On detection, treatment and prevention of complications in paediatric cataract surgery

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Cover illustration: The eye of an infant one month after cataract surgery.

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To my family

ABSTRACT

On detection, treatment and prevention of complications in paediatric cataract surgery

Purpose: To find and validate methods for diagnosis, treatment and prevention of complications in paediatric cataract surgery.

Background: Cataract and glaucoma are major treatable blinding conditions in children. Surgery for cataract in children and for its major complications, secondary glaucoma (SG) and visual axis opacification (VAO), are performed in general anaesthesia in the child. Knowledge on detection, indication and treatment as well as complication rates and risks are important to make the right decisions.

Methods: Data on diagnosis, treatment and outcome for children subjected to surgery was retrieved from medical records or from the Paediatric Cataract Registry (PECARE).

Results: Refractive change mapping is an effective method to follow development after early cataract surgery enabling detection of SG. Glaucoma treatment with chamber angle surgery and shunt draining device is safe and reduces pressure levels adequately. Visual acuity (VA) levels seems good. With primary implantation of bag-in-the-lens intraocular lens (BiL-IOL), the rate of VAO is low, 4.6%. Comorbidity is common and SG more frequent in eyes with early surgery for congenital cataract; Surgery in infants before 5 weeks of age has a high SG rate but results in higher corrected distance visual acuity levels compared to surgery between 5 and 12 weeks of age. Performing surgery between 5 weeks and 2 years of age resulted in a SG rate of 6.7% with primary implantation of a BiL-IOL. In a Swedish registry cohort of paediatric cataract surgeries <8 years of age and a mean follow-up of 3.31 years, the incidence of surgically treated SG was 23.7%. The majority was early-onset (< 1 year after surgery). With 58.3% infants (surgery within 3 months of age) this rate is fair. The incidence of late-onset glaucoma was low but the time span too short for prediction.

Conclusion: Early detection and treatment of congenital cataract and SG are important for good VA results during childhood. Chamber angle surgery and shunt draining device lower pressure adequately in cases of SG. With primary implantation of a BiL-IOL the VAO rate was 4.6% in children from 2 weeks to 16 years of age. High rates of SG are obtained when performing surgery during the first 5 weeks. Postponing surgery to after 5 weeks of age seems to reduce the rate of early-onset secondary glaucoma. The low SG incidence for surgery after 5 weeks of age indicates safety from a glaucoma perspective for implantation of BiL-IOL in children over 5 weeks of age.

Keywords: paediatric cataract, paediatric glaucoma, primary intraocular lens, visual axis opacification.

SAMMANFATTNING PÅ SVENSKA

Om upptäckande av komplikationer, deras behandling och förebyggande vid kataraktkirurgi på barn.

Katarakt innebär att ögats lins är grumlig. Hos äldre är detta mycket vanligt och åtgärdbart med en rutinmässig operation. Katarakt hos barn är ovanligt (årlig förekomst av nya fall är 36/100 000). Barn med medfödd katarakt riskerar en svår, bestående synnedsättning på grund av uteblivna stimuli till synbanor och synbark. För att hindra detta måste katarakten åtgärdas inom de första två till tre levnadsmånaderna. Tidig operation innebär dock en risk, både på grund av sövning och ökat antal ögonkomplikationer.

Avhandlingen utvärderar aktuella tekniker för operation av katarakt hos barn samt upptäckt, orsak och behandling vid uppkomna komplikationer. Avhandlingen vill visa på frekvensen av komplikationerna efterstarr (grumling av synaxeln) och glaukom (högt ögontryck, som hos barn tänjer ut ögat, gör hornhinnan disig och skadar synnerven). Den söker också faktorer av betydelse för utveckling av glaukom efter kataraktoperation och om tidig operation förbättrar synutveckling och påverkar frekvensen sekundärglaukom.

Genom tidig diagnos och behandling vid glaukom minskar risken för skador på ögat och i delarbete 1 har vi undersökt om ögats brytkraft kan användas för att påvisa ökad tillväxt som är en viktig markör för glaukom hos barn. Slutsats: brytkraften förändras snabbt vid glaukom och är därmed en bra markör för glaukom.

Vid barnglaukom är förstahandsvalet operation. Delarbete 2 har utvärderat två kirurgiska åtgärder som används specifikt på barn: kammarvinkelkirurgi och inläggning av shunt. Arbetet belyser effektiviteten för behandling av primärt och sekundärt glaukom. Slutsats: 2/3 av ögonen med glaukom får en adekvat trycksänkning med ett eller två ingrepp. De använda metoderna har dessutom fördelen att inte påverka de områden av ögat som används vid glaukomkirurgi hos vuxna.

I delarbete 3 har vi utvärderat en nyutvecklad konstgjord ögonlins gjord för att blockera linscellers överväxt av synaxeln. Slutsats: efterstarrfrekvensen på 5% ligger klart under vad man förväntar hos barn där man inte opererar in någon konstgjord lins vilket gör linsen lämplig vid kataraktkirurgi på barn.

I delarbete 4 har vi sökt faktorer av betydelse för att förutsäga uppkomst av glaukom och orsaker till låg synskärpa efter operation för katarakt med linsen

i arbete 3. Slutsats: frekvensen av glaukom är samma som i tidigare studier då ögat lämnas utan inopererad lins och att drabbade ögon främst är de som har annan ögonsjuklighet eller opereras första levnadsmånaden. Samtidigt gav operation första månaden i denna studie högre synskärpa jämfört med de som opererats efter en månad för tät medfödd katarakt.

I delarbete 5 har vi undersökt förekomsten av glaukom efter kirurgi för katarakt på barn i Sverige. Barnkataraktregistret PECARE, startat 2006, där alla operationer av katarakt på barn under 8 års ålder registreras ger oss i Sverige en unik möjlighet att samla data från ett geografiskt område och följa upp under lång tid. En tidigare PECARE-studie har visat att man med BB-screening fångar upp och opererar täta katarakter tidigare i Sverige än i andra länder. Arbetet kan därför påvisa en högre frekvens av glaukom under första levnadsåret jämfört med andra länder. Dock är antalet fall av glaukom med debut efter första levnadsåret färre än i andra länder. Det verkar som att ögats beskaffenhet i kombination med operation ger glaukom.

Avhandlingens slutsatser är:

- Ögats förändring i brytkraft är ett bra mått på tillväxt och kan användas för att hitta glaukom efter kataraktkirurgi på barn.

- Att kammarvinkelkirurgi som förstahandsval och Molteno-Shunt som andrahandsval sänker trycket adekvat och verkar hållbart vid barnglaukom oavsett orsak.

- Att den typ av intraokulär lins som används ger en god synutveckling och lägre risk för efterstarr jämfört med andra likvärdiga tekniker.

- Att vi hittar barnen och opererar dem tidigt i livet i Sverige och förekomsten av glaukom efter operation av katarakt på barn är något högre första tiden efter operation men verkar hamna på samma nivåer som i andra studier efter några år.

- Att registerdata från PECARE, möjliggör större datamängder och säkrare underlag för framtida strategier.

LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. Alf Nyström, Kristina Lundqvist, Johan Sjöstrand. Longitudinal change in aphakic refraction after early surgery for congenital cataract. *J AAPOS*. 2010 Dec;14(6):522-6.

II. Madeleine Zetterberg, Alf Nyström, Lada Kalaboukhova, Gunilla Magnusson. Outcome of surgical treatment of primary and secondary glaucoma in young children. *Acta Ophthalmol*. 2015 May;93(3):269-75.

III. Alf Nyström, Nawaf Almarzouki, Gunilla Magnusson, Madeleine Zetterberg. Phacoemulsification and primary implantation with bag-in-the-lens intraocular lens in children with unilateral and bilateral cataract. *Acta Ophthalmol*. 2018 Jun;96(4):364-370.

IV. Alf Nyström, Gunilla Magnusson, Madeleine Zetterberg. Secondary glaucoma and visual outcome after paediatric cataract surgery with primary bag-in-the-lens intraocular lens. *Acta Ophthalmol*. 2019 Sep 11.

V. Alf Nyström, Birgitte Haargaard, Annika Rosensvärd, Kristina Tornqvist, Gunilla Magnusson. The Swedish national paediatric cataract registry (PECARE): incidence and onset of post-operative glaucoma. *Manuscript 2019*.

CONTENT

ABBREVIATIONS

BCVA	best corrected visual acuity
BiL	bag-in-the-lens
CCT	central corneal thickness
CDVA	corrected distance visual acuity
CI	confidence interval
ECCE	extra-capsular cataract surgery
IATS	Infant Aphakia Treatment Study
IOL	intraocular lens
IOP	intraocular pressure
LEC	lens epithelial cells
LogMAR	logarithm of the Minimum Angle of Resolution
Nd-YAG	neodymium-yttrium aluminium garnet
PCO	posterior capsule opacification
PECARE	The Paediatric Cataract Registry
PFV	persistent foetal vasculature
SD	standard deviation
SG	secondary glaucoma
SRK/T	Sanders Retzlaff Kraff /Theoretical
VA	visual acuity
VAO	visual axis opacification

GLOSSARY

Accommodation	adjusting focus to permit imaging of objects at varying distances
Afferent	conducting incoming impulses to the brain
Amblyopia	developmental disorder with a reduced vision of less than 0.5 (20/40) in both eyes or a difference of more than two lines with the worse-seeing eye less than 0.5 (20/40) (here in eyes with a history of cataract)
Aphakia	condition with no lens in the eye
Bag, or capsular bag	a sac-like structure remaining within the eye following the removal of the lens content from the eye
Bag-in-the-lens	a technique for fixation of an intraocular lens
Canal of Schlemm	a circular canal collecting the drained aqueous humour from the anterior chamber to the collecting vessels and into the veins
Capsulorhexis	a usually circular hole made in the lens capsule by tearing
Cataract	a change in the crystalline lens affecting translucency
Chamber Angle	the anterior angle between the base of the iris and cornea where fluid is diverted from the eye through the trabecular meshwork and the canal of Schlemm

Ciliary body	part of the eye that includes the ciliary muscle, which controls the shape of the lens and the ciliary epithelium which produces the aqueous humour
Ciliary processes	part of the ciliary body, which the crystalline lens is attached to through the zonules
Ciliary sulcus	a pouch between the iris and the ciliary processes
Congenital	present from birth
Cortex	the outer layers of the lens
Critical period	period for visual development when blocking of visual stimuli will permanently affect vision
Crystalline lens	the natural lens in the eye
-ectomy	suffix indicating surgical removal
Elschnig pearls	new formation of lens epithelial cells after cataract surgery
Emmetropia	the refractive status of the eye at which objects at far distance creates a sharp image in the retinal plane
Glaucoma	disease characterized by high intraocular pressure related damage to the eye
Haptics	parts of the intraocular lens manufactured to keep the lens in place

