

**AN INVESTIGATION INTO THE
APPLICATION OF LIGHT SOURCES IN THE
TREATMENT OF GLAUCOMA**

by

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ABSTRACT: AN INVESTIGATION INTO THE APPLICATION OF LIGHT SOURCES IN THE TREATMENT OF GLAUCOMA.

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Glaucoma is a blinding disease characterized by damage to the optic nerve and often caused by an increase in the intra-ocular pressure.

Glaucoma affects from 2% to 8% of the South African population, depending on race and age. Primary Open-angle Glaucoma (POAG) is found mostly in patients above the age of 40 years. POAG is more prevalent in black people, with the number of black persons contracting the disease double that of persons of European origin.

In South Africa, the prevalence of blindness is estimated to be 0,6%, thus 240 000 out of a total of 40 million. Glaucoma is responsible for an estimated 20% of the total number of blind people, thus approximately 48 000.

The treatment of glaucoma in Africa, and particularly in rural areas, presents many unresolved problems. Conventional conservative treatment with eye drops is difficult, due to the following reasons:

- ~ Logistical problems of providing patients with a supply of medication.
- ~ Appropriate use of drops requires education, together with a high degree of personal compliance.
- ~ Cost of medical treatment.

Patients require life-long treatment. Eye drops cost approximately R100,00 per person per month. Thus, over a ten-year period, the cost would be R12 000,00 per person and R576 million for the estimated 48 000 sufferers.

Conventional surgery is not very effective, due to the following reasons:

- ~ Scarring takes place at the surgical site.
- ~ Can be performed only in main centres with microsurgical facilities and competent staff.
- ~ Requires travelling expenses, not only for surgery, but also for periodical follow-up examinations.
- ~ Surgical complications are not uncommon.

Conventional laser surgery is not effective, for the following reasons:

- ~ Can be performed only in main centres with laser surgery facilities and competent staff.
- ~ Requires travelling expenses, not only for surgery, but also for periodical follow-up examinations.
- ~ Complications of surgery are not uncommon.

This dissertation describes an investigation concerning treatment of glaucoma, with specific reference to the use of optical energy sources.

The spectral transmission of the human sclera is investigated. Alternative methods of sourcing optical energy to the ciliary processes are presented and compared.

Results obtained can be summarized as follows:

- ~ The spectral transmission of the sclera was measured.
- ~ Trans-scleral transmission was measured to be very low (less than 5%).

The result was confirmed by means of histological investigation, where high scleral absorption was found.

- ~ Since no well-defined transmission window could be found, the application source need not be monochromatic.
- ~ Results published in literature were found to be inconsistent.

OPSOMMING: 'N ONDERSOEK NA DIE TOEPASSING VAN LIGBRONNE IN DIE BEHANDELING VAN GLOUKOOM.

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Gloukoom is 'n siekte van die oog wat tot blindheid kan lei. Dit word gekenmerk deur skade aan die optiese senuwee en word dikwels deur 'n toename in intra-okulêre druk veroorsaak.

Gloukoom kom voor in 2% tot 8% van alle mense in Suid-Afrika, afhangend van ras en ouderdom. Primêre Oophoek-Gloukoom (POHG) is mees algemeen by mense ouer as 40 jaar. POHG kom ook meer by swart mense voor en die aantal swart persone wat die siekte het, is twee keer meer as mense van Europese herkoms.

In Suid Afrika is ongeveer 0,6% van die bevolking blind - dus 240 000 mense uit 'n totale bevolking van 40 miljoen. Gloukoom is die oorsaak van blindheid by 20% van alle mense wat blind is, dus ongeveer 48 000.

Die behandeling van gloukoom in Afrika, en meer spesifiek in afgeleë gebiede, word bemoeilik deur verskeie onopgeloste probleme. Konvensionele konserwatiewe behandeling met oogdruppels is moeilik, om die volgende redes:

- ~ Logistiese probleme om pasiënte van medikasie te voorsien.
- ~ Korrekte toediening van medikasie vereis onderrig asook 'n hoë mate van selfdisipline.
- ~ Koste van medikasie.

Pasiënte moet lewenslank behandel word. Oogdruppels kos ongeveer R100,00 per persoon per maand. Oor 'n tien-jaar periode is die koste dus R12 000,00 per persoon en R576 miljoen vir die 48 000 pasiënte in Suid Afrika.

Konvensionele chirurgie is nie doeltreffend nie, om die volgende redes:

- ~ Letsels vorm waar die wond was.
- ~ Operasies kan slegs in hoofsentra gedoen word waar mikrochirurgie-fasiliteite bestaan, met kundige personeel.
- ~ Die hoë koste van vervoer, nie net vir chirurgie nie, maar ook vir opvolgbesoeke.
- ~ Komplikasies wat op chirurgie volg is nie ongewoon nie.

Konvensionele laserbehandeling is nie doeltreffend nie, vanweë die volgende redes:

- ~ Behandeling kan slegs in hoofsentra uitgevoer word waar laserfasiliteite bestaan, met kundige personeel.
- ~ Vervoerkostes, nie net vir toediening nie, maar ook vir opvolgbesoeke.
- ~ Komplikasies na toediening is nie ongewoon nie.

Hierdie verhandeling beskryf 'n ondersoek na die behandeling van gloukoom, met spesifieke verwysing na die gebruik van ligbronne.

Die spektrale transmissie van die menslike sklera is ondersoek. Alternatiewe metodes om optiese energie aan die siliêre prosesse toe te dien, word voorgestel en vergelyk.

Resultate verkry kan soos volg opgesom word:

- ~ Die spektrale transmissie van die sklera is bepaal.
- ~ Die transsklerale transmissie van die sklera is laag (minder as 5%).

Hierdie resultaat is bevestig deur 'n histologie-ondersoek, waar die sklerale absorpsie hoog was.

- ~ Omdat geen transmissievenster by die sklera gemeet kon word nie, was dit nie nodig dat die energiebron monochromaties moes wees nie.
- ~ Resultate gepubliseer in die literatuur stem dikwels nie ooreen nie.

KEYWORDS

Glaucoma, Intra-ocular Pressure, Sclera, Laser, Optical Transmittance, Optical Energy, Optical Power, Spectral Transmittance, Transmittance, Optical Transmission

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Without any of you, this would not have been possible.

ABBREVIATIONS AND ACRONYMS

ACGIH	American Conference of Governmental Industrial Hygienists
ALT	Argon Laser Trabeculoplasty
DLCPC	Diode Laser Cyclophotocoagulation
IOP	Intra-ocular Pressure
POAG	Primary Open-angle Glaucoma
TALC	Transpupillary Argon Laser Cyclophotocoagulation
TSCPC	Transscleral Cyclophotocoagulation
XPRP	Panretinal Xenonphotocoagulation

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1. INTRODUCTION

1.1 Overview

This dissertation describes an investigation concerning treatment of glaucoma which took into consideration the cost and treatment constraints typical of remote and rural areas, with particular application to rural African areas.

Two specific aspects are addressed in this regard, namely a background study on the clinical aspects of glaucoma, with reference to optical sources, and an experimental investigation of the spectral characteristics of the sclera of the human eye.

For the development of a treatment device and a method for the treatment of glaucoma, parameters of interest that were investigated include the following:

- ~ The spectral characteristics of specific parts of the eye (mainly sclera and ciliary body).
- ~ Optimum optical power levels and energy levels.
- ~ Application methods.

The experimental investigation in this study was focused on the first two parameters.

1.2 Objectives

The objectives of the development of an appropriate treatment method are as follows:

- ~ To determine the optical transmission properties of the human sclera.
- ~ To determine optimal laser or other application methods and power levels.

The reason for determining the optical transmission properties of the human sclera is to enable the researcher to specify the optimal application wavelength. The optimal wavelength is that wavelength where the best scleral transmission is achieved. This will lead to the design of an apparatus which can be used for the controlled and effective partial destruction of the ciliary body.

1.3 Document Layout

The research part of this dissertation starts with an overview of the anatomy and geometry of the human eye (Chapter 2). It is followed by a description of glaucoma and the treatment of the disease (Chapter 3). Chapters 2 and 3 are included to enable the reader with limited knowledge of ophthalmology to follow the remainder of the dissertation.

Chapter 4 presents a summary of results and methods published in accredited journals. The existing research is critically evaluated and the most important findings are published in Table 4.1. The results as found in a number of reports are also presented in Appendix A. This is quite an exhaustive summary and may be helpful to both the engineer and the ophthalmologist.

Chapter 5 describes three methods used to determine the spectral transmission of the sclera. Results obtained during these tests are published, as well as the advantages and disadvantages of the methods used. Graphical layout is presented in such a way that the reader should be able to repeat the investigation, using similar equipment.

A few experimental sources were used in Chapter 6 to apply optical energy to scleral specimens. The treated scleral specimens were then subjected to histological investigations. Results and methods are presented.

During the course of the investigation (Chapters 5 and 6) it became clear that an emulated eye would be a valuable instrument. The construction of such an eye is presented in Chapter 7, i.e. an eye is constructed and evaluated. It is then used for measuring some optical parameters which have relevance to the human eye.

The conclusion is presented in Chapter 8. Some suggestions for future research are also listed.

1.4 **Method**

The method used to complete this study is shown in Figure 1.1. The approach was to start with a literature study. If all laser (the initial choice of applicator) parameters could be established, using the literature, research could continue by using these as a baseline. It was found, however, that the laser parameters published in the research literature were not well defined and were also inconsistent. The next step was thus to measure the scleral transmission. Specification of a specific laser would have been relatively easy if a well-defined scleral transmission window could be found. This was not the case. Alternative methods had to be investigated, and the efficiency of these applicators had to be determined.

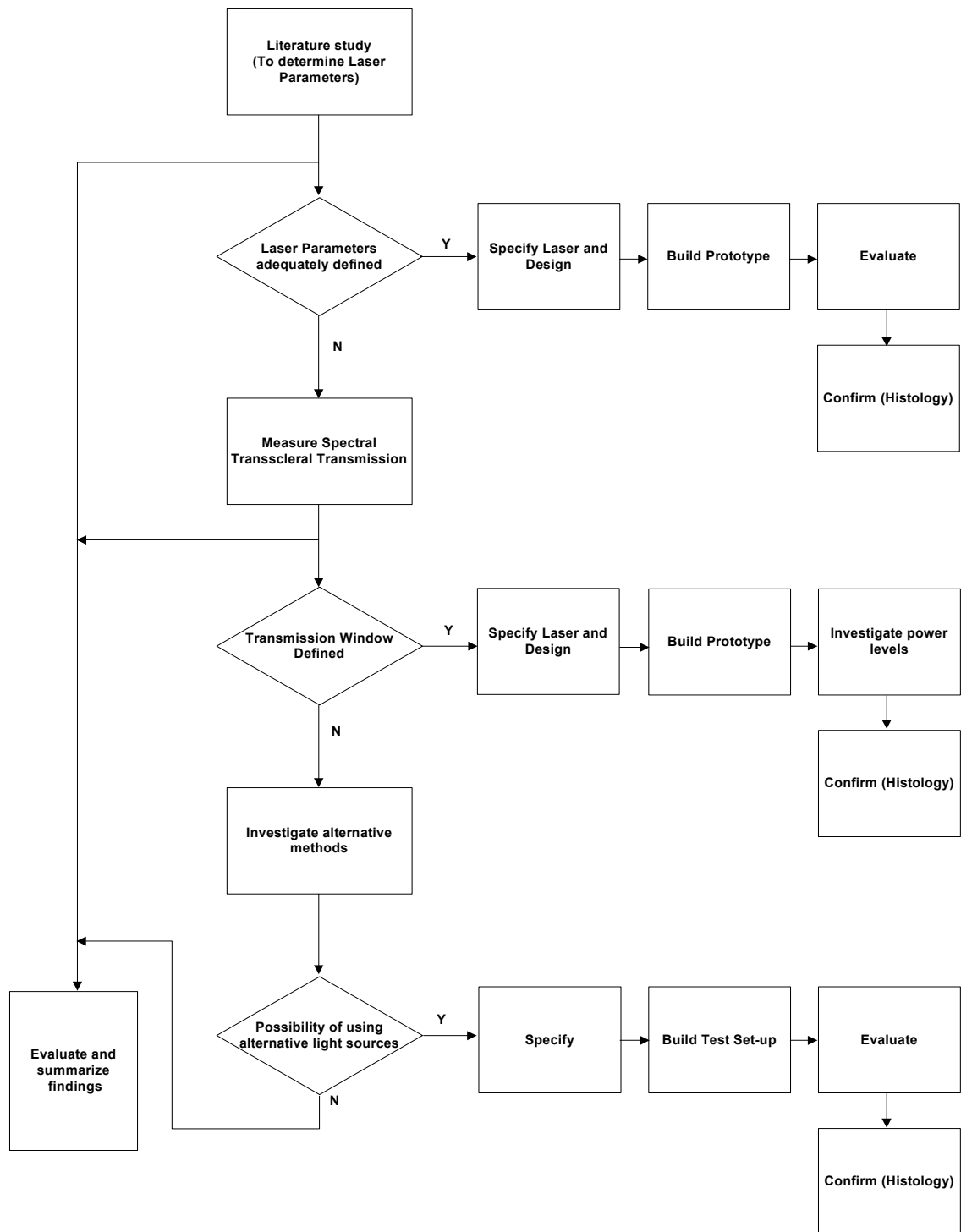


Figure 1.1
Study method and approach

2. BACKGROUND

2.1 Anatomy and Geometry of the Eye

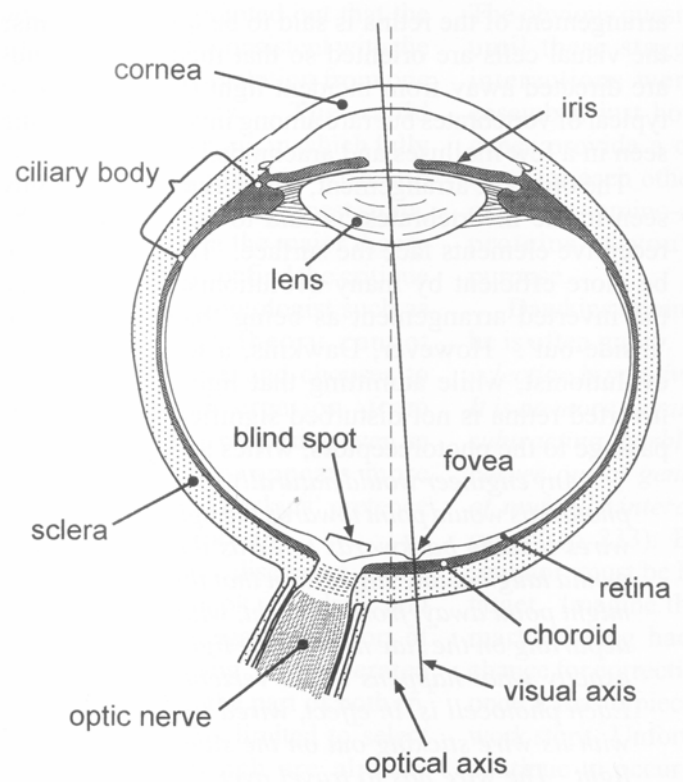


Figure 2.1
Eye anatomy (Gurney [1])

The “anterior chamber” is situated between the cornea, the iris and the lens.

The “posterior chamber” is situated between the lens and the retina.

The “optic disc” is where the optic nerve enters the eye.

The “limbus” is where the sclera meets the cornea.

The eye can be partitioned into two semi-spherical chambers of two different sizes. One chamber is placed behind the lens and the other in front of the lens.

The smaller chamber is placed anteriorly and is transparent. The anterior chamber has a radius of about 8 mm. The anterior chamber is bordered by the cornea (anterior) and the lens (posterior). The anterior chamber is filled with aqueous humor.

The larger chamber is placed posteriorly and is opaque. The posterior chamber has a radius of approximately 12 mm and is bordered by the lens (anterior) and the retina (posterior). The posterior chamber is filled with the vitreous humor, which is a colourless, transparent gel.

The area where the sclera and the cornea meets is called the corneoscleral junction, sclerocorneal junction or limbus (Thomas [2]).

The characteristics of these structures are important in understanding the causes and treatment of glaucoma.

2.2 The Anterior Chamber

The anterior chamber consists of two smaller chambers, namely the smaller anterior chamber and the smaller posterior chamber.

The smaller anterior chamber is the cavity behind the cornea and in front of the iris. The volume of the smaller anterior chamber is about 0,2 ml. The corner between the cornea, sclera, ciliary body and the iris is at the peripheral margin of the chamber. The trabecular meshwork is also situated here, with its channels for drainage of the aqueous humor.

The smaller posterior chamber is the slit-like cavity between the iris and the lens. Peripherally it is bordered by the ciliary body. The volume of the smaller posterior chamber is about 0,06 ml.

2.3 Background to Glaucoma

Glaucoma is a disorder of the smaller anterior chamber. The ciliary processes of the ciliary body produce a clear fluid which is called the aqueous humor. The aqueous humor flows through the pupil into the smaller anterior chamber. It drains out of the anterior chamber through the trabecular meshwork.

The function of the aqueous humor is to supply the metabolic needs of the lens and the cornea. The lens and the cornea do not have a blood supply. By means of its pressure, the aqueous humor also supports the wall of the eyeball and maintains its optical shape. The normal rate of formation of aqueous humor is 2 to 6 F l/min.

