The Artisan aphakia intraocular lens in the paediatric eye

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Chapter 1

GENERAL INTRODUCTION
1.1 INTRODUCTION

A clear and well-centered crystalline lens is essential for good vision. Blurring of the lens, resulting in a decrease in quality of vision, is called a cataract. Cataracts occur mainly in elderly people, but can also appear in newborns and children, in which cases they are called congenital or juvenile cataracts. A decrease in vision can also be caused by a dislocation of the crystalline lens, which can be a symptom of syndromal diseases, and is often encountered in Marfan syndrome. Dislocation can also be caused by trauma to the eye. In the case of trauma, the lens dislocation is often accompanied by a cataract.

This thesis reports the follow-up of children with congenital or juvenile cataracts and children with crystalline lens dislocation due to either trauma or Marfan syndrome who underwent lens surgery with the implantation of an artificial intraocular lens to replace the crystalline lens which was either dislocated or affected by a cataract.

1.2 THE CRYSTALLINE (NATURAL) LENS

1.2.1 Anatomy and function

The crystalline lens is a transparent and biconvex structure, situated between the iris and the vitreous body. It is held in place by a suspensory system composed of suspensory ligaments, the zonulæ of Zinn, which are attached on the one side to the ciliary body, and on the other to the equatorial region of the natural lens (Figure 1). The principal component of the suspensory ligaments is the glycoprotein fibrillin².

Figure 1. The position of the crystalline (natural) lens in the eye, and its relation to the ciliary body, the suspensory ligaments and the cornea
Adapted from: Encyclopedia Britannica.
The lens continues to grow throughout life\textsuperscript{1,3}. At birth, the lens has an equatorial diameter of 6.5 millimeter and an anteroposterior thickness of 3.5 millimeter. The crystalline lens has a single layer of epithelial cells at its anterior and is completely enveloped by a collagenous capsule, the basement membrane of the epithelium. The epithelial cells at the equatorial region of the lens develop throughout life to form spindle-shaped secondary fibres. Newly formed fibres have a complicated architectural form. They are arranged into zones where fibres growing from different directions meet and form sutures. The oldest cells are most central, whereas the younger cells are more peripheral. Both an embryonic and a fetal nucleus are present at birth. The fetal nucleus is distinguished from the embryonic nucleus by Y-shaped upright sutures anteriorly and inverted Y-shaped sutures posteriorly. Lens fibres developing after birth contribute to the adult nucleus. The lens nucleus is made up of densely compacted lens fibres\textsuperscript{4}. The cortex is comprised of the most superficial and youngest layers between the capsule and the adult nucleus\textsuperscript{1}. The lens fibres in the lens cortex are less densely packed. By early adulthood, the lens has a stable equatorial diameter of approximately nine millimeters and an anteroposterior depth of five millimeters\textsuperscript{4}.

The natural lens contributes about 15-20 diopters (D) of the approximately 60 D of convergent refractive power of the average human eye. When the natural lens is removed from the eye during lens surgery, there is a loss of convergent refractive power. Aphakic eyes are hyperopic, except for eyes that are extremely myopic before lens surgery. The aphakic refractive error can exceed 30 diopters, depending on the biometric properties of the eye (mainly the axial eye length and curvature of the cornea), and the age of the patient. In order to achieve good vision, aphakia should be corrected. This can be done using glasses, contact lenses, and artificial intraocular lenses. In this thesis, the focus is on the correction of aphakia in children with intraocular lenses.

1.2.2 Abnormalities of the crystalline lens in children

There is a wide range of abnormalities in size, shape, position, and transparency that can occur in the crystalline lens. Some of these abnormalities, such as primary aphakia, lens coloboma, and microspherophakia are seen rarely. Other abnormalities, such as cataracts and dislocated lenses, are more commonly encountered by the ophthalmologist.

In this thesis, paediatric patients with aphakia after surgery for cataract (congenital, juvenile and traumatic) or lens dislocation (either due to Marfan syndrome or trauma) are reported. These lens abnormalities will therefore be discussed in greater detail.

**Cataracts**

The most common anomaly found in the crystalline lens is a cataract. In case of cataract,
Opacification of the crystalline lens results in mild to severe loss of vision.

In adults, the most common cause of cataracts is aging. Less frequently, adult cataracts result from other causes such as trauma, metabolic disease (diabetes), uveitis, glucocorticoid drugs, or previous intraocular surgery such as pars plana vitrectomy.