Hyperopia	condition where the eyeball is optically too short and the image is focused behind the eye. Lenses or accommodation are needed to focus the image in the retinal plane
Intraocular lens	artificial lens inserted into the eye
In-the-bag	technique for fixation of an intraocular lens by inserting it inside the capsule of the crystalline lens
Lens	(1) short for “crystalline lens” (2) a device focusing light rays to form an image
Lens sutures	the areas in the crystalline lens where the fibres join during the development of the lens. The sutures are a common site for cataract in infants
Myopia	the eyeball is optically too long and the image is focused in front of the retina. Lenses or shortening the distance to the object is needed to focus the image on the retinal plane
Neurons	impulse-conducting nerve cells
Nystagmus	involuntary repetitive movements of the eye
Opacification	a blurring of vision, e.g. caused by covering by tissue or thickening of tissue
Ophthalmoscopy	inspection of the inner eye using an ophthalmoscope
Pars Plana	part of the wall of the eye-ball posterior to the iris with no retina

Phacoemulsification	disintegration, using ultrasound and suction removal of contents in the crystalline lens in cataract surgery
Polar	anterior or posterior centre of the crystalline lens
Pseudophakia	condition of having an artificial lens in the eye
Pulverulent/Pulveruscent	consisting of small dots or grains
Refraction	the ability of the eye to deflect light to a focus
Retinopathy	disease of the retina
Retina	light absorbing part of the eye where light is being transformed into neural signals
Retinoscopy	an objective way of determining the refractive status of the eye by observing the change of direction of imaged light with different lenses held in front of the eye
Sensitive period	time when visual input is most important for visual development
Shunt	a device, to divert fluid. Here, usually a silicone tube that is used to divert the aqueous humour bypassing the chamber angle outflow, to an external reservoir
Soemmerring's ring	secondary cataract formation after surgery or trauma to the lens which is shaped like a doughnut-like ring

Sanders Retzlaff Kraff /Theoretical	a formula for intraocular lens power calculation
Trabecular meshwork	the filter in the chamber angle in front of Schlemm's canal
Visual acuity	the resolution capacity of the eye
Visual axis	the central pathway through the eye when the eye is aligned
Visual axis opacification	any condition that occludes the optic pathway into the eye, such as fibrosis of the capsule or lens epithelial cells
Vitrectomy	surgical removal of the vitreous or part of the vitreous body behind the lens
Zonula	band or meshwork connecting the lens to the ciliary processes

1 INTRODUCTION

1.1 BACKGROUND

Cataract, glaucoma and retinopathy of prematurity are the major treatable blinding conditions in children in Sweden (Blohme & Tornqvist 1997). This thesis deals with surgery for cataract in children and its two major complications, secondary glaucoma (SG) and visual axis opacification (VAO). The incidence of congenital cataract in Sweden is 36 cases per 100,000 births a year (Abrahamsson et al. 1999).

The work of Wiesel and Hubel on visual deprivation in cats made it apparent that there is a critical period for visual development in mammals. This is not only a functional entity but also neurons are structurally altered from lack of visual input (Wiesel & Hubel 1963). This makes it plausible that there is a period during which an occlusion of an eye will result in permanent reduction of vision, as supported by several studies. (Lloyd et al. 1995; Birch & Stager 1996; Lambert et al. 2006; Birch et al. 2009; Sjostrand et al. 2011).

1.2 CORTICAL PATHWAYS

Not only the visual acuity (VA) is affected in paediatric cataract. Afferent visual signals are necessary for the development of normal cortical pathways and to block infantile nystagmus, which otherwise may start at birth but more usually at the age of 2-3 months (Brodsky & Dell'Osso 2014). Nystagmus can develop even in children with as short a deprivation period as 3 weeks (Abadi et al. 2006). However, during this sub-cortical or latent period, transient visual disturbance does not appear to impact the eventual visual outcome. This period could be up to 6 weeks for human infants with unilateral visual deprivation (Birch & Stager 1996; Lundvall & Kugelberg 2002a; Lundvall & Kugelberg 2002b; Lloyd et al. 2007). In a study by Lambert (Lambert et al. 2006) the majority of children (10 out of 16) with nystagmus at their first visit were 12 weeks of age and older, but five out of 16 already had nystagmus at between 8 and 12 weeks. Other studies have not shown preoperative nystagmus to be an indicator of poor VA outcome but postoperative nystagmus is (Young et al. 2012).

1.3 CONGENITAL CATARACT

Congenital cataract is a condition in which the crystalline lens has not developed into the clear image-forming part of the anterior segment of the eye but is partly or wholly affected/deranged (Figure 1A) (Lambert & Drack 1996; Taylor 1998) (Lloyd et al. 2007). The cataract can occlude the eye and its severity depends on the density of the cataract or, rather, on the quality of the image-forming parts of the lens that are clear. This means that different cataract types may have a different impact on image formation. a device, to divert fluid. Here, usually a silicone tube that is used to divert the aqueous humour

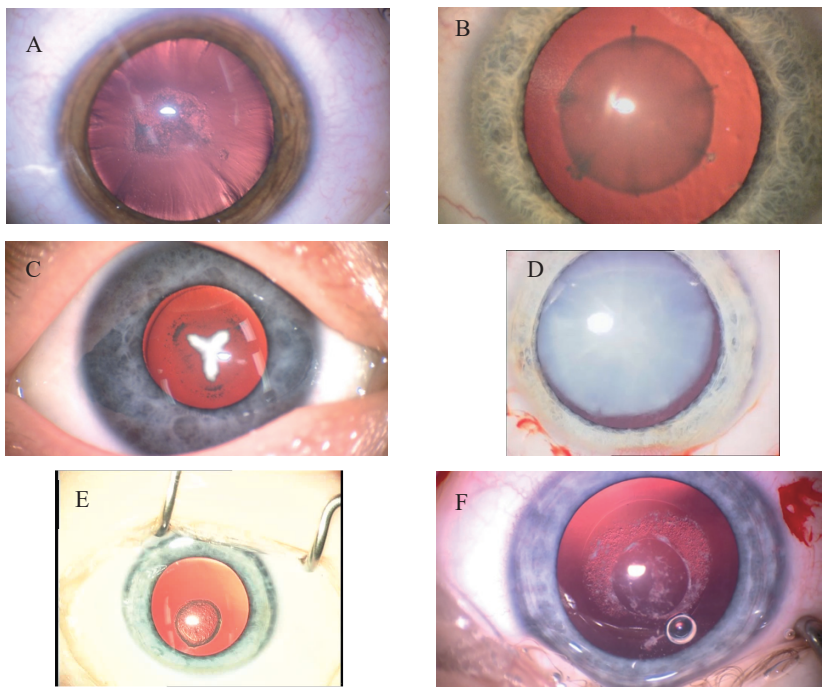

Figure 1. :(A) Posterior polar cataract forming a cloud in the cente, in combination with a cortical spoke-shaped cataract. (B) Zonular cataract with a central opacity and a cortical cataract, called "riders", in the layer surrounding it. (C) Sutural cataract forming a "Y"-shaped cataract in the centre and a mild nuclear opacification. (D) An almost dense white cataract with a clear zone in the periphery. (E) Lenticonus -an area of interface dysgenesis between the lens and vitreous has caused a disruption of the posterior capsule usually bending backwards. (F) Defect in the posterior capsule after the lens content has been removed.

Cataract can either be defined by its morphology as polar, zonular, sutural or dense/total (Figure 1A-D) or by the type of lens opacification into, e.g. pulverulent, coralliform or cerulean(Lambert & Drack 1996; Taylor 1998; Forster et al. 2006). Posterior lenticonus, an area of interface dysgenesis between the lens and vitreous can also form a cataract (Figure 1E), and leave a defect after removal (Figure 1F). Different morphology also has a different impact because the origin of the condition determines the size and location of the lens opacity. Descriptive morphology may also be more important in determining the underlying genetic cause of lens opacities (Taylor 1998) (Trumler 2011) (Shiels et al. 2010) although it appears that the same mutation may cause different types of morphology (Berry et al. 2018).

1.4 THE OPTIC LENS

The task of the optic lens is to focus an object onto the image plane, point by point. Every part of the lens contributes to this and the larger the lens the brighter the image (Smith & Atchison 1997). When it comes to the eye, brightness is of most interest close to the limits of perception (Cornsweet 1970). Vision is not experienced as worse in normal indoor light than outdoors on a clear day despite a massive difference in brightness. For a child with cataract this means that there is a need for surgery only if the image-forming capacity of the lens is so poor that it prevents visual development. For the newborn child, this means that it occludes the image and for infants, toddlers and children below the age of 8 years, that visual development stops or declines. The upper age limit for children with cataract to treat amblyopia is more uncertain and improvement is seen even after eight years of age (Sjostrand et al. 2011; Writing Committee for the Pediatric Eye Disease Investigator et al. 2019).

To determine whether a cataract occludes an image, either inspection of the fundus through ophthalmoscopy, or examination with retinoscopy, is suitable. Retinoscopy is a way to objectively measure the refraction of an eye. This is done through a slit light, which is passed across the pupil in a slow movement and by changing the power of the correcting lens held in front of the eye while looking for the change in direction. The possibility to observe an image of the slit light through the optic media of a child's eye means that the cataract is not occluding and the child should be scheduled to visual follow-ups before decision on surgery is made. Methods for objectively grading cataracts in

children have been developed but it is important to combine these with image analysis (Forster et al. 2006) (Figure 1A-E).

1.5 LENS AND ANTERIOR CHAMBER FORMATION

The human lens is derived from the optic vesicle surface ectoderm. In the fourth week of the embryo's formation lens cells elongate to form a placode that further develops to form a lens vesicle. Primary lens fibres elongate filling the vesicle from the posterior to the anterior end during the following week. In a third elongation phase equatorial cells differentiate into secondary (cortical) lens fibre cells from the nucleus to the periphery (Piatigorsky 1981). The growth rate is high and the lens continues to grow considerably during the first year (Bluestein et al. 1996). The anterior chamber formation begins with differentiation of mesodermal tissue. Corneal endothelium and later, irido-pupillary lamina forms and the corneal stroma develops during the second month (McMenamin 1989). For the following stage, two different theories are proposed, one supported by Barkan (Barkan 1955) postulating the splitting of a membrane (Barkan's membrane), the other posting a backward slipping of structures in the periphery of the angle. (Anderson 1981).

1.6 SCREENING FOR CATARACT AND TIMING OF SURGERY

In order to detect cataracts in newborn babies we need a good screening system. Sweden has such a system, and 75% of the cataracts in newborns are identified within 42 days of birth (Magnusson et al. 2013). If the presence of occlusion is known, when is the optimal time to remove the cataract? Looking at the effects of occlusion, the potential of higher VA levels drops week by week after birth until 14 weeks of age (Birch & Stager 1996; Birch et al. 2009). After 14 weeks, visual development is not as sensitive and the results levels out (Lin et al. 2017) (Wright et al. 1992). This means the sooner the condition is addressed the better which has been supported by numerous studies for more than two decades (Watts et al. 2003) (Birch & Stager 1996; Birch et al. 2009) (Lundvall & Kugelberg 2002a; Lundvall & Kugelberg 2002b).

