CRS

2023 ANNUAL MEETING & EXPO

JULY 24-28, 2023

THE FUTURE OF DELIVERY SCIENCE

Paris Hotel » Las Vegas, NV, USA

Wireless theranostic smart contact lens for monitoring and control of intraocular pressure in glaucoma

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POSTECH
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HARVARD MEDICAL SCHOOL

Stanford University

PHI BIOMED™

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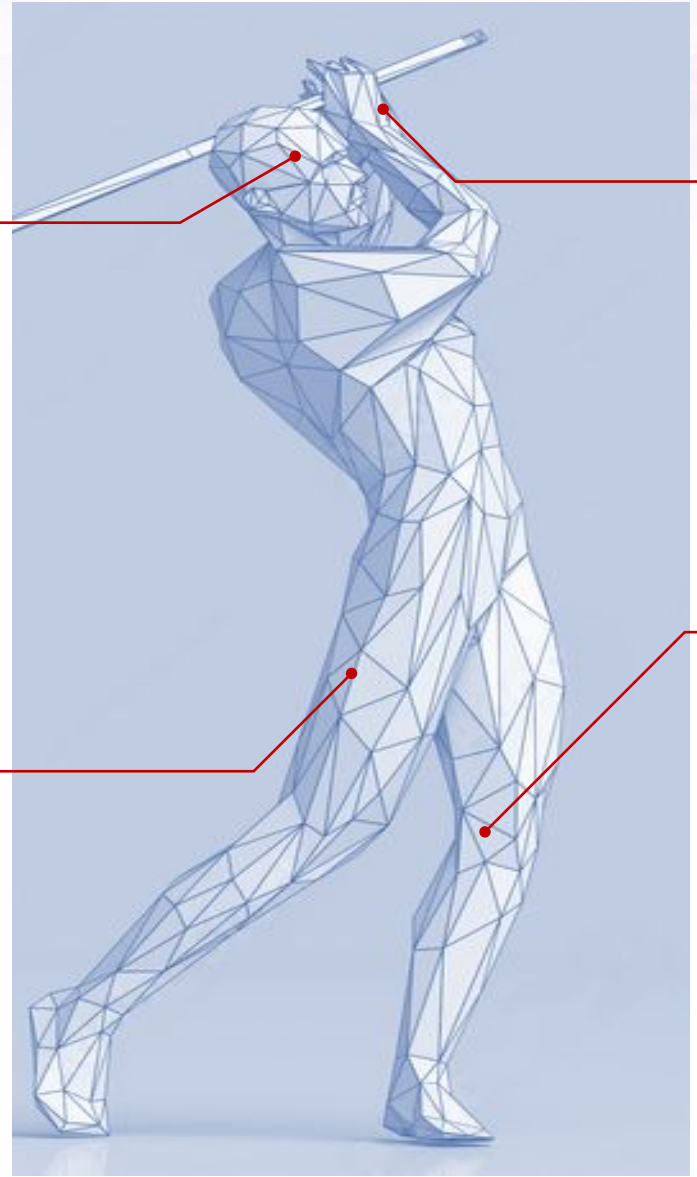
- Multifunctional Nanomaterials

I. Introduction

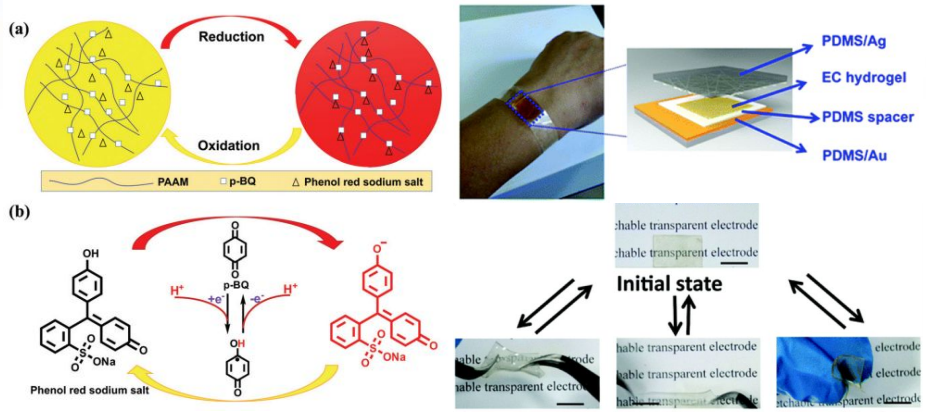
❖ Futuristic wearable electronic systems and devices

I. Introduction

❖ Stretchable electronic devices

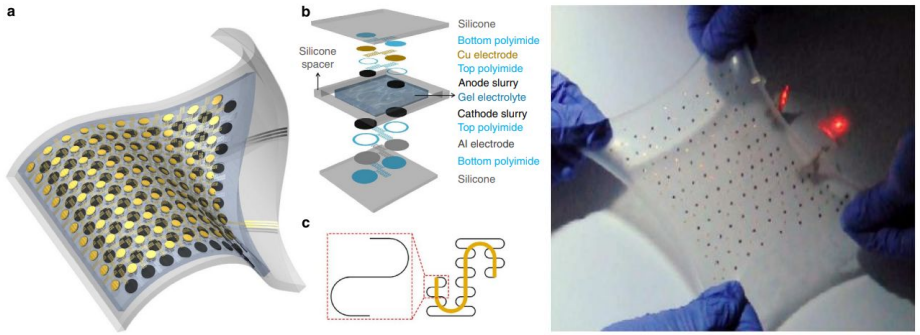


Stretchable display



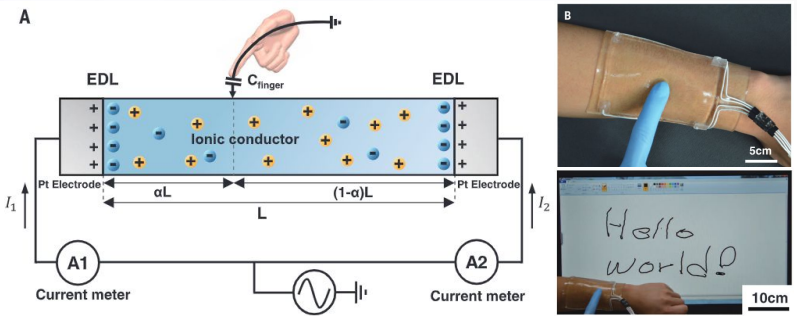
J. Mater. Chem. C **7**, 9481-9486, 2019

Stretchable battery



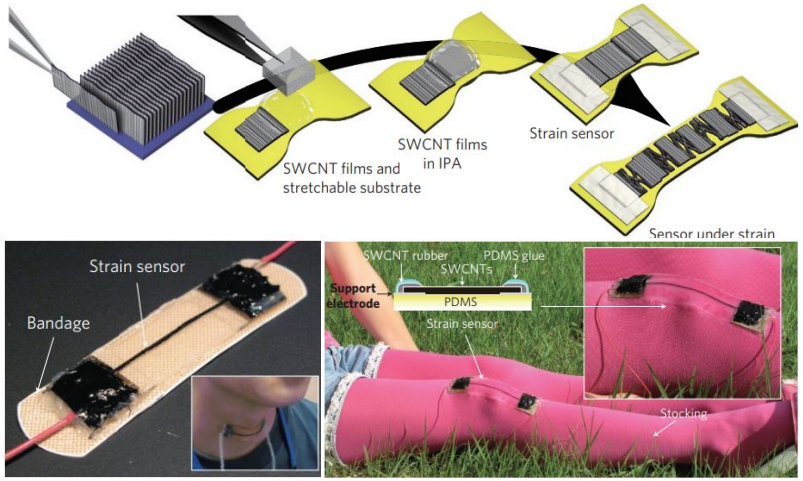
Nature Commun. **4**, 1-8, 2013

Stretchable touch panel



Science **353** 682-687, 2016

Stretchable sensor



Nature Nanotechnol. **6**, 296-301, 2011

❖ Wearable electronic medical devices market

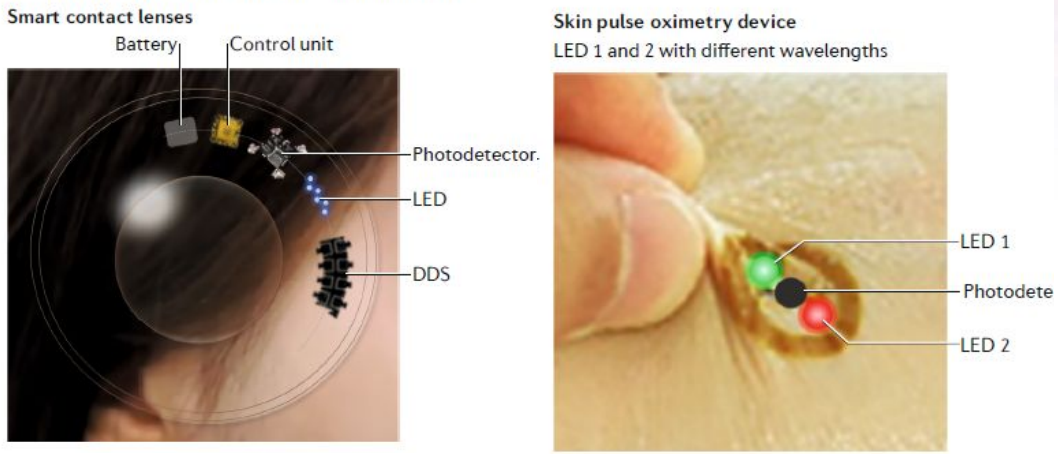
❖ Multifunctional materials for smart healthcare devices

NATURE REVIEWS | MATERIALS

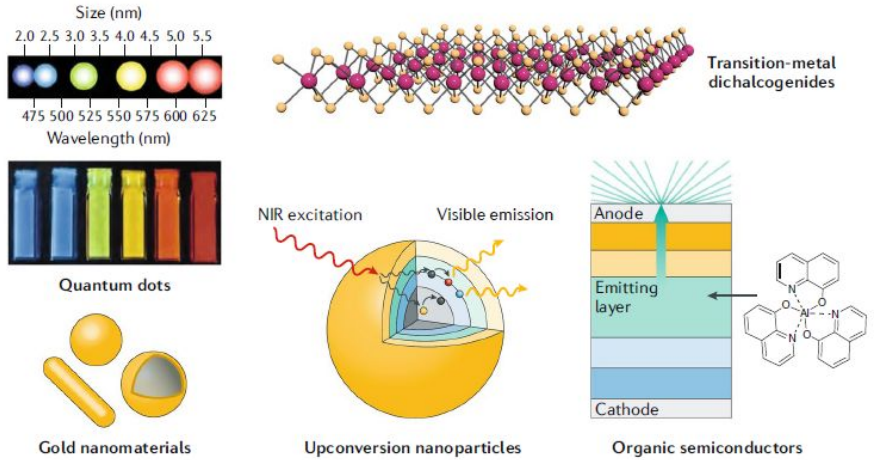
Multifunctional materials for implantable and wearable photonic healthcare devices

Geon-Hui Lee[1,2,9], Hanul Moon[2,3,9], Hyemin Kim[4,9], Gae Hwang Lee[2,5], Woosung Kwon[6], Seunghyup Yoo[3], David Myung[2,7], Seok Hyun Yun[8], Zhenan Bao[2]* and Sei Kwang Hahn[1,2,4]**

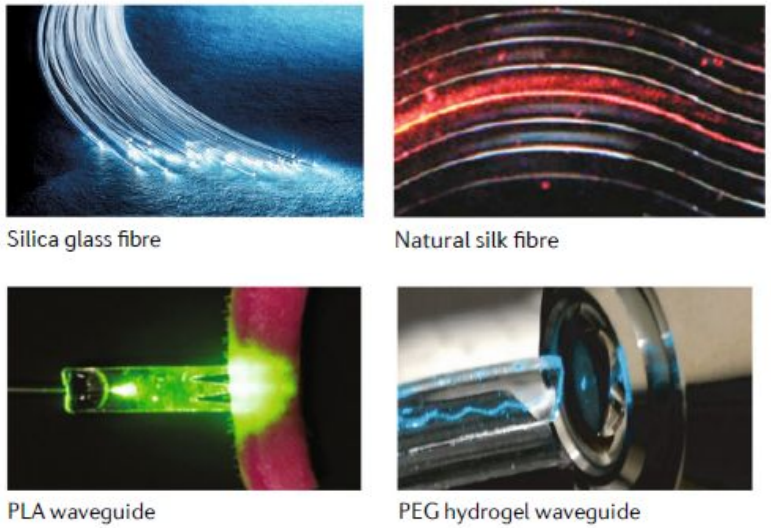
[Nature Reviews Materials 2020, IF = 83.5, Citation 350]



Light-responsive materials



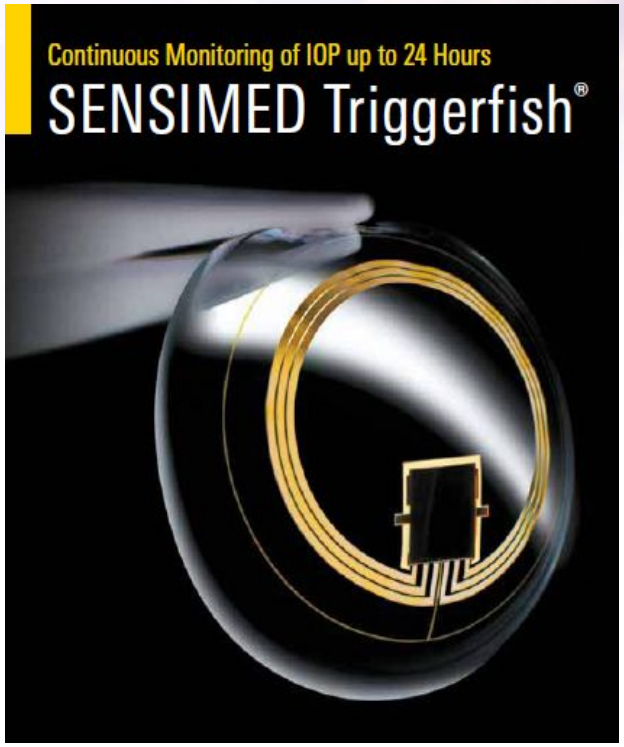
Light-delivering materials

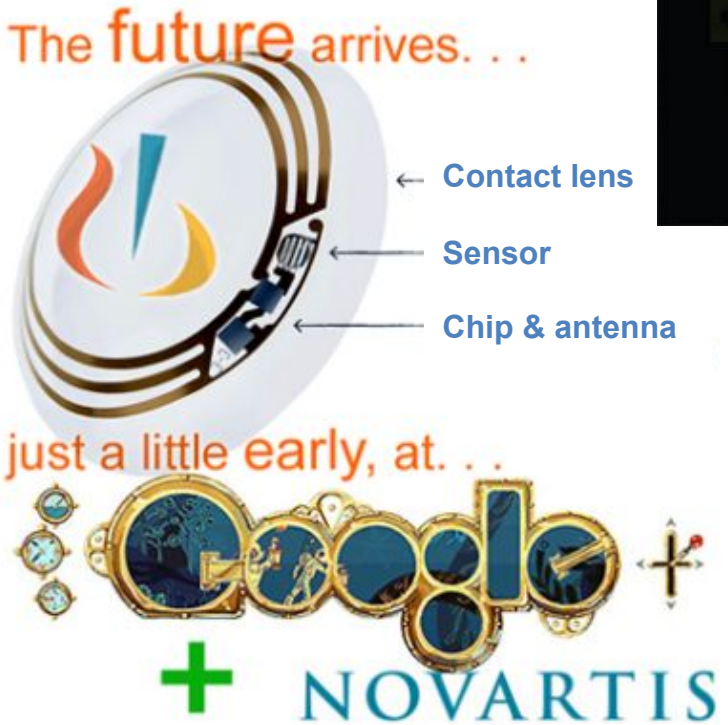


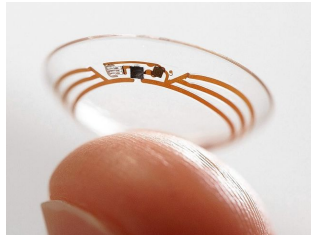
2. Smart Electrochemical Contact Lenses

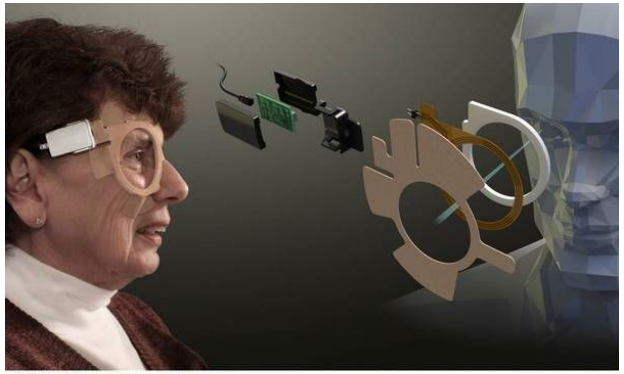
- Smart Electrochemical Contact Lens
- Smart Photonic Contact Lens
- Smart Piezoelectric Contact Lens

2. Smart Electrochemical Contact Lens



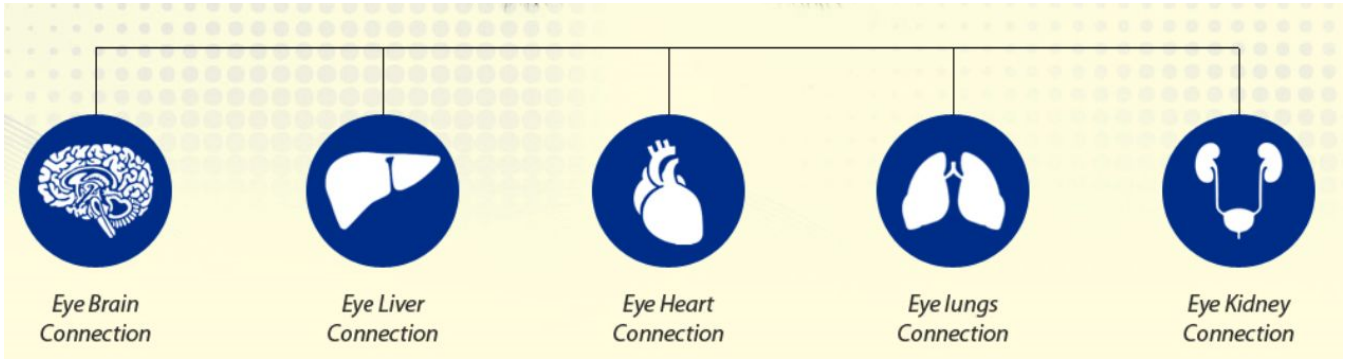






2. Smart Electrochemical Contact Lens

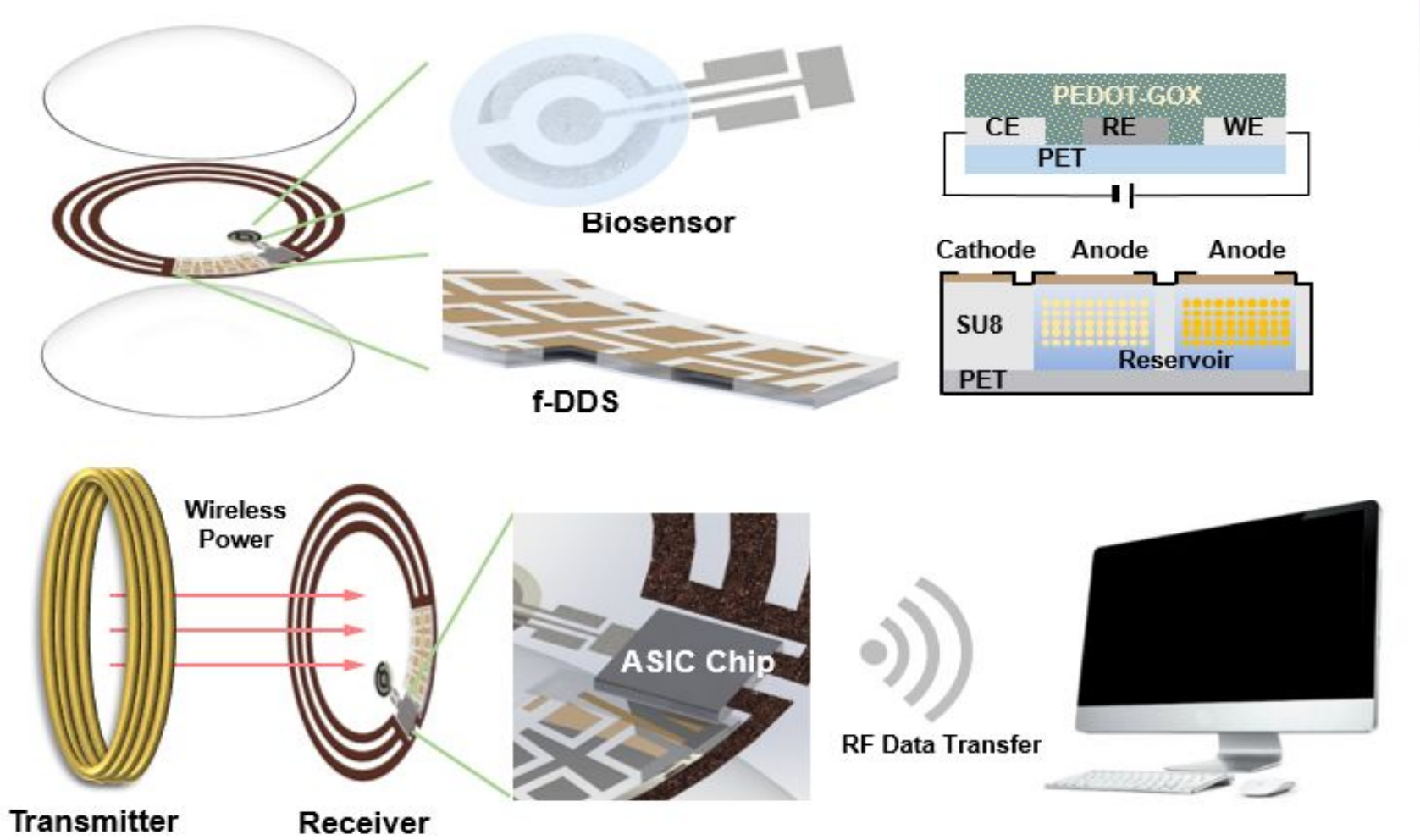
❖ **Eye as an interface between the human body and an electronic device**



