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Research Article

Contact Lens that Enabled Early Diagnosis for Diseases Induced by Oxidative Stress and Potassium Ion (K+) in Ocular Tissues

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ABSTRACT

The present study used sensor technology to design a lens that could replace a docto.r It consists of an oxidative stress sensor, a (K+) ion sensor and a pressure sensor placed on a Lotrafilcon A silicone hydrogel lens for early diagnosis, as well as a recording and display device that the user can use on their own, recording 24 hours a day and alerting when needed. Additionally, power will be provided to the sensors for data transmission via an external wireless power transfer device. The oxidative stress sensor detects oxidative stress in the structures of the eye and indicates that the patient may have an abnormal condition like diabetic retinopathy, glaucoma and cataracts. Likewise, the (K +) ion sensor detects the (K +) ion concentration in the ocular cells and detects abnormal conditions where the concentration is elevated. The pressure sensor allows the intraocular pressure of patients diagnosed with glaucoma to be kept under control. This way, diseases can be diagnosed early, and continuous monitoring and control of the disease will be ensured. This will prevent the user from having to make frequent visits to the hospital, while also reducing the workload.

Keywords: *Cataract, Contact lens, Diabetic retinopathy, Migraine, Oxidative stress, Potassium ion (K+) sensor.*

Oküler Dokularda Oksidatif Stres ve Potasyum İyonunun (K+) Tetiklediği Hastalıklarda Erken Teşhis İmkâni Sağlayan Kontakt Lens

ÖZ

Çalışmada, bir doktorun yerini alabilecek bir lens tasarlamak için sensör teknolojisi kullanıldı. Erken teşhis için silikon hidrojel lens olan Lotrafilcon A üzerine yerleştirilecek oksidatif stres sensörü, (K+) iyon sensörü ve basınç sensörünün yanı sıra kullanıcının kendi başına kullanabileceği bir kayıt ve görüntüleme cihazından oluşur, 24 saat kayıt yapar ve gerekirse uyarı verir. Ek olarak, harici bir kablosuz güç aktarım cihazı aracılığıyla veri iletimi için sensörlere güç sağlanacaktır. Kullanılan oksidatif stres sensörü ile göz yapılarında oksidatif stres saptanır, hastada diyabetik retinopati, glokom ve katarakt için anormal bir durumun ortaya çıkabileceği anlaşılır. Aynı şekilde (K +) iyon sensörü de oküler hücrelerdeki (K +) iyon konsantrasyonunu tespit eder, konsantrasyonun arttığı anormal durumları tespit eder. Kullanılacak basınç sensörü ile glokom tanısı alan hastaların basıncı kontrol altında tutulur. Oluşabilecek hastalıkların erken teşhisi, eğer bir hastalık varsa hastalığın sürekli izlenmesi ve kontrolü sağlanacaktır. Bu, kullanıcının sürekli hastaneye gitmesini önlerken aynı zamanda iş yükünü de azaltacaktır.

Anahtar Kelimeler: *Katarakt, Kontakt lens, Diyabetik retinopati, Migren, Oksidatif stres, Potasyum iyon (K+) sensörü*

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I. INTRODUCTION

People's desire for individualized healthcare has grown dramatically as their living levels and quality of life have improved. Despite this desire, proper illness diagnosis and therapy are presently available. [1]

Since the eye is a structure directly connected to nerve cells, the damage caused by these diseases in the body is usually irreversible. For this reason, the early detection opportunity provided by the use of lenses is a promising method to prevent these damages. Wearable medical gadgets that are personalized to the individual, convenient, and capable of getting real-time information about the health of the human body are in high demand.[2-7]

Previous studies on electronic contact lenses have generally focused only on the pressure parameter in the eye and aimed to control glaucoma, not diagnose it.

For example, in the 11th issue of Clinical Ophthalmology published in 2017, Grace E. Dunbar, Bailey Yuquan Shan and Ahmad A. Aref used a CLS Triggerfish device with a soft silicone contact lens that remained on the ocular surface for 24 hours. They used pigs in their experiments and showed a high correlation between CLS output and intraocular pressure. The working principle of the Triggerfish cls is simply stated as follows; the contact lens receives information from the power meter and transmits it to an adhesive antenna placed on the patient's eye area, and the antenna in turn sends information to the wearable recorder worn by the patient. [8]