In children, the cause of cataracts is unknown (idiopathic) in most cases. Among the most common non-idiopathic causes of bilateral cataracts are autosomal dominant hereditary cataracts (about 30% of all cases), metabolic disorders, genetically transmitted syndromes, and intrauterine infections. Unilateral cataracts are mostly idiopathic but can be associated with other lens or eye abnormalities, such as posterior lenticonus and persistant fetal vasculature. Cataracts in children can be the result of a blunt or perforating trauma, in which case the cataract is almost always unilateral. In children, bilateral cataracts are more common than unilateral cataracts. A complete list of etiological causes of paediatric cataracts can be found in Table 1.

The incidence and prevalence of congenital and infantile cataracts varies from country to country. The prevalence has been reported as 1-15 per 10,000 children worldwide. A birth prevalence of bilateral cataract of 1-3 per 10,000 in industrial countries is estimated, a number which is likely higher in developing countries, because of an increased exposure to infectious disease and other potential etiologic factors in the latter countries. Each year almost three children of every 10,000 born in the United Kingdom will have a congenital or infantile cataract (both unilateral and bilateral) diagnosed by their first birthday. An adjusted cumulative incidence at one year of age of 2.5, at five years of age of 3.2 and at 15 years of age of 3.5 per 10,000 was reported. The incidence of congenital cataracts (both unilateral and bilateral) reported in Sweden was 36 cases per 100,000 live births.

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Table 1. Etiology of cataracts in childhood
Adapted from: Taylor, Paediatric Ophthalmology and Strabismus.


Traumatic cataracts
Both blunt and perforating trauma can cause cataracts. These traumatic cataracts can be a part of a larger trauma to the anterior and posterior segment, including damage to other tissues, such as the cornea and iris tissue, vitreous and retina. Eye injuries are a significant cause of ocular morbidity in children\textsuperscript{11-13}. In children younger than 14 years old the majority of eye traumas occur at home, caused by tools or toys in younger children and as a result of sport accidents in older children\textsuperscript{12}. Boys are more frequently involved in eye trauma, with a ratio of approximately 3:1\textsuperscript{12,14-16}. Blunt trauma is more frequently encountered than perforating trauma in children\textsuperscript{12,16}.

Lens dislocation (ectopia lentis)
Dislocation of the crystalline lens can be caused by trauma or can be due to non-traumatic causes. Trauma is the most common cause of acquired lens dislocation. Both blunt and penetrating eye injuries can cause dislocation of the lens.

Non-traumatic lens dislocation can occur as an isolated anomaly (simple \textit{ectopia lentis}), or can be associated with pupillary abnormalities in the ocular syndrome \textit{ectopia lentis et pupillae}, or can be a part of a systemic disease, storage disease or syndromal abnormality. Lens dislocation is a known feature in, to name but a few conditions, Marfan syndrome, homocysteinurie, and Weill Marchechani syndrome.

The systemic disorder that accounts for most cases of lens dislocation is Marfan syndrome\textsuperscript{17}. Dislocation of the crystalline lens occurs in about 50-80\% of patients with Marfan syndrome\textsuperscript{18-20}. Marfan syndrome is a connective-tissue disease, inherited in an autosomal dominant manner, and mainly caused by mutations in the \textit{FBN1} gene, encoding fibrillin. It affects the optical, skeletal, and cardiovascular systems\textsuperscript{21}. Marfan syndrome has a frequency of approximately 1 in 10.000 live births\textsuperscript{17,22}. The clinical diagnosis is made using the Ghent nosology\textsuperscript{23,24}, a set of clinical criteria outlined by international expert opinion to facilitate accurate recognition of this genetic syndrome. The Ghent nosology comprises a set of major and minor manifestations in different body systems\textsuperscript{24,25}. The major ophthalmic diagnostic criterion is dislocation of the crystalline lens.

1.3 Crystalline lens/ cataract surgery and intraocular lenses

1.3.1 Introduction
Nowadays, cataract surgery is one of the most common elective surgeries performed. In the US, it is estimated that almost 1.5 million adult cataract surgeries are performed each year\textsuperscript{26}. In the Netherlands the number of eyes operated on to solve cataracts is approximately 150.000 per year\textsuperscript{27}. Cataract surgery is a technique described since ancient...
history. During the latter half of the past century, cataract surgery has evolved greatly. The development of phacoemulsification and the artificial intraocular lens could be considered as the two most important developments in the ophthalmic surgical field.

1.3.2 Historic overview of surgical techniques

The first reports on crystalline lens treatment date from the fifth century BC. At that time, the goal of the technique of couching was to dislocate the crystalline lens away from the visual axis, into the vitreous humour. In the mid 1600s extracapsular cataract extraction (ECCE) was developed. With this technique, the crystalline lens was removed from the eye, rather then dislocated into the vitreous. The anterior lens capsule was opened and the lens nucleus was expressed through a corneal wound. All procedures were performed without antiseptics or anaesthetics.