However, early surgery increases the risk of complications to occur. Surgery in infants before 1 month of age in general contains an anaesthetic risk (Neumann & von Ungern-Sternberg 2014). Previous work at our clinic showed that surgery before 11 days of age dramatically increased the numbers

of eyes that developed SG (Magnusson et al. 2000) and similar findings were published by Lundvall (Lundvall & Zetterstrom 1999). Today, we consider the first month to be a high-risk period for cataract surgery with regard to SG development (Vishwanath et al. 2004), (Lambert 2016). For two decades until 2015 there was a consensus in Sweden on early surgery to achieve the highest possible VA levels and surgery was frequently scheduled for between 2 and 6 weeks. To enable us to identify and evaluate dense congenital cataracts before 2 weeks of age and gain the possibility of early surgery, we need a good screening system as mentioned above.

1.7 TREATMENT FOR PAEDIATRIC CATARACT

Although treatment of cataract is essentially surgical, medical (*i.e.* non-surgical) treatments also exist, as in children with galactokinase deficiency, where avoiding milk may reduce the nuclear part of the cataract (Stambolian 1988). Apart from this the treatment for paediatric cataract today is surgery. Until the 1950s prognosis for cataract surgery in children was poor. Surgical attempts by Saunders in London and Gibson in Birmingham in the early 19th century had few followers and the eyes frequently ended up inflamed and with membrane formation. Optic iridectomy, where a part of the iris is removed to make a clear opening peripheral to a partial cataract was an attempt to manage cataracts without touching the lens with its known complications and aphakia (Costenbader & Albert 1957).

Shortly afterwards, aspiration of soft cataracts was described by Scheie (Scheie 1960). In this method, the peripheral and posterior parts of the capsule were left as in cataract surgery in adults, so-called “extra-capsular cataract extraction” (ECCE). Modifications of this method are still the golden standard, with the eye left without a substitute for the crystalline lens (i.e. aphakic) in very young infants.

As vitreous surgery with microsurgery and cutters became available, the cutters were also used for removing as much of the lens as possible, i.e. performing a lensectomy (Peyman et al. 1978). The removal of the entire lens and posterior capsule was more effective against posterior capsule opacification or visual axis opacification (VAO), a common cause of reoperation (Taylor 1981) (Vasavada & Desai 1997) however even in these cases VAO occurred (Morgan & Karcioglu 1987). An alternative approach was to make an opening in the posterior capsule as part of the primary surgery

(Parks 1983), which could also be performed from behind through pars plana (Buckley et al. 1993).

When phacoemulsification of cataract was introduced in adults, it was no longer necessary to make a large opening in the eye and the anterior capsule to remove the nucleus. It was also possible to use this technique in children (Hiles & Wallar 1974). A circumscribed hole in the anterior capsule was made, a so-called "capsulorhexis", to keep the integrity of the lens and provide a stable fixation of the IOL (Gimbel & Neuhann 1990) (Figure 2). In children, this method was refined to include the posterior capsule, initially for the prevention of extension of tears (Castaneda et al. 1992). Keeping the lens periphery provided a better possibility for secondary lens implantation either in the sulcus or in the lens bag after removal of lens material, both of which methods were safer than those of secondary IOL anchoring. Anterior vitrectomy was also performed to prevent lens epithelial cells (LECs) from migrating over the visual axis (Vasavada & Desai 1997). A prospective study comparing pars plana lensectomy with ECCE and IOL, and finally ECCE with posterior chamber IOL, posterior capsulotomy plus anterior vitrectomy, concluded that the latter, had the highest chance of achieving a clear visual axis in children with 2 to 8 years of age (Basti et al. 1996).

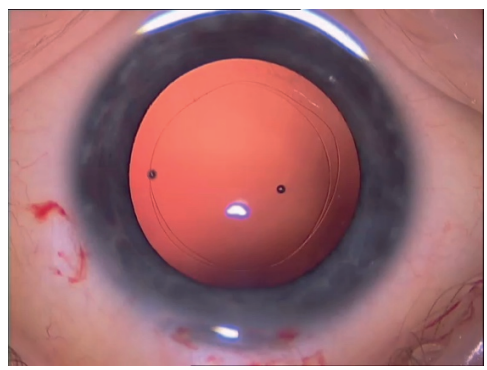

Figure 2. Two symmetrical circular tears called "capsulorhexis" before implantation of an intraocular lens (IOL)

Primary intraocular lens implantation: The first intraocular lens (IOL) implantation in adults was performed by Harold Ridley in 1949 (Ridley 1952) and despite being controversial at the time, IOLs have caused no controversy since the late 1970s. In children however, and especially in infants and children below 2 years of age, there is still no consensus despite decades of use even in the very young. In 1996, Wilson discussed IOL implantation in the care of children and concluded that "it appears that IOL implantation has become the

standard of care, at least for children beyond the first 2 years of life". (Wilson 1996; Lundvall & Zetterstrom 2006) Membrane formation was suggested to be a result of IOL-induced uveitis (Nishi 1988) and high rates of re-operations were due to secondary cataract formation and VAO with a need for more treatments under general anaesthesia (Plager et al. 2011; Plager et al. 2014; Solebo et al. 2018).

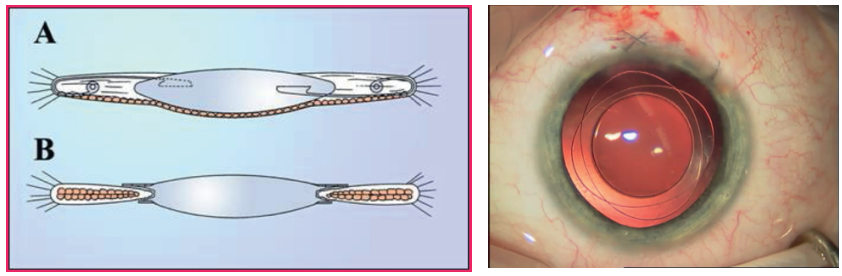

Figure 3. Left: Bag-in-the-lens (BiL) fixation (below), preventing lens epithelial cell (LEC) overgrowth as in the lens in the bag (above). With permission Professor Marie-José Tassignon. Right: (BiL)-IOL implanted in an eye of a child.

To address this problem, several methods have been proposed. Design of the IOL shape with sharp edges (Nishi et al. 2000) Optic capture as described by (Gimbel 1996) are both measures to prevent VAO. In the latter strategy, the lens haptics are placed in the bag and the optic of the IOL is pushed down under a somewhat smaller posterior capsulorhexis to facilitate adhesions between the anterior and posterior capsule and thus to prevent migration of LECs. Another strategy to prevent VAO is provided by the bag-in-the-lens (BiL)- IOL, where an anterior and posterior capsulorhexis of the same size are created (Figure 2). The BiL-IOL is inserted by sliding the anterior and posterior capsule blades along a groove of the IOL (Figure 3) to put the capsules together and to block LECs otherwise likely to migrate through adhesions (Kappelhof et al. 1987) or out of the lens capsular bag and over the visual axis (see Figure 4) (Tassignon et al. 2002).

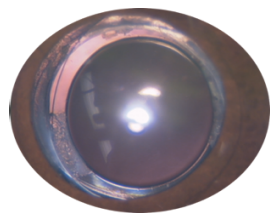

Figure 4. Lens epithelial cells (LECs) are here prevented by adhesions from migrating across the optical zone.

1.8 VISUAL REHABILITATION AND RESULTS

Unilateral cataract is not as much a threat to the child´s vision or activities in daily life as is bilateral cataract. It is, however, a challenge for the ophthalmologist. With a healthy second eye, the visual system has to adapt to a far worse optic situation in the affected eye. The likelihood to achieve higher VA in an eye with unilateral cataract is by far worse, (Vaegan & Taylor 1979). The goal of surgery for unilateral cataract is not necessarily to provide an equal visual situation on both sides but, rather, to add visual field support and an insurance in case of an injury or disease on the contralateral side.

Bilateral cataract is a major threat to visual development and a frequent cause of blindness in children world-wide foster (Foster & Gilbert 2003). The only treatment is surgery. In children in contrast to adults, surgery alone is not enough to gain good VA. After surgery, artificial lenses will have to take over the lost refractive function of the lens. Whether these artificial lenses are spectacles or contact lenses there will be a constant need for re-assessment to determine the refractive power in order to provide good-enough image forming properties on the retina.

1.8.1 INTRAOCULAR LENSES

The use of IOLs is not a controversy in adult cataract surgery. In children, on the other hand, great many difficulties make authors question their use especially in infants below 3 months of age. Size and growth is one important question when the crystalline lens grows (Bluestein et al. 1996). The commonly used technique in adults, the in-the-bag placement of an IOL, keeps the lens capsule open; in children, since they have a high proliferation rate of the LECs, the incidence of VAO is high. Ophthalmologic practice in the United States has shown a decline in primary IOL implantation as choice of treatment for very young infants after unfavourable reports from the Infant Aphakia Treatment Study (IATS) (Poole et al. 2019). From 7 to 24 months of age, IOLs are considered safe and results are good. However, the rate of retreatment due to VAO is still high in the IOL group (Bothun et al. 2019). As a result of retreatments in the IOL group, the recommendation from the investigators of the ioLunder2 study in the British Isles, was not to use IOLs in children under the age of 2 (Solebo et al. 2018), the main reason being the high rate of VAO in this group. Hence, VAO has to be addressed if primary IOL implantation is to be an option in infants.

1.8.2 CONTACT LENSES

There are many advantages to using contact lenses in aphakic children. They usually stay in the right position and vision is more normal because of the less pronounced magnification compared with spectacles. There is also the possibility to change power whenever needed because of ocular growth. The average growth of the eye, as measured in contact lens power, will decrease the required optical power by > 10 dioptres during the first years (Morris et al. 1979; Moore 1989). Ocular growth will also affect the required shape of the contact lens. Good visual results are obtained with corneal contact lenses during the first 3 years (Lorenz & Worle 1991).

Contact lens measures

Three measures are of importance to define the properties of a contact lens: (1) the refractive power; (2) the size of the lens (lens diameter); and (3) the basal curve, which is the radius of the globe formed by the posterior surface of the contact lens. A fourth measure may also be of importance in high power contact lenses, namely, the optic zone. With a small optic zone, the lens will be thinner and easier to fit. Unfortunately, the fit of the lens is even more important in these cases, since a small optic zone has to be better centred more accurately in order to cover the pupil. High-power contact lenses do not give the same magnification as do spectacle lenses. The refractive power is usually high, which is a major argument for using contact lenses rather than spectacles.

1.8.3 SPECTACLES

At first glance, the use of spectacles may seem an easy way to correct refractive errors in children. Three mayor obstacles are evident: (1) the power of the lenses; (2) the importance of alignment; and (3) the difference between the eyes. In the IATS, the correction for children with IOL was spectacles only (Infant Aphakia Treatment Study et al. 2010). With small noses, heavy lenses and large differences between the eyes, this task is not easy.

1.8.4 MEASUREMENTS IN CHILDREN

The measurements initially obtained under general anaesthesia from the infant's eye at the investigation prior to surgery provide the basis for further calculations (Flitcroft et al. 1999). As the instruments for measurement are made to fit adults, values obtained in infants are much less accurate, because calibration measures are in the borderline range for infant eyes.

The three most important measurements in order to determine IOL power prior to surgery are:

- Keratometry – the assessment of the anterior curvature of the cornea.
- Axial length – the distance from the apex of the cornea to the retinal surface.
- Refractometry – measurement of the refractive power of the eye.

