Simerdip Kaur takes a look at the latest ophthalmology-related news stories and asks which are scientific reality and which are 'fake news'.

Headline: Glucose-sensing contact lenses replace the finger prick test!

The concept of contact lenses was first illustrated by Leonardo da Vinci in 1508, although it was only in 1887 when the first glass contact lens was manufactured [1]. These proved to be very heavy and covered the entire surface of the eye, thus making it unfit for purpose until later in 1939 when the first plastic contact lens was designed. Over the years, plastic contact lenses have become more sophisticated and evolved to the various types available today including soft, gas permeable and silicone hydrogel. These lenses cover only the corneal surface, but scleral lenses are also available.

This seemingly small device has had life changing effects in correcting refractive errors for some patients. Recent technological advances could allow them to have more than just an optical function. Wearable technologies such as fitness bands and watches acting as monitors of physical activity are increasingly popular in society today. These gadgets are now also being developed to monitor for signs of disease through associated physiological changes in the human body.

This has led to the innovation of a 'smart contact lens' which aims to provide a non-invasive solution to measuring blood glucose with the use of tear glucose level instead.

Curiosity in tear glucose levels dates back decades to the 1930s when researchers sought various methods to measure it [2]. Glucose in the aqueous component of the tear film is obtained from ultrafiltration of plasma in the acinar region of the lacrimal and accessory glands [3]. Tear glucose levels in normal individuals have been found to range between 0.0 and 3.6 milimoles per litre [2]. Diabetic patients have higher tear glucose levels measuring up to 4.7 milimoles per litre [2,4]. The tear glucose levels obtained were varied depending on the methods used, for example, non-invasive, chemical or mechanical tear stimulation, as well as the volume of tears obtained which were usually highest with mechanical stimulation [2].

One of the earliest studies of contact lens tear glucose measurements was conducted by March et al. in 2004 on five patients with type two diabetes [5]. Their device consisted of a fluorescence sensor on a modified contact lens and the signal was captured with a hand-held photofluorometer. A notable issue with this study is that the absolute fluorescent signal was not calibrated for absolute glucose concentrations so this had to be adjusted for each subject in the study in addition to the small sample size. Nevertheless they demonstrated a correlation in tear and blood glucose concentration with a rise in the former after an oral glucose tolerance test [2].

Similarly, in 2011 Zhang et al. developed a fluorescent-based contact lens sensor using porous nanostructure optical probe labelled with a lectin protein with specific binding affinity to glucose [6]. Their research mainly focused on the development of the porous material and studying its properties, proving that it was suitable for sensing glucose continuously for up to five days in in-vitro settings only [6].

Google also announced their efforts in producing the 'Google Contact Lens' in collaboration with Novartis in 2014 [7]. Their design included a contact lens implanted with a wireless microchip containing an antenna to transmit glucose readings to a smart device. The lens contains a pinhole to allow the tears to drain towards a glucose sensor embedded within the soft lens material. This lens was due to be launched within five years, however, this has slowed down due to technical issues.

In 2016, a separate team in South Korea led by Kim et al. developed a multifunctional sensor applied within a contact lens to monitor both glucose in tears and intraocular pressure (IOP) using the resistance and capacitance of the electronic device [8]. Their device is made of a transparent and flexible sensor made of graphene – a form of carbon, and its hybrid materials on a soft contact lens with metal nanowires. They performed in-vivo testing using this contact lens on rabbits and noted that the contact lens and sensor remained stable even after eye-blinks and that the rabbit tolerated it well. They successfully obtained tear glucose readings wirelessly two hours after feeding the rabbit and the values on the sensors frequency reflection curve were higher than the pre-prandial results, indicating glucose binding in the tear fluid [8].

The studies discussed so far offer a glimpse into some of the research currently taking place in non-invasive glucose monitoring via contact lens use. However, the implementation of smart contact lenses to measure tear glucose as a substitute for the finger prick test remains contested due to the reasons below.

First and foremost, a clear association between tear and blood glucose readings needs to be established. Studies using mechanical stimulation of tears show correlation with blood glucose whilst chemical stimulation does not. This is expected due to the leakage of glucose from conjunctival epithelial cells and the interstitial space, as well as from the aqueous layer of the tear film [2]. Other factors affecting tear film evaporation such as changes in ambient temperature levels, humidity and the use of a contact lens also alter tear glucose levels [9]. Additionally, the mechanical irritation caused by a contact lens can directly stimulate tear production and thus affect tear glucose concentration [2]. Thus at this stage it is not possible to validate that tear glucose is a true reflection of blood glucose levels.

Ultimately, these smart contact lenses need to be tested on human subjects with large sample sizes over a longer duration of time to ascertain their accuracy and reliability in comparison with blood glucose measurements. Other factors to consider include the cost implication, suitability of use in patients with existing ocular surface disease or those whom already wear vision-correcting contact lenses, infection risk and patients with phobia too. Although it is an exciting development in the field of medical technology, the finger prick test remains for now.

References

1. Contact Lens Manufacturers Association www.contactlenses.org/timeline.htm
2. Baca JT, Finegold DN, Asher SA. Tear glucose analysis for the noninvasive detection and monitoring of diabetes mellitus. *The Ocular Surface* 2007;**5(4)**:280-93.
3. Ferris J: *Basic Sciences in Ophthalmology: a self-assessment text*. BMJ Books; 1999.
4. Lewis JG, Stephens PJ. Tear glucose in diabetes. *Br J Ophthalmol* 1958;**42**:754-8.
5. March WF, Mueller A, Herbrechtsmeier P. Clinical trial of a noninvasive contact lens glucose sensor. *Diabetes Technol Ther* 2004;**6**:782-9.
6. Zhang J, Hodge W, Hutnick C, Wang X. Noninvasive diagnostic device for diabetes through measuring tear glucose. *J Diabetes Sci Technol* 2011;**5(1)**:166-72.
7. Google. Official Blog. https://googleblog.blogspot.co.uk/2014/01/introducing-our-smart-contact-lens.html
8. Kim J, Kim M, Lee M-S, et al. Wearable smart sensor systems integrated on soft contact lenses for wireless ocular diagnostics. *Nature Communications* 2017;**8**:14997.
9. Willcox MDP, Dartt DA. Complexity of the tear film: Importance in homeostasis and dysfunction during disease. *Exp Eye Res* 2013;**117**:1-3.

SECTION EDITOR

Simerdip Kaur,

Ophthalmology Specialty Trainee Year 1, KSS Deanery, UK.

E: simerdip.kaur@hotmail.com