When the rate of production of aqueous humor exceeds the drainage rate of the trabecular meshwork, pressure builds up in the anterior sphere. The pressure build-up is transferred to the posterior sphere as well. Positive pressure is then also applied to the optic disc. Cupping of the optic disc takes place and this leads to optic atrophy. Blindness eventually sets in.

The pressure in the eye can be measured, and this is called Intra-ocular Pressure (IOP). Normal IOP is 10 - 20 mmHg (1,3 kPa - 2,6 kPa).

Glaucoma is the leading cause of new cases of blindness in the USA (Babak *et al* [3]). By the year 2000, the number of people with primary glaucoma in the world was estimated at almost 66,8 million.

One percent of Africans are blind, with cataract, trachoma and glaucoma listed as the three leading causes of blindness (Lewallen *et al* [4]). Lewallen *et al* [4] also comments that the bulk of blindness in Africa is preventable or curable.

In developed countries, fewer than 50% of those with glaucoma are aware that they have the disease. **It is estimated that the rate of known disease in the developing world is even lower.** (Quigly [5])

3. TREATMENT

3.1 Introduction

Many methods of treatment exist for glaucoma. This document deals with only one method, which is called Transscleral Cyclophotocoagulation (TSCPC). The aim of TSCPC is to destroy parts of the ciliary body in order to limit production of aqueous humor. Optical power is applied, from the outside of the eye, towards the ciliary body in order to achieve ciliary ablation, and thus coagulation of the ciliary tissue. For optical power to reach the ciliary body, it has to pass through the sclera.

Loss of vision in glaucoma is irreversible. The purpose of the treatment is thus to prevent further loss of vision. IOP must be controlled constantly. Usually, ciliary ablation was reserved as a treatment for eyes with poor vision and difficult, severe glaucoma that was uncontrolled by medication, despite numerous previous surgeries.

The objective of ciliary ablation is to slow down formation of aqueous humor, bringing inflow into a better balance with outflow, which is usually severely impeded in eyes affected by glaucoma (Bron *et al* [6]).

Sivak-Callcott *et al* [7] list the preferred surgical treatments for glaucoma as trabeculectomy with antimetabolite therapy, aqueous shunt implants and diode laser cyclophotocoagulation.

3.2 Background

Bietti [8] noted the fact that the idea of acting, in some way, on the ciliary body to reduce the aqueous output in order to lower IOP is not a recent therapeutic advance. He stated that Hancock had already suggested it in 1861, and that it was supported by Abadie (1910) and Fiore (1929).

The use of optical power to ablate the ciliary body was first proposed by Weekers and co-workers in 1961. Weekers *et al* [9] used a xenon arc for photocoagulation. This was the first step in the development of transscleral photocoagulation. In 1972, Beckman *et al* [10] and [11] reported transscleral cyclodestruction, using a ruby laser (Beckman *et al* [10]), and they also experimented with a neodymium YAG laser (Beckman *et al* [11]).

In the years immediately after 1972, cyclocryotherapy (as first proposed by Bietti [8] in 1950) remained the cyclodestructive treatment of choice for patients with glaucoma. Because of the unavailability of suitable lasers, Polack *et al* [12] as well as McLean *et al* [13] were the pioneers in the application of cyclocryotherapy.

In 1985, Wilensky *et al* [14] reported the results of transscleral Nd:YAG cyclophotocoagulation in pigmented rabbit eyes. This initiated the first research to define the laser parameters necessary to produce a sustained decrease in IOP.

A panretinal photocoagulation with the xenon arc (XPRP) was used by Schiødt *et al* [15] to reduce IOP in normotensive diabetic eyes by 2 to 3 mmHg. Panretinal photo coagulation was also used by Kaufman *et al* [16] to demonstrate that denervation of the ciliary muscle is achieved.

Pratesi [17] was the first to use diode lasers in medical applications in 1984. In 1990, Finger *et al* [18] used a 4,6 GHz microwave applicator to ablate the ciliary body in rabbit eyes. They claimed that some of the advantages of this method were the ability to control the depth of heat treatment (by frequency selection) and the possibility of tissue with low water content (such as the sclera) to remain relatively unaffected.

Coleman *et al* [19] experimented with using ultrasound for ciliary ablation. Ultrasonic energy was used to treat 69 patients with uncontrolled, elevated IOP. Thinning of scleral collagen was experienced together with focal damage to the ciliary epithelium.

Some other causes of glaucoma were also investigated. One of these is a special case of glaucoma which is called ‘malignant’ or ‘ciliary block’ glaucoma. Shaffer [20] suggested that the condition was caused by posterior misdirection of aqueous humor.

Herschler [21] stated that swelling of the ciliary processes, initiated by inflammation or miotics, may cause a critical compromise of an already anatomically narrow lens equator/ciliary body space, and this will have the effect that a relative block of forward aqueous flow will occur.

Pustovalov *et al* [22] compiled an overview on the use of infrared laser diodes in the treatment of glaucoma, using TSCPC. Most of the commercially available devices were listed, together with some basic specifications. They also mentioned that 4085 medical diode lasers had been sold in the world (in 1999) for a total amount of 22,75 million US dollars. It is thus a method which is gaining acceptance world-wide.

3.3 Application Method

An optical power source delivers optical power which is then delivered to the eye, using a light pipe such as a large-core optical fibre. The output of the optical fibre is then aimed at the eye.

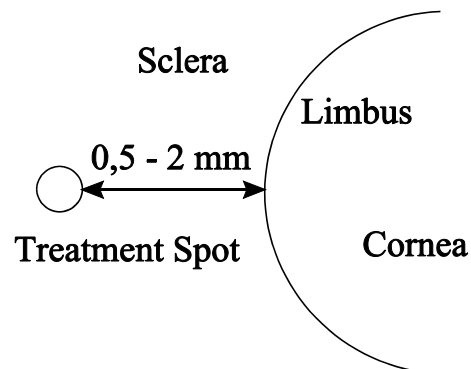


Figure 3.1

Application distance from limbus is shown as the ‘treatment spot’

The curved line shows the limbus, the cornea is visibly clear and the sclera white

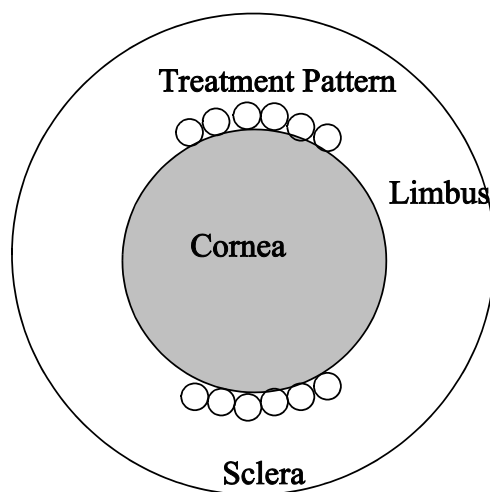


Figure 3.2

Typical application pattern as seen from the front of the eye

The ciliary body is behind the limbus and can not be seen from the outside.

The optical power is applied 0,5 to 2 mm posterior to the limbus (Figure 3.1) in a pattern as shown in Figure 3.2. Ablation of the ciliary processes is usually irreversible, therefore care is taken to ablate the correct area. External positioning of the applicator probe is important to ensure that optical energy is applied to the ciliary processes that are not visible from the outside of the eye.

3.4 Tissue Response to Laser Radiation

An explanation of the general physics of lasers is presented by Polanyi [23]. The physics of specific lasers is also covered, except that of diode lasers.

Any laser which is directed towards tissue produces an incident beam, which then strikes the tissue. Some part of the incident beam is reflected and the remainder enters the tissue. The reflected part of the beam has two light components, namely diffuse and regular. The regular, reflected light has an angle of reflectance equal to the angle of the incident beam. The angles of reflectance for diffuse light are random and uniformly distributed.

The part of the incident beam that enters the tissue is absorbed and scattered internally. A part of the incident beam may be transmitted right through the tissue, depending on the optical density of the tissue.

The deposition of heat in tissue is due only to light photons that are absorbed in the tissue. The extent of thermal destruction of tissue by near-infrared as well as visible lasers is dependent on heat deposition in the tissue and heat transfer within the tissue.

Evaporation of water is an important heat sink for laser energy, and steam can carry heat away from the primary region of laser exposure (Jacques [24]). Smith *et al* [25] showed that the absorption of optical energy by tissue varies, depending on wavelength, beam diameter, pulse length, pulse power, coherence and angle of incidence.

Jacques [24] noticed that the variety of interactions between laser and tissue can make dosimetry a non-linear, dynamic process. (This observation of Jacques [24] is in agreement with the results obtained during this study.) His research showed that the physical mechanisms of interaction between laser and tissue can be characterized as photochemical, photothermal and photomechanical processes.

Welch [26] evaluated different models which can be used for calculations of heat absorption in tissue. He noted that the thermal properties of tissue vary, depending on temperature and water content. He further suggested that the thermal response has often been calculated by using linear models with constant coefficients that presume exponential absorption of laser irradiation with penetration depth. It is also noted that, for weakly absorbing tissues, light scattering (and therefore not transmittance) dominates all optical properties. Light scattering thus becomes a dominant factor in the visible and near-infrared wavelength regions.

Unfortunately, Welch [26] does not comment on power density levels.

Simmons *et al* [27] evaluated the relative effect on tissue when optical energy is supplied by using a Nd:YAG laser and also a semiconductor diode laser, both continuous wave. They used two human autopsied eyes (from one donor) and performed contact transscleral cyclophotocoagulation on the eyes.

In the work of Simmons *et al* [27], delivery of optical power was through a 600 F m optical fibre. Tissue response was viewed by using a high-magnification videographic recording technique to analyse real-time laser effects. In addition to this, tissue was also studied by means of light microscopy. Different tissue responses were noted. Nd:YAG laser lesions were characterized by prominent whitening of tissue and contraction of the ciliary epithelium. Diode laser lesions had less whitening and the tissue contraction appeared to be deeper in the ciliary body.

Stolzenburg *et al* [28] reported that mild burns of the ocular surface occurred during all non-contact and contact TSCPC procedures.

Blasini *et al* [29] suggested that direct damage to the ciliary epithelium is the most likely mechanism of reduced aqueous production following laser photocoagulation.

Preussner *et al* [30] developed an experimental system which is aimed at preventing application of excessive optical energy. Optical power is applied by using an optical fibre. An optical detector is placed next to the application fibre and is used to detect reflected optical energy. Typical graphs of reflected optical power were generated, and these were used as reference graphs in a computer program. A computer is then used to interrupt optical power delivery before a ‘pop’ takes place. (When optical energy is applied to tissue, the tissue will eventually evaporate, causing an audible ‘pop’ noise, which is known as the ‘pop’ effect.) It is thought that a ‘pop’ is indicative of a certain power level.

Walland [31] stated that the ‘pop’ encountered in DLCPC has been used as a crude dosimetry indicator and presumably represents tissue disruption rather than coagulation.

The permeability of the human sclera was investigated by Olsen *et al* [32]. They referred especially to the effect of diode laser application on the permeability of the sclera. Their results showed that age, cryotherapy and also diode laser treatment do not alter the permeability of the sclera. They also reported that surgical thinning significantly increases permeability.

3.5 Ocular Hazards

It was suspected that a significant amount of light can enter the eye through the sclera and not only through the normal corneal entrance. Smith *et al* [25] describe a series of measurements in which they attempted to find an answer to the question of exactly how much optical energy reaches the posterior part of the eye, in order to assess the risk of damage to the retina during TSCPC.

They used a ruby laser and a neodymium laser to apply optical power to the eyes of rabbits. Optical power was applied behind the limbus and perpendicular to the sclera. Forty-four rabbits’ eyes were irradiated by the ruby laser, with exposure levels ranging from 10 to 352 Jcm⁻². Twenty-six rabbits’ eyes were irradiated by a neodymium laser, with exposure levels ranging from 30 to 375 Jcm⁻². Laser-induced damage was then assessed in various parts of the eyes. Threshold damage was also established. This was 60 Jcm⁻² for the neodymium laser and 30 Jcm⁻² for the ruby laser.

According to Smith *et al* [25], an unexpected effect was the production of cataracts. This was observed within 5 days of treatment in 9 (out of 25) of the rabbits. It has been suggested that the cataracts were due to heat transfer from the ciliary body but this could not be confirmed. Cataract formation may be an important reason for doing both *in vitro* and *in vivo* experimentation with a new treatment method.

Myers *et al* [33] performed TSCPC on four cadaver eyes (ages over 70 years) in an effort to measure scattered laser energy reaching the posterior pole. The reason for this measurement was to find a cause for the high incidence of post-operative visual loss after TSCPC treatment. Optical energy was measured with a photodiode through a 7 mm hole in the posterior pole. ACGIH guidelines were used to calculate allowable energy exposures for a diode laser (Iris Medical Instruments) and a Nd:YAG laser (Microruptor).

Applied optical power levels varied from 1,75 W to 3 W, with duration times of 2 seconds for the diode laser (thus 3,5 J to 6 J). Optical power was delivered by using a 600 Fm optical fibre, applied 1,2 mm posterior to the limbus. Applied optical energy level for the Nd:YAG laser was 8 J. Optical energy was delivered by using a 600 Fm optical fibre, applied 1,4 mm posterior to the limbus. Myers *et al* [33] came to the conclusion that 3 to 5% of delivered laser power reaches the posterior pole. They also noted that exposure energies may approach or exceed ACGIH guidelines. Another factor mentioned was that, if intensity of scattered laser energy varies markedly over the posterior pole, some areas of the retina may be exposed to energies further in excess of ACGIH guidelines.

3.6 Human Scleral Optical Properties

It is important to measure human scleral spectral transmittance, as this dictates the optimum wavelength of a possible optical source.

Vogel *et al* [34] experimentally investigated the optical properties of the human sclera adjacent to the limbus. They used five laser sources of different wavelengths.

These were a He-Cd laser (442 nm), an argon ion laser (514 nm), a He-Ne laser (633 nm), a diode laser (804 nm) and a Nd:YAG laser (1064 nm). The optical power of all laser sources was applied to scleral samples of autopsied eyes. Total transmittance, absorption, reflection and angular distribution of transmitted and reflected light were measured by using a specially manufactured integrating sphere. A 600 Fm optical fibre was used for delivery of optical power and this was used in both contact (the exiting tip of the optical fibre touching the sclera) and non-contact (exiting tip of the optical fibre not touching sclera) modes.

Scleral transmittance was measured by Vogel *et al* [34] to be 6% at 442 nm, 35% at 804 nm and 53% at 1064 nm. These measurements were taken with the optical fibre in non-contact mode.

Optical fibre contact led to an increase of transmittance, with a factor of 3,5 at 442 nm, 2,0 at 804 nm, and 1,5 at 1064 nm.

Nemati *et al* [35] used the eyes of four rabbits to measure transmittance, absorption and scattering of the conjunctiva, sclera and ciliary body individually. Scleral transmittance was measured to be 0,9% at 400 nm, 40% at 800 nm and 60% at 1064 nm.

4.1 Optical Power Application Methods and Power Levels

A summary of application methods and power levels is presented in Appendix A. This tabled summary is not as exhaustive as the information presented in this chapter but it was impossible to include all the information in Appendix A, which can be used as a quick reference.

Herschler [21] used a standard argon laser (Coherent Radiation) to apply energy directly through the cornea. He was able to reach the ciliary processes through the cornea because peripheral iridectomies had been performed on all the patients at an earlier stage. Laser power varied from 0,3 W to 0,1 W. The duration of treatment was 0,1 s and the sizes of the applicator probes were 100 Fm and 200 Fm. Applied energy was therefore 10 mJ to 30 mJ.

Cantor *et al* [36] used a Nd:YAG (Lasag Microruptor) laser to apply energy to rabbit eyes. They investigated the role of pigmentation in differing energy levels of application. To do this they used the eyes of pigmented rabbits as well as those of albino rabbits. Optical power was applied through the sclera and perpendicular to it. Pulse energies of 1,95 and 2,15 J were used.

Assia *et al* [37] investigated the use of a diode laser (Microlase). Wavelengths of 780 nm and 830 nm were used. Power settings of 1000 and 1200 mW were studied, as were pulse durations of 0,2, 0,4, 0,5, 0,6, 0,7 and 1 s. Applicator probes were 100 Fm, 200 Fm and 500 Fm. Optical power was applied through the sclera, 1 to 2 mm posterior to the limbus. Assia *et al* [37] also repeated their experiments, using a Nd:YAG laser (Microruptor). With this laser, energy levels of 2, 4, 6 and 8 J were studied.

Schuman *et al* [38] used a Nd:YAG laser for the treatment of 140 eyes (136 patients). The average age of the patients was 61 years, with a range of 2 to 90 years. Optical powers of 7 to 9 W were used, with an application time of 0,7 s in both cases. The diameter of the applicator was 600 F.

Lee [39] investigated the use of transpupillary argon laser cyclophotocoagulation (TALC) in the treatment of 14 patients with aphakic glaucoma. The average age of the patients was 61 years, with a range of 39 to 82 years. The TALC treatment was performed, using specially designed lenses and mirrors. The argon laser was used to apply optical power of 1 W, with spot sizes of 50 and 100 Fm for durations of 0,1 and 0,2 s. The laser beam was aimed directly over the ciliary processes, and only one process was coagulated at a time.

