

Smart contact lenses: How far has glaucoma treatment gone?

Ognjenka Rahić^{1*}, Jasmina Hadžiabdić¹, Amina Tucak-Smajić¹, Merima Sirbubalo¹,
Lamija Hindija¹, Marija Glavaš-Dodov², Edina Vranić^{1*}

¹University of Sarajevo - Faculty of Pharmacy, Zmaja od Bosne 8, 71000 Sarajevo, Bosnia and Herzegovina

²Faculty of Pharmacy, University Ss. Cyril and Methodius, Majka Tereza 47, 1000 Skopje, N. Macedonia

Introduction

Glaucoma, known as the "silent thief of vision", is the most common cause of treatable blindness worldwide, with a prevalence expected to be around 112.0 million by 2040 (Tham et al., 2014). Glaucoma is the common name for a group of progressive, neurodegenerative diseases caused in most cases by elevated intraocular pressure (IOP).

IOP reduction is the primary goal of glaucoma treatment, as studies have shown that it can prevent the development and progression of glaucoma (Heijl et al., 2002). Treatment of glaucoma, like other chronic disorders, has two major drawbacks: first, there are the disadvantages of conventional ophthalmic dosage forms, such as low drug bioavailability and quick drainage due to lacrimation. The second issue is patients' non-adherence, which is primarily due to their forgetfulness (Kass et al., 2002). To provide the best possible treatment for patients, extensive research is conducted in two directions: therapy optimization and the development of innovative drug delivery systems.

IOP monitoring Contact lenses (CLs)

Contact lenses (CLs) have been developed as one of solutions to these problems because they are non-invasive, come into direct contact with the eye, and can be worn on the cornea with minimal discomfort for the patients. There are numerous IOP monitoring (smart) CLs and antiglaucomatous drug-eluting CLs.

The gold standard for IOP monitoring is the Goldmann applanation tonometer. Its main drawback is need for anesthesia, as tonometer's tip must be pressed onto the cornea surface. In line with that goes the fact that its positioning requires trained personnel. And lastly, it provides the IOP levels in an awake state and in an

upright position during office hours. This cannot give the optimal picture of a patient's IOP levels, as it is known that IOP levels fluctuate considerably during sleep and with eyes closed (Renard et al., 2010). As solution to these problems, several different IOP monitoring CLs have been developed.

Triggerfish[®], commercially developed by SENSIMED based on research by Leonardi et al., was the first IOP monitoring CLs approved by European Regulatory Authorities in 2009 and by the FDA in 2016 (Chen et al., 2021). Triggerfish[®] is a device that combines smart CLs with electromechanical microsensor to detect spontaneous circumferential changes in the corneoscleral region. The information from the CLs is wirelessly received by the adhesive SENSIMED Triggerfish[®] antenna, which is positioned around the eye. The data is then sent from the antenna to the portable recorder via a small flexible connection. During the monitoring session, the patient's recorder records the data collected. The data is uploaded from the recorder to the software already installed on the practitioner's computer through Bluetooth at the end of the recording period. This device records the IOP profile over a 30-second period every 5 minutes during a 24-h period (Dunbar et al., 2017).

Pang et al. created CLs with a Wheatstone bridge circuit in 2019 to increase the detection of weak eyeball deformations, which is advantageous for high sensitivity and precision. Two active and two passive strain gauges were created using lithography and deposition techniques. A contact lens shape was created using a thermal model and then encased in a biocompatible polydimethylsiloxane (PDMS) layer. It had a good dynamic reaction to IOP changes at varied speeds (Pang et al., 2019).

Another idea is to use microfluidics in CLs to detect IOP. They are made up of PDMS soft CLs with embedded micro-fluidic channel that is partially filled

with incompressible fluid. This device displays the changing volume of the microchannel as the fluid displaces in response to any volume change. Patients who are wearing these CLs will take pictures of them with their phones throughout the day (Campigotto et al., 2020).

By superimposing a camera-captured image onto the micropattern of the contact lens using a computer-assisted virtual reference image, Lee et al. constructed CLs with moiré patterns of concentric circles that detected IOP changes. This device also allowed for the elution of integrated drug from a thermo-responsive nanogel drug carrier (Lee et al., 2020).

Kim et al. developed and tested a soft CLs for continuous IOP monitoring with a smartphone in volunteers. A strain sensor, a wireless antenna, capacitors, resistors, stretchy metal interconnectors, and an integrated circuit for wireless communication are all included in the CLs. The CLs were able to accurately measure IOP without causing inflammation (Kim et al., 2021).

Dou et al. designed a wearable CL IOP sensor based on a platinum strain gauge coated in a polyamide insulating layer and packaged in transparent PDMS using a micro-electro-mechanical method. It demonstrated outstanding repeatability and a dynamic responsiveness to varying IOP change speeds (Dou et al., 2021).