Keratometry is performed by mirroring an object on to the corneal surface and measuring the angel at which the rays of the image are falling on the image are reflected back. This can be done either manually, as with the Javal-Schiötz keratometry, where two illuminated objects, a rectangle and a staircase, mounted on a circular ruler, are imaged onto the corneal surface. Changing the distances until their edges meet in a straight line obtains the angle. This angle is converted to the radius of the measured object's surface (Figure 5).

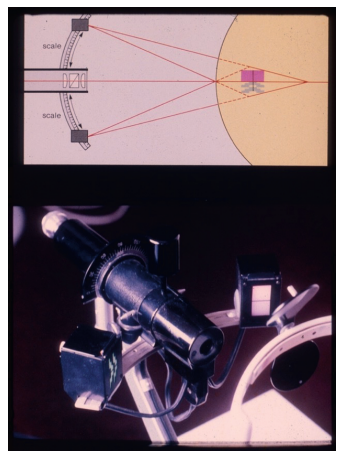

Figure 5. Javal-Schiötz keratometer for measuring corneal radius.

The same principle is used with an automatic portable keratometer and in adults these measurements coincide (Manning & Kloess 1997). With knowledge about the radius and the refractive power of cornea, two measures may be obtained; (1) the measured radius in millimetres and (2)the calculated refractive power of the surface in dioptres (Trivedi & Wilson 2008). Measurement of the radius is important with regard to the shape of the basal curve of the contact lens and for calculation of the corneal power, which together with the axial length and the position of the lens will give the eye's refractive power. However, the change in corneal curvature is rapid during the first 2 months in life (Inagaki 1986) and the prediction error is larger in small corneal radii (Tromans et al. 2001). Most parameters in studies apply to older

children (Mutti et al. 2005) (Sorsby et al. 1961; Wood et al. 1996) and focus on refractive growth.

The axial length in infants is obtained using ultrasound to measure the time from signal to echo from a surface of the eye perpendicular to the in-coming ultrasound wave (Fledelius 1976). To convert time to distance, the speed of sound in the medium has to be known (Jansson 1963). The velocity in the lens of a child may differ from that of an adult (Hoffer 1994). To establish whether a surface is perpendicular, the amplitude of the sound wave is used as best predictor. The higher the amplitude, the more perpendicular the surface. Four surfaces are possible to obtain; the corneal surface, the surface of the anterior lens capsule and that of the posterior lens capsule, and the surface of the inner limiting membrane of the retina. When the amplitude is as high as possible for all these surfaces, the alignment is reasonably good. With many measures to take into account, however, there is a problem of repeatability (Zadnik et al. 1992)

Lens Power Formulas:
Two general types of formulas are used for lens power calculations: (1) theoretical formulas, in which measured distances and corneal curvature are used to calculate the optic power of the eye, such as proposed by Hoffer (Hoffer 1993) and (2) empirical regression, in which a curve is drawn based on previous results. The most common formula, the SRK/T formula, has a modification to accommodate both short and long eyes (Retzlaff et al. 1990). We have used the SRK/T, which in our experience is better for power calculations in children than expected.

Problems in biometric measurements, with focus on measurements in children
Corneal measurements. The cornea is smaller in children than in adults and as the shape of the cornea is not spherical this means that the smaller the diameter, the more peripheral is the measurement. With a shape closer to an ellipse, a peripheral measurement will have a flatter curvature than will a value obtained closer to the central axis, which is steeper. As this is the case, the theoretical central value in a child will have a shorter radius and a higher refractive power than indicated by keratometry. This may affect both the prediction on IOL calculation as well as the shape of the base curve of the contact lens. Furthermore, the refractive power of the cornea is not related to the surface alone, but to a combination of the curvature of the anterior and posterior surface, the refractive index, the thickness of the cornea and the size of the pupil. To our knowledge, there is no research addressing these issues in children with cataract.

Ultrasound measurements. The velocity of the sound differs between different materials. Regarding the values for the aqueous humour and vitreous body in a child average velocity of sound of 1532m/s is probably fairly accurate (Hoffer 1994). The value for the lens, however, is probably not as accurate because the calibration is made in adult cataract patients who have a denser lens with higher velocity compared with most children with cataracts (Hoffer 1994). The only way to validate these measures is through retinoscopy. In a child with rapid change in refractive power this has to be performed shortly after surgery which usually is difficult and even in older children gives variable measurements and has repeatability issues (Hirsch 1956).

1.9 AMBLYOPIA

Vision at birth is very poor but develops rapidly during the first three months in life. Deprivation of vision during the first weeks in life results in a permanent reduction in VA. The critical period has been stated to be 1- 8 weeks of age (Wright 1995). In a study by Lambert (Lambert et al. 2006) nystagmus at first visit before surgery was significantly associated with low VA even after accounting for age at surgery here too the surgery performed before 10 weeks of age resulted in higher VA. Amblyopia therapy (full-time patching) in an eye with a partial cataract without surgery was successful in most children with unilateral media opacity (Bradford et al. 1992), This means that in eyes with a good enough image, patching is the right treatment. However, when vision declines the usual way to treat amblyopia is with extended patching. In the case of existing cataract, however, cataract surgery should be considered before extensive patching. One study reports that, in children with unilateral cataract, early surgery and intense patching may lead to the same visual level in the aphakic eye as in the healthy other eye during the first 2 years of life. However, in that study the utmost care was taken and the compliance was almost 80% in the majority of cases despite a very intense schedule. They also report that intensive occlusion deprives the occluded eye (Lloyd et al. 1995).

Thompson et al report a loss of recognition in the fellow phakic eye, which was not seen in severe untreated unilateral children. They interpret this as a probable iatrogenic effect (Thompson et al. 1996). In another study, reported by Taylor, a loss in low spatial frequencies in the better eye after patching (Taylor 1998). The adherence to patching is important for the outcome and for this reason the IATS included patching diaries for a 7-days per year (Bothun et al. 2019).

1.10 COMPLICATIONS

Even with optimal management, patients will still experience complications. The two major complications in paediatric cataract surgery are VAO and SG (Plager et al. 2014; Solebo et al. 2018). One might therefore expect SG and VAO as complications in children after cataract surgery. Other complications are endophthalmitis (infection in the eye-bulb) (Gharaibeh et al. 2018), cystoid macular oedema (Kirwan & O'Keeffe 2006), which are both extremely rare in children and retinal detachment that may come very late, decades after surgery (Haargaard et al. 2014).

1.10.1 SECONDARY GLAUCOMA

Glaucoma in childhood is intraocular pressure (IOP)-related damage to the eye. The causes of increased pressure are several but glaucoma secondary to child cataract surgery is an entity of its own (Weinreb et al. 2013). Pressure in the eye derives from aqueous humour produced in the eye by the ciliary body and the pressure rises if the outflow is blocked in any way.

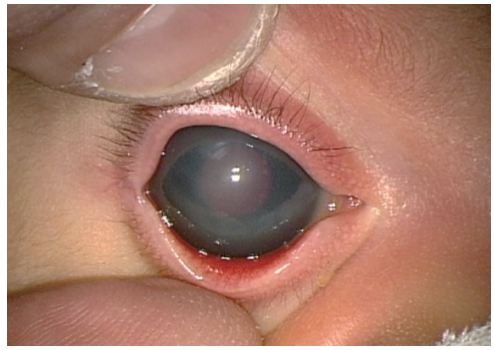

Figure 6. Enlarged, hazy cornea.

Diagnosis

The most significant signs of glaucoma development are tearing, blepharospasm, light sensitivity, corneal haze and enlargement of the eye bulb (Weinreb et al. 2013) (Sampaolesi & Caruso 1982) (see Figure 6). In a child below 3 years of age, increased pressure makes the bulb expand more than that in normal growth (buphthalmos). This fact has been known for decades and increased axial length is one of the criteria in establishing glaucoma in an infant (Sampaolesi & Caruso 1982). It is also more reliable than pressure measurements. Pressure measurements in children have many errors. A child resisting the examination can easily squeeze the measured pressure to above 30mmHg. Methods for measurement of pressure are dependent on the central

corneal thickness (CCT) and radius. Increased CCT is not uncommon in children after cataract extraction (Lupinacci et al. 2009) and may therefore produce falsely high IOP. The relation between CCT and pressure measurements in children is not simple, and to reduce presumed pressure after high CCT values is questionable (Chen et al. 2004) On the other hand, anaesthesia usually lowers the pressure (ketamine and chloral-hydrate are exceptions)(Self & Ellis 1977). Though true IOP-values are difficult to achieve in children there are other measures that are more readily obtained, such as corneal diameter and axial length.

High pressure makes the eye expand. This is first seen as a myopic shift in refraction (Egbert & Kushner 1990), which initially is reversible if pressure is lowered surgically. Secondly, the cornea becomes enlarged and less curved. This is much more obvious at observation but may mask the myopic shift since a less curved cornea results in a hyperopic shift. The follow-up protocol is therefore of major importance to find signs of glaucoma after surgery for paediatric cataract in the first months in life.

If enlargement is an important sign, does an IOL cause a change in growth of the eye? The axial growth of the pseudophakic eye has been reported as normal in some reports (Hussin & Markham 2009) while others have reported a less pronounced myopic shift in pseudophakic children (Superstein et al. 2002). With a BiL-IOL, the forces on the zonulae may differ from an in-the-bag implantation, more resembling the aphakic architecture during the first months. Opposed to this remains the fact that, in our study, very few eyes developed SG after the first 5 weeks, at which time the size has not yet changed substantially.

Cause

If the signs of SG are clear, the cause of SG is more uncertain. Several theories have been suggested. Post-operative inflammation after cataract extraction has been demonstrated to lead to membrane formation in the eye (Nishi 1988). Other causes that have been discussed are surgical trauma, blockage by LECs in the trabecular meshwork, LEC exposure (Walton 1995), change in anterior segment architecture either by the change of angle growth (Reme & d'Epinay 1981) which has been reported in late-onset glaucoma (Kang et al. 2006) or due to the angle (Anderson 1981) and the impact on the maturation process of the endothelial cells. Risk factors appear to be young age (Vishwanath et al. 2004) (Watts et al. 2003; Lawrence et al. 2005; Trivedi et al. 2006), although glaucoma still develops if surgery is postponed until after 1 year (Asrani & Wilensky 1995) as well as biometric data such as small corneal diameter (Wallace & Plager 1996) and pupil (Mills & Robb 1994), coexisting persistent

foetal vasculature (PFV) (Kuhli-Hattenbach et al. 2008) or other ocular pathology, surgical factors such as posterior capsulotomy and anterior vitrectomy, and also retained LECs.

The glaucoma rate seems to be equal in case with total lens removal and cases where the periphery of the lens capsule is left intact (Stech et al. 2019). Some authors have found a protective effect of primary IOL implantation (Asrani et al. 2000; Lawrence et al. 2005) (Mataftsi et al. 2014), while others have not (Chak et al. 2008; Wong et al. 2009; Kirwan et al. 2010). Asrani and co-authors have suggested two theories on the protective function of the IOL - one being a chemical hypothesis, were vitreal substances are blocked from entering the anterior chamber; the other being a mechanical hypothesis whereby the zonulae help support the structure in the chamber angle (Asrani et al. 2000). A recent study showed that the horizontal size of Schlemm's canal is smaller in accommodation in eyes that have had surgery for cataract compared with normal eyes (Daniel et al. 2019) which could be a biomechanical explanation for glaucoma secondary to cataract surgery in children.