BCC Research, Genetic Engineering & Biotechnology News, Acu Eye Zone

2. Smart Electrochemical Contact Lens

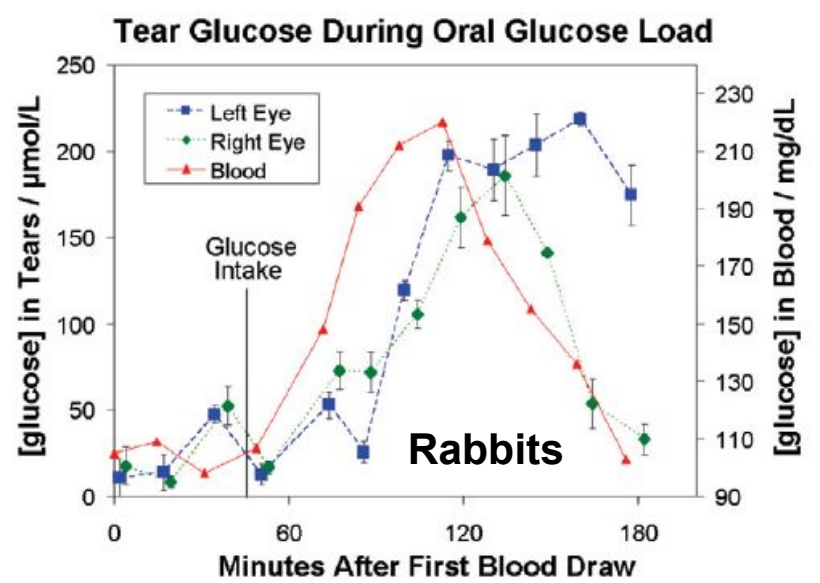
❖ Smart electrochemical contact lens for monitoring and control of diabetes



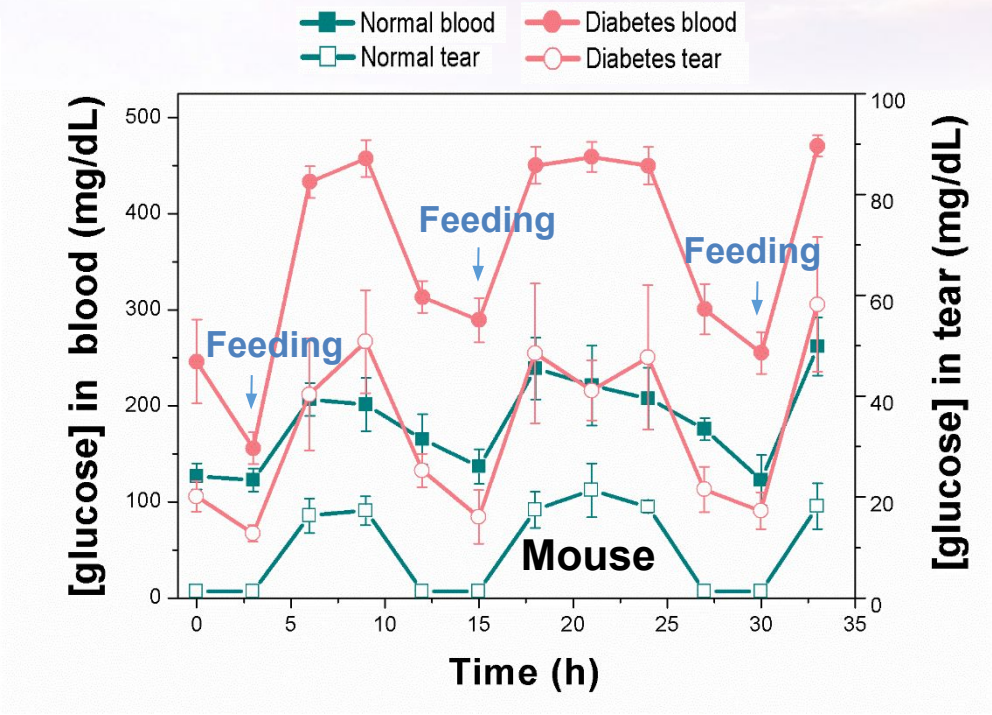
Hahn *et al.* Science Advances, 6, eaba3252 (2020)

2. Smart Electrochemical Contact Lens

❖ Strong correlation between glucose concentration in tear & blood



[Source: Ocular Surface 5, 280, 2007]

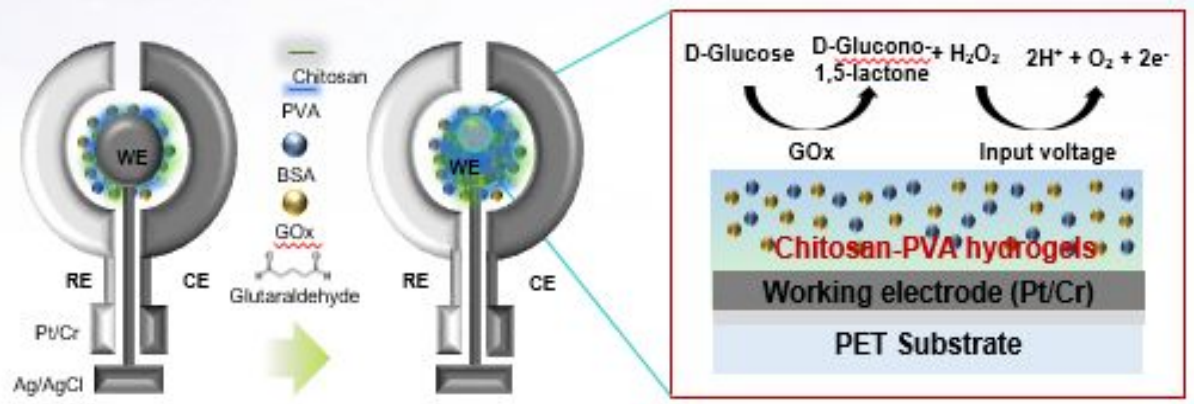


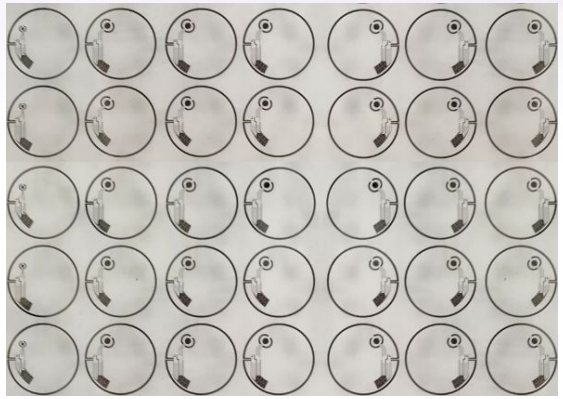
Type	Samples	Mouse	Rabbit	Human
Normal	Blood (mg/dL)	120~250	140~200	100~140
	Tear (mg/dL)	0~20	0~36	0~20
Diabetes	Blood (mg/dL)	150~500	150~400	126~200
	Tear (mg/dL)	15~60	15~60	40~100

Ocular Surface 5, 280 (2007)

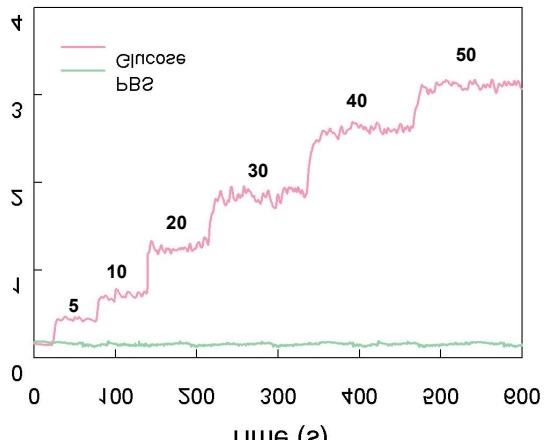
2. Smart Electrochemical Contact Lens

❖ 3-Electrodes glucose biosensor system

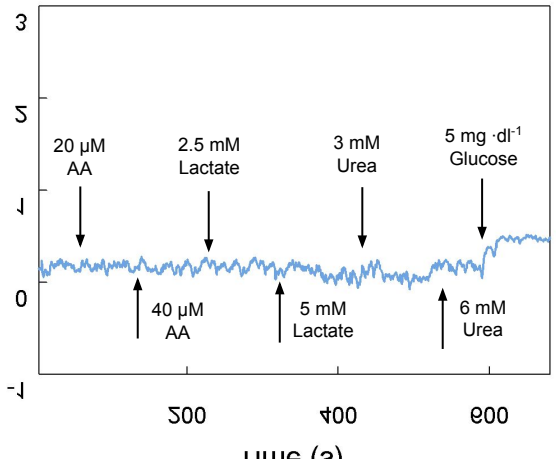




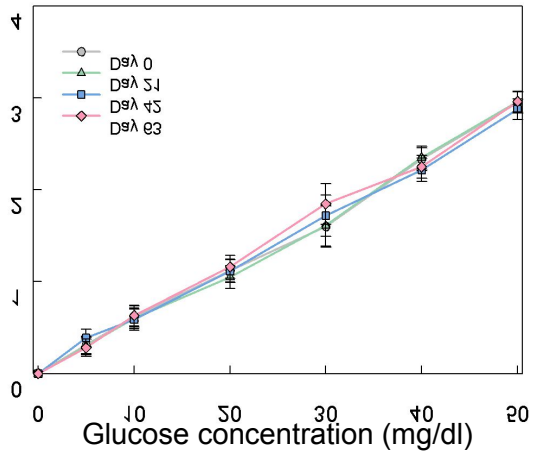
In vitro glucose detection



Glucose-specific detection



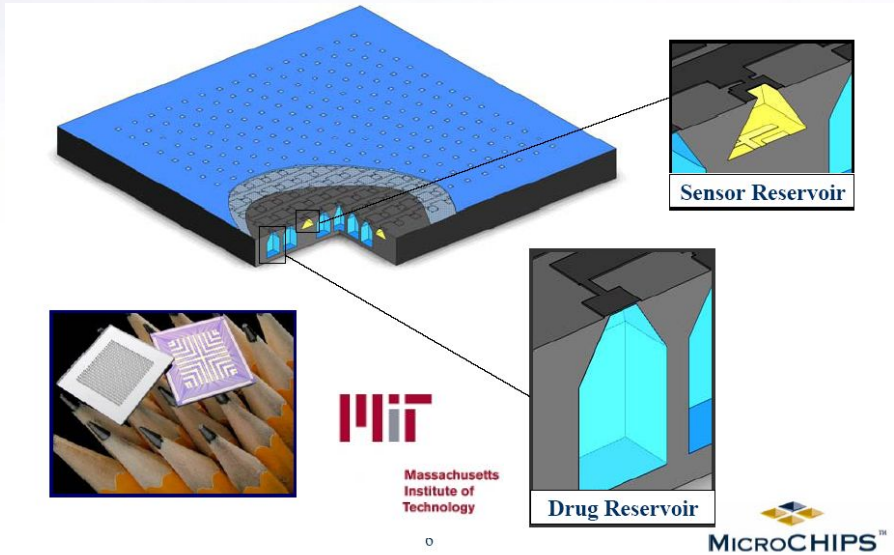
Long-term storage stability

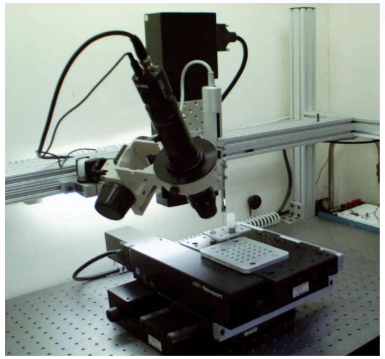


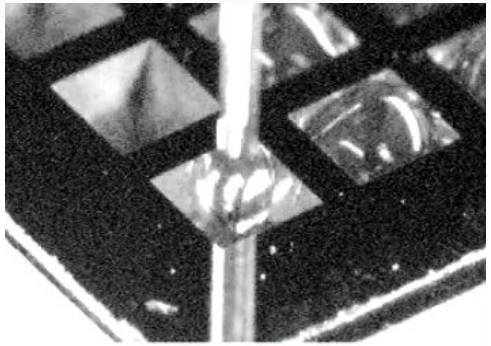
Hahn *et al.* Science Advances, 6, eaba3252 (2020)

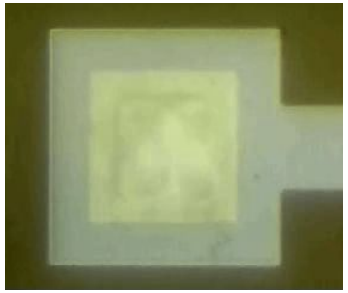
2. Smart Electrochemical Contact Lens

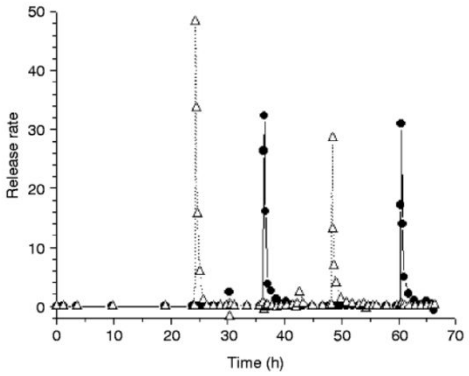
- Gold coated drug reservoirs developed by Robert Langer at MIT

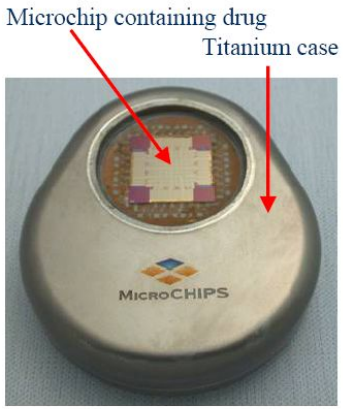


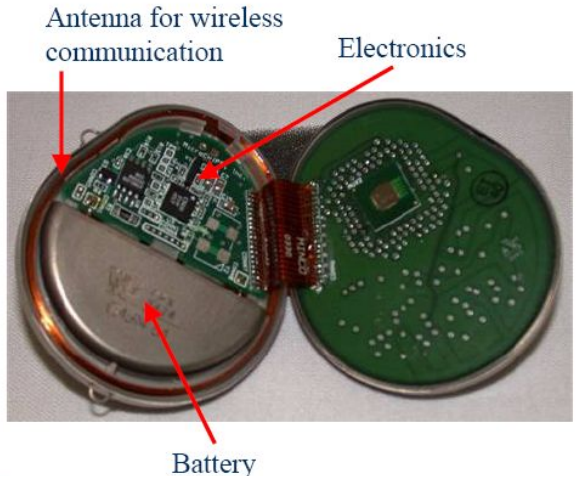








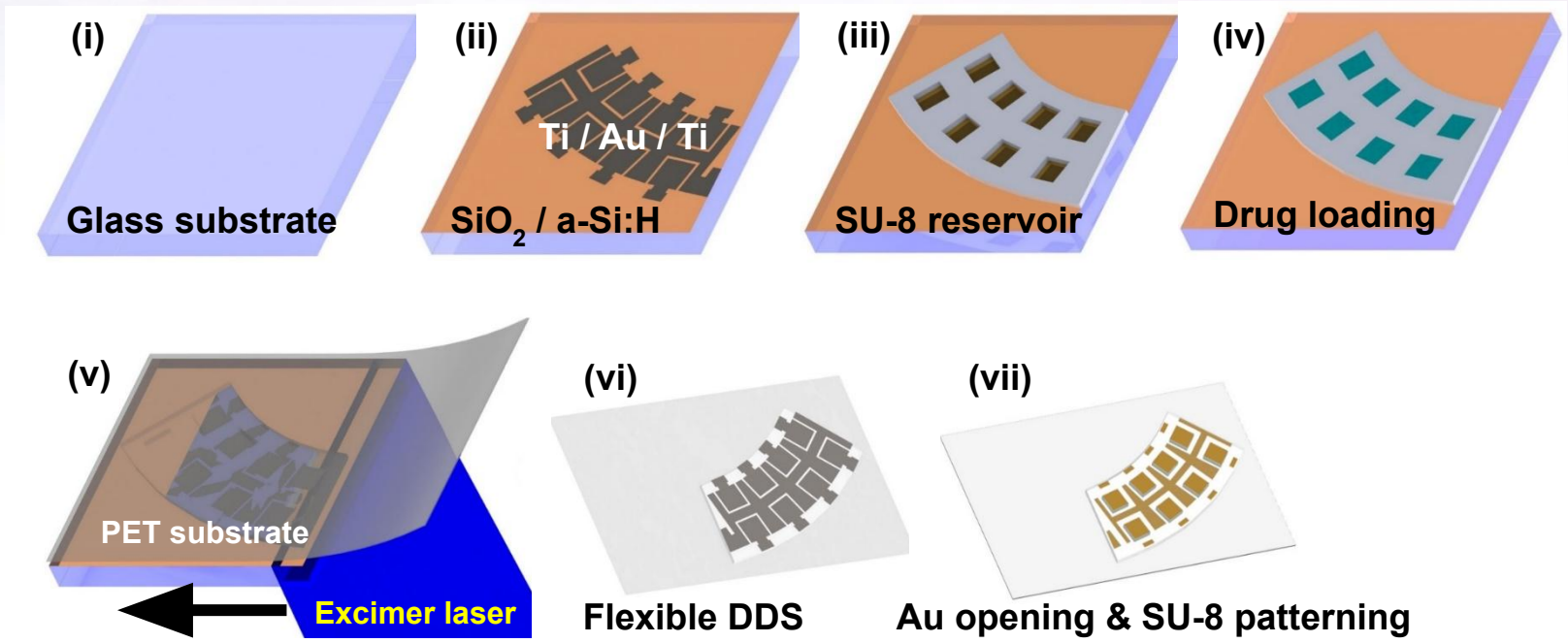


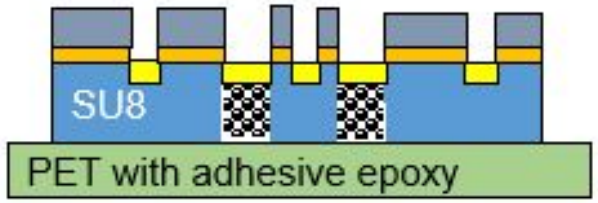


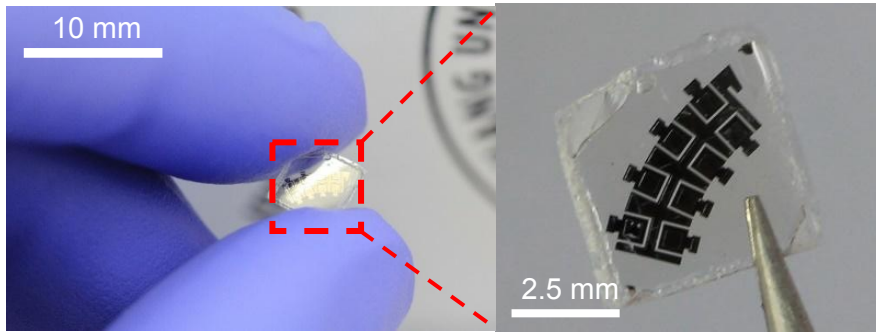
Modern Biopharmaceuticals, Wiley

2. Smart Electrochemical Contact Lens

❖ Fabrication of flexible drug delivery systems (f-DDS)

