BIOCOMPTABILITY STUDY
OF AN ARTIFICIAL SWITCHABLE IRIS

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Abstract

English
This dissertation presents the progress towards an active contact lens with integrated liquid crystal cell, with a focus on the biocompatibility of the lens. Firstly the dimensions of the lens are examined to increase comfort of the patient. The results show that the lens bearing must be on the sclera and therefore a diameter of 15.6mm is suggested, based on the Jupiter design.

Secondly, cellulose tricacetate, is proposed as alternative material for PET. Several parameters, which determine the biocompatibility are defined and tested on this material. We can conclude that the most important parameter is the oxygen permeability.

The outcome of the tests says that, even though cellulose triacetate, has not yet been used as substrate material, it possesses significant positive qualities for lens design compared to PET, such as a higher oxygen permeability, but also a high optical quality, and wettability, and a certain stiffness as well as a sufficient flexibility.

However, there must be searched for materials with a higher oxygen permeability and also the effect of the LCD on the latter parameter must be investigated. Although the material may not be the ideal answer, it is a positive progress towards the realization of biocompatible LCD integrated contact lenses.

Nederlands
Tijdens dit onderzoek is er gepoogd een antwoord te vinden voor de biocompatibiliteit van een actieve lens met geïntegreerde vloeibare kristallen. Allereerst worden de afmetingen en vormgeving van de lens bepaald om het comfort van de patient te verhogen. Uit de resultaten is gebleken dat voor een verhoogd comfort de lens op de sclera moet rusten en dus bij voorkeur een diameter van 15.6 mm bevat, gebaseerd op het Jupiter ontwerp.

Verder, wordt cellulose triacetaat naar voor geschoven als alternatief voor PET. De parameters, die de biocompatibiliteit van de lens bepalen werden vastgelegd en getest op dit materiaal. Geconcludeerd kan worden dat de belangrijkste parameter voor een contact lens de zuurstofdoorlatbaarheid is.

Deze testen wijzen uit dat, hoewel cellulose triacetaat voorafgaand nooit als substraat materiaal is gebruikt, het materiaal wel degelijk goede contactlens eigenschappen bevat vergeleken met PET, zoals een hogere zuurstofdoorlatbaarheid, maar ook een goede optische kwaliteit, een hydrofiel gedrag en een prima evenwicht tussen sterkte en flexibiliteit.

Echter dient er gezocht te worden naar materialen met een hogere zuurstofdoorlatbaarheid en het effect van de vloeibare kristallen op deze parameter. Alhoewel cellulose triacetaat misschien niet het ideale antwoord is op de onderzoeks vraag, bracht het ons toch dichter bij de realisatie van biocompatible LCD geïntegreerde contactlenzen.
Dans cette étude, on a tenté de trouver une réponse à la biocompatibilité d’une lentille active avec des cristaux liquides intégrés. Tout d’abord, les dimensions et conception de la lentille est déterminée afin d’augmenter le confort du patient. Les résultats ont montrés que pour atteindre un confort élevé, la lentille doit être mise sur la sclère et qui de préférence doit avoir un diamètre de 15,6 mm, basé sur le concept de Jupiter.

En outre, triacétate de cellulose est présenté comme une alternative au PET. Les paramètres qui déterminent la biocompatibilité de la lentille ont été enregistrés et testés sur ce matériel. On peut conclure que le paramètre le plus important pour une lentille de contact est la perméabilité à l’oxygène.

Bien que triacétate de cellulose n’a jamais été utilisée en tant que matériau de la lentille, ces tests démontrent que le matériel contient en effet des bonnes capacités de lentille de contact comme une perméabilité à l’oxygène acceptable. Mais aussi une bonne qualité optique, un comportement hyrodfile et un bon équilibre entre la force et la flexibilité.

Cependant, la recherche des matériaux ayant une perméabilité à l’oxygène plus élevée, est nécessaire ainsi que la recherche sur l’effet du display sur ce paramètre.

Bien que triacétate de cellulose n’est peut être pas la réponse idéale à la question de recherche, on se retrouve quand même plus proche de la réalisation des matériaux de lentille biocompatible pour des lentilles de contact intégrée au ACL.

Key words
Contact lens - Iris - LCD - Biocompatibility - Lens Design
Preface

This dissertation forms the capstone within the master of biomedical engineer, a study with a wide range of technical, functional and medical disciplines, at the Universities of Ghent (UGent) and Brussels (VUB). It is written under the teaching supervision of Professor Herbert De Smet and Jelle De Smet.

The intent of the thesis is to study the implementation of an artificial switchable iris and its biocompatibility. An alternative material for polyethylene theraphthalate is suggested. The diagram presented at page 2 resembles a short overview of the content of this research.

The result is the product of an intensive but instructive process about the challenges within engineering and medicine, a field that in the future will only grow in attention.

This thesis would not have been made without the help and support of many. I would like to extend my sincere gratitude to all those who made it possible

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Contents

List of Figures .......................................................... xi
List of Tables ............................................................ xiii
Introduction ............................................................... xiv
Thesis Outline ............................................................. 2

1 The Human Eye ......................................................... 3
   1.1 Anatomy and Physiology of the Human Eye ......................... 5
   1.2 Dimensions and Shape of the Human Eye .......................... 9
   1.3 Eye diseases .......................................................... 10
   1.4 Treatment ............................................................ 11
   1.5 Conclusion ........................................................... 12

2 Contact lenses .......................................................... 13
   2.1 History ............................................................... 15
   2.2 Material Properties ............................................... 18
      2.2.1 Oxygen Permeability ......................................... 18
      2.2.2 Water content ................................................ 20
      2.2.3 Wettability .................................................... 20
      2.2.4 Attraction of Proteins and lipids ........................... 22
      2.2.5 Refractive Power ............................................. 23
      2.2.6 Mechanical Properties ..................................... 24
   2.3 Relationships between Material Properties ...................... 27
      2.3.1 Dk vs. Young’s Modulus .................................... 27
CONTENTS

4.2.4 Water Vapor Transmission ........................................ 67
4.2.5 Wettability ..................................................... 71
4.2.6 Water Content .................................................. 74
4.2.7 Color and light transmittance ................................... 76
4.2.8 Mechanical Properties .......................................... 77
4.3 Fabrication process with TAC ...................................... 80
4.4 Conclusion ......................................................... 81

5 Conclusion/Discussion ................................................ 83
# List of Figures

1.1 The human eye and its composition ............................................... 5  
1.2 Delation and constriction of the iris (based on (3)) .......................... 7  
1.3 Dimensions of the anterior ocular surface .................................... 8  
1.4 Dimensions of the human eye (based on (5)) .................................. 8  
1.5 Limbal and scleral shape profile (based on (7)) ............................... 9  
1.6 Disorders of the eye surface ....................................................... 10  
1.7 Different solutions for iris damage .............................................. 11  
2.1 The lens surface exists of hydrophobic (yellow) and hydrophilic (blue) groups. A moist environment will attract the hydrophilic groups (based on (19)) ................................................................. 21  
2.2 Wetting angles for various wetting properties .................................. 21  
2.3 Papillary conjunctivitis ............................................................... 22  
2.4 A. Single refraction; B. Double refraction ...................................... 23  
2.5 A. a true elastic material; B. a visco-elastic material; C. a strong and brittle material; D. A strong and tough material (based on (29)) .......... 25  
2.6 Correlation between Young’s modulus and oxygen permeability measured for A. hydrogel lenses; B. rigid gas permeable lenses (based on (31) and (32)) ................................................................. 27  
2.7 Relationship between oxygen permeability and water content for hydrogel lenses at 35°C (based on (14)) ......................................................... 28  
2.8 Relationship between oxygen permeability and water vapor transmission for polyethylene films (based on (33)) ........................................... 29  
2.9 Relationship between oxygen permeability and water vapor transmission for different CA compositions (based on (55)) .......................... 30
LIST OF FIGURES

2.10 Chemical structure of conventional hydrogel monomers (based on (36)) . . 35
2.11 Chemical structure of rigid lens materials (based on (38)) . . . . . . . . . 36

3.1 Composition of the artificial iris (based on (42)) . . . . . . . . . . . . . . 45
3.2 Step 1-5 activation of the liquid crystals with increasing light intensity . . 46
3.3 A. helical structure of a liquid crystal molecule; B. deactivated condition of
the crystals; C. activated condition of the crystals (based on (45)) . . . . . 47
3.4 A. deactivated condition of the crystals in the contact lens; B. activated
condition of the crystals in the contact lens (based on (44)) . . . . . . . . 48
3.5 Steps within the fabrication process of the LCD in PET (based on (2)) . . 49
3.6 Proposed fabrication method: late cutting the lens by use of buttons . . . 50
3.7 Dimensions of a scleral lens design with 5 curves (based on (37)) . . . . 52
3.8 artificial iris design with central opening: A. no activation; B. activation
of one ring; C. activation of a couple rings; D. activation of all rings (based
on (46)) . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . 53

4.1 Polyethylene theraphthalate . . . . . . . . . . . . . . . . . . . . . . . . . 57
4.2 Cellulose triacetate . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . 58
4.3 Thermogravimetric analyzer . . . . . . . . . . . . . . . . . . . . . . . . . 60
4.4 TGA degradation of PET and TAC . . . . . . . . . . . . . . . . . . . . . 62
4.5 TGA degradation of PET and TAC . . . . . . . . . . . . . . . . . . . . . 63
4.6 DSC curves of PET and TAC . . . . . . . . . . . . . . . . . . . . . . . . . 65
4.7 Principle of OTR test . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . 66
4.8 Principle of WVTR test . . . . . . . . . . . . . . . . . . . . . . . . . . . . . 67
4.9 WVTR curve of PET without pedot and SiO\textsubscript{2} layers at 23°C . . . 69
4.10 WVTR curve of PET without pedot and SiO\textsubscript{2} layers at 38°C . . . . 69
4.11 WVTR curve of PET with pedot and SiO\textsubscript{2} layers . . . . . . . . . . 70
4.12 WVTR curve of TAC with pedot and SiO\textsubscript{2} layers . . . . . . . . . 70
4.13 Schematic of a drop on a non-wetting solid material. . . . . . . . . . . . . 72
4.14 OCA 20 video based optical contact angle measurement system . . . . . 72
4.15 SCA measurements . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . 73
LIST OF FIGURES

4.16 SCA measurements of TAC before and after 30 seconds. 74
4.17 water content of PET and TAC measured every 10min. 75
4.18 Principle of the spectrophotometer 76
4.19 UV-curves of PET and TAC 77
4.20 Components of the universal testing machine 77
4.21 typical stress-strain curve for polymers (based on (59)) 78
4.22 Dimensions of the samples 79
4.23 Stress-strain curve of PET and TAC 79
4.24 A. TAC-film before thermal treatment; B. TAC-film after thermal treat-
ment 80
4.25 TAC-film molded at 125°C; A. deformations at the edge; B. deformations
at the center 81
LIST OF FIGURES
## List of Tables

2.1 Refractive indices of various materials (birefrigent material) . . . . . . 24
2.2 Young’s Modulus of various general materials . . . . . . . . . . . . . . . . 26
2.3 Overview lens types . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . 32
2.4 Classification soft lenses . . . . . . . . . . . . . . . . . . . . . . . . . . . 34
2.5 Overview characteristics of every lens material . . . . . . . . . . . . . . . 38
2.6 Group suffix . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . 39
2.7 Code for various Dk values . . . . . . . . . . . . . . . . . . . . . . . . . . 40
3.1 Jupiter scleral lens design in multiple overall diameters [mm] . . . . . . 51
3.2 Minimum thicknesses for different materials [mm] . . . . . . . . . . . . 52
4.1 Weight of samples before test . . . . . . . . . . . . . . . . . . . . . . . . . 74
Introduction

The human eye is a powerful object, and can take on different tasks at the same time. It enables people to distinguish millions of colors and shapes, adjusts easily to shifting light conditions, transmits information to the grey mass at a rate, technology hasn’t been able to peer with. As science never stops, nor is satisfied and always wants to improve, it mostly aims to be as efficient as nature’s creations or even wants to surpass nature’s creations. And thus scientists also challenge to mimic the working of the human eye on several levels. Until now, people seeing the world with data superimposed on their visual field was only limited to the science fiction movies like the Terminator. In stories by the science fiction author Vernor Vinge, characters rely on electronic contact lenses, rather than smartphones or brain implants as in reality, for wireless access information, which appears right before their eyes. These fantasies might seem far-fetched, but scientists aspire to make this fantasy come true (1).

Today, a prototype contact lens with simple built-in electronics is already within reach. The Center for Microsystems (Cmst) in Ghent developed a lens embedding a liquid crystal display (LCD) with basic patterns and limited pixels. The lens can be used for multiple purposes, for example to mimic the iris. In this case the lens turns darker as the light intention increases, and thus controlling light transmission through the eye.

Four fundamental challenges stand in the way in building an electronic switchable iris. As flexible LCDs are not designed to be transformed into spherical shapes, the first challenge is to create a very thin, spherically curved substrate with active layers. "By using new kinds of conductive polymers and integrating them into a smooth spherical cell", as J. De Smet quoted, the first challenge is already fulfilled (2). Secondly, the display must be powered autonomously and adapt to the conditions of the moment. That leads to the third challenge, which is that the lens should be photosensitive. The liquid crystals activate when the light intensity increases. Finally, the whole system needs to be completely safe and comfortable for the eye. So before a LCD can go into the eye, it must be embedded in a biocompatible substance, that doesn’t cause damage to the eye nor to the LCD. It must also have the right dimensions to be comfortable to wear for the patient.

This dissertation studies the latter challenge, the implementation and biocompatibility of the artificial switchable iris. It discusses the material use and the challenges ahead. Its goal is to find answers to the following questions.

- How can the contact lens be poured into the correct form? What is the correct implementation? What are the design parameters of the lens?
- How can the lens be made biocompatible with the eye? What are the requirements to be in contact with the eye without eye or lens damage? How can we reach the highest comfort for the patient?
Chapter I is an introduction to the anatomy, physiology and dimensions of the human eye. The goal is to make the reader familiar with the medical terms before moving on to the quest for answers. Chapter II gives an overview of the contact lens types, their history and their material use. Also the properties of an ideal lens are mentioned. The latter is important knowledge before designing a lens and selecting the proper lens material. Chapter III discusses the proper implementation of the artificial iris. It reasons about the composition of the lens, the measurements and the developing process. Finally chapter IV reviews the laboratory work. It deals with the materials that are selected and tested, explains the different tests that are performed and eventually discusses the results. Every chapter is followed by a small conclusion to keep the overview over the thesis. Likewise there is a thesis outline inserted for a clear view on the content of this research.

Finally, I would like to inform that the figures used in this paper are based on already existing figures and the units, used over the research, are based on the SI system.
LIST OF TABLES
Chapter 1

The Human Eye
1.1 Anatomy and Physiology of the Human Eye

The human eye is one of nature’s remarkable creations. We use our eyes in almost every activity we perform, whether reading, working, cooking, opening a door, writing a letter, driving a car, or in countless other ways. Most people probably would agree that sight is the sense they most value. The eye allows us to see and interpret the shapes, colors, and dimensions of objects in the world by processing the light they reflect or emit. It accommodates to changing lighting conditions and focuses light rays originating from various distances from the eye (3).