Because magnesium homeostasis is so tightly linked to calcium, sodium, and potassium homeostasis, any changes in magnesium homeostasis are bound to be associated with calcium, sodium, and potassium homeostasis, and vice versa. Clearly, changes in magnesium homeostasis can have a major impact on cellular and molecular activities, as well as constitute the basis of various clinical diseases.The lens, in particular, is as vulnerable to alterations in magnesium homeostasis as any other organ in the body. The structural and functional integrity of the lens, which is critical in transmitting light to the retina, is heavily reliant on the preservation of intracellular and extracellular ionic homeostasis. [9]

As a result, failure of Na+/K+ATPase in the presence of magnesium deprivation results in intracellular potassium depletion (Bara et al. 1993; Iezhitsa 2005; Iezhitsa and Spasov 2008) and intracellular sodium buildup. [10-11]. Oxidative stress is known to play a significant role in the pathogenesis of age related macular degeneration . [12]

The ocular disorders related to the anterior segment of the eye, including dry eye, keratoconus, conjunctiva, uveitis, and cataract, share similar characteristics that facilitate their diagnosis. Moreover, these diseases present a complex pathophysiology related to oxidative stress, tissue damage, and inflammatory pathway. [13]

The aim of this study is to enable early diagnosis of diseases such as diabetes, glaucoma, migraine and cataracts that cause specific symptoms in the eye, as well as diseases caused by specific reactions in the structures of the eye, using sensors embedded in a silicone hydrogel lens implanted in the eye.

In this study, the initial symptoms of diseases that can be diagnosed, the progression of the diseases and the damages to the person as a result of the diseases are explained in detail under the section titled literature summary. The equipment used in the lens and its principle of operation are detailed in the section titled materials and method.

Thanks to the lens designed in this study, it will be possible to develop more personalized treatment methods for users and improve the quality of their lives.

II. SUBJECT, SCOPE AND LITERATURE SUMMARY

The accuracy of IOP measured by conventional techniques such as Goldmann applanation tonometry is highly dependent on corneal stiffness.

In addition, it usually requires a visit to the doctor's office. Therefore, multiple or continuous measurement of IOP in glaucoma patients may better aid in the diagnosis, monitoring and management of the disease [14].

In such cases, telemetric detection is a viable way to meet this requirement. Thanks to telemetry, data can be collected externally from implanted sensor devices without wires.[15]

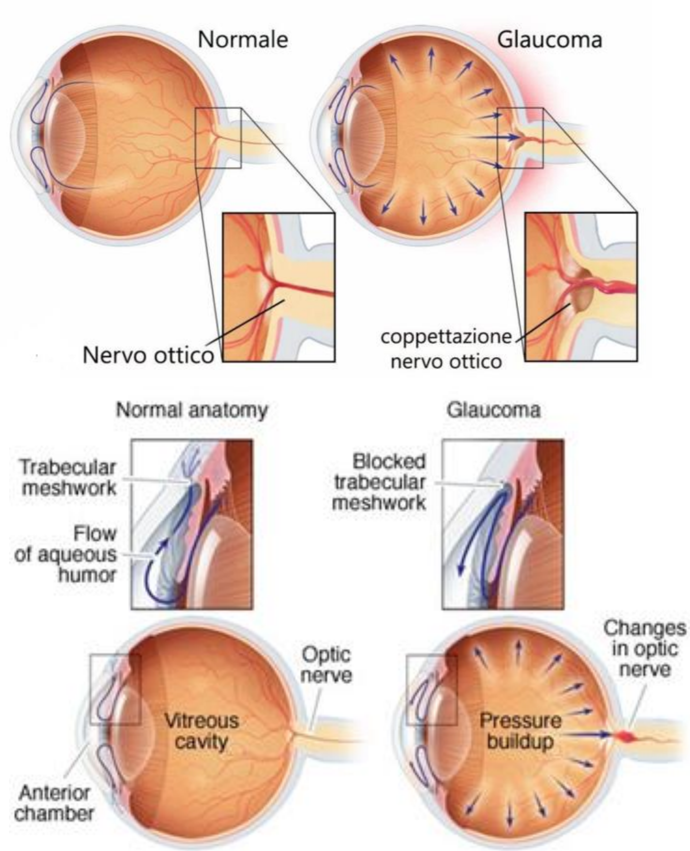

Figure 1. *The appearance of the optic nerve in the normal eye and the eye with glaucoma [15]*

In most glaucoma patients, when fluid intake is less than the flow rate, intraocular pressure rises above the normal range due to increased resistance to fluid flow in the exit pathway, which leads to the loss of optic nerve tissue. Untreated peripheral vision problems can cause blindness [16]. This condition is painless and cannot be recognized directly or indirectly without pressure measurements. Therefore, accurate measurement of intraocular pressure is important in glaucoma patients [17].