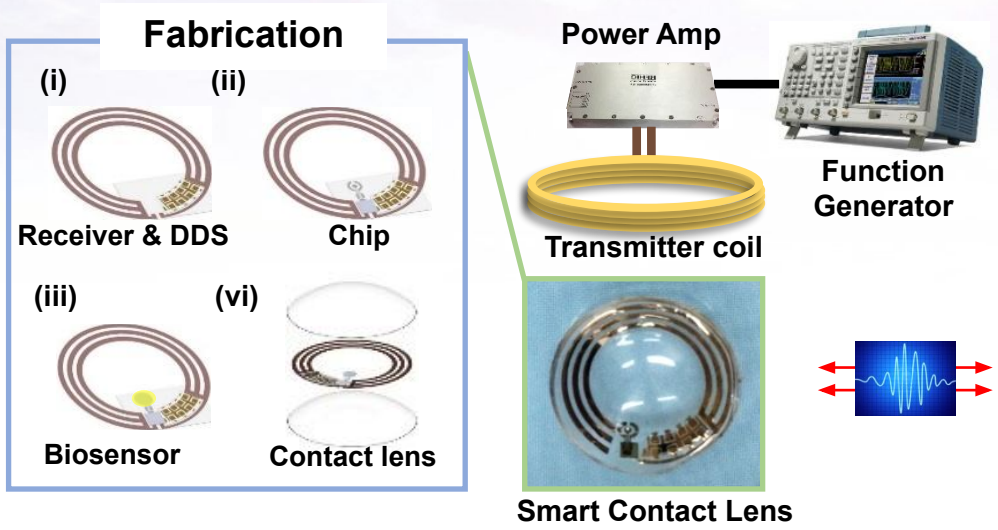


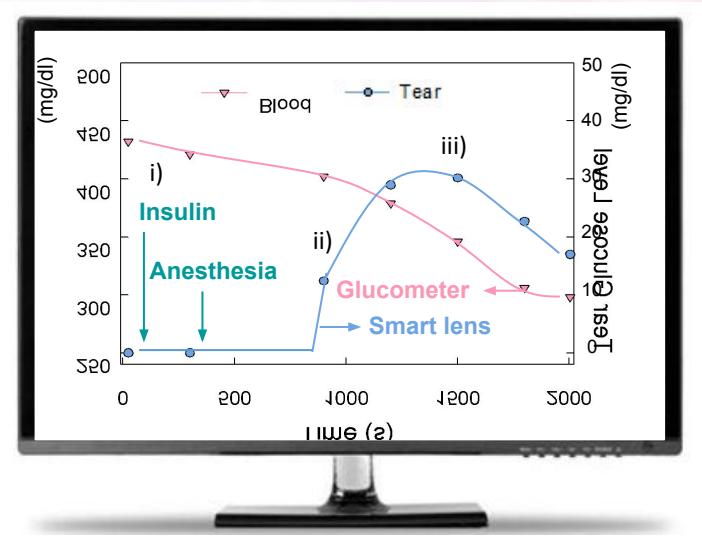




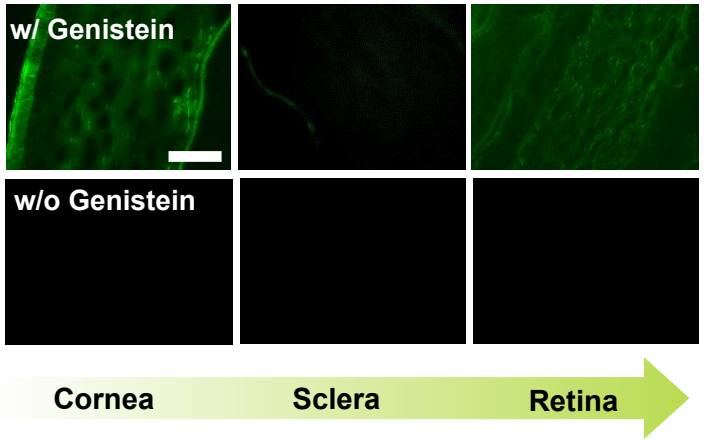
2. Smart Electrochemical Contact Lens

❖ Theranostic application of smart contact lens





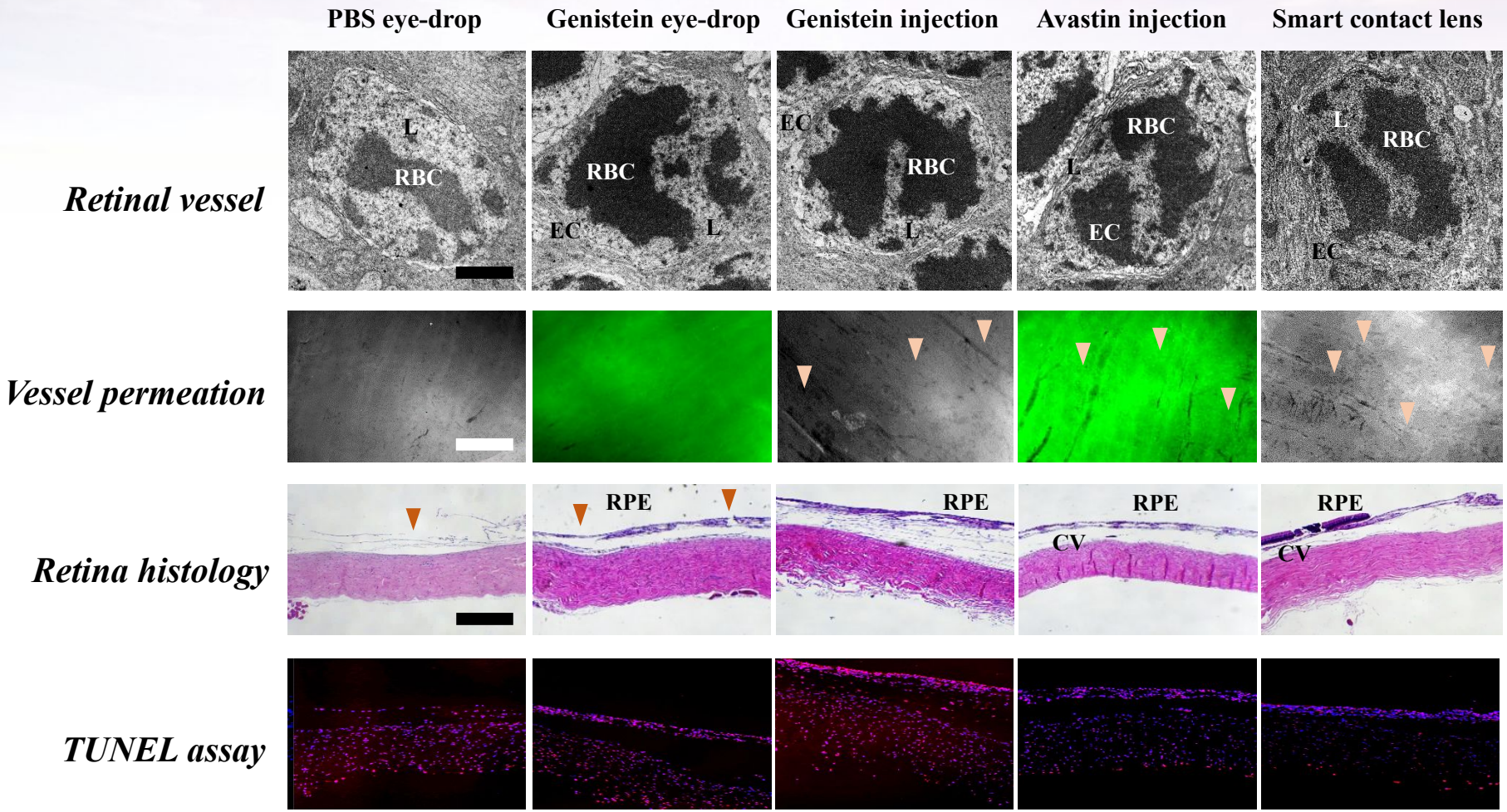
***In vivo* genistein detection**



Hahn *et al.* Science Advances, 6, eaba3252 (2020)

2. Smart Electrochemical Contact Lens

❖ Smart contact lens for therapeutic applications on diabetic retinopathy

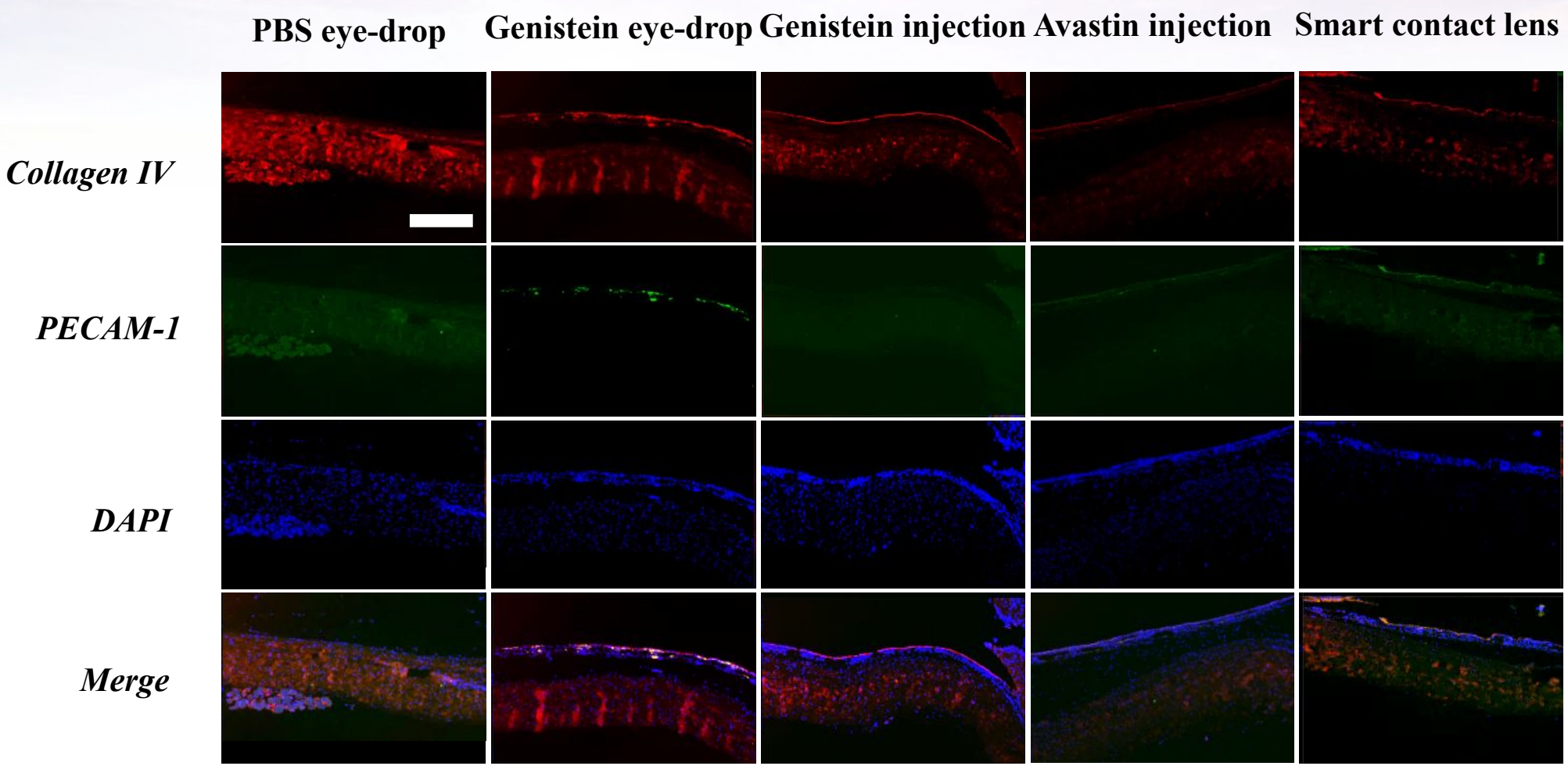


(L: lumen of vessel, EC: endothelial cell, RPE: retinal pigment epithelium, CV: choroidal vessel)

Hahn *et al.* Science Advances, 6, eaba3252 (2020)

2. Smart Electrochemical Contact Lens

❖ Immunohistochemical analysis for the therapeutic effect



Hahn *et al.* Science Advances, 6, eaba3252 (2020)

2. Smart Electrochemical Contact Lens

❖ Smart contact lens for diabetes diagnosis and therapy

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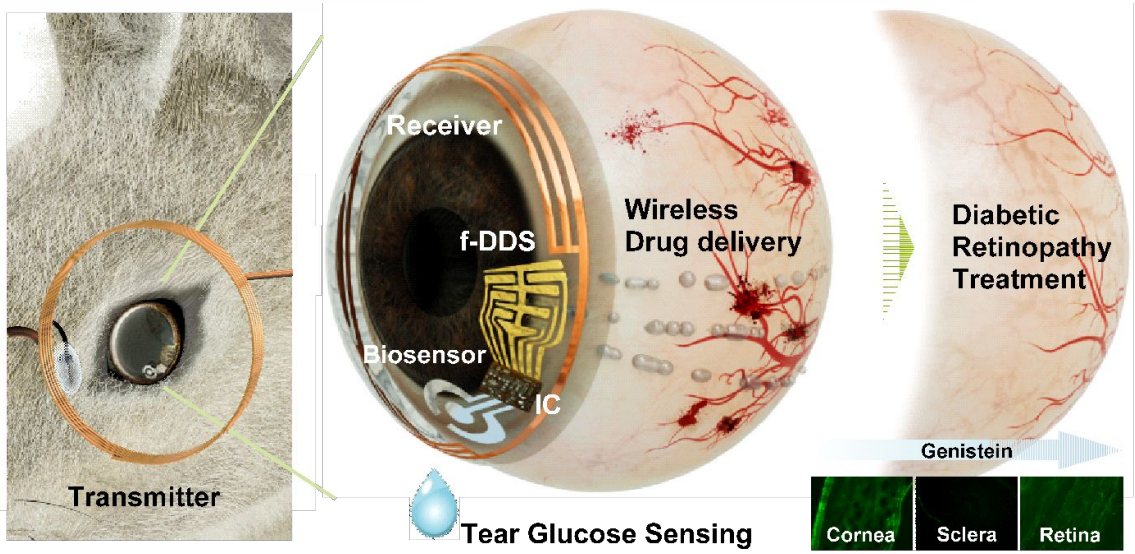
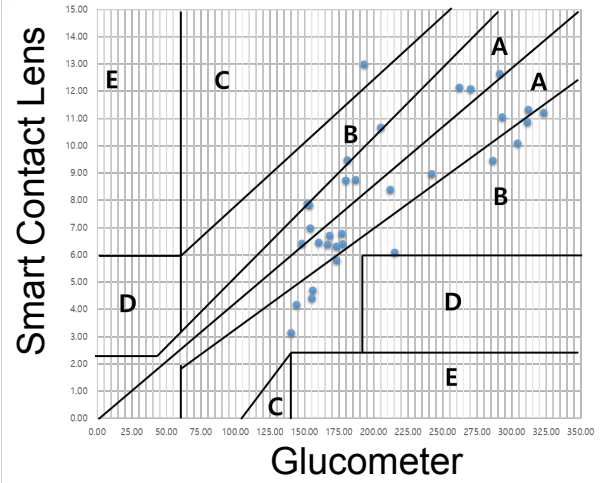
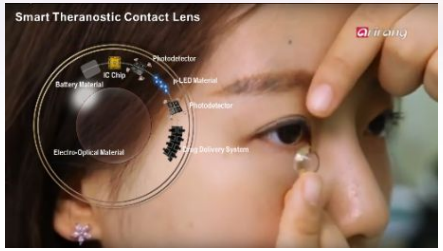




90% Accuracy with Glucometer

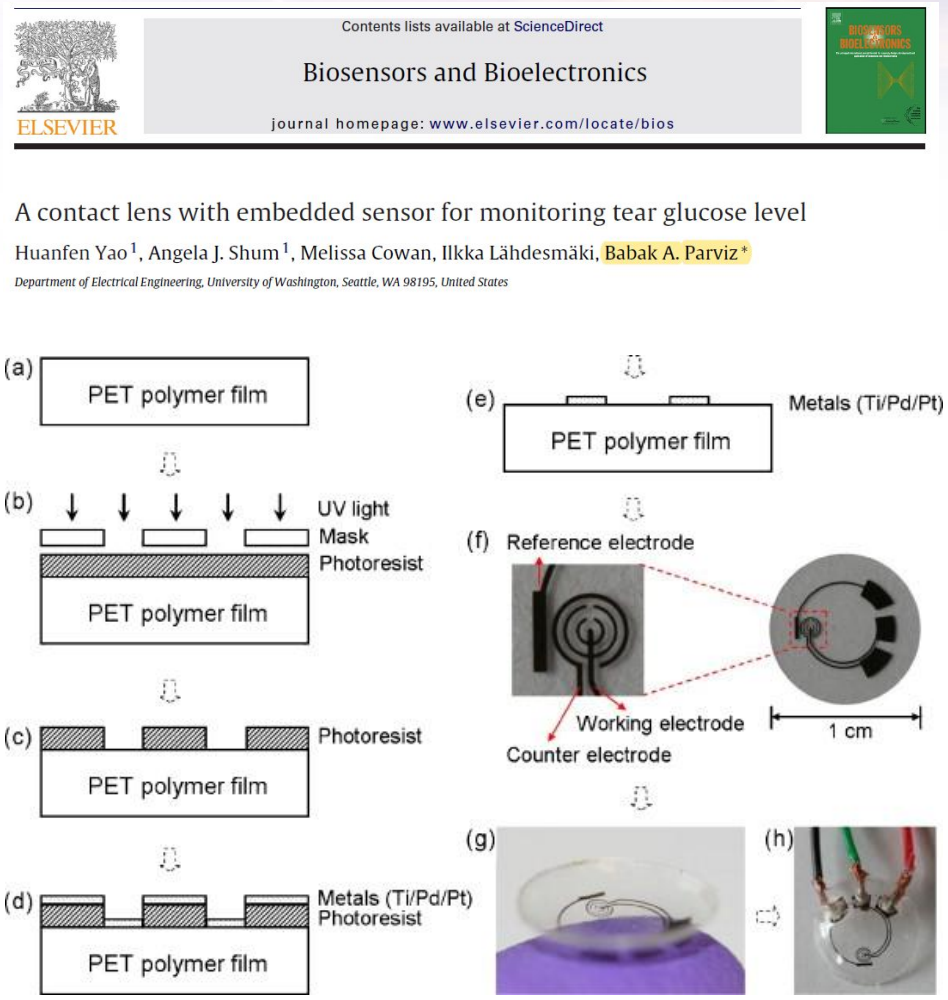


U.S.News & World Report · EurekAlert! AAAS · UPI · ScienceDaily · VentureBeat · Daily Mail

wissenschaft.de · acrofan · HealthDay News for Healthier Living · 毎日新聞社 · Asian Scientist · India TV