As light waves enter the pupil and cross the lens, they are focused on the back of the eyeball. Subsequently the light is converted into impulses by the photoreceptors and conveyed to the brain where an image is perceived. Figure 1.1 pictures the composition of the human eye(4).

![Figure 1.1: The human eye and its composition](image)

**Cornea**

The front of the eye is protected by a transparent layer, the cornea. It is also the primary structure that helps to focus the incoming light, the secondary structure is the lens. The cornea is transparent due to the fact that it contains hardly any cells and no blood vessels. This avascular property of the cornea obstructs the adequate blood flow to supply the eye of enough oxygen, or to remove enough carbon dioxide. Therefore, the cornea relies on its exposure to the air for aid and has an oxygen consumption of about 1-10 ml/h/cm$^2$ (37). There is a constant presence of tension, which is the driving force to move oxygen into the cornea. The oxygen tension has a value of 155mmHg at sea level when the eye is open. Further, the cornea has the highest concentration of nerve fibers of all body structures, about 70 to 80 sensory nerves (37). In other words, the
cornea is the most sensitive part of the human body.

Sclera
At the boarders of the iris, the cornea continuously proceeds into the sclera, which is the white, opaque portion of the eye. The transition zone between the sclera and the cornea is called the limbus. The sclera contains collagen and elastic fibers and provides protection and serves as an attachment for the extra-ocular muscles, which move the eye. The nerves in the sclera are less sensitive than in the corneal part of the eye. This is because the nerves are less diffusive and isolated while passing the scleral layer and thus less delicate. The sclera is covered with a mucous membrane, the conjunctiva, consisting of loose connective transparent tissue. It is loose to allow free and independent movement of the globe. As the conjunctiva is not a real structure, it follows the scleral shape, the surface will later on be referred to as the scleral surface.

Choroid
The choroid is the second layer around the eye and lies between the sclera and the retina. It consists of blood vessels, which supply the retina with nutrients. Furthermore, this layer is dark colored, so it can also absorb light that isn’t absorbed by the retina to minimize the amount of light, bouncing around the eye.

Retina
The retina is the inner layer of the eye and is composed of nerve tissue. The layer contains light receptors, which receive, absorb and process the incoming light and eventually send it through the optic nerve to the brain. At a given point, the optic nerves have to enter the retina in order to enable the connection with the brain. This spot is called the optic disc. It is a blind spot that is not sensitive to light due to the absence of photoreceptor cells.

Macula
There is a small sensitive area within the retina on the back of the eyeball, called the macula. The latter controls the central vision and has a central spot, a small yellowish mass, that provides the clearest vision. When looking directly at an object, it will form an image on the macula.

Iris
The colored disc we see is called the iris. It is a thin diaphragm, containing mostly connective tissue and smooth muscle fibers. Its function is to control the amount of incoming light. When the light intensity is high, the iris contracts to reduce the amount of light entering the eye. Conversely, it expands its opening, also called the pupil, when the light intensity decreases. Figure 1.6 represents the principle of the iris.
1.1. ANATOMY AND PHYSIOLOGY OF THE HUMAN EYE

Figure 1.2: Delation and constriction of the iris (based on (3))

The Lens
The lens is located directly behind the iris. While light travels through the lens, it is focused on the retina. The lens itself is a membrane-like elastic structure that is under constant tension. When looking at a close object, more tension will be released, and thus the lens surface becomes more convex (a rounder or more global configuration) in order to focus better at a near distance. This adjustment in lens shape, to focus at various distances, is referred to as the accommodative process and is associated with a concurrent constriction (decrease in size) of the pupil.

Vitreous Humour
80 Percent of the eye volume consists of a clear gel, called the vitreous humour. It fills the inside chamber of the eyeball and is transparent and colorless. Its main function is to help keep the retina in place.

Tear Fluid
The surface of the eye is coated with a layer of tear. It keeps the surface moist, removes foreign bodies, provides bacterial action as protection and acts as a lubricant for eyes and lids on blinking. The tear fluid consists of water, enzymes, proteins, lipid sodium, calcium and biocarbonates.

Eyelid
The eyelids most important role is to protect the eyeball and to spread the tear fluid even over the corneal surface. By blinking it pumps vital tear lipids in the lids, it mixes, distributes, and drains tear fluid and it spreads the tear film over the corneal surface. Thus the blinking action is vital for a stable tear film, if this was absent or improper, it would result in dry eyes. Between blinks, the tear film thins via evaporation and exits into the fornices. Blink is a frequent event in the normal eye, occurring 6 times per minute, 8000 to 9000 times per day or 3 million-plus times per year.
CHAPTER 1. THE HUMAN EYE

Figure 1.3: Dimensions of the anterior ocular surface

Figure 1.4: Dimensions of the human eye (based on (5))
1.2 Dimensions and Shape of the Human Eye

Figure 1.4 sums up the different measurements and parameters of the eye. The refractive index is represented as n. The latter is explained in section 2.2.5 on page 23.

The book 'A guide to scleral fitting' by Eef van der Worp (7) looks at the anterior ocular surface. Figure 1.3 shows that the free space on the scleral surface is disrupted by the insertion of the eye muscle. It appears that in the temporal, superior and inferior direction there is roughly 7 mm of space between the limbus and the insertion of the eye muscle. However, on the nasal side there is only 5 mm of space. With an average corneal diameter of 11.8 mm, it means that horizontally, 22.00 to 24.00 mm is the maximum physical diameter for a contact lens before it may interfere with the location of the eye muscle insertion, assuming the lens does not move.

Finally, the human eye is not shaped like a perfect sphere, especially the limbal zone deviates from this hypothesis. Eef van der Worp (7) provides excellent graphs visualizing the curving of the eyeball surface. The figure represents the limbal and scleral shape profile. The limbal shape is an important parameter for the fitting of lenses. Note on figure 1.5 that the cornea is steeper than the sclera. The limbal zone is rather straight (tangential) before getting steeper again. Within the limbal zone the angle difference is 1.8°, which is almost flat in comparison with the sclera. In the scleral zone the angle difference is larger, approximately up to 6.6°.

![Figure 1.5: Limbal and scleral shape profile (based on (7))](image-url)
1.3 Eye diseases

Different diseases or incidents on the surface of the eye can damage or distort vision. There can be disorders of the conjunctiva, the lens, the sclera, the cornea or the iris. One of the most common eye diseases is cataract, a disorder of the lens, it becomes clouded and thus decreases the vision. Another common disease is conjunctivitis or also called pink eye. It occurs on the top most layer of the eye. Conjunctivitis is caused by a viral or bacterial infection and results in redness and itch. Other possible disorders are keratoconus, a degenerative disorder where the cornea undergoes structural changes, and scleritis, an inflammation of the sclera. One can elaborate on the existing eye diseases, only there are so many of them that this thesis will focus on the disorders of the iris.

The iris can be damaged by a genetic disease. Persons who suffer of aniridia have a damaged or absent iris (8). As already mentioned, the iris controls the amount of incoming light. Therefore persons with aniridia are very photosensitive. As the iris also helps with focusing the view, these people have additional problems with creating a clear view. This disease is mostly associated with keratoconus, which results in a very irregular surface of the cornea. Likewise there is an increased sensitivity of the cornea. For these reasons aniridia patients have difficulties wearing contact lenses on the cornea.

Another genetic disease that affects the iris is coloboma. A coloboma is a hole in one of the structures of the eye, such as the iris. The effects a coloboma has on the vision can be mild or more severe depending on the size and location of the gap, but are always associated with photosensitivity and glare.

Also albinism can cause visible problems. In this case the pigment is absent, which makes the iris transparent and thus ineffective in filtering the incoming light. Like persons with aniridia or coloboma, also albinism patients suffer of photosensitivity and glare.

However, not only genetic diseases but also incidents during life can cause a damaged iris. For example, if a tumor is formed close to or in the surface of the iris. The only solution is to remove the tumor and thus a part of the iris, causing a hole in the diaphragm. Next to this the patient can have a trauma, which affects the iris.

Figure 1.6: Disorders of the eye surface
1.4 Treatment

Nowadays there are only passive solutions for a damaged iris. There is the permanent solution, which contains the implantation of a colored disc, designed according to the dimensions of the other normal iris. Such a prosthetic iris must be placed during surgery, which includes health risks. Another disadvantage is the high costs, as the surgery and implant are non-refundable. Alternatively, the patient can choose for the temporary solution, wearing contact lenses with a print. The latter is mostly used for patients with a trauma or a removed tumor. Unfortunately these contact lenses are easy to loose and practicing sports, like swimming, is not recommended.

The greatest disadvantage of both treatments is that they are static and do not adapt to the brightness level present at that moment. In low light conditions, little light waves are entering the eye, causing difficulties with vision. Conversely, when the light intensity is high in the room, still too much light waves are allowed to enter the human eye, leading to only a partial relief of photosensitivity and glare. The ideal treatment would be an implant that mimics the natural iris and adapts to the light intensity that is present in the room at that moment. Consequently we would have a total relief of photosensitivity and glare problems.

The Center for Microsystems (Cmst), a research center that encourages the co-operation between Imec and the University of Ghent, is investigating this active solution at the moment (2). The goal is to create a lens that becomes darker as the light intensity increases, controlling the light transmission through the eye and thus mimicking the principle of the natural iris. This is made possible by embedding a liquid crystal display (LCD) with a limited amount of pixels into a lens substrate. The result is a total relief of photosensitivity and glare problems, no health risks due to eye surgery, an increase of vision acuity and lower costs.

At the moment the design of the lens is not yet made biocompatible. There is need for further research towards the corresponding design with the human eye. The research should focus on the required dimensions, the composition, as well as the biocompatibility of the lens. The latter is important to prevent irritation or permanent damage that the lens might inflect on the eye.

Figure 1.7: Different solutions for iris damage
1.5 Conclusion

When designing a contact lens it is important to first study the human eye and its dimensions. Looking at the components of the eye we can conclude that the cornea and the sclera are the main structures for lens design. The cornea is much more sensitive than the sclera. Especially people with aniridia have a very sensitive and irregular cornea.

The iris is responsible for the amount of incoming light and helps to focus vision. When the iris is damaged the light transmission is uncontrolled, resulting in photosensitivity and glare.

The eye surface is covered with tear fluid, consisting of water, enzymes, proteins, lipid sodium, calcium and biocarbonates. This implies that the lens must be able to resist these components. While designing the lens, we must keep in mind that the eye is not a perfect sphere, but exists of several curves. The cornea is steeper than the sclera and the transition zone, called the limbus is more or less flat.

As the eye is depending on contact with the environment for oxygen exchange, the lens must be permeable for oxygen.

We can conclude that there are 2 major questions that must be answered before the switchable iris can be worn by the patient.

- What are the dimensions the lens should be having? What are the design parameters for a correct implementation?
- Is the lens biocompatible? Which parameters make the lens biocompatible with the human eye?

In the next chapters we will investigate these questions and try to answer them as accurate as possible.
Chapter 2

Contact lenses
2.1 History

The development of the contact lens was an interesting project during the past decades. The highlights are presented in the timeline on the preceding page. It is assumed that the history starts with the theories of Leonardo da Vinci around 1508 (9). He was the first person who illustrated the initial concept of the contact lens. Leonardo suggested to use a water-filled hemisphere to cover the eye, which was actually worn remarkably like a contact lens. He substituted the refractive power of the curved glass to improve the clarity of the image received by the retina. His ideas far exceeded the ability of the technology of his times to actually implement them. However he stated an important principle for contact lens design. He could eliminate the cornea as a refractive surface, substituting the refractive index of a curved, clear lens in its place, and positioning that lens directly on the eye.

Almost a century and a half later, in 1636, the philosopher-mathematician Renee Descartes suggested placing a lens directly upon the cornea and not including the sclera, which would be the most effective method as Leonardo suggested (9). By the use of a water-filled tube, with a lens placed on one end and on the other end the cornea edges of the eye, he demonstrated the cornea’s role in astigmatism (optical defect in which vision is blurred due to an irregular or toric curvature of the cornea or lens) and could neutralize the cornea.

The British astronomer Sir John Herschel conceptualizes in 1827 the practical lens design. He proposed taking an actual mold of the eye, by using a glass lens, and grinding the inside and outside curvature to conform as close as possible to the shape of the cornea of the patient and correct its irregularity. But it would last until 1884 to actually see the development of a real contact lens. As the technology of glass blowing, lens grinding and the development of anesthesia became accurate, it was possible to develop actual contact lenses by molding.

Around 1887-1888, two important scientists earned their place in the history of contact lenses (10). The first was Friedrich Muller, who was a German maker of artificial glass eyes. He designed a transparent glass blown lens for a patient to protect a diseased eye. This invention became used on regular base for many years. The second scientist worth mentioning is a Swiss physician, A.E. Fick. He used Muller’s lenses to manufacture the first glass lens to correct vision, which appeared to be the first true contact lens. He designed both scleral and corneal lenses. He experimented using casts of cadaver eyes and proposed that correct fitting was possible by using spherical shapes for both the cornea and sclera. He was also the first to use the ophthalmometer to fit contact lenses. Edouard Kalt, working in France during the same time, devoted most of his efforts in scleral lenses to fitting keratoconics, and established the principle of three point touch, which is a standard still used today by many contact lens fitters with keratoconus patients. Unfortunately, these lenses, progressed by these scientists were uncomfortable and thus most people still preferred the use of spectacles when it was
CHAPTER 2. CONTACT LENSES

possible. The lenses were only used in cases where the cornea needed protection from infections and encrustations of the eyelids.

By the beginning of the 20th century a plateau had been reached in the development of contact lenses (9). Researchers realized that glass was relatively heavy. Furthermore it was dangerous for the eye when it broke, and was impermeable for oxygen. Wearing these large, scleral lenses resulted in discomfort, irritation, swelling, infection or other damage. And thus, glass contact lenses were available but were used for a brief period and on a limited scale only for occasional therapeutic purposes. The development of contact lenses thus remained static at this point, waiting for supporting technology to catch up.

This catch up came around in the 1930s. In 1936 the Rohm and Hass company introduced transparent Methyl Metacrylate in the United States. William Feinbloom successfully used this plastic to construct contact lenses, making them lighter and more convenient (10). Istvan Gyorffy (1937) in Hungary began to use polymethyl methacrylate (PMMA) to make scleral lenses from moulds, taken of the human eye (11). The step from plastic scleral to plastic corneal lenses, a lens that only covers the cornea, was a short but difficult one and was accomplished by Kelvin Tuohy in 1947. The modern era of contact lenses had begun (10).

Tuohy and others tasked a lot of time and energy in investigating the design of corneal plastic contact lenses (11). The result was a small, light lens that conformed very closely to the shape of the central cornea. The PMMA or hard corneal contact lenses for correcting refractive errors became commercially available in the early 1950s. And for the next two decades, they were virtually the only type of lenses used. PMMA was called the first generation of modern contact lenses. However, PMMA is, like glass, not permeable for oxygen and thus the search for a better material continued.