From the mid 1700s intracapsular cataract extraction (ICCE) was preferred. The lens with its capsule was removed from the eye in toto, using manual pressure and later more advanced devices as erysophakes, cryoprobes and specialised forceps. Problems related to retained lens material, causing inflammation, as encountered with ECCE, were solved by this ICCE technique. However ICCE also had disadvantages and high rates of complications.

With the introduction and development of irrigation and aspiration systems (latter half of 19th century, first half of 20th century) it became possible to remove all cortical lens material after the lens nucleus was removed. This caused a shift from ICCE to modern methods of ECCE. After opening the anterior lens capsule and removing the nucleus, the remaining cortex could now be removed from the capsular bag with these irrigating devices. Advantages of the modern ECCE technique comprised a smaller incision, maintenance of a separation between anterior and posterior compartments of the eye, thus eliminating forward movement of the vitreous, and more possibilities for intraocular lens (IOL) positioning. The introduction of the binocular operating microscope (mid 20th century) fine suture material, and modern sterilization techniques increased surgical success and reduced the number and the severity of complications.

In 1967, Charles Kelman invented phacoemulsification. Phacoemulsification uses an ultrasonically driven tip to fragment and emulsify the lens nucleus. The lens fragments are then aspirated through a hollow needle and removed from the eye. After nucleus removal, the cortex is removed using an automated irrigation/aspiration system. Viscoelastic agents are now used to create space in the anterior chamber of the eye, thus preventing contact between the tip of the phacoemulsification handpiece and the corneal endothelium. This modern ECCE technique made it possible to remove the hard nucleus from the eye through a small incision, and resulted in faster surgery, less complications and faster recovery and improvement of visual acuity. The conversion to phacoemulsification led to a substantial increase in cataract surgery during the
period of 1980 tot 2004\textsuperscript{16}. During this period the number of cataract operations that were performed in the Netherlands increased from approximately 10,000 in 1980 to approximately 135,000 in 2004\textsuperscript{27}. With the further development of instruments and intraocular lenses which can be inserted through an incision of only a few millimetres, we are now able to create self-sealing corneal wounds. Efforts to reduce incision size have led to the development of ‘microincisional’ cataract surgery (MICS), a technique that permits cataract removal through incisions ranging from 1.0–1.5 millimetres\textsuperscript{33}.

1.3.3 Historic overview of the use of intraocular lenses

Before 1949, cataract surgery resulted in aphakia, and patients were destined to wear high hyperopic spectacles that were of considerable weight and that caused magnification and distortion to the peripheral vision. Scleral contact lenses and eventual corneal lenses were used when available and possible\textsuperscript{29}.

The development of IOL implantation began in 1949, with the identification of polymethylmethacrylate (PMMA) as an inert material, which could serve as a substitute for the crystalline lens. With the observation that fragments of plexiglass (PMMA, Perspex) from shattered cockpit windshields were tolerated well by the eyes of British pilots in World War II, Sir Harold Ridley began the era of IOL implantation\textsuperscript{34}. After the first implantation of a Ridley lens in 1949, numerous surgical techniques, intraocular lens designs for placement in the anterior and posterior chamber, and materials were developed and used\textsuperscript{35}.

From 1975 to the mid eighties rapid and highly innovative IOL developments took place. At the same time phacoemulsification was becoming more widespread. The Artisan lens was introduced by professor Jan Worst from Groningen, the Netherlands, in 1978. Earlier Cornelius Binkhorst, also from the Netherlands, pioneered the use of pupil and iris fixated IOLs.

The first generations of intraocular lenses were made of PMMA. PMMA is a rigid material and lenses made from it require a large incision and hence sutures to seal the wound. Foldable IOLs, made of silicone and acrylic, were introduced in the 1980s\textsuperscript{29}. These IOLs could be implanted in the eye through smaller incisions thus allowing sutureless surgery and reduced astigmatism. The availability of small-incision foldable IOLs was the factor that influenced the majority of ECCE surgeons to convert to using phacoemulsification.

From 1986 to 1997, PMMA was the preferred optic material by members of the American Society of Cataract and Refractive Surgery (ASCRS). In 1998, it dropped to second place and acrylic became the preferred optic material. In 2002, acrylic was preferred by the majority of cataract surgeons\textsuperscript{36}.

Cataract surgery has improved tremendously and doctors and patients expectations have grown accordingly. The postoperative goals have shifted from improved vision...
towards perfect vision, preferably without glasses. After the implantation of single focus intraocular lenses the patient is dependent on glasses for near or for far. To overcome this possible disadvantage intraocular lenses that provide refractive correction for both near and distance, accommodating and multifocal IOLs, are being developed\textsuperscript{38,39,40}.