2. Smart Electrochemical Contact Lens

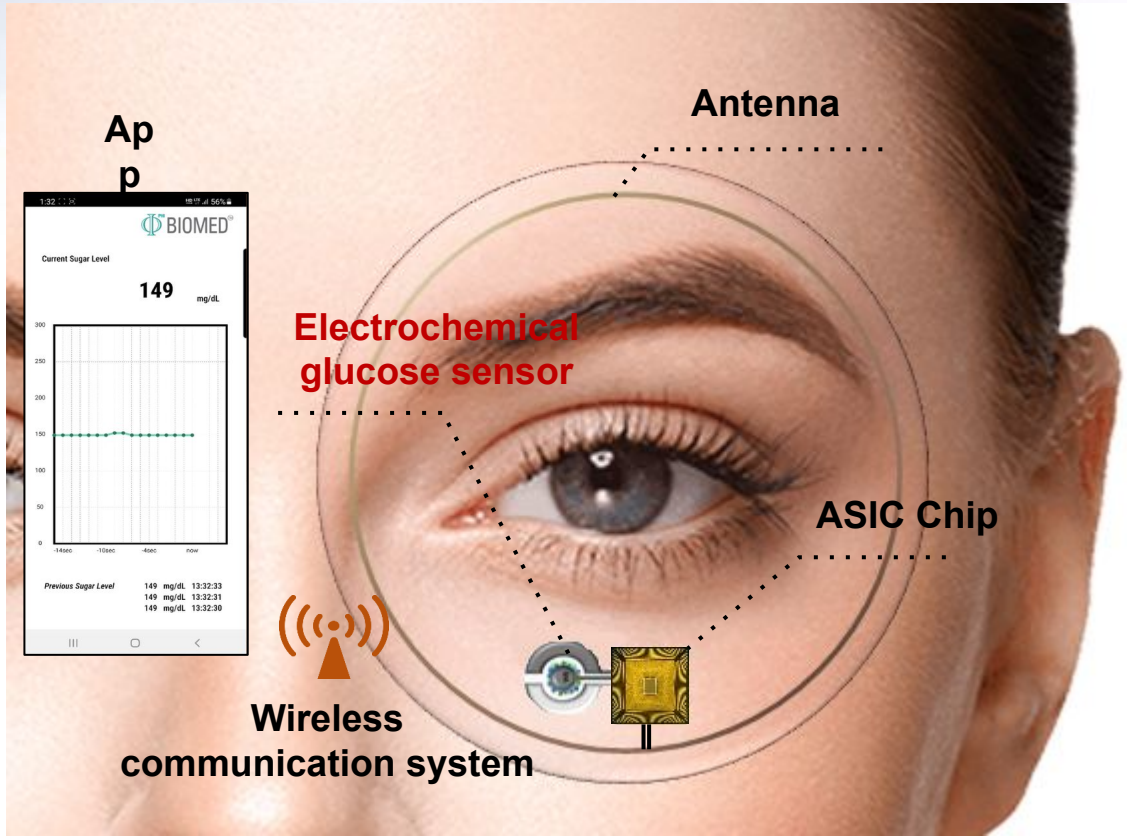
❖ Google lens for diabetes diagnosis



Enzyme layer: GOx +Ti sol-gel layer + **Nafion layer → Low diffusion flux, sensitivity, response time**

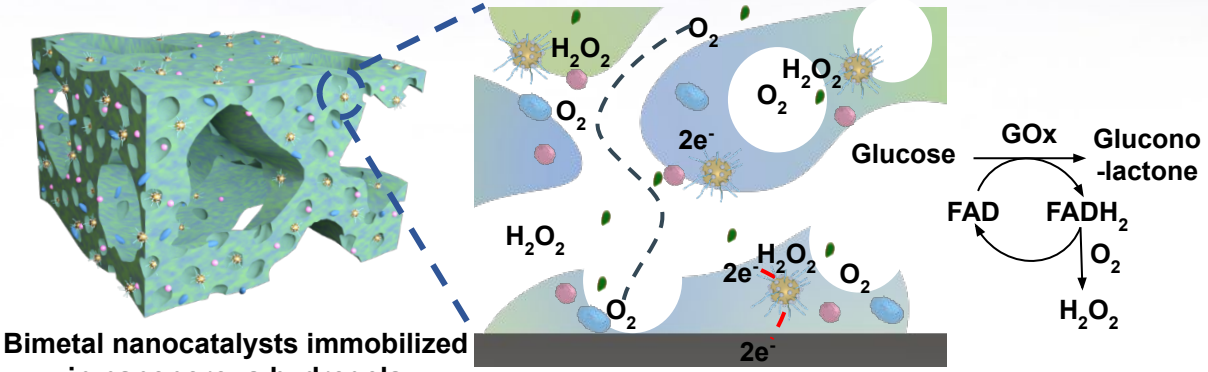
2. Smart Electrochemical Contact Lens

❖ Smart contact lens for highly sensitive and long-term stable diabetes diagnosis



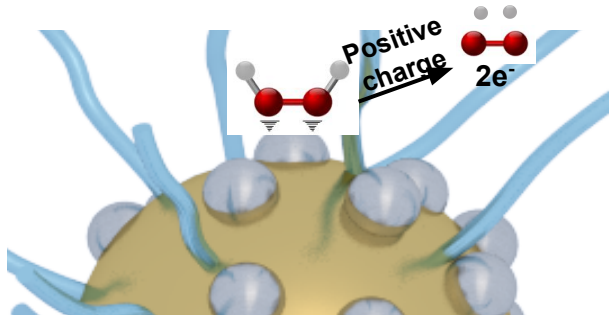
Core Tech: **Bimetal nanocatalysts and glucose oxidase immobilized in nanoporous hydrogels**

Nanoporous hydrogel



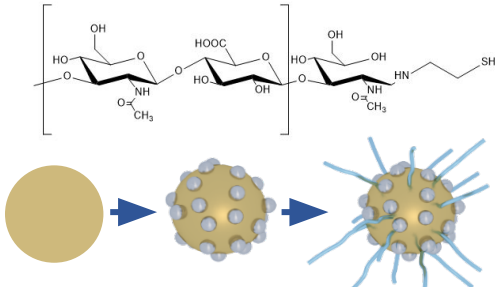
HA-Au@Pt BiNCs

$H_2O_2 + Pt(OH)_2 \leftrightarrow Pt(OH)_2 + 2H^+ + 2e^- + O_2$



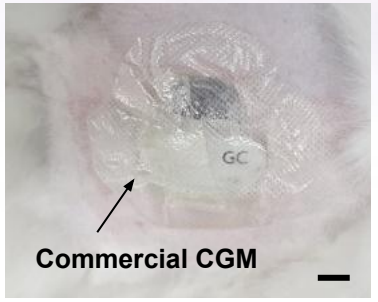
Highly efficient H_2O_2 decomposition

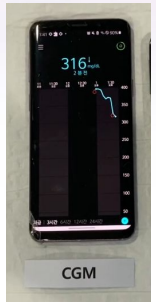
end HA-SH

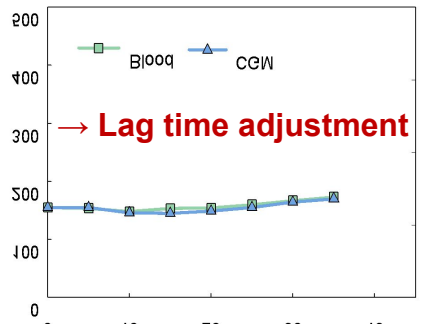


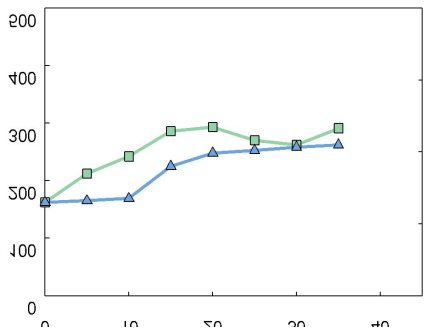
2. Smart Electrochemical Contact Lens

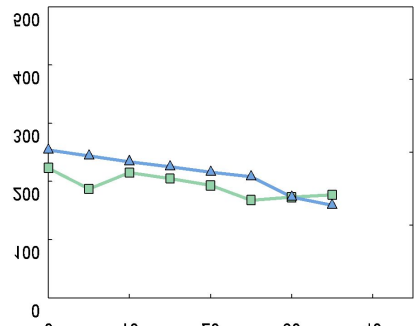
❖ Smart contact lens for long-term stable and highly sensitive diabetes diagnosis

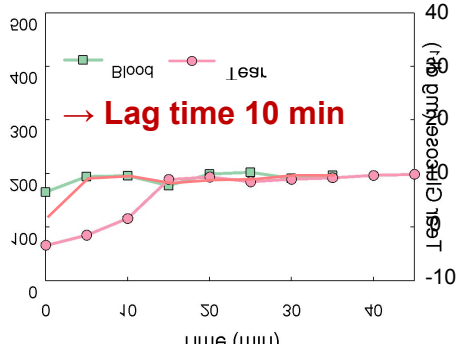


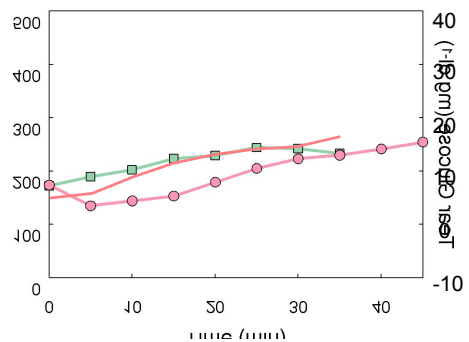


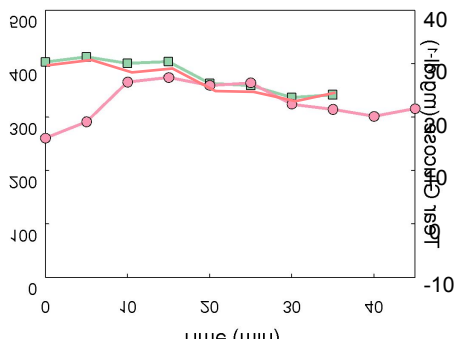




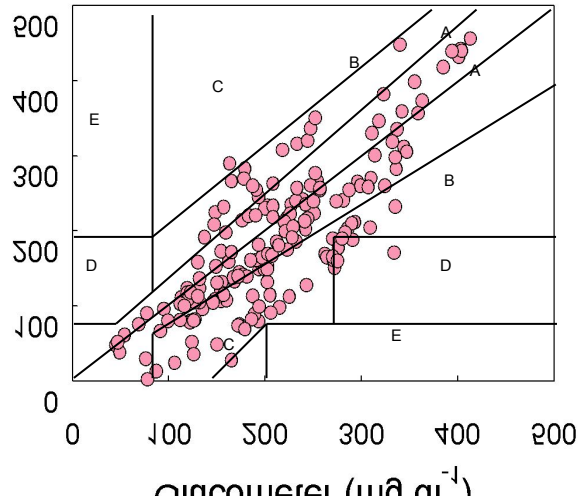








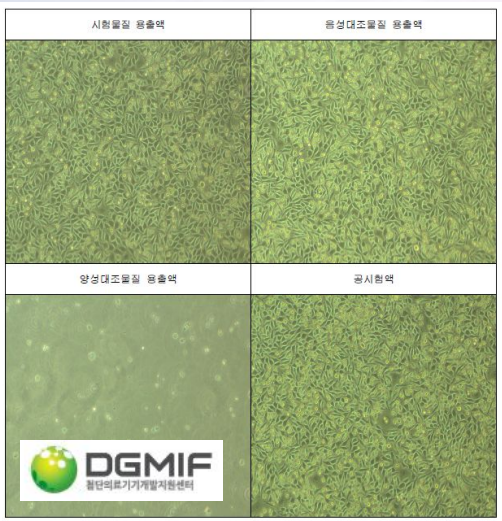
[Clark-error grid analysis]

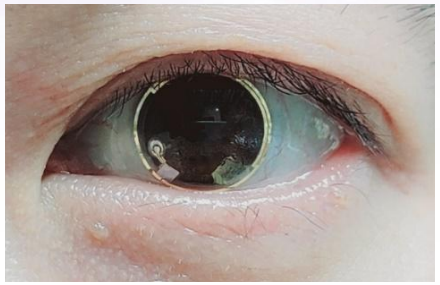


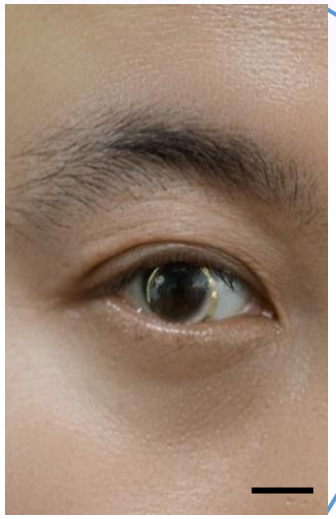
Hahn *et al.* Advanced Materials, 34, 2110536 (2022)

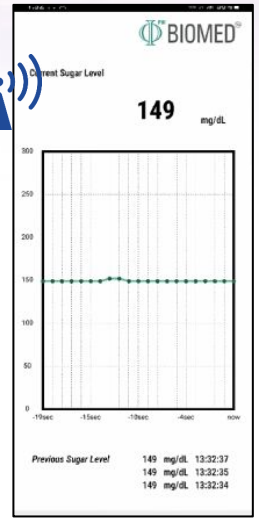
2. Smart Electrochemical Contact Lens

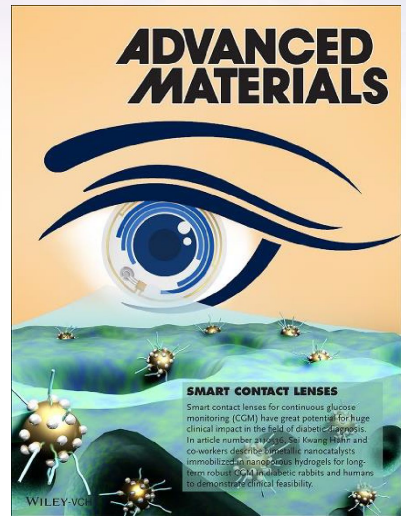
❖ Biological and electrical safety of smart contact lens for diabetes diagnosis



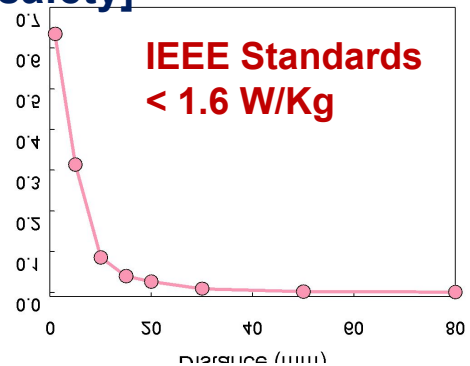


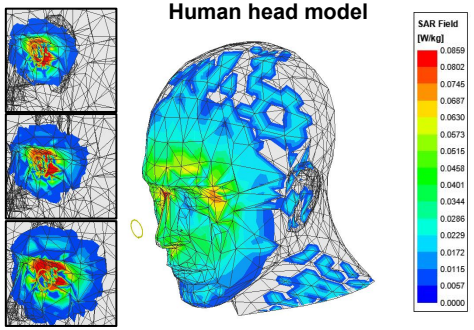




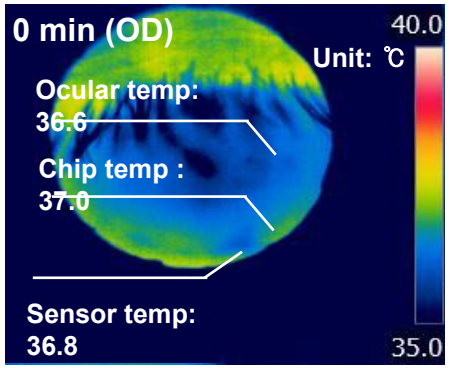


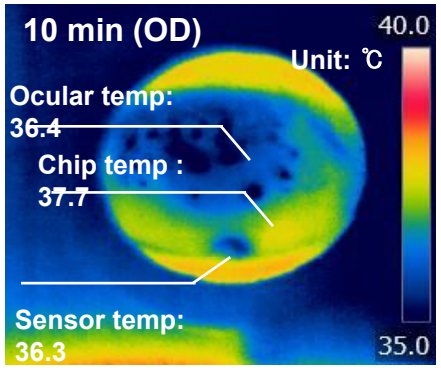
[Electromagnetic wave safety]

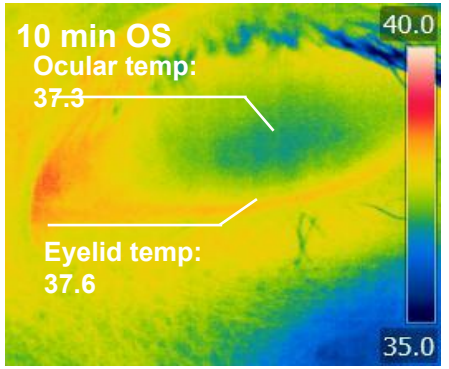




[Thermal safety]





