

The SENSIMED Triggerfish contact lens sensor for continuous 24-hour recording of ocular dimensional changes in people with or at risk of developing glaucoma

Medtech innovation briefing

Published: 19 November 2014

www.nice.org.uk/guidance/mib14

Summary

The SENSIMED Triggerfish is a contact lens sensor that continuously measures changes in ocular dimensions, which are related to changes in intraocular pressure (IOP, or pressure in the eye). It is designed to record patterns of IOP-related changes over 24 hours, and is intended to be used in people with or at risk of glaucoma.

Effectiveness	Adverse events and safety
<ul style="list-style-type: none">• Thirteen publications were identified involving a total of 237 patients (from 5 patients in the smallest to 40 in the largest). Of these studies, 9 were observational, 2 were interventional, and 1 was a trial register record.• No studies were identified showing agreement with a reference standard for monitoring IOP, or which included clinical efficacy outcomes.• There is uncertainty about how well dimensional changes measured by the SENSIMED Triggerfish reflect true fluctuations in IOP.• No evidence was identified to show that 24-hour recording with the SENSIMED Triggerfish leads to improved clinical outcomes for patients, such as control of IOP, progression from ocular hypertension (OHT) to glaucoma, or vision loss. One study reported that therapy was changed in 11 patients (73%) following results of 24-hour recording with the SENSIMED Triggerfish.	<ul style="list-style-type: none">• Of the 13 studies included in the analysis, 10 reported mild or moderate adverse events and 2 reported severe adverse events. Device-related adverse events tended to resolve quickly.• Patient comfort or tolerability was reported in 5 studies and found to be good. Poor tolerability of the device resulted in incomplete monitoring with the SENSIMED Triggerfish in 4 people out of the 63 people taking part in 3 of these studies.

Cost and resource use	Technical factors
<ul style="list-style-type: none">• Initial outlay for the SENSIMED Triggerfish system is approximately £5923 for hardware and software. Each use of the device is estimated to cost £424–£549 in single-use consumables, plus clinician time.• The SENSIMED Triggerfish sensor is fitted and removed by an ophthalmologist or appropriately trained optometrist. The results must be separately analysed and interpreted.• There is no published evidence reporting cost or resource use.	<ul style="list-style-type: none">• The SENSIMED Triggerfish measures ocular dimensional changes captured at the corneoscleral junction area. The device uses this information to produce a qualitative profile of relative IOP-related peaks and patterns over 24 hours.• The SENSIMED Triggerfish measures ocular dimensional patterns in electrical units (millivolts), which cannot be directly compared with conventional IOP measurement devices such as Goldmann Applanation Tonometry (GAT).• The patient wears the device for 24 hours while they go about usual activities (with some exceptions such as while showering, swimming or driving).

Introduction

Glaucoma is a disease in which the optic nerve becomes damaged, leading to progressive vision loss. Damage occurs because of raised pressure inside the eye (intraocular pressure, or IOP). Raised IOP (described as ocular hypertension, or OHT) is caused by a build-up of the fluid (aqueous humour) within the eye. This can happen when the drainage tubes within the eye (called the trabecular network) become blocked, so the aqueous humour cannot drain out of the eye properly. The most common form of glaucoma is chronic open-angle glaucoma (COAG), which develops slowly and can cause blindness

(NHS Choices Glaucoma). Open-angle glaucoma is a chronic and progressive condition in which visual field loss is associated with morphological changes, which occur at the optic nerve head and retinal nerve fibre layer in the absence of other ocular disease (European Glaucoma Society, 2008).

COAG is usually asymptomatic until irreversible vision loss has occurred. The peripheral vision is lost first before the damage progresses inwards in the visual field. In England, approximately 480,000 people have COAG. Among those of white European family origin, around 2% over the age of 40 years and 10% of those aged over 75 years have COAG. People of African or African-Caribbean family origin have a higher risk of developing the disease. Other risk factors include short-sightedness, ocular hypertension and family history of glaucoma. People with diabetes may also be more at risk of developing glaucoma (NHS Choices Glaucoma).

OHT is defined as pressure in the eye consistently greater than 21 mm Hg, and it affects 5% of people aged over 40 years in the UK. This equates to around 1 million people (Burr et al. 2012).

People who have or who are at risk of developing COAG, including those with OHT, need regular monitoring to prevent their vision deteriorating any further. All COAG treatments aim to reduce IOP to a level low enough to limit disease onset or progression. Treatment can be in the form of medication (eye drops which either increase the flow of aqueous humour out of the eye or reduce its production), laser treatment to open up the trabecular meshwork (trabeculoplasty), or surgery (most commonly trabeculectomy to remove part of the meshwork, allowing the aqueous humour to drain properly). Some people's glaucoma continues to progress despite IOP-lowering treatment; indeed, 1 study suggests that glaucoma may progress in up to 45% of people, regardless of treatment (Heijl et al. 2002).

Technology overview

This briefing describes the regulated use of the technology for the indication specified, in the setting described, and with any other specific equipment referred to. It is the responsibility of healthcare professionals to check the regulatory status of any intended use of the technology in other indications and settings.

About the technology

CE marking

The SENSIMED Triggerfish was CE-marked in May 2010 as a Class IIa medical device, under the description of 'medical device telemetry applications for recording IOP [intraocular pressure]-related patterns'. The sensor, antenna, data cable, software, and data recorder are included in this CE mark.

Description

The SENSIMED Triggerfish contact lens sensor is a minimally invasive medical device designed to provide continuous 24-hour recording of ocular dimensional changes (changes in the shape of the eye), related to intraocular pressure fluctuations.

The device has the following single-use components:

- A disposable, soft, contact lens containing a sensor. The lens is made from pure silicone with an oxygen plasma surface treatment, and is worn for 24 hours. The sensor is 585 micrometres thick in the centre and 260 micrometres thick in the periphery. The contact lens diameter is 14.1 mm. The lens is available in 3 curvature radius sizes: 8.4 mm (steep), 8.7 mm (medium) and 9.0 mm (flat). It is fitted like an ordinary contact lens following appropriate measurements of the eye. The lens has an oxygen transmissibility of 119 Dk/t units, which exceeds the levels recommended for normal contact lenses in order to avoid hypoxia of the cornea.
- A self-adhesive, flexible, disposable antenna which is placed on the skin around the eye for a single 24-hour period.
- A booklet where the patient can record relevant information to help to understand the patterns recorded in ocular dimensional changes. This may include meal times or periods of sleep or physical activity.
- A pouch that holds the recorder. This is single-use for hygiene reasons.

The SENSIMED Triggerfish also has the following reusable components:

- A recorder which is worn around the person's neck in the pouch. Following a recording session, they attend a consultation with an ophthalmologist or optician, where the system is removed. After this consultation, the collected data is retrieved from the recorder, via the Bluetooth USB adapter.
- A data cable which connects the antenna to the recorder.
- The Bluetooth USB adapter which transfers data from the recorder to a computer.
- The battery charger for the recorder.
- Software for the clinician to visualise the results from the recording session.

The sensor works by measuring minute changes in the dimensions of the eye (the ocular dimensions) through a strain gauge in the contact lens. These patterns are the result of changes in the production and outflow of aqueous humour, combined with the biomechanical properties of the eye walls. Changes in both IOP and in ocular dimensions are caused by the same factors, and so it is assumed that the profiles are closely related. The manufacturer states that by measuring the patterns of ocular dimension changes, the SENSIMED Triggerfish can reveal changes in IOP over the course of 1 whole day and night. The sensor records for 30 seconds at 5 minute intervals over 24 hours. The information is transmitted wirelessly from the sensor to the antenna, and then transferred via a wire from the antenna to the recorder. At the end of a 24-hour recording session, data are transferred from the recorder via a Bluetooth adapter to a computer for analysis. A clinician views the data through computer software which filters out peaks and 'noise' caused by eye blinks.

Data from the sensor are measured in electrical units (millivolts) referenced against a starting value of 0 at each recording session. For this reason, data from the SENSIMED Triggerfish cannot be directly compared with results from currently used IOP measurement devices such as Goldmann Applanation Tonometry (GAT), which measure pressure in millimetres of mercury (mm Hg). Furthermore, the SENSIMED Triggerfish produces a qualitative profile of relative intraocular pressure peaks and patterns over 24 hours, whereas GAT gives definitive IOP values at a fixed time point. SENSIMED Triggerfish is not designed to replace definitive IOP measurements (in mm Hg) with a contact tonometer such as GAT.

Intended use

The SENSIMED Triggerfish device is indicated for continuous recording of IOP-related

patterns in ocular dimensions for up to 24 hours in people with glaucoma, at risk of glaucoma, or with suspected high intraocular pressure. The safety and tolerability of the device has only been evaluated in adults aged over 18 years.