1.4 **CRYSTALLINE LENS SURGERY AND INTRAOCULAR LENSES IN CHILDREN**

1.4.1. *Surgical technique in paediatric eyes*

Many surgical techniques used in adult cataract surgery have been adopted and modified for the paediatric patient\textsuperscript{41}. In comparison with adult eyes, paediatric eyes have greater elasticity of the lens capsule and lower scleral rigidity. These differences make the anterior capsulotomy more difficult and cause a narrower and less stable anterior chamber. In children there is a higher incidence of posterior capsule opacification, necessitating primary management of the posterior capsule \textsuperscript{41}. The advent of vitreous suction cutting devices in the mid 1970s to the early 1980s revolutionized paediatric cataract surgery\textsuperscript{42,43}. These devices provided the new possibility of managing the posterior capsule and anterior vitreous more easily, and thereby addressed the complication of posterior capsule opacification.

*Preferred practices*

The current consensus in paediatric cataract removal is that the surgery includes a superior limbal or scleral incision, manual curvilinear anterior capsulorhexis, irrigation and aspiration of the lens material and sutured closure of the wound\textsuperscript{41,44,45}. The majority of surgeons perform a posterior capsulotomy and an anterior vitrectomy, in particular in patients younger than 5-7 years of age\textsuperscript{41,45,46}. The use of high viscosity viscoelastic agents to maintain anterior chamber stability and to deal with the high vitreous pressure in the paediatric eye, is recommended in paediatric cataract surgery\textsuperscript{41,45,46}. The use of Trypan blue dye, to stain the lens capsule, is shown to improve the rate of complete capsulorhexis\textsuperscript{47}, and is helpful when a red reflex is absent.

1.4.2 *Complications after surgery*

**PCO**

The most frequent complication after paediatric cataract surgery is posterior capsule opacification (PCO), also known as visual axis opacification (VAO). The incidence of PCO decreases with increasing age of the child\textsuperscript{41}. To reduce the incidence of PCO, primary management of the posterior capsule and anterior vitrectomy are recommended, especially in children below the age of 5-7 years.
Glaucoma

Glaucoma is one of the most severe complications after cataract surgery in children. It is most common encountered in children that were operated at a very young age. Several studies report an increased risk of secondary glaucoma when surgery has been performed in the first months of life.48-51

Inflammation

In children, there is a more pronounced inflammatory reaction after eye surgery, even more so in newborns and infants. Antimicrobial, and anti-inflammatory eye drops are used during the postoperative weeks, to prevent fibrinous uveitis and endophthalmitis. Subconjunctival or intracameral injection of antibiotics and steroids after paediatric cataract surgery is recommended by some authors,5,52,53 also because frequent administration of eyedrops can be challenging in children and can cause missed doses and non-compliance.

Endothelial cell loss

The normal decline in endothelial cell density in adults has been reported to be 0.3% to 0.6% per year. After cataract surgery in adults the rate of endothelial cell loss continues at a higher rate of about 2.5%. A normal decrease in endothelial cell density ranging from 1.1% to 2.9% per year was reported in infancy and childhood. No reports on the decline in endothelial cell density after paediatric cataract surgery can be found. Since 1990 only a few studies on the corneal endothelium after paediatric cataract surgery have been published. In 1992 Kora et al.57 reported an endothelial cell loss of 6%, three years after cataract extraction with implantation of an in-the-bag posterior chamber IOL in six paediatric eyes. Six years later Basti et al.58 presented a prospective study on the corneal endothelium of 18 eyes after surgery for congenital or developmental cataract and implantation of an in-the-bag posterior chamber IOL. They reported an endothelial cell loss of 5.3-7.5%, three months after surgery. More recently, two retrospective studies reporting the endothelial cell density after congenital cataract surgery without IOL implantation, were published59,60. In both retrospective studies no significant differences in endothelial cell density were found in the eyes of patients operated for congenital cataracts when compared to the eyes of non-operated control patients after a mean follow-up of 10.7 years59 and 13 years60.

1.4.3 Intraocular lenses in children

History and current preferences

Prior to the era of intraocular lens implantation in children, aphakia was corrected by aphakic glasses (Figure 2) or contact lenses. Aphakic glasses are rarely used nowadays. Contact lenses remain a useful means in the treatment of aphakia, especially in infants.
who are operated for congenital cataract extraction shortly after birth or during the first year of life\textsuperscript{61,62}.

Hiles and Binkhorst pioneered the use of IOLs in children in the 1970s and 1980s. Irido-capsular fixation, two-loop Binkhorst IOLs, iris clip IOLs and iris sutured lenses were implanted before 1982\textsuperscript{63,64}. Since 1982, posterior chamber lenses were considered appropriate for paediatric use\textsuperscript{64}, yet before the mid 1990s, IOL implantation in children was mostly investigational\textsuperscript{63,65}.

