Optical diagnostic techniques in ophthalmology

de Kinkelder, R.

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SUMMARY

Many inherited and acquired diseases or disorders show up in the posterior part of the eye, the retina. Eye diseases like age related macular degeneration (AMD) and glaucoma, the two major causes of blindness in the western world, but also systemic diseases like diabetes mellitus, manifest in the retina, the latter one as diabetic retinopathy. The ability to image through the windows to the soul and the development of techniques to visualize the retina has always been of great interest. Many optical techniques have been developed in the last 16 decades to assist physicians in an accurate diagnosis of eye diseases. To determine the added value of these optical techniques, they have to be (clinically) tested, evaluated and validated, preferably on samples that can accurately assess the precision and accuracy of the tested device. This thesis evaluates optical techniques that are used in day-to-day clinic, in particular the high resolution retinal imaging technique optical coherence tomography (OCT), but also psychophysical tests that asses the amount of macular pigment using heterochromatic flicker photometry (HFP) and a system that uses rarebit testing to detect AMD in an early stage. Furthermore, a retinal motion tracker based on a scanning laser ophthalmoscope (SLO) is proposed that can detect and correct retinal motions during OCT imaging.

Chapter 1 gives an introduction into the eye’s anatomy and three mayor eye diseases, i.e. AMD, glaucoma and amblyopia, are discussed briefly because these diseases are topic of research for this thesis. Furthermore, an overview of optical imaging techniques that have been developed since the first fundus images in 1891 by the German ophthalmologist Gerloff. The optical imaging techniques used in this thesis, i.e. OCT, SLO, HFP and Macubit testing are discussed in more detail.

Before OCT system can be used in clinical practice they need to be calibrated on device independent, reproducible samples that mimic the relevant tissue geometry and optical properties. In Chapter 2 a phantom eye is presented that determines the accuracy and precision RNFL thickness measurements of commercial SD-OCT systems. Twelve SD-OCT systems of four manufacturers were tested. All systems combined overestimated the 49 µm thick phantom RNFL thickness on average by 18 µm. Within brands, thickness measurements differed statistically significant for one Topcon, one RTVue and one Cirrus. Between brands, thickness determined with RTVue and Topcon differed statistically significant from Cirrus and Spectralis. The maximum difference between mean thicknesses is 3.6 µm within brands and 7.7 µm between brands.

One of the in chapter 2 evaluated SD-OCT systems is used to measure the thickness of the entire retina in amblyopic and healthy children. In chapter 3 we present the results of the thickness measurements using this SD-OCT system. The correlation
between the axial length of the eye and the retinal thickness between the two groups are compared. Although the mean axial length of amblyopic and fellow eyes is shorter compared to healthy eyes, the retinal thickness is not larger. Furthermore, the linear correlation between axial length and retinal thickness found in healthy eyes seems to be lost in the eyes of amblyopic children.

Structural information is important for an accurate diagnosis of eye diseases but axial and lateral motions create imaging artifacts and degrade the resolution of scanning optical imaging techniques. In chapter 4 the cause of axial motions during OCT scanning of the retina is investigated. Understanding the cause of these motions can lead to improved OCT image quality and therefore better diagnosis. Twenty-seven measurements were done on 5 subjects. We collected spectral-domain OCT images at the macula over periods up to 30 seconds. We calculated the axial shift of every average A-scan with respect to the previous average A-scan by calculating the cross-correlation. The frequency spectrum of the calculated shifts versus time was determined. The heart rate was determined from blood pressure measurements at the finger using an optical blood pressure detector. The fundamental frequency and higher order harmonics of the axial OCT shift were compared with the frequency spectrum of blood pressure data. In addition, simultaneous registration of the movement of the cornea and the retina was done using a dual reference arm OCT set-up and movements of the head were also analyzed. We conclude that axial motion artifacts during OCT volume scanning of the retina are caused by movements of the whole head induced by the heartbeat.

High resolution imaging is of great importance for an accurate diagnosis of diseases that affect the retina. However, the image quality is degraded by involuntary lateral eye motions that occur in the same time scale as the scan rate of retinal imaging techniques. Increasing the imaging speed may reduce the influence of eye motions, but the amount of light that returns in the optical system is also reduced. Therefore these lateral and rotational eye motions need to be corrected actively and as accurate as possible. In chapter 5, a line scan scanning laser ophthalmoscope is presented for active motion tracking to correct for the involuntary lateral motions by the patient. The tracker is tested on a phantom eye and a healthy volunteer. The tracker can accurately correct eye motions before the next image is acquired (21 frames per second) and the residual motions are decreased when the frame rate is increased.

Besides structural information the functional state of the retina is an important parameter to diagnose eye diseases that affect this retinal function. To evaluate the protective function of macular pigment the MPOD value needs to be assessed accurately. Macular pigment is assumed to protect the eye from ultra violet light and could cause development of AMD. In chapter 6 we evaluate a new
commercially available device that measures the amount of MPOD using HFP against another, well-established, device using HFP and the MPR. The repeatability of this new device, the Macuscope, was low (i.e. wide limits of agreement) and MPOD values correlated poorly with the fundus reflectance method, and agreed poorly with the well-established device, QuantifEye, the tested Macuscope protocol seems less suitable for studying MPOD.

Detecting AMD in an early stage is important to start treatment of this disease preventing loss of vision. In chapter 7 we show the results of measurements on the detection of early-AMD using a Macubit probing test. This device has been tested on 12 patients suffering from AMD in an early stage, but still with good vision, and a healthy control group. Compared to a healthy control group, the Macubit hit rate was significantly lower for the patient group, while the visual acuity was not different. Consequently, the Macubit device can detect functional losses that cannot be detected by a visual acuity chart and could therefore be an efficient tool to detect early AMD and monitor treatment effects in that stage.

Chapter 8 discusses the added value of the used optical imaging techniques that give structural information about the retina. The use of normative databases with RNFL thickness measurements is discussed in more detail and the fact that motion artifacts should not always be considered as noise. Furthermore, psychophysical testing can give information about the functional state of the retina and can be of additional value to structural imaging techniques like OCT.