Also worth mentioning is the accomplishment of Norman Bier. In 1945 the food and drug administration (FDA) granted him a patent for the fenestration of PMMA scleral lenses. This ventilates the cornea and creates an air bubble which moves on excursions of the eye (11). In this way the oxygen permeability problem was partly overcome.

Next in progression were the Czechoslovakian chemists Wichetrle and Lim, who in 1961 introduced the second generation of contact lenses, soft contact lenses, using a hydrophilic material, called hydrogel polymers (10). The basic hydrogel plastic is hydroxyethyl-methacrylate (HEMA), although new hydrogel materials and other soft-lens plastics have recently been developed. These plastics absorb water (as much as 85 to 90 percent by weight) and become soft and flexible in proportion to their absorbency. Due to this flexibility they were comfortable on the eye, but also difficult to handle. Furthermore they were of poor optical quality, and raised questions about the absorption of bacteria and proteins. Because of this they were not a practical alternative to hard lenses for a decade or more after their invention. It took several years to improve the material and lens design of soft lenses.
2.1. HISTORY

After a few years of experimentation and improvement, Wichterle granted to National Patent Development Corp. (NPD), a U.S. firm, exclusive Western Hemisphere, rights to the new hydrogel materials and to a new molding process, now called spin casting, for the fabrication of hydrogel contact lenses. NPD, in turn, licensed Bausch & Lomb Inc. to use these product and process patents. In 1971, after considerable improvement and careful testing, Bausch & Lomb obtained approval from the U.S. Food and Drug Administration to sell hydrogel lenses in the United States. After several years, other firms began to obtain similar approvals for their hydrogel lenses, and many firms are now on the market.

The decade of the 1970s thus marked the introduction, acceptance, and ultimate dominance of soft lenses over the older PMMA hard lenses. But as the decade ended a new type of lens, formulated as the third generation, was introduced. This lens was the first gas-permeable hard lens, made of either cellulose acetate butyrate (CAB), PMMA-silicone combinations, or pure silicone (13). These lenses allow oxygen to reach the cornea through the lens as soft lenses do, while also offering the optical clarity and ease of handling of hard lenses. In 1978, the first gas-permeable hard lenses were approved for use in the United States, and recently, other designs followed.

In 1979 the Polycon lens was launched by Syntex Ophthalmics (13). Irving Fatt, an American chemist, who worked with Wichterle, moved to London, got U.S. FDA approval of a PMMA-silicone copolymer lens and made this gas-permeable contact lens material widely available. He also carried out some groundbreaking studies into oxygen tension and permeability, for example he introduced the Dk-system for measuring the oxygen permeability (see 2.2.1 on page 18).

During the next 20 years the focus was set on improving the materials and their use. overnight wear of gas permeable contact lenses; daily and monthly disposable soft contact lenses became available.

The most recent development in the history of contact lenses is the introduction of silicone hydrogels for soft contacts in 2002. By using this new material, ophthalmologists are able to reach much higher oxygen permeability than had been possible until this moment. Finally 3 years ago (2010) the material was available for widespread use.

Nowadays a wide range of precision-made, carefully fitted, and extensively used contact lenses represents the contributions of a large number of scientific areas and industrial sectors which played key roles. These include: physics, biology, and chemistry and their continually expanding theoretical and empirical foundations; precision glassmaking, which made possible early lenses of thin optical glass; the plastics industry, which has developed an expanded inventory of sophisticated polymer plastics that are the foundation of today's contact lenses; the precision machine tool industry, which has provided ultra-fine grinding, lathing, and molding machines for lens finishing; the optical instruments industry, for its provision of precise ophthalmic measurement and examination technology and eye-care practitioners and technical personnel, who have utilized the new technologies and encouraged their evolution.
2.2 Material Properties

It is essential to know all the required features the ideal lens must contain. Once all the necessary information is gathered, the selection of the material for the lens can begin. The following properties determine the lens and its biocompatibility:

- oxygen permeability
- water content
- wettability
- attraction of proteins and lipids
- refractive power
- mechanical properties

2.2.1 Oxygen Permeability

As mentioned in the first chapter, the cornea requires an aerobic metabolism for oxygen supply. Contact lens wear can obstruct this transport. As a result contact lens users will prefer a material with proven high oxygen performance.

The oxygen permeability of a material is referred to as the Dk-value (15) (16).

\[ P = D \times k \] (2.1)

With \( P \) as the permeability coefficient. \( D \) is the diffusion coefficient, a measure of how fast dissolved molecules of oxygen can move within the material. It is influenced by the flexibility of the polymer chain and the free volume within the polymer. \( k \) is a solubility coefficient and provides information about the amount of oxygen molecules dissolved in the material. It is influenced by the chemical interaction between polymer and oxygen molecules. A given definition for Dk (37)'The Dk is a rate of oxygen flow under specified conditions through a unit area of the contact lens material of a unit thickness when subjected to unit pressure differences'. Furthermore, the Dk is independent of the shape or thickness of the material. However, it varies with the temperature. With a higher temperature there is an increasing Dk-value.

Taking the thickness into account, the term oxygen transmissibility is used. The latter is a feature of a finished contact lens and defines the ability of the lens to allow oxygen to move from anterior to posterior surface within a certain thickness. As the thickness increases, the oxygen transmissibility decreases (14).
\[ P = \frac{D \times k}{t} \]  

For clinical situations it is more relevant to consider the amount of oxygen which actually reaches the cornea surface per unit time. Fick introduced a formula which defines the amount of oxygen that moves from the anterior to posterior surface, which can be rewritten (14).

\[ J = A \times \frac{D \times k}{t} \times (P_1 - P_2) \]  

or rewritten

\[ \frac{J}{A} = \frac{D \times k}{t} \times (P_1 - P_2) \]  

The flux decreases with the contact lens thickness and hydration. By using oxygen flux the difference in oxygen tension across the lens is taken into account. The oxygen tension difference is the driving force for oxygen transmission. Normally, the oxygen tension at the anterior side is constantly around 159 mmHg when the eye is open, and 59 mmHg in closed condition (14). At the posterior side the oxygen tension depends on the lens transmissibility. The greater the difference, the greater the driving force and thus the faster the oxygen transmission occurs. However, there is a maximum limit. When the oxygen tension on the anterior side is equal to the tension at the posterior side there is no longer any driving force present. But the tension is difficult to measure. So Brennan proposed a parameter, the equivalent oxygen percentage (EOP), which provides an indirect measure of the oxygen tension beneath the contact lens (14).

There are three parameters that will influence the oxygen performance. The first parameter is the material chemistry. A tight and close packaging doesn’t allow oxygen transmission. The less tight the arrangement of polymer chains is, the higher the rate of oxygen diffusion.

Another parameter that will result in a better oxygen performance is an increased water content (specific for soft lenses). The water content acts as a plasticizer that permits greater flexibility to the polymer chain, which encourages the diffusion (more at 2.2.2 on page 20).

Finally, the thickness will affect the oxygen performance. An increasing thickness of the lens results in a decreasing transmissibility. Thus the lens must be as thin as possible. However if the lens is too thin it can suffer from deformation, it can be too fragile to handle, and it can have a diminished structural integrity, which results in a greater tendency to tear. It also leads to dehydratation, which can lead to corneal staining, and wrinkling behavior.
2.2.2 Water content

Water content refers to the amount of water held by the contact lens and is specific for hydrogel lenses. This is caused by the fact that the polymer network in a hydrogel contains hydrophilic groups. It swells in water, which causes it to become soft and to take on elastic properties, i.e. the water acts as a plasticizer. The polymers are cross-linked, forming chemical bridges that link one chain to another, in order to give them increased physical stability. In addition to cross-links, chains are also connected to each other and the polymer chains intermingle randomly, like individual strands being rolled up together (17).

The material will always reach an equilibrium, commonly termed as the equilibrium water content (EWC) of a hydrogel and is defined as:

\[
EWC = \frac{\text{weight of water in polymer}}{\text{total weight of hydrated polymer}} \times 100\% \quad (2.5)
\]

The EWC of a hydrogel may vary with temperature and pH.

The water content of hydrogels ranges from a low content of 24% to a high content of 80%. A greater water content gives rise to a higher oxygen permeability. However a large water content also leads to a lower refractive index. The latter is explained into more detail in 2.2.5 on page 23. Another disadvantage is the risk of dry eyes for the patient. As contact lenses need to stay hydrated, they will make use of the present wet environment, which is the present tear fluid. A high water content lens would need more tear fluid to stay moist than a low water content lens.

2.2.3 Wettability

Wettability is the formation of a continuous fluid film on a solid surface. It is also called the hydrophilic behavior of the surface of a material and gives information about the adhesion of a liquid to a solid. A good wettability of the contact lens is necessary for a good vision and is supported by a stable uniform tear film over the surface of the contact lens.

The surface of a contact lens is dynamic, which means that the lens molecules continuously rotate to and away from the surface. If a hydrophilic group rotates to the surface and finds water at this surface, it will tend to stay stable. Likewise if it finds air it will try to rotate away causing an unstable dry microenvironment, which on his turn results in discomfort for the patient. Figure 2.1 displays the hydrophilic (blue) and hydrophobic (yellow) groups of a polymer molecule and visualizes their rotations (19).

So a dry microenvironment at the lens surface favors hydrophobic groups, while a wet microenvironment will prefer hydrophilic groups. As the eye surface is a wet environment hydrophilic behavior of the lens leads to a higher comfort for the patient. However, a too high wettability can disrupt vision throughout the wearing period.
2.2. MATERIAL PROPERTIES

Figure 2.1: The lens surface exists of hydrophobic (yellow) and hydrophilic (blue) groups. A moist environment will attract the hydrophilic groups (based on (19)).

The wettability of a contact lens depends on 3 parameters (19):

- surface tension of the tear fluid
- surface tension of the lens material
- interfacial tension between them

Figure 2.2: Wetting angles for various wetting properties

Figure 2.2 represents various wetting angles(19). When the angle is greater than 90° the drop shape is spherical, which indicates a bad wettability. Conversely, if the drop
shape approaches a flat shape and the contact angle is smaller than 90°, it provides a good wettability.

Surface molecules of the contact lens can lower their surface tension by covering themselves with liquid. As molecules always aim for as less tension as possible, a lens material with a high surface tension will have a better wettability. Also the wearing period of the lens may influence the wettability behavior of the lens material. Over time, the movement of hydrophobic proteins to the interface of the tear film with the lens can cause the lens to become more and more dry. When that happens, the lens is less lubricated and there is greater tension interaction between the lens and the tear film, resulting in an increased discomfort with time. This brings us to the next property.

2.2.4 Attraction of Proteins and lipids

Most contact lenses consist of monomers and cross-linked materials that have charges on the monomers. These charges attract proteins, which also have charge distributions and are positively charged amino acids. Thus they attract the negatively charged (anionic) lens material surface. The attraction results in the formation of a biofilm on the lens. The biofilm causes loss of the ocular properties and give the contact lens a yellowish color. Likewise the biofilm on the lens surface can also produce an immune response. Antibodies are produced, resulting in papillary conjunctivitis(20). Therefore the lens must resist to the deposition of a biofilm on the lens and thus the attraction of proteins.

Figure 2.3: Papillary conjunctivitis

The protein and lipid interactions with contact lenses were found to be material- and time-dependent. Proteins are absorbed very quickly, from the moment the lens is put in the eye. It is not a process which takes days or weeks to start. Absorption is essentially a one-way process and therefore the effects become worse in time. For soft lenses, if proteins are absorbed into the matrix of a lens, there is effectively less space for water and the more protein present in the lens, the lower the water content of the lens, resulting in a lower oxygen permeability.

The attraction is also related to the material ionicity (22). Traditionally, it are ionic lenses which adsorb easily proteins. The ionicity of the lens material is discussed in 2.5.1 on page 33.
2.2.5 Refractive Power

The refractive power of a contact lens is responsible for the correction of vision of the patient. It is directly linked with the refractive index, a dimensionless unit, and describes how light propagates through the optical device.

\[ n = \frac{c}{v} \]  

(2.6)

The refractive index is referred to as \( n \), \( c \) is the speed of light in vacuum and \( v \) is the speed of light through the lens material. For example, water has a refractive index of 1.33, meaning that light travels 1.33 times faster in vacuum than in water (23) (24).

The refractive index has a significant influence on lens design, as the refractive index determines the thickness and curvature of the contact lens (25). The natural lens has refractive index of approximately 1.4. The refractive index of the contact lens must be a fraction higher as it is at a greater distance from the focal spot. The higher the refractive index, the better the vision. Likewise, the higher the refractive index, the thinner the lens can be designed.

![Figure 2.4: A. Single refraction; B. Double refraction](image)

According to Figure 2.4 A we can say:

\[ n_1 \times sin(\theta_1) = n_2 \times sin(\theta_1) \]  

(2.7)

The given equation is for a single refraction. However, there are also double refractions (figure 2.4 B), also termed as birefringence. Birefringence differs from single refraction as a single ray of unpolarized light entering a medium is split into two rays, each traveling in a different direction. When a material has a high refractive index that is double breaking, it can blur the vision of the patient. Thus for lens design a material with a single breaking index is favored. Table 2.1 provides a summary of the refractive indices of various materials.
# CHAPTER 2. CONTACT LENSES

Table 2.1: Refractive indices of various materials (*birefrigrent material)

<table>
<thead>
<tr>
<th>Material</th>
<th>Refractive Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vacuum</td>
<td>1</td>
</tr>
<tr>
<td>Air</td>
<td>1.000277</td>
</tr>
<tr>
<td>Water</td>
<td>1.3330</td>
</tr>
<tr>
<td>Diamond</td>
<td>2.419</td>
</tr>
<tr>
<td>Human Cornea</td>
<td>1.380</td>
</tr>
<tr>
<td>Human Lens</td>
<td>1.406</td>
</tr>
<tr>
<td>CAB</td>
<td>1.47</td>
</tr>
<tr>
<td>PMMA</td>
<td>1.49</td>
</tr>
<tr>
<td>SA</td>
<td>145</td>
</tr>
<tr>
<td>FSA</td>
<td>147</td>
</tr>
<tr>
<td>PET</td>
<td>1.4-1.6*</td>
</tr>
</tbody>
</table>

## 2.2.6 Mechanical Properties

A contact lens is subjected to external forces: removal or eye movement can cause irreversible deformation or fracture, both during handling and the manufacturing process. This can result in a decrease in optical performance, discomfort or even complete disintegration (27).

The ultimate goal of lens design is comfort and good vision. An important characteristic of a contact lens material is its ability to maintain its physical dimensions, or return to its original shape (27). This can be achieved by high levels of flexibility, but a high flexibility is limited by the reduction in durability. Therefore the lens must be light weighted to be comfortable, but must also be strong to avoid tearing and scratching. Also a high E-modulus is demanded for the ease of handle and comfort, not only for the patient, but also for the manufacturer. On the other hand, higher modulus has mechanical effects associated with lens wear by some patients, it can lead to discomfort or infections including papillary conjunctivitis (30). The ease of manufacturing the lens and the reliability of the quoted parameters and dimensional stability will be influenced by the mechanical characteristics of the contact lens material.

