CHAPTER 10

Summary & Samenvatting

Summary

The number of people with glaucoma has been estimated at 66.8 million, with 6.7 million suffering from bilateral blindness. This makes glaucoma the second leading cause of irreversible blindness worldwide. When left untreated, glaucoma results in visual field loss and eventually in blindness. In considering the diagnosis of glaucoma, the physician will evaluate the intraocular pressure, the optic nerve head and the visual field. This seems to be a straightforward diagnostic process, but, surprisingly, there is still no consensus on the criteria for the signs on which the diagnosis is based.

Glaucoma is a progressive optic neuropathy characterized by death of retinal ganglion cells (RGC). The course of events that eventually leads to death of these cells is not exactly known. As the RGCs die, the retinal nerve fiber layer (NFL), which is made up of the axons of the RGCs, thins. Scanning laser polarimetry (SLP) is an imaging technique that can detect glaucoma by assessing the thickness of the retinal NFL.

SLP came onto the market in 1993. The working principle is based on the NFL being form-birefringent. As a polarized beam of laser light is sent through the NFL, a shift in polarization occurs. This phase shift is called retardation and is thought to be linearly correlated with NFL thickness, as has been shown in a monkey model. In the past, SLP has shown to discriminate well between normal and glaucomatous eyes. The first scanning laser polarimeter that came onto the market was called the Nerve Fiber Analyzer (NFA). When the research described in this thesis began, the instrument had recently undergone extensive hard- and software revisions and was henceforward called the GDx. The goal of this thesis was to investigate the clinical performance of the GDx (mainly its ability to discriminate between healthy and glaucomatous eyes) and to explore ways of how to improve this.

We found that some images in some patients reproduced poorly. This turned out to be caused by eye movements during image acquisition, resulting in what we called "motion artifacts". These motion artifacts went undetected by the system's built-in image quality check. In *chapter 2*, we demonstrated that motion artifacts led to an increase in retardation values. In glaucomatous eyes, motion artifacts might lead to overlooking the disease. In following normal eyes, a baseline image with motion artifacts followed by an image without motion artifacts may mimic progression.

In *chapter 3*, the reproducibility of measurements was studied. It was found that the reproducibility of measurements was high, and that it hardly differed between single images and mean images. It also varied across different parameters. We therefore calculated limits of agreement separately for every parameter. These limits may later serve as critical values for progression. For example, limits of agreement for the superior maximum parameter in normal subjects were 7.2 microns. This meant that any measured change in this parameter would not be statistically significant until it exceeded these 7.2 microns.

The normal population, when measured with the GDx, is characterized by a large variation in NFL thickness and orientation. A typical pattern, coined 'split bundles' by us, was described and illustrated in *chapter 4*. We found that it was a common

finding in healthy individuals with a prevalence of almost 8%. We also examined the effect of superior split bundles on the parameters and found that the superior maximum parameter was lower in cases with a split bundle. We argued that, in patients with a split bundle, an abnormal 'superior maximum' parameter, otherwise a potential indicator of glaucoma, should not readily be interpreted as abnormal.

The GDx has a built-in normative database against which all calculated parameters are tested. For subjects of different age or race, a separate database exists, because both factors are known to affect the thickness of the nerve fiber layer. In *Chapter 5* we described that human strabismic amblyopia was not correlated with a difference in NFL thickness. This meant that for amblyopic eyes the standard database could be used, and that there was no need to construct a separate database for these patients.

Chapter 6 is a case report of a patient that was followed after the onset of an anterior ischemic optic neuropathy (AION). A part of the optic nerve is damaged by a perfusion insufficiency. This usually results in a decrease in visual acuity and visual field damage. The case report shows a progressive decrease in NFL thickness over the course of 4 weeks, as measured with the GDx.

To increase the power of the GDx to discriminate between normal eyes and glaucomatous eyes, several authors have developed new GDx parameters. In *chapter 7*, we determined the sensitivity and specificity of 4 such new parameters, and compared the values with those of the 14 standard parameters. We found that the Number had a sensitivity and specificity for detecting glaucoma of 77% and 89%, respectively. None of the other parameters, including the new ones, discriminated better than the Number. Some of the existing parameters performed poorly, suggesting that those might better be left out of the printout altogether.

In *chapter 8*, an experiment is described where we tested our clinical impression that an expert clinical judgement of the entire printouts would yield a better discrimination between normal and glaucomatous eyes than a mere interpretation of the parameters. Both observers performed better than the Number at a cut-off value of 23, especially in the group with mild glaucoma. In this chapter, we have also described how we interpreted the clinical GDx data. A more detailed explanation has been translated into the Rotterdam GDx Course, and over the past few years it was presented to ophthalmologists and technicians worldwide. Recently, an interactive CD-ROM version of the Rotterdam GDx Course has become available. The CD can be found in the appendix.

In summary, the GDx provides fast, objective and quantitative data on NFL thickness. The applicability and reproducibility of measurements are high and the image acquisition is user and patient friendly. The GDx yields useful sensitivity and specificity values for the detection of glaucoma, whereas its role in follow-up remains to be investigated. As it stands, the GDx holds insufficient validity to serve as a single test for glaucoma. It does, however, provide a very useful addition to the existing tests we run in patients to make the correct diagnosis.