Advanced diagnostic tools utilizing novel Micro-Electromechanical Systems (MEMS) have been pursued to provide detailed and continuous IOP histories[18]. However, from a practical point of view, the most difficult obstacle to clinical use is the surgical piercing of the cornea by the practicing clinician. Due to this, there is a demand for a minimally invasive sensor. Tonometry-like systems for IOP measurement that can be placed in the echocardiographic field have emerged as a new and exciting research area for MEMS applications. [19].

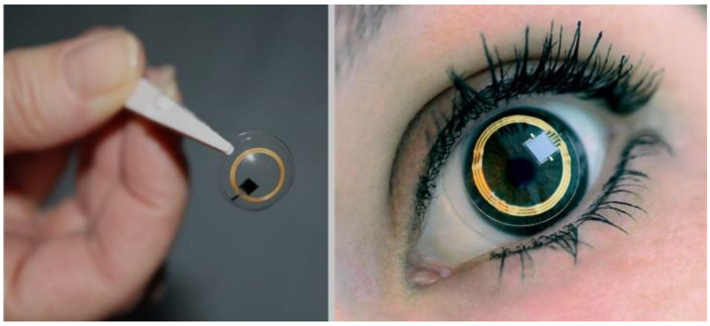

Figure 2. *A lens study with Bio-MEMS sensors .[18]*

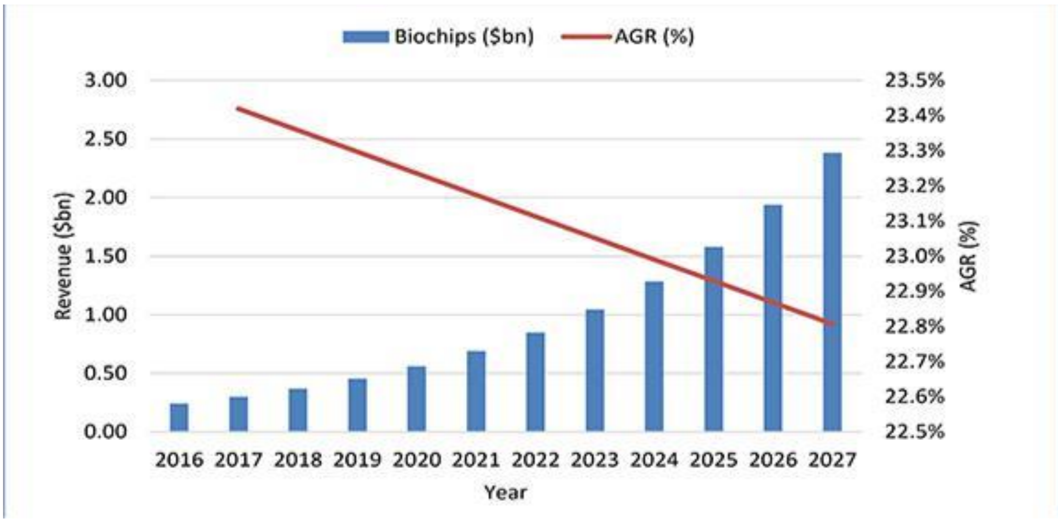

Figure 3. *Graph of Global implantable Bio-MEMS and Biochip usage.[19]*

Studies in Iran have shown that the mortality rate from some common diseases is very high and most of the deaths in these patients are due to lack of timely medical attention. It was concluded that the risk of death would be greatly reduced if patients were diagnosed or given medical care in a timely manner [20]. Using the Internet of Things, we developed glasses that have sensors inside to detect your eyes and send relavent information such as blood flow and eye fatigue to your smartphone. Based on appropriate algorithms, the smartphone detects optic nerve hypoperfusion, congestion or damage and sends an alert to the patient's mobile device.

This information, together with patient data, can be sent to doctors and emergency hospitals. Emergency hospitals can take immediate initiatives for patients. The patient can then be transferred to a medical center. Based on the information that the Internet of Things sends to health centers, doctors can take the necessary steps before patients reach the hospital. It can protect patients from the risk of blindness and complications. The glasses use voice alerts to notify you of the results. The color of the glasses frame indicates the patient's condition. Green: good condition; yellow: warning; red: danger for emergency patients. The glasses can also detect eye diseases such as cataracts, intraocular pressure, glaucoma and age-related macular degeneration (AMD). [20] Eye disease notifications and data analyzed over time can be displayed graphically, along with information about the patient's condition. In an emergency, the data can be sent to an ophthalmologist.

The advantages of this method are as follows.