The first important parameter is stress. One can distinguish tensile stress, compressional, flexural or torsional stress, shear, impact or tear stress. In polymer industry, and thus also the contact lens area, tensile stress is the most frequently considered and measured.

\[
\tau = \frac{F}{A}
\]  

with \( \tau \) the tensile stress, \( F \) the applied force and \( A \) the cross-sectional area of the sample. The unit of stress is the called Pascal, which is expressed as Newton per square meter [Pa = 1N/m²].

The strain at yield point is also a useful indicator of the strength of a material. Strain
2.2. MATERIAL PROPERTIES

describes the deformation of the sample in the direction of the applied force. It is referred to as the elongation $\varepsilon$, i.e. the percent change in length of the sample relative to the initial length of the sample (29).

$$\varepsilon = \frac{L - L_0}{L_0} \times 100\%$$

(2.9)

where $L_0$ is the initial length of the sample and L.

Finally there is the modulus of elasticity, the E-modulus, or better known as Young’s modulus. This parameter describes how well the material resists the deformation. A higher modulus indicates a stiffer contact lens.

$$E = \frac{\tau}{\varepsilon}$$

(2.10)

The Young’s modulus of an elastic material is a constant value, i.e. the stress is proportional to the applied strain. According to figure 2.2 the modulus can be determined from the slope of the stress-strain curve, created during tensile tests. The shape of this curve indicates whether a material is strong and tough or strong and brittle. Stress-strain curve B approaches the behavior of a contact lens material.

However, few contact lens materials are truly elastic and are actually classified as viscoelastic. For viscoelastic materials, the Young’s modulus varies with the amount of

Figure 2.5: A. a true elastic material; B. a visco-elastic material; C. a strong and brittle material; D. A strong and tough material (based on (29))
stress applied. The value quoted for Young’s modulus for these materials is usually the initial value at very low strains where the proportionality of stress to strain is maximum (28). Table 2.2 gives some values for the Young modulus for various general materials (29).

<table>
<thead>
<tr>
<th>Material</th>
<th>Young Modulus ( MPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diamond</td>
<td>1200 000</td>
</tr>
<tr>
<td>Stainless steel</td>
<td>200 000</td>
</tr>
<tr>
<td>Rubber</td>
<td>10-100</td>
</tr>
<tr>
<td>Cornea</td>
<td>0.45-10</td>
</tr>
<tr>
<td>PMMA</td>
<td>1800-3100</td>
</tr>
<tr>
<td>CAB</td>
<td>2400-4100</td>
</tr>
<tr>
<td>PET</td>
<td>2000-27 000</td>
</tr>
<tr>
<td>polyHEMA</td>
<td>3.7</td>
</tr>
</tbody>
</table>
2.3 Relationships between Material Properties

2.3.1 Dk vs. Young’s Modulus

A link exists between the oxygen permeability (Dk) and the modulus of a contact lens material, although there is a difference in soft and rigid lens behavior.

For soft contact lenses it is proven that with an increased modulus follows an increased Dk-value. In 2007 Loretta Szczotka-Flynn studied the behavior of various hydrogels from different companies (31). For example, the lens material with the highest Dk (lotrafilcon A) is the stiffest, and the lowest-Dk material (galyfilcon A) is the most flexible. However, one lens material stands outside this continuum: comfilcon A. This lens is unusually soft for its given Dk value (31). The lens has a Dk of 128, yet a relatively low modulus. This can be explained by its composition. In contrast to the other hydrogels, it has no TRIS-based or PVP-based chemistry. Macromers are the only source of silicone. As already mentioned, the silicone increases the water content and due to the macromers, the lens still keeps its flexibility. Thus for hydrogels it is possible to predict the relationship in a limited way.

![Figure 2.6: Correlation between Young’s modulus and oxygen permeability measured for A. hydrogel lenses; B. rigid gas permeable lenses (based on (31) and (32))](image)

In contrast, rigid contact lenses with a high modulus have low oxygen permeability. The Scottish optometrist W.R. Stevenson tested several rigid lens materials, including PMMA, silicone acrylates (Boston Equalens), etc (32). Figure 2.6 B shows that there is an inverse correlation between Dk-value and the E-modulus of the rigid lens material. PMMA has the lowest Dk of the lens materials tested and had the highest Young’s modulus, while the highest Dk lens material tested (Fluoroperm 90) had the lowest
modulus. Therefore, one may expect a greater flexibility in lens materials of higher oxygen permeability.

One notable exception to this rule is cellulose acetate butyrate (CAB). CAB is a material with a low Dk-value, but is relatively flexible.

### 2.3.2 Dk vs. Water Content

Water content is a property specific for soft lenses, as these lens materials absorb easily fluid. In contrast, rigid lens materials absorb little water, which results in a very low water content. But unlike hydrogels, rigid materials don’t make use of the water content to transmit oxygen through the lens. Therefore the link between Dk and the water content is only discussed for hydrogels.

As one can predict, knowing that the water transports oxygen, Dk increases as water content increases. Figure 2.7 shows that the relationship between water content and permeability is not a linear, but an exponential one (14)

![Figure 2.7: Relationship between oxygen permeability and water content for hydrogel lenses at 35°C (based on (14))](image)

Efron and Morgan described the exponential relationship between the oxygen permeability and the water content with the following formula (14):

$$Dk = A \times e^{BW}$$  \hspace{1cm} (2.11)

W represents the water content of the lens. A and B are constants for the given temperature. Morgan and Efron proposed values for the constants A and B at 35°C, which
is the surface temperature of the eye. Thus the equation becomes:

\[ Dk = 1.67 \times e^{0.0397^W} \]  

(2.12)

Recently, silicone was added to the hydrogels, creating a total new type of lens. Here the water content can be decreased, while still maintaining a high Dk-value (see page 33). As Figure 2.7 illustrates, they have a different ratio between Dk and water content at a lower amount. For the latter the equation is inapplicable.

Every factor, which influences the water content will indirectly also affect the oxygen transmission. Factors that can have an influence can include PH, temperature and dehydratation of the lens.

2.3.3 Dk vs. Water Vapor Transmission

There is little known about the link between oxygen and water vapor transmission for contact lenses in general. However, for some materials, used for packaging, there are existing studies (33) that prove this link. For polyethylene (PE), figure 2.8 illustrates that these parameters are directly linked together.

![Figure 2.8: Relationship between oxygen permeability and water vapor transmission for polyethylene films (based on (33))](image)

These results can be modeled with the following equation:

\[ OTR = 470 \times WVTR \]  

(2.13)

This means that only one of these permeation tests need to be performed. WVTR measurements can be used to accurately predict the OTR.

Also a link between OTR and WVTR for cellulose acetate (CA) with varying compositions is found (55). The study proves the high water affinity of cellulose acetate. Also
Figure 2.9: Relationship between oxygen permeability and water vapor transmission for different CA compositions (based on (55))

CA has a high oxygen transmission, which can be reduced by the presence of nanofillers. For CA the link can be modeled as followed:

For CA without nano-fillers, as this is the case for the research concerning an artificial iris, the link can be approximated with the following equation:

\[ OTR = 0,6 \times WVTR \]  \hspace{1cm} (2.14)
2.4 Lens Design

Different classifications of contact lenses are used by ophthalmologists. The lenses can be divided according to their primary function, material use, wear schedule, replacement schedule or lens design. The most common used and most appropriate division for this thesis is the division according to material and/or design. As lenses are classified by design, there exist three groups:

- corneal contact lenses
- corneo-scleral contact lenses
- scleral contact lenses

**Corneal Lenses**
The size of the lens will determine the amount of acceptable bearing and clearance as well as the fluid dynamics. The corneal lens is the smallest lens (8 mm to 12.5 mm) and is completely supported by the cornea. They are easy to handle by the consumer and are inexpensive. Nowadays the corneal lenses are the most common used lens type in Belgium. The reason for this is probably the preference of the ophthalmologists and the ease of learning how to fit the lens. These lenses can be permanent or disposable. Permanent lenses need to be properly cleaned and cared for. The disposable are often worn continuously for a day or in a period of a month, and thrown away when removed. However, corneal lenses are not a good option for diseased or irregular corneas, as patients can’t support these lenses.

**Corneo-scleral Lenses**
The next category in lens types, increasing in size, is the corneo-scleral lens. The corneo-scleral lenses exhibit corneal bearing, similar to the corneal design, and a thin rim of scleral touch. They range in size from 12.5mm to 15mm, and have a larger size than corneal lenses. The larger diameter means less lid interaction and very little adaptation is necessary. Therefore corneo-scleral lenses may provide better comfort, centration, and stability compared to the corneal rigid lenses. Nearly anyone who can wear corneal lenses could be wearing corneo-scleral lenses instead. These lenses are inexpensive, but initially not easy to fit. Corneo-scleral lenses are not an option for too diseased corneas due to the bear lens pressure.

**Scleral Lenses**
Scleral lenses completely cover the cornea and place all lens bearing on the sclera. They are further subdivided into mini- and large-scleral lenses. The mini-scleral lenses range in size from 15mm to 18mm, and the large scleral lenses (the largest existing lenses) range from 18 to 25mm. Lens diameter choice is depending on the patient’s eye dimensions. The major advantage of this lens type is that these lenses can be worn by
persons with irregular corneal surface. As already mentioned the sclera is much less sensitive than the cornea. So, lenses that rest primarily or exclusively on the sclera may induce less sensation than smaller lenses that rest upon the cornea. This is interesting for example for people with aniridia or iris damage, as their cornea is extremely sensitive and irregular. Also when there is no contact with the cornea there is no mechanical damage possible by the lens material. In some patients the corneal tissue is damaged. Scleral lenses trap a reservoir of fluid behind the lens. This fluid acts as a protection layer for the cornea, reduces the mechanical stress to the cornea, and may even allow it to heal in some cases. In small diameter lenses like the corneal or corneo-scleral lenses the tear reservoir capacity is typically small to non existent. Corneal lenses can become decentered, and may even become dislodged. Since scleral extend under the upper and lower lids, they rarely dislocate. For scleral lenses it is important to choose materials with a Dk-value higher than 100, because they semi-seal the eye. This makes tear exchange relatively slow as compared to corneal lens design. Finally, to prevent lens flexure scleral lenses are often manufactured with a thickness 4 times greater than corneal lenses. If lens flexure occurs, there is a risk of creating a negative pressure under the lens, which results in limbal swelling.

Table 2.3 presents a short overview of the three lens types.

<table>
<thead>
<tr>
<th>Table 2.3: Overview lens types</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corneal lens</td>
</tr>
<tr>
<td>8-12.5mm all lens bearing on cornea</td>
</tr>
<tr>
<td>no tear reservoir limited tear reservoir capacity</td>
</tr>
<tr>
<td>easy to handle and fit good comfort</td>
</tr>
<tr>
<td>not for irregular corneas</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
2.5 Lens Materials

Classified by material, the contact lenses are divided into three types:

- soft contact lenses
- rigid contact lenses
- hybrid contact lenses

2.5.1 Soft Lenses

Soft lenses contain hydroxyl or hydroxyl and lactam groups. These allow them to absorb and hold water, within the polymer chains, and thus the spaces between the chains expand. In the dehydrated state most hydrogels are hard and brittle. However, due to the hydrogels, which are hydrophilic, the lens swells in water, causing it to become soft and flexible. So it takes on elastic properties, i.e. the water acts as a plasticizer. In contrast to rigid lenses, soft lenses can be folded so that the edges meet and when released they will return to their normal shape. The structure of hydrogel material is composed as a long backbone of a variety of chemical groups. The function of these chemical groups, or monomers, is to attract and bind water.

Due to their flexibility they adapt the shape of the eye from just about the moment they make contact with the eye. They give much more initial comfort to the wearer than hard lenses, which is their greatest advantage. Because of their good initial comfort many people prefer hydrogel contact lenses.

Unfortunately, the durability of a soft contact lens is not as good as for rigid lenses. Because of their flexibility they are easy to tear and sensitive to scratches. Also protein deposit clouds the lenses over time. While blinking, soft lenses are more likely to distort. The eyes must then refocus, which can lead to a decrease in visual acuity.

Other disadvantages of soft lenses include relatively less visual acuity than with rigid lenses, absorption of chemicals from topically applied ophthalmic products, and the requirement of more lens-cleaning and disinfecting products.

FDA divided hydrogel polymers into four groups according to table 2.4, based on water content and electrostatic charge (ionicity) of the material. The electrostatic charge is obtained by the removal of the hydrogen atom in the carboxyl group.

For protein deposition, the ionicity and the water content of the lens material are the main influencing parameters.

Group 1 generally shows lower protein deposition. Due to their low water content, these lenses are typically the thinnest types of lenses. In contrast, group 4 shows the highest protein deposition, and is therefore more suitable for a short life span like in the case of
CHAPTER 2. CONTACT LENSES

Table 2.4: Classification soft lenses

<table>
<thead>
<tr>
<th>Category</th>
<th>Water content</th>
<th>Electrostatic charge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>Low water</td>
<td>Non-ionic</td>
</tr>
<tr>
<td></td>
<td>&lt;50% H₂O</td>
<td></td>
</tr>
<tr>
<td>Group 2</td>
<td>High water</td>
<td>Non-ionic</td>
</tr>
<tr>
<td></td>
<td>&gt;50% H₂O</td>
<td></td>
</tr>
<tr>
<td>Group 3</td>
<td>Low water</td>
<td>Ionic</td>
</tr>
<tr>
<td></td>
<td>&gt;50% H₂O</td>
<td></td>
</tr>
<tr>
<td>Group 4</td>
<td>High water</td>
<td>Ionic</td>
</tr>
<tr>
<td></td>
<td>&gt;50% H₂O</td>
<td></td>
</tr>
</tbody>
</table>

Disposable lenses. These materials are relatively porous, negatively charged networks. They are the only group into which the positively-charged proteins are able to diffuse.

More recently, hydrogel materials is categorized into two groups, according to their Dk-value.

- conventional hydrogel materials, today referred to as low-Dk materials
- silicone hydrogels, today referred to as high-Dk materials

The 4 groups in table 2.4 contain both, conventional and silicone, hydrogel materials.

**Conventional Hydrogels**

Frequently used monomers in conventional hydrogels are N-vinyl pyrrolidone (NVP), methyl-methacrylic acid (MMA), glycedyl methacrylate (GMA), and hydroxy-ethyl-methacrylate (HEMA)(36). Cross-links can be modified to accomplish a greater stability.

HEMA-based hydrogels are made of polymerized 2-hydroxy-ethyl methacrylate monomers which can be cross-linked with ethylene glycol dimethacrylate (EGDMA). The hydroxyl group will bind with the water molecules, resulting in a hydrated polymer matrix. Contact lenses made from polyHEMA contain approximately 38-40% water in hydrated state (group 1 in table 2.4)(36).

When MMA and NVP are linked up into an MMA/VP copolymer, a completely new material is obtained with very different characteristics to the HEMA/VP copolymer. For this combination, contact lenses with a water content up to 60-85% can be obtained.