Treatment

Although an entity of its own, treatment of glaucoma secondary to cataract surgery shows much resemblance to treatment of primary congenital glaucoma, the Golden standard of which is goniotomy described by Barkan (Barkan 1938). It was originally applied in adult glaucoma by Carlo de Vincentiis (DeVincentiis 1893). Trabeculotomy was described by Smith using a nylon thread (Smith 1960). At about the same time Burian described trabeculotomy using a specially adapted instrument, the trabeculotome (Burian 1960). Results on outcome of goniotomy and trabeculotomy seem to be similar (McPherson & Berry 1983; Hoskins et al. 1984), although goniotomy has less favourable outcome in children above the age of three (deLuise & Anderson 1983). While new methods are available, goniotomy and trabeculotomy are still the methods with the most long-lasting effect (Morales et al. 2013). A comparison between goniotomy and 360 degree trabeculotomy was in favour of trabeculotomy (Mendicino et al. 2000). This is interesting as there have been reports on the wrong direction of the thread (Neely 2005) and there was no mention of how the selection was made.

Different theories have been proposed on the histopathological background of congenital glaucoma. Barkan presented a theory involving a membrane and incomplete cleavage of angular tissues (Barkan 1955),but there are no histological evidence of a such structure. Gonioscopy, however, gives the impression of substance in front of the angle (see Figure 7, left). According to Anderson, "If the resistance is due to the compacted trabecular sheets, an

incision through the trabecular sheets would relieve the compaction and could account for the rather striking success of goniotomy or trabeculotomy in infantile glaucoma" (Anderson 1981). In 1972, two routes by which fluid leaves the anterior chamber were described, namely through the trabecular meshwork and through the uveal meshwork (Inomata et al. 1972). The consequence for surgical decision making is that the method should deal with the origin of both.

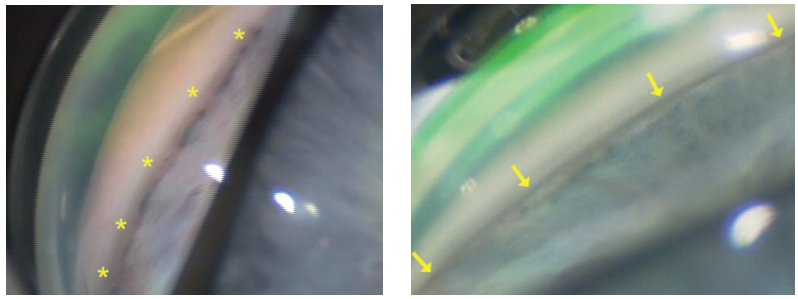

Figure 7. Left: Dysgenetic chamber angle seen through a gonioscopic mirror and in the centre of the picture showing bridges of abnormal uveal meshwork (next to yellow stars) creating an anterior insertion of the iris base covering the trabecular meshwork. Right: The incised and separated uveal meshwork after trabeculotomy, black line indicated by yellow arrows.

The timing of the procedure seems to be of importance. The greatest success rate (97%), with the least number of procedures, is achieved from the third to the fifth month (Haas 1968), and rates stay >75% during the first year (deLuise & Anderson 1983). According to Haas, once the pressure has been stabilized for a year, the likelihood of maintaining pressure levels is high.

Similar results have been obtained with goniotomy for primary congenital glaucoma in East Africa, and with the more scar-forming tissue in a Black population, this is particularly promising (Bowman et al. 2011). The combination of trabeculotomy with trabeculectomy has not been proved to be better (Khalil & Abdelhakim 2016). The surgical technique for chamber angle surgery in the papers presented in this thesis was a radial incision without a scleral flap, and a trabeculotomy with the use of Harms trabeculotome (Harms & Dannheim 1970), in combination with viscoelastic injection (Tamcelik & Ozkiris 2008), (Figure 7, right). Antimetabolites were not used to avoid long-time risks in children (Mendicino et al. 2000). The treatment outcome of angle surgery in primary congenital glaucoma has been described by some as better than the outcome in SG or in cases of comorbidity, but the difference is limited and VA is stable (Kargi et al. 2006). A recent Cochrane analysis was unable to

show a single method that is superior in primary congenital glaucoma (Ghate & Wang 2015).

If angle surgery turns out to be insufficient, a drainage tube device is employed where a silicone tube is inserted into the anterior chamber through a scleral canal. The tube ends with some sort of plate sutured to the sclera, 8-12mm posterior to the limbus, to maintain an open area for formation of a filtering bleb. The three most common drainage tubes are Ahmed (Coleman et al. 1995a; Coleman et al. 1995b), Baerveldt (Fellenbaum et al. 1995) and Molteno (Molteno 1969) implants. These drainage tube devices have been reported to be more efficient than filtering surgery (Tanimoto & Brandt 2006). Filtering surgery in children would need an antimetabolite due to the excessively good healing capacities in children. The antimetabolites most frequently used are mitomycin C and, less commonly 5-fluoro-uracil. They are efficient in preventing healing but at the same time confer a life-long risk of bad healing in the treated area and therefore a risk for late infections (e.g. endophthalmitis) (Waheed et al. 1998; Mendicino et al. 2000; Gharaibeh et al. 2018). Drainage tube devices have specific risks as well, among which, penetration of the tube through the conjunctiva and hypotony are the most described (Munoz et al. 1991). In case of hypotony, however, the tube can easily be plugged from the anterior chamber and drainage can be visualized by B-scan (Figure 8).

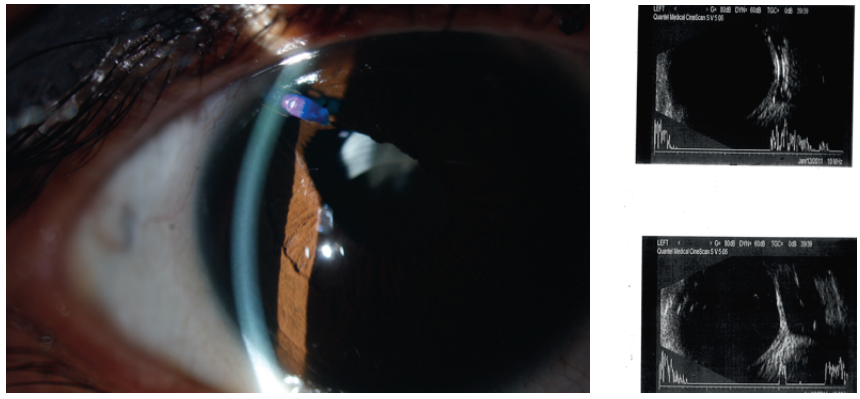

Figure 8. A Molteno tube with a prolene suture plug, inserted in the anterior chamber (left). Ultrasound B-scan of a Molteno tube without (top right) and with drainage (bottom right). A clearly visible space with fluid can be seen behind the bulb.

Prognosis

Long-term follow up in primary congenital glaucoma shows a lack in progression in almost 60% of cases after > 30 years (de Silva et al. 2011).
If these results hold, there is a reasonable chance of good long-term visual function even in children affected by SG as long as the initial pressure-lowering effect is good and the glaucoma is handled before the pressure has caused too much damage. The prognosis for chamber angle surgery treatment in congenital glaucoma has in a study shown better in children with surgery after the second and to the fifth month with a 97% success rate (Haas 1968). Even though these numbers are quite reassuring, for the patient, SG still poses a threat to vision.

1.10.2 VISUAL AXIS OPACIFICATION AND POSTERIOR CAPSULE OPACIFICATION

Visual axis opacification(VAO) and posterior capsule opacification (PCO) are the most frequent complications in paediatric cataract surgery (Vasavada et al. 2011) (Plager et al. 2014; Solebo et al. 2015). There is a strong inverse relationship between age and incidence of PCO (Astle et al. 2009) (Hosal & Biglan 2002) (Plager et al. 2011). Growth rate in LECs is high during the first 6 months when the lens increases from 6 to 7.7 mm in diameter (Bluestein et al. 1996) and the likeliness of VAO formation is not only great; the condition also is often not, unlike in adults, treatable with Nd-YAG lasers due to unsatisfactory results (Hutcheson et al. 1999; O'Keefe et al. 2001). The Nd-YAG laser is good at disrupting membranes, but newly formed LECs, i.e. Elschnig pearls (Elschnig 1911), represent more extensive newly formed tissue (Kappelhof et al. 1986) and are not as easily treatable because of the volume involved.

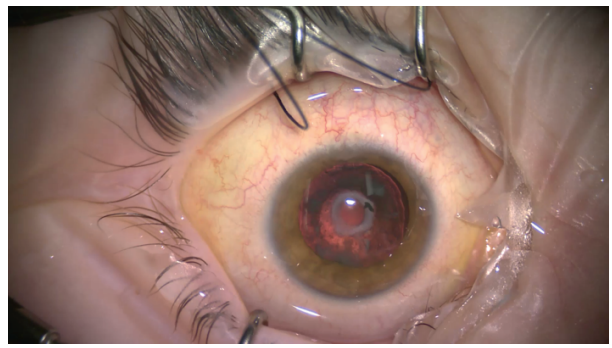

Figure 9. Adhesions of the anterior and posterior capsule forming a circular fibrotic ring in the centre, with lens epithelial cells (LECs) filling the periphery of the lens.

Diagnosis

Like cataract, PCO and VAO are diagnosed through biomicroscopic examination and retinoscopy. Secondary cataract formation was described by Soemmerring in 1828 (von Soemmerring 1828), and this doughnut-shaped ring, consisting of the peripheral lens capsule and lens cells at different degrees of degeneration still bears Soemmerring's name (Kappelhof et al. 1987), (Figure 9). In children with primary removal of the central part of the posterior capsule, the fibrosis is not as much of a threat but migration of LECs cannot be prevented (Vasavada et al. 2011) (Astle et al. 2009) (Figure 10).

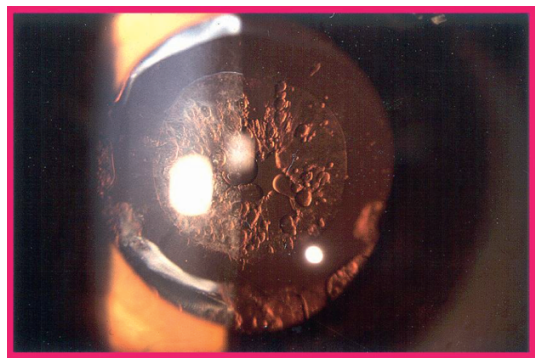

Figure 10. Lens epithelial cells (LECs), or Elschnig pearls covering the opening in the posterior capsule. With permission Professor Marie-José Tassignon.