Kosoko *et al* [40] used a diode laser (Oculight Slx) with a special probe for the treatment of refractory glaucoma in 27 patients. Kosoko *et al* [40] used a laser diode at a wavelength of 810 nm as a source, and an optical fibre with a diameter of 600 Fm was used for delivery of optical power. The applied optical power ranged from 1,5 to 2 W, and the duration of application was 2 s in all cases. The number of patients treated was 27, with an average age of 62,2 years (range of 32 to 85).

Schuman *et al* [41] carried out a comprehensive study to investigate the effects of semiconductor diode laser (Nidek DC-1200) contact transscleral cyclophotocoagulation in human cadaver eyes, using gross examination, light microscopy and scanning electron microscopy to determine optimum treatment parameters. Laser diodes transmitting in two different wavelengths were used, namely 818 nm and 850 nm. Power was set at 900 mW for the 818 nm unit and at 1, 2, 2,3, 2,7, or 3 W for the 850 nm unit. Delivery times were 1, 2, 3, 4 and 5 s, and 22 cadaver eyes were used. The diameter of the applicator probe was 600 Fm, and the probe was placed 1 to 1,25 mm posterior to the limbus.

Bock *et al* [42] used a diode laser (Iris Medical Instruments) for the treatment of a variety of pediatric glaucomas. The treatment group consisted of 26 eyes from 20 patients. Patients ranged in age from 6 months to 27,2 years (10 patients were younger than 10 years of age). Application optical power ranged from 1,8 W to 2,4 W, applied for 2 s. Optical power was delivered by means of a standard G-probe from Iris Medical Instruments.

Hampton *et al* [43] reported on the clinical results of a comprehensive pilot study to evaluate transscleral Nd:YAG laser cyclophotocoagulation in 100 patients and treating 106 eyes (mean age 58 and range 11 to 87 years). They used a Nd:YAG laser (Microruptor 2) and applied optical energy levels of between 7 and 8 J for a duration of 20 ms. The laser applications were positioned 1,5 mm posterior to the limbus.

Nissen *et al* [44] used a xenon lamp to perform panretinal photocoagulation on 12 eyes. The average age of the patients was 32 years. (The xenon lamp is a wide-band optical power source.)

A krypton laser (Lasertek 41 AKTrKr) was used by Immonen *et al* [45] for the treatment of 62 eyes (57 patients). The fibre optic probe was held perpendicularly to the sclera, 1,2 to 3 mm behind the limbus. The applied optical power was 400 to 500 mW, with a duration of 10 seconds.

Fankhauser *et al* [46] studied the effects of various laser sources upon the ciliary body via the transscleral route, using 16 autopsied eyes. The lasers they used were a Nd:YAG (Microruptor 2 at 1064 nm), a blue argon cw laser at 488 nm, a green argon cw laser at 514 nm and also a He-Ne laser at 633 nm. The He-Ne laser was operated at an optical power of 20 mW and each of the two argon lasers at 500 mW. The Nd:YAG laser was used at 6 to 7 J. Pulse durations were 10 ms and 20 ms. The lasers were all applied to the sclera of the eyes. Forward scattering, backward scattering and transmittance through the sclera were measured. The light scattering effect produced by the sclera was characterized by rotating an optical fibre through almost 360° around the specimen.

Gaasterland *et al* [47] used a diode laser (IRIS Medical Instruments) for ciliary ablation in severe glaucoma. Optical power was delivered by using a 600 µm optical fibre probe, and the power was applied 1,2 mm posterior to the limbus. Applied optical power varied from 1,75 W to 2 W, with a duration of 2 s. The application group consisted of 21 eyes.

Moriarty [48] presented a list of the advantages and disadvantages of the use of diode lasers in ophthalmology.

Patel *et al* [49] described the application of vitrectomy and transvitreal endophotocoagulation on the ciliary processes of 16 human eyes of 18 patients. The average age of the patients was 54, years and the ages ranged from 15 to 82 years. An argon laser was used, with optical power delivery of 500 to 700 mW. Durations lasted from 0,5 to 1 s. The laser applicator probe was positioned 2 to 4 mm from the ciliary processes, and photocoagulation was applied under direct visualization.

Allingham *et al* [50] used 27 enucleated human eyes to evaluate TSCPC, using a Nd:YAG (Surgical Laser Technologies) laser. All donated eyes were from caucasians individuals aged 56 to 83 years. Optical power was delivered by using a 700 Fm optical fibre. The optical fibre was placed perpendicular to the sclera at varying distances posterior to the limbus (0; 0,5; 1,0; 1,5 mm). The optical power settings used were 5, 7, 9 and 11 W, with a constant pulse duration of 0,7 s.

Blasini *et al* [29] performed TSCPC on five patients, 24 to 72 hours before enucleation for blind, painful eyes. They used a Nd:YAG (Microrupter 2) laser, and applied optical energy levels of between 2 and 8 J. Optical power was delivered by using an optical fibre that was positioned 0,5 - 3 mm posterior to the limbus. Application duration time was set at 20 ms.

Peyman *et al* [51] used a diode laser (Iris Medical Instruments) with an output optical power of 1 W to perform TSCPC on five rabbits' eyes. Applied optical power was 300 - 400 mW, with a duration time of 0,5 s. Optical power was delivered by means of a 200 Fm optical fibre.

Hennis *et al* [52] used a semiconductor diode laser (Microlase) to perform TSCPC on 14 patients with glaucoma. Wavelengths of the diode laser were 780 nm and 830 nm, and the laser was used as a slit-lamp attachment. The duration of the application was 990 ms, with a 100 Fm spot size and applied optical power of 1,2 W. Applications were placed 1 mm posterior to the limbus. Fourteen eyes from 14 patients were treated. The average age of the patients was $69,9 \pm 13$ years, ranging from 38 to 84 years.

Wright *et al* [53] reviewed the records of 35 patients (35 eyes) treated with a Nd:yAG laser (Microruptor). Applied optical energy varied from 3,4 to 8,6 J, and the duration was set at 20 ms. The mean age of the patients was $64,5 \pm 18,1$ years, with a range of 16 to 89 years.

Hennis *et al* [54] used a semiconductor diode laser with a slit-lamp delivery system to perform TSCPC on four cadaver eyes. The laser (Microlase, Keeler Instruments) incorporated two diodes with wavelengths of 780 and 830 nm. Applied optical power was 1,2 W, with pulse durations of 0,2 to 1 s. Optical energy was delivered by means of 100, 200 and 500 Fm optical fibres.

Federman *et al* [55] described the use of sapphire ceramic crystals as delivery medium for TSCPC. An argon laser was used, with optical power output of 1 W, for a duration of 1 s.

Bloom *et al* [56] used a diode laser (Iris Medical Instruments) for the treatment of advanced glaucoma in 195 patients (210 eyes). The mean age of the patients was 51 years, with a range of 1 year to 89 years. The wavelength of the laser was 810 nm, and applied optical power was 1,5 W, with an application duration of 1,5 s.

Spencer *et al* [57] analysed the results of IOP reduction in glaucoma, following TSCPC with a repeatable standard protocol. They used a diode laser (Iris Medical Instruments) with a wavelength of 810 nm. Applied optical power was 2 W, with an application duration of 2 s. A 600 Fm optical fibre was used for delivery of optical energy and it was placed 1,2 mm posterior to the limbus. Treatment was completed on 58 eyes of 53 patients. The average age of patients was 59,9 years, with a range of 15 to 93 years.

Wong *et al* [58] designed and tested a glass-ball tip fitted at the delivery end of the optical fibre. The ball tip focused optical energy to a spot size of 740 Fm and 2,1 mm away from the surface of the ball lens. They used this method, together with a diode laser (wavelength of 810 nm), to do TSCPC on 33 glaucoma patients. The patient group consisted of 25 Chinese, 6 Malays and 2 Indians. Average patient age was $57,4 \pm 13,6$ years, ranging from 22 to 79 years. The optical power delivered by the laser was 1,8 to 2 W, with an application duration of 0,3 to 0,5 s.

Azuara-Blanco *et al* [59] described the treatment of a 45-year-old man. TSCPC was used, with an optical power level of 2 W and a duration of 2 s.

Walland [31] decided on a dosage-standardized treatment for 30 patients. A diode laser (Iris Medical Instruments) with a wavelength of 810 nm was used. Applied optical power was 1,5 W, for a duration of 1,5 s.

Preußner *et al* [60] investigated the effect of different beam diameters of the optical power delivery system. Optical fibres with diameters of 350 Fm and 2 mm were evaluated. A lamp with a filament was used, with an optical power output of 15 W and an exposure time of 5 to 10 s before bleaching was noticed.

4.2 Results

Herschler [21] reported that all patients showed deepening of the anterior chamber after the application of the laser. The deepening continued to full depth over the next three to five days.

Cantor *et al* [36] reported marked destruction of the ciliary body in pigmented rabbits' eyes, but no histological effects were observed in albino rabbits' eyes.

Regarding the evaluation of laser-induced damage to the ciliary body in transscleral cyclophotocoagulation, Assia *et al* [37] stated that ciliary process blanching, shrinking and pigment dispersion were believed to represent laser burns because the latter probably indicated destruction of the ciliary body epithelium and stroma. Assia *et al* [37] reported that a thermal reaction at the ciliary processes was observed when energy was applied 0,5 to 1 mm posterior to the limbus, using 0,84 to 1,2 J of energy. They also reported that spot size had little effect on the quality of the lesion induced. Applications 2 mm behind the limbus showed a thermal reaction only in the pars plana.

Schuman *et al* [38] measured the mean IOP of 136 patients at $35,2 \pm 1,59$ mmHg. This was measured before transscleral photocoagulation. Six months after treatment, the mean IOP was $18,4 \pm 1,16$ mmHg, which indicates that the mean IOP was reduced by almost 50%. As Schuman *et al* [38] were able to apply the treatment to a fairly large number of patients, some other interesting results were also published. Seventeen of the patients were non white, and there was no significant correlation between race and treatment group. It was also reported that non-white patients had a significantly greater increase in cellular reaction and flare at 1 hour and 1 week than white patients. Non-white patients also had significantly more post-operative pain than white patients.

Lee [39] reported that the applied laser energy was sufficient to produce a concave brown burn, with pigment dispersion and/or gas bubble production. The IOP-lowering effect after the TALC procedure was unstable and not uniform. It ranged from no change in IOP in 4 eyes, to appreciable reduction of the IOP in ten eyes.

Kosoko *et al* [40] measured a 44% reduction in IOP, which before treatment with the diode laser was measured to be $37,8 \pm 12,1$ mmHg. Two years after treatment the IOP was measured to be 20,3 mmHg.

Using semiconductor laser diodes on cadaver eyes, Schuman *et al* [41] reported that exposures of less than 2 J produced no visible damage. A 2 to 3 J exposure produced mild whitening of the ciliary processes, while 4 to 5 J exposures created more intense whitening of the processes. Energies higher than 5 J often produced explosive tissue damage. The optimum application optical power for contact transscleral diode laser cyclophotocoagulation in cadaver eyes was found to be between 3 J and 4,5 J.

Bock *et al* [42] measured the average pretreatment IOP to be $34,2 \pm 10,4$ mmHg. The pretreatment IOP ranged from 15 to 62 mmHg. Six months after the initial procedure, the mean decrease in IOP for all eyes was $10,3 \pm 14,7$ mmHg. The authors noted a greater tendency towards failure in patients with congenital glaucoma.

Hampton *et al* [43] measured the average pretreatment IOP of 106 eyes to be 38 mmHg, and the IOP ranged from 18 to 80 mmHg. For after-treatment evaluation, a range of 7 to 20 mmHg was considered to be a success. After 6 months the treatment of 65 eyes was considered to have been successful. Of the 65 eyes, 14 had to be treated for a second time or more.

Nissen *et al* [44] measured the average pretreatment IOP of 12 eyes to be 30 mmHg. Four months after treatment, the average IOP measured 20 mmHg. Unfortunately, only the spot size of the xenon lamp was recorded. No energy levels are reported and also no durations. These omissions are disappointing because no data is available with regard to applied optical power levels.

Immonen *et al* [45] used a krypton laser for transscleral contact cyclophotocoagulation. The IOP decreased from the baseline mean of $34,8 \pm 11,0$ mmHg to $20,4 \pm 8,3$ mmHg within 10 days and to $20,9 \pm 9,1$ mmHg six months post-operative. The optical power levels used by Immonen *et al* [45] can be delivered by most krypton laser units used for retinal photocoagulation. This is advantageous, since retinal krypton lasers are available in many centres, and no new equipment is therefore needed for cyclocoagulation.

Fankhauser *et al* [46] found that a beam, tangentially oriented and positioned 0,5 to 1 mm posterior to the limbus, has a high probability of hitting the ciliary body and damaging the ciliary processes. They also reported that by using the Nd:YAG laser, an increase in forward scattering, from 5% to 61%, and a decrease in backward scattering, from 45% to 4%, was obtained, in comparison to values obtained when using the blue argon laser.

Gaasterland *et al* [47] measured the average baseline IOP of 21 eyes to be 32,6 mmHg (range 16 to 70 mmHg). After treatment with a diode laser, the average IOP for 14 of the 21 eyes was 19 mmHg, measured 11 months after treatment.

Patel *et al* [49] measured the average IOP of 16 eyes to be 39 mmHg (range 25 to 50 mmHg) before treatment (vitrectomy and transvitreal endophotocoagulation). After treatment, the mean IOP was 20 mmHg for 14 of the 16 eyes. Patel *et al* [49] also reported that the immediate result of treatment was whitening and shrinkage of the ciliary processes. This effect was sometimes accompanied by an audible ‘popping’ sound.

Allingham *et al* [50] reported that optical fibre placement 0,5 mm posterior to the limbus produced lesions that were centred either on the ciliary processes or just at the anterior slope of the ciliary processes. With the optical fibre positioned 1 mm posterior to the limbus, the lesions were localized to the middle and posterior part of the ciliary processes. With the optical fibre placed at 1,5 mm behind the limbus, only the most distal portions of the ciliary processes were reached. Allingham *et al* [50] also reported that 5 W optical power produced no visible lesions. Gray burns were produced by the 7 W setting, and the 9 W setting produced circular, whitish lesions. With the 11 W setting, crater formation was initiated in the ciliary processes.

Blasini *et al* [29] carried out a histological study and found disruption of the ciliary epithelium.

Peyman *et al* [51] reported that ciliary body coagulation was achieved at an optical power level of 300 to 400 mW. Histological examinations demonstrated thermal destruction of the ciliary body processes. They (Peyman *et al*) do add, however, that the reaction was not predictable.

Hennis *et al* [52] stated that the mean pre-operative IOP was $34,8 \pm 13$ mmHg, and the mean IOP six months after a single treatment was $24,3 \pm 18$ mmHg. Laser treatment was considered successful in 10 of the 14 patients. Hennis *et al* [52] also reported that the results were inconsistent among individuals. In some patients, an adequate IOP effect was maintained, whereas in others the IOP became uncontrolled after the first post-operative month. No certain reasons for treatment failure could be formulated. Some complications included mild uveitis and conjunctival burns at the site of laser applications.

Wright *et al* [53] used a Nd:YAG laser and reported a mean pretreatment IOP of $37,9 \pm 11,0$ mmHg. Mean post-treatment IOP was $21,2 \pm 12,9$ mmHg. Wright *et al* [53] also reported that multiple treatments of TSCPC may be required for long-term IOP control. They also noted that Nd:YAG TSCPC may control IOP but is not always a vision-saving procedure.

Hennis *et al* [54] used a posterior photographic technique and light microscopy for evaluation of the TSCPC effects of a laser diode. They reported that optical power of 1,2 W and a pulse duration of 1 s was able to produce a grossly visible lesion in the ciliary body. The reaction of the latter was also observed as tissue blanching, shrinkage and pigment dispersion. Ciliary body reaction was observed histologically as coagulation necrosis and epithelial cell disruption. Hennis *et al* [54] also reported that variations in size of the delivery optical fibre did not significantly affect the results.

Fiore *et al* [61] reported scleral thinning after Nd:YAG TSCPC. They stated that a patient (30-year-old male) received applications of 4,8 mJ of optical energy, using a Nd:YAG laser (Microruptor). Treatment was repeated 18 days later, using applications of 5,03 mJ of optical energy. Six weeks after the second treatment, scleral thinning was noted at a spot 2 mm posterior to the limbus. This case was not histologically confirmed, but Fiore *et al* [61] reported that the appearance, location, pattern and occurrence suggested that the area of scleral thinning was caused by laser treatment.

Bloom *et al* [56] measured mean pretreatment IOP as $34,1 \pm 10,6$ mmHg. After a period of 10 months, the mean IOP was $20,1 \pm 9,3$ mmHg. They noted that, to reduce IOP to a satisfactory level, multiple applications were required. No patients were followed up for long periods and (according to Bloom *et al* [56]), it is not known what will happen to IOP control in the longer term (longer than 2 years).

Spencer *et al* [57] reported that the IOP of 58 eyes was followed for 6 to 37 months. Mean pretreatment IOP was 33,0 mmHg, reducing to an average of 16,7 mmHg at the final visit. They also stated that they had applied the same level of optical power and duration to all patients.