Finally, there are contact lenses with glycedyl methacrylate (GMA), which is more hydrophilic than HEMA, as the monomer contains two hydroxyl groups. It can be used in 2 combinations. Firstly, GMA can be combined with MMA to produce materials which have water contents in the range of 30-42%. These materials are stiffer and stronger than HEMA hydrogels. Secondly, it can be linked up with HEMA to construct a contact lens with a high water content and a non-ionic characteristic. Water content can go up to
2.5. LENS MATERIALS

70%. The latter is relatively deposit resistant and insensitive to pH-variations in a range of 6-10 pH (36).

Oxygen permeability for all of these hydrogels, is essentially established by the water content, since oxygen is able to pass through the water rather than through the material itself (36). So for conventional hydrogels, the oxygen permeability increases logarithmically with an increasing water content. Unfortunately, a high water content results in a higher thickness.

Silicone Hydrogels
The most recent development is the silicone hydrogel contact lens. Groups containing silicon-oxygens (silicones) are linked together to increase oxygen permeability. For conventional hydrogels, the oxygen permeability increases logarithmically with an increase in water content. However, increasing the water content, also increases adsorption of tear fluid and decreases the durability. By the addition of silicone groups there is a significant enhancement of oxygen transmission, without increasing the water content. This can be explained as oxygen is more soluble in silicone than it is in water, whereas, for a conventional hydrogel, oxygen is more soluble in water than in polyMMA or in one of the other polymers. Also a relative high modulus is possible due to these silicone groups and the thickness can be reduced, compared to conventional hydrogels.

But silicone based materials are hydrophobic, therefore a surface treatment or additional
2.5.2 Rigid Lenses

![Chemical structure of rigid lens materials (based on (38))](image)

As rigid lenses are less flexible than soft lenses, there is the risk that the movement of the lens is limited. The lens must be able to slide and move over the corneal surface with each blink to enhance oxygen permeation. This oxygenation process in hard contact lenses is often referred to as "tear pump phenomenon" whereby the corneal surface is provided with oxygen-coated tears. Since they are firm they retain their shape better when you blink, so the eye does not have to refocus as much.

Advantages of hard contact lenses include a high refractive index, ranging from 1.46 to 1.50 (23). They also have excellent visual acuity, durability (life span of 2-4 years), ability to withstand acids, and no sensitivity reactions when placed on the cornea. They require almost no water to maintain their shape, so they won’t pull the moisture away from the eyes. An advantage of RGP contacts is that they are made of a firm plastic, so they have a high resistance against scratches or tearing. They also harbor fewer protein deposits from the tear film, a property that benefits the health and comfort of the eye. Disadvantages of hard lenses include a longer adaptation time, and poor oxygen permeation for certain materials.

Rigid lens materials are divided into rigid non-gas permeable (RNGP) and rigid gas permeable lenses (RGP). Non-gas permeable lenses are made of PMMA which was the first material used for polymer based lenses. It was an ideal polymer to be used for rigid contact lenses as it is cheap, easy to handle, and an inert and stable material. However, PMMA allows little to no oxygen transmission through the material, it has a Dk-value of 0.1 (40). Therefore PMMA is no longer used for lens design.

Today’s materials used for manufacturing RGPs are Cellulose Acetate Butyrate (CAB), Silicone Acrylate (SA) and Fluorsilicone Acrylate (FSA).
2.5. **LENS MATERIALS**

**CAB**
Cellulose acetate butyrate was the first material to replace PMMA. It has a reasonably good wettability due to the large number of polar hydroxyl groups, which are capable of hydrogen bonding with an aqueous wetting solution such as tear fluid (37). Because of a high Young modulus it has a high breakage rate. It is also relatively inert, so there is little attraction of proteins. However it has a low Dk-value. For that it is now rarely used. It also scratches easily and is difficult to manufacture due to its dimensional instability. The latter problem can be mainly overcome by the moulding method. CAB lenses, for example, transmit more oxygen than PMMA lenses, but are not as stable as PMMA. Moreover, preservatives such as benzalkonium chloride affect CAB and change the lens surface.

**SA**
SA is a combination of modified methyl-metacrylate (MMA), which provides the rigidity and good optical qualities, and silicone, which enhances the oxygen permeability. Cross-links are also applied to improve the mechanical properties of the lens. Furthermore, to get a good wettability, wetting agents such as methacrylic acid, are added (40). It are the minor variations in concentrations of monomers, wetting agents and cross-linkers that vary the formulations of these materials.

The advantage is that this material is widely available and is mechanical stable. It has mostly a low to medium Dk-value, ranging from 14 to 60. SA lenses have a good dimensional stability and a high resistance against scratches. Also a good vision is achieved with limited lens flexure (37). SA also withstands high temperatures, which makes it easy to manufacture them. Unfortunately, the material attracts proteins. And, when compared with PMMA, due to the hydrophobic silicone components, the surface wettability is lower.

**FSA**
Unlike SA material, the added components, which increase oxygen permeability in FSA materials are silicone-oxygen (Si-O-Si) structures in the side groups of the basic PMMA backbone (39). Adding fluorine-components to the silicone acrylate enhances the transmission of oxygen through the polymer, and thus higher Dk-values (above 100) can be achieved. This is because the oxygen molecules prefer to dissolve into fluorinated materials. In essence, the FSA polymer absorbs oxygen from the atmosphere and the Si-O-Si components move the oxygen through the polymer. The fluorine also improves the wettability and deposit resistance.

Disadvantage of this material is that it becomes very brittle when the thickness is too small (37). During manufacturing it is also required to be handled with care. When compared to PMMA lenses, the FSA based lenses have greater mass and decreased stability.
2.5.3 Hybrid Lenses

Hybrid lenses have adopted the benefits of both rigid and soft lenses. A hybrid contact lens is made up with a gas permeable center that is surrounded by a hydrophilic soft outer ring. New technology has blended together the visual acuity of the rigid gas permeable lenses and the flexibility and comfort of the soft contact lenses. However, these lenses are, like soft lenses, very fragile. The main disadvantage is their low Dk-value (generally between 5 and 15).

2.5.4 Overview Lens Materials

Table 2.5 summarizes the characteristics of the materials used for contact lens design.

<table>
<thead>
<tr>
<th></th>
<th>Conventional Hydrogels</th>
<th>Silicone Hydrogels</th>
<th>PMMA</th>
<th>CAB</th>
<th>SA</th>
<th>FSA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dk</strong></td>
<td>8-44</td>
<td>61.5</td>
<td>0.1</td>
<td>4-8</td>
<td>14-60</td>
<td>40-150</td>
</tr>
<tr>
<td><strong>water content [%]</strong></td>
<td>20-75</td>
<td>32</td>
<td>N.A.</td>
<td>N.A.</td>
<td>N.A.</td>
<td>N.A.</td>
</tr>
<tr>
<td><strong>wetting angle [°]</strong></td>
<td>20-72</td>
<td>17-22</td>
<td>70</td>
<td>34</td>
<td>25-30</td>
<td>3-50</td>
</tr>
<tr>
<td><strong>attraction of proteins</strong></td>
<td>high</td>
<td>high</td>
<td>low</td>
<td>low</td>
<td>medium</td>
<td>low</td>
</tr>
<tr>
<td><strong>RI</strong></td>
<td>1.46-1.37</td>
<td>1.39</td>
<td>1.49</td>
<td>1.47</td>
<td>1.46-1.48</td>
<td>1.41-1.53</td>
</tr>
<tr>
<td><strong>Young’s Modulus [MPa]</strong></td>
<td>0.3-0.5</td>
<td>1.1</td>
<td>2000</td>
<td>1500</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2.6 International Standard Method for Classification

When looking for the proper lenses it is important to understand the coding of the different lens types. The international standard method for classification of both rigid and soft contact lens materials is BS EN ISO 11539:1999, published in 1999 by the European Standard (35). Each material is classified by a six part code:

prefix - stem - series suffix - group suffix - Dk range - modification code

Prefix and series suffix
Prefix is a term that is administrated by the United States Adopted Names (USAN) Council. It is optional for other countries.

Stem
The stem refers to the water content of the material. There are two types of stems used, filcon and focon. The filcon stem is affixed to the prefix and is applied for hydrogel materials with a water content more than 10 percent. The focon is affixed to the prefix and is applied for materials which contain less than 10 percent water by mass, which are non-hydrogel materials.

Series Suffix
Like the prefix, the series suffix is also a term administrated by the United States Adopted Names (USAN) Council. It indicates the revision level of the chemical formula. The letter A is used for the first formulation, B for the second etc.

Group Suffix
Group suffix is based on the type of stem. When the stem refers to soft material, the group suffix will indicate if the hydrogel is ionic or non-ionic and specifies the amount of water content. If it is a rigid material, the group suffix will determine if the material contains silicone and/or fluorine. The group suffix is detailed in the following table.

<table>
<thead>
<tr>
<th>Group Suffix</th>
<th>Filcon (soft lenses)</th>
<th>Falcon (rigid lenses)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>&lt;50% EWC, &lt;1% ionic monomer</td>
<td>no silicone, no fluorine</td>
</tr>
<tr>
<td>II</td>
<td>&gt;50% EWC, &lt;1% ionic monomer</td>
<td>silicone, no fluorine</td>
</tr>
<tr>
<td>III</td>
<td>&lt;50% EWC, &gt;1% ionic monomer</td>
<td>silicone, fluorine</td>
</tr>
<tr>
<td>IV</td>
<td>&gt;50% EWC, &gt;1% ionic monomer</td>
<td>no silicone, fluorine</td>
</tr>
</tbody>
</table>

Dk Range
The fourth part of the code gives information about the oxygen permeability, described by the Dk range. The code part is represented by a number, starting with 1, and increases with increasing Dk range. Table 2.7 gives the possible coding.
Table 2.7: Code for various Dk values

<table>
<thead>
<tr>
<th>Code</th>
<th>Dk</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>&lt;1</td>
</tr>
<tr>
<td>1</td>
<td>1-15</td>
</tr>
<tr>
<td>2</td>
<td>16-30</td>
</tr>
<tr>
<td>3</td>
<td>31-60</td>
</tr>
<tr>
<td>4</td>
<td>61-100</td>
</tr>
<tr>
<td>5</td>
<td>101-150</td>
</tr>
<tr>
<td>6</td>
<td>151-200</td>
</tr>
<tr>
<td>7</td>
<td>Increasing with 50 Dk units</td>
</tr>
</tbody>
</table>

Surface Modification Code

Sometimes the surface of the contact lens is modified, having different chemical characters from the bulk material. The last part of the code is added when dealing with a modified surface and determines the new surface properties.
2.7 Conclusion

We can conclude that the most meaningful parameter for contact lenses is the oxygen permeability. It is of great importance that the lens allows oxygen transmission to maintain a healthy eye. This property is referred to as the Dk-value. The higher the Dk is, the greater the oxygen transmission is through the lens.

According to several studies, one can link the oxygen transmission to the water vapor transmission rate. For PE there is a direct link.

Although Dk is an important parameter, there are several other parameters that determine the comfort of the patient, like the wettability, water content, attraction of proteins, mechanical property, refractive index, and lens design.

The wettability is called the hydrophilic behavior of the lens, and determines how well a fluid film is formed on the lens surface. The wettability must be as high as possible, as a low wettability results in discomfort and low vision quality.

Water content is a parameter specific for soft lenses. A high water content gives rise to a high Dk-value. But a high water content means also a high absorbance of fluids and thus the lens will make use of the present wet environment. The attraction of tear fluid may lead to dry eyes or even infection. Additional, a high water content can also lead to a lower refractive index. Further the attraction of proteins must be kept low to prevent infections and to prevent a decrease in vision quality.

For a good vision quality, a high refractive index is favored. Supplementary the index must be single breaking. Birefringence leads to a blur vision, as it divides the incoming light waves into 2.

We have to keep in mind that the contact lens also must possess a certain stiffness to enhance the ease of handling by the consumer and the manufacturer. This is determined by the Young’s modulus. The latter can be linked to the Dk-value for both soft and rigid lenses. For soft lenses the modulus increases with increasing oxygen permeability. This can be explained by the water content, as they are responsible for both. However for rigid materials, the Dk-value decreases with increasing Dk-value. The stiffer the material, the stiffer the bindings, and the harder it is for the oxygen to pass these stiff bindings.

As for the lens design, for patients suffering of aniridia, lens bearing on the corneal surface is a ‘no go’, as the disease mostly is accompanied by an irregular and sensitive cornea. Therefore, the lens design is limited to a scleral lens design. As scleral lenses have large dimensions, the chosen material must have a certain stiffness. Otherwise the lens is difficult to handle by the patient as well as by the manufacturer, and the lens becomes very brittle and easy to scratch. Thus, the lens must be made of rigid materials. Overlooking the available rigid lens materials it is already possible to eliminate PMMA because of its zero Dk-value. Also CAB is not recommended due to its low oxygen permeability. Materials that are qualified are SA and FSA.
Moreover, the lens must follow the shape of the eye surface as close as possible. So, like the eye surface (seen in chapter I) the lens will have several curves. This will be determined in the next chapter.

Finally, we must keep in mind if the lens is very expensive, the interest of the consumer will diminish. The costs of a contact lens are influenced by the availability of the chosen material, the type of lens, the manufacturing process and the demand of the market.
Chapter 3

Implementation of the Artificial Iris
CHAPTER 3. IMPLEMENTATION OF THE ARTIFICIAL IRIS
3.1 Composition

Defining the design of the lens includes determining the components and their composition, the dimensions and shape, and finally, selecting the proper materials. In the previous chapter, we determined that the general lens shape should use a scleral design due to the sensitivity of the diseased or damaged cornea. Thereby the material range has been limited to rigid lens materials, as these are the only kind that ensure enough support for the large dimensions of the contact lens. Before setting the values for each dimension, one must know the various components, as these will have a direct effect on the design.

Current technology of the artificial iris consists of 3 main components.

- Flexible, spherically shaped LCD (consisting the liquid crystals and the substrate)
- Driver electronics (energy and LCD driving)
- Biocompatible body

Firstly, the liquid crystal cell is enclosed by flexible substrates, forming the LCD, and sealed at the edges. Electronics are made of inorganic materials, require high temperatures and contain chemicals that are not biocompatible with the eye, which complicates their integration. One must assure the display doesn’t make contact with the human eye and leakage is avoided.

It is important that the flexible substrate is biocompatible and allows the transmission of oxygen through the lens. At the moment the flexible substrate exists of PET, which has zero Dk and thus is not permeable for oxygen, an unacceptable property for a modern contact lens. Hence, an alternative high Dk- material must be suggested. This will be further investigated in chapter IV.

Additional, the inner side of the flexible substrate is covered with a transparent conductive layer, which supports the function of the liquid crystals. To control the behavior of the LCD, a driver chip is applied.
Finally, all the components are embedded in a biocompatible body. The embedding is defined by the dimensions, materials and fabrication method.

In the following subsections the different components as well as the functioning of the lens are discussed into more detail.

### 3.2 Principle

To mimic the function of the natural iris, the lens is divided into rings, in decreasing radius towards the center. As the iris constricts at a larger brightness, the lens must behave in the same way. Thus with increasing light intensity, more circular pixels are activated, illustrated by figure 3.2. At a maximal brightness the activated pixels cover the entire iris.