Cause

Visual axis opacification may have different origin and processes. Foreign body reaction, inflammation and trauma (Fagerholm & Philipson 1979). The epithelial cells may undergo fibrous metaplasia and form secondary membranes (McDonnell et al. 1984), which is common during the first year (Astle et al. 2009) but occurs at the greatest rate when surgery is performed before 6 weeks of age (Watts et al. 2003). The largest volume comes from LEC proliferation, forming first syncytial posterior capsule opacification and later Elschnig pearls (Apple et al. 1992).

Treatment

The most common treatment in adult VAO is Nd-YAG laser. A pulse disrupts the membrane which in adults is normally comparatively thin and has few or no epithelial cells (Aron-Rosa et al. 1980). In children, the problem is that the anterior vitreous membrane is left as a carrier for LECs and the reopacification rate is high (Hutcheson et al. 1999). Some authors recommend surgery rather than Nd-YAG laser (Mullner-Eidenbock et al. 2003).

The earliest surgical treatment, discission, is a procedure in which membranes in the pupillary area are cut with a long blade through an incision in the anterior chamber of the eye. The method works because of the pressure from the vitreous body through the capsular tear in the presence of an open wound on the surface of the eye and with no IOL in the way. With modern microsurgery through closed small incisions, and a combination of fibrosis and LECs migrating over the optical axis discission has little or no use in children. Vitreous fragmentation, cutting and aspiration using a pars plana approach are currently the accepted way to clear the optic axis in the presence of fibrosis or migrating LECs (Vasavada et al. 2011).

In adults, either treatment is likely only to be used once while in children re-treatments are common (Plager et al. 2014; Solebo et al. 2015). Without posterior capsulotomy almost all infants need a secondary procedure to treat VAO (Vasavada & Chauhan 1994). Recent studies have identified VAO as the most frequent cause of re-operation in children under the age of 2 and consequently as a reason to advise against the use of intra-ocular lenses in children. (Plager et al. 2014; Solebo et al. 2018) The results have already been adapted by surgeons (Poole et al. 2019).

1.11 OCULAR COMORBIDITY

In children with cataract, ocular comorbidity and coexisting systemic malformation or disease are common. Down Syndrome (Haargaard & Fledelius 2006) Lowe's syndrome (Kruger et al. 2003) Foetal Alcohol Syndrome (Stromland 1985) Stickler syndrome (Seery et al. 1990) and Alport syndrome (McCarthy & Maino 2000). In unilateral cataracts ocular comorbidity PFV and microphthalmos (Weiss et al. 1989a; Weiss et al. 1989b) are most common. But ocular comorbidity is also common in bilateral cataracts aniridia, lens coloboma and embryotoxon being examples.

1.11.1 PERSISTENT FOETAL VASCULATURE

In the foetus, proliferating, transient blood vessels not respecting borders arise and normally disappear again. Those that persist at birth are termed persistent foetal vasculature (PFV)(Mutlu & Leopold 1964; Goldberg 1997). This phenomenon was first described as one of the causes of leukocoria but was later described more specifically (Reese & Payne 1947). From anterior to posterior, these blood vessels may have adhesions to the cornea (Peters' anomaly) and shallow anterior chamber, pupillary membrane (Figure 11A), irido-hyaloid vessels more spherical anteriorly shifted lens, centrally dragged ciliary processes (Figure 11B), persistent hyaloid artery (Figure 11C),

peripapillary and macular traction (Figure 11D) with macular engagement, dysplasia and failure to develop foveal pit, and tent-shaped retinal detachment. (Laatikainen & Tarkkanen 1982; Mullner-Eidenbock et al. 2004a; Mullner-Eidenbock et al. 2004b).

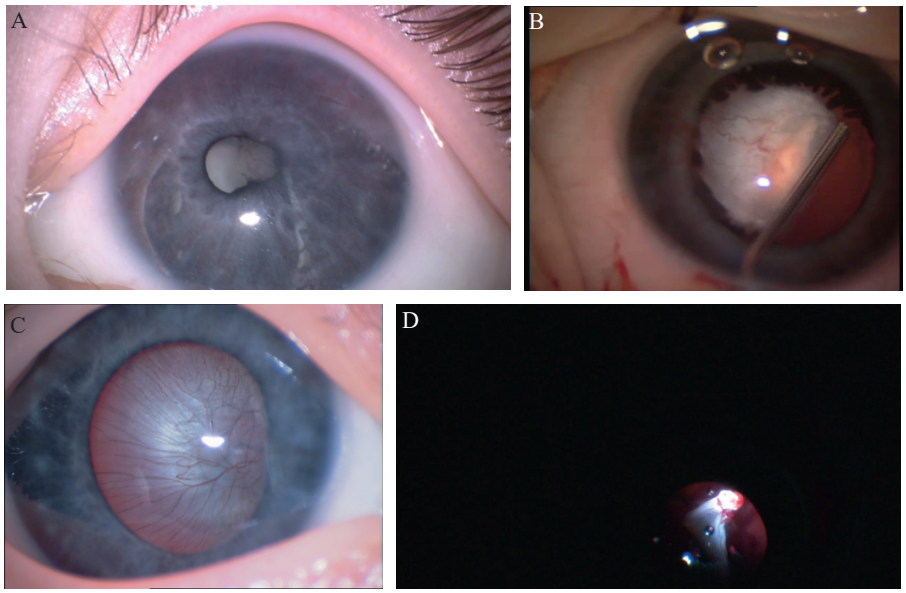

Figure 11. (A) Persistent foetal vasculature (PFV): shallow anterior chamber, adhesions to central cornea and vessels passing the border from the iris to the lens. (B) Centrally dragged ciliary processes and a vascularized membrane posterior to the lens. Vessels can be seen passing from the iris into the lens. (C) Vascular membrane on the lens and a hyaloid artery continuing backwards. (D) Hyaloid artery with membrane, continuing to the foveal area.

Different stages from very mild to serious pre-pupillary membrane have been described (Mullner-Eidenbock et al. 2004b). Studies have proposed that PFV increases the risk for SG (Kuhli-Hattenbach et al. 2008; Kuhli-Hattenbach et al. 2016) as well as for other adverse events (O'Keefe et al. 2001), (Morrison et al. 2011). Vishwanath et al. did not find a difference in glaucoma rate between eyes with PFV and eyes with "isolated congenital cataract" (Vishwanath et al. 2004), but stated that they "did not have sufficient numbers to conduct separate risk factor analyses for unilateral cataracts". Persistent foetal vasculature is more common with unilateral cataracts (Mullner-Eidenbock et al. 2004b), while other common ocular malformations are usually bilateral.

1.11.2 EMBRYOTOXON

Remnants of mesenchymal cells on the posterior surface of the cornea are sometimes seen near the limbal rim in children as a sign of incomplete formation of the chamber angle. This means an increased risk of glaucoma without cataract surgery; Ozeki et al reported a prevalence of open-angle glaucoma in these children of 11.2% (Ozeki et al. 1997).

1.11.3 ECTROPION UVEAE

Ectropion uveae is a condition where an overgrowth of pigment epithelium cells on the anterior surface of the iris are visible in the pupillary area and dysgenesis in the irido-trabecular region. This means an increased risk of glaucoma (Kumari & Saha 2018).

2 AIM

The aim of this thesis was to find and validate methods for diagnosis, treatment and prevention of complications in paediatric cataract surgery.

Specific aims

Paper I – To characterize the longitudinal changes in refraction in aphakic eyes after early surgery for congenital cataract, and evaluate this change as a non-invasive indicator of disturbances in ocular development.

Paper II –To describe a paediatric cohort surgically treated for primary glaucoma and secondary glaucoma with regard to incidence, visual outcome and control of IOP.

Paper III –To report the outcome and evaluate the results of IOL-implantation in children with primary implantation of BiL-IOL with regard to eligibility, possible complications and VA results.

Paper IV –To determine predictors of secondary glaucoma and poor visual outcome after cataract surgery with primary BiL-IOL in children.

Paper V –To report cumulative incidence and time of onset of postoperative glaucoma in a paediatric registry-based cohort with early cataract surgery.

3 PAPERS

3.1 BACKGROUND OF THE PAPERS

3.1.1 PAPER I

Until the first decade of this century there was no method available to precisely measure IOP in an unsedated small child. Today, in the Nordic countries, rebound tonometry (Lundvall et al. 2011) (iCare Finland OY, Vantaa, Finland) is used for IOP measurement in small children. However rebound tonometry has many sources of error. These include high pachymetry values and false high values when children are tense (Martinez-de-la-Casa et al. 2009). Low values seem more reliable (Dahlmann-Noor et al. 2013).

Clinical signs such as corneal oedema, obvious difference in size between the right and left cornea or increased excavation of the optic disc were clinical ways to diagnose glaucoma, unless the patient was examined under general anaesthesia.

Prior to the appearance of these signs, the axial length increases. Axial length is a way to validate pressure levels over time in children (Sampaolesi & Caruso 1982). It can be measured by ultrasonography, which is most common in babies but requires general anaesthesia in a small child to obtain the needed precision. Alternatively, it can be measured optically (Fledelius et al. 2014). Additional optic measurements are standard routine in most eye clinics that handles small children. A retinoscopy value is needed to check on refraction, and for prescribing glasses or contact lenses. But it also provides a check on the optical length of the eye. The ocular tissues of infants are soft. High pressure will extend the walls and the eye will expand. The value can fluctuate, meaning that if the pressure normalizes the globe may decrease in size. There is therefore good sense in using this standard measure to rapidly identify change and act immediately to stop progression of the disease. Even today with better possibilities of measuring the pressure, determining axial length can help in distinguishing between a false or a temporarily high value from a true damaging pressure.

3.1.2 PAPER II

Treatment of glaucoma in childhood differs from treatment of adult glaucoma. In childhood, surgery is often the first line of treatment (Haas 1968) since medication alone rarely show sustained efficacy for glaucoma in infants and young children (Weinreb et al. 2013). Pharmaceutical treatment rarely lowers

the pressure enough and the issue of treatment over the lifespan together with the compliance issue requires other treatment strategies. Dysgenesis of the trabecular meshwork in congenital glaucoma and angle structural changes in children after cataract surgery are suggested to be major reasons for development of glaucoma in these groups (Kang et al. 2006). As a consequence, if surgery shall have a preventive role for future glaucoma it is probably the correct first approach. For angle surgery, two methods are available. Trabeculotomy means finding the canal of Schlemm from the outside and opening the trabecular meshwork into the anterior chamber towards the centre of the eye (Burian 1960; Tamcelik & Ozkiris 2008). The alternative method goniotomy in which the chamber angle is opened from the inside (Barkan 1938) with a sharp knife. This has the disadvantage of needing a clear view through the cornea, which usually is not available in children with glaucoma because of corneal oedema.

Both methods have the same potential in children up to the age of 3, according to the literature (Hoskins et al. 1984). We chose trabeculotomy (Burian 1960) with the methods described by Harms (Harms & Dannheim 1970) and the modification of Tamcelik (Tamcelik & Ozkiris 2008) because of the potential to treat most of the paediatric glaucoma children regardless of corneal status. This method has also been used in children up to 12 years, with good results. (Luntz 1984) (but with less effect in anomalous eyes) (McPherson & McFarland 1980).

