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Contact lens assisted imaging with integrated flexible handheld probe for glaucoma diagnosis

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ABSTRACT

Angle closure glaucoma accounts for majority of the bilateral blindness in Asian countries such as Singapore, China, and India. Abnormalities in the optic nerve and aqueous outflow system are the most indicative clinical hallmarks for glaucoma of this clinical subtype. Traditional photographic imaging techniques to assess the drainage angle are contact based, and may expose patients to risk of corneal abrasion and infections. In addition, these procedures require the use of viscous ophthalmic gels as coupling medium to overcome the phenomenon of total internal reflection at the tear-air interface. In this paper, we propose an integrated flexible handheld probe consisting of a micro color CCD video camera and white light LEDs. The handheld probe is able to capture images of the fundus and opposite iridocorneal angle when placed at the central cornea or limbus respectively. Here, we propose the use of hydrogel contact lens as an index matching medium and better protective barrier, as an alternative to conventional ophthalmic gels. The proposed imaging system and methodology has been successfully tested on porcine eye samples, *ex vivo*. With its high repeatability, reproducibility, and a good safety profile, it is believed that the proposed imaging system and methodology will complement existing imaging modalities in the diagnosis and management of glaucoma.

Keywords: Glaucoma, iridocorneal angle imaging, fundus imaging, integrated flexible handheld probe, contact lenses

1. INTRODUCTION

In the trabecular outflow route, aqueous humour exits the anterior chamber of the eye via the trabecular meshwork. It then passes through the Schlemm's canal and collector channels, and drains into the aqueous veins and episcleral vessels^[1]. Angle-closure or closed-angle glaucoma is the narrowing and closing of the iridocorneal angle, which is the area between the cornea and the iris. It is characterized by the anatomical predisposition of narrow angles with iridocorneal contact. The narrow angle obstructs trabecular outflow and increases intraocular pressure overtime, resulting in irreversible optic nerve damage. It is estimated that in 2020, 79.6 million people will be affected by open-angle and angle-closure glaucoma, with primary angle closure glaucoma being most prevalent in Asian countries such as Singapore, China, and India^[2].

Due to the inconsistencies in signs and symptoms among the various clinical subtypes, a comprehensive glaucoma examination usually comprises of five initial tests: tonometry, perimetry, pachymetry, ophthalmoscopy, and gonioscopy. This is followed by the careful assessment and evaluation of the optic nerve and anterior chamber angle, which are critical and essential to the diagnosis and follow-up treatment of glaucoma. While stereo images of the optic nerve provide important information about the color, shape, and cup to disc ratio of the optic nerve^[3], the width of the iridocorneal angle is closely associated to the trabecular outflow rate^[4]. Our group has recently published a review paper on the progress in anterior chamber angle imaging techniques, highlighting the advantages and limitations of existing imaging methods^[5]. Some of these limitations include patient discomfort, physician compliance, time-consuming image acquisition, and the need for trained and experienced operator. Instrumentations and optical configurations that were conceptualized from fiber optics and bulk optics have been applied widely in bio-imaging and metrology^[6-18].

In this context, we introduce an integrated flexible handheld probe consisting of a micro color CCD video camera and white light LEDs for the pre-clinical imaging of the fundus and iridocorneal angle. For this investigation, we choose etafilcon A hydrogel contact lenses over ophthalmic gels or saline solutions as index matching medium. This safer,

simpler, and cost-effective medium can overcome the phenomenon of total internal reflection (TIR) at the tear-air interface.

When light travels from a medium of higher optical density to a medium of lower optical density, it will refract or bend away from the normal. Figure 1 shows a schematic illustration of light transmission from the anterior chamber to air. θ_1 is the angle of incidence onto the posterior cornea; θ_2 is the angle of refraction in cornea; θ_3 is the angle of incident onto the anterior cornea; and θ_4 is the angle of refraction in air. The critical angle, θ_c , at the tear-air interface is approximated to be 46° . Under normal conditions, light from the iridocorneal angle region undergoes TIR at the tear-air interface because they reach the interface at an angle shallower than θ_c , and visualization of the anterior chamber angle structures is not possible.