Paediatric IOL implantation evolved as adult IOL implantation techniques and IOL materials improved. An increasing number of surgeons now accept IOL implantation for the correction of aphakia in children. In fact, IOL implantation has become a standard procedure in older children\textsuperscript{43,65}.

In 1994, 46\% of members of the American Association of Paediatric Ophthalmology and Strabismus (AAPOS) and 27\% of members of the ASCRS responded on a survey that they were implanting IOLs in children. The majority implanted lenses in children older than six years\textsuperscript{66}. Six years later, in 2001, 89.5\% of AAPOS respondents and 93.8\% of ASCRS respondents implanted IOLs in children. At that time 81.9 \% of AAPOS members and 54.2\% of ASCRS members had implanted an IOL in children under the age of 2 years old\textsuperscript{45}.

Thus, intraocular lenses are being increasingly used to optically correct aphakia in children with good visual results. However, their use during early infancy remains controversial because of the increased incidence of complications in these infantile eyes, and the difficulty of accurately predicting the most appropriate lens power to insert. The number of surgeons implanting lenses in children under two years of age has increased\textsuperscript{44,45}, yet primary IOL implantation in infants, especially under the age of 6
months, is still controversial and caution when considering IOL implantation in infants is advocated\(^{44,67}\).

**IOL material in children**

PMMA IOLs were implanted in paediatric eyes in the 1980s and early 1990s. Since more than 50 years PMMA, as an inert material, has proved to be well accepted by the human eye. The reduced incidence of posterior capsule opacification (PCO) after implantation of hydrophobic acrylic IOLs in adults, prompted paediatric cataract surgeons to use these lenses in paediatric eyes\(^{42}\). Also in children less PCO was reported after implantation of hydrophobic IOLs\(^ {68}\). Another advantage of these foldable lenses, was the possibility of smaller incision surgery\(^ {65}\). The hydrophobic acrylic IOL is nowadays the first choice of many paediatric cataract surgeons\(^ {68-73}\). The 1-piece AcrySof IOL was preferred for in-the-bag implantation, and the 3-piece AcrySof IOL for sulcus fixation in a survey among US and non-US member of the American Association for Paediatric Ophthalmology and Strabismus\(^ {74}\).

1.4.4. Special indications for intraocular lenses in children

**Secondary implantation of an intraocular lens in children.**

Primary IOL implantation has become a standard procedure in children. Yet in the case of cataract surgery in infants and very young children, many surgeons still choose to leave the eye aphakic (see chapter 1.4.2). These eyes are candidates for secondary lens implantation at an older age, especially in case of problematic contact lens or spectacle wear. IOL implantation after traumatic aphakia is also often performed as a secondary procedure. Secondary posterior chamber lenses can be implanted in children who have adequate posterior capsule to support the lens, either within the bag or in the ciliary sulcus. A technique for placing a secondary intraocular lens within the capsular bag has been described and successfully performed\(^ {75}\). Yet reconstruction of the capsular bag is technically difficult in most cases, due to fusion of the anterior and posterior capsule. Secondary IOLs are usually placed in the ciliary sulcus\(^ {76-78}\). In the absence of capsular support, secondary IOLs can be sutured in the posterior chamber to either the sclera or iris or can be placed in the anterior chamber, either angle supported or iris-fixated.

**Intraocular lenses in case of an absence of capsular support in children.**

In some cases of aphakia, the lens capsule of the natural lens is absent or not stable enough to support an IOL. Important causes of absence of capsular support in children are trauma and lens dislocation due to systemic disease (see chapter 1.2.2).

Despite advancements in surgical techniques and technology, lens dislocation with loss of significant zonular support in children, presents a challenge for cataract extraction and IOL implantation\(^ {42}\). Various techniques and IOLs are used in the absence of a stable
capsular bag. Transscleral sutured posterior chamber IOLs, sutured capsular tension rings with in-the-bag posterior chamber IOLs (PCIOLs), iris-fixated PCIOLs and open loop anterior chamber IOLs are used. The Artisan aphakia IOL, the subject of this thesis, is a treatment option in these cases and favourable outcome has been reported. No studies comparing the different IOL options in children are available. A more favourable outcome of scleral sutured PCIOLs when compared to angle supported anterior chamber IOLs was reported in a small retrospective study ten years ago. As yet, there is no consensus as to which IOL offers the best solution for paediatric aphakia in the absence of capsular support.