The manufacturer states that IOP-lowering medication (eye drops) can be administered as usual by people wearing the sensor, and that sterile artificial tears can be used to hydrate the eye if needed. The manufacturer also states that people wearing a hearing aid can use the SENSIMED Triggerfish, and that it is not contraindicated in pregnant or lactating women.

According to the manufacturer's instructions for use, the SENSIMED Triggerfish should not be used by people with:

- active eye disease, eye injury or eye abnormality affecting the cornea, conjunctiva, or eyelids
- a history of eye or eyelid infections including blepharitis and sties
- a history of adverse effects associated with wearing contact lenses, including intolerance and abnormal ocular response to contact lenses
- active inflammation or infection of the eye
- corneal vascularisation
- insufficiency of lachrymal secretion
- corneal hypoesthesia
- a known allergy to silicone
- skin irritations, certain allergies, eczema, or other indications against wearing patches.

People must not bathe, shower or swim while wearing the device because there is a risk of electric shock. They must not wear full metallic frame glasses and should limit the use of mobile phones and radios to minimise interference with the recording signal. People are also advised not to drive while wearing the sensor.

Setting and intended user

Having examined the patient's eye for contraindications (including a test of visual acuity,

central corneal radius and thickness measurement, slit lamp examination [including the conjunctiva and cornea], and intraocular pressure tonometry), a clinician with appropriate training must fit the SENSIMED Triggerfish. Following eye measurements, the device should be fitted in the same way as a regular contact lens. An ophthalmologist or optometrist with appropriate training is needed to interpret the results of the SENSIMED Triggerfish.

Patients may follow their routine activities over the 24-hour period while the device records, including sleeping (but excluding driving or water-based activities, as described above).

Current NHS options

NICE's guideline on [glaucoma](#) recommends that GAT should be used to measure IOP in people with chronic open-angle glaucoma (COAG) or OHT, and those who are suspected of having COAG. GAT is a contact technique for measuring pressure in the eye, in which the patient is given anaesthetic eye drops before the pressure inside the eye is measured by applying force directly to the cornea. Non-contact devices that measure pressure in the eye are available, but GAT is considered to be the most accurate (Guidance on the referral of glaucoma suspects by community optometrists, Royal College of Optometrists 2010).

NICE's guideline on [glaucoma](#) recommends that as well as GAT, people with COAG, OHT or suspected COAG are offered central corneal thickness measurement, gonioscopy, standard automated perimetry for visual field testing, and optic nerve examination using a slit lamp. The results of these tests indicate the risk of OHT and glaucoma progression, and therefore the level of clinical supervision and treatment needed. The guideline recommends that people with OHT or suspected COAG are assessed at regular intervals (from every 4–6 months for people at high risk of COAG to 12–24 months for people at low risk). Intervals for assessment of people with confirmed COAG are based on their risk of progression to sight loss, and range from every 2–6 months to every 6–12 months. NICE recommends that an optometrist or ophthalmologist should perform GAT at every clinical assessment.

It is recognised in literature that IOP levels fluctuate throughout a 24-hour period. Some studies suggest that IOP values tend to peak at night (Bagga et al. 2009), whereas others report that peak IOP levels are reached in the morning (David et al. 1992). Because GAT measurements are usually taken during office hours, peak IOP levels may be missed or underestimated. Fluctuating IOP levels in themselves may contribute to glaucoma

progression, although there remains uncertainty about this (Caprioli 2007).

Because the peak IOP value may be underestimated in a single appointment, some NHS patients are referred for phasing. At a phasing clinic, a patient's IOP is measured using GAT every hour or 2 hours throughout the span of a regular working day (Moodie et al. 2010). Full, 24-hour recording of IOP is not routinely conducted in the NHS and needs in-patient care (NIHR Horizon Scanning Centre 2012).

NICE is not aware of other devices available to the NHS that have a similar function to the SENSIMED Triggerfish.

Costs and use of the technology

The following are list prices provided by the UK distributor of the SENSIMED Triggerfish device (Kestrel Ophthalmics) for July 2014 (excluding VAT):

- Sensor (steep, medium, flat; single use): £750 for a box of 2
- Antenna, packaged by pack of 3, left or right (single use): £54
- Data recorder: £3350
- Data cable: £534
- Battery charger: £22
- Software: £2000
- Software update (per year): £680
- Bluetooth USB stick: £17
- Sleeve for recorder (single use, 25 units): £20
- User manual: £20
- Patient booklet (single use, to be given to each patient, 12 units): £4
- Fitting guide for sensor: £2
- Quick setup guide: £2

- Carrying case: £150

From these list prices, it is estimated that each 24-hour use of the SENSIMED Triggerfish device would cost £424–£549 in single-use consumables, plus clinician time. The anticipated lifespan of the recorder and cable are not known, but both have 2-year warranty periods. Information from the manufacturer suggests that the battery supports at least 300 cycles of charge/discharge. Software updates are provided by the manufacturer with no additional charge.

The device calibrates automatically at start-up so no manual calibration is needed. No maintenance contracts are available; in the case of a faulty recorder, the UK distributor would provide a replacement.

The UK distributor offers training to NHS staff on how to use the SENSIMED Triggerfish device. Distributor representatives attend initial patient fitting sessions to resolve any issues.

The SENSIMED Triggerfish is intended as an adjunct to IOP measurement with tonometry techniques such as GAT. The following NHS tariffs for outpatient attendance (2013–14) relating to ophthalmic services have been provided for information (Payments by results tariff 2013–14):

- First attendance, single professional: £106
- First attendance, multi-professional: £108
- Follow-up attendance, single professional: £60
- Follow-up attendance, multi-professional: £87

No published costs were found for the cost of daytime or 24-hour phasing clinics.

Likely place in therapy

The SENSIMED Triggerfish is currently used in some NHS and private hospitals as part of research studies, and so its place in guiding treatment or improving monitoring is not clear.

The manufacturer suggests that the SENSIMED Triggerfish would be useful in cases where recording takes place before and after an intervention such as a change in medication or

surgery. This may provide information on whether an intervention has been effective in lowering IOP.

The SENSIMED Triggerfish may also be of benefit where there is a suspicion that fluctuating IOP levels are contributing to disease progression, or where peak IOP levels are being missed during daytime measurements.

Specialist commentator comments

The specialist commentators were in agreement that continuous recording of IOP-related changes over 24 hours would give a more precise and reliable measurement of IOP compared with single clinic visits. It would also identify IOP-related patterns and this may allow clinicians to better assess patients' responses to treatment and adjust accordingly. Patients with fluctuating IOP readings across single clinic visits, and those with good IOP control, or normal-tension glaucoma, but worsening visual fields may benefit particularly from 24-hour IOP recording. This could potentially benefit patients by reducing the number of clinic visits needed. It may also suggest a more appropriate course of treatment and limit unnecessary treatment changes.

However, the specialist commentators noted that the SENSIMED Triggerfish device's place in managing glaucoma is uncertain: published studies are limited to small patient numbers, and the validity of SENSIMED Triggerfish as a method for measuring IOP-related patterns remains unproven. The device does not directly measure IOP, and agreement studies are needed to confirm the association between SENSIMED Triggerfish and a reference standard such as GAT. In addition, there is uncertainty about whether IOP fluctuations are indeed a risk factor for glaucoma. It was noted that factors influencing 'calibration' between SENSIMED Triggerfish and GAT are unlikely to be stable over time or between patients. Ultimately further studies are needed to support the use of the SENSIMED Triggerfish in managing glaucoma.

All specialist commentators agreed that the cost of the single-use SENSIMED Triggerfish device was high and that, on currently available evidence, its cost effectiveness cannot be determined.

It was noted that a clinician with experience in contact lens fitting should oversee placement of the device. Patients may be required to wait in the clinic following fitting of the contact lens, which could impact resource use and service throughput. A specialist commentator noted that tests of visual acuity, central corneal thickness and radius

measurements, slit lamp examination, and IOP would be routine in a NHS glaucoma clinic, and so may not need to be repeated during fitting of the device.

Various factors relating to the material the lens is made of (such as oxygen transmissibility, thickness and wettability) are related to the likelihood of adverse effects occurring. Correct fitting of the lens is important to prevent adverse effects and ensure accurate corneal curvature measurements. It was noted that measurements made by the device may be complicated by factors such as blinks, eye movement, corneal hydration and oxygenation, although the manufacturer states that the SENSIMED Triggerfish software can filter the effects of blinking out of the measurements. As such, more information is needed on lens parameters and fitting considerations.

A specialist commentator suggested that there may be more adverse effects with the SENSIMED Triggerfish than with general contact lenses. Another specialist commentator was uncertain about whether the lens can be cleaned with soft lens solution or saline if dropped during fitting. The manufacturer clarified that a lens should not be used if its sterility cannot be guaranteed, for example if it has been dropped. A specialist commentator noted that it was unclear whether the device could be used following trabeculectomy or aqueous shunt glaucoma surgery. The manufacturer stated that it is possible to use the SENSIMED Triggerfish device in some people who have had these procedures, depending on the position of the bleb, as advised by the physician.