Figure 1. Schematic illustration of light transmission from the anterior chamber to air.

2. METHODOLOGY

2.1 Sample preparation

From the continuous endothelial lining of the aqueous outflow channels in the anterior chamber, to the close structural resemblance of the retina structures in the vitreous chamber^[19], the porcine eye has high morphological similarities to that of the human eye. Moreover, it is a validated model for glaucoma studies^[20]. The right eye of five randomly selected pigs (*Sus scrofa domestica*) was enucleated at the local abattoir. The eyes were transported and kept on ice until the investigation began. All extra-ocular tissues, including the lacrimal gland and conjunctivas, were removed before fixation onto custom eye holders. The experiment was conducted in accordance to the regulations of Agri-Food & Veterinary Authority of Singapore and Nanyang Technological University's regulations on biosafety.

2.2 Imaging system

The distal end of the handheld probe is designed using computer-aided design software, SolidWorks. It is 26 mm in diameter, and has a 3 mm x 3 mm imaging conduit in the center. The imaging conduit houses a micro color CCD video camera (IntroSpicio™ 115, Medigus Ltd., Israel). The CCD has 291,000 effective numbers of pixels (500 longitudinal x 582 lateral) and each pixel measures 2.95 μm (horizontal) x 1.90 μm (vertical) in size. It has a working distance of 20 mm, a field of view of 140° , and a frame rate of 30 frames per second. The CCD is coupled to a video processing unit, which is in turn connected to a desktop monitor for image display. The imaging conduit is surrounded by four illumination conduits at a 71° angle with respect to the illumination plane. Each of the illumination conduit has an internal diameter of 5 mm, and is fitted with a 20° viewing angle white light LED with a maximum luminous intensity of 7000 mcd (LM520A, Seoul Semiconductor Co., Ltd, Korea). The illumination and viewing angles are selected based on a Lambertian approach for isotropic luminescence across the entire field of view. The brightness of the LEDs can be adjusted using a potentiometer. The design of this handheld probe fulfils the safety directions recommended by the International Commission on Non-ionizing Radiation Protection^[21]. A schematic of the distal end of the handheld probe is shown in Figure 2.

Figure 2. Schematic of the (a) top view and (b) side view of the distal end of the handheld probe.

2.3 Imaging method

A 8.8 mm back curvature, 14.0 mm diameter etafilcon A contact lens (Acuvue, Johnson & Johnson Vision Care Inc., Florida, USA) is positioned precisely onto the cornea of the *ex vivo* porcine sample. Since the direct view of the iridocorneal angle is obstructed by the scleral overlap, the handheld probe is placed at the limbal region to image the iridocorneal angle region at the opposite quadrant. With a field of view of 140° , only three images have to be acquired for a complete view of the anterior chamber angle. For fundus imaging, the probe is placed at the central cornea such that the imaging axis coincides with the optical axis of the eye. The handheld probe is able to capture either single frame images or a fast kinetic series. The imaging schemes for anterior and posterior chamber imaging are illustrated in Figure 3(a) and 3(b) respectively.

Figure 3. The imaging schemes for (a) iridocorneal angle imaging and (b) fundus imaging.

3. RESULTS AND DISCUSSION

The history of contact lenses can be dated back to the da Vinci era^[22]. From a protruding contact lens, to one that was affixed with wax, we have progressed to biocompatible hydrogel contact lenses for refractive error correction, therapeutic, and aesthetic purposes. Safety, vision, and comfort are the primary attributes of contact lens performances. The etafilcon A hydrogel contact lenses used in this study have a refractive index of 1.4, 70% minimum light transmittance, hydrophilic surface character, and 58% water content. These contact lenses have been cleared by regulatory bodies in terms of safety and efficacy. It should be fairly noted that the use of etafilcon A hydrogel lenses as

index matching medium does not eliminate the risk of infections such as microbial keratitis. The rates and severity of infections are however low, and hence there is lesser risk of resultant reduction in visual acuity^[23, 24]. Moreover, etafilcon A contact lenses have minimal physiological effects and a low rate of adverse events^[25, 26]. Examinations similar to indentation gonioscopy can be performed safely since the hydrogel lenses double up as a protective barrier against corneal abrasions and epithelial injuries. On comfort, these lenses are easy to apply and remove due to its hydrophilicity. All the above factors are critical, when choosing an alternative index matching medium since glaucoma is a chronic condition that requires life-long review, even after successful control of the intraocular pressure.