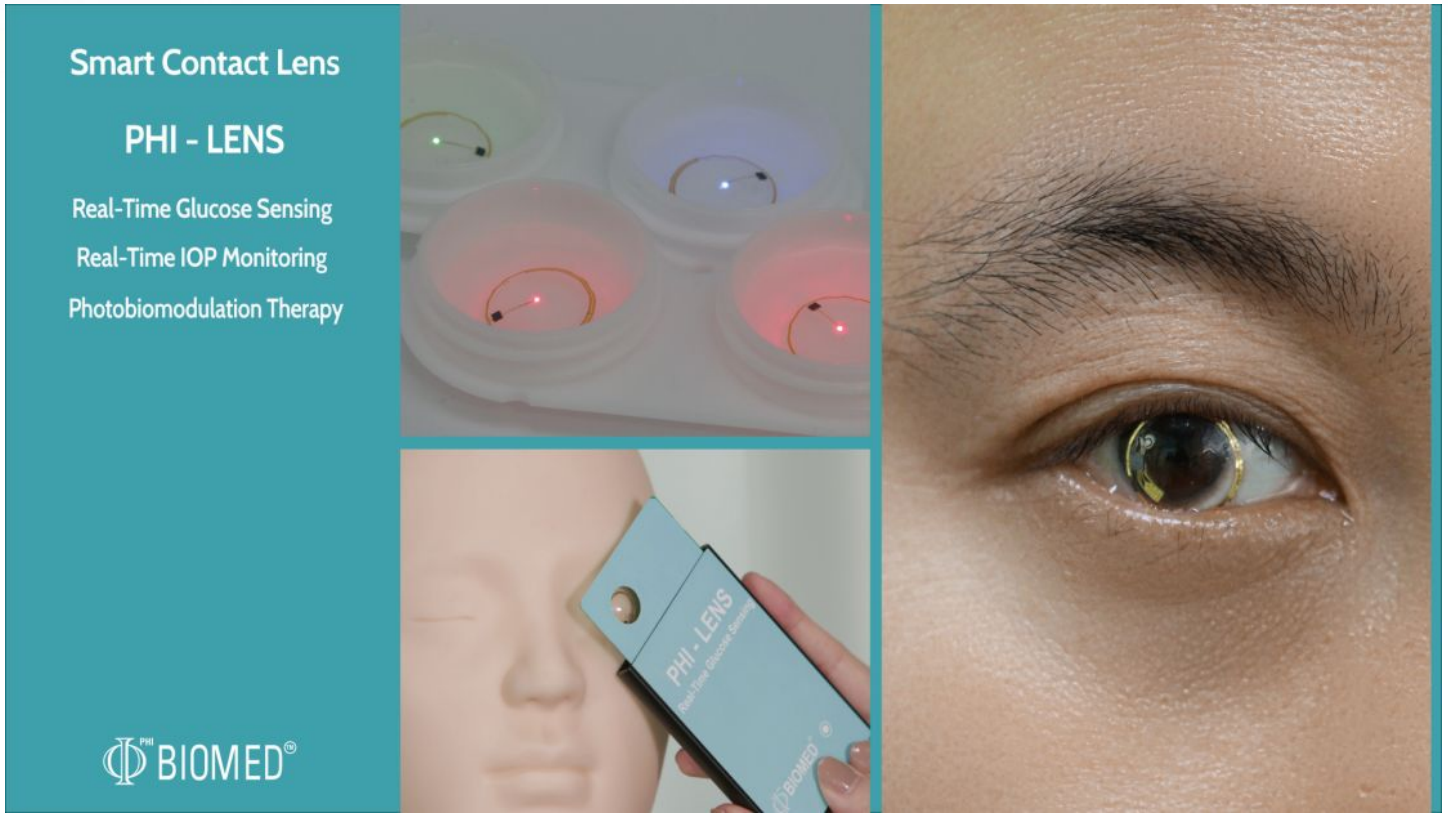


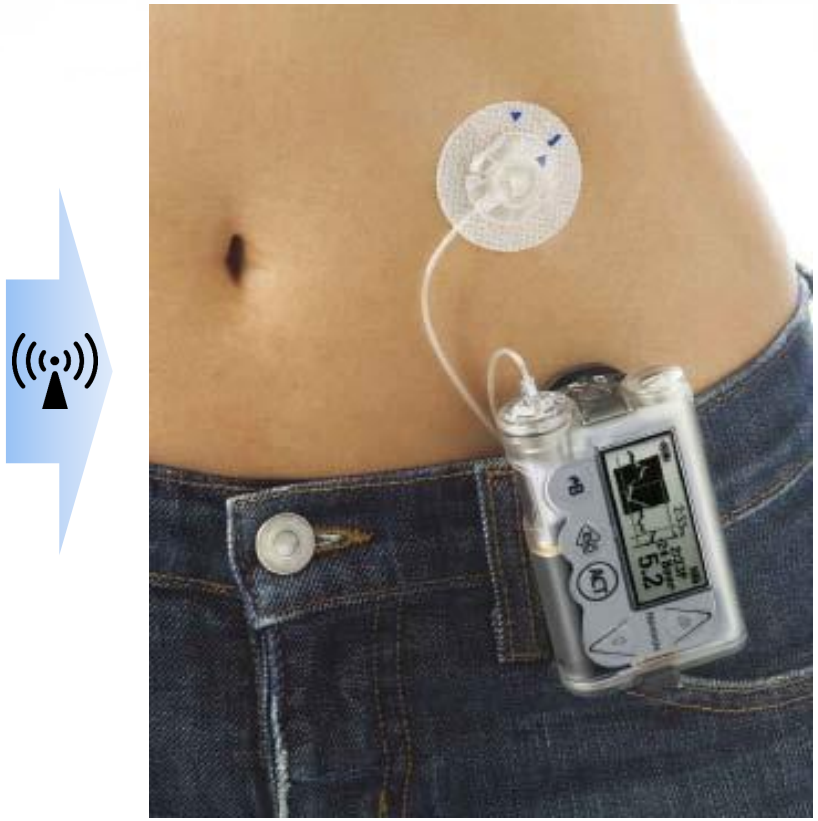
Hahn *et al.* Advanced Materials, 34, 2110536 (2022)

2. Smart Electrochemical Contact Lens

Summary Smart contact lens for diabetes diagnosis and therapy

- Smart contact lens in combination with insulin pump for diabetes theranosis





3. Smart Photonic Contact Lens

- Smart Electrochemical Contact Lens
- Smart Photonic Contact Lens
- Smart Piezoelectric Contact Lens

3. Smart Photonic Contact Lens

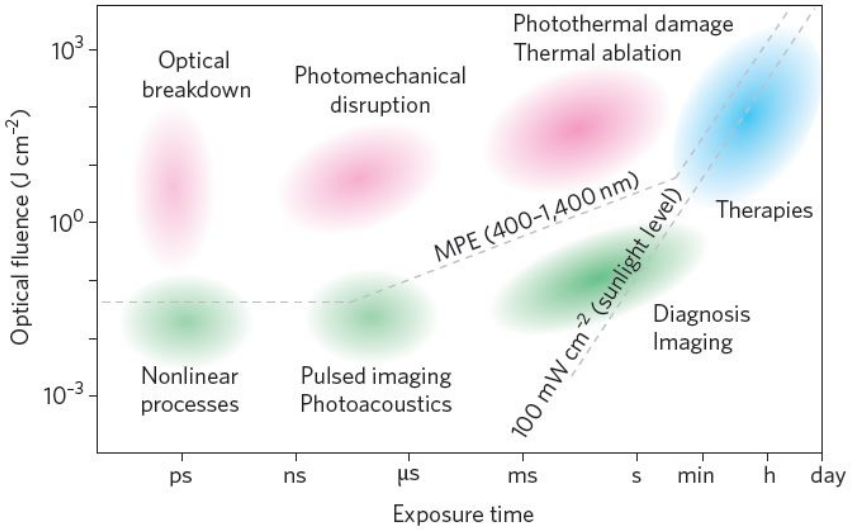
❖ Photomedicine for diagnosis and therapy

nature biomedical engineering
REVIEW ARTICLE
PUBLISHED: 10 JANUARY 2017 | VOLUME: 1 | ARTICLE NUMBER: 0008

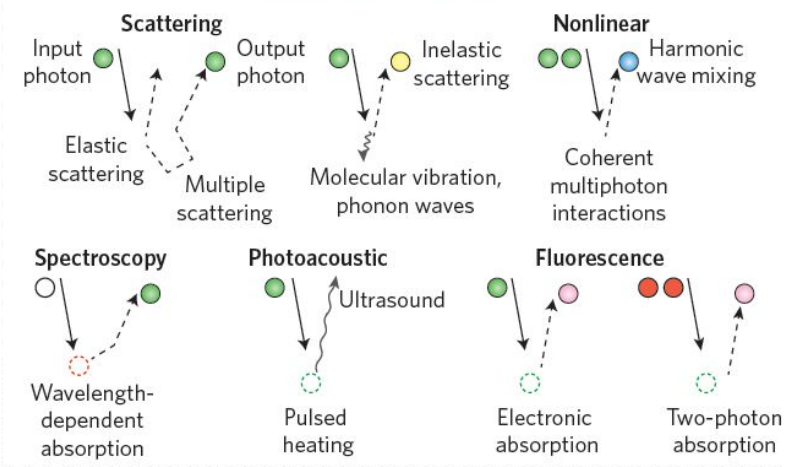
Light in diagnosis, therapy and surgery

Seok Hyun Yun[1,2,3*] and Sheldon J. J. Kwok[1,3]

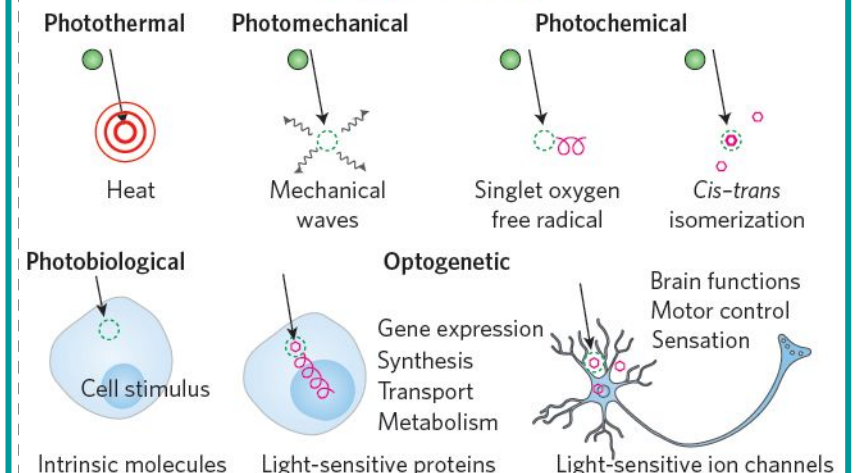
[Nature Biomedical Engineering 2017;1:0008]



Diagnostics and imaging

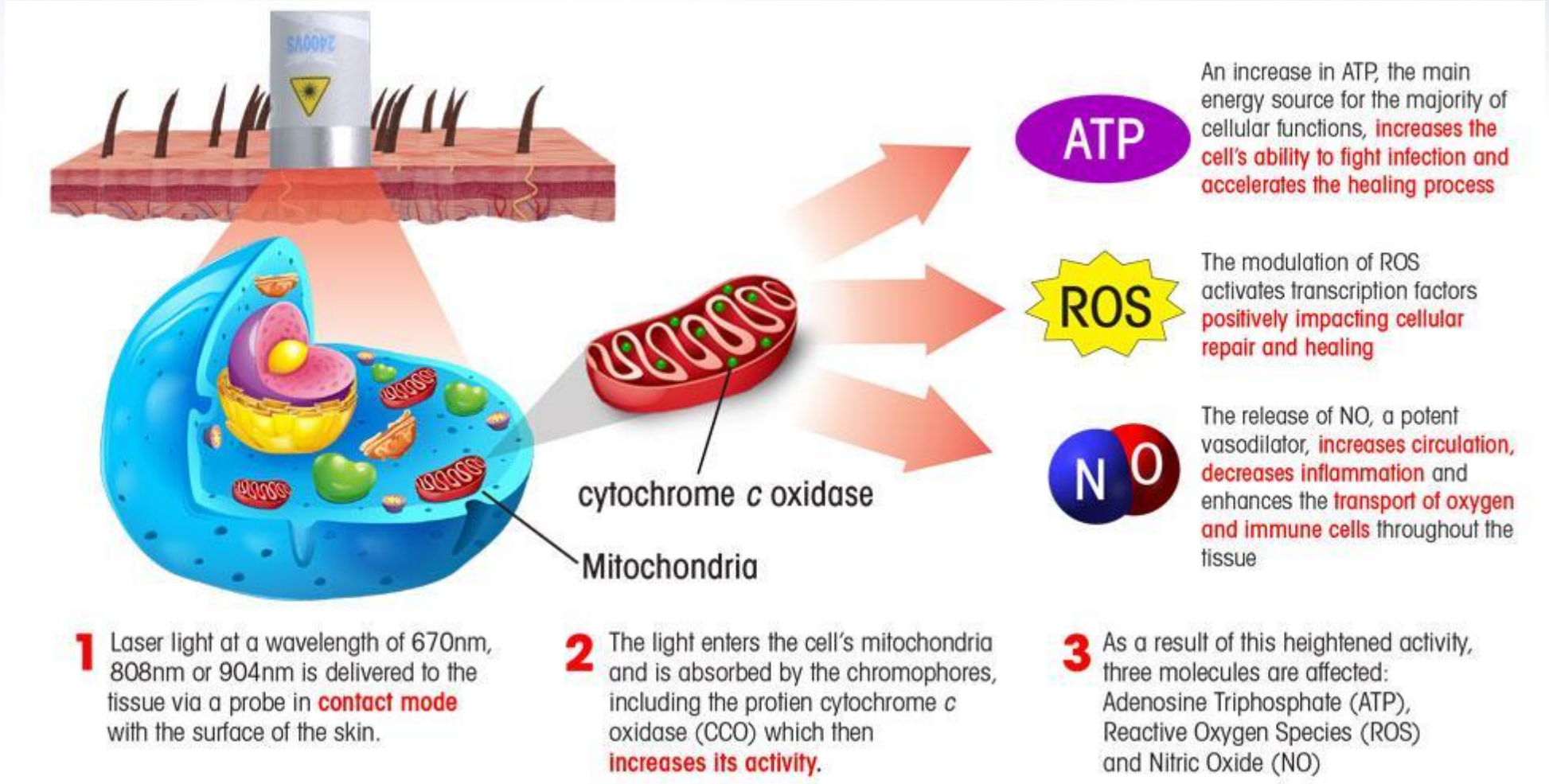


Surgery and therapy



3. Smart Photonic Contact Lens

❖ The photobiomodulation mechanism for light therapy in tissue



Hahn *et al.* Nat. Rev. Mater. 5, 149 (2020)

3. Smart Photonic Contact Lens

❖ Wearable photonic devices

Photobiomodulation

Purpose: Skin rejuvenation, hair growth, and wound healing

Display

Purpose: To deliver the information for users

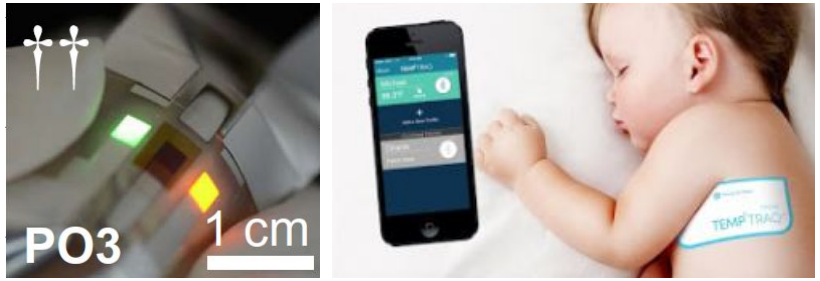
fNIRs

Purpose: To measure the brain activity using oxygen consumption in brain

Life cycle

Purpose: To control sleep by changing serotonin secretion using blue light

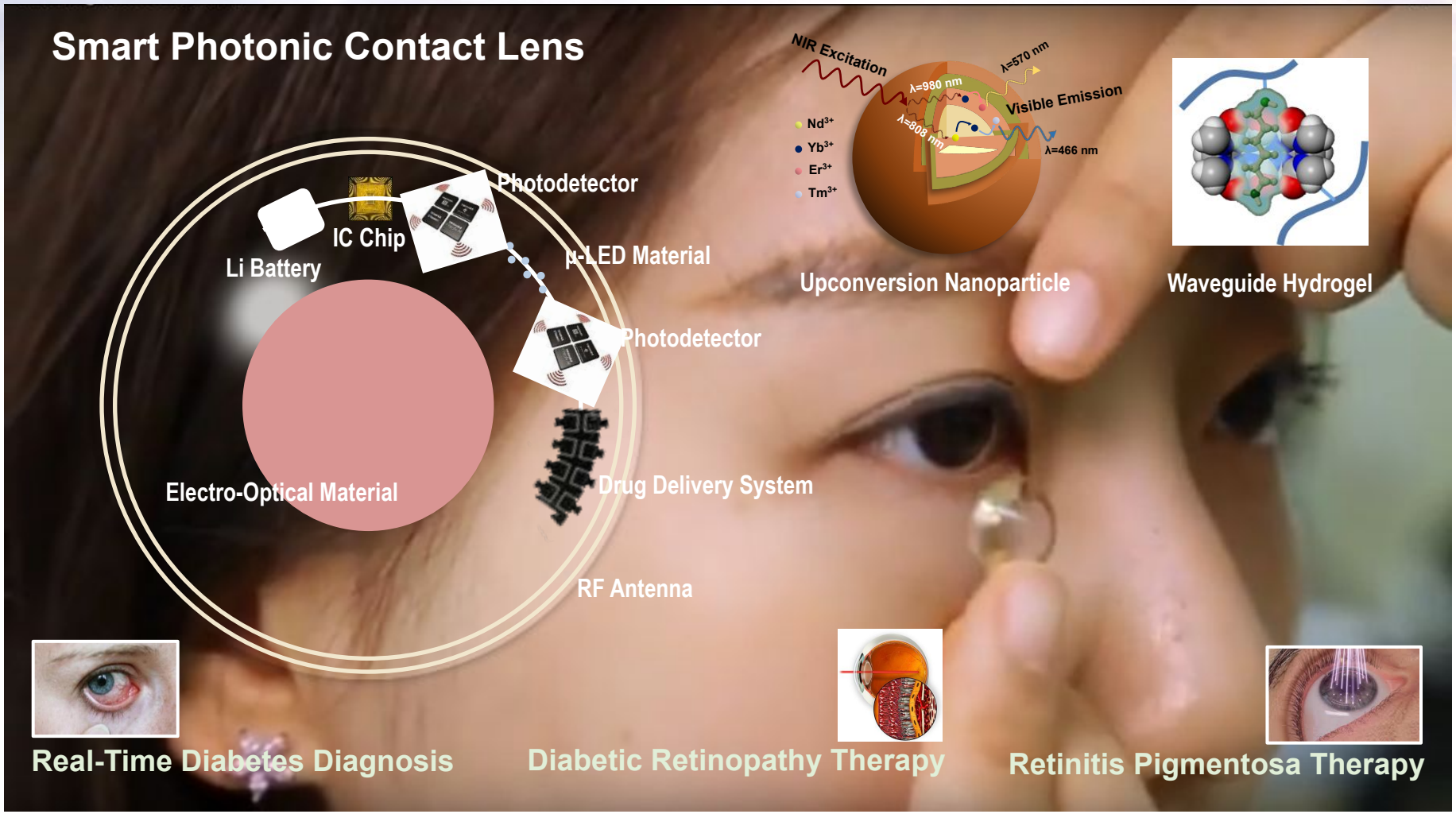
Pulse oximetry



Purpose: To measure oxygen concentration in blood using light absorption change

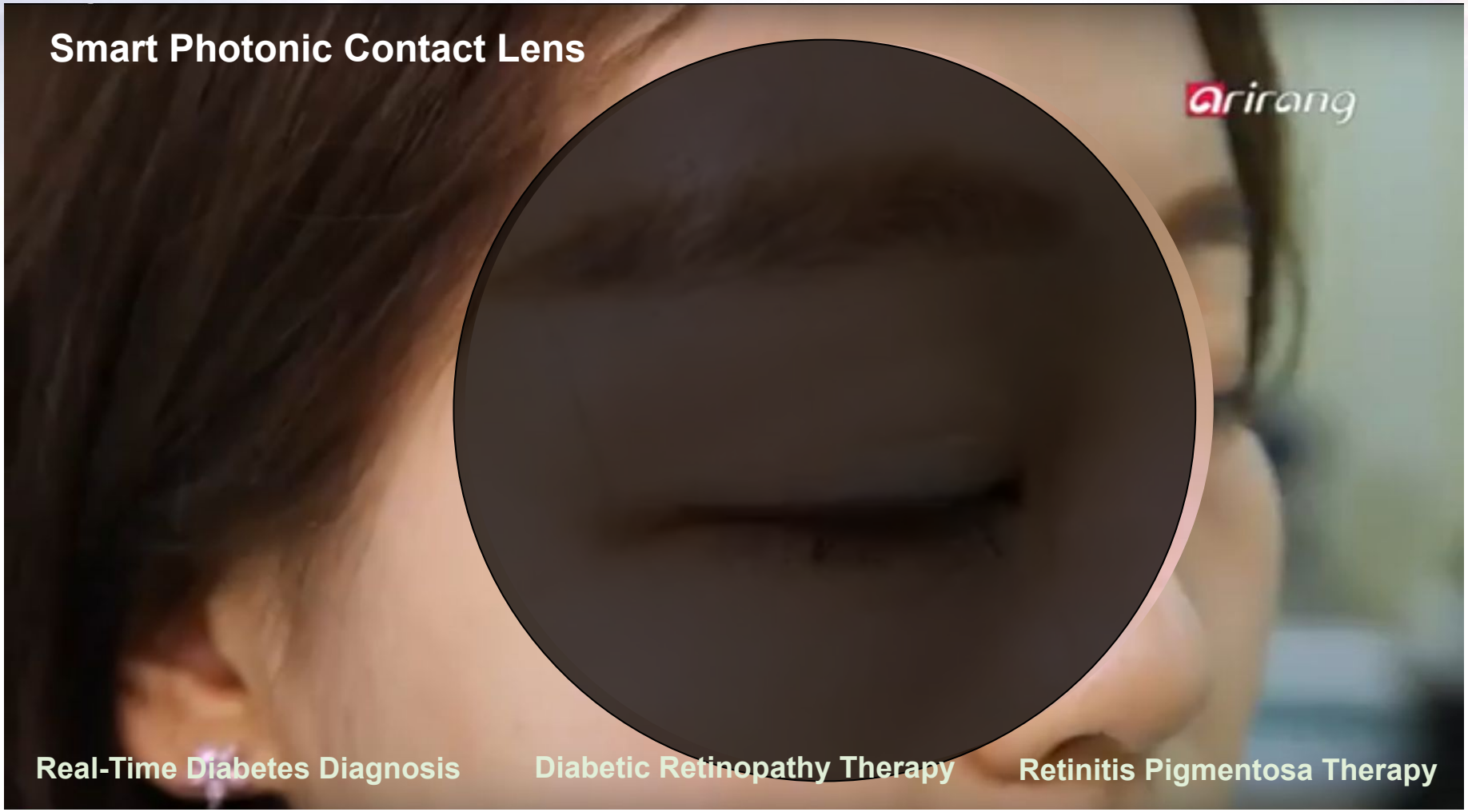
- fNIR: functional near-infrared spectroscopy