The manufacturer's list of contraindications was considered to be extensive and may limit the population in whom the device can be used. Metallic framed spectacles are common among people in whom the SENSIMED Triggerfish is likely to be used, and this contraindication may affect people's daily activities while wearing the device. Moreover, further detail is needed on the contraindication of 'insufficiency of lachrymal secretion' because this is more common in older people.

Equality considerations

NICE is committed to promoting equality and eliminating unlawful discrimination. We aim to comply fully with all legal obligations to:

- promote race and disability equality and equality of opportunity between men and women

- eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief, in the way we produce our guidance (these are protected characteristics under the Equality Act 2010).

Age is a protected characteristic defined in the Equality Act (2010). Older people are at increased risk of developing glaucoma; improved management of pressure in the eye may reduce the risk of vision loss and therefore improve quality of life.

Vision loss may be classified as a disability which is a protected characteristic defined in the Equality Act (2010). Improved management of IOP may reduce the risk of vision loss and therefore improve quality of life.

People of African-Caribbean family origin are at increased risk of COAG.

People of Asian family origin are at increased risk of acute angle-closure glaucoma.

Evidence review

Clinical and technical evidence

No studies reporting direct agreement of SENSIMED Triggerfish with a reference standard such as Goldmann Applanation Tonometry (GAT) were identified. No studies with clinical effectiveness outcomes, such as rates of progression to COAG or vision loss, were found.

In preparing this briefing 13 studies were identified which contained relevant outcomes, including studies on the safety and tolerability of the SENSIMED Triggerfish device in healthy people. Of these 13: 9 were open, observational studies (Agnifili et al. 2014; De Smedt et al. 2012; Faschinger and Mossbock 2013; Freiberg et al. 2012; Hervas et al. 2013; Lorenz et al. 2013; Mansouri and Shaarawy 2011; Mansouri et al. 2012; Mottet et al. 2013 [both Faschinger and Mossbock 2013 and Hervas et al. 2013 were letters to journal editors]; 3 were open interventional studies in which recording took place before and after IOP-lowering drugs or surgery with no reference diagnostic (Hollo et al. 2014; Pajic et al. 2011; Tojo et al. 2013); and 1 was an observational study, the results of which were presented only in a clinical trial register (NCT01390779). The details and results of these studies are provided in tables 1 to 13.

Safety

Table 14 summarises the safety outcomes as reported by 9 of the 13 studies. Commonly reported adverse events were diffuse conjunctival keratitis, superficial punctate keratitis, blurred vision, sensor pressure mark, corneal abrasion, ocular hyperaemia, discomfort/irritation, conjunctivitis and mild corneal abrasion or erosion.

No serious adverse events were reported. Among the 40 people in the Lorenz et al. (2013) study, 5 severe adverse events were reported: 3 corneal epithelial defects, 1 incidence of severe pain, and 1 conjunctival erythema. The study did not report the total number of adverse events. Mansouri et al. (2012) described 2 people who had 5 adverse events of conjunctival hyperaemia (5 of 149 [3%] events), which were classified as severe. All adverse events in this study resolved in the 24 hours after the device was removed.

Patient comfort and tolerability

According to the 5 of the 13 studies which reported these outcomes, the SENSIMED Triggerfish was generally well tolerated.

Technical results

One study reported fair to good reproducibility in pairs of SENSIMED Triggerfish readings 1 week apart (Mansouri et al. 2012). However, a letter to the editor did not report this reproducibility (Faschinger and Mossbock 2013). There is uncertainty about the SENSIMED Triggerfish's ability to accurately and reproducibly measure IOP-related patterns over 24 hours, and this is compounded by there being no studies which directly measure its performance against a reference technique such as GAT. There are, however, validity outcomes in the included studies which give an indication of the device's recording capabilities (reported in table 14).

Table 1 Summary of the observational study: Agnifili et al. (2014)

Study component	Description
Objectives/hypotheses	To examine the circadian IOP-related patterns in healthy people and in people with POAG and NTG using the SENSIMED Triggerfish.

Study design	Open, uncontrolled, observational study.
Setting	Patients were consecutively enrolled and measured with the SENSIMED Triggerfish. Patients were enrolled from an ophthalmology clinic in Italy (no dates provided).
Inclusion/exclusion criteria	Healthy eyes showed a BCVA $\geq 20/40$, refractive error < 4 dioptres and mean IOP < 18 mm Hg, CCT ranging from 530 micrometres to 560 micrometres, the absence of signs of glaucomatous optic neuropathy and normal visual-field test. Inclusion criteria for POAG and NTG eyes were a BCVA $\geq 20/40$, refractive error ≤ 4 dioptres (spherical equivalent) and CCT ranging from 530 micrometres to 560 micrometres. The initial diagnosis of POAG needed an indication in the patient chart of an untreated IOP of 24-37 mm Hg, the absence of secondary glaucoma and the presence of glaucomatous optic neuropathy. The diagnosis of NTG needed untreated mean diurnal IOP ≤ 21 mm Hg from diagnosis to enrolment as indicated by the patient chart, IOP asymmetry < 4 mm Hg and open iridocorneal angle.
Primary outcomes	24-hour SENSIMED Triggerfish pattern (secondary outcomes were sub-period patterns, peaks and prolonged peaks).
Statistical methods	Growth modelling to address within-person and between-person variability simultaneously.
Participants	10 healthy patients, 10 patients with POAG and 10 with NTG.
Results	See table 14.
Conclusions	Adverse events were reported during lens wear. No changes in visual acuity were found after sensor removal and no patients requested removal of the sensor. Mean SENSIMED Triggerfish patterns were significantly different between healthy, POAG, and NTG groups.
Abbreviations: BCVA, best corrected visual acuity; CCT, central corneal thickness; IOP, intraocular pressure; NTG, normal tension glaucoma; POAG, primary open angle glaucoma.	

Table 2 Summary of the observational study: De Smedt et al. (2012)

Study component	Description
Objectives/ hypotheses	To evaluate the tolerability, comfort, and reliability of the signal transmission of the SENSIMED Triggerfish used for 24-hour IOP-related fluctuation recording in humans.
Study design	Open, uncontrolled, observational study (healthy volunteers).
Setting	Healthy volunteers were recruited in to the study and fitted with SENSIMED Triggerfish (8.7 mm curvature radius prototype). Patients were seen by the investigators at 5 minutes, 30 minutes, 4 hours, 12 hours and 24 hours after fitting of the SENSIMED Triggerfish. Full eye examinations were done before and after SENSIMED Triggerfish sensor placement. Dates and setting were not reported.
Inclusion/ exclusion criteria	Inclusion: aged >21 years, not pregnant, not suffering from glaucoma/ ocular surface disorder, no ocular surgery in past 3 months.
Primary outcomes	No primary outcome reported. Other outcomes included BCVA, subjective wearing comfort (scored between 0 and 10; 0=intolerable; 10=perfect), position and surface wetting ability of the sensor and its mobility on blinking and adverse events.
Statistical methods	Wilcoxon signed rank test for analysis of the differences in parameters over time.
Participants	10 healthy volunteers.
Results	See table 14.
Conclusions	Subject-reported comfort score was acceptable. Visual acuity reduced during and immediately after SENSIMED Triggerfish wear and mild and moderate adverse events were reported. Three patients needed antibiotic treatment for corneal abrasion.
Abbreviations: BCVA, best corrected visual acuity; IOP, intraocular pressure.	

Table 3 Summary of the observational study: Faschinger and Mossbock (2013) (letter to editor)

Study component	Description
Objectives/ hypotheses	Not specified
Study design	Open, semi-comparative, observational study (healthy volunteers). Letter to editor.
Setting	Healthy people were monitored with the SENSIMED Triggerfish in 1 eye and simultaneously measured with applanation tonometry 5 times in the other eye (total duration approximately 2 hours). Head and body positions were changed during this period to artificially induce IOP changes. The procedure was repeated 2–8 weeks later in all 5 patients.
Inclusion/ exclusion criteria	Young people with healthy eyes (no further information provided).
Primary outcomes	Not reported.
Statistical methods	None reported.
Participants	5 people with healthy eyes.
Results	See table 14.
Conclusions	Applanation tonometry and the SENSIMED Triggerfish did not produce similar curves during change in body and head positions. Applanation curves appeared reproducible but those from the SENSIMED Triggerfish did not.
Abbreviations: IOP, intraocular pressure.	