The lens must darken as the light intensity rises, hence a photosensitive element should be included in the electronics. However, this is not been developed yet and still needs more investigation. As this is not within the scope of this dissertation, the lens will be controlled via an external power source.

![Figure 3.2: Step 1-5 activation of the liquid crystals with increasing light intensity](image)

### 3.3 Flexible LCD

Firstly, the design of the active part and its pixelisation is part of a second dissertation, investigated by Pieter De Backer. As this research focuses on the overall design and biocompatibility of the lens and its materials, only a short introduction will be given. More detailed information about the active part can be found in the dissertation 'Design and Fabrication of a Tunable Artificial Iris' by Pieter De Backer (46).

In general, liquid crystals are molecular rigid rods, with dipole and/or easily polarizable substances. These molecules exhibit properties of both a conventional liquid as of a solid crystal, meaning that they flow like liquids, but the molecules are oriented in a crystal-like way. Because of their anisotropic molecular shape, other properties such as their refractive index are also anisotropic and thus generally tend to be birefringent. As a result, the polarization state of light traveling through liquid crystal can be altered.
3.3. **FLEXIBLE LCD**

This principle is used in LCDs of which we can see a Twisted Nematic configuration in figure 3.3. Here, linearly polarized light enters the cell and meets the liquid crystals, which are organized in a helical structure. In normal conditions, the light follows the twist of the molecules and exits through the secondary linear polarizer. At the inner side of the cell (on both sides) one can find a transparent conductive layer (generally indium tin oxide, but in flexible displays often a conductive flexible polymer). When a voltage is applied, the resulting electric field reorients the liquid crystal molecules and the helix will unwind to varying degrees, depending on the voltage. The orientation of the linearly polarized light will not be parallel to the secondary polarizer anymore and the light will be (partly) absorbed.

However, standard polarizers used in LCDs are too thick to be used in a contact lens. Therefore, a different configuration is used, where an absorbing dye is dissolved in the liquid crystal.

![Figure 3.3](image_url)

**Figure 3.3:** A. helical structure of a liquid crystal molecule; B. deactivated condition of the crystals; C. activated condition of the crystals (based on (45))

Next to this, as mentioned in the subsection 3.2 the lens must become darker when activated and not the other way around. Hence, the initial position of the crystal rods is perpendicular to the substrates to allow for sufficient light transmission. Applying an electrical field forces them to reorient in a helix and absorb the incoming light, and thus the lens becomes darker. When the electrical field is turned off, the crystal molecules will relax and return to their perpendicular orientation and light will again be able to pass through.

As already mentioned in the previous chapter, the contact lens follows the curved surface of the eye, hence for the artificial iris design a curved display is required.
3.4 Fabrication Process of the LCD

Now the composition and principle is known, the fabrication of the LCD is explained: how is the flexible substrate formed and how are the liquid crystals applied? The different steps during the process are summarized by figure ??.

**Step 1: Preparation of the PET-samples**
Prior to the fabrication process the samples are cleaned. Two identically films with a thickness of 0.05mm are placed into a beaker filled with acetone was used for cleaning PET, so during the first trial acetone is also used for cleaning the TAC-films. The beaker with samples is placed for 5 minutes in a trill plate bath to assure no dust remains on the samples. Afterwards the samples are washed with water and dry cleaned.

**Step 2: Lamination**
The glass carriers are spin coated with a temporary adhesive (a solution of wax and ethanol), then they are pre-heated up to 95°C, to finally laminate the PET-films onto the glass carriers. During the lamination, the films must be applied as homogeneous as possible to prevent the formation of air bubbles or wrinkles.

**Step 3: Photolithographic layer**
Pedot and SiO2 is evaporated on the PET-surfaces. These layers will enhance the conductivity of the liquid crystals. Subsequently a photoresist, with spacer balls namely
SU8 3010, with a thickness of 0.01mm, is spin coated and patterned onto the PET-films.

**Step 4: Composition**
On one sample a UV-curable glue (UVS91) is dispensed in circular pattern with a small interruption, that will be required in step 6 for the filling with liquid crystals. The second glass carrier with the laminated TAC-film is sandwiched with the first, and the resulting composition is illuminated with UV-light to activate the glue and to delaminate the glass barriers on the films.

**Step 5: Cutting**
Next, the glass carriers are removed and a CO2-laser cuts out the substrates along the circular glue patterns, resulting in flat cut-out lenses. As wireless powering is not yet performed in this stadium of the research, an additional rectangular area, for the external electrical contacts, is foreseen. Due to the thermal ablation of the CO2laser, the external opening provided in step 4 is sealed and needs to be re-opened with an excimer laser. The latter perforates the first TAC-film and stops at a depth of 0.01mm in the second film, and thus re-opening the entrance for the liquid crystals.

**Step 6: Molding**
Then the lens is brought at a temperature above the glass transition temperature, ap-
proximately 125°C, so the lens can be shaped easily. Afterwards the lens is molded with a spherical aluminium mold.

**Step 7: Liquid crystal cell**
Finally the curved lens is filled with liquid crystals, via the provided entrance, and sealed. The result is a curved flexible substrate with integrated liquid crystals.

### 3.5 Embedding

#### 3.5.1 Materialization and fabrication method

The embedding is determined by the dimensions, fabrication method, and materialization. The initial goal of this dissertation was to investigate all three factors and the materials of the flexible substrate. Unfortunately, due to limited access to contact lens materials and information concerning manufacturing methods, the research is restricted to the materials of the flexible substrate.

However, a proposal can be offered for elaboration in further investigation. Late cutting is a commonly used technique for fabrication of rigid contact lenses. Hence this technique can be applied to compose the contact lens. For this, the biocompatible embedding material is button shaped. The LCD and unpolymerized RGP material, is placed between the male and female button. Subsequently, the lens is milled and sandwiched, forming the artificial iris (figure 3.6).

![Figure 3.6: Proposed fabrication method: late cutting the lens by use of buttons](image-url)
3.5.2 Dimensions

As for the dimensions, mentioned in the previous chapter, the contact lens will be of scleral size, because all lens bearing is on the less sensitive part of the eye, the sclera and thus more comfort is provided for the patient.

The lens can possess several curvatures, going from bicurve (2 peripheral zones), tricurve (3 peripheral zones) to multicurve (3 or more peripheral zones). The multicurved lens is preferred as it has a better adaption to the corneal surface shape than bi- or tricurved contact lenses.

Lately, the company Visionary optics, specialized in contact lenses, has launched a new scleral lens design, called Jupiter. As it already received positive reactions of optahlmol-ogists and patients, the artificial iris will be based on this design. The Jupiter Scleral Lens falls into multiple overall diameters (summarized in table 3.1) depending on the dimensions of the patients eye. A scleral lens with a diameter of 15.6mm is most common size used and fits 90% of the eyes. For this reason a scleral lens with these measurements is best suited for future embedding of our artificial iris.

<table>
<thead>
<tr>
<th>Chord diameter</th>
<th>base curve</th>
<th>second corneal curve</th>
<th>limbal curve</th>
<th>landing curve</th>
<th>edge lifting curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>15.0</td>
<td>8</td>
<td>+1.7</td>
<td>+0.9</td>
<td>+0.5</td>
<td>+0.4</td>
</tr>
<tr>
<td>15.6</td>
<td>8.6</td>
<td>+1.7</td>
<td>0.9</td>
<td>0.5</td>
<td>0.4</td>
</tr>
<tr>
<td>18.2</td>
<td>8.2</td>
<td>+2.0</td>
<td>+1.0</td>
<td>+1.5</td>
<td>0.5</td>
</tr>
<tr>
<td>18.8</td>
<td>8.2</td>
<td>+2.6</td>
<td>+0.7</td>
<td>+1.5</td>
<td>+0.5</td>
</tr>
<tr>
<td>20.2</td>
<td>8.2</td>
<td>+2.7</td>
<td>+0.7</td>
<td>+2.1</td>
<td>+0.5</td>
</tr>
</tbody>
</table>

The Jupiter lens exists of 5 curves, 3 curves that form the corneal chamber (optical zone and limbal curve) and 2 curves, which form the periphery of the lens, including the landing and edge fitting curves (figure 3.7) (41). The optical zone creates the desired optical effect and is determined by the base curve and second corneal curve. The back surface of the optical zone approximately aligns the corneal surface. The limbal curve will define the sagittal depth of the lens. The landing curve is the only curve to touch the sclera. An even pressure distribution is needed in the landing zone in order to provide a homogeneous corneal clearance. Finally, the edge lifting is requisite in order for lenses to move.

Taking the thickness into account, there is a distinction between center thickness and edge thickness. Table 3.2 provides a summary of minimum thicknesses for various rigid lens materials. It can be said that the center thickness should not be less than 0.14 mm with most rigid materials, due to lens flexure. For edge thickness a minimum of 0.12 mm is required. A 'sharp' edge shape must be avoided as this causes discomfort and makes the lens fragile.
Table 3.2: Minimum thicknesses for different materials [mm]

<table>
<thead>
<tr>
<th>Material</th>
<th>Center Thickness</th>
<th>Edge Thickness</th>
</tr>
</thead>
<tbody>
<tr>
<td>PMMA</td>
<td>0.10</td>
<td>0.12</td>
</tr>
<tr>
<td>CAB</td>
<td>0.16</td>
<td>0.12</td>
</tr>
<tr>
<td>SA</td>
<td>0.15</td>
<td>0.13</td>
</tr>
<tr>
<td>FSA</td>
<td>0.14</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Due to limited tools, this design is not yet implemented in the current technology. This is subject for future development.

Figure 3.7: Dimensions of a scleral lens design with 5 curves (based on (37))
3.6 Alternative Design

The most important parameter is the oxygen transmission of the lens. Over time many scientists have searched for the ideal lens material. Thus, when designing an artificial iris, it is logical to select a material with a high Dk-value. However, the material may have a high Dk, but the lens can still have a very low oxygen transmission, due to the display. If choosing a high-Dk material is not enough, one can apply a central opening in the LCD to enhance the oxygen transmission to the cornea, as this region will never be darkened (the natural iris, never closes fully, and always has a certain opening, the pupil). The design and principle with the LCD is given by figure 3.8.

![Figure 3.8: artificial iris design with central opening: A. no activation; B. activation of one ring; C. activation of a couple rings; D. activation of all rings (based on (46))](image)

Problem with this fenestration is that the lenses are weakened mechanically with the risk of rupturing (37). Another disadvantage is that in some cases it causes discomfort, or visual disturbance on blinking. There is also the risk of stacking secreted tear fluid at the boarders of the hole. And finally, while applying an opening in the center, the lens loses its function as vision improve/correction.

All of these disadvantages can disappear by filling the hole in the LCD with the RGP material of the embedding biocompatible body. Further examination of this proposal is required in order to detect the factors that cause discomfort or impede the fabrication process.
3.7 Conclusion

We can resume that the scleral lens will have a diameter of 15.6mm, based on Jupiter design, so the lens possesses 5 curves, including an optical zone and a landing curve. This design was favored as it fits 90% of the eyes. Different thicknesses for center and edge of the contact lens are necessary to provide a high comfort level.

The landing curve is the only part of the lens that is in contact with the sclera. The optical zone will exist of a liquid crystal cell. On his terms, the cell will be divided into 5 or more ring structures. With increasing light intensity, more rings will be activated towards the center of the lens. Future research can replace the manual control device by a photosensitive system. The solar energy can be used for both activation of the system as for the power supply.

As for the composition, one should prevent leakage of the liquid crystals, as this can cause an allergic or irritating reaction. Therefore the liquid crystals are surrounded by a flexible substrate, forming the LCD, and then embedded in a biocompatible body. For the latter a fabrication process is suggested, namely late cutting buttons.

At the moment the flexible substrate is made of PET. However, this material has no oxygen permeability, which is an unacceptable property for modern contact lenses. Hence, a material with a higher Dk and thus biocompatible properties, should be proposed. But how do we know if the chosen material is biocompatible with the eye? This question, as well as a material proposal are discussed in the next chapter.

Finally, if material selection is not enough to provide a high enough oxygen transport, a design with a central hole in the LCD, wherein the hole is filed with RGP material of the embedding can be suggested. Filling the hole with RGP material enhances the oxygen transmission, like in modern contact lenses.
Chapter 4

Biocompatibility of the Artificial Iris
4.1 Material Choice

4.1.1 PET

This chapter focuses on the material of the flexible substrate. At the moment, the substrate is designed with poly-ethylene theraphtalate (PET). It is a plastic resin and the most common type of polyester. Two monomers, modified ethylene glycol and purified terephthalic acid, are combined to form the polymer called polyethylene terephthalate. The choice for PET was based on similar research, where they already worked with PET, like the development of an integrated biosensor in a contact lens(47)(48). It was also chosen due to its stable structure and resistance against high temperatures during the design process. Another advantage is that the material is convenient to handle, it owns a certain stiffness, but is still easily to manipulate. Furthermore, it can be made transparent and is versatile, it is light weighted, a high refractive index and has a high scratch resistance.

PET is widely used for the fabrication of plastic bottles, but also for producing foils, plastic cutlery, (figure 4.1), etc. Additional the polyester is recyclable. Up to 100% of a PET package can be made from recycled PET, and the material can be recycled again and again. It can be reused for the fabrication of bottles, but can also be made into fiber for carpets, fabric for t-shirts or fleece jackets, fiberfill for sleeping bags, winter coats, industrial strapping, food packaging, etc. So PET has a wide range of applications.

However, this material is not oxygen permeable and thus not biocompatible with the eye. Another disadvantage is the fact that the refractive index is birefrigent, which can blur the vision. For these reasons other materials must be evaluated.

4.1.2 TAC

Cellulose triacetate, or shortly TAC, is manufactured from cellulose and a source of acetate esters. During the fabrication of triacetate the cellulose is completely acetylated in contrast with regular cellulose acetate. Further, triacetate has a significantly greater heat resistant than cellulose acetate.

A notable remark is that the regularity of the cellulose chain and extensive hydrogen bonding between hydroxyl groups cause cellulose to be a tightly packed crystalline ma-
CHAPTER 4. BIOCOMPATIBILITY OF THE ARTIFICIAL IRIS

Figure 4.2: Cellulose triacetate

material, which is insoluble. Therefore cellulose cannot be processed in melt condition or in solution. However, cellulose derivatives in which there is less hydrogen bonding are processable (50).

The advantages are that the material has transparent properties and excellent optical clarity, aspects necessary for contact lens design. It possesses a good wrinkling resistance during temperatures lower than the glass temperature. Furthermore it also can resist high manufacturing temperature, up to 140\(^\circ\)C, has a good dimensional stability, and a good physical strength. Hence, the material is easy to manipulate during manufacturing.

In the past, TAC was especially used for the manufacture of movie rolls. Nowadays TAC is typically used for the design of glasses, the creation of fibers and film bases, membranes in devices for kidney dialysis and drug delivery systems. The latter 2 applications prove the acetate is biocompatible with human fluids, such as blood and stomach acid. As it is used as a semi-permeable membrane for osmotic drug delivery systems, the material must possess a certain permeability. In general as the acetyl content increases in TAC films, the permeability of the lens decreases (49).