If angle surgery turns out not to be sufficient, drainage tube devices have proven to be more efficient than filtering surgery (Tanimoto & Brandt 2006). Filtering surgery in children, i.e. trabeculectomy, has to be complemented by antimetabolites because of children's excessively good healing capacity, which at the same time has the disadvantage of a life-long risk of bad healing (Mendicino et al. 2000).

3.1.3 PAPER III

The most common complication after child cataract surgery is visual axis opacification (VAO). A previous study from our department reports a 31% incidence of VAO after surgery in children without IOL implantation (Magnusson et al. 2000). In the late 1990s the implantation of IOLs was applied to still younger eyes. The results regarding VAO showed a substantial rate of VAO especially in the infants below the age of 1 year (Lundvall & Zetterstrom 2006) (Astle et al. 2009). Hydrophobic IOL material has been reported to protect against VAO in adults (Li et al. 2013) as well as in children (Mullner-Eidenbock et al. 2003). An IOL with conventional design would still

have a high risk of a second surgery at a time when it would not have any benefit for the child. Aphakia gives the opportunity to perform a secondary implant whenever chosen.

The new BiL-IOL concept had the potential to change this (Tassignon et al. 2002). Instead of implanting the IOL in the capsular bag where the IOL keeps the anterior and posterior capsule apart, and allowing LECs to migrate and proliferate, the capsule is opened both in the anterior and in the posterior part with two 5mm large capsulorhexes. The capsular rims are then inserted in a groove at the IOL equator thus preventing LECs from migrating out of the lens-bag and in front of the optic axis.

The BiL-IOL has previously been proved efficient in reducing VAO in a paediatric cohort with an 8.7% rate (4/46) eyes (Van Looveren et al. 2015). The IOL is made of hydrophilic acrylic, which has been suggested to have better biocompatibility compared with hydrophobic IOLs (Abela-Formanek et al. 2011), This is advantageous when inflammation is the cause of VAO. Another big advantage was the prospective of easy lens exchange if the growth of the eye differs from expected and a lens exchange would be needed for refractive reasons, as described by Ni Dhubhghaill et al (Ni Dhubhghaill et al. 2015). The technique was introduced at the Department of Ophthalmology, Sahlgrenska University Hospital, in 2009 and this study was a follow-up.

3.1.4 PAPER IV

With good results for VAO and excellent postoperative status the incidence of glaucoma could be expected to also be low when inflammation, exposition of vitreous substances and LECs have any part in SG (Nishi 1988; Walton 1995) (Asrani et al. 2000). However, the numbers were the same as previously reported from our Department in children with aphakia (Magnusson et al. 2000). Visual acuity development is the reason for early surgery and the VA results on surgery at different ages are of importance in the decision on when to perform surgery (Birch & Stager 1996; Birch et al. 2009) This study is a more in-depth analysis of SG in the same cohort as included in Paper III, focusing on predictive factors and visual development in children who developed SG postoperatively.

3.1.5 PAPER V

In rare conditions the task of gathering large enough numbers is always a challenge. The Pediatric Cataract Registry (PECARE) is collected data on a geographic basis. The registry started in 2006 and all cataract procedures in Sweden below the age of 8 years are now entered in PECARE. The registry,

includes data on cataract such a density, type, and PFV, along with biometric data, VA and refraction, comorbidity, when and by whom the cataract was discovered, consanguinity, heredity and other diseases at the time of operation. It has four follow-up reports at the child's age of 1, 2, 5 and 10 years, respectively (Appendix).

3.2 MATERIAL AND METHODS

3.2.1 PAPER I

Paper I is a retrospective analysis of longitudinally measured refraction of aphakic eyes of children at different ages after cataract surgery. The study was longitudinal and the measurements were repeated for every child. Normal growth curves, calculated as contact lens power (optic) change, were constructed. The individual curve for each individual eye was overlaid to validate the assumption that eyes follow a predetermined curve.

Materials: The cohort were children from a study of congenital cataracts in western Sweden (Abrahamsson et al. 1999), investigated at a single centre with comparatively few investigators.

3.2.2 PAPER II

Paper II is a cross-sectional retrospective cohort study on results after paediatric glaucoma surgery. The incidence of glaucoma, type of surgery, pressure-lowering efficacy and VA results at follow-up are presented. The surgical methods used were mainly angle surgery and a drainage shunt device (Molteno valve). The surgery therefore comprised: (1) nasal trabeculotomy; (2) temporal trabeculotomy, (3) upper temporal Molteno implant; and (4) lower temporal Molteno implant.

Materials: The cohort in this study were children who had surgery at a single centre by the same surgeon (Alf Nyström). Follow-up was at different sites depending on the referral hospital.

3.2.3 PAPER III

Paper III and IV are cross-sectional retrospective cohort studies on results of child cataract surgery.

Paper III is a study on primary implantation of BiL-IOLs at Sahlgrenska university hospital. The preoperative morbidity of the eyes as well as systemic

disease, complication rate, (mainly VAO and SG) and corrected distance VA (CDVA) results are included.

3.2.4 PAPER IV

Paper IV is a more thorough analysis of SG in the eyes included in Paper III. The time of cataract surgery for the children who developed glaucoma and the VA levels obtained at surgery at different ages (weeks after birth) are analysed. Occurrence of comorbidity, visual acuity and complications are the results.

Materials: The first 109 cataract surgeries in 84 children who received a BiL-IOL were included. The children were followed up at different hospitals according to their place of residence.

3.2.5 PAPER V

Paper V is a registry-based study of children prospectively reported to PECARE, and the incidence of glaucoma after paediatric cataract surgery in children aged 0-8.

Materials: The study included all children in Sweden with a cataract extraction performed between 2007 and 2014 at different sites by different surgeons and different ophthalmologists doing the follow-up according to a protocol.

3.3 STATISTICAL PROCEDURES

3.3.1 PAPER I

For statistical calculations, second-degree polynomial, logarithmic, and exponential fitting models were tested. The regression line with the greatest R^2 value was considered the best fit. Microsoft Excel (Microsoft Corporation Redmond WA, USA) was used for all calculations.

3.3.2 PAPER II – IV

Visual acuity was converted to logMAR before performing arithmetic operations. Mean and standard deviation (SD) and/or medians with ranges are given as appropriate. Student's t-test for two independent samples and the Mann–Whitney U-test were used for continuous parameters, and the chi-square test for small samples (Fisher's exact test) was used for categorical data. A p-value < 0.05 was considered statistically significant. Binary logistic regression using a backwards, conditional stepwise approach when entering

covariates was used to analyse possible predictors for SG and for poor visual outcome. For the analysis, SPSS version 22 or 23 for Mac (SPSS Inc., Chicago, IL, USA) was used as statistical software.

3.3.3 PAPER V

The data in the PECARE were collected at specific time points, namely at the ages of 1, 2, 5 and 10 years. The occurrence of glaucoma was registered at these, but actual onset of glaucoma was somewhere between the last visit without glaucoma and the first visit with registered glaucoma. A date for first glaucoma onset was randomly imputed somewhere between the first visit with glaucoma and the last visit without glaucoma. A uniform distribution with a pre-specified seed value was used for this imputation. The cumulative incidence curve was adjusted for multiple eyes per subject (Ying & Wei 2007). This means that the statistical model used for Kaplan-Meier is a frailty model analysis which takes into account that multiple measurements can be derived from the same patient. Categorical variables were described by number and percentage and continuous variables by means, SD, medians, minimums and maximums. All analyses were performed with SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA).

3.4 RESULTS AND DISCUSSION OF SPECIFIC PAPERS

Complications will occur in surgery. With knowledge about previous results, we can make decisions for future surgery. The papers were investigations of diagnosis, incidence, management and outcome of paediatric cataract with focus on the main complications VAO and SG.

Paper I investigates a diagnostic tool in diagnosis of glaucoma, secondary to cataract surgery in children. Growth curves show growth of the normal eye after cataract surgery with aphakia.
Paper II examines the outcome of glaucoma surgery for primary glaucoma and SG in childhood.
Paper III is on the outcome after cataract extraction and primary BiL-IOL implantation in children with cataract in Sahlgrenska University Hospital.
Paper IV is an analysis of predictors for and outcome of SG and VA among the children reported in Paper III.
Paper V is a Registry-based study on glaucoma that uses PECARE data.

3.4.1 PAPER I

Refractive growth curves are similar in shape to growth curves of length, weight and head circumference (Wikland et al. 2002). Abnormal curves, i.e. curves that deviate from the shape of normal eyes, may indicate glaucoma development after early cataract surgery.

Previous investigations have shown comparison of the rate of refractive growth (McClatchey & Parks 1997). New here is the shown linearity in growth for every eye during the first 3 years of life. The result is a model for eye growth with the potential to target glaucomatous eyes as pathological. It is important to identify and quickly diagnose glaucoma without uncertainty or postponement of diagnosis or treatment.

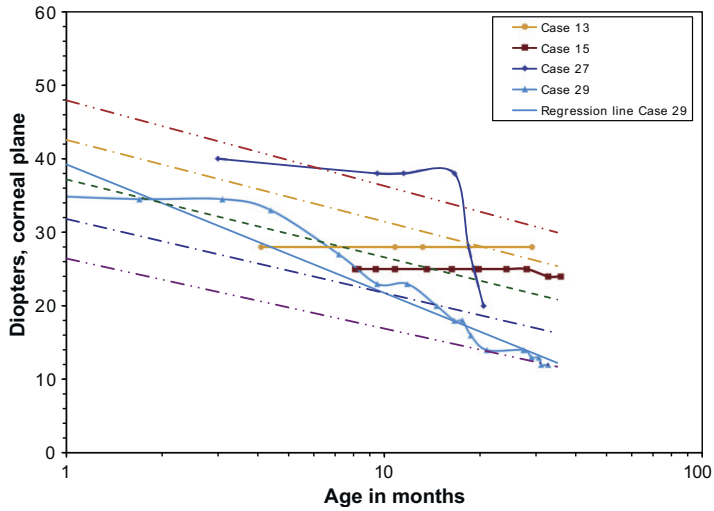

Figure 12. Curves of aberrant growth - no growth cases 13 and 15; glaucoma with rapid change, case 27; and an eye from a child with Down syndrome, case 29. The x-axis shows age in months (logarithmic) and the y-axis the refraction in diopter. Normal change (dotted) and ±1 and ±2SD are indicated (dash-dotted).

In Paper I we demonstrate that the ocular growth in most children follows logarithmic growth curves. Besides showing normal growth, three types of aberrant curves emerged from the model: (1) eyes that developed glaucoma; (2) eyes of children with Down's syndrome; and (3) a category of otherwise healthy eyes that during the time of measurement experienced no change at all (see Figure 12). Diagnosis of glaucoma secondary to cataract surgery in children, as compared with primary congenital glaucoma, is often difficult to make in time for adequate treatment. When the classic signs of corneal oedema and corneal growth occur, pressure has often been high for a considerable

period of time. Pressure measurements in children are often hard to interpret because of bad cooperation and abnormally high corneal thickness, both providing falsely high values (Dahlmann-Noor et al. 2013). Axial eye growth is usually the first sign that an eye has had a pressure high enough to affect the globe and this should raise the suspicion of glaucoma (Figure 13). In the event of this early and comparably safe diagnostic sign the child should be scheduled for a thorough investigation under general anaesthesia to confirm the diagnosis.