Wong *et al* [58] reported a mean pretreatment IOP of $40,6 \pm 10,7$ mmHg (with a range of 22 to 67 mmHg and a mean IOP of 22 mmHg at 18 months). They also reported that no significant correlation could be found between total laser energy delivered and change in IOP. Another conclusion which Wong *et al* [58] made is that lowered IOP did not necessarily preserve vision.

Azuara-Blanco *et al* [59] measured the pretreatment IOP of one patient as 45 mmHg. One day post-operatively the IOP was 20 mmHg. Two weeks after treatment, the patient presented with malignant glaucoma. Azuara-Blanco *et al* [59] warned that TSCPC can be the cause of severe complications.

Walland [31] treated 30 patients, and after a mean follow-up of 10,4 months, the post-operative mean IOP was $25,8 \pm 17,7$ mmHg. The preoperative IOP was $49,4 \pm 11,2$ mmHg. Walland [31] also reported that almost no audible ‘pops’ had been experienced during treatment. A gradual rise in the mean IOP after DLCPC was apparent with the specific laser settings used.

Due to this, almost a third of all cases were retreated. It is not known whether this apparent recovery of ciliary body function would still occur at alternative laser settings. Walland [31] also commented that optimum energy levels for DLCPC still had to be established in order to predict and plan IOP outcome.

Pustovalov *et al* [22] reported that TSCPC, using a laser diode, usually provides positive results but these can still be accompanied by undesirable side effects such as coagulation of the sclera and the vitreous body, mechanical ruptures, haemorrhage etc.

Sabri *et al* [62] reported on a case of scleral perforation following contact transscleral cyclodiode treatment. It was noted, however, that the sclera had thinned as a result of previous ocular surgery.

Han *et al* [63] determined the effect of transscleral diode photocoagulation on the tensile strength of the sclera, using an experimental rabbit model. Their verdict was that no significant weakening could be detected.

4.3 **Race**

Although investigating different treatment methods for different races was not one of the primary objectives of this study, any information with regard to race on the subject of glaucoma would be an asset, and it was decided to include some information on this subject.

It is unfortunate that most of the studies completed do not mention race but only age and sometimes gender. This situation makes it difficult to draw any conclusions on the grounds of race with regard to response to laser treatment.

Although the procedure was not TSCPC but laser trabeculoplasty, it is worth mentioning the study completed by Wise [64]. Laser trabeculoplasty was used for the treatment of 150 eyes from 113 patients. Results were carefully monitored up to ten years after treatment. Wise [64] stated that the eyes of non-white patients responded as well as the eyes of white patients. A limited investigation with regard to race was done during this study. The results of the investigation described in this dissertation are in agreement with those of Wise [64].

Hennis *et al* [52] treated 14 patients with glaucoma. Two patients were white and twelve were black. No difference in treatment success was reported.

Wright *et al* [53] treated 35 patients, using a Nd:YAG laser. Twenty patients were white, 4 black and 11 Hispanic. No difference in treatment success was reported.

Spencer *et al* [57] treated 58 eyes, using a diode laser. They applied standardized optical energy settings to all eyes, and the ‘pop’ manifested sometimes. They noted that they did not find a particular association between race and hearing the ‘pops’.

Although Wong *et al* [58] treated exclusively Asian patients, unfortunately no mention is made about possible race differences with regard to treatment methods and response. Applied optical energy levels were lower (540 mJ to 1 J) than those recommended by most other researchers. It is not clear whether this could be attributed to race or to a slightly different application method.

Josefson [65] reported on a seven-year study conducted by the National Eye Institute in the USA. The trial involved 332 black patients and 249 white patients. Researchers found that black patients responded better to laser surgery, whereas white patients responded better to trabeculectomy treatment of glaucoma. No mention was made of the application of TSCPC.

Oh *et al* [66] completed a gonioscopic study in an attempt to determine racial (and other) differences in the anterior chamber. The anterior chamber was studied in 291 patients who included Afro-Americans, Caucasians and Far East Asians. No significant difference was found between the angle width of these three groups, but the iris joins the sclera more anteriorly in Asians, slightly more posteriorly in Afro-Americans and most posteriorly in Caucasians.

Congdon *et al* [67] developed a novel method (using biometric gonioscopy) for making measurements in the anterior chamber in order to compare the anterior chamber angles of people of European, African and east-Asian descent, aged 40 years and older. Fifteen persons of each gender, from each race and from each decade, from 40 to 70 years old, were evaluated. No significant difference in angle measurement between black, white and Chinese races could be established. Younger people of Chinese race appeared to have deeper anterior chamber angles than white or black people, whereas the angles of older Chinese were significantly narrower. They conclude that the failure to detect a difference in angle measurements between these major three groups was surprising, especially if taking into account that the prevalence of angle closure is much higher among Chinese.

Higgenbotham *et al* [68] examined baseline differences between black and white glaucoma patients. A total of 332 black patients (451 eyes) and 249 white patients (325 eyes) were monitored. Higgenbotham *et al* [68] came to the conclusion that visual field defects are more severe in blacks than whites.

4.4 Discussion

When attempting to determine the applied optical energy range needed for diode TSCPC, results presented in literature differ dramatically. Indeed, Pastor *et al* [73] conducted a literature search (in 2001) for the years 1968 to 2000 on the subject of cyclophotocoagulation. They retrieved 130 citations, and 34 of these articles were reviewed. They summarized the results as follows: ‘The predominant problem with all studies on cyclophotocoagulation is the lack of a uniform definition of success, which makes comparisons difficult’. Pastor *et al* [73] also stated: ‘Most of the literature consists of non-comparative case series that provide evidence that is limited and often not convincing’. They concluded: ‘There is insufficient evidence to definitively compare the relative efficacy of the cyclophotocoagulation procedures for glaucoma’. Schlote *et al* [74] evaluated the efficacy and safety of TSCPC in refractory, advanced glaucoma. They considered it a safe method of treatment but did add that repeated treatments are often necessary. They also commented that success of treatment depends on the age of the patients, previous surgery and the type of glaucoma. Kirwan *et al* [75] commented on the use of diode cyclophotocoagulation in the management of glaucoma in pediatrics. They noted that some effective control of IOP was achieved, although cyclodiode treatment was not sufficient to reduce the number of medications.

Minimum applied optical energy level ranges from 100 mJ (Assia *et al* [37]) to 3,5 J (Gaasterland *et al* [47]). Similarly interesting is the maximum applied optical energy level, which ranges from 200 mJ (Peyman *et al* [51]) to 4,8 J (Bock *et al* [42]). Schuman *et al* [41] reported that energy levels of more than 5 J produced explosive tissue damage.

The least applied optical energy needed for ablation of the ciliary body is reported by Herschler [21], (30 mJ) but this is only when the energy is applied transpupillary.

When performing TSCPC (using laser sources of all types) on patients, the standard method of measurement was the subsequent lowering of IOP: ([31], [37], [38], [40], [42], [43], [44], [45], [47], [49], [52], [53], [56], [57], [58], [69], [70], [71] and [72]).

TSCPC applied to rabbits' eyes, enucleated eyes and cadaver eyes was evaluated by using different inspection techniques. Blanching and shrinkage of the ciliary body were used by [29], [36], [37], [51], [54] and [60] to evaluate destruction of the ciliary body. White lesions were also reported by [50] and [55]. It is also interesting to note that Hennis *et al* [54] was able to produce a grossly visible lesion in the ciliary body, at an energy level of only 1,2 W.

Positioning of the optical fibre seems to be decided on with [29], [31], [36], [37], [38], [40], [41], [43], [45], [46], [47], [50], [52], [53], [54], [57], [58] and [69] suggesting that it (when using contact TSCPC) should be 0,5 to 2 mm posterior to the limbus. Only [70], [71] and [72] claim that the application position can be as far posterior as 3 mm. Assia *et al* [37] stated that optical energy should not be applied more than 2 mm posterior to the limbus, as this is likely to miss the ciliary body.

According to Assia *et al* [37], the applied spot size is not important and can vary from 100 to 500 Fm. Others ([31], [38], [40], [41], [42], [47] and [57]) used a spot size of 600 Fm, with similar results, while Wong *et al* [58] used a 740 Fm spot size. The smallest spot size was 50 Fm, applied by Lee [39], and also boasting satisfactory results.

The exact effect of laser applications on the ciliary body is not unanimously agreed on. Another problem exists when determining laser energy application levels, using cadaver or enucleated eyes. The question is how representative these measurements are in comparison to those obtained from living eyes. Parver [77] shows that when the eye is exposed to a light source, the absorption of light by the retina and the choroid can raise local tissue temperatures above body temperature.

Under these circumstances, the choroid acts as a heat sink, dissipating heat by convection and conduction through the blood stream. Parver *et al* [77] mentioned the fact that blood flow to the choroid is exceptionally high, but very little oxygen (about 5%) is extracted in the choroid. They also showed that the rate of blood flow into the choroid increases when light intensity into the eye is increased. Gearrets *et al* [78] were able to produce photocoagulation lesions in dead animals, with light intensities well below those needed in live animals, and it was presumed that this was the case because no blood flow was available to remove the applied heat.

These findings raise the question of applied optical power levels again. It is probable that energy levels determined by means of tests using *in vivo* samples may not be applicable to treatment of patients. It is difficult, however, to practically measure energy levels *in vitro*.

Table 4.1 presents a summary of results achieved after application of TSCPC. Successful treatment can be described as in the case in which IOP was lowered after one treatment, and 12 cases are reported. All other outcomes can be described as unsuccessful, and 14 such cases are reported. Another issue is the question of when the lowering of IOP can be described as successful. All quoted studies measured the IOP six months to two years after application. It could not be established what the result would be more than two years after application. On the other hand, unsuccessful cases can be confirmed, since they failed soon after application.

TABLE 4.1

Results: Summary of Findings of TSCPC Application

Summary of Results	Reference
IOP lowered after one treatment	[38], [40], [42], [43], [44], [45], [47], [49], [52], [53], [57], [58]
IOP lowered after multiple treatments	[31], [43], [53], [61], [56]
IOP lowering unstable and not uniform	[39]
IOP lowering failure in congenital glaucoma	[42]
IOP lowering failure	[47], [49]
Complications such as mild uveitis and conjunctival burns.	[52], [59], [22]
Scleral thinning	[61]
No vision preservation	[58]

5.1 Introduction

Spectral transmittance of the sclera is determined experimentally in order to specify a light source with a wavelength that will enable optical power to reach the ciliary processes without adversely affecting scleral tissue. This chapter describes three methods that are used to determine the spectral transmittance of the sclera.

The first method uses a monochromator with an optical bench. This is a typical set-up that can be assembled in an electro-optics laboratory. It makes use of standard optical components. The layout and test set-up are described in paragraph 5.3.

The second method makes use of a spectrophotometer. The test set-up for this method is described in paragraph 5.4.

The third method employs the use of a radiometer. The test set-up for this method is described in paragraph 5.5.

The monochromator method is manually assembled and as such also has to be calibrated manually. The spectrophotometer as well as the radiometer are instruments that are calibrated by an accredited facility. Manufacturer's instructions and procedures must be followed in order to use the instruments.

5.2 Specimen

5.2.1 Statistics

All specimens were received after removal from fresh cadavers and after removal of the corneas. Specimens were supplied by the Pretoria Eye Institute. Ages differed from 2 years old to 63, with a mean age of 32 years. Nine pairs of eyes were younger than 32 years of age and six pairs were older than 32 years. Fifteen pairs of eyes were prepared and tested. Twelve pairs belonged to males and two to females. Seven pairs of eyes belonged to persons from Caucasian origin and five pairs to black persons. Unfortunately, no eyes were available from persons who originated from the East, such as Indian, Chinese and Japanese people. Both the gender and race of one pair of eyes are unknown.

5.2.2 Preparation

All specimens were supplied in a frozen condition by the Pretoria Eye Institute. Specimens were frozen within two hours after removal from the body and were then kept frozen (at between -9 EC and -16 EC, which was the operating range of the freezer used) until needed for measurement. Four hours before measurement, all specimens were removed from the freezer and allowed to stabilize at room temperature (19 EC to 25 EC).

Specimens were received without corneas and thus usually also without ciliary bodies and trabecular meshworks. (The trabecular meshwork is situated anterior to the iris. Figure 2.1.) Some specimens were received with these two parts still intact, but not attached to the remainder of the eyes. It was then impossible to use the ciliary body as well as the trabecular meshwork in an experimental set-up.

In order to isolate scleral transmittance measurement, the choroid was removed in all circumstances (except where stated otherwise). Specimens were then cut into quarters. A transmittance measurement was done in each quarter to ensure the integrity of results obtained from each eye. On some specimens this proved to be difficult in practice, and in such cases specimens were cut only in half to simplify mounting.

Specimens were mounted in an experimental apparatus to ensure that the measurement beam was applied close (0,5 to 2 mm (refer to Figure 2.2)) to the limbus in specimens where the limbus was clearly defined. Where it was not clearly defined, the measurement beam was applied as close as possible to where the limbus would have been.

5.3 Method 1: Monochromator

5.3.1 Method and Experimental Layout

Figure 5.1 presents a diagram describing the experimental layout. A wide-band light source (in this case a quartz halogen lamp, but it can be any other wide-band source) is used to produce the optical energy used as input for the set-up. Two lenses are then used to focus the light from the source onto the input slit of the monochromator. This specific configuration was used for focusing because of the availability of components. Before entering the monochromator, the light passes through a mechanical optical chopper, which is a slotted rotating disc. The chopper provides input to the phase lock amplifier which is used to remove the dc component of background light. This chopper forms part of the radiometer, which is used to measure optical energy or power. Inside the monochromator, a neutral density filter can be fitted to control incoming light levels. Light intensity can also be adjusted by adjusting the optical intensity output of the source, if the source used allows it. The monochromator is used to remove a single wavelength from the incoming wide-band light.

The required wavelength can be selected by the researcher by rotating the grating, using a crank handle. Light consisting of a single wavelength is focused on the output slit of the monochromator. This light enters an optical fibre which channels it to the sample holder, where it is applied to the sample. Any large-core optical fibre (a step index optical fibre with a core diameter of more than 300 μm and (for this application) the core diameter should preferably not exceed 900 μm . This is to limit application spot size, which, in turn, may complicate placement of the probe) can be used, but the larger the core diameter of the optical fibre, the better, since more optical energy can be transferred. The output of the optical fibre is mounted in order to gently touch the sclera sample.

The sclera sample is mounted in the open (vertically) without being clamped by glass plates, unless specified differently. It is mounted by using the two horizontal bars of a standard lens holder. The upper part of the sample (sclera) makes contact with the upper bar of the lens holder, and the lower part of the sample (sclera) makes contact with the lower bar of the lens holder (Figure 5.2).

The sample can now be clamped on both sides but experience showed that the sample was able to stay in place firmly without clamping, simply using the adhesive properties of the sclera, since it is still wet after removal from the growth medium.

The monochromator is adjusted to the required wavelength. The radiometer is then used to measure the optical power with no sample installed. This measurement is the reference value. The radiometer is then used to measure the optical power with a sample installed. The transmittance can then be calculated. This completes one test. The monochromator is adjusted to a different wavelength and the process is repeated. The system is calibrated by using an accredited neutral density filter in place of the scleral sample.