Table 4 Summary of the observational study: Freiberg et al. (2012)

Study component	Description
Objectives/hypotheses	Investigate the effect of overnight wear of the SENSIMED Triggerfish on CCT.
Study design	Open, uncontrolled, observational study
Setting	Patients were monitored with the SENSIMED Triggerfish in hospital during their sleep period (no dates reported). The device was randomly installed in 10 right and 10 left eyes. Comprehensive eye assessment including GAT measurement was done before the device was inserted and after it was removed. One eye was monitored and the opposite eye (without sensor) was used as control.
Inclusion/exclusion criteria	<p>Inclusion criteria: patients over 18 years of age diagnosed with either ocular hypertension or glaucoma. Adults scheduled to be hospitalised as part of their standard glaucoma care.</p> <p>Anti-glaucomatous drug treatment, if any, had to be stable since at least 4 weeks prior to study entry.</p> <p>Exclusion criteria: contact lens wear within the last 2 years, ocular surface status preventing contact lens fitting or ocular surgery within the last 3 months.</p>
Primary outcomes	Effect of overnight wear of the SENSIMED Triggerfish on CCT. Other outcomes included effect of on peripheral corneal thickness, CCR and safety.
Statistical methods	Corneal thickness was assessed by computing Spearman correlation coefficients. Paired t-tests or Wilcoxon signed rank tests were used as appropriate.
Participants	20 patients with glaucoma (15 included in primary data, all 20 evaluated for safety)
Results	See table 14.
Conclusions	Adverse events were reported including severe ocular hyperaemia and bacterial conjunctivitis. No changes in visual acuity were reported.

Abbreviations: CCT, central corneal thickness; CCR, central corneal radius; GAT, Goldmann Applanation Tonometry.

Table 5 Summary of the observational study: Hervas Ontiveros et al. (2013) (letter to editor)

Study component	Description
Objectives/ hypotheses	No objectives reported
Study design	Open, uncontrolled, observational study. Letter to editor.
Setting	Patients had 24-hour recording with the SENSIMED Triggerfish in hospital in Spain (6 patients completed the recording). GAT measurements were taken at the start, middle and end of this 24-hour period. One patient had GAT measurements taken at 3-hour intervals.
Inclusion/ exclusion criteria	Aged 18–85 years with similar open angle glaucoma diagnosed in both eyes and topical antihypertensive treatment stable for at least 4 weeks. Included patients had not had any type of eye surgery in the past 6 months.
Primary outcomes	No primary outcomes defined. Other outcomes were tolerability and serious adverse events.
Statistical methods	None reported.
Participants	8 patients with open angle glaucoma.
Results	See table 14.
Conclusions	Device tolerability issues were reported and no severe adverse events were reported.
Abbreviations: GAT, Goldmann Applanation Tonometry.	

Table 6 Summary of the interventional study: Hollo et al. (2014)

Study component	Description
Objectives/hypotheses	To evaluate 24-hour continuous recording of IOP-related patterns with the SENSIMED Triggerfish to detect prostaglandin-induced IOP reduction.
Study design	Interventional study.
Setting	Between October 2011 and February 2012, patients with ocular hypertension and POAG were recruited in Hungary. All glaucoma medications were stopped for 6 weeks prior to study IOP-related measurements. One eye from each patient had 24-hour measurements 3 times, 4 days apart (twice with the SENSIMED Triggerfish and once with GAT). GAT measurements were taken at 6 time points with the patient in a sitting position during hospitalisation. SENSIMED Triggerfish curves were obtained in an outpatient setting. Patients then had IOP-lowering therapy (travoprost) for 3 months, after which 24-hour monitoring was done with GAT and the SENSIMED Triggerfish (separated by 4 days). Eye examination was done before and after sensor placement.
Inclusion/exclusion criteria	<p>Inclusion criteria: all patients were aged 18 years and over. Ocular hypertension was defined as untreated IOP consistently >21 mm Hg, open anterior chamber angle, reproducible normal visual field, and no glaucomatous optic nerve head and retinal nerve fibre layer damage. POAG was defined as typical glaucomatous optic nerve head and retinal nerve fibre layer damage, reproducible glaucomatous visual field deterioration with automated threshold perimetry, untreated IOP>21 mm Hg, open anterior chamber angle, and no sign of any secondary glaucoma (further inclusion criteria are provided in the full text).</p> <p>Exclusion criteria: any uncontrolled systemic disease, known intolerance to contact lens material and topical prostaglandin analogue medication, IOP>40 mm Hg during the washout period, and participation in any clinical drug trial 30 days before the enrolment.</p>

Primary outcomes	No primary outcome described. Other outcomes included safety, effect of IOP-lowering medication on the SENSIMED Triggerfish and GAT curves, comparison of GAT values before and after sensor fitting with first and last 50 minutes of SENSIMED Triggerfish measurements, and effect of change in sitting position.
Statistical methods	Pearson correlation for relationship between GAT IOP values measured immediately before and after SENSIMED Triggerfish curves, and the difference between the first and last 50-minute periods of the SENSIMED Triggerfish curves. Friedman test to investigate treatment-related change in the mean and SD values of the complete SENSIMED Triggerfish curves. Paired t-test was used to compare mean GAT measurements before and after IOP-lowering drugs.
Participants	9 patients (4 with ocular hypertension; 5 with POAG).
Results	See table 14.
Conclusions	IOP-lowering medication changed the shape of GAT curves but not SENSIMED Triggerfish curves. No correlation was seen in the difference between the first and last SENSIMED Triggerfish measurements compared to the first and last GAT measurements. The authors suggest that these results show limited agreement between methods.
Abbreviations: GAT, Goldmann Applanation Tonometry; IOP, intraocular pressure; POAG, primary open angle glaucoma; SD, standard deviation.	

Table 7 Summary of the observational study: Lorenz et al. (2013)

Study component	Description
Objectives/hypotheses	To investigate tolerability and safety of the SENSIMED Triggerfish for 24-hour intraocular pressure recording in healthy people and age-matched glaucoma patients.
Study design	Open, uncontrolled, observational study.

Setting	Healthy people and patients with glaucoma had 24-hour recording with the SENSIMED Triggerfish (8.7 mm curvature radius only) as part of this study in Germany (no dates provided). Comprehensive eye assessment including GAT measurement was done before the device was fitted and after it was removed. Discomfort levels were scored. Patients were asked to apply their topical anti-glaucoma medication as usual.
Inclusion/exclusion criteria	Inclusion criteria: male or female, 18–80 years old; healthy person or treated glaucoma patient; cylinder refraction of $\leq \pm 2$ dioptres in the study eye; visual acuity of 20/80 or better in the study eye. Exclusion criteria: people wearing contact lenses in the last 2 years; people with contraindications for wearing contact lenses; history of refractive surgery; history of intraocular surgery in the last 3 months; severe dry eye syndrome; keratoconus or other corneal abnormalities; conjunctival or intraocular inflammation; pregnancy and lactation; simultaneous participation in other clinical trials.
Primary outcomes	Primary end point was the level of patient-reported discomfort in the study eye at 24 hours using a VAS (0=no discomfort; 100=very severe discomfort). Secondary end points included the following parameters which were measured as change from baseline for the study eye: BCVA, pachymetry, corneal epithelial staining, conjunctival erythema and corneal topography.
Statistical methods	VAS scores for healthy people and glaucoma patients were compared using independent groups' Wilcoxon rank-sum test.
Participants	20 healthy people and 20 age-matched patients with glaucoma.
Results	See table 14.
Conclusions	Patients found the SENSIMED Triggerfish device tolerable and reasonably comfortable. Mild and severe adverse events were reported, including corneal epithelial defects, pain, and conjunctival erythema, all of which resolved within 2 days. Ocular parameters such as conjunctival oedema and erythema were significantly changed following sensor wear.
Abbreviations: BCVA, best corrected visual acuity; GAT, Goldmann Applanation Tonometry; IOP, intraocular pressure; VAS, visual analogue scale.	

Table 8 Summary of the observational study: Mansouri and

Shaarawy (2011)

Study component	Description
Objectives/ hypotheses	None reported.
Study design	Open, uncontrolled, observational study.
Setting	Consecutive patients with progressive open angle glaucoma had 24-hour ambulatory IOP-related change recording with the SENSIMED Triggerfish in Switzerland (no dates reported). Patients were asked to grade their average level of ocular comfort.
Inclusion/ exclusion criteria	Patients with progressive open angle glaucoma despite medical treatment and controlled IOPs during office hours.
Primary outcomes	No primary outcome defined; other outcomes were safety and comfort.
Statistical methods	None reported.
Participants	15 patients with glaucoma (12 with POAG and 3 with pseudoexfoliative glaucoma).
Results	See table 14.
Conclusions	Results suggested reasonable tolerability and comfort. Minor complications were reported, but no serious adverse events.
Abbreviations: IOP, intraocular pressure.	

