within. Distortion of the connections can lead to false readings and may lead to complete failure in recording if it is attempted to re-fit the Sensor subsequent to removal. Moreover, there is a risk that breakage of a metal internal component could occur, protrusion of which through the silicone could lead to a corneal injury if re-use is attempted.
Conclusion
The SENSIMED Triggerfish® Sensor benefits the patient by monitoring the trend in ocular dimensional changes through a specific combination of safety, comfort and precision electrical engineering. These cornerstones are severely compromised by wear and removal. For these reasons the product has obtained CE-mark for single use up to 24 hours only. **Re-use of the Sensor is unsafe and off-label use; it is the manufacturer’s restriction that re-use should never be attempted.**

Fig 1. Left, The SENSIMED Triggerfish® Sensor with a degraded surface treatment clearly showing hydrophobicity.
Right, The SENSIMED Triggerfish® Sensor with intact surface treatment demonstrates high wettability.