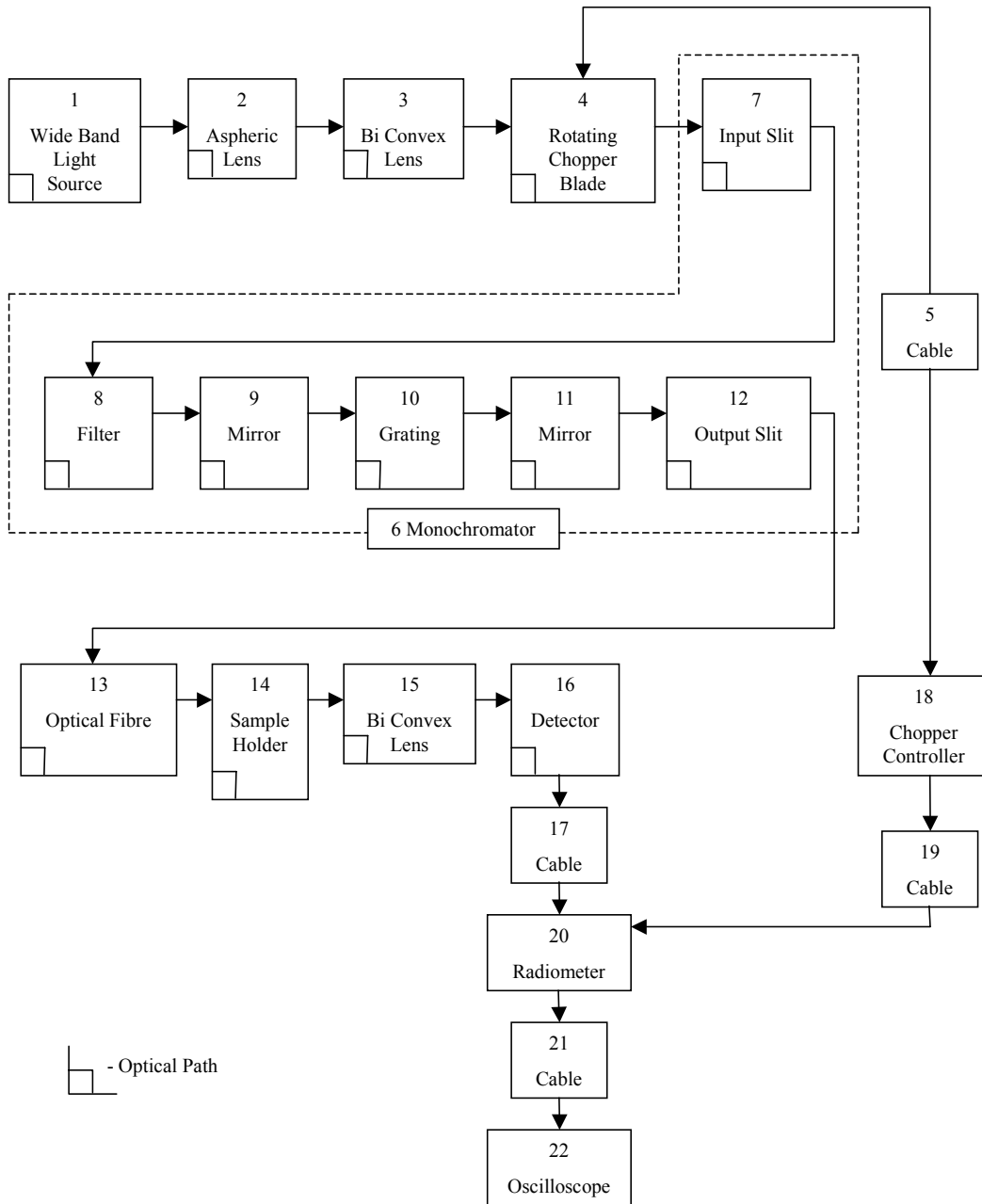


Figure 5.1

Monochromator: spectral transmittance measurement
(Monochromator with optical bench, integration sphere not used)

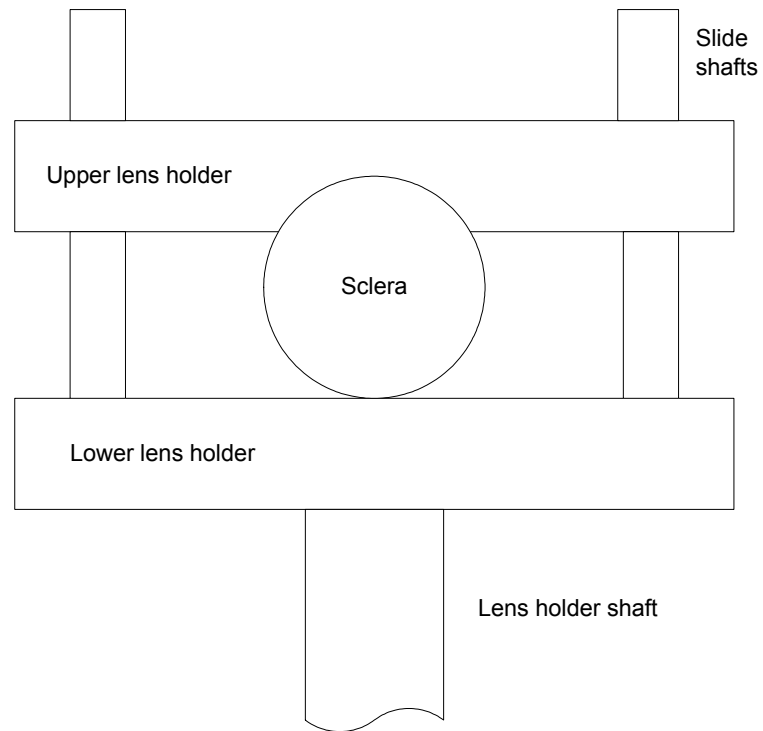


Figure 5.2

Mounting of scleral tissue to lens holder

This method has the following advantages:

- ~ The optical power is delivered by means of an optical fibre, which is a realistic method, since it is currently used by ophthalmologists.
- ~ The sclera sample is mounted vertically and in free space without deforming the specimen.
- ~ Scattered light in the forward direction is included in the measurement.

This method has the following disadvantages:

- ~ The range of wavelengths that can be measured is from 400 nm to 1100 nm (typical Si region). (The ideal range would be 100 nm to 12000 nm, as this will include sources from the ultraviolet wavelength region to the infrared wavelength region.)
- ~ Back-scattered light is not measured because no detector is fitted behind the specimen.
- ~ The measurement process is labour-intensive and time-consuming, with one set of measurements taking up to 1 hour.

5.3.2 Component Description

Table 5.1 gives a description of the components used in the measurement set-up in Figure 5.1

Table 5.1

Monochromator: List of Components

Number	Description	Technical Detail
1	Wide-band light source	100 W halogen lamp
2	Aspheric lens	Diameter = 60 mm Focal length = 39 mm Melles Griot 01LAG017
3	Bi-convex lens	Diameter = 110 mm Focal length = 150 mm
4	Rotating chopper blade	Stanford Research Systems Model SR540, set at 32 Hz
5	Cable	Conveys bidirectional data
6	Monochromator	Jarrel Ash Scale in D
7	Removable and adjustable input slit	Set at 1 mm
8	Removable filter	RG715
9	Mirror	
10	Grating	
11	Mirror	
12	Removable and adjustable output slit	Set at 1 mm
13	Optical fibre	Core diameter = 1 mm
14	Sample holder	
15	Bi convex lens	Diameter = 50 mm Focal length = 100 mm
16	Detector	Laser precision Si probe
17	Cable	Conveys detector signal to radiometer.
18	Chopper controller	Stanford Research Systems Model SR540
19	Cable	Conveys chopper signal to synchronized radiometer
20	Radiometer	Laser Precision Corp
21	Cable	Conveys received signal to oscilloscope
22	Oscilloscope	20 MHz bandwidth
23	Wavelength measurement intervals	10 nm

5.3.3 Results

Results are presented in Table 5.2

TABLE 5.2
Monochromator: Maximum Transmittance

Sample Number	Maximum Transmittance and at Wavelength of Maximum Transmittance
1A	4,7% at 1100 nm
4A	5% at 1100 nm
5A	3,7% at 1100 nm
6A	9,3% at 1100 nm

5.4 Method 2: Spectrophotometer

5.4.1 Method

A Perkin Elmer Lambda 9 US/VIS/NIR spectrophotometer is used. The sclera sample is prepared and mounted between two standard laboratory glass plates, which is not ideal, as deformation of the sample may be induced. The sample is inserted into the apparatus and the spectral transmittance is measured automatically by means of a computer. The transmittance results are stored in software and also printed. The spectrophotometer automatically compensates for reflection from glass plate surfaces. The applied beam is circular and 5 mm in diameter. (The sample should thus be larger than 5 mm in diameter, which is possible.)

This method has the following advantages:

- ~ The process is automated and quick. (Typical measurement time is less than 5 minutes.)
- ~ The range of wavelengths which can be covered is 400 nm to 2000 nm.
- ~ Scattered light from the glass surfaces is automatically compensated for.

This method has the following disadvantages:

- ~ The applied beam is 5 mm in diameter, which is not representative of the method currently used by ophthalmologists.
- ~ The sample is mounted between standard laboratory glass plates and some compression is thus applied to the sample.

5.4.2 Results

Graphs 1 to 5 in Figure 5.3 correspond to five samples of human eyes (sample numbers 2B, 4B, 5B, 6B and 7B). All these measurements were completed by using a Perkin Elmer Lambda 9 spectrophotometer. The spectral transmittance was measured by using Method 2. In all cases, the choroid was removed before the test.

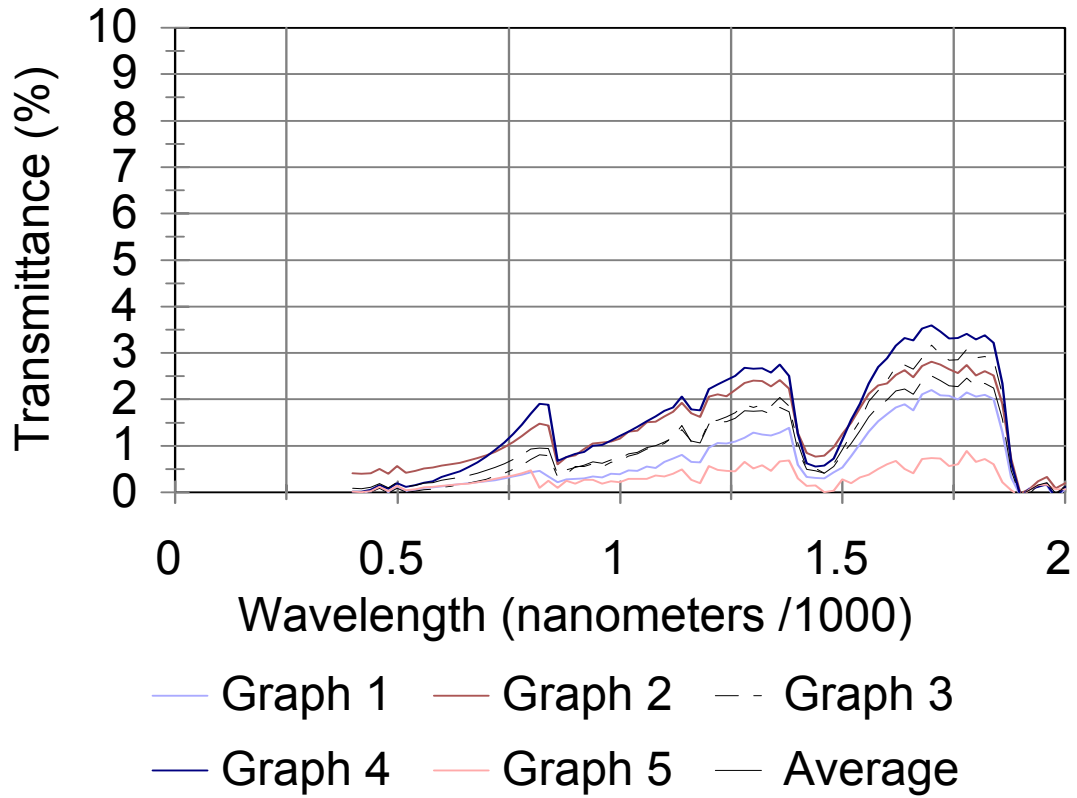


Figure 5.3
Spectrophotometer: Spectral transmittance

5.5 Method 3: Radiometer

5.5.1 Method

A Bomem radiometer is used as a measurement apparatus. The measurement set-up is dictated by the Bomem apparatus layout, which can be used in only one way. A black body is used as an energy source. The temperature of the black body is set at 700 EC. The sclera sample is prepared and mounted between the black body and the radiometer. The sample is mounted in a standard Bomem mounting plate, which is supplied with the radiometer. This mounting plate is specially manufactured to be installed in the optical path inside the radiometer. The spectral transmittance is measured automatically. Results are stored by using dedicated software but can also be printed. A pinhole is positioned right next to the sclera sample. The applied beam is circular and 5 mm in diameter. (The sample should thus be larger than 5 mm in diameter, which is possible.)

This method has the following advantages:

- ~ The process is automated and quick. (Typical measurement time is less than 5 minutes.)
- ~ The range of wavelengths that can be covered is 2000 nm to 12000 nm.

This method has the following disadvantage:

- ~ The applied beam is 5 mm in diameter, which is not representative of the method currently used by ophthalmologists.

5.5.2 Description and Results of Sample

Maximum transmittance figures are presented in the last column of Table 5.3 and the spectral transmittance is presented in Figure 5.4.

TABLE 5.3

Radiometer: Maximum Transmittance

Sample Number	Wavelength (nanometres/1000)	Maximum Transmittance
8A	2 - 6	3%
8B	2 - 12	4,5%
9A	2 - 6	1,5%
9B	2 - 6	0,6%
10A	2 - 12	4,5%
10B	2 - 6	0,1%
11A	2 - 6	0,2%
11B	6 - 9	0,02%
12A	6 - 9	0,03%
12B	6 - 9	0,01%
13A	6 - 9	0,01%
13B	6 - 9	0,01%
14A	6 - 9	0%
14B	6 - 9	0%
15A	6 - 9	0,01%
15B	6 - 9	0,01%

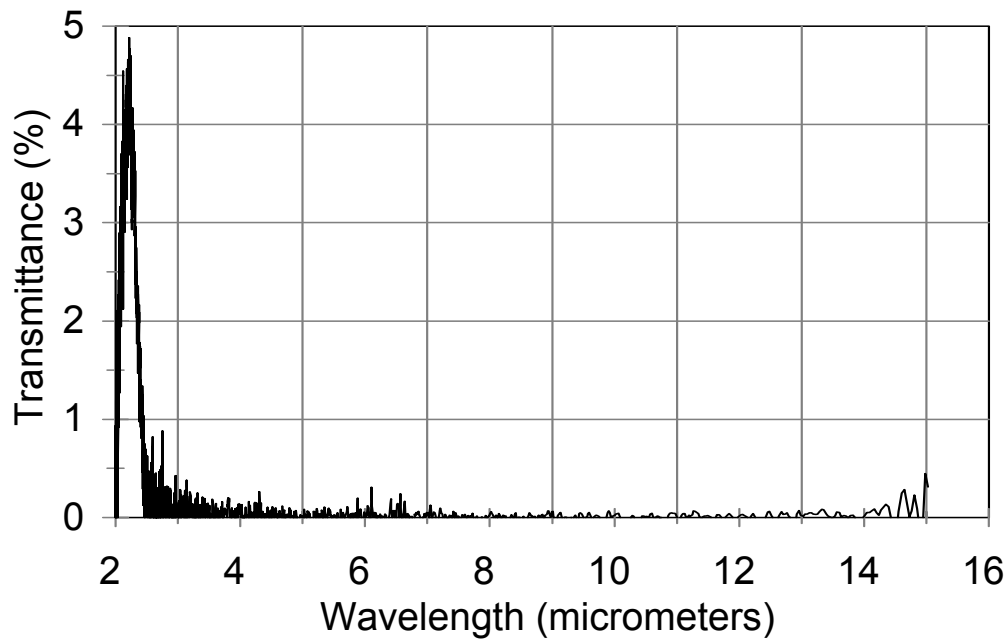


Figure 5.4

Radiometer: Spectral transmittance

Note that the y-scale is different from that of Figure 5.3

5.6 Discussion

Results are displayed in Table 5.2, Figure 5.3 and also Table 5.3. The maximum scleral transmittance measured in Table 5.2 was 9,3% at 1 100 nm. Results presented in Figure 5.3 include measurements up to a wavelength of 2 000 nm. The maximum transmittance is less than 4%. Table 5.3 shows the spectral transmittance up to a wavelength of 12 000 nm. The maximum transmittance still remains very low. The calculated average transmittance measured for white persons was 2,6% and the average transmittance measured for black persons was 3,1%.

According to the presented results, the transmittance of the human sclera is very limited, indeed to the point where the application of any transscleral optical energy becomes impractical, since there is little to be gained.

Certain factors could have influenced the results. These are the time taken from death to removal of the eye, or the specific solution that was used for storage of the specimen. Storage temperature is also important.

As far as could be established, the results presented in this chapter constitute the first attempt at a continuous scleral transmittance measurement of the human sclera. The graphs presented in Figure 5.3 are unique in that none such measurement could be found during scrutiny of 120 related journal articles. A well-known result is that of Vogel *et al* [34], where transmittance was measured at three wavelengths.

As described in paragraph 3.6, Vogel *et al* [34] measured scleral transmittance of 6% at 442 nm, 35% at 804 nm and 53% at 1064 nm. It is not clear why there are differences in the outcomes of measurements. When attempting to isolate differences in experimental set-ups, it was found that there were vital differences. This study used eyes that were frozen before use. The exact method of preparation of the specimens used by Vogel *et al* [34] is not known. The ages of the donors used by Vogel *et al* [34] are not known, whereas the average age of donors used in this study was 32 years.

6.1 Introduction

In order to evaluate the damage achieved on the choroid and ciliary body, it was decided to execute a test in which white light is applied to the anterior side of the sclera.

Two white-light sources were used to evaluate the concept. The one is a xenon lamp and the other a quartz halogen lamp. Each of these sources has its own unique properties and advantages as well as disadvantages. Two of the advantages of using a wide-band source are simplicity and cost. Both these parameters are important in the development of an applicator that can be used in rural areas. This is especially applicable to the use of the quartz halogen lamp, which is easy to obtain and also cost-effective. The xenon lamp is not quite in this category, as it is still expensive and not that easy to obtain. It was included because (depending on model) it is able to deliver high optical power in the visible wavelength region.

The wide-band sources can be used directly in an optical system or they can be connected to optical fibres or other components such as pinholes. A small spot size is required in the application of optical energy to the sclera. The reason for this is that the application of energy should be localized and controllable. An optical fibre is the ideal instrument to accomplish this. The spot size can be adjusted by using optical fibres with different core diameters. In this study, pinholes were also employed because optical fibres with the required diameters were not always available. In practice, the use of a specific wide-band source will be dictated by factors such as size, power consumption, efficiency, cooling, cost and also replaceability.