Table 9 Summary of the observational study: Mansouri et al. (2012)

Study component	Description
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Objectives/ hypotheses	To examine the safety, tolerability, and reproducibility of the SENSIMED Triggerfish device.
Study design	Open, uncontrolled, observational study.
Setting	Patients with suspected glaucoma and established glaucoma received 2, 24-hour recording sessions with the SENSIMED Triggerfish with a 1-week interval. Behaviour and sleep were not controlled. Patients had an eye examination before and after 24-hour recording.
Inclusion/ exclusion criteria	<p>Suspected glaucoma was defined as those people with eyes with abnormal-appearing optic discs without repeatable abnormal standard automated perimetry results. Patients suspected of having glaucoma also included those with eyes with an IOP > 22 mm Hg but with healthy-appearing optic discs and without repeatable abnormal standard automated perimetry results. Established glaucoma was defined as people having at least 2 consecutive, reliable and repeatable standard automated perimetry examinations with either a pattern standard deviation outside the 95% confidence limits or a glaucoma hemifield test result outside the 99% confidence limits.</p> <p>Inclusion criteria: aged 18–80 years, best-corrected visual acuity of 20/80 or greater in the study eye, spherical refraction between –5 and 3 dioptres, cylinder correction of 2 dioptres or less, and open angles on gonioscopy (further inclusion criteria reported in full text).</p> <p>Exclusion criteria: previous glaucoma surgery or any intraocular surgery 3 months before study inclusion, known intolerance to silicone, contraindications for contact lens wear, severe dry eye disease, keratoconus, or other corneal abnormality.</p>
Primary outcomes	Primary safety outcomes were adverse events (defined as any change from baseline in relevant ocular parameters, as assessed by the investigator or the patient) and subjective comfort level measured on a VAS (0=no discomfort; 100=very severe discomfort). Secondary outcomes were reproducibility of the SENSIMED Triggerfish patterns on 2 separate readings.
Statistical methods	Reproducibility of signal patterns was assessed using Pearson correlations.

Participants	40 patients (21 with suspected glaucoma and 19 with established glaucoma).
Results	See table 14.
Conclusions	Adverse events were reported in the majority of patients; most were classified as mild, and 2 were severe. All adverse events resolved within 24 hours and no serious adverse events were reported. Tolerability scores were encouraging. Correlation between repeated SENSIMED Triggerfish curves was fair to good.
Abbreviations: IOP, intraocular pressure; VAS, visual analogue scale.	

Table 10 Summary of the observational study: Mottet et al. (2013)

Study component	Description
Objectives/ hypotheses	To evaluate 24-hour IOP rhythm reproducibility during repeated continuous 24-hour IOP monitoring with NCT and the SENSIMED Triggerfish in healthy people.
Study design	Observational, uncontrolled, open study.
Setting	Volunteers at a referral centre of chronobiology in France had 4 24-hour IOP monitoring sessions over 6 months. The IOP-related patterns of the first eye were continuously recorded using the SENSIMED Triggerfish and the IOP of the opposite eye was measured hourly using NCT. Two sessions with NCT measurements in 1 eye and SENSIMED Triggerfish measurements in the opposite eye, 1 session with SENSIMED Triggerfish measurements in only 1 eye, and 1 session with NCT measurements in both eyes were performed.
Inclusion/ exclusion criteria	Inclusion criteria: people free of sleep disturbance, endocrine illness or ocular disease (spherical equivalent between -1 and +1 dioptre), with regular lifestyle habits and a habitual total sleep time of approximately 8 hours. Exclusion criteria: people who worked shifts, had taken a transmeridian flight less than 2 months before the beginning of the study, had any medical treatment, or smoked.

Primary outcomes	A nonlinear regression analysis was used to model the 24-hour IOP curve. Comparison of curve characteristics was done and agreement evaluated .
Statistical methods	Model was fitted to the SENSIMED Triggerfish data. ICC was used to measure reproducibility. A Bland-Altman plot was used to compare different methods.
Participants	12 young healthy adults.
Results	See table 14.
Conclusions	The SENSIMED Triggerfish produced a reproducible curve in healthy people but the relative variation in electrical signal cannot be used to estimate IOP measurements in mm Hg.
Abbreviations: ICC, intraclass correlation; IOP, intraocular pressure; NCT, non-contact tonometry.	

Table 11 Summary of the interventional study: Pajic et al. (2011)

Study component	Description
Objectives/ hypotheses	To perform 24-hour recording in 5 patients with NTG in the presence and absence of anti-glaucomatous treatment.
Study design	Interventional study.
Setting	Patients who were untreated or with IOP-lowering drugs stopped for a minimum of 6 weeks and were recorded with the SENSIMED Triggerfish for 24 hours. Patients then had IOP-lowering medication for at least 6 weeks. SENSIMED Triggerfish recording was then done again. Recording was conducted in an ambulatory setting in Switzerland (no dates reported). GAT IOP measurements were taken before and after SENSIMED Triggerfish recording. Patients were instructed to use their IOP-lowering medication as usual during SENSIMED Triggerfish recording.

Inclusion/exclusion criteria	NTG was defined as IOP without treatment less than 21 mm Hg on diurnal testing, gonioscopic open anterior chamber angle, typical glaucomatous optic disc damage with glaucomatous cupping and loss of neuroretinal rim, visual field defect compatible with the glaucomatous cupping and progressive damage.
Primary outcomes	No primary outcome was defined. Other outcomes included description of SENSIMED Triggerfish output with and without IOP-lowering drugs, relationship between GAT values before and after SENSIMED Triggerfish recording and the respective initial and final SENSIMED Triggerfish output.
Statistical methods	Pearson correlation was used to compare patient patterns over 2 sessions.
Participants	5 patients diagnosed with NTG
Results	See table 14.
Conclusions	SENSIMED Triggerfish profiles were repeatable and highly individual. The effect of IOP-lowering medication was not reflected in all SENSIMED Triggerfish patterns, and there was no relationship between GAT IOP values and SENSIMED Triggerfish output (no analysis reported).
Abbreviations: GAT, Goldmann Applanation Tonometry; IOP, intraocular pressure; NTG, normal tension glaucoma.	

Table 12 Summary of the trial record: NCT01390779, Efficacy of 24-hour IOP recording with the SENSIMED Triggerfish

Study component	Description
Objectives/hypotheses	Assess the safety and effectiveness of the SENSIMED Triggerfish device in continuous recording of relative IOP-related patterns.
Study design	Open, uncontrolled, observational study.

Setting	Patients were recruited between July 2011 and May 2012 and had 24-hour recording with the SENSIMED Triggerfish in 1 randomly selected eye, while in a sleep laboratory. An eye examination was done at screening and before and after the device recording.
Inclusion/exclusion criteria	<p>Inclusion criteria: diagnosis of POAG, including normal tension glaucoma, or healthy people, including people with ocular hypertension for whom no evidence or suspicion of structural or functional glaucomatous damage exists, no anti-glaucomatous drug treatment or washed-out for 4 weeks, IOP symmetry of ± 3 mm Hg between fellow eyes, aged 18-80 years.</p> <p>Exclusion criteria: patients who had eye surgery in the last 3 months, corneal or conjunctival abnormality hindering contact lens adaptation, wear of full frame metallic glasses during SENSIMED Triggerfish recording, severe dry eye, secondary forms of open angle glaucoma, allergy to corneal anaesthetic.</p>
Primary outcomes	The SENSIMED Triggerfish device's capacity to detect changes in IOP-related patterns from wake to sleep, and its ability to detect ocular pulse frequency concurrent to heart rate.
Statistical methods	Not reported.
Participants	33 patients with or without glaucoma (32 completed).
Results	See table 14.
Conclusions	These preliminary results in a trial record showed that the SENSIMED Triggerfish is associated with adverse events but none was serious.
Abbreviations: IOP, intraocular pressure; POAG, primary open angle glaucoma.	

Table 13 Summary of the interventional study: Tojo et al. (2013)

Study component	Description
Objectives/hypotheses	To examine the effects of SLT on IOP-related patterns in patients with normal tension glaucoma using the SENSIMED Triggerfish.

Study design	Interventional study.
Setting	Patients were recruited between April 2012 and November 2012 in a hospital in Japan. All patients had SLT, and had IOP measurement and 24-hour recording with the SENSIMED Triggerfish before and after treatment.
Inclusion/exclusion criteria	<p>Diagnosis of NTG was made if all of the following criteria were satisfied: presence of glaucomatous optic disc neuropathy with corresponding visual field defects; a threshold examination of Swedish interactive thresholding algorithm 30-2 program showing 'outside normal limits' in a glaucoma hemifield test and a cluster of 3 contiguous points on the pattern deviation plot depressed at $p < 5\%$ level; an open angle by gonioscopy; and a baseline IOP < 21 mm Hg.</p> <p>Inclusion criteria: NTG for over 20 years, BCVA ≥ 0.3, spherical equivalent < -6 dioptres, and no clinical problems in the ocular surface for wearing contact lens for 24 hours.</p> <p>Exclusion criteria: pseudo exfoliation syndrome, neovascular glaucoma, steroid glaucoma, primary angle closure glaucoma, history of ocular trauma, history of retinal diseases or uveitis, history of vitrectomy, and history of laser trabeculoplasty or other glaucoma surgeries.</p>
Primary outcomes	No primary outcome was defined. Other outcomes included range of IOP-related patterns measured by the SENSIMED Triggerfish before and after SLT (including nocturnal and diurnal measurements), complications and corneal changes.
Statistical methods	The range of IOP-related patterns, which was defined as the difference between the maximum and minimum value during the course of 24 hours, was calculated from the data of IOP-related patterns. Wilcoxon signed-rank test was used for statistical analyses.
Participants	10 people with NTG.
Results	See table 14.