3. Smart Photonic Contact Lens



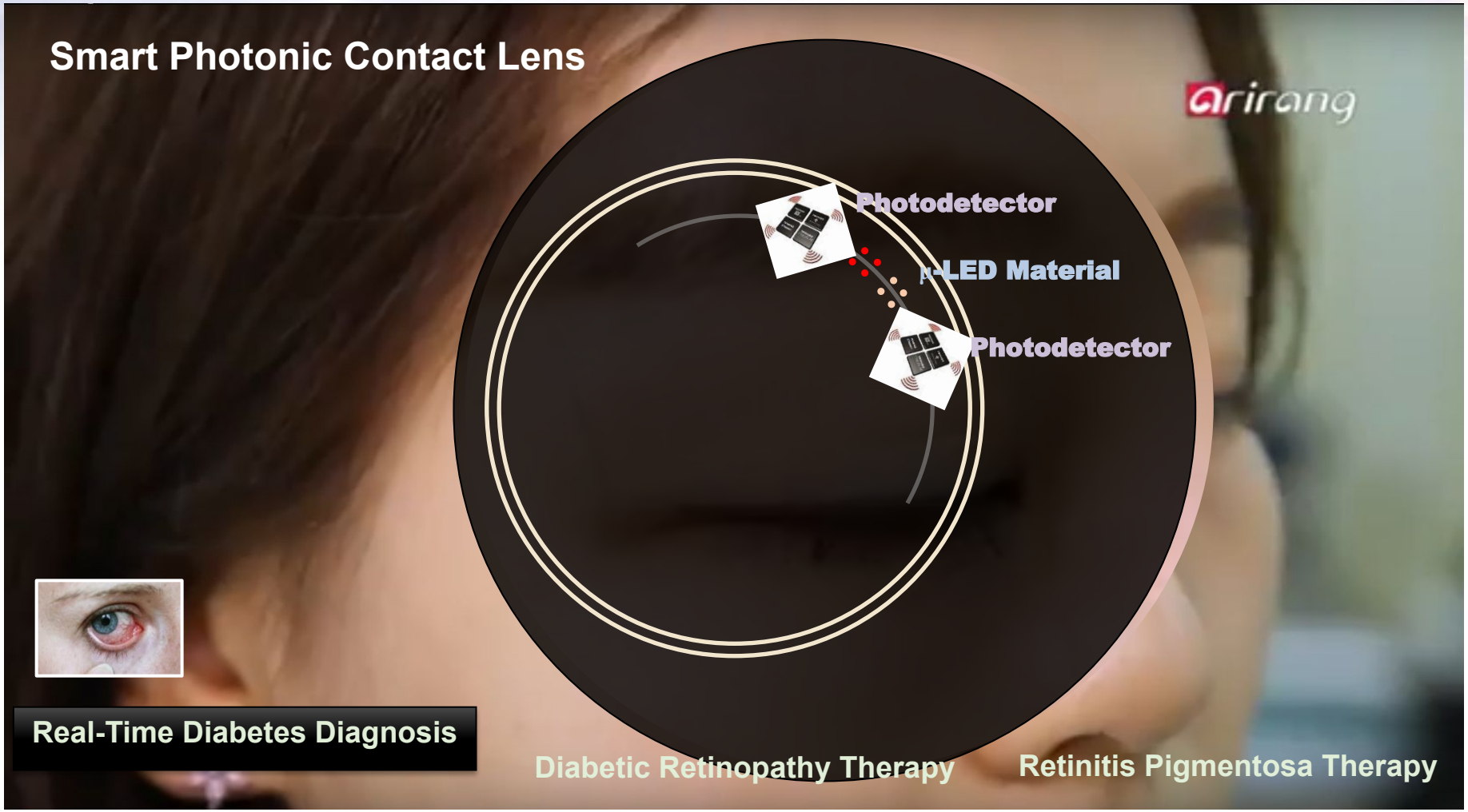
US Patent 15/522,816, EU Patent 16783461.3, PCT/KR2017/015243, Korean Patent 10-2017-0059225

3. Smart Photonic Contact Lens



US Patent 15/522,816, EU Patent 16783461.3, PCT/KR2017/015243, Korean Patent 10-2017-0059225

3. Smart Photonic Contact Lens

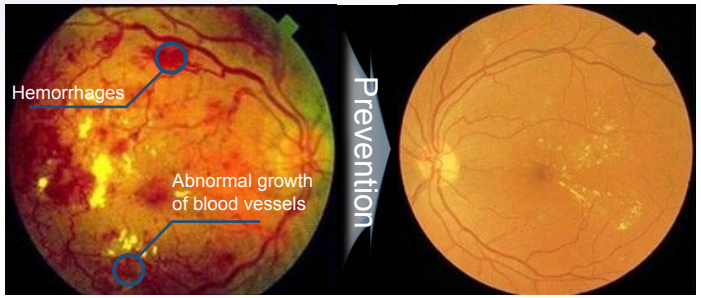


US Patent 15/522,816, EU Patent 16783461.3, PCT/KR2017/015243, Korean Patent 10-2017-0059225

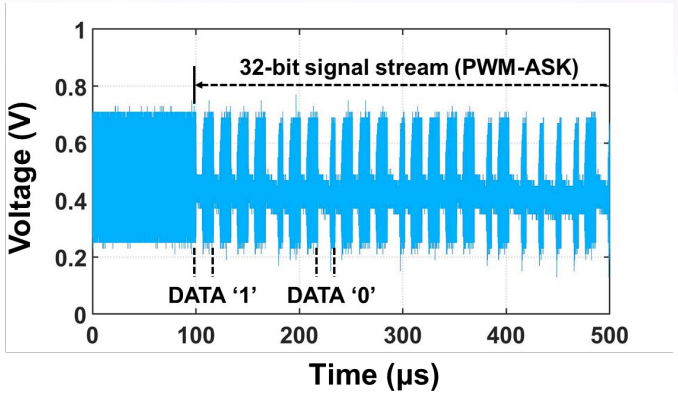
3. Smart Photonic Contact Lens

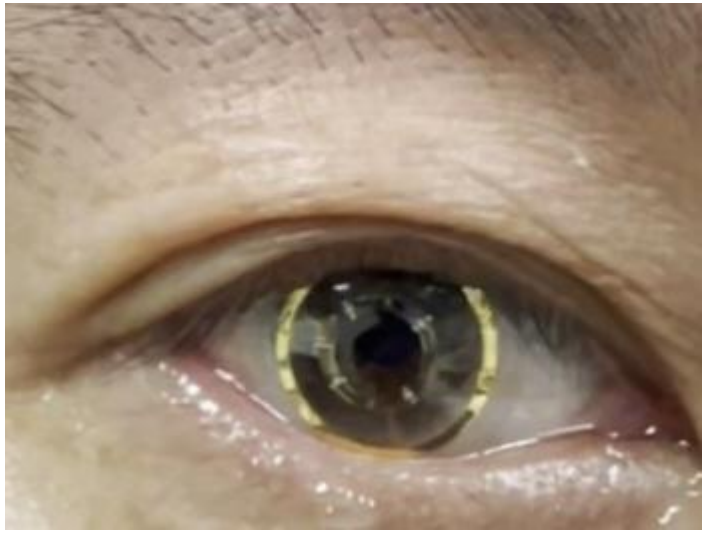
Summary

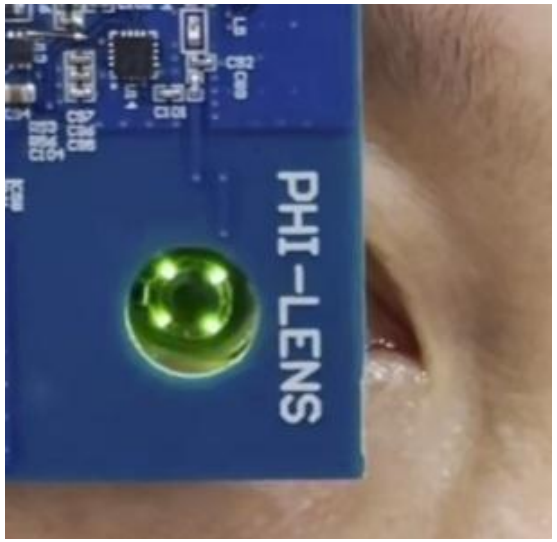
Smart photonic contact lens for diabetic retinopathy phototherapy

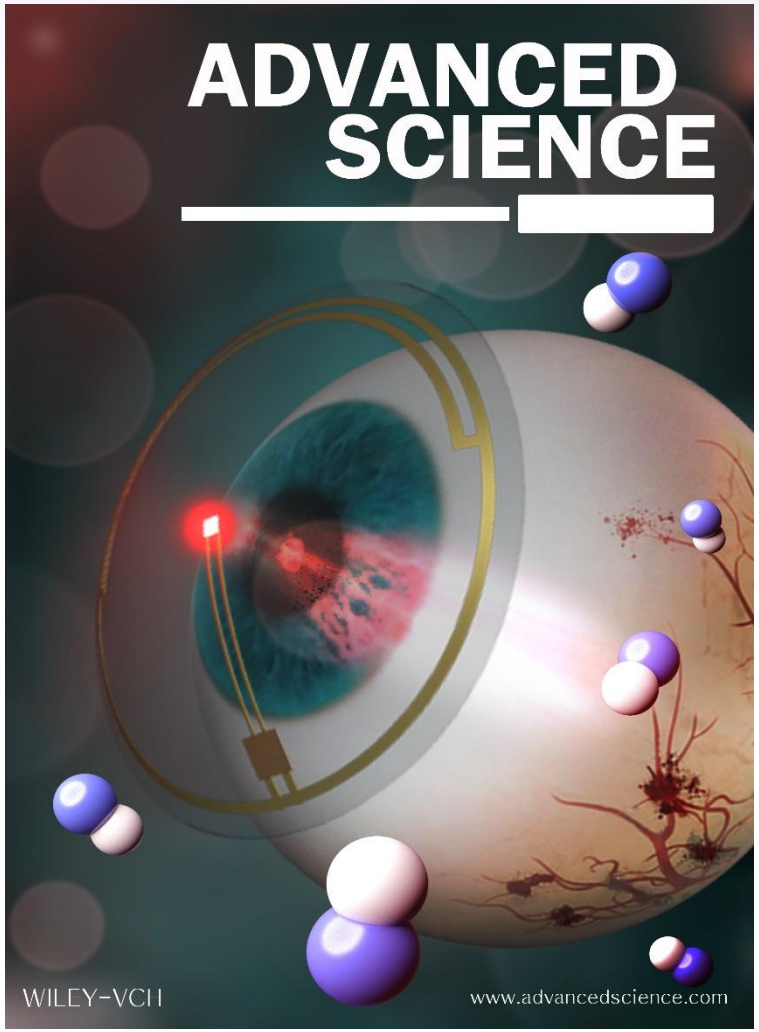


Diabetic retinopathy Normal







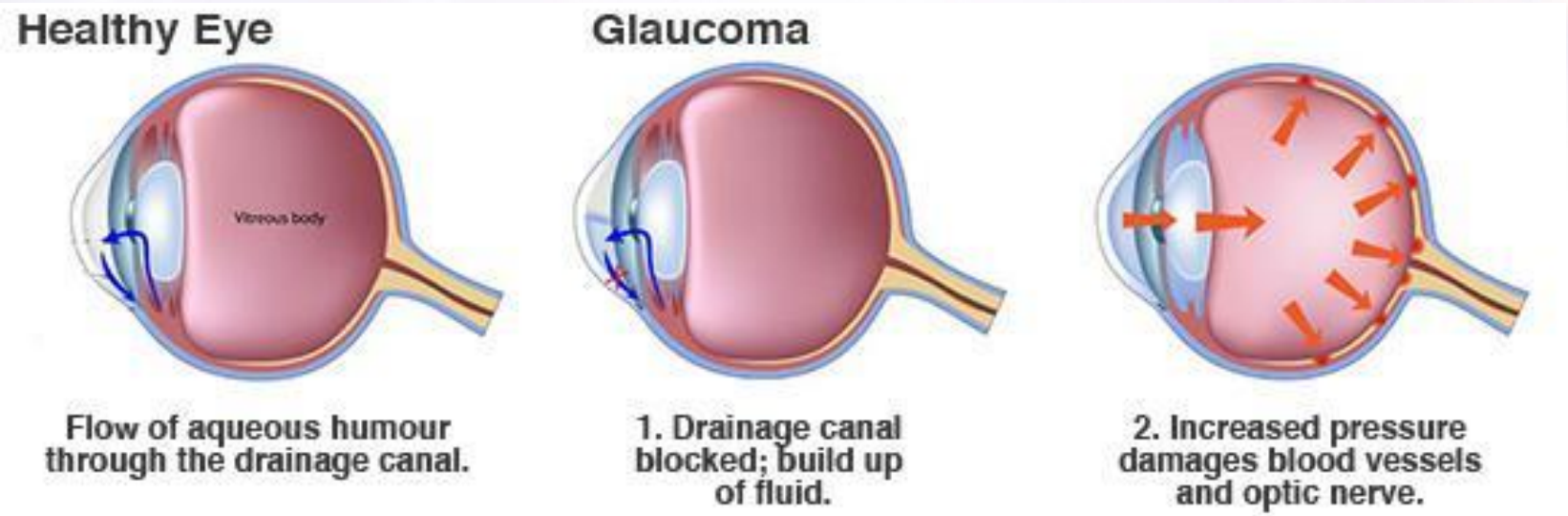


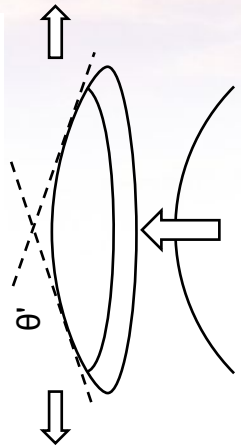
4. Smart Piezoelectric Contact Lens

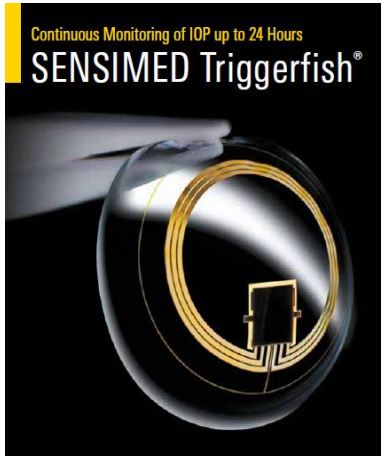
- Smart Electrochemical Contact Lens
- Smart Photonic Contact Lens
- Smart Piezoelectric Contact Lens

4. Smart Piezoelectric Contact Lens

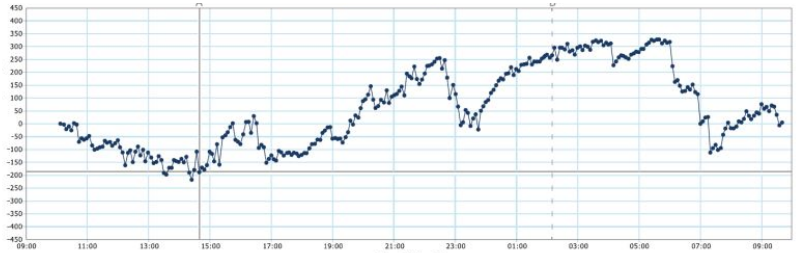
❖ Development and symptoms of glaucoma





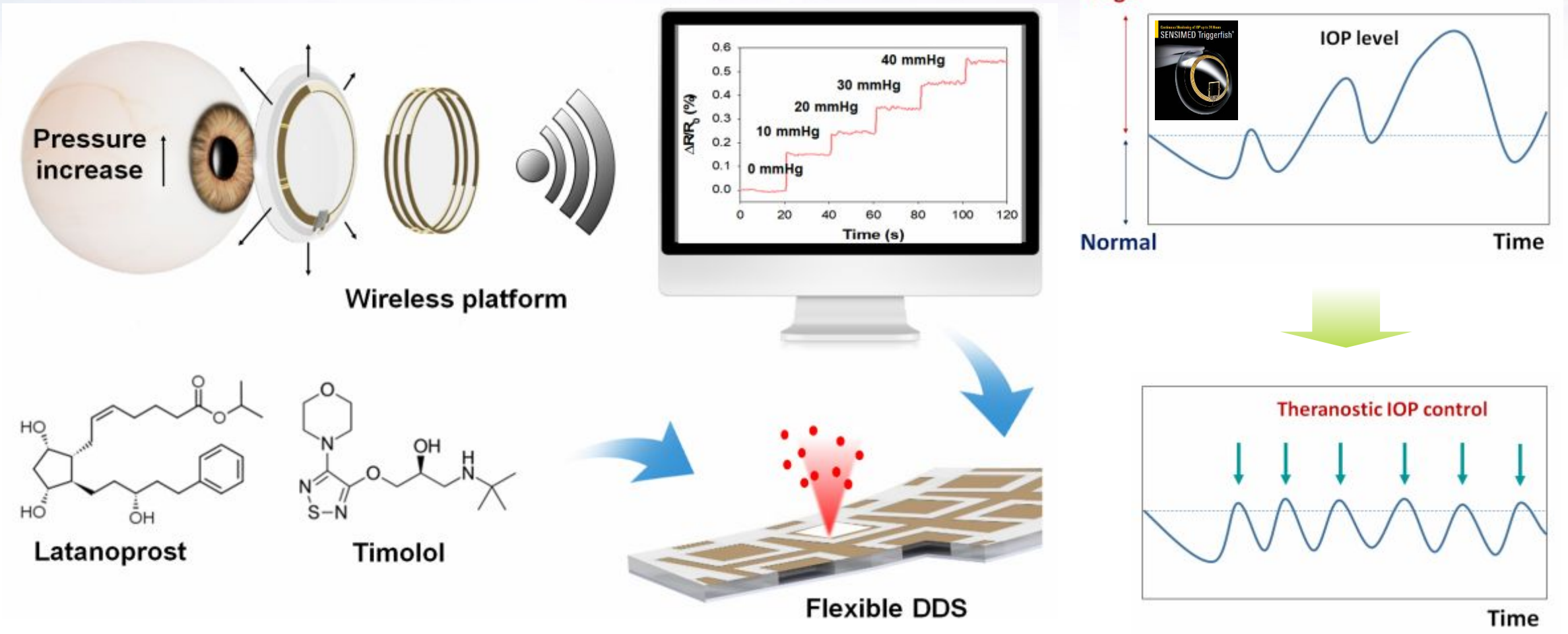


"Sensimed has developed a paradigm shift in glaucoma to continuously and non-invasively monitor individual intraocular pressure."