6.2 Xenon Arc Lamp

6.2.1 Set-up

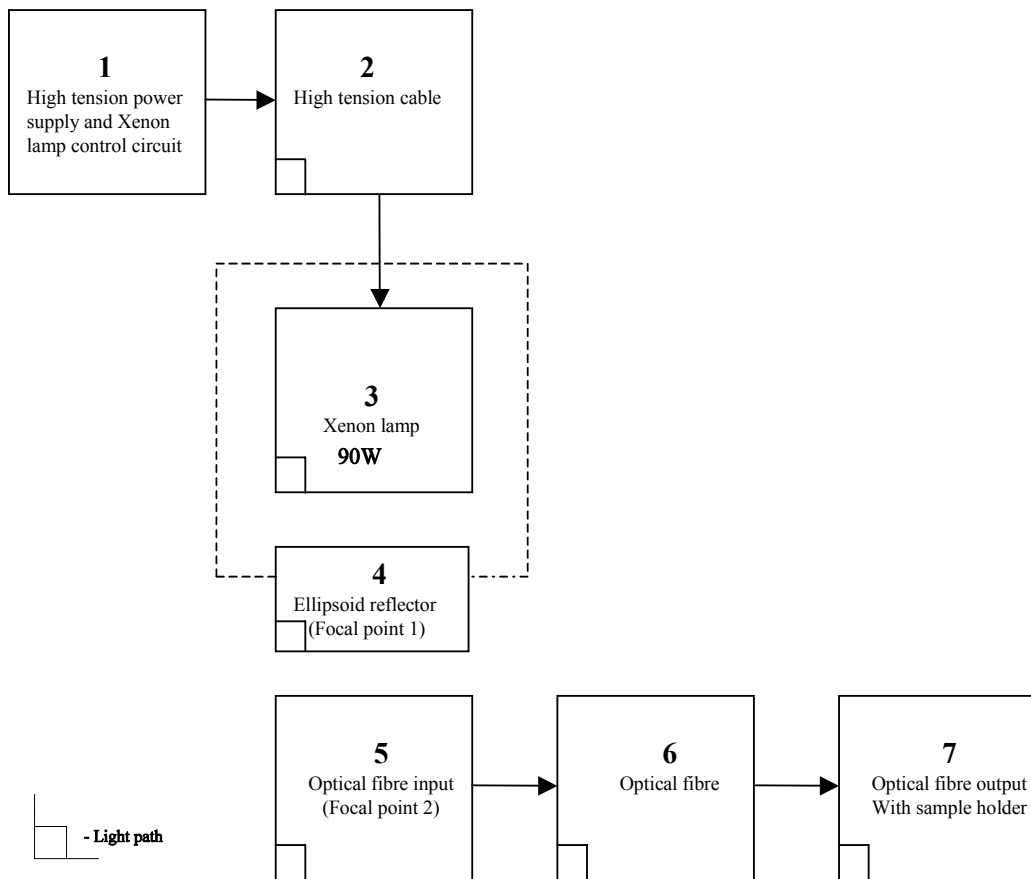


Figure 6.1 :
Xenon arc lamp

The source used in this experiment was a xenon lamp. The xenon lamp needs a high-voltage power supply as well as a control circuit to function. The control circuit also modulates the lamp, in this specific case at 5 kHz. (This frequency is used as it is suggested by the lamp manufacturer.) Start-up current of the xenon lamp is between 6,5 A and 7 A. After modulation, the applied current decreases to between 3,5 A and 4 A. As with most xenon arc lamps, heat generation of the lamp proved to be severe (prolonged use can damage the input tip of the optical fibre), and it was necessary to use forced cooling (laboratory fan, Rotron Caravel, 250 V) to control the generated heat.

The xenon lamp was then mounted in one of the two focal points (focal point 1) of an ellipsoid reflector. One end of an optical fibre was mounted close to the reflector but not exactly on the remaining focal point (focal point F2) of the ellipsoid reflector. This was not technically possible, due to the size and proximity of the ellipsoid reflector.

The other end of the fibre was used to deliver optical power to the sample.

6.2.2 Results

Optical output power exiting the optical fibre (before a sample was inserted in the set-up) was measured with an EG&G model 550-1 radiometer/photometer. The optical power exiting the optical fibre was measured at 222 mW/mm².

Samples number 16A and 16B (human) were used for evaluation. The sample was prepared and mounted as described in paragraph 5.3.1. The human eye was cut in half. The sclera and choroid were left intact.

The tip of the optical fibre was then pressed gently against the outside of the sclera. From the opposite side, the inside surface of the choroid was closely monitored and also photographed to record any change in colour of the choroid.

Whitening and/or blanching of the choroid/ciliary body is often recognized by ophthalmologists to indicate tissue damage. (This is described by [36], [29], [48], [35],[50], [49], [53], [54] and [59]).

6.3 Quartz Halogen Lamp with Optical Fibre

6.3.1 Set-up

The set-up is presented in Figure 6.2.

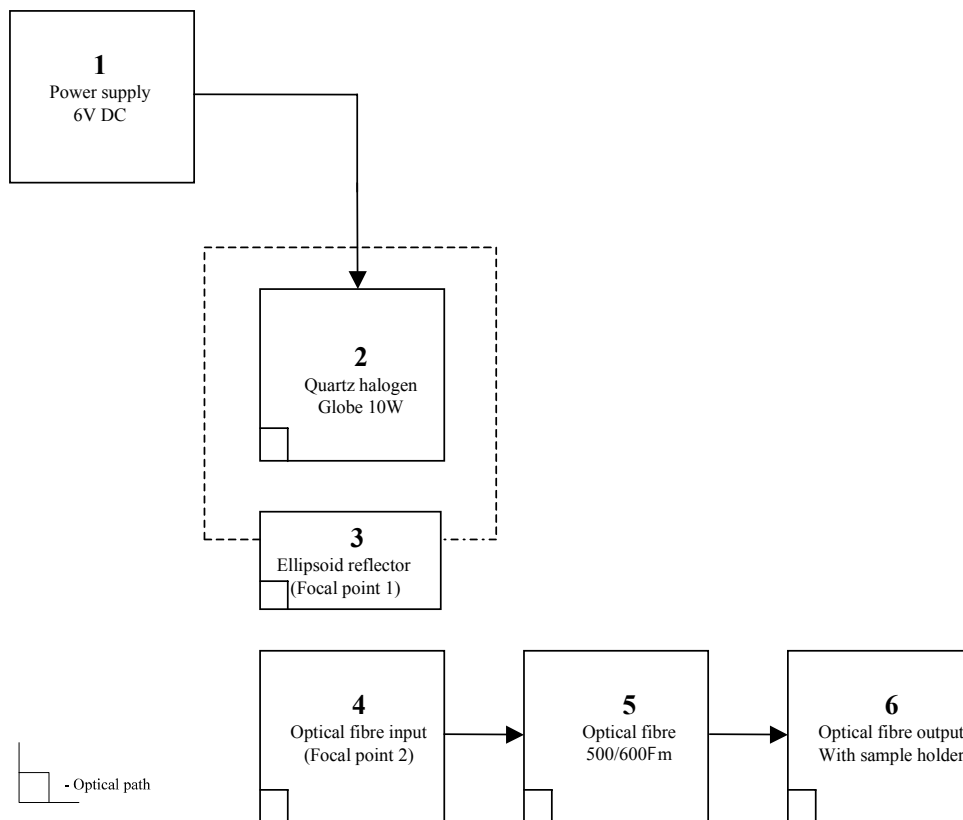


Figure 6.2
Quartz halogen lamp with optical fibre

A 10 W quartz halogen globe is used as a wide-band source. This specific source was selected because of the minute size of the filament, which measured approximately 1,5 mm by 1 mm. The source is powered by a DC power supply, which is set at 6 V, 2 A. An ellipsoid reflector is used to couple optical power into a 500/600 Fm optical fibre. The wide-band source is positioned on the one focal point of the ellipsoid reflector (focal point F1) and the optical fibre is positioned on the other focal point (focal point F2). Micro-positioning equipment was required to ensure optimum optical coupling. This set-up proved to be ideal, as the numerical aperture of the optical fibre matched with the ellipsoid reflector. The specific optical fibre as well as ellipsoid reflector were chosen because of availability.

6.3.2 Results

The optical power exiting the optical fibre was measured by using an EG&G (model 550-1) radiometer/photometer with a silicon probe. The optical power was measured to be 0,56 Wmm⁻². It is important to note that this was the optical power measured in the silicon wavelength region. The actual wide-band optical power is estimated to be much more, since optical power is delivered in the near-infrared region (at least up to 2 Fm) as well. A calibrated pyroelectric probe (or similar device) was unfortunately not available, with the result that the optical power delivered in the near-infrared region could not be measured.

6.4 Quartz Halogen Lamp with Pinhole

6.4.1 Set-up

The set-up is presented in Figure 6.3

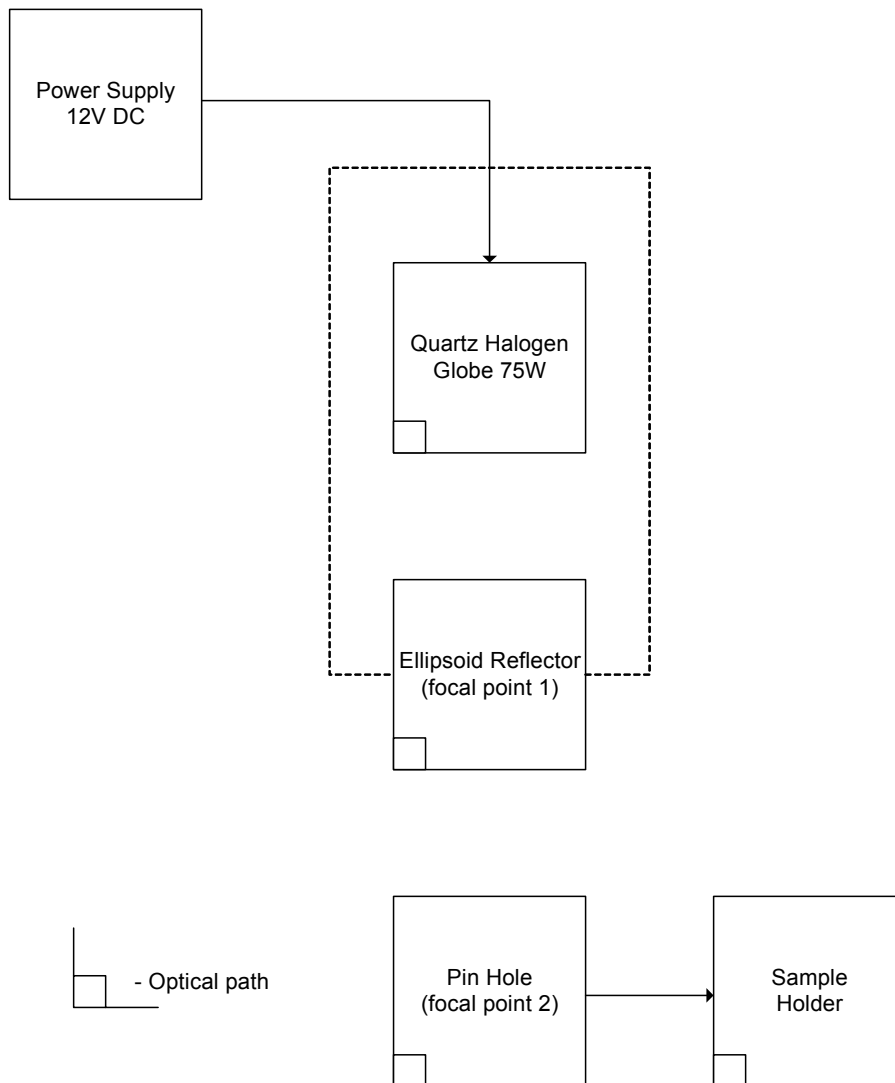


Figure 6.3
Quartz halogen lamp with pinhole

This method is similar to the method described in paragraph 6.3, except for the optical fibre, which is substituted by a pinhole. This is done in order to experiment with different sizes of pinholes so that the effect of different energy levels as well as different sizes of pinholes can be investigated. The same result can be achieved by using large-core optical fibres with different core sizes. The only difference is that large-core optical fibres are relatively expensive and difficult to obtain.

A 75 W quartz halogen globe is used as a wide-band source. This specific source was selected for high optical power. The source is powered by a DC power supply which is set at 12 V, 8 A. An ellipsoid reflector is used to focus optical power onto the pinhole. The wide-band source is positioned on the one focal point of the ellipsoid reflector (focal point F1) and the pinhole is positioned on the other focal point (focal point F2) of the ellipsoid reflector. Micro-positioning equipment was required to ensure optimum optical coupling. The specimen is placed as close to the rear of the pinhole as possible.

6.4.2 Specimens

At this stage of the investigation it became necessary to switch over from using human sclera to those of porcine sclera. This change was decided on because of the following problems experienced in the use of human sclera:

- ~ Availability of human eyes became limited, with typical times to wait in the order of two or three months.
- ~ High HIV infection rate.
- ~ High hepatitis infection rate.

The question to consider next was how close the porcine sclera is to that of a human. Olsen *et al* [87] investigated the thickness and surface area of porcine sclera. They used a hundred and twenty-eight porcine globes for the evaluation and concluded that porcine scleral thickness is very similar to human scleral thickness. Olsen *et al* [87] also commented that (in their view) the porcine sclera is an excellent model for studying human trans-scleral drug delivery.

On the other hand, Vogel *et al* [34] stated that a porcine sclera is 27 to 36% thicker than that of a human sclera, especially in the limbal region. According to Vogel *et al* [34], the absorption of porcine sclera is less than that of human sclera. The results as published by Vogel *et al* [34] are not in agreement with the results of the investigation as published by Olsen *et al* [87]. The reason for the discrepancy is not clear.

It was decided to proceed with tests, using porcine sclera, and an agreement was reached with a supplier who was able to supply porcine eyes. An advantage was that the eyes could be harvested 2 hours after death, which meant that the eyes could be treated without being frozen first.

6.4.3 Results

Two pig's eyes were treated, as shown in Figure 6.3. Each eye was treated at two spots. The posterior part of the eye was then opened with a 5 to 7 mm slit, and the eye was preserved in a formaldehyde solution (34 to 38%, BV 331). The slit was made to allow the eye to absorb the formaldehyde.

The eyes were then delivered to the National Health Laboratory Service (Tshwane Academic Division) for a histological investigation and description. (The report can be found in Appendix D.)

The pathologist from the National Health Laboratory reported severe thermal damage and degeneration of the sclera. The change is most obvious at the outer aspect (anterior) of the sclera, especially in the area of the ciliary body. The change is also noticed posteriorly. In some areas, splitting of tissue is visible. The area of the canal of Schlemm as well as the trabecular mesh-work shows little change.

The ciliary body looks relatively normal. The area of the eye not treated shows none of the changes. (The histology report was unfortunately written in Afrikaans but a summary is presented here for the benefit of the English reader.)

The damaged sclera in conjunction with the relatively undamaged ciliary body points to optical energy being absorbed in the sclera to such a point that the ciliary body is not reached. No or little energy is absorbed in the ciliary body and that is why it remains unscathed.

With the first set of eyes, a pinhole of 4 mm was used. Optical power was measured to be 13,8 mW. As the application time was 30 minutes per spot, total energy delivered was 23,4 J per spot.

6.4.4 Discussion

The energy applied (23,4 J) is approximately twice to three times the energy used by [2], [6], [7], [12], [15], [17], [20] and [23]. These applications were all of the scleral contact type, which means that energy transfer was more efficient than in the case where the pinhole is used. (The pinhole method is a non-contact method.)

As already mentioned, degeneration of the sclera is noted as well as very little damage to the ciliary body. This is in line with the low scleral transmittance figures (for human sclera) obtained in Chapter 5.

On the other hand, Vogel *et al* [34] suggests that the absorption of porcine sclera is less than that of human sclera, although it was not explicitly measured. Olsen *et al* [87] is the only study on porcine sclera which could be traced and no comment is printed regarding porcine scleral transmittance and/or scleral absorption. It is also important to note that the choroid was left intact for this evaluation.

The results of this study support the results obtained by Olsen *et al* [87] but are in contradiction with the results obtained by Vogel *et al* [34]. Using the porcine sclera, it was shown that the absorption of the sclera is high. Olsen *et al* [87] states that the human sclera is very similar to porcine sclera, and it can thus be deduced that the human scleral absorption will also be high. This result is also supported by the findings published in Chapter 5.

6.4.5 Summary

The area to be treated in the eye is the ciliary body. Experimental application of wideband light-sources showed that most of the optical energy is absorbed in the sclera and does not reach the ciliary body.