Conclusions	The range of IOP-related patterns measured by the SENSIMED Triggerfish over 24 hours showed no statistically significant difference before and after SLT. The range of nocturnal fluctuations was significantly different before and after SLT. Minor complications were reported which resolved quickly and without treatment
Abbreviations: BCVA, best corrected visual acuity; IOP, intraocular pressure; NTG, normal tension glaucoma; SLT, selective laser trabeculoplasty.	

Table 14 Summary of results from non-randomised studies

Study	Agnifili et al. 2014
Design	Open, uncontrolled, observational study, n=30
Safety	4 people (13.3%; 3 with glaucoma and 1 without) reported blurred vision; 30 patients (100%) reported diffuse conjunctival hyperaemia; 12 study eyes (40%) developed superficial punctate keratitis and 2 eyes (6.7%) showed a conjunctival pressure mark from the contact lens sensor edge. No significant changes in BCVA were found after sensor removal.
Technical information relating to measurement capabilities	Differences in SENSIMED Triggerfish trends between patients with and without glaucoma were seen ($p < 0.05$). Other outcomes were reported but not relevant.
Study	De Smedt et al. 2012
Design	Open, uncontrolled, observational study, n=10
Patient tolerability/ acceptability	Comfort scores did not change significantly from 8.35/10 at 5 minutes after fitting to 7.5/10 at 24 hours after fitting (it is not clear whether the sensor was in place at the 24-hour time point). The minimum detectable difference was 1.84 ($p = 0.16$).

<p>Safety</p>	<p>9 patients (90%) had localised fluorescein-positive staining and 1 (10%) had generalised staining after device removal; 3 (30%) had a corneal epithelial micro-defect/abrasion for which ofloxacin antibiotics were prescribed (resolved quickly). Contact lens impression mark was seen in 8 patients (80%).</p> <p>BCVA significantly reduced while wearing the SENSIMED Triggerfish (1.07 to 0.85; p=0.008). This reduction did not continue beyond 48 hours after removal of the device.</p> <p>Lubrication of the sensor lens surface was good in 9 eyes (90%) at baseline, but 1 eye showed hydrophobic spots. There was no significant change in this parameter after 30 minutes or 4, 12 and 24 hours. Lens mobility reduced during the 24 hours in which the SENSIMED Triggerfish was in place; during the final visit no spontaneous mobility was present in 9 eyes (90%) and in 1 eye (10%) it was difficult. At 24 hours the push-up test was difficult in all eyes. Decentration of the sensor lens in the vertical axis was seen in 7 patients; the authors report that this may indicate a too tight fit. At the time of publication only 1 lens size was available (8.7 mm curvature radius).</p> <p>In 2 patients disconnection between cable and antenna was seen.</p>
<p>Technical information relating to measurement capabilities</p>	<p>Other outcomes reported but not relevant.</p>
<p>Study</p>	<p>Faschinger and Mossbock 2013 (letter to editor)</p>
<p>Design</p>	<p>Open, semi-comparative, observational study, n=5.</p>
<p>Technical information relating to measurement capabilities</p>	<p>Applanation tonometry (method not specified) showed an increasing slope when patients were positioned to artificially increase IOP (supine or with head and thorax down). No agreement in curve profiles were seen between applanation and the SENSIMED Triggerfish, and no statistics were reported. Repeated applanation curves looked similar on the publication graph, whereas repeated SENSIMED Triggerfish curves looked less similar.</p>
<p>Study</p>	<p>Freiberg et al. 2012</p>

Design	Open, uncontrolled, observational study, n=20
Safety	<p>4 adverse events were reported (20%). 1 patient reported moderate eye irritation and blurred vision; another had severe ocular hyperaemia and was diagnosed with a bacterial conjunctivitis.</p> <p>Issues not defined as adverse events were superficial punctate keratitis in 10 eyes (50%), conjunctiva contact lens sensor edge pressure mark in 2 eyes (10%), and diffuse conjunctiva hyperaemia in all study eyes (100%).</p> <p>No significant changes in BCVA were reported (no data reported).</p>
Technical information relating to measurement capabilities	Mean ultrasound CCT changed from 523 to 537 micrometres ($p=0.015$) in the eyes wearing the SENSIMED Triggerfish device, and from 518 to 522 micrometres in the opposite eyes ($p=0.206$).
Study	Hervas Ontiveros et al. 2013
Design	Open, uncontrolled, observational study, n=8.
Diagnostic accuracy/ efficacy	Authors report that 1 patient was surgically intervened following high IOP measurements during the trial, although it is unclear whether SENSIMED Triggerfish or GAT measurements provided this information.
Patient tolerability/ acceptability	2 patients (25%) did not complete SENSIMED Triggerfish recording due to device intolerance (both reported discomfort such as a foreign body feeling and moderate conjunctival hyperaemia).
Serious adverse events	None.
Technical information relating to measurement capabilities	Other outcomes reported but not relevant.
Study	Hollo et al. 2014
Design	Interventional study, n=9.

Safety	<p>100% of patients had mild transient conjunctival hyperaemia which resolved within 48 hours after SENSIMED Triggerfish recording; 1 patient (11%) had moderate discomfort and corneal epithelial defects which healed spontaneously in 1 day; 1 patient (11%) had mild corneal epithelium erosion with no discomfort which also healed spontaneously within 1 day; 1 patient (11%) had acute conjunctivitis treated with topical levofloxacin medication which healed in 4 days.</p>
Technical information relating to measurement capabilities	<p>Comparison of the means of 3 SENSIMED Triggerfish curves (2 untreated baseline curves and 1 curve under treatment with IOP-lowering medication) showed no difference (152.94, 142.35, and 132.98 au; $p=0.273$). Differences in mean GAT measurements over 24 hours before and after treatment were significantly different (22.91 ± 5.11 mm Hg after wash-out of medication and 8.24 ± 2.49 mm Hg at 3 months of IOP-lowering treatment ($p < 0.001$). This suggests that IOP-lowering medication did not change the shape of 24-hour SENSIMED Triggerfish curves, in contrast to GAT measurements.</p> <p>Mean differences in GAT IOP values from immediately before SENSIMED Triggerfish fitting and immediately after its removal did not differ significantly from zero, either when the untreated baseline values (mean difference: -0.722 mm Hg) or the values measured under treatment (mean difference: 0.111 mm Hg) were compared ($p=0.083$ and 0.884 respectively). In contrast, when the mean value of the first 50-minute period of the SENSIMED Triggerfish curve was subtracted from the mean of the last 50-minute values, the difference was significant for both the untreated and the treated periods (mean difference: 233.56 and 203.34 au; $p=0.001$ and <0.001 respectively).</p> <p>No correlation was seen between the difference of the first and last 50-minute periods of the SENSIMED Triggerfish curves (mean values) and the corresponding difference of the first and last GAT IOP values either at baseline (Pearson correlation, $r=-0.223$; $p=0.546$) or under treatment ($r=0.320$; $p=0.402$).</p>
Study	Lorenz et al. 2013
Design	Open, uncontrolled, observational study, $n=40$.