The correction of aphakia in the absence of capsular support in adults also remains a subject of debate. A meta analysis of the safety and efficacy of open loop anterior chamber IOLs, scleral sutured posterior chamber IOLs, and iris sutured posterior chamber IOLs in eyes with absence of capsular support in adults, revealed no differences between the IOLs. The Artisan lens was not included in this analysis. A comparable visual outcome and incidence of intraoperative and postoperative complications in adult eyes with Artisan aphakia IOLs compared to eyes with sulcus sutured IOLs after a mean of 14 months of follow-up was reported.

More recently, two comparative studies on the Artisan aphakia IOL versus iris fixated posterior chamber IOLs and versus scleral fixated PCIOLs were published. Both studies included only eyes of patients with Marfan syndrome and report comparable results of visual outcome and corneal endothelial cell density when compared to the posterior chamber IOLs. A higher number of lens dislocations was found in the iris sutured and scleral sutured lenses, when compared to the Artisan aphakia IOL after 1 year of follow-up.

Multifocal and accommodating lenses in children

There is an interest in using multifocal IOLs among surgeons performing paediatric cataract surgery. The loss of accommodation, which results from loss of the crystalline lens, has more impact on the visual function and development in the paediatric patient than in the adult patient. Therefore the use of multifocal IOL might be beneficial in children. Very little literature is available on the use of multifocal IOLs in children. Difficulty with precise biometry, centration of the IOL, unknown increase in axial length, optical abberations, and amblyopia must be addressed before multifocal IOLs can be recommended for routine use in children. No reports on the implantation of accommodating IOLs in children are available.

At present, the use of multifocal IOLs in children is investigational and controversial. Spectacle independence is the primary goal of these expensive lenses, a goal that cannot be achieved in the growing eye of a child. Loss of clear vision due to optical aberrations, decrease of contrast, straylight and glare can exacerbate amblyopia. Consequently,
surgeons should hesitate to implant a premium IOL in a paediatric eye.

1.4.5 The outcome after cataract/ lens surgery in children

Refractive outcome

Refractive changes that occur with aging in normal, healthy, phakic eyes of children are influenced by three variables that ideally change in concert to maintain emmetropia: axial length, corneal curvature, and natural lens growth. Removal of the crystalline lens changes one of these three important variables, causing an aphakic refractive error, which must be corrected. The implantation of a fixed power IOL in the aphakic growing paediatric eye will lead to changing refractive errors in time. Children implanted with an IOL will need glasses for far and near in addition to the IOL. The paediatric cataract surgeon must choose an IOL power that will give a certain initial postoperative refractive error. Some surgeons choose emmetropia or myopia to help in the early management of amblyopia, others choose hyperopia that varies with age at surgery, to reduce the child's ultimate myopia. The first option might be preferable in unilateral cataracts, were there is a high risk of anisometric amblyopia. In bilateral cataract cases, where there is a lower risk of amblyopia, initial higher hypermetropia and consequently less myopia in adulthood, might be preferable. Undercorrection of plus 6 to plus 7 diopters (D) at the age of one, plus 5 D at the age of two, plus 4 to plus 5 D at the age of three, plus 2 to plus 3 D at the age of five, and 0 to plus 1.5 D at the age of 7 and older is suggested by different authors.

Another difficulty determining the final refractive outcome in children is that the inaccuracy of the initial IOL power calculation is high. Continuous research is performed on these issues in the growing paediatric eye.

Visual outcome and amblyopia

Human vision requires precise collaboration of all elements of the visual system, from the eye to the visual cortex in the brain. There is a sensitive period, during which time the immature and developing visual system retains plasticity and can thus be influenced. The sensitive period in humans is approximately 8 years. Any disturbance of vision can negatively affect the immature visual system, causing visual impairment, which is called amblyopia, or lazy eyes. The most common causes of amblyopia are strabismus, high asymmetric refractive errors, and deprivation due to organic causes, for example cataract, crystalline lens dislocation or ptosis. The risk for amblyopia remains, also after these causes have been treated. For example, amblyopia has been found to be the major cause of residual visual deficit after paediatric unilateral and bilateral cataract.

In children, the visual outcome and the risk of amblyopia after lens surgery depends on many factors, including the age at onset of the lens disease, the age at the time of the surgery, the indications for surgery (cataract/ trauma/ dislocated lens), the presence of associated ocular abnormalities, whether the cataract is unilateral of bilateral, and the...
compliance with optical correction and amblyopia treatment.

A large retrospective study on the visual outcome after cataract surgery and IOL implantation showed a mean visual acuity of 20/80 in unilateral cases and 20/34 in bilateral cases\textsuperscript{107}. A worse visual acuity was reported in children that were operated under the age of one, with a visual acuity in unilateral cases of 20/258 and in bilateral cases of 20/60. Early detection and timely surgery of lens abnormalities that interfere with the visual development as well as meticulous correction of refractive errors and well monitored amblyopia treatment, are of great importance when treating children after lens surgery.