In addition to elevated IOP, it has been demonstrated that Matrix Metalloproteinase-9 (MMP-9) is overexpressed in glaucoma patients' tears. With this in mind, Ye et al. developed optical-based dual-function CLs for simultaneous detection of IOP and MMP-9. IOP is measured by changing the color of an antiopal structure, which eliminates the need for complicated electronics. The quantification of MMP-9 is achieved in genuine tear samples using the peptide modified gold nanobowls surface-enhanced Raman scattering substrate. The structural color is created by selective diffraction of light from a unique 3D periodic structure, and it may be modified by changing the periodic structure's refractive index or lattice spacing. Because these CLs use structural color, any potential electronic component eye harm can be avoided (Ye et al., 2022).

Conclusion

Since glaucoma is very important health concern worldwide, researchers are persistent in their efforts to find solution to prevent and cure glaucoma more effectively, due to several limitations of traditional medication as well as patient nonadherence. One of the pathways they are taking is to identify best possible instrument for IOP monitoring that will be most convenient for patients, as IOP elevation and variation are key risk factors of glaucoma progression. Concept behind employing CLs in IOP monitoring is that when IOP

varies, so does eye curvature. Electronic parts make up most CLs, with detection software on computer or smartphone. However, most recent study is focused on finding way to avoid using electronics and instead employ less irritating approaches.

References

- Campigotto, A., Leahy, S., Zhao, G. et al., 2020. Non-invasive intraocular pressure monitoring with contact lens. *Br. J. Ophthalmol.* 104, 1324-1328. <https://doi.org/10.1136/bjophthalmol-2018-313714>
- Chen, X., Wu, X., Lin, X. et al., 2021. Outcome, influence factor and development of CLS measurement in continuous IOP monitoring: A narrative review. *Cont. Lens Anterior Eye* 44, 101376. <https://doi.org/10.1016/j.clae.2020.10.006>
- Dou, Z., Tand, J., Liu, Z. et al., 2021. Wearable contact lens sensor for non-invasive continuous monitoring of intraocular pressure. *Micromachines* 12, 108. <https://doi.org/10.3390/mi12020108>
- Dunbar, G.E., Shen, B.Y., Aref, A.A., 2017. The Sensimed Triggerfish contact lens sensor: efficacy, safety, and patient perspectives. *Clin. Ophthalmol.* 11, 875-882. <https://doi.org/10.2147/OPHTH.S109708>
- Heijl, A., Leske, C., Bengtsson, B. et al., 2002. Reduction of intraocular pressure and glaucoma progression. *Arch. Ophthalmol.* 120, 1268-1279. <https://doi.org/10.1001/archophth.120.10.1268>
- Kass, M.A., Heuer, D.K., Higginbotham E.J. et al., 2002 The Ocular Hypertension Treatment Study. *Arch. Ophthalmol.* 120, 701-713. <https://doi.org/10.1001/archophth.120.6.701>
- Kim, J., Park, J., Park, Y.-G. et al., 2021. A soft and transparent contact lens for the wireless quantitative monitoring of intraocular pressure. *Nat. Biomed. Eng.* 5, 772-782. <https://doi.org/10.1038/s41551-021-00719-8>
- Lee, S.-H., Shin, K.-S., Kim J.-W. et al., 2020. Stimulus-responsive contact lens for IOP measurement or temperature-triggered drug release. *Transl. Vis. Sci. Technol.* 9, 1-9. <https://doi.org/10.1167/tvst.9.4.1>
- Pang, Y., Li Y., Wang, X. et al., 2019. A contact lens promising for non-invasive continuous intraocular pressure monitoring. *RSC Adv.* 9, 5076-5082, doi: 10.1039/c8ra10257k
- Renard, E., Palombi, K., Gronfier C. et al., 2010. Twenty-four hour (nyctohemeral) rhythm of intraocular pressure and ocular perfusion pressure in normal-tension glaucoma. *Invest. Ophthalmol. Vis. Sci.* 51, 882-889. <https://doi.org/10.1167/iovs.09-3668>
- Tham, Y.C., Li, X., Wong, T.Y. et al, 2014. Global prevalence of glaucoma and projections of glaucoma burden through 2040: A systematic review and meta-analysis. *Ophthalmology* 121, 2081-2090. <https://doi.org/10.1016/j.ophtha.2014.05.013>
- Ye, Y., Ge, Y., Zhang, Q. et al., 2022. Smart contact lens with dual-sensing platform for monitoring intraocular pressure and matrix metalloproteinase-9. *Adv. Sci.* 9, 1-11. <https://doi.org/10.1002/advs.202104738>