7.1 Introduction

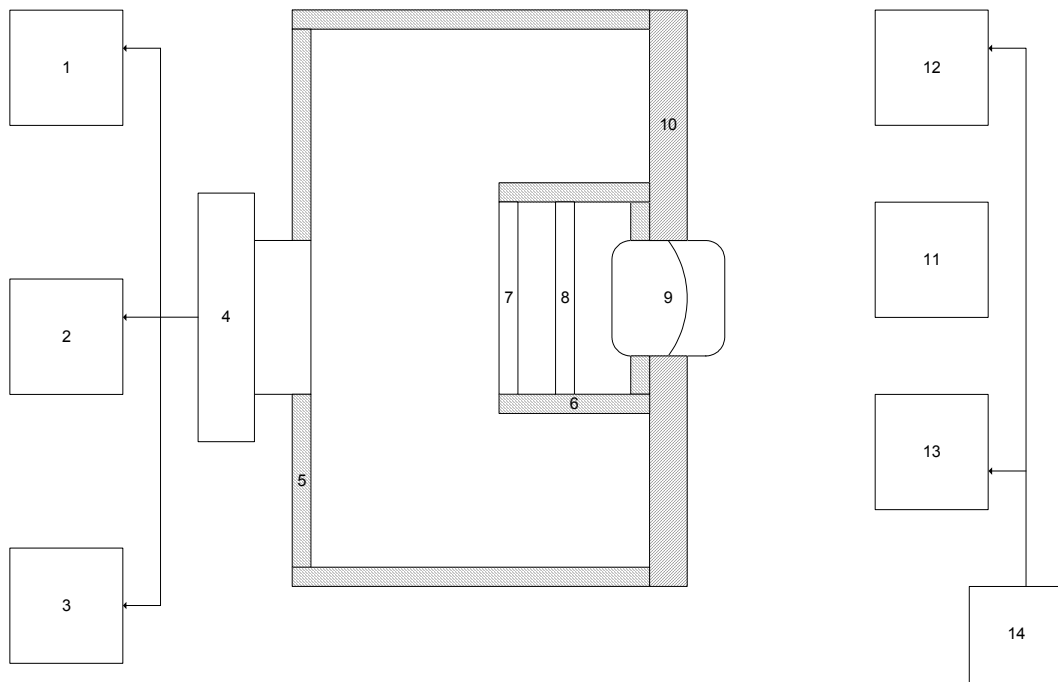
As already reported, Vogel *et al* [34] measured scleral transmittance and they achieved a number of 38% at 632 nm. How does this affect the retina? If the scleral transmittance is high at a visible wavelength such as 632 nm (the same wavelength as a HeNe laser), what amount of light will reach the retina and what effect will this have on light perception? It is true that the choroid was removed for all scleral transmittance measurements, and the next question is thus what is the transmittance and absorption of the choroid? To measure the transmittance of the choroid is not a trivial task, as the choroid is a very thin membrane. If the absorption of the choroid is high, how is the energy (in the form of heat) dissipated? Absorption of the light energy in the choroid will depend on pigmentation, and experience (by dissecting 15 pairs of eyes, as shown in Appendix E) showed that choroid pigmentation may vary from black to light tan. (It could not be established whether pigmentation depends on age, race or gender.) Possibly, thickness of the choroid also varies. Indeed, Cantor *et al* [36] reported destruction of the ciliary body in pigmented rabbits' eyes, but no histological effects were observed in albino rabbits' eyes.

A high transmittance of visible light through the sclera and choroid will be registered on the retina as stray light or background noise, which will reduce the ability of the eye to produce a high-contrast picture.

It was decided that a test had to be designed and executed which can be used for the evaluation of the signal as registered by the retina, as well as the perception of stray light (noise) on the retina. To evaluate this effect, it was decided to construct an 'emulated eye', using optical components and mechanical hardware.

7.2 The Ideal Hardware

A piece of hardware was designed which can be used for measurements and applications where a simulated eye is required. The experimental layout is shown in Figure 7.1.



Figur

e 7.1

Proposed construction of an emulated eye

The various parts and components of the eye are described in Table 7.1.

TABLE 7.1
EMULATED EYE: DESCRIPTION OF COMPONENTS

Item Number	Component	Interface	Description
1	Oscilloscope	Connects to output of CCD imager.	20 MHz bandwidth with TV triggering.
2	Video Monitor	Connects to output of CCD imager.	High-resolution black and white video monitor.
3	Video Printer	Connects to output of CCD imager.	High-resolution black and white video printer or a frame- grabber card with high resolution can also be used. Active area should be as large as possible, with a one-inch sensor would be ideal if it can be obtained.
4	CCD Imager	Mechanically mounted in mechanics which forms part of the eyeball (outer casing).	Black and white CCD imager with high resolution and Si sensor is sufficient.

Item Number	Component	Interface	Description
5	Outer Casing	Simulates the eyeball and as such provides structural integrity and mounting for all other components, mechanical and optical. Can also be in a spherical shape if a CCD imager with a similar shape can be procured.	Machined from metal. Circular, with dimensions of 25 * 25 mm.
6	Inner Casing	Provides mounting facility for optical components.	Machined from metal.
7	Photometric Filter	Mounted in the optical path.	Photometric filter to simulate eye response.
8	Mechanical Iris	Mounted in the optical path.	Mechanical iris from which the opening can be adjusted from 8 mm to 3 mm in diameter.
9	Doublet	Mounted in optical path.	Simulates the combined optical effect of both the cornea and lens. Diameter should be 8 to 10 mm and focal length should be 20 to 25 mm to achieve an F# number of 6.

Item Number	Component	Interface	Description
10	Diffused Glass Plate	Mounted to the outer casing.	This component simulates the sclera. It should be interchangeable and at least two plates should be available: one with a transparency of 38% and the other with a transparency of 10%.
11	Resolution Chart	CCD focussed at resolution chart.	Standard resolution chart or any other suitable object.
12 and 13	Floodlights	Lights directed towards diffused glass plates.	Floodlights with high intensity (typical 500 W) and of which intensity can be adjusted.
14	Floodlight controller	Connected to flood-light inputs.	Should be able to adjust flood-light intensity from completely switched off to maximum intensity.

The functioning of the emulated eye is described as follows: The CCD imager simulates the retina. It would have been ideal if the active area covered the complete rear side of the eyeball but this is not practical, as the active area is dictated by the size of commercially available devices.

The doublet simulates the optical system of the eye, which consists of cornea and lens. The image is thus projected onto the CCD (retina), using the doublet (cornea and lens).

The sclera is simulated by the diffused glass of different transparencies. Stray or unwanted light is generated by the floodlights, then passes through the diffused glass and is registered on the retina as noise. The practical effect is that contrast of the final picture is affected. The intensity of the floodlights can be adjusted to evaluate the effect of different noise levels on the retina.

Without having the mechanical construction facility to manufacture the simulated eye as described in Figure 7.1, it was decided to build a similar system, using optical bench components. This system is described in paragraph 7.3.

7.3 An Emulated Eye on an Optical Bench

The experimental layout is shown in Figure 7.2.

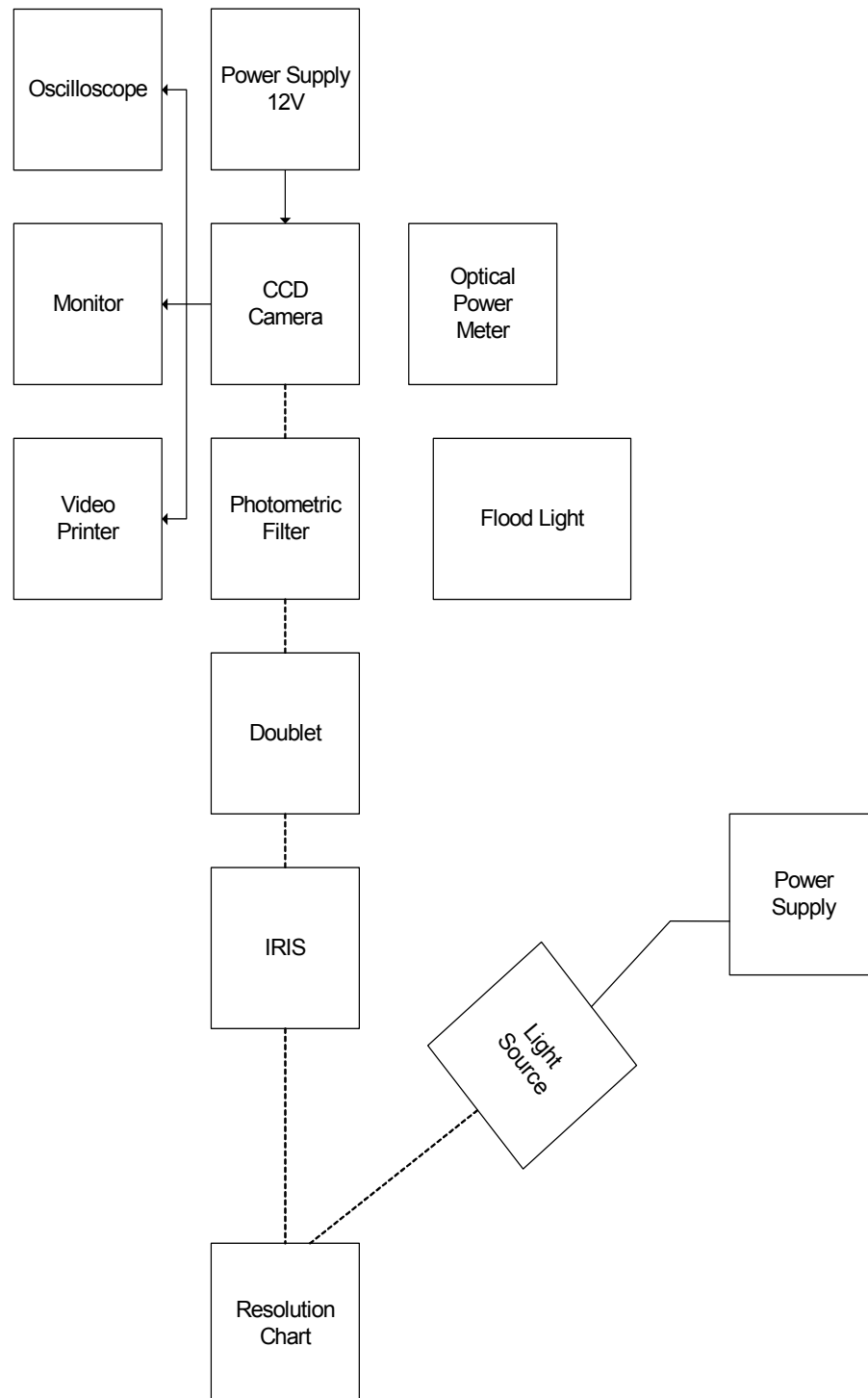


Figure 7.2

An emulated eye, using an optical bench

A CCD camera is used without a doublet lens to simulate the retina. A doublet is used for the simulation of the eye lens as well as that of the cornea. The doublet was specified to be as close to the optical components of the eye as possible. The human eye has a focal length of 22 to 24 mm, and the maximum opening of the iris is 6 to 7 mm. This means that the F# number of the complete eye is about 6. The doublet that was used had a focal length of 30 mm and a diameter of 32 mm. A mechanical iris was used to limit the incidence beam diameter to 5 mm in order to achieve a F# number of 6 for the optical system.

All optical components were mounted on optical benches. A resolution chart was mounted at a distance of 1 m and illuminated by means of a DC light source. The doublet was then moved until a high-contrast picture appeared on the video monitor.

In this set-up, no sclera is present. An additional light source (flood-lamp) is used to illuminate the complete optical system. This then represents light entering through the sclera. To simulate the condition where the sclera is not transparent at all, the flood-lamp is switched off and only the resolution chart is illuminated. The complete system is tested in a dark room.

The flood-lamp is switched on to simulate various light levels entering the sclera. The optical power meter is used to measure light levels reaching the retina (CCD camera). The flood-lamp thus generates stray light, which reaches the retina through the sclera.

The output of the CCD camera is connected to a video monitor, a video printer and also an oscilloscope. The oscilloscope is used (in TV-triggering mode) to measure contrast levels and also offset levels.

7.4 Results

The flood-lamp was used at two different light levels to evaluate the effect of stray light reaching the retina (CCD camera). Light level is measured in optical power reaching a specified area. In this case it is measured as FWcm^{-2} . The video signal is displayed on an oscilloscope and the amplitude is measured in mV.

The first flood- (stray) light level was measured to be 2FWcm^{-2} . The video signal contrast was measured to be 906 mV.

The second flood- (stray) light level was measured to be 6FWcm^{-2} . The video signal contrast was measured to be 500 mV.

The two video signal oscilloscope traces are presented in Figures 7.3 and 7.4. (All measurement parameters were identical for the two traces.) The two oscilloscope traces are to be read by comparing the one to the other. The y-axis in both cases shows the amplitude (mV) of the video signals, while the x-axis shows the time (s).

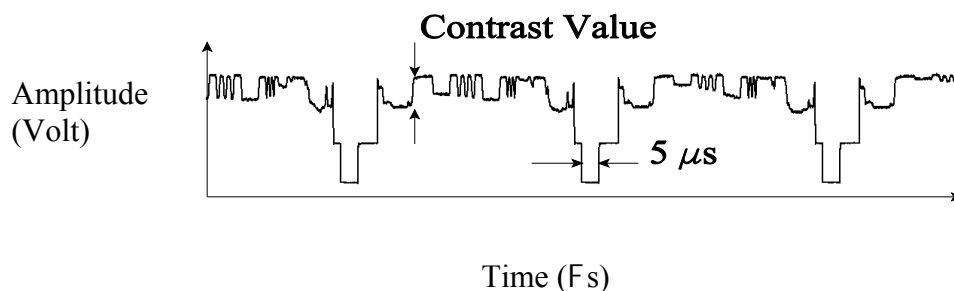


Figure 7.3

Video signal for flood light level 2FWcm^{-2} .

Contrast value: 906 mV

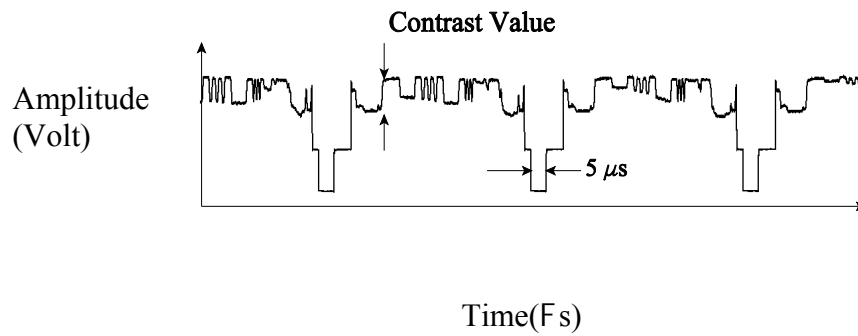


Figure 7.4

Video signal for floodlight level 6 F W cm^{-2} .

Contrast value : 500 mV

The two video printer pictures are presented in Figures 7.5 and 7.6.
(All measurement parameters were identical for the two prints.)

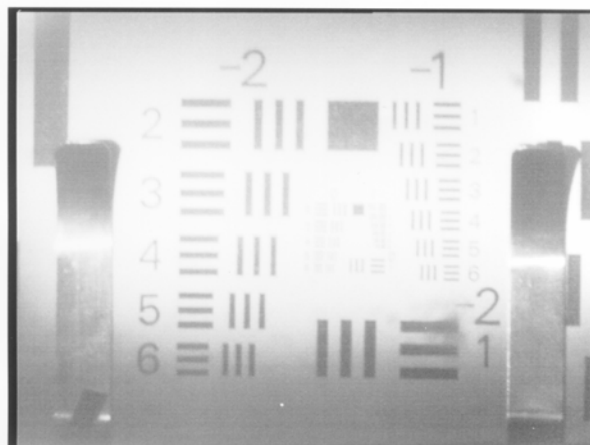


Figure 7.5

Resolution chart video for floodlight level 2 FWcm².
(Contrast value: 906 mV)



Figure 7.6

Resolution chart video for floodlight level 6 FWcm².
(Contrast value: 500mV)

When comparing Figure 7.3 with Figure 7.4, and Figure 7.5 with Figure 7.6, a difference in the contrast value (y-axis in Figure 7.3 and Figure 7.4) can be read from the oscilloscope but it can also be seen on the monitor. The contrast value in Figure 7.3 and Figure 7.5 is 906 mV, whereas the value in Figure 7.4 and Figure 7.6 is 500 mV. The only difference was the amount of stray light reaching the CCD (retina) from the side, thus through the emulated sclera. In practice this means that the higher level of stray light on the CCD (retina) reduced the sensor's ability to produce a high-contrast image. This simple experiment shows that a high transmittance of light (in the visible spectrum) through the sclera is likely to reduce the ability of the eye to produce high-contrast images. In the one case, the floodlight level is 30% of that in the higher illumination case. This corresponds to the claim of Vogel *et al* [34], that a 38% scleral transmittance can be expected at 632 nm. According to this experiment, a high scleral transmittance will probably present the retina with a problem in the form of stray light, hence Vogel's results are unlikely.

8. CONCLUSION

8.1 Discussion

This study started off with an investigation into the application of light sources in the use of transscleral cyclophotocoagulation in the treatment of glaucoma.

Due to the method used, the transmittance of optical energy through the sclera is of vital importance. The logical information to be used here is a spectral transmittance curve of the human sclera. This was not available but Vogel *et al* [34] did publish transmittance values which were measured at four selected wavelengths (paragraph 3.6).

A spectral transmittance curve was then generated, using different test methods, in Chapter 5. All these measurements showed a transmittance value much lower than that proposed by Vogel *et al* [34]. The measurements also indicated that a monochromatic light source is not necessary but a wide-band light source can be used as an applicator.

The next step was to apply wide-band light energy to specimens and to evaluate the results by carrying out a histological investigation. Results obtained here also indicated a low scleral transmittance. (The histological investigation indicated high energy absorbency of the sclera, which points to low transmittance.)

The author is of the opinion that discrepancies exist in the application of energy through the sclera. It is certainly true that successes are reported but methods are not standardized, and the huge variation in applied energy is a cause for concern. (This is discussed in paragraph 4.4.) Pastor *et al* [73] as well as Kirwan *et al* [75] also voiced their concerns.