I. Identifies possible eye problems.
2. Cheap and easy to use; allows everyone to get information at every level.
3. Prolongs healthy vision.
4. Reduces medical costs.

5. Language assistance can be provided for the visually impaired.
6. Accurate communication of information regarding eye health to ophthalmologists, emergency patients and their relatives.
7. Specification of the geographical location of patients and their relatives using GPS for emergencies.
8. Early detection of stroke and macular degeneration risk, preventing blindness and complications. [20]

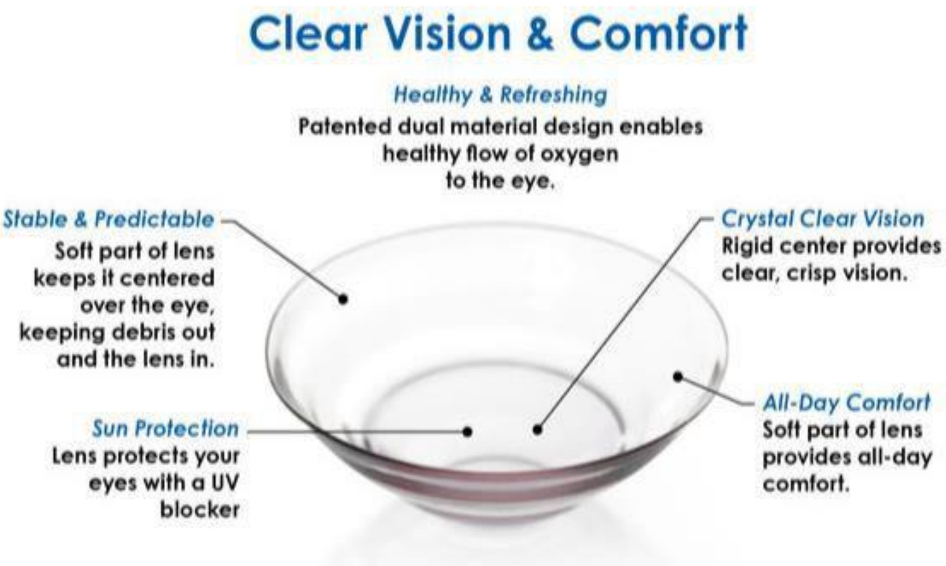

Figure 4. *The convenience and advantages of the lens to be used in the Project .[20]*

Diabetic eye disease is a group of eye diseases that affect people with diabetes. These diseases include diabetic retinopathy, diabetic macular edema (DME), cataracts, glaucoma and others. All types of diabetic eye disease can lead to severe vision loss and blindness. Diabetic retinopathy is a change in the blood vessels of the retina that causes bleeding, leaking and blurred vision. Diabetic retinopathy is the leading cause of blindness in diabetics and working-age adults. DME is a result of diabetic retinopathy, which causes swelling of the macula, a region of the retina. Early detection, treatment, regular check-ups and care can prevent vision loss due to diabetic eye disease. [21]

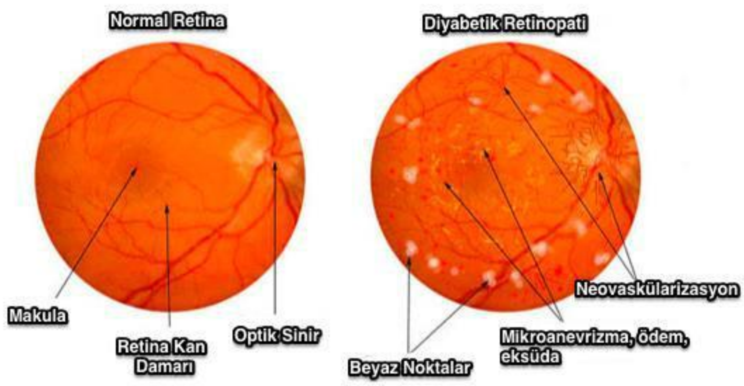

Figure 5. *Ratina image in normal eye and diabetic eye [21]*

Since migraine and glaucoma are two diseases in which vascular and neurologic factors are effective, we think that CCT (central corneal thickness) value in migraine patients is a point that should be paid special attention in the evaluation of glaucoma.[22.23].

CCT value has gained great importance in the clinical examinations of patients with glaucoma and OHT in recent years. The IOP value has been found to be lower than normal in patients with thin corneas and higher in patients with thick corneas.[24,26].

When determining the corneal thickness of the patient, taking at least 3 measurements close to each other, performing the measurements at approximately the same time of the day and excluding corneal pathologies in patient selection may increase the reproducibility of pachymetry. Age and corneal curvature may affect corneal thickness over the years. Studies have shown that patients with ocular hypertension have a thicker CCT and those with normotensive glaucoma have a thinner than normal CCT [27,28].