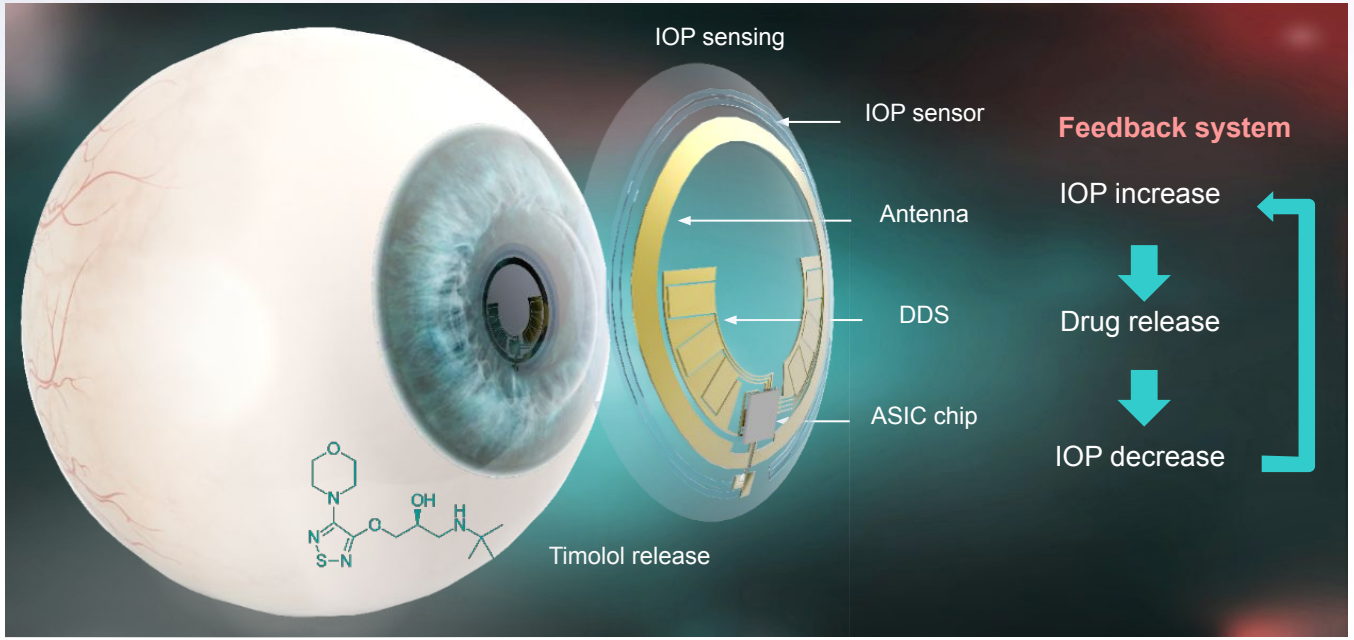
4. Smart Piezoelectric Contact Lens

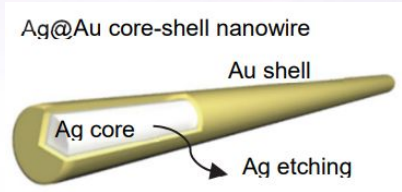
❖ Design of transparent AuHNW IOP sensor and DDS on smart contact lens

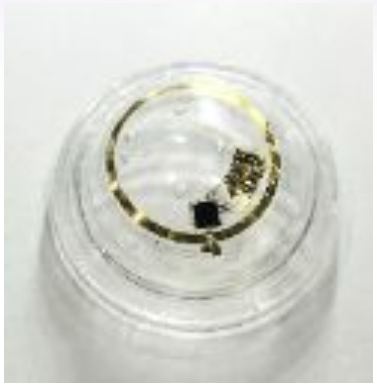


4. Smart Piezoelectric Contact Lens

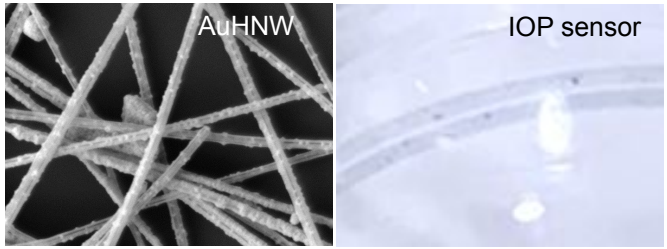
❖ Design of biocompatible AuHNW IOP sensor on smart contact lens



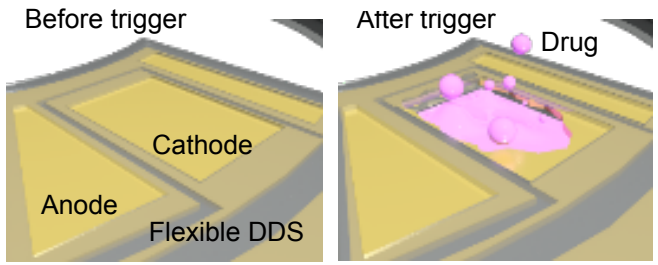


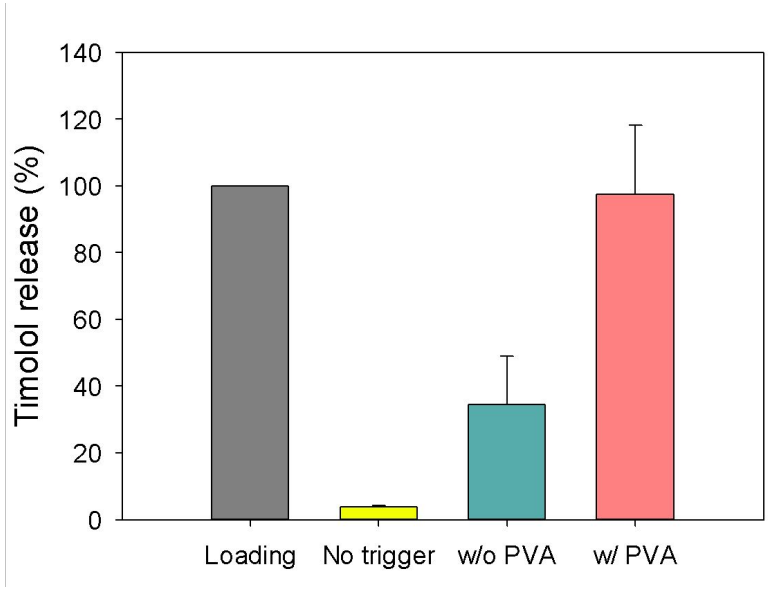


IOP sensor



Flexible DDS

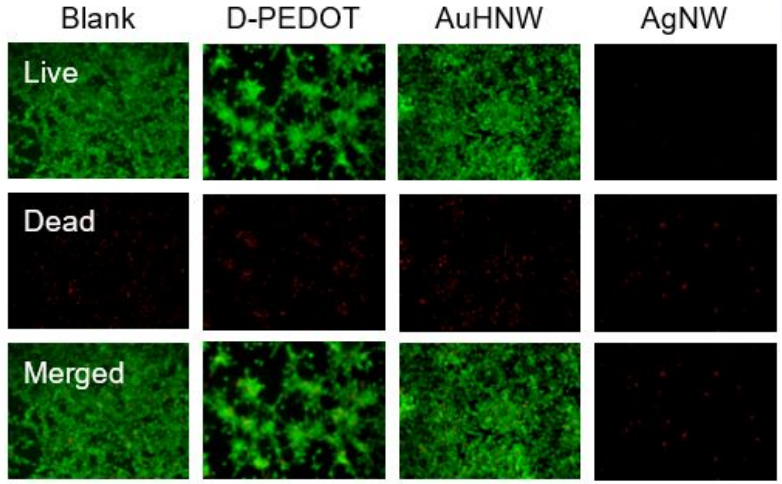


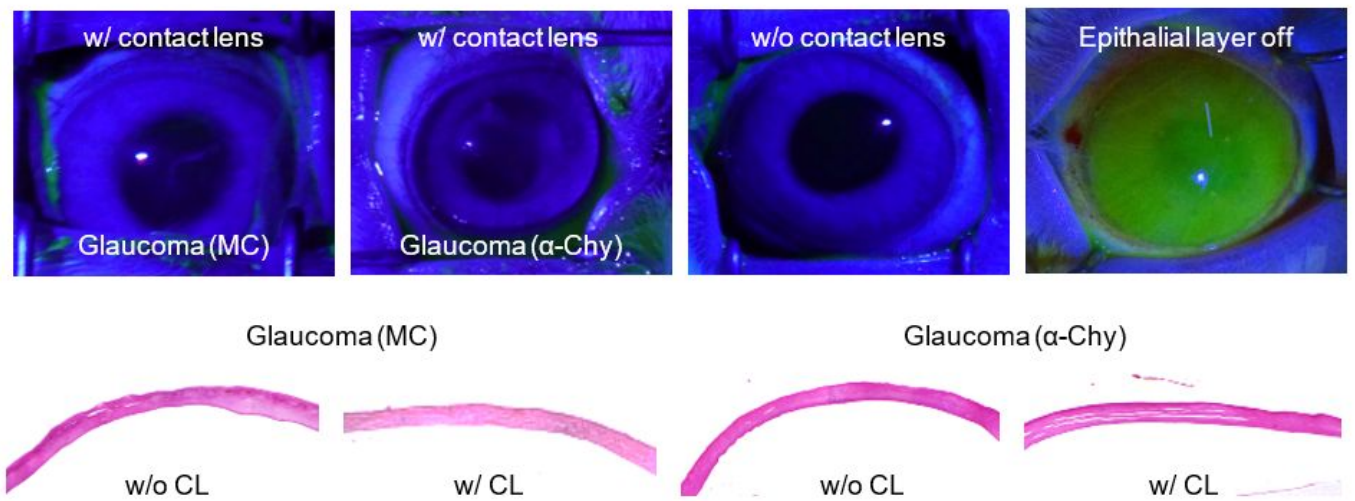


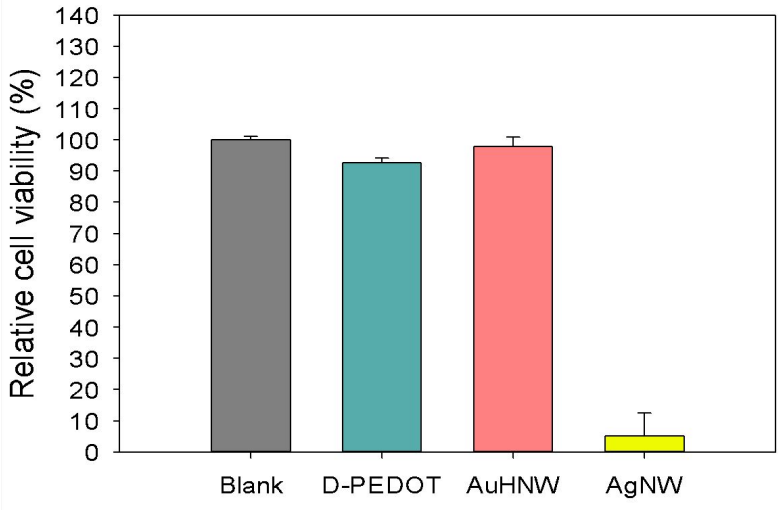
Hahn *et al.* Nature Communication, 13:6801 (2022)

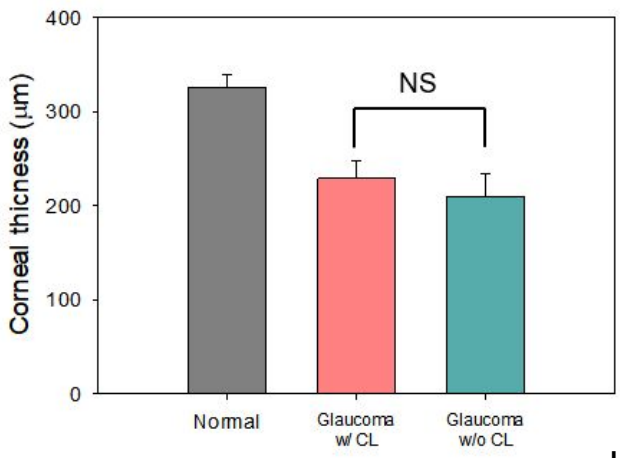
4. Smart Piezoelectric Contact Lens

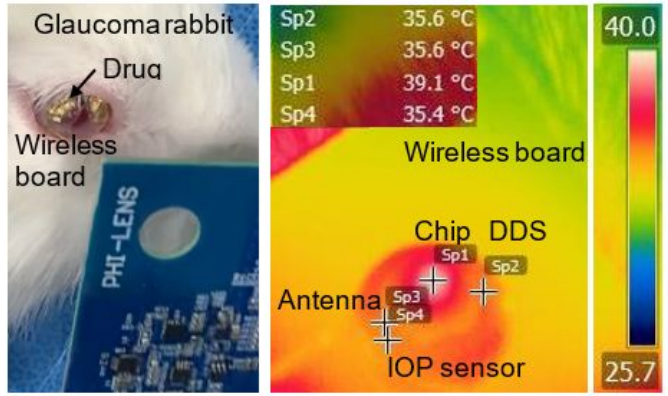
❖ Biological and electrical safety of smart contact lens for glaucoma IOP theranosis







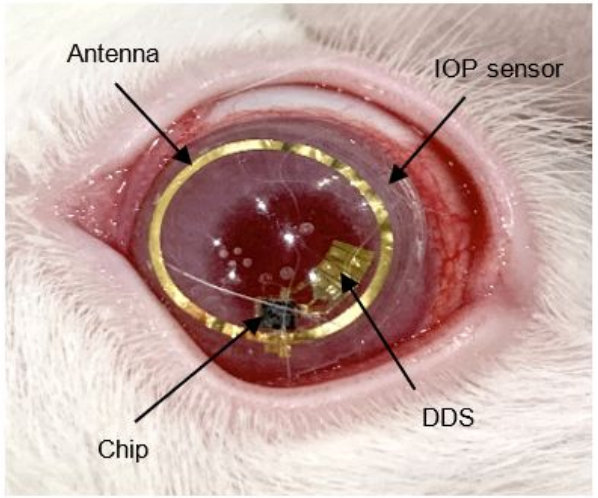


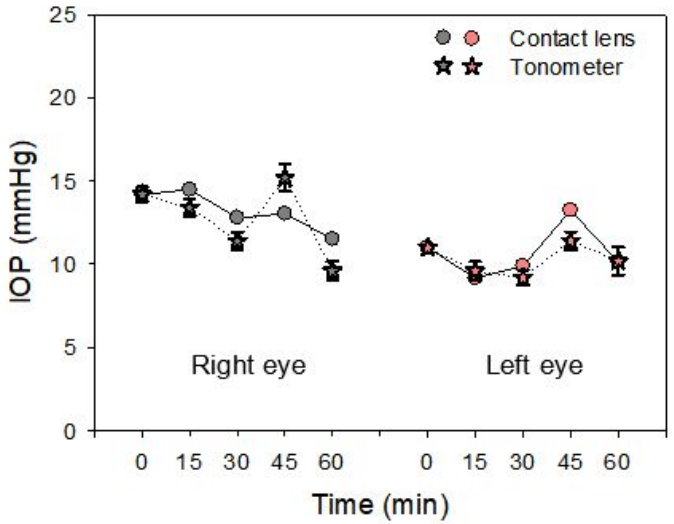


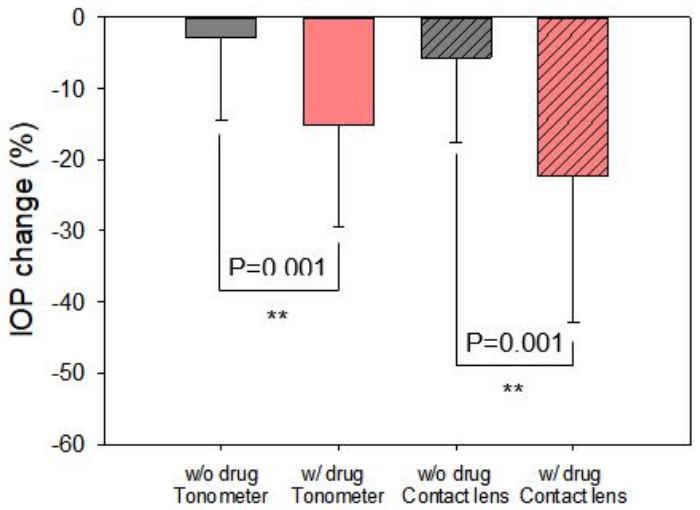
Hahn *et al.* Nature Communication, 13:6801 (2022)

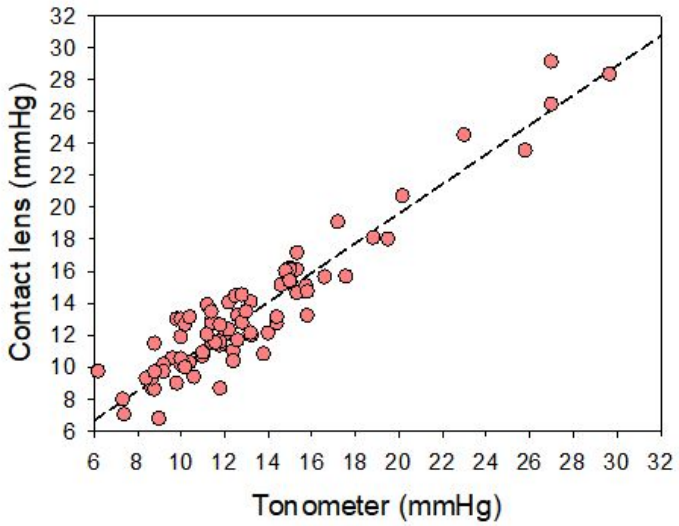
4. Smart Piezoelectric Contact Lens

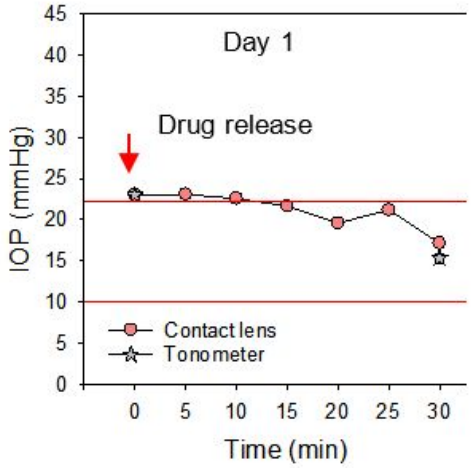
❖ *In vivo* monitoring and control of IOP by wireless smart contact lens