But why choose TAC? It would have been better to examine materials like FSA or SA, as suggested in this dissertation, but, unfortunately, the availability of these materials was limited. Contacting companies, which provide lens materials wasn’t easy, and even more difficult was convincing them to corporate with the project by providing us with material samples. This did not raise their interest as they are used to deliver material in large quantities to major industrial players.

Due to these conditions, we were forced to search for alternative materials. Looking at the history, the ability to use TAC as a substrate has not yet been explored, nor is there evidence of unsuitability of TAC. Due to the exceptional qualities mentioned here, the prospects to use it for designing the flexible substrate seem positive.

Another advantage if choosing TAC as substrate material, is its availability as preprocessed films, which was not the case for SA or FSA. Firstly, one must investigate the biocompatibility of TAC as well as its effect on the fabrication process.
4.2 Testing the Lens

The Food and Drug Administration (FDA) is an organization that exercises a multifaceted role regarding the industry around medical devices, drugs, food cosmetics, and veterinary medicine. Its mission is to enforce the Federal Food, Drug and Cosmetic Act (Act). FDA not only acts as an industry regulator but also as a protector for the consumer and as a scientific advisor (51).

Before a product can be made available on the market, scientists must first determine a product’s ultimate safety profile. It takes about 10-15 years to develop one new product, e.g. a drug or an implant, from the time it is discovered to when it is available for treating patients. The product undergoes several testing stages. The first stage is to develop a material that meets the basic requirements of the device and collect data on materials comprising the device. The second step is to test this in vitro (cell culture) and/or in vivo on animals that are close related to the human structure. In this way it is possible to predict their behavior when in contact with the human body. The last step is to test this on humans. Firstly on a small group of volunteers, secondly at a large scale. If the product survives all these tests it is declared as safe and biocompatible with the human body. The product can finally be sold and used by patients.

Concerning contact lenses, these are regulated under the authority of the medical device amendments, which is the responsibility of the Center for Devices and Radiological Health (CDRH), within the FDA (51). The center is involved in standards development for all medical devices and regulation supporting a safe use of the device, including the contact lens area. For the latter, the contact lens must include testing the following properties and additionally these tests must have a positive result, according to FDA guidance (52), before its release on the market:

- oxygen permeability
- wettability
- mechanical properties
- water content
- color and light transmittance
- refractive index
- biocompatibility with the eye

The goal of the biocompatibility tests is to measure how compatible the device is with the biological system, in this case the compatibility of lenses with the eye. Thus we need to determine the influence of the lens and if it has any potentially harmful physiological effects. The tests include investigating cytotoxicity, sensitization arrays, ocular irritation
and implementation. But as this research contains cell culture, in vitro and in vivo research, these are the last steps to approve safe use of the contact lens. First the lens needs to meet all of the other tests, performed during the first stage of product development. As in vivo and in vitro tests are far away future materials, this thesis will focus on the primary tests.

In what follows, the different tests that are performed for this research (FDA recommended and self proposed tests) will be explained into more detail. First the theory is given, then the lab results are analyzed and discussed.

4.2.1 Chemical Properties

Thermogravimetric Analyzer

Precursory to the DSC, a thermogravimetric analysis (TGA) is performed to determine the critical temperatures where degradation occurs. TGA is a technique in which the mass of a substance, in this case lens material sample, is subjected to a controlled temperature program in a controlled atmosphere. Upon heating a material, the difference in mass is monitored as a function of the temperature. When mass loss occurs, it indicates that a degradation of the sample takes place (54).

The TGA instrument can quantify thermostability of polymers, their degradation temperature, their chemical composition and non-organic residue in polymer compounds (53). For this research only degradation of the polymers is monitored and no thermostability is examined.

Figure 4.3: Thermogravimetric analyzer
4.2. TESTING THE LENS

The TGA instrument exists of the following components (53):

- furnace (RT+5°C - 1000°C)
- micro balance
- autosampler tray for the sample
- control unit
- heat exchanger to control the temperature
- gas flow meters to control the flow rate

Supplementary, figure 4.3 shows a schematic arrangement of the components of a TGA instrument. The TGA curves are plotted with the mass change ($\Delta m$) expressed as a percentage on the vertical axis and normally temperature (T) or, when preferred, time (t) on the horizontal axis.

A sample of 1mg weight is placed on the auto-sampler tray. The test starts mostly at a temperature of 30°C (higher than room temperature). Calibration is executed with a rate of 10°C/min. Purging happens through balance housing with a dry inert gas (most commonly nitrogen). Also, only reactive/corrosive gases are introduced through sample area/furnace housing. The purge gases flow rate are for the furnace 60ml/min and for the balance 40ml/min. Thus the total flow rate is 100ml/min(53).

Lab Results

During this research, the TGA Q50 model of TA instruments is used. Prior, the program calculates the extrapolated onset temperature that denotes the temperature at which the weight loss begins. Figures 4.4 and 4.5 contain TGA-curves for PET and TAC, showing weight change as function of the temperature. For every mass variation, the temperature and weight change is given. As the temperature increases, water evaporates leading to decrease in weight of the sample.

The onset temperature indicates the start of a significant degradation. The degradation behavior of the two materials is different. PET has a very clear behavior with 2 delimited zones. PET undergoes thermal degradation beginning at 399°C and with a total mass loss of 86.42%. At approximately 800°C there remains a small amount of inert residue (7.43%).

TAC demonstrates relatively more complex decomposition behavior and shows three important zones(55), so degradation happens in 2 steps.

The first zone corresponds to losing its water of crystallization at 206.12°C. The second one represents the cellulose acetate decomposition. This reaction takes place over an
extremely narrow temperature range of only 20°C for 1% to approximately 78% conversion. The last zone is the carbonization of the degraded products to ash, with remaining an inert residue of 7.867%. Melts are formed at 369.68°C.

Figure 4.4: TGA degradation of PET and TAC
Figure 4.5: TGA degradation of PET and TAC
4.2.2 Physical Properties

Differential Scanning Calorimeter

The differential scanning calorimetry method (DSC) is used to determine the physical properties of a material, but also various chemical properties can be termed. It is important to determine these properties as the material must resist the manufacturing methods and be optimal for the human eye temperature. During the DSC test degradation of the material must be avoided. It consists of a DSC cell and a control unit, which are connected to a liquid nitrogen cooling accessory (LNCA). DSC is a software-controlled measurement and analysis of the heat flow. One must increase/decrease the temperature of a sample in comparison to a reference while the sample is heated/cooled at the same rate. Further, the tests are performed under a controlled atmosphere, i.e. helium.

Using DSC it is possible to determine endo- and exothermic processes (physical and chemical changes) like:

- melting and boiling points
- crystallization time and temperature
- percentage of crystallinity
- heats of fusion and reactions
- rate and degree of curing
- changes in heat capacity (glass transition)

A sample of 1mg weight is used, and the start temperature is approximately 30°C (higher than room temperature). Calibration is executed with a rate of 10°C/min. When reaching the liquid modus, the material is cooled down by the furnace to 500°C, and then it is cooled by air.

The test is performed twice. The first heating up is performed to erase the thermal history and to guarantee a good thermal contact with the tray. Subsequently the polymer is cooled under controlled conditions, as the cooling rate defines the crystallization, so the faster the cooling happens, the less crystalline the material will be. After this controlled cooling different samples can be compare accurately. Then, the cycle is repeated and the glass transition temperature and degree of crystallization can be determined.

Lab Results

During this research, the DSC Q2000 model of TA instruments is used. DSC curves of PET and TAC are shown in figures 4.6. The glass transition temperature is characterized by a dip in the curve. The point of recrystallization and the melting point result
in exothermal and endothermal peaks. For polymer the onset temperature is used as melting temperature and not the peak. Glass transition temperature is defined as the inflection point.

From figure 4.6 it can be concluded that TAC (131°C) has a higher glass temperature than PET (82°C). However TAC shows a weakening already before the glass temperature. Furthermore, PET will also reach faster his liquid state at a melting temperature of (241°C). At (271°C) TAC will become liquid.

![Figure 4.6: DSC curves of PET and TAC](image)
4.2.3 Oxygen Transmission

Coulometric method

The oxygen transmission rate, or OTR, of a contact lens can be measured according to the coulometric method or the polarographic analysis. As the latter is not used for this research, only the coulometric method will be explained. In general, coulometry is a dynamic electrochemical analysis for determining the amount of a substance released during electrolysis, in which the number of coulombs used is measured. The measuring devices is called a coulometric sensor.

Conceptually the test device operates as follows:

A closed chamber is on one side filled with dry nitrogen and on the other side filled with oxygen. The test film is clamped in centre of the chamber and acts as a membrane. The membrane separates the nitrogen flow from the oxygen flow. The partial pressure difference creates a driving force for the oxygen molecules to diffuse through the membrane to the lower pressure side. The test film determines the oxygen permeation, and is continuously measured by the coulometric sensor in the outgoing nitrogen flow.

The OTR test is taken under standard environmental conditions, namely at a temperature of 23°C and a humidity of 0%. The oxygen gas passes through the chamber during a given period, mostly 24h.

The method requires careful control of all measurement and environmental conditions to achieve reliable results. The following factors can be kept constant:

- Temperature
- Clamping force
- Oxygen concentration in the PBS

The following uncontrollable factors can cause measurement errors.
4.2. TESTING THE LENS

- Boundary layer effects
- Lens dehydration
- Edge effects

Lab Results

As the budget for a dissertation is limited and an OTR test is performed by specialized companies (especially in the sector of food packaging), and thus costs money (i.e.; approximately 310 euro), it was not possible to execute this test. As mentioned before it is actually the most important parameter for lens design and as Dk can be linked to the modulus and water vapor transmission (seen in section 2.3 page 27), these test will indirectly give an approximation of the oxygen transmission of the materials.

4.2.4 Water Vapor Transmission

Coulometric method

The coulometric method can also be used to determine the water vapor transmission rate, or WVTR, of the contact lens. In this case oxygen is replaced by mixture of water vapor with nitrogen, or also called wet nitrogen. The membrane defines the water vapor permeation, and is continuously measured by an infrared detector at the outgoing flow of the dry nitrogen. The principle of the WVTR test:

![Figure 4.8: Principle of WVTR test](image)

The WVTR test is taken under standard environmental conditions, namely at a temperature of 38°C and a humidity of 90%. The water vapor passes through the chamber during a given period, mostly 24h. Like the OTR test the method requires careful control of all measurement and environmental conditions to achieve reliable results, and the same factors can not be manipulated to avoid measurement errors. Values are expressed in g/m²/24day in metric (or SI) units.
Lab Results

Firstly it is worth mentioning that the test is performed with Aquatran tool. This tool is often employed in the food packaging industry and is used to measure the water vapor transmission through barrier layers. As these layers should not be permeable for water vapor, the Aquatran sensor is extremely sensitive to determine the smallest transmission. In contrast, the lens material for this dissertation should allow and even support this transmission. Therefore saturation of the sensor is possible, as the tool should determine the opposite for what it is designed for.

Aquatran operates in a temperature range of 5 – 50°C and a test range of 0.0005 – 5g/m²/day. To avoid saturation, the test surface is limited and a mask of 1m² is mount instead of the general 5m². Subsequently both samples are tested when already treated with pedot and SiO₂ to define the influence of these layers. Will they serve as barriers and lower the WVTR, or enhance the water vapor transmission?

The test is performed twice for each material sample. First, conditions of 23°C and 100% RH are set, and during the second trial the standardized conditions of 38°C and 90% are maintained.

For PET a WVTR of 5g/m²/day is reached for test conditions of 100% RH and 23°C. During the second trial a WVTR of approximately 12.1 – 12.6g/m²/day is reached.

Surprisingly, when investigating PET with coating, the WVTR becomes greater, so the pedot and SiO₂ layers do not serve as barriers. The latter can be explained by the plasma treatment.

As for TAC, the upper limit (250g/m²/day) was exceeded for both conditions, so we can conclude that the WVTR of TAC minimal 20 to 50 times greater is than the WVTR of PET. And also for coated TAC saturation occurs after 20 minutes.

In section 2.3 page 27 we made a careful inference that with an increasing WVTR an increasing OTR corresponds. So TAC will have a greater OTR than PET.
4.2. TESTING THE LENS

Figure 4.9: WVTR curve of PET without pedot and SiO₂ layers at 23°C.

Figure 4.10: WVTR curve of PET without pedot and SiO₂ layers at 38°C.
CHAPTER 4. BIOMATERIALS OF THE ARTIFICIAL IRIS

Figure 4.11: WVTR curve of PET with pedot and SiO$_2$ layers

Figure 4.12: WVTR curve of TAC with pedot and SiO$_2$ layers
4.2. TESTING THE LENS

4.2.5 Wettability

Surface Contact Angle Test

The wettability of a solid material depends on the surface energy and thus on the contact angle with the fluid. Therefore a surface contact angle test, or SCA test, is performed to define indirectly the wettability of the contact lens.

First the drop orientation is determined by choosing the method. There are 2 methods available for measuring the contact angle:

- sessile drop method for solid surfaces. The drop is 'sitting', resting on the table.
- captive bubble method for liquids. The drop is floating in a fluid against the sample bottom.

For this research the sessile drop method is chosen.

Secondly, the instrument is set up. The sample is mold on the holder so the baseline is perfectly horizontal. The test fluid is placed in the syringe. Further the camera angle is adjusted by using FTA standards. The protruding height is nominally the radius, so the contact angle is 90°. The ball diameter is an even millimeter number, such as 4 or 6mm, with a tolerance of approximately 2,5µm. The baseline must be applied manually. This is used to explore the sensitivity to the vertical baseline position. The next step is the calibration. Followed by the fluid loading. Set the syringe internal diameter so the pump will be calibrated. This is done on the 'pump tab'. And finally the drop is dispensed. When you pump more viscous fluids, the pumping rate must be slowed to accommodate the pressure drop across the needle. Mostly the pump program is aspirating at a rate of 0.125µl/s in the final phase of the run (57).

Two principal assumptions are made during this test (57). First of all, the drop is symmetric which means it is irrelevant from which direction the drop is viewed. And secondly, the drop is not in motion which means that interfacial tension and gravity are the only forces shaping the drop. Contact angles are calculated by the slope of the tangent to the drop at the liquid-solid-vapor interface line (19).

The angle is defined by the program as the angle made by the intersection of the liquid-solid interface and the liquid/air interface. It can be alternately described as the angle between solid samples surface and the tangent of the droplets ovate shape at the edge of the droplet. The profile of a symmetric shaped liquid drop is described by the Young-Laplace equation (60):

\[ \gamma_{lv} \cdot \left( \frac{1}{R_1} + \frac{1}{R_2} \right) = \Delta \rho \cdot g \cdot z(x,y) \]  \hspace{1cm} (4.1)

The smaller the measured contact angle Θ, the better is the wetting between liquid and solid. If the angle is much larger than 90°, the material has a bad wetting. However, when the angle is much smaller than 90°, and even approaches zero, it indicates a good wetting.
Lab Results

The test is performed using the OCA 20 instrument, a video based optical contact angle measurement system (58). With the OCA 20 instrument it is possible to calculate more than the contact angle. It permits to determine the surface free energy of solids and their components. But also the surface and interfacial tension of liquids can be calculated, as well as the wetting behavior of liquids on solid surfaces and the wetting envelope and work of adhesion.