Past literature and related scientific data shed light on the importance of this particular subject and the growing interest around it. Studies on the diagnosis of eye disease are generally focused on glaucoma, and there is a lack of studies regarding the use of lenses in diagnosing other eye diseases.

Lenses, one of the most common and comfortable to use medical devices today, will become even more useful when intergrated with the features focused on in this study and will soon be a life-saving device for patients who have a genetic predisposition or are in an at-risk group.

III. UNIQUE VALUE

Our work draws attention to international research in related scientific fields and seeks solutions to current problems It focuses on early diagnosis of diseases such as diabetes, glaucoma, migraine and cataracts, which are frequently encountered in certain age groups due to genetic predisposition. This study also focuses on designing a system that is easy to use while providing accurate data efficiently.

Since the lens used in the study is a silicone hydrogel contact lens suitable for continuous use, it will be very easy for users to integrate this lens into their daily lives. As a result, patients who need to visit the hospital frequently for disease control will be able to reduce the frequency of visits, which will reduce the workload of doctors. Furthermore, patients will not need to visit the hospital as often during treatment and follow-up, which will help prevent overcrowding in hospitals. This will also provide an effective solution to combat infections and diseases that can be transmitted within the hospital, preventing the spread of infectious diseases in these environments. It is expected that there may be some problems that may arise due to the customization, cost and in-vivo use of the lens. Previous studies on electronic contact lenses have drawn attention to problems such as the need for power supply when a wireless antenna is not used.

IV. MATERIALS AND METHOD

Certain calculations need to be performed to accurately measure, identify and diagnose various problems such as retinal detachment, gas bubbles in the eye, etc. and to develop good treatment plans.

Classically, the eye P-V relationship is characterized by the Friedenwald coefficient of eye hardness, K. According to Gloster (1965), it correlates relative changes in intraocular pressure (P) with relative changes in intraocular volume (V).

$$\frac{DP}{P} = k\frac{DV}{V} = KDV \quad (1)$$

Ocular Compatibility

The relationship between corneal cupping pressure and volume can be defined in terms of ocular compliance as follows:

$$\phi = \frac{DV_\phi}{DP} \approx \frac{V_\phi}{P} \tag{2}$$

In other words ϕ =DVϕDP≈VϕP

In these formulas, intraocular pressure (P) represents the change in intraocular volume (Vϕ) per unit change in intraocular pressure (P). ϕ can also be interpreted as the slope of the relationship between eye volume and pressure. A smaller slope indicates a less flexible or stiffer corneal shell. ϕ = 1/(KP). As can be seen in the Friedenwald model (equation 1), eye alignment is highly dependent on intraocular pressure.

Alternatives to the Friedenwald model describing the P-V relationship of the eye can be derived from first principles (McEwen and St. Helen, 1965; Woo et al., 1972; Collins and van der Werff, 2013). For example, using Laplace's law and Fung's structural equation for the collagen keratoscleral envelope σ = A(e αε - 1) (Fung, 1967), and assuming small stresses and uniform mechanical properties, one obtains the formula for ocular compatibility.

$$\phi = \phi_R\left(\frac{P_{r,\phi} + \gamma}{P + \gamma}\right) \tag{3}$$

Here φr is defined as the reference application that has passed on the basis of Pr, φ reference [see Figure (Etik et al., 2004) and Material S1]. Pr,φ can be selected as desired, but the physical value of intraocular pressure is a natural choice. In equation (3) (Sect. Material S1), the term γ is a function of material properties and eye shape, but in this study it is considered as an empirically specified parameter. In the special case γ = 0 (equation 3), the Friedenwald model reduces to the following: ϕ = r r (P r ,ϕ/ P). where K = 1/(ϕ r P r,ϕ).

This study aims to use a Lotrafilcon lens fitted with three bio-sensors to provide early diagnosis and monitering of diabetic retinopathy, glaucoma, migraine and cataracts triggered by oxidative stress formation, increased pressure and extracellular potassium ion (K+) accumulation in the eye.

A sensor that can detect free radicals that cause oxidative stress will be used for early diagnosis of diabetic retinopathy, glaucoma and cataracts, a potassium (K+) sensor that can detect increased extracellular ion concentrations will be used for early diagnosis of migraine, and a pressure sensor will be used sensor to ensure control in diagnosed glaucoma patients.