Since the experimental results are reproducible, only the results from one sample are presented in this proceeding. Figure 4 shows images of the iridocorneal angle captured with the flexible handheld probe, using the hydrogel contact lens as an index matching medium. Even though the porcine eye is heavily pigmented, it can be seen from Figure 4(a) that the normal iris processes are reaching towards the scleral spur. This indicates an open angle. In Figure 4(c), a state of high intraocular pressure was induced in the *ex vivo* samples by deliberately injecting fluids into the vitreous chamber. The injection was done via a 29-gauge needle syringe. The increase in pressure caused the iris to close up towards the cornea, narrowing and occluding the iridocorneal angle. Figure 4(b) and 4(d) are indentation examinations of the eye before and after the injection. Under normal physiological conditions in Figure 4(b), the iris moved readily when the cornea is indented. In Figure 4(d) where angle-closure glaucoma was induced, the iris may be in contact or become adhere to the cornea. Fundus images can be captured with or without the hydrogel contact lens. Its principle is analogous to direct ophthalmoscopy, which can be explained by the reversibility of light. Here, the pupil functions as both the entrance and exit for the illuminating and imaging light rays respectively. The optic disc and retina can be directly imaged. Clinicians and vision researchers are therefore able to examine the color and shape of the optic nerve. Figure 5 shows the fundus image of the *ex vivo* porcine sample.

Figure 4. Images acquired using the integrated flexible handheld probe, with the hydrogel contact lens as an index matching medium. (a) shows an open angle where the iris processes are seen reaching towards the scleral spur. (b) is the indentation examination of the same eye where the iris is flattened as the cornea is indented. (c) shows a closed angle of the same eye after deliberately injecting fluids into the vitreous chamber. The increase in pressure caused the iris to close up towards the cornea, narrowing and occluding the iridocorneal angle. (d) is the indentation examination of the eye after injection. Part of the iris root is adhered to the cornea.

Iridocorneal images acquired from the integrated flexible handheld probe are comparable to gonioscopy images. Clinicians and vision researchers can easily differentiate a closed angle from an open angle. The possibility of

indentation examination enables the classification and appropriate management of pathological conditions such as plateau iris and peripheral anterior synchia. Imaging with the handheld probe requires minimal expertise, and the procedure can be performed with the patients in an upright seated position. It takes about 1 min and 1 to 2 min per eye for fundus and iridocorneal angle imaging respectively. The photographic documentations allow the monitoring of treatment responses and pathological changes overtime. In addition, these images can be used as patient education tools to help them better understand their conditions.

Figure 5. Fundus image of the *ex vivo* porcine eye captured using the integrated flexible handheld probe.

4. CONCLUSION

In this study, hydrogel contact lens is used as an alternative method to overcome the phenomenon of TIR at the tear-air interface to allow the display, capture, and recording of images at the iridocorneal angle region, using an integrated flexible handheld probe. The hydrogel contact lens also serves as a better mechanical protective barrier against epithelial injury, as compared to the conventional ophthalmic gel or saline solution, which is commonly used in contact procedures such as gonioscopy and RetCam. It does not introduce any imaging artefacts, and can give good quality digital images. Fundus imaging can be performed with or without the hydrogel contact lens. The imaging capability of the proposed method is demonstrated using *ex vivo* porcine samples, with high reproducibility and repeatability. Future work includes the integration of near infrared imaging modality and the *in vivo* imaging of small animal models. With more translational studies and research, it is envisaged that its applications can be extended to the surgical management and follow up procedures of microinvasive glaucoma surgeries (MIGS) and goniosynechiolysis (GSL).

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