1.5 THE ARTISAN APHAKIA IOL

1.5.1 History and development

In 1978 Professor Jan Worst in Groningen, the Netherlands, developed the Lobster Claw or Iris Claw lens. Using an earlier model, the Slotted Medallion lens, he sometimes observed that some iris tissue was caught in the slot of this lens. This clasping of iris tissue proved to be a serendipitously discovered new possibility for stable fixation of an intraocular lens. Based on the grip of the claws of a lobster, professor Worst developed an anterior chamber IOL, fixated to the iris with 2 claws. The claws of the lens are attached to the iris, without sutures, by enclavation of a fold of iris tissue of the virtually immobile midperiphery of the iris stroma (Figure 3). Therefore the IOL does not interfere with the normal vasculature and nerve supply\textsuperscript{87,108}. The Artisan aphakia IOL is a one-piece PMMA lens with an optic diameter of 5.0 millimetres, a body diameter of 5.4 millimetres, and an overall diameter of 8.5 millimetres\textsuperscript{108}.

In 1986 the name of the Iris Claw lens was changed into Artisan aphakia IOL. In 1997 an improved vaulted design of the Artisan aphakia IOL was introduced. The lens configuration was made vaulted to create distance to the iris and enclavation was made

![Figure 3. An example of the Artisan aphakia IOL in a paediatric eye](image)
Jan Worst implanted the first Iris Claw lens in 1978. Initially, he implanted this lens only as a secondary implant in the case of traumatic cataracts. Soon afterwards, he used it as a primary implant in ECCE as well as in ICCE cases and later on after the first cases of phacoemulsification. Nowadays, with the widespread use of phacoemulsification, the implantation of a posterior chamber in-the-bag IOL is the preferred technique. Therefore, at the present time, the Artisan aphakia IOL is mainly used as a back-up lens for complicated cataract surgery with insufficient capsular support, as a secondary implant, for example after a traumatic cataract, or in case of non-traumatic dislocated lenses. The Artisan aphakia IOL has been implanted in approximately 450,000 aphakic eyes worldwide. In 1986 the concept of the Iris Claw lens was modified to be used in the phakic eye for the purpose of treating refractive errors. This phakic version of the Artisan IOL was further developed and after approval of the US Food and Drug Administration in 2004, it was brought on the market under the name Verisyse IOL.

1.5.2 The use of the Artisan lens in children

The Artisan aphakia IOL

In 1980 Worst started to implant the Iris Claw lens in paediatric eyes. He observed that the Iris Claw IOL could be removed and exchanged with minimal surgical trauma, and one of his considerations for the use of this IOL in children, was the possibility of future IOL exchange in the growing paediatric eye. Worst developed two Paediatric Artisan aphakia lenses with
a smaller optic size of 4.4 millimetres, a body diameter of 4.4 millimetres, and smaller overall diameter of 6.5/7.5 millimetres respectively, to fit the smaller paediatric eye. Since the first publication on the use of the Artisan aphakia IOL in children by van der Pol and Worst, in 1996, only two reports on the use of this IOL in children were published. In these two studies, the Artisan aphakia IOL was used for the correction of aphakia in the absence of capsular support, due to idiopathic crystalline lens dislocation or crystalline lens dislocation as a result of Marfan syndrome. In the Netherlands the Artisan aphakia IOL is used as a first choice IOL in children that lack the necessary capsular support to implant an in-the-bag or sulcus IOL and is implanted either as a primary or secondary procedure.

**The Artisan/Verisyse phakic IOL**

The phakic Artisan IOL has also been used in paediatric patients. Phakic IOLs in children are incidently used in children who have significant anisometropia or bilateral ametropia and who are not able to comply to refractive correction by spectacle or contact lens wear, amongst other, mentally impaired children. Their use is still controversial.

**The Artisan Iris Reconstruction IOL**

A special design of Artisan IOL is the Artisan Iris Reconstruction implant (Figure 5). The Artisan Iris Reconstruction IOL is designed for anterior segment reconstruction of eyes in which asymmetric iris damage has occurred. The Artisan Iris Reconstruction IOL is a tailor-made polymethylmethacrylate IOL with a coloured iris diaphragm to treat aphakia as well as iris defects. These lenses are available in various dioptric powers and colours (brown, blue, green, and black).

![Figure 5. An example of the Artisan Iris Reconstruction IOL in a paediatric eye.](image)

### 1.5.3 The corneal endothelium

**Introduction**

The proximity of the Artisan lens to the innermost cell layer of the cornea, the endothelium has led to concern regarding the possible damage of this cell layer due to...
the insertion and presence of this IOL. The barrier and pump functions of the endothelial cells are responsible for maintaining corneal transparency. Human corneal endothelial cells are considered to be non-proliferative in vivo, and a significant loss of endothelial cells, due to (surgical) trauma, dystrophy, contact lens wear or disease can lead to corneal decompensation, resulting in a decreased corneal clarity.