The Lotrafilcon A silicone hydrogel lens was considered to be the most suitable lens for this study. This is due to many reasons, such as advances in the manufacturing processes of Lotrafilcon A lenses, their continuously improving design, low cost and sharp image properties. Furthermore, this lens has the highest oxygen permeability among silicone hydrogel lenses. The fact that it is a widely used and highly biocompatible material was another reason for choosing Lotrafilcon A.

Data detection can be performed externally, without the use of wires, via telemetry from an implanted detection device.

The sensors inside the lens will store the received data in an Arduino-based recording device for 24 hours, and then provide an easy-to-understand warning to the user via the biotelemetry system system in the case a warning is required. The telemetry system used transmits this information to the user via radio frequency. Recent technological advances have also made it possible to integrate microelectronic circuit structures into silicone hydrogel contact lenses such as Lotrafilcon A and to use the lens continuously.

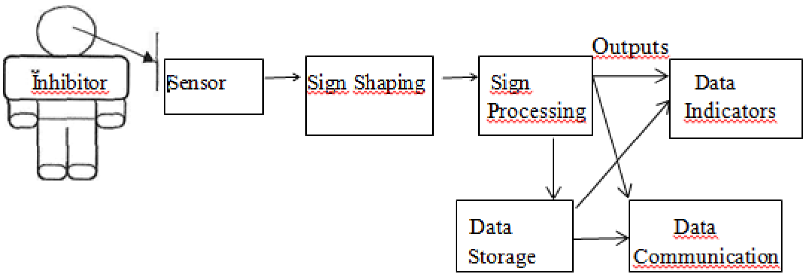

Figure 6. *Block diagram of the simple telemetry system that will also be used in the Lotrafilcon A Lens*

The recording device uses a wireless antenna to read sensor data, and the power required by the sensors is provided by a wireless power transmission device. Power will also be transmitted through the antenna placed on the lens to send data, providing two channels in one. Power will be provided to the sensor by wirelessly charging it for a certain period of time per day via a charger.

The lens design was carried out with the Progineer program. The codes for the 3 sensors to be used in the lens were written using the Arduino program.

A. ARDUINO CODE FRAGMENT FOR THE OXIDATIVE STRESS SENSOR;

```
If(analogRead (Oxydative stress=0) )
{ Console.Writeline(“Normal Seviye”);
Else
Console.Write1ine(“Tehlikeli Durum”);
Retum(Oxydative stres);
```

B. ARDUINO CODE FRAGMENT FOR THE (K+) SENSOR;

```
If(analogRead((K+)>50))
Console.Writeline("Potassium concentration is rising.”);
Else If(analogRead((K*)<50 &&(K+)40))
Console.Writeline(“Potassium concentration is at a normal level”);
Else(“(K*)<40)
Conso le. Writeline("Potassium concentration is falling.”);
Return (K*);
```

C. ARDUINO CODE FRAGMENT FOR THE PRESSURE SENSOR;

```
If(analogRead (Eye pressure>12 && Eye pressure<18))
Console.Writeline("Normal Level");
Else
Conso le.Write1ine("Dangerous Situation");
Return(Eye pressure);
```

In addition, with three sensors to be placed in the contact lens for the study, the lens will be designed to complete its work in such a way as to communicate with the patient or doctor by transmitting the signals it receives about changes in pressure, color and shape in the eye to a telemetry system. The sensors to be used in the study are MEMS sensors. The lens design will be carried out using the Solidworks 2016 program.

V. CONCLUSION

With the lens developed in this study, changes in parameters such as oxidative stress, potassium ions (K+) and pressure, which are involved in the pathophysiology of many eye-related diseases, will be detected at an early stage. This will be a new and promising step for preventive medicine and treatment methods, which have become increasingly important in recent years. The study can be produced using mobile patient systems and Internet of Things (IoT) technology.

When put into the service of patients, it is an application that will improve the quality of life of patients, especially those in at risk groups. The study, intended to advance the field of electronic contact lens applications, will shed light on future studies on this subject.

Along with the developing technology, a biocompatible micro-sized power supply can be developed and integrated into the lens without an external charger. The functions of the different types of sensors can be combined in a single sensor and the work can be carried out at lower cost.

Although cataract surgery is one of the the most common and successful ophthalmic procedures with recent advances in recent years, methods to prevent or delay tar formation still remain a hot area of research, as previous studies in the literature have shown. In addition to possible postoperative complications, cataract surgery itself is highly stressful [29].

With this study, early diagnosis and medicated treatment will be possible, which will be more economical and reduce workload for medical staff and facilities, and patients will regain their health earlier.