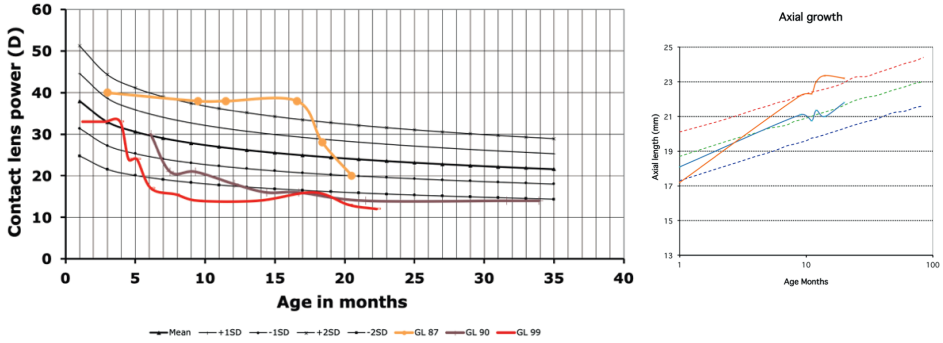

Figure 13. Left: Curves of three eyes with change in refraction and suspected glaucoma - all with a refractive change of > 2 standard deviation (SD). The x-axis shows age in months and the y-axis the refraction in dioptre. Normal change and ±1 and ±2SD are indicated. Right: Axial growth of an aphakic eye with glaucoma (orange colour). The x-axis shows age in months and the y-axis the axial length in mm. Normal growth and 95% CI (dotted) lines. (Sampaolesi).

3.4.2 PAPER II

With an incidence of 4.3 cases per 100.000 live births of primary congenital glaucoma in a western Swedish cohort and a rate of 13% of glaucoma secondary to cataract surgery, the numbers presented in Paper II are very close to previous studies indicating a representative sample for conclusions. Incidence and outcome are in accordance with previous studies (McGinnity et al. 1987) (Magnusson et al. 2000; Papadopoulos et al. 2007). Chamber angle surgery, sometimes combined with a shunt and without the use of antimetabolites, seems to have good potential to reduce pressure sufficiently (from 31.5 ±8.1mmHg to 17.1 ±4.4 mmHg) in primary glaucoma and SG in a paediatric glaucoma cohort. With a mean number of 2.3 pressure-lowering

procedures/eye the method seems to be comparable to similar studies (Alsheikheh et al. 2007). For those 32% with only one pressure-lowering procedure and a mean follow-up of 6.8 years, treatment may also be considered as successful.

This retrospective follow-up of eyes treated with pressure-lowering surgery for primary glaucoma and SG covers a 9-year span from 2002 to 2010. Median time from cataract surgery to glaucoma diagnosis was 3.8 months (range 1.6 months to 4.3 years) a comparatively short time compared to other studies where 6-8 years are common (Chak et al. 2008; Comer et al. 2011; Lambert et al. 2013). The median follow-up time was almost 4.98 years (range 0.33-11.04 years). In the entire cohort, 45% of the eyes had a VA of ≥0.3 in the glaucomatous eye at last follow-up. The possibility of keeping these levels is probably good according to a study by Kargi (Kargi et al. 2006) but in the study of long-term results by de Silva (de Silva et al. 2011), multiple regression did not find factors associated with good visual prognosis.

3.4.3 PAPER III

This is a retrospective follow-up of the 5 first years after primary implantation of the BiL-IOL, an IOL made with the purpose of reducing VAO in eyes after cataract surgery. In contrast to earlier studies with primary IOL implantation in children with high rates of secondary VAO (O'Keefe et al. 2001; Plager et al. 2014; Solebo et al. 2018), the present study showed only 4.6% (5/109 eyes) of VAO at a median follow-up of 2.9 years (range 7 months to 5.8 years).

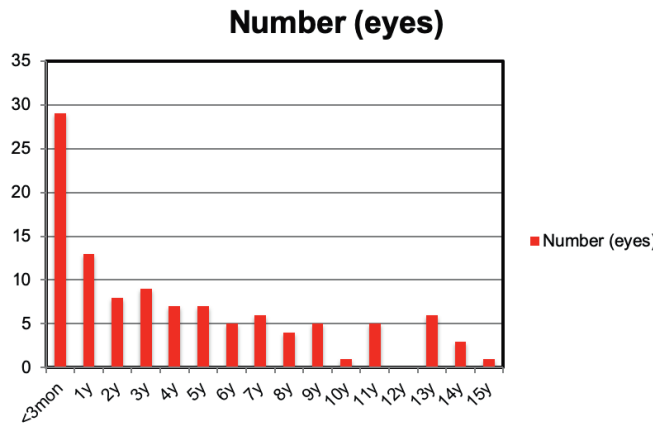

Figure 14. Number of eyes included in the Study III, by age (e.g. 2y stands for >1 and <2years).

In the study, all children with a BiL-IOL implanted at our clinic, 109 eyes of 84 children, were included. The median age at surgery was 2.5 years ranging from 2 weeks to 14.1 years, 22.6% of the children being 12 weeks or younger with a mean age of approximately 3 years at last follow-up. Among these, 24 eyes (16 children) were <6 weeks old at surgery. This age distribution of the children corresponded to that of all cataract surgeries in children in Sweden (based on PECARE data) (see Figure 14 and 16).

During the study period, 21 eyes were left aphakic, mostly because they did not meet the inclusion criteria of large enough biometric measures or because of conditions preventing the creation of an appropriately sized capsulorhexis. Glaucoma was seen in 15 eyes (13.8%), which is close to 12% seen in a previous study in western Sweden (Magnusson et al. 2000). Other studies on infantile cataract have also shown similar numbers, with 19% (Plager et al. 2014) and 13% (Kirwan et al. 2010) incidence of SG.

Apart from VAO and SG, some complications specific to the BiL-IOL occurred. The most common of these was incarceration of the iris in the rim of the lens, often managed by mydriatic drops. In eight eyes (7.3%) surgical correction had to be undertaken due to BiL-IOL incarceration in the pupil or luxation into the vitreous had to be undertaken, at least two of which had traumatic origin. Hydrophilic IOLs have the rare disadvantage of calcium deposits on the surface and in this study, one IOL had to be replaced for this reason. The exchange IOL was also a BiL-IOL and no deposit were seen at the endpoint of the study. Altogether, the re-operation rate for VAO and other complications than glaucoma was 14.7%. Ocular comorbidity was more frequent among children with unilateral cataract, with PFV being most frequent (22.5%). Even with the bilateral cataracts, PFV was the most frequent ocular comorbidity (5.8%). Among the bilateral cataracts, 54.5% of the children had a coexisting systemic disease or malformation. This was less often present in children with unilateral cataract children (15%). The difference in both ocular comorbidity and coexisting systemic disease was statistically significant between unilateral and bilateral cases.

Visual acuity was good in the majority of bilateral cases, with 55.6% attaining a CDVA of ≥0.5 decimal. This is somewhat inferior to another published study on BiL-IOL in children, where 86.7% reached ≥0.5 (Van Looveren et al. 2015). Unilateral cataracts are expected to perform worse and 37.5% attained a CDVA of ≥0.5 decimal in the present study. The results of the unilateral cataracts were more equal to the 31.2% reaching ≥0.5 in the study by van Looveren et al.

The CDVA results of the study are more difficult to interpret. Most of the dense bilateral congenital cataracts were still very young at the time of the last VA tests. This may explain the difference between mean and median CDVA among the bilateral cataracts: a median of 0.22 logMAR (0.6 decimal) with 55.6% scoring ≥0.5 decimal, versus a mean of 0.42 logMAR (approximately 0.4 decimal). Among the bilateral cataracts, 20% had a VA between 0.3 and 0.5 decimal, which is a normal value for a bilateral cataract at the age of 3 and is expected to increase (Magnusson et al. 2002) (Birch et al. 2009). With the exception of three eyes (one with +9.75 and two in a child with Down syndrome with -12) the children over the age of 5 had a mean refraction of -0.30±2.8 D.

Often studies exclude cases with comorbidity from evaluation (Solebo et al. 2015; Kuhli-Hattenbach et al. 2016; Lin et al. 2017) (Lambert et al. 2013). Comorbidity seems to be quite common among children with congenital cataract and can be expected to be so. In the present study, all comorbidity cases were included. With 54.5% of the bilateral cataracts having a coexisting systemic disease or malformation and 35.0% of the unilateral cataract cases having coexisting ocular comorbidity, it appears that children with comorbidity constitute a fairly large proportion of the paediatric cataract cases. It is probably reasonable to assume that with increased knowledge in the field of genetics, more systemic involvement will be found (Gillespie et al. 2014). This may also affect results regarding SG after cataract surgery in infants.

In this study, 13.8% of the eyes developed glaucoma after a mean time interval of 15 ±8.4 weeks and a range of 5-34 weeks, i.e. most glaucoma developed within a little more than half a year after surgery, which is a comparatively short time. (Magnusson et al. 2000; Haargaard et al. 2008; Comer et al. 2011) As well as the major complications of VAO and glaucoma, there is a surgical concern regarding lens luxation. Children can be quite aggressive in their way they rub their eyes after surgery and even parents with an initial inexperience in contact lens handling may interfere with the quite delicate structures shortly after surgery. In the present study, 7.3% of the children required surgery for repositioning of the lens.

3.4.4 PAPER IV

This paper is a follow-up on glaucoma and VA of study III. In this study, only children in the early surgery group (surgery within 3 months of age) developed glaucoma, with one exception and this child's treatment was postponed to the later time of treatment because of an intraocular haemorrhage at birth. Even among the early group time for surgery differed significantly between those

who developed glaucoma and those who did not. Mean age at surgery in the glaucoma group was 3.5±1.1 weeks, compared with 5.7±3.3 weeks for those who did not develop glaucoma. Within the first 5 weeks SG was common after surgery.

Corrected distance visual acuity differed both between the two groups in the early surgery group (≤12weeks) and between the early and late surgery groups. In the early surgery group, the glaucoma children with surgery at 3.5 weeks had a CDVA of 0.56 (range 0.4-1.0) logMAR (0.28decimal), a significantly better result compared with the non-glaucomatous children with a CDVA of 0.89 (range 0.7-1.6) (p=0.016) who had surgery at 5.7 weeks. Interesting also is that only one patient in the glaucoma group had a CDVA of < 0.1 decimal. Studies have reported equal results in VA between glaucomatous eyes and those without (Comer et al. 2011), but low CDVA results are common in eyes with SG (Freedman et al. 2015) (Lambert et al. 2013). Surgery in the third week compared with the sixth week rendered higher VA levels and higher levels of early-onset SG.

Corrected distance visual acuity was significantly better in the late surgery group but these children were older (median 7 years, range 2.8 – 17.2 years) at the time of the last visit compared with 3±1.34 years for the early group. The development of CDVA was slower but was considered appropriate compared with a cohort of children without cataract (Figure 15).