**Imaging of the corneal endothelium**

The corneal endothelium can be photographed with special cameras. A non-contact specular microscope was used in the studies that are presented in this thesis. Non-contact specular microscopy is a widely used method to image and study the corneal endothelium. Semi automated software is available to study both quantitative and qualitative aspects of the endothelium.

**Endothelial cell density**

Shortly after birth, the human cornea has approximately 6000 endothelial cells per square millimetre of posterior corneal surface. This number decreases rapidly during infancy, and continues to decrease during life (Figure 6). The normal annual decline in ECD ranges from 2.9% during infancy and childhood to 0.3-0.6% throughout adult life. A normal ECD ranging from 2407 to 2977 cells/mm² in the third decade of life are found in normal human eyes in different populations. Endothelial cell loss is followed by migration and spreading of neighbouring endothelial cells. The exact lower limit of endothelial cells that is necessary to keep the cornea clear is not known, but is estimated to be about 500 cells/mm².

![Figure 6. Decrease of the endothelial cell density during life](From Armitage et al., Invest Ophthalmol Vis Sci 2003 Aug;44(8):3326-31)
Morphology of the corneal endothelium
The normal configuration of the corneal endothelial cell is hexagonal (Figure 7). A significant disruption in the regular hexagonal pattern is called pleomorphism. The coefficient of variation of cell size (CV) is the standard deviation of the cell area divided by the mean cell area. The CV increases when the differences in cell size increase and is called polymegathism. An increase in CV and a decrease in percentage of hexagonal cells occurs with age\(^{131}\). However, pleomorphism has also been described in healthy eyes of children\(^{132}\).

![Figure 7. The hexagonal pattern of the corneal endothelium](image)

1.5.4 The Artisan aphakia IOL and the corneal endothelium

Only two studies reporting on the endothelial cell density after Artisan aphakia IOL implantation in children are available. Lifshitz et al.\(^92\) reported on four eyes of three children with idiopathic dislocated lenses implanted with an Artisan aphakia IOL. The postoperative endothelial cell counts of the operated eyes of two unilaterally operated patients were compared to the fellow un-operated eyes. No cell loss in the operated eyes was found after eight months of monitoring. Aspiotis et al.\(^91\) reported on seven eyes of five young patients with lens dislocation due to Marfan syndrome and implanted with an Artisan aphakia IOL. At two and six months of monitoring no reduction in the number of endothelial cells was observed when compared to before the surgery.

Guell et al. prospectively studied adult eyes that were implanted with the Artisan
aphakia IOL. The clinical outcome of 16 eyes of 14 adult patients with secondary Artisan aphakia IOL implantation after aphakia due to various causes was reported. A mean endothelial cell loss of 7.8% during the first 12 months after the surgery with a cumulative loss of 10.9% for the first 3 postoperative years is reported. The authors suggest that the endothelial cell loss might therefore be most likely related to the surgery for the secondary Artisan aphakia IOL implantation.

Recently, two randomised studies were performed, reporting on the endothelial cell density of the eyes of adult patients with Marfan syndrome, implanted with the Artisan aphakia IOL. Hirashima et al. reported the endothelial cell density of 31 eyes of 16 adult Marfan patients, preoperatively, and at 3, 6, and 12 months postoperatively. One eye of the patients was implanted with an Artisan aphakia IOL and the other eye was implanted with an iris sutured posterior chamber IOL. Six months after surgery the endothelial cell loss in the eyes implanted with the Artisan IOL was 8%, in comparison to 10% in the iris fixated posterior chamber IOL.

Zheng et al. performed a randomised study to compare the outcome after either Artisan aphakia IOL or scleral fixated posterior chamber IOL implantation in the eyes of patients with Marfan syndrome. The endothelial cell loss was 13.3% and 19.3%, 3 and 12 months after surgery in the eyes implanted with an Artisan aphakia IOL. This was comparable to the cell loss in eyes implanted with the scleral sutured posterior chamber IOL.

Studies of the corneal endothelium in human donor corneas indicate that corneal endothelial cells in younger donor eyes have a higher proliferative capacity than older human corneal endothelial cells. This might explain the limited endothelial cell loss that was found in children after Artisan aphakia IOL implantation, when compared to the outcome in the adult eyes. Only short term follow-up of the corneal endothelium after Artisan aphakia IOL implantation in children is reported. In this thesis the long-term clinical outcome and complications as well as the long-term outcome of the corneal endothelium after Artisan aphakia IOL implantation in paediatric eyes is reported.
References


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Chapter 1