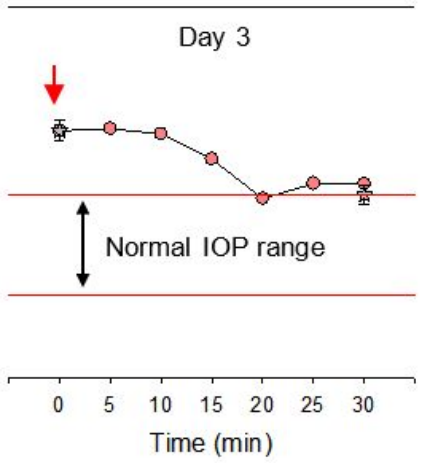


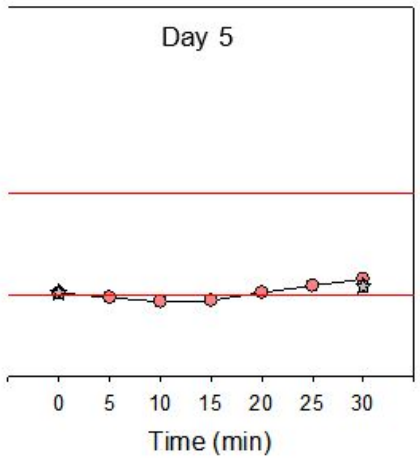








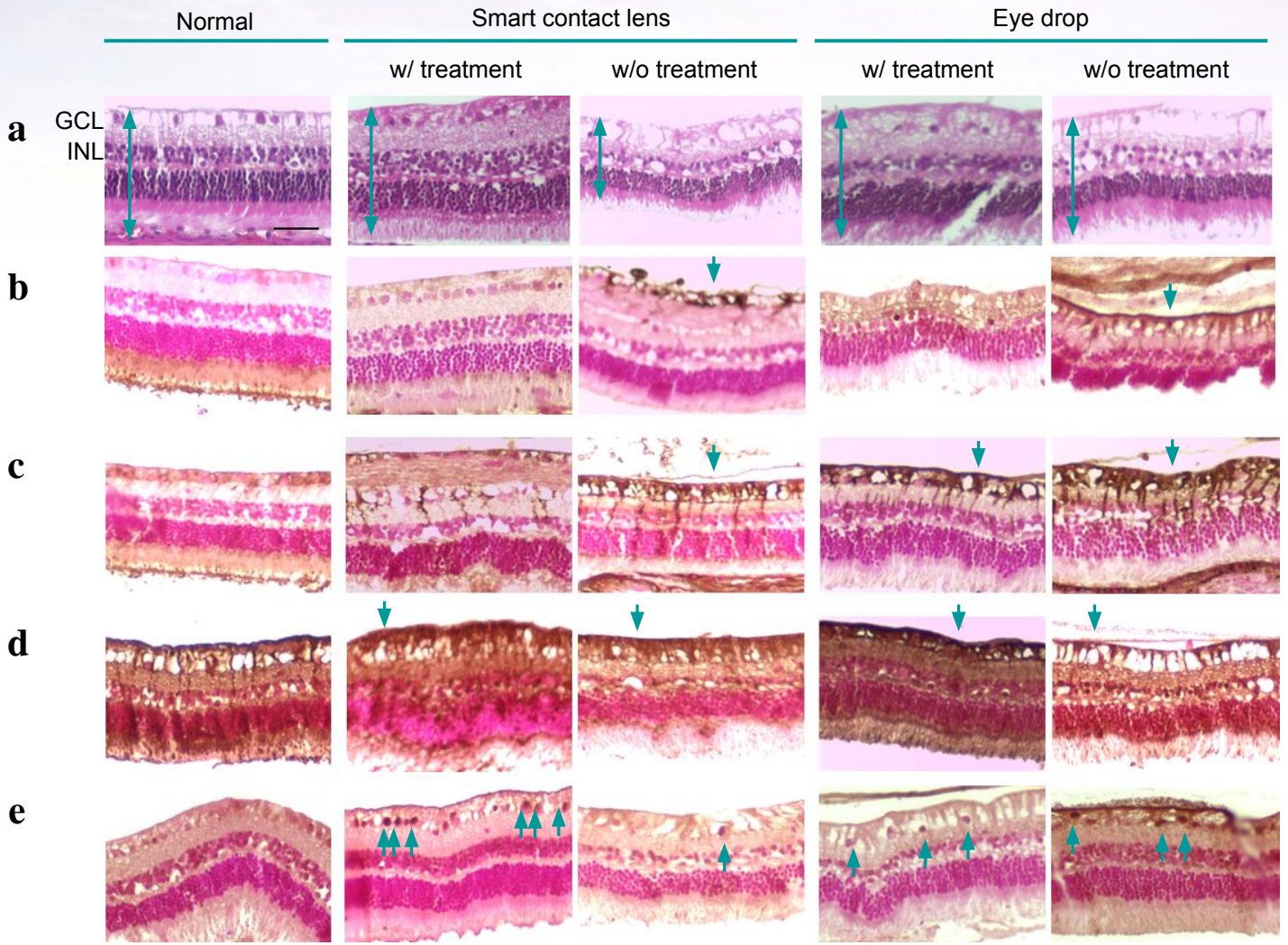




Hahn *et al.* Nature Communication, 13:6801 (2022)

4. Smart Piezoelectric Contact Lens

❖ *In vivo* monitoring and control of IOP by wireless smart contact lens



***In vivo* therapeutic effect by theranostic smart contact lens and eye drop in glaucoma rabbits induced by injecting methylcellulose. a**, OM images for retinal histology. OM images for immunohistochemical analyses for **b**, GFAP, **c**, CD11b, **d**, BDNF and **e**, Brn3a. Arrows indicate the expression of each marker (scale bar, 100 μm).

Hahn *et al.* Nature Communication, 13:6801 (2022)

4. Smart Piezoelectric Contact Lens

Summary Smart piezoelectric contact lens for theranostic IOP management in glaucoma

nature communications

Article

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Wireless theranostic smart contact lens for monitoring and control of intraocular pressure in glaucoma

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Check for updates

Tae Yeon Kim[1], Jee Won Mok[2], Sang Hoon Hong[1], Sang Hoon Jeong[1], Hyunsik Choi[3], Sangbaie Shin[3], Choun-Ki Joo[2] & Sei Kwang Hahn[1,3]

Glaucoma is one of the irreversible ocular diseases that can cause vision loss in some serious cases. Although Triggerfish has been commercialized for monitoring intraocular pressure in glaucoma, there is no smart contact lens to monitor intraocular pressure and take appropriate drug treatment in response to the intraocular pressure levels. Here, we report a precisely integrated theranostic smart contact lens with a sensitive gold hollow nanowire based intraocular pressure sensor, a flexible drug delivery system, wireless power and communication systems and an application specific integrated circuit chip for both monitoring and control of intraocular pressure in glaucoma. The gold hollow nanowire based intraocular pressure sensor shows high ocular strain sensitivity, chemical stability and biocompatibility. Furthermore, the flexible drug delivery system can be used for on-demand delivery of timolol for intraocular pressure control. Taken together, the intraocular pressure levels can be successfully monitored and controlled by the theranostic smart contact lens in glaucoma induced rabbits. This theranostic smart contact lens would be harnessed as a futuristic personal healthcare platform for glaucoma and other ocular diseases.

Glaucoma is a chronic eye disease requiring continuous medical care for patients' life time. Intraocular pressure (IOP) is one of the most important indicators of glaucoma[1,2]. Glaucoma patients are generally recommended for monitoring IOP and reducing IOP to a lower range. Accordingly, the appropriate IOP control is currently the only available first medical care for glaucoma patients. Commercial tonometers such as a rebound tonometer and a Goldmann applanation tonometer (GAT) have been used for the static IOP measurements in the clinic[3]. However, these measurements have some challenges. GAT can be inconvenient due to time and space constraints. Although home tonometry is portable, patients need to carefully follow the manual for accurate detection. These can significantly interrupt the daily life of patients. Furthermore, it is difficult to collect many data from the conventional static IOP measurements in a single day and to monitor the IOP fluctuation of patients. This may cause inappropriate treatment to patients, because the IOP can change time to time[4,5]. Recently, eye drop solutions are the important first medical treatment for the IOP control of glaucoma patients[6–8]. However, it is highly challenging to achieve the high adherence of glaucoma patients. The method and time of drug treatments as instructed have not been followed by many glaucoma patients[9]. Furthermore, each patient can have a different therapeutic effect of drugs, which necessitate a different drug dose for each person[10]. Accordingly, it is important to monitor continuous IOP changes in real-time and delivers drugs in response to the IOP profiles.

Smart contact lenses can provide a new paradigm in glaucoma as a promising alternative to conventional management methods with non-invasive, continuous IOP monitoring and on-demand drug delivery[11,12]. In particular, recent smart contact lenses based on strain

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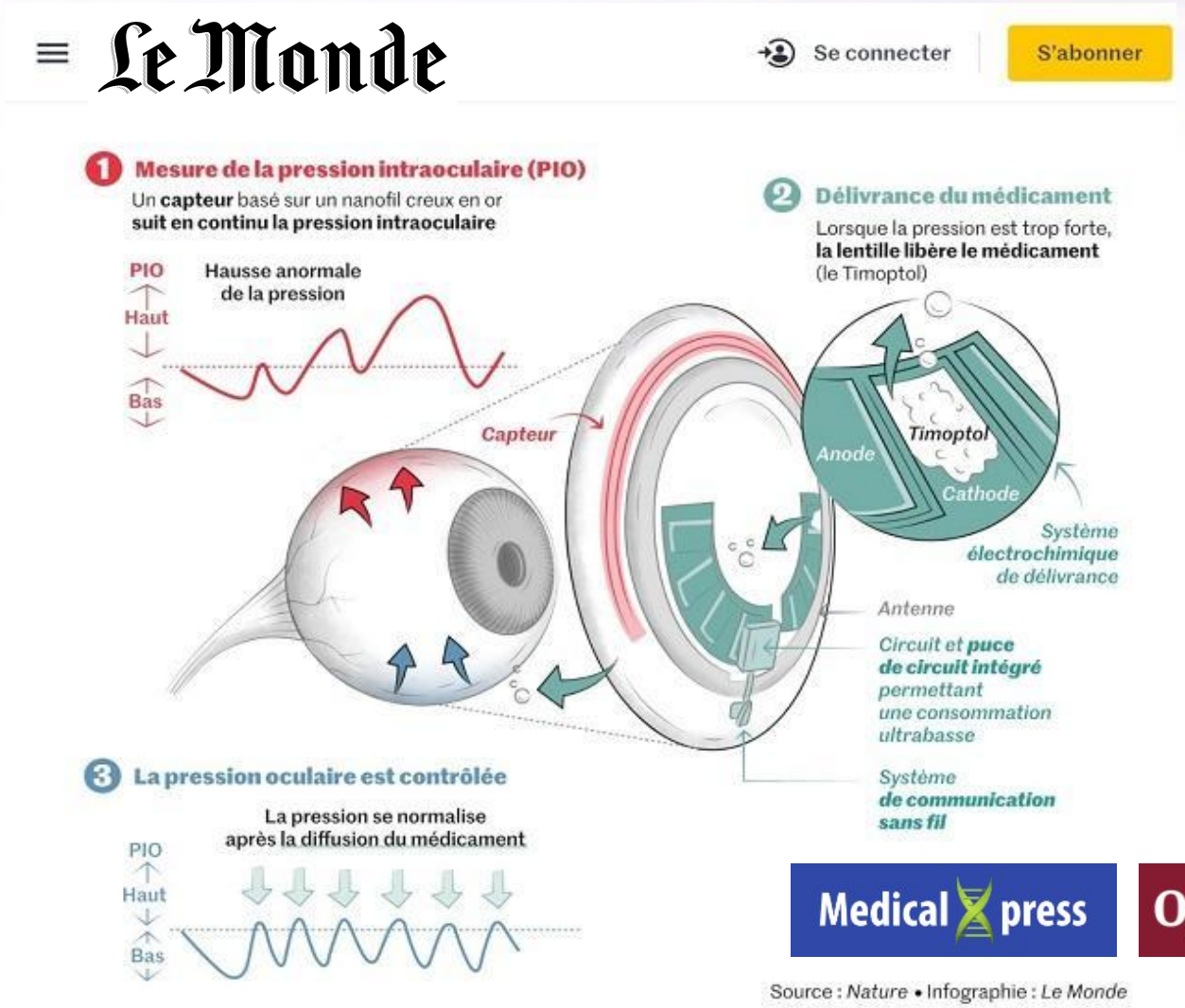
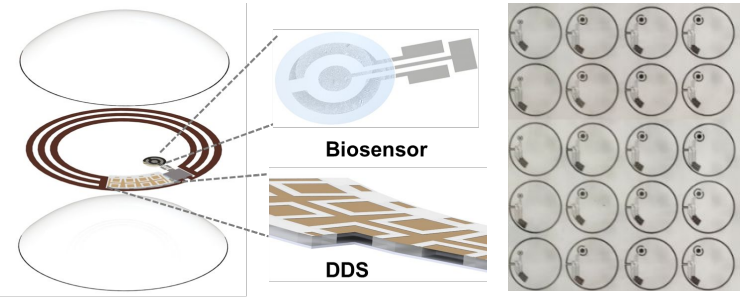
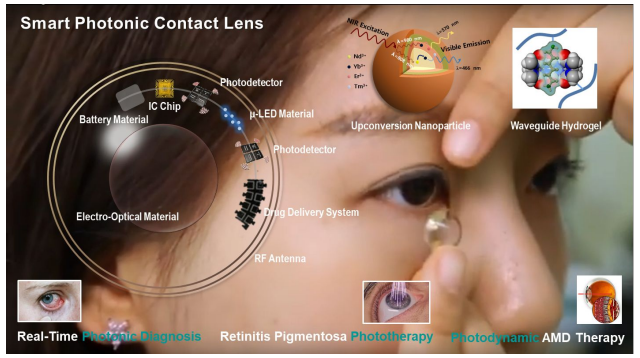


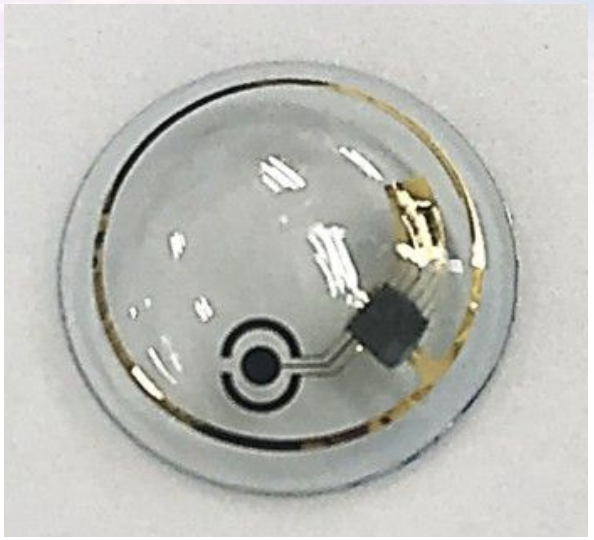
5. Summary for Smart Theranostic Contact Lens

Smart Electrochemical Contact Lens

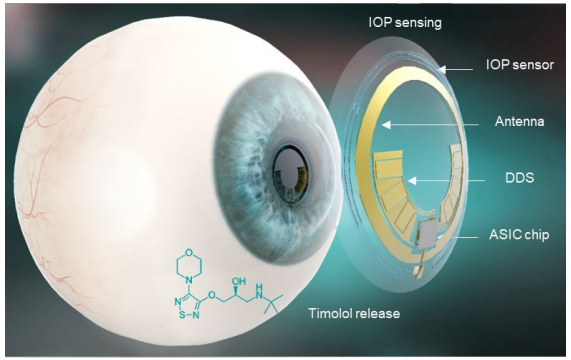


Smart Photonic Contact Lens

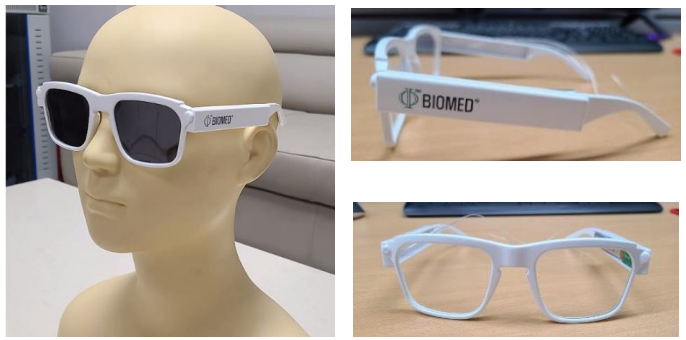




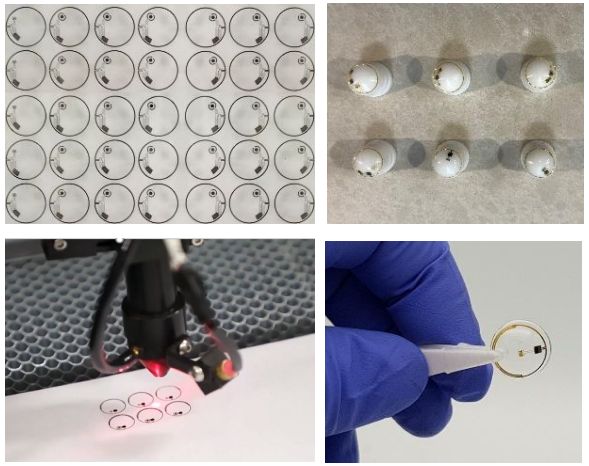
Smart Theranostic Contact Lenses for Diabetes and Ocular Diseases



Smart Piezoelectric Contact Lens

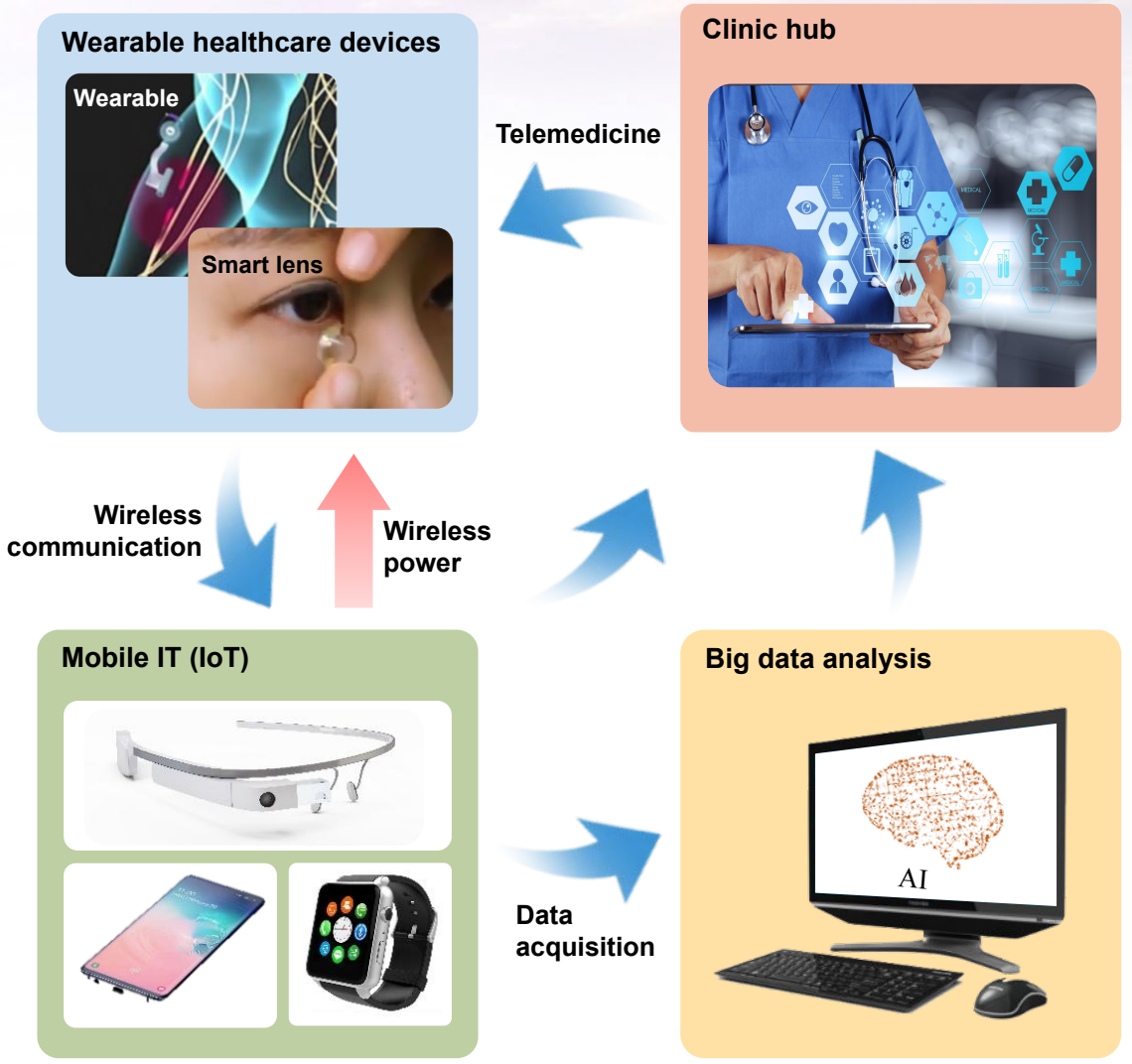


Smart Glasses for Ubiquitous Healthcare



5. Smart Healthcare Contact Lens and Glasses

❖ Wireless smart contact lens and glasses for ubiquitous healthcare in Industry 4.0



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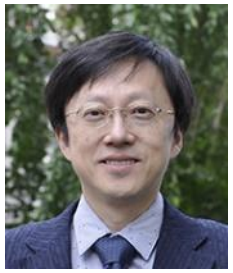

Thank You for Your Kind Attention !!!

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