Thanks to this lens, which is designed for preventive purposes in case of genetic predisposition, patients can recognize the disease and apply preventive treatments while they are still at the onset of these diseases.

It is thought that this is a study that will help the country stand out in the international arena and take a leading position in health.

VI . RESOURCES

[1] Hunkyu Seo, Won Gi Chung, Yong Won Kwon, Sumin Kim, Yeon-Mi Hong, Wonjung Park, Enji Kim, Jakyoung Lee, Sanghoon Lee, Moohyun Kim, Kyeonghee Lim, Inhea Jeong, Hayoung Song, and Jang-Ung Park, “Smart Contact Lenses as Wearable Ophthalmic Devices for Disease Monitoring and Health Management”, *Chem. Rev*. vol.123, no19, pp 11488−11558, 2023

[2] Shirzaei Sani, E. Xu, C. Wang, C. Song, Y. Min, J. Tu, J. Solomon, S. A. Li, J. Banks, J. L. Armstrong, D. G. Gao, W. “ A Stretchable Wireless Wearable Bioelectronic System for Multiplexed Monitoring and Combination Treatment of Infected Chronic Wounds”. *Science Advances*, 2023. 9 (12), No. eadf7388,

[3] Wang, M.; Yang, Y.; Min, J.; Song, Y.; Tu, J.; Mukasa, D.; Ye, C.; Xu, C.; Heflin, N.; McCune, J. S.; Hsiai, T. K.; Li, Z.; Gao, W. A "Wearable Electrochemical Biosensor for the Monitoring of Metabo-lites and Nutrients". *Nat. Biomed. Eng*. 2022, 6 (11), 1225−1235.

[4] De la Paz, E.; Maganti, N. H.; Trifonov, A.; Jeerapan, I.; Mahato, K.; Yin, L.; Sonsa-ard, T.; Ma, N.; Jung, W.; Burns, R.; Zarrinpar, A.; Wang, J.; Mercier, P. P. A "Self-Powered Ingestible Wireless Biosensing System for Real-Time in Situ Monitoring of Gastrointestinal Tract Metabolites". *Nat. Commun*. 2022, 13 (1), 7405.

[5] Song, J. W.; Ryu, H.; Bai, W.; Xie, Z.; Vázquez-Guardado, A.; Nandoliya, K.; Avila, R.; Lee, G.; Song, Z.; Kim, J.; Lee, M.-K.; Liu, Y.; Kim, M.; Wang, H.; Wu, Y.; Yoon, H.-J.; Kwak, S. S.; Shin, J.; Kwon, K.; Lu, W.; Chen, X.; Huang, Y.; Ameer, G. A.; Rogers, J. A. "Bioresorbable, Wireless, and Battery-Free System for Electrotherapy and Impedance Sensing at Wound Sites". *Science Advances* 2023, 9 (8), No. eade4687.

[6] Jiang, Y.; Trotsyuk, A. A.; Niu, S.; Henn, D.; Chen, K.; Shih, C.-C.; Larson, M. R.; Mermin-Bunnell, A. M.; Mittal, S.; Lai, J.-C.; Saberi, A.; Beard, E.; Jing, S.; Zhong, D.; Steele, S. R.; Sun, K.; Jain, T.; Zhao, E.; Neimeth, C. R.; Viana, W. G.; Tang, J.; Sivaraj, D.; Padmanabhan, J.; Rodrigues, M.; Perrault, D. P.; Chattopadhyay, A.; Maan, Z. N.; Leeolou, M. C.; Bonham, C. A.; Kwon, S. H.; Kussie, H. C.; Fischer, K. S.; Gurusankar, G.; Liang, K.; Zhang, K.; Nag, R.; Snyder, M. P.; Januszyk, M.; Gurtner, G. C.; Bao, Z. "Wireless, Closed-Loop, Smart Bandage with Integrated Sensors and Stimulators for Advanced Wound Care and Accelerated Healing". *Nat. Biotechnol*. 2023, 41 (5), 652−662.

[7] An, B. W.; Shin, J. H.; Kim, S.-Y.; Kim, J.; Ji, S.; Park, J.; Lee, Y.; Jang, J.; Park, Y.-G.; Cho, E.; Jo, S.; Park, J.-U. "Smart Sensor Systems for Wearable Electronic Devices". *Polymers* 2017, 9 (8), 303.

[8] Grace E Dunbar Bailey Yuguan Shen Ahmad A Aref . "The Sensimed Triggerfish contact lens sensor: efficacy, safety, and patient perspectives". *Clinical Ophthalmology* 2017:11 875–882 8 May 2017

[9] Renu Agarwal, Igor Iezhitsa, Puneet Agarwal, Alexander Spasov, "Magnesium deficiency: Does it have a role to play in cataractogenesis?", Experimental Eye Research 101 (2012) 82-89.

[10] Bara M, Guiet-Bara A, Durlach J (1993) "Regulation of sodium and potassium pathways by magnesium in cell membranes." *Magnes Res* 6(2):167–177

[11] Iezhitsa IN (2005) "Potassium and magnesium depletions in congestive heart failure–pathophysiology, consequences and replenishment." *Clin Calcium* 15(11):123–133

[12] Renu Agarwal, lgor Iezhitsa, Puneet Agarwal, "Pathogenetic role of magnesium deficiency in ophthalmic diseases", *Biometals* (2014) 27:5–18

[13] Azza Dammak, Cristina Pastrana, Alba Martin-Gil, Carlos Carpena-Torres, Assumpta Peral Cerda, Mirjam Simovart, Pilar Alarma, Fernando Huete-Toral and Gonzalo Carracedo, "Oxidative Stress in the Anterior Ocular Diseases: Diagnostic and Treatment", *Biomedicines* 2023, 11, 292**.**

[14] R. A. Moses, "The Goldmann applanation tonometer," Amer. J. *Ophthalmo*l., vol. 46, no. 6, pp. 865–869, Dec. 1958.

[15] K. C. Katuri, S. Asrani, and M. K. Ramasubramanian, “Intraocular pressure monitoring sensors,” *IEEE Sensors* 1., vol. 8, no. 1, pp. 12 - 19, Jan. 2008.

[16] L. Martinez, R. Giannetti, M. Rodriquez, “Design of a system for continuous intraocular pressure monitoring,” *In: Instrumentation and Measurement Technology Conference,* Como, Italy, 2004.

[17] K. C. Katuri, M K. Ramasubramanian, S. Asrani, “ A Surface Micromachined Capacitive Pressure Sensor for Intraocular Pressure Measurement, *” IEEE ASME Int. Conf. on Mechatronics and Embedded Systems and Applications* , pp. 149-154, 2010.

[18] C. Collin, “Miniature passive pressure transensor for implanting in the eye,” *IEEE Transactions on Biomedical Engineering* (Volume: BME-14, Issue: 2, April 1967)
Page(s): 74 - 83

[19] P. Walter, U Schnakenberg, “Development of a completely encapsulated intraocular pressure sensor,” *Ophthalmic Research*, vol. 32, no. 26, pp. 278-284, 2000.

[20] Internet of Things in Eye Diseases, Introducing a New Smart Eyeglasses Designed for Probable Dangerous Pressure Changes in Human Eyes (2017 International Confarence on Computer and Applications)

[21] The National Eye Institute (NEI) (September 2015)

[22] Migren Hastalarında Merkezi Kornea Kalınlığın Değerlendirilmesi. Mehmet COŞKUN . Karabük Üniversitesi Göz Hastalıkları Anabilim Dalı, Karabük (*Bozok Tıp Derg* 2017;7(1):59-63)

[23] Coşkun, Mehmet. “Migren Hastalıklarında Merkezi Kornea Kalınlığının Değerlendirmesi ”.www.dergipark.gov.tr.dergipark.gov.tr/article-file/292642 Access Address on March 25, 2019

[24] Argus VA: Ocular hypertension and central corneal thickness.*Ophthalmology*. 1995;102:1810-1812.

[25] Ventura AC, Bohnke M, Mojon DS: “Central corneal thickness measurements in patients with normal tension glaucoma, primary open angle glaucoma, pseudoexfolia tion glaucoma, or ocular hypertension”. *Br J Ophthalmol*. 2001;85:792-795.

[26] Ko Y-C, Liu CJ-I, Hsu W-M: “Varying effects of corneal thickness on intraocular pressure measurements with different tonometers”.*Eye*. 2005;19:327-332

[27] Brandt JD, Beiser JA, Kass MA, et al.: “Central corneal thickness in the Ocular Hypertension Treatment Study (OHTS)”. *Ophthalmology*. 2001;108:1779-1788.

[28] Gordon MO, Baiser JA, Brandt JE, et al.: T”he ocular hypertension treatment study: Baseline factors that predict the onset of primary open-angle glaucoma”. *Arch Ophthalmol*. 2002;120: 714-720.

[29] Hasim, Z,. Zarina, S,. “ Osmatik Stress induced oxidative damage; Possible machansim of cataract formation in diabetes ” *Journal of Diabetes and its Compilcations*, 2012.