Patient tolerability/ acceptability	<p>95% of patients with glaucoma (19/20) agreed to use the device again. Mean discomfort measured on a VAS was 21.82 (range 7–67, median 13.5) in the healthy group and 26.8 (range 0–71, median 22) in patients with glaucoma. Mean VAS for all patients was 24.3.</p> <p>38 patients (95%) completed the study; 1 patient without glaucoma did not continue with monitoring due to improper device fitting (the device was too big and did not stay in place); 1 patient with glaucoma discontinued the study due to severe foreign body sensation and pain. The device was removed after 40 minutes and deterioration of corneal epithelial staining was detected. Discomfort had resolved after 1 hour. Retrospective analysis of the device by the manufacturer showed an incorrect encapsulation of the microelectronic components.</p>
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Safety	<p>A total of 32 patients had an adverse event (80%) which was probably or definitely related to the study device (table below). All adverse events resolved within 2 days.</p> <ul style="list-style-type: none">• Any adverse event: 80% of all participants (75% of healthy participants; 85% of glaucoma patients).• Corneal epithelium defect: 58% of all participants (45% of healthy participants; 70% of glaucoma patients).• Visual acuity reduced: 20% of all participants (20% of healthy participants; 20% of glaucoma patients).• Foreign body sensation: 15% of all participants (10% of healthy participants; 20% of glaucoma patients).• Conjunctival hyperemia: 15% of all participants (10% of healthy participants; 20% of glaucoma patients).• Eye irritation: 8% of all participants (0% of healthy participants; 15% of glaucoma patients).• Lacrimation increased: 5% of all participants (5% of healthy participants; 5% of glaucoma patients).• Eye pain: 5% of all participants (0% of healthy participants; 10% of glaucoma patients).• Conjunctivitis bacterial: 5% of all participants (10% of healthy participants; 0% of glaucoma patients).• Conjunctival haemorrhage: 3% of all participants (0% of healthy participants; 5% of glaucoma patients).• Eyelid oedema: 3% of all participants (5% of healthy participants; 0% of glaucoma patients).• Sicca syndrome: 3% of all participants (0% of healthy participants; 5% of glaucoma patients).• Abnormal sensation in eye: 3% of all participants (5% healthy participants; 0% glaucoma patients).
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	<ul style="list-style-type: none"> • Visual impairment: 3% of all participants (0% of healthy participants; 5% of glaucoma patients). • Discomfort: 3% of all participants (0% of healthy participants; 5% of glaucoma patients). • Administration site reaction (injury): 3% of all participants (0% of healthy participants; 5% of glaucoma patients). <p>The following study parameters showed statistically significant changes when compared before and after fitting of the SENSIMED Triggerfish device: conjunctival oedema, (mean change=0.18; p=0.0016); conjunctival erythema (mean change=1.05; p<0.001); epithelial defects (mean change=1.08; p<0.001); lid oedema (mean change=0.16; p=0.063).</p>
Serious adverse events	No serious adverse events were reported; 11% of adverse events were deemed severe: corneal epithelial defects (n=3), sharp pain in the eye (n=1) and conjunctival erythema (n=1). All adverse events resolved within 2 days.
Study	Mansouri and Shaarawy 2011
Design	Open, uncontrolled, observational study, n=15.
Diagnostic accuracy/ efficacy	Following the findings of 24-hour recording with the SENSIMED Triggerfish, therapy was changed in 11 patients (73%).
Patient tolerability/ acceptability	13 patients (87%) completed 24-hour SENSIMED Triggerfish recording. Of the 2 who did not, 1 had pre-existing severe dry eye disease and discontinued IOP-related recording after 13 hours due to device intolerance; the device malfunctioned in the other. Average patient score for comfort was 7 out of 10.
Safety	5 minor complications were reported: 1 case of corneal erosion in a patient with severe dry eye disease and 4 cases of superficial punctate keratitis. All complications resolved after 24 hours.
Serious adverse events	None (0%)

Study	Mansouri et al. 2012
Design	Open, uncontrolled, observational study, n=40.
Patient tolerability/ acceptability	Mean comfort score for all patients was 27.2 out of 100 (SD 18.5) in the first recording session with SENSIMED Triggerfish and 23.8 (SD 18.7) in the second session a week later. Poor tolerability was reported in 4 patients in the first session and 3 patients in the second session.
Safety	151 adverse events were reported, of which 149 (in 38 patients) were device-related (142 were classified as mild). There were 77 in the first session and 72 in the second; 2 patients had moderate adverse events (1 superficial punctate keratitis and 1 blurred vision); 33 (82%) had blurred vision, 32 (80%) had hyperaemia of the bulbar alpebral conjunctiva, and 6 (15%) had superficial punctate keratitis. All adverse events resolved within 24 hours and there was none in the opposite eye. 15% of patients developed corneal staining. Technical issues which prevented complete data recording occurred in 4 cases: battery insufficiency (2), disconnection of device (1) and unknown (1).
Serious adverse events	No serious adverse events were reported during the study. Two patients exhibited conjunctival hyperaemia that was qualified as severe (5 of 149 events) but these severe adverse events were resolved within 24 hours.
Technical information relating to measurement capabilities	Correlation of two 24-hour recording sessions was $r=0.59$ (defined as a fair to good correlation).
Study	Mottet et al. 2013
Design	Open, uncontrolled, observational study, n=12.

<p>Technical information relating to measurement capabilities</p>	<p>ICCs were measured to compare SENSIMED Triggerfish measurements across repeated visits. ICCs were significant (indicating fair to good agreement according to the authors) for 9 of 25 readings for the device.</p> <p>Results show that the SENSIMED Triggerfish cannot estimate the absolute value of IOP in mm Hg when using pre- and post-SENSIMED Triggerfish GAT measurements or when using pre- and post-SENSIMED Triggerfish NCT measurements.</p> <p>It is not possible to use the relative change in SENSIMED Triggerfish signal multiplied by the IOP measured before the SENSIMED Triggerfish fitting to estimate the absolute IOP at each point of the 24-hour session.</p> <p>Regarding the pre-session and post-session measurements with GAT and NCT, the agreement on the change in IOP between the SENSIMED Triggerfish and NCT or GAT was also poor. Bland-Altman analyses suggest that SENSIMED Triggerfish overestimates the large IOP changes compared with NCT.</p>
<p>Study</p>	<p>Pajic et al. 2011</p>
<p>Design</p>	<p>Interventional study, n=5.</p>
<p>Technical information relating to measurement capabilities</p>	<p>In 3 patients absolute device output values were generally lower with IOP-lowering treatment than without, and for 2 patients SENSIMED Triggerfish output was lower in the control session (without IOP-lowering treatment) than in the treated session (the publication text contains an error relating to this point; the figures are assumed to be correct). There was no relationship between the reference GAT IOP values before and after device recording and the respective initial and final device output (no statistical testing done).</p>
<p>Study</p>	<p>Trial record (NCT01390779): Efficacy of 24-hour IOP recording with the SENSIMED Triggerfish</p>
<p>Design</p>	<p>Open, uncontrolled, interventional study, n=33.</p>
<p>Safety</p>	<p>Adverse events were recorded in 15 of 33 patients: 8 (24%) ocular hyperaemia, 7 (21%) punctate keratitis, 5 (15%) eye pressure mark, 1 (3%) blurred vision, 1 (3%) eyelid oedema and 1 (3%) corneal disorder.</p>

Serious adverse events	0 (0%)
Study	Tojo et al. 2013
Design	Interventional study, n=10.
Safety	Minor complications were reported in some cases (number not reported), such as conjunctivitis, slight hyperaemia, or peripheral corneal oedema in the eyes following SENSIMED Triggerfish wear for 24 hours. These complications resolved within a few days (exact duration not reported) and without treatment. Visual acuity did not change before or after SLT.
Serious adverse events	No serious complications were observed.
Technical information relating to measurement capabilities	Mean IOP measured by tonometry at 1 month was significantly reduced following SLT (p=0.002). This was not reflected in the SENSIMED Triggerfish results (measured post-operatively at 1-2 months); there was no significant change in 24-hour IOP changes before and after SLT (p=0.77). Nocturnal changes were significantly different before and after SLT (p=0.014).
Abbreviations: BCVA, best corrected visual acuity; GAT, Goldmann Applanation Tonometry; ICC, intraclass correlation; IOP, intraocular pressure; n, number of patients; NCT, non-contact tonometry; NTG, normal tension glaucoma; POAG, primary open angle glaucoma; SD, standard deviation; SLT, selective laser trabeculoplasty; VAS, visual analogue scale.	

Nine newly-completed or ongoing trials on the SENSIMED Triggerfish device were identified:

- Study ID 12426: Continuous Recording of Short Time Fluctuations in Intraocular Pressure using the Sensimed Triggerfish Sensor (Observational). This trial has completed recruitment (in follow-up) and has not been published.