The use of a wide-band source as illuminator shows promising results in other areas of the body. It is also interesting to note that Gordon *et al* ([88] and [89]) as well as Feuermann *et al* [90] successfully demonstrated surgery on rat livers, using the sun as a wide-band source. This information was published recently and research is continuing.

The question of choroid transmittance is not mentioned by any author, and this may be important. It is thus suggested that this parameter should be investigated further. The transmittance of the choroid may explain the differences in results of different studies.

The conclusion of this study can be summarized as follows:

- 8.1.1 The question of spectral scleral transmittance (including choroid) has not been resolved.
- 8.1.2 Energy levels when using TSCPC are not standardized. It is true, however, that if the problem stated in paragraph 8.1 can be addressed effectively, the energy level problem will also be solved to a large degree.
- 8.1.3 A wide-band source can be used for treatment since it offers many advantages whilst being able to deliver the correct energy levels.
- 8.1.4 A hardware model is suggested, which can be a useful tool when attempting research on the eye.

8.2 Suggested Further Research

As already mentioned, some questions still remain. In order to better understand the application of TSCPC and solve related problems, the following questions have to be addressed:

- 8.2.1 The optical scleral transmittance and absorption of the choroid must be investigated, using a wide variety of human samples.
- 8.2.2 Standardized energy levels for TSCPC must be investigated, using a wide variety of human samples.
- 8.2.3 The question of different energy levels for *in vitro* and *in vivo* applications should be researched further.
- 8.2.4 Energy levels reaching the retina should be confirmed.

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APPENDIX A

Summary of Application Methods and Power Levels for TSCPC

(Unless otherwise noted)

Item	Type of Laser (Unless otherwise noted)	Applied Optical Power	Application Time	Applied Energy	Application Diameter	Application Method	Number of Patients	Results	Reference
1	Argon	0,3 W - 1 W	0,1 s	30 mJ - 100 mJ	100 - 200 Fm	Through iridectomy hole.	6	Deepening of the anterior chamber.	Herschler [21]
2	Nd:YAG	Not supplied	20 ms	2 - 8 J	Not supplied	Contact through sclera, 0.5 - 3 mm posterior to limbus.	5 enucleated eyes	Damage to ciliary epithelium	Blasini <i>et al</i> [29]
3	Diode 810 nm	1,5 W	1,5 s	2,25 J	600 Fm	Contact through sclera: 1,2 mm posterior to limbus.	30	Final IOP: 25,8 mmHg Multiple treatments.	Walland [31]
4	Nd:YAG 1064 nm	Not supplied	Not supplied	1,95 - 2,15 J	Not supplied	Contact, through sclera, 1 mm posterior to limbus.	Rabbits	Ciliary body destroyed in pigmented eyes.	Cantor <i>et al</i> [36]

Item	Type of Laser (Unless otherwise noted)	Applied Optical Power	Application Time	Applied Energy	Application Diameter	Application Method	Number of Patients	Results	Reference
5	Diode 780 nm, 830 nm	1 W; 1,2 W	0,1; 0,4; 0,5; 0,6; 0,7 s	100 mJ - 840 mJ	100, 200, 500 Fm	Contact through sclera: 0,5 - 2 mm posterior to limbus.	Cadaver	Blanching and shrinking of ciliary body	Assia <i>et al</i> [37]
6	Nd:YAG	Not supplied	Not supplied	2, 4, 6, 8 J	100, 200, 500 Fm	Contact through sclera: 0,5 - 2 mm posterior to limbus.	Cadaver	Blanching and shrinking of ciliary body	Assia <i>et al</i> [37]
7	Nd:YAG	7 W - 9 W	0,7 s	4,9 - 6,3 J	600 Fm	Contact through sclera: 0,5 - 1 mm posterior to limbus.	136	35,2 mmHg IOP reduced to 18,4 mmHg after 6 months.	Schuman <i>et al</i> [38]
8	Argon	1 W	0,1 - 0,2 s	0,1 - 0,2 J	50 Fm, 100 Fm	Through pupil	14	Results unstable and not uniform.	Lee [39]
9	Diode 810 nm	1,5 - 2 W	2 s	3 - 4 J	600 Fm	Contact through sclera: 1,2 mm posterior to limbus.	27	Final IOP: 20 mmHg after 2 years	Kosoko <i>et al</i> [40]

Item	Type of Laser (Unless otherwise noted)	Applied Optical Power	Application Time	Applied Energy	Application Diameter	Application Method	Number of Patients	Results	Reference
10	Diode 818 nm 850 nm	0,9 - 3 W	1, 2, 3, 4, 5 s	0,9 J - 4,5 J	600 Fm	Contact through sclera: 1 - 1,2 mm posterior to limbus.	22 cadavers	2 J: no damage 2 - 3 J: mild whitening 4 - 5 J: intense whitening > 5 J: explosive damage	Schuman <i>et al</i> [41]
11	Diode 810 nm	1,8 - 2,4 W	2 s	3,6 - 4,8 J	600 Fm	Contact through sclera; position not supplied	26	Final IOP: 24 mmHg after 6 months (adults) No decrease in congenital glaucoma.	Bock <i>et al</i> [42]
12	Nd:YAG	Not supplied	20 ms	7 - 8 J	Not supplied	Contact through sclera: 1,5 mm posterior to limbus.	100	Final IOP: 7 - 20 mmHg in 65 eyes No IOP lowering in 14 eyes.	Hampton <i>et al</i> [43]

Item	Type of Laser (Unless otherwise noted)	Applied Optical Power	Application Time	Applied Energy	Application Diameter	Application Method	Number of Patients	Results	Reference
13	Xenon	Not supplied	Not supplied	Not supplied	4,5 deg	Panretinal	12	Final IOP: 20 mmHg	Nissen <i>et al</i> [44]
14	Krypton (550 nm)	400 - 500 mW	10 s	4 - 5 J	Not supplied	Contact through sclera: 1,2 to 3 mm posterior to limbus.	62	Final IOP: 20,9 mmHg after 6 months	Immonen <i>et al</i> [45]
15	Nd:YAG	Not supplied	Not supplied	6 - 7 J	Not supplied	Contact through sclera: 0,5 to 1 mm posterior to limbus.	16 cadavers	Not supplied	Fankhauser <i>et al</i> [46]
16	He-Ne	20 mW	10 ms - 20 ms	200 - 400 mJ	Not supplied	Contact through sclera: 0,5 to 1 mm posterior to limbus.	16 cadavers	Not supplied	Fankhauser <i>et al</i> [46]
17	Argon 488 nm 514 nm	500 mW	10 ms - 20 ms	5 - 10 J	Not supplied	Contact through sclera: 0,5 to 1 mm posterior to limbus.	16 cadavers	Not supplied	Fankhauser <i>et al</i> [46]

Item	Type of Laser (Unless otherwise noted)	Applied Optical Power	Application Time	Applied Energy	Application Diameter	Application Method	Number of Patients	Results	Reference
18	Diode 810 nm	1,75 - 2 W	2 s	3,5 - 4 J	600 Fm	Contact through sclera: 1,2 mm posterior to limbus.	21	Final IOP: 19 mmHg after 11 months.	Gaasterland <i>et al</i> [47]
19	Argon	500 - 700 mW	0,5 - 1 s	250 - 700 mJ	Not supplied	Vitrectomy and transvitreal endophotocoagulation.	16	Final IOP: 20 mmHg in 14 eyes after 6 months.	Patel <i>et al</i> [49]
20	Nd:YAG	5, 7, 9, 11 W	0,7 s	3,5; 4,9; 6,3; 7,7 J	700 Fm	Contact through sclera: 0,5 - 1,5 mm posterior to limbus.	27 cadavers	White lesions	Allingham <i>et al</i> [50]
21	Diode 810 nm	300 - 400 mW	0,5 s	150 - 200 mJ	700 Fm	Contact through sclera	5 rabbits	Damage to ciliary processes. Results unpredictable.	Peyman <i>et al</i> [51]
22	Diode 780 nm 830 nm	1,2 W	990 ms	1,2 J	100 Fm	Contact through sclera: 1 mm posterior to limbus.	14	Results inconsistent and also complications.	Hennis <i>et al</i> [52]

Item	Type of Laser (Unless otherwise noted)	Applied Optical Power	Application Time	Applied Energy	Application Diameter	Application Method	Number of Patients	Results	Reference
23	Nd:YAG	Not supplied	20 ms	3,4 - 8,6 J	Not supplied	Contact through sclera: 1 - 3 mm posterior to limbus.	35	Final IOP: 21,2 mmHg Multiple treatments needed.	Wright <i>et al</i> [53]
24	Diode 780 nm 830 nm	1,2 W	0,7 - 1 s	0,7 - 1,2 J	100, 200, 500 Fm	Contact through sclera: 0,5 mm posterior to limbus.	4 cadaver eyes	Blanching, shrinkage and pigment dispersion	Hennis <i>et al</i> [54]
25	Argon	1 W	1 s	1 J	Not supplied	Contact through sclera.	1 cadaver eye	Lesion with increased pigmentation.	Federman <i>et al</i> [55]
26	Diode 810 nm	1,5 W	1,5 s	2,25 J	Not supplied	Contact through sclera.	210	Final IOP: 20,1 mmHg Multiple treatments needed.	Bloom <i>et al</i> [56]

Item	Type of Laser (Unless otherwise noted)	Applied Optical Power	Application Time	Applied Energy	Application Diameter	Application Method	Number of Patients	Results	Reference
27	Diode 810 nm	2 W	2 s	4 J	600 Fm	Contact through sclera: 1,2 mm posterior to limbus.	58	Final IOP: 16,7 mmHg	Spencer <i>et al</i> [57]
28	Diode 810 nm	1,8 - 2 W	0,3 - 0,5 s	540 mJ - 1 J	740 Fm	Contact through sclera: 1,5 mm posterior to limbus.	33 (Asian)	Final IOP: 22 mmHg No vision preservation	Wong <i>et al</i> [58]
29	Diode	2 W	2 s	4 J	Not supplied	Contact through sclera.	1	Malignant glaucoma	Azuara-Blanco <i>et al</i> [59]
30	Bulb	15 W	8 - 10 s	120 - 150 J	350 Fm - 2 mm	Contact through sclera.	Porcine eyes	Bleaching	Preußner <i>et al</i> [60]
31	Nd:YAG	Not supplied	Not supplied	4,8 mJ, 5,03 mJ	Not supplied	Contact through sclera.	1	Scleral thinning	Fiore <i>et al</i> [61]
32	Nd:YAG	4 W	0,5 s	2 J	Not supplied	Contact through sclera: 1,5 mm posterior to limbus.	23	Final IOP: 25 mmHg	Brancato <i>et al</i> [69]

Item	Type of Laser (Unless otherwise noted)	Applied Optical Power	Application Time	Applied Energy	Application Diameter	Application Method	Number of Patients	Results	Reference
33	Nd:YAG	Not supplied	20 ms	0,5 - 2,75 J	Not supplied	Non-contact through sclera, 3 mm posterior to limbus	32	Final IOP: 21 mmHg	Schwartz <i>et al</i> [70]
34	Nd:YAG	Not supplied	20 ms	1,8 - 3 J	Not supplied	Non-contact through sclera, 2 - 3 mm posterior to limbus	40	Final IOP: 21 mmHg	Devenyi RG <i>et al</i> [71]
35	Nd:YAG	Not supplied	20 ms	3,5 - 4,5 J	Not supplied	Non-contact through sclera, 2 - 3 mm posterior to limbus	32	Final IOP: 22 mmHg	Klapper <i>et al</i> [72]
36	Diode	1,5 - 2 W	2 s	3 - 4 J	Not supplied	Contact through sclera.	11 (eyes)	Final IOP: 14.5 mmHg after 52 weeks.	Han <i>et al</i> [79]
37	Diode	Not supplied	Not supplied	Not supplied	Not supplied	Through sclera	21 (eyes)	Final IOP: 13,6 mmHg after 26,9 months	Semchyshyn <i>et al</i> [80]

Item	Type of Laser (Unless otherwise noted)	Applied Optical Power	Application Time	Applied Energy	Application Diameter	Application Method	Number of Patients	Results	Reference
38	Diode	1,5 W	1,5 s	2,25 J	Not supplied	Through sclera	28 (eyes)	Final IOP: 15 mmHg after 6 months.	Shah <i>et al</i> [81]
39	Diode	Not supplied	Not supplied	Not supplied	Not supplied	Through sclera	30	Final IOP: 20,8 mmHg after 1 year. Medications decreased from 2 to 1,8	Hawkins <i>et al</i> [82]
40	Diode	1,25 - 1,5 W	1,5 - 2,5s	2,25 - 3,125 J	Not supplied	Through sclera	92 (eyes)	Final IOP: 22 mmHg in 48% of eyes after 13,2 months.	Egbert <i>et al</i> [83]
41	Diode	Not supplied	Not supplied	Not supplied	Not supplied	Through sclera	20 (22 eyes)	IOP controlled in 77,3% of all patients after 12 months.	Schlote <i>et al</i> [84]

Item	Type of Laser (Unless otherwise noted)	Applied Optical Power	Application Time	Applied Energy	Application Diameter	Application Method	Number of Patients	Results	Reference
42	Diode	Not supplied	Not supplied	Not supplied	Not supplied	Through sclera	30	Final IOP: 26 mmHg after 6 months. Pain relief was also successfully provided in hypertensive glaucomatous eyes.	Martin <i>et al</i> [85]
43	Krypton	300 - 500 W (Note 1)	10 s	3 - 5 kJ	Not supplied	Contact through sclera	22 (27 eyes)	Final IOP: 22,6 mmHg after 2 years.	Raivio <i>et al</i> [86]

Note 1 (from Item 43): It is clear that this level of optical power is dangerously high, especially at an application time of 10 seconds. The author was contacted (via e-mail) and asked for comment but no reply was received. (I suspect that the optical power should have been printed as 300 - 500 mW.)

GLOSSARY OF TERMS

Ablation	Removal of a part, pathway, or function .
Aphakic	An eye from which the crystalline lens has been removed.
Atrophy	A decrease in size of an organ or tissue.
Beta blockers	Eye drops which help to decrease the flow of aqueous humor into the eye.
Bleaching	Whitening of tissue by means of the application of energy.
Coagulate	To solidify; to change from a fluid state to a semisolid mass.
Congenital	Present at birth.
Cryotherapy	The therapeutic use of cold.
Cyclophotocoagulation	Alteration of proteins in ciliary body tissue by means of the use of light energy in the form of ordinary light rays or a laser beam.
Disruption	Separate forcibly; interrupt flow of continuity.
Dysfunction	Abnormal, inadequate or impaired action of an organ or part.
Hyperopic/hyperopes	Far-sightedness (incoming collimated light rays focus behind the retina and not exactly on the retina)
<i>In vitro</i>	An <i>in vitro</i> test is done in the laboratory, usually involving isolated tissue, organ or cell preparations.
<i>In vivo</i>	An <i>in vivo</i> test is one performed on a living organism.

Miotics	Eye drops which help to increase the flow of aqueous humor out of the eye.
Myopic/myopes	Nearsightedness (incoming collimated light rays focus in front of the retina and not exactly on the retina)
Necrosis	The death of areas of tissue or bone, surrounded by healthy parts.
Neuropathy	Any disease of the nerves.
Neutral density filter	These are filters which have a very flat wavelength response and are used to attenuate light in a calibrated, chromatically invariant fashion.
Nystagmus	Constant, involuntary, cyclical movement of the eyeball.
Permeability	The capability of allowing the passage of fluids or substances in solution.
Photocoagulation	Alteration of proteins in tissue by the use of light energy in the form of ordinary light rays or a laser beam.
Pop	When optical energy is applied to tissue, the tissue will eventually evaporate, causing an audible ‘pop’ noise which is known as the ‘pop’ effect.
Predispose	The potential to develop a certain disease or condition in the presence of specific environmental stimuli.
Stroma	Foundation-supporting tissues of an organ.
Trabeculoplasty	Laser energy is directed towards the trabecular meshwork. Energy is applied in an effort to open closed drain channels.
Transmission	Radiometric term which describes a <i>process</i> .

Transmissivity	Radiometric term which describes a property of a <i>generic material</i> .
Transmittance	Radiometric term which describes a property of a <i>specific sample</i> .
Uveitis	A term referring to the inflammation of the choroid, ciliary body and/or iris.
Wide-band light source	These are multichromatic light sources. Although they transmit light consisting of multiple wavelengths, spectral transmittance may not be flat.

APPENDIX C

SAMPLE DETAIL AND HISTORY

Sample Number	Date Received	Age	Gender	Race
1A and 1B		43		Unknown
2A and 2B	05/2000	28	Male	White
3A and 3B	15/06/2000	49	Male	White
4A and 4B	21/07/2000	26	Male	White
5A and 5B	21/07/2000	2	Male	White
6A and 6B	27/07/2000	40	Male	Black
7A and 7B	27/07/2000	38	Male	White
8A and 8B	09/09/2000	51	Male	White
9A and 9B	09/09/2000	63	Male	White
10A and 10B	09/09/2000	30	Male	Black
11A and 11B	08/08/2001	23	Female	Unknown
12A and 12B	08/08/2001	20	Male	Unknown
13A and 13B	08/08/2001	23	Male	Unknown
14A and 14B	08/08/2001	24	Male	Unknown
15A and 15B	10/10/2001	20	Female	Unknown

APPENDIX D

National Health Laboratory Service Reports