On figure 4.14 the following components are represented:
4.2. TESTING THE LENS

- high speed video system with CCD camera (A)
- up to 4 manual or motor-driven and software controlled dosing units (B)
- sample stage, adjustable in three axis (C)

As the lens will be in contact with tear fluid, artificial tear fluid is composed. For the amount of 100ml tear fluid:

- 0.670ml sodium chloride
- 0.200ml sodium bicarbonate
- 0.008ml calcium chloride
- 100.0ml purified water

After applying a tear drop on the samples, the following results are obtained:

For every sample the test is performed 3 times for 30s. Every second an image is taken, so the end result is the average of the contact angles of every image. For PET:

- 75.6° with a standard deviation of 2.2°
- 74.9° with a standard deviation of 2.4°
- 75.4° with a standard deviation of 1.9°

For TAC:

- 60.4° with a standard deviation of 0.3°
- 58.6° with a standard deviation of 0.9°
- 61.7° with a standard deviation of 0.9°
CHAPTER 4. BIOCOMPATIBILITY OF THE ARTIFICIAL IRIS

The contact angle of the PET/tear drop interface is around $75^\circ$ and for TAC/tear drop interface $60^\circ$. The contact angle with TAC is smaller than with PET, so TAC is more hydrophilic than PET. We can not say that the TAC sample is hydrophilic as the tear drop is still convex. We can conclude that TAC has a better wettability than PET, which is a positive result, as a good wettability is necessary for contact lenses.

However, after comparing the TAC sample measurements taken before and after 30 seconds (figure 4.16), we see the baseline moves upwards. This means the TAC film takes up some of the tear fluid and the material swells. If this swelling is of large dimensions it can cause discomfort for the patient as well as lower the quality of vision. Therefore a water content test is performed.

![Figure 4.16: SCA measurements of TAC before and after 30 seconds.](image)

### 4.2.6 Water Content

Six Samples of 1x1cm are prepared for each material. All of the samples are weighed before the test. Sequentially, they are placed in 2ml of artificial tear fluid. Every 10min

<table>
<thead>
<tr>
<th>Weight measuring</th>
<th>PET</th>
<th>TAC [mg]</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.61</td>
<td>5.91</td>
<td></td>
</tr>
<tr>
<td>7.02</td>
<td>6.20</td>
<td></td>
</tr>
<tr>
<td>6.70</td>
<td>6.21</td>
<td></td>
</tr>
<tr>
<td>7.20</td>
<td>6.60</td>
<td></td>
</tr>
<tr>
<td>6.98</td>
<td>6.44</td>
<td></td>
</tr>
<tr>
<td>6.88</td>
<td>6.75</td>
<td></td>
</tr>
</tbody>
</table>

the samples are weighed. During the test, the tear fluid and the samples are placed in an environment similar to that one of the human eye, thus conditions of $37^\circ$C and Ph of 7.2-7.4 are maintained.
Lab Results

As expected PET absorbs little to almost no tear fluid and is satisfied after 20min. In contrast, TAC expands to 20% of its volume, but will be stable after 40min. This expansion is not significant and doesn’t exceed the maximal thickness of 120 µm. So it will not disturb the eye conditions or result in discomfort.

Figure 4.17 illustrates the results.

![Figure 4.17: water content of PET and TAC measured every 10min.](image-url)
4.2.7 Color and light transmittance

Spectrophotometer

The color and light transmittance of a contact lens is examined with a spectrophotometer. As light passes through the monochromator the chosen wavelength is selected, sequently the light wave travels through the sample, after which it is detected how much light waves were able to pass through the material. The more light waves are detected, the higher the light transmittance through the material is and thus the higher the refractive index.

![Principle of the spectrophotometer](image)

Figure 4.18: Principle of the spectrophotometer

Beer Lamberts law represents the relationship between transmittance and intensity of the light wave

\[ T = \frac{I}{I_0} \]  

(4.2)

with \( T \) the transmittance and \( I \) the (initial) intensity.

Lab results

For this test Uvikon xl of Bio-tek instruments is used. As figure 4.19 shows, TAC has a higher light transmission than PET. This is a positive result, as PET already showed an excellent refractive index, however it is birefringent. Thus an even higher light transmission for TAC, which possesses a single breaking index, can only enhance choosing TAC above PET.
4.2. TESTING THE LENS

4.2.8 Mechanical Properties

Universal Testing Machine

The universal testing machine or material testing machine can define the tensile stress and compressive strength of materials and consists of the following components, represented by figure 4.20

When a material is subjected to a high load, it undergoes a certain deformation, and
when this load is repeated frequently, the deformation can become permanently. In the testing of contact lenses a valuable examination is the time-dependent deformation and subsequent recovery under periods of load and removal. During repeated load, the viscoelastic nature of contact lens materials can cause permanent deformation, which will have a negative effect on the stability of the contact lens during wear (29).

Figure 4.21 shows a typical stress-strain behavior of a polymer subjected to a tensile test, taken over the entire strain range and the ultimate failure. For sufficiently low stresses and strains, the polymer behaves as a linear elastic material. In this zone the material will return to its initial dimensions after load release, so the deformation is only temporary.

The point where the behavior starts to be non-linear is called the yield point and indicates the onset of plastic (i.e. permanent) deformation. Beyond the yield point the material stretches out considerably and a "neck" is formed; this region is called the plastic region. Further elongation leads to an abrupt increase in stress (strain hardening) and the ultimate rupture of the material. At the rupture point the corresponding stress and strain are called the ultimate strength and the elongation at break, respectively. The stress-strain behavior of a polymeric material depends on various parameters such as molecular characteristics, microstructure, strain-rate and temperature.

![Stress-strain curve for polymers](image)

Figure 4.21: typical stress-strain curve for polymers (based on (59))

Each sample has a thickness of 0.05 mm, similar to the thickness used for the flexible substrate, and a width of 18 mm. The extension rate is set on 1 mm/min.

**Lab Results**

The test is performed with an Instron type 5885H.
4.2. TESTING THE LENS

As expected, PET has a greater load resistance than TAC, which possesses brittle characteristics compared to PET. This could be predicted as TAC was easy to tear during handling and cutting. However, TAC shows for small load a more elastic behavior than PET. So, although PET has greater mechanical properties than TAC, it does not influence the choice for TAC as substrate material, as the contact lens will not be subjected to extreme deformation by the patient. During fabrication the material will have to resist greater forces, but here the material is used in a higher temperature range, namely around its glass transition temperature, which means it will be more elastic.

In section 2.3.1 page 27 a link between Dk and modulus for rigid materials was given. It says that the greater the modulus, the lower the Dk value. Hence, TAC must have a greater Dk-value than PET.

When applying the young’s modulus equation (stress over strain) TAC has a modulus of almost 8 MPa, which is still high compared to hydrogels, which have a modulus of approximately 0.3-1.1 MPa.

Notable is the fact that it is possible that TAC has a higher value than is represented here, due to already existing micro-cracks that could be initiated during the cutting out of the samples or fabrication process of the material. However, the difference will not be significant.
CHAPTER 4. BIOCOMPATIBILITY OF THE ARTIFICIAL IRIS

4.3 Fabrication process with TAC

To finish, the fabrication of the flexible substrate is performed with TAC instead of PET. The different fabrication steps of 3.4 on page 48. However, as this method is based on the properties of PET, some complications occurred when replacing PET by TAC.

Firstly, during the cleaning, we observe that acetone is not a good cleaning choice, as the TAC-material dissolves completely. Thus ethanol is chosen alternatively.

After lamination, one can see that several air bubbles have formed underneath the layer (figure 4.24 A.). This is a result of a bad adhesion behavior. To improve the adhesion of TAC a thermal treatment is performed. After a thermal treatment of 5 min up to 95°C, the air bubbles disappear (figure 4.24 B.), which implies that the TAC-film must possess a certain oxygen permeability.

Also during molding some complications appear. Normally the material has to be heated above its glass transition temperature, which is 140°C for TAC, to easily deform the materials to the shape of the lens. Therefore TAC is heated up to 150°C. However, TAC becomes very soft and adapts easily every defect (a groove or a pit) of the mold as can be seen at figure 4.25. When lowering the temperature to 111°C the material becomes less editable and the lens shows a more homogeneous surface.

This strange observation can be explained by the TGA test results in 4.2.1 page 60. One can see that TAC starts already weakening at a temperature of 111°C, thus it becomes already deformable at this temperature. Therefore the temperature can be lowered, so the material is deformable, but still not to weakened to adapt every error of the mold.
4.4 Conclusion

A final complication appears during the pedot patterning, which was not as successful as with PET. More research is required to solve this complication.

4.4 Conclusion

Although PET has many advantages, there are 2 main reasons why PET is an unacceptable choice as substrate material. Firstly, it does not allow oxygen transmission, and secondly it has a double breaking refraction, which causes a blur vision. Due to limited budget and tools, the common materials used in lens industry were difficult to find.

Then TAC raised our interest to use as substrate material, as it showed a lot of good properties. It owns a high refractive index, is already used as biomaterial and has a great availability as preprocessed film. So parameters of TAC were examined, such as the wettability, mechanical properties, water vapor transmission, etc. Unfortunately the oxygen transmission could not be performed due to limited budget.

Overlooking the test result, we can conclude TAC scores better than PET concerning biocompatibility. First of all it shows a better wettability and a high single breaking refractive index, which solves the birefringent problem of PET. Secondly it has a very high water vapor transmission, which can relate to a high oxygen transmission. Also the fact that it has a lower young’s modulus than PET, suggests a higher oxygen permeability than PET. Further TAC possesses a better wettability. It uptakes some fluid, but this is limited.

Consequently, TAC is definitely a good alternative for the substrate, compared to PET. In the future, more research must be done concerning its oxygen transmission, the fabrication methods, attraction of proteins, etc.
Chapter 5

Conclusion/Discussion
The human eye can be seen as one of the most important sensory organs of the human body, as we use it during almost all activities in our life. When vision is obstructed, it limits the patient's personal freedom excessively. This project investigates a treatment for people with a damaged iris, due to a disease, trauma, or tumor. The iris controls the incoming amount of light and helps focusing the image. Persons with a damaged iris are very photosensitive, as they can no longer control the amount of incoming light. For them an active solution with a total relief of photosensitivity is offered by this study: the artificial switchable iris, a contact lens, which adapts to light intensity, and thus mimics the function of the natural iris.

However, the study of the latter is still in its infancy, so there are still many questions that need to be answered. Within this dissertation, two questions were studied, focusing on the biocompatibility of the lens.

- What are the design parameters of the artificial iris for a correct implementation?
- Is the lens biocompatible with the human eye and which parameters define this?

**Implementation of the Artificial Iris**

As for the first question, one must know that patients with a damaged iris additionally suffer from a high sensitive and irregular corneal surface. This important fact eliminates already every lens design with bearing on the cornea and thus a scleral lens design is suggested. Currently, the Jupiter scleral lens design is launched by the company Visionary Optics, which has a diameter of 15.6 mm and fits 90% of the eyes. Therefore, the Jupiter lens is used as basis for our artificial iris design. As the lens has a reasonable large size, it must possess certain stiffness. Consequently, the lens will be made of rigid material. Because of limited tools, this design is not yet implemented in the current technology and thus is subject for future development.

Designing is not only determining the dimensions but also selecting the proper composition and fabrication process. At the moment, the lens has three components. The first component is the driver, which covers the energy and LCD driving. The LCD is the second component and consists of the liquid crystals sealed in a flexible substrate. The last component encloses the first two and is the biocompatible body, made of a rigid material.

Due to the limited availability of fabrication methods, only a proposal could be made for the fabrication of the lens. Lathe cutting is a commonly used technique for the construction of rigid lenses and uses buttons. The buttons are individually mounted on spinning shafts and are shaped with computer-controlled precision cutting tools. After the front and back surfaces are shaped with the cutting tool, the finished lenses then undergo quality assurance testing.

**Biocompatibility of the Artificial Iris**

When investigating the second question, concerning the biocompatibility, one must first
collect and analyze the parameters, which determine a good contact lens. Six properties define the biocompatibility of the contact lens:

- a high oxygen permeability
- a good wettability
- a balanced water content (only applicable for soft lenses)
- little to no attraction of proteins and fats
- a high refractive index
- good mechanical properties, meaning, a good stiffness- flexibility balance

The parameter with the greatest influence is the oxygen permeability. The latter is necessary as the eye depends on the contact with its environment for oxygen supply. Therefore the oxygen transmission through the lens will be the main property the lens material must have. The initial biocompatibility study included the study of material use for the flexible substrate as well as for the biocompatible body. However, some complications crossed the road and thus the focus of this dissertation is limited to the material choice of the flexible substrate.

At the moment PET is used. Although PET has many advantages, there are 2 main reasons why PET is an unacceptable choice as substrate material. For one thing, it does not allow oxygen transmission, and secondly it has double breaking refraction, which causes a blur vision. Due to limited budget and tools, the common materials used in lens industry were difficult to find.

TAC was proposed as alternative material. Overlooking the test result, we can conclude TAC scores better than PET concerning biocompatibility. First of all it shows a better wettability and a high single breaking refractive index, which solves the birefringent problem of PET. Secondly it has a very high water vapor transmission, which can relate to a high oxygen transmission. Also the fact that it has a lower youngs modulus than PET, suggests higher oxygen permeability than PET. Further TAC possesses a better wettability. It uptakes some water, but this is limited. Consequently, TAC is definitely a good alternative for the substrate, compared to PET. In the future, more research must be done concerning its oxygen transmission, the fabrication methods, attraction of proteins, etc.

**Future Development**

We can conclude that the road to a contact lens with an integrated LCD is still long, there are still a lot of questions and pathways to investigate. In the extension of this project, we must examine the proposed fabrication process, determine the oxygen transmission onto more detail, implement the suggested dimensions and fabrication process.
There are materials, which possess higher Dk-values, like silicone acrylate and fluor-silicone acrylate, and will probably be better options, but the limited availability of these materials did not allow to explore these possibilities. Hence, investigating other acceptable materials is subject for future research.

Nevertheless, TAC is a step in the right direction. Based on the test results of this dissertation we can decide that, in comparison with PET, TAC is a better material choice for the flexible substrate. Therefore, we recommend replacing PET by TAC in all further research.

In the future, such contact lenses may also be used for other purposes than the treatment of damaged irises. It can even be used for bifocal designs or technological gadgets. The lens will receive data from external platforms, like cell phones or computers, and provide visual information to the consumer. The long-term goal is to create a display embedded in a contact lens that can be worn comfortable and without complications over a long time of wear. The contact lens will include a pixel array, optical improvements for the patient, an antenna for receiving the data, a power base like a battery or wireless charger, and pixel control.

We can conclude that there is still a lot of research needed, but according to this dissertation there is great promise in applying a LCD in contact lenses, concerning the biocompatibility part. The knowledge gained during this investigation can also be extended to other applications.
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