- [NCT01972997](#): A Single-center, Randomized, Double-blinded, Prospective Study to Assess the Changes in the 24-hour IOP (Intraocular Pressure) Pattern in Relation to SENSIMED Triggerfish Sensor Sizes in Healthy Subjects. This trial has completed but has not been published.
- [NCT01906138](#): A Prospective, Open Label Study Assessing the 24-hour Intraocular Pressure Pattern Monitored by SENSIMED Triggerfish in Primary Angle Closure and Primary Angle Closure Glaucoma Patients, Before and After Laser Peripheral Iridotomy. This trial has completed but has not been published.
- [NCT01906502](#): A Prospective, Open Label Study to Assess the 24-hour IOP Pattern Recorded With SENSIMED Triggerfish in a Healthy Population. This trial has completed but has not been published.
- [NCT01767753](#): A Prospective, Observational, Open Label Study to Assess the 24-hour IOP Fluctuation Pattern Recorded With SENSIMED Triggerfish in Patients With Primary Open-angle Glaucoma, Before and After Selective Laser Trabeculoplasty. This trial has completed but has not been published.
- [NCT01467453](#): Clinical Application of Sensimed Triggerfish Sensor (TS) With Wireless Signal Transmission for Continuous Intraocular Pressure Measurement. The trial record indicated that this study is currently recruiting participants (estimated completion date December 2012).
- [NCT01507584](#): The Effects of the Water Drinking Test on Intraocular Pressure of Glaucoma Patients Undergoing 24 Hour Continuous Monitoring With the SENSIMED Triggerfish. The trial record indicated that this study is currently recruiting participants (estimated completion date Sept 2012).
- [NCT01912599](#): Pilot Study on Ambulatory Intraocular Pressure and Blood Pressure Monitoring in Glaucoma. This trial has completed but has not been published.
- [NCT02030886](#): A Single-center, Open Label, Prospective Study Assessing the 24-hour IOP Patterns Using SENSIMED Triggerfish in Ocular Hypertensive Patients Newly Converted to Glaucomatous Disease Versus Stable Ocular Hypertensive Patients. The trial record indicated that this study is currently recruiting participants (estimated completion date October 2014).

Costs and resource consequences

No published evidence relating to the cost or resource consequences of using the SENSIMED Triggerfish in the NHS was identified for this briefing.

In order to provide 24-hour recording with the SENSIMED Triggerfish device, an NHS eye clinic would need to purchase a SENSIMED Triggerfish sensor, antenna, sleeve and booklet for every patient. In cases where patients are monitored before and after an intervention, such as medication or surgery, each patient would require another sensor, antenna, sleeve, and booklet. The clinic would also need to buy at least 1 each of the reusable data recorder, cable, battery charger and Bluetooth stick. In addition, it would need a computer with the SENSIMED Triggerfish software installed.

If another SENSIMED Triggerfish lens needs to be used because of an ill-fitting lens, patient discomfort, or after a lens is dropped or damaged during fitting, its cost would be doubled.

It is assumed that an NHS eye clinic would have the necessary equipment to perform eye examinations before and after placement of the SENSIMED Triggerfish sensor.

Each patient would require at least 2 sessions with an appropriately trained ophthalmologist or optometrist for the fitting and removal of the SENSIMED Triggerfish sensor. An eye examination including visual acuity, central corneal radius and thickness measurement, slit lamp examination, and IOP tonometry should be done during the SENSIMED Triggerfish fitting session. Slit lamp examination and tonometry should be done after the device is removed, as well as analysis of the SENSIMED Triggerfish output. There is no information on the time taken to carry out these sessions. There is also uncertainty as to how existing ophthalmology services would manage this additional staff need.

Strengths and limitations of the evidence

The key limitation of the available evidence was that no studies investigated the impact of the SENSIMED Triggerfish device on clinical outcomes, such as progression to glaucoma or vision deterioration. There was no evidence that having a better understanding of IOP-related patterns using the SENSIMED Triggerfish over 24 hours influenced the need for or success of any subsequent treatment. None of the selected studies show agreement between the SENSIMED Triggerfish and a reference standard, such as GAT (although correlations were analysed in some cases), and therefore there was no evidence

that the SENSIMED Triggerfish provided more informative results than conventional techniques.

An important barrier to interpretation of the study findings on the SENSIMED Triggerfish in its current form is that it records dimensional changes related to IOP patterns using a millivolt scale, which cannot be referenced or calibrated to a standard measure of IOP in mm Hg. Also, the patterns that the SENSIMED Triggerfish produces are qualitative, and the values that would indicate inadequate management of ocular hypertension have not yet been defined.

All studies included in this briefing had small sample sizes (the largest was 40 patients) and most did not report whether patients were consecutively recruited, therefore introducing the risk of selection bias. Despite being of interest from a safety point of view, inclusion of healthy adults may reduce the generalisability of results to people with suspected or established glaucoma.

Given the nature of the device, blinded studies would be inappropriate. There is a risk of reporting bias in open-label studies published to date, specifically in outcomes such as patient-reported adverse events and tolerability. Many studies provided neither clear definitions of what constitutes an adverse event or complication, nor descriptions of tolerability measures.

Two letters to editors (Faschinger and Mossbock 2013; Hervas et al. 2013) and 1 trial register entry (NCT01390779) were included in the evidence for this briefing. These publications have not been peer-reviewed and contained limited information on their methodology. As such, the results should be interpreted with caution.

Seven publications reported either financial support from or conflicts of interest from the authors. This may be a further source of bias.

Relevance to NICE guidance programmes

NICE has issued the following guidance:

- [Glaucoma quality standard](#) (2011) NICE quality standard 7
- [Glaucoma: Diagnosis and management of chronic open angle glaucoma and ocular hypertension](#) (2009) NICE guideline CG85

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The SENSIMED Triggerfish contact lens sensor for continuous 24-hour recording of ocular dimensional changes in people with or at risk of developing glaucoma (MIB14)

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NCT01390779 Trial Record: Efficacy of 24-hour Intraocular Pressure Fluctuation Recording With the SENSIMED Triggerfish Contact Lens Sensor (Principle investigator: John HK Lui)

Pajic B, Pajic-Eggspuchler B, Haefliger I (2011). Continuous IOP fluctuation recording in

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Search strategy and evidence selection

Search strategy

The following search strategy was used to search Ovid MEDLINE(R) 1946 to June Week 3 2014

1. (triggerfish and (lens or sensor or glaucoma or intra-ocular or intraocular or ocular)).ti,ab.
2. (Sensimed and triggerfish).ti,ab.
3. (Contact lens* adj5 (sensor or monitor*)).ti,ab.
4. ((Intra-ocular or intraocular) adj3 pressure adj3 (monitor* or measure*) adj5 lens*).ti,ab.
5. (Ocular adj5 telemetry adj5 sensor).ti,ab.
6. ((24-hour or continuous) adj3 intraocular adj3 pressure adj3 monitor*).ti,ab.
7. Tonometry, Ocular/ and Intraocular Pressure/ and Contact Lenses/
8. or/1-7

The following databases were also searched:

- Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations 30 June 2014.
- Embase 1974 to 2 July 2014.
- PsycINFO 1806 to June Week 4 2014.
- DARE (includes Cochrane library, NHS EED, HTA, CRD).

- Scopus (4 July 2014).

The above searches returned 306 references, and 196 references after duplicate removal.

Thirty-four trials on Triggerfish contact lens sensor (CLS) were identified in the preparation of this briefing.

Evidence selection

Retrieved references were independently sifted by 2 researchers using the following criteria:

- Population: adults with glaucoma, suspected glaucoma, ocular hypertension, normal tension glaucoma or healthy subjects.
- Intervention: SENSIMED Triggerfish contact lens sensor.
- Comparator: standard care (any tonometry device) or no comparator.
- Outcomes: safety (adverse events and complications), patient tolerability or acceptability, reproducibility of Triggerfish measurements, agreement with gold standard (Goldmann Applanation Tonometry; GAT), diagnostic accuracy compared with GAT, clinical outcomes such as control of intraocular pressure or progression to glaucoma or vision loss.

Exclusion criteria:

- non-English language (with no available translation)
- not relevant to selection criteria
- animal studies
- poster presentations (with no full text available)
- case reports with 2 or fewer participants.

In preparing this briefing, 23 published papers were identified relevant to the Triggerfish for monitoring intraocular pressure, 12 of which were excluded as they did not meet the inclusion criteria. The UK distributor provided a list of 19 published articles and 26 conference poster presentations which had either already been identified or did not meet

the inclusion criteria. Ultimately, 11 references met the selection criteria and were included in this briefing (Agnifili et al. 2014; De Smedt et al. 2012; Faschinger and Mossbock 2013; Freiberg et al. 2012; Hervas et al. 2013; Hollo et al. 2014; Lorenz et al. 2013; Mansouri et al. 2012; Mansouri and Shaarawy 2011; Mottet et al. 2013; Pajic et al. 2011). A single study with accompanying results was identified from a clinical trials register (NCT01390779) and included in this briefing.

Changes after publication

December 2015: One word replaced in the Adverse events and safety section of the summary table. One sentence added to the conclusions in table 13.

About this briefing

Medtech innovation briefings summarise the published evidence and information available for individual medical technologies. The briefings provide information to aid local decision-making by clinicians, managers, and procurement professionals.

Medtech innovation briefings aim to present information and critically review the strengths and weaknesses of the relevant evidence, but contain no recommendations and **are not formal NICE guidance**.

Development of this briefing

This briefing was developed for NICE by Cedar. The [interim process and methods statement](#) sets out the process NICE uses to select topics, and how the briefings are developed, quality assured and approved for publication.

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ISBN: 978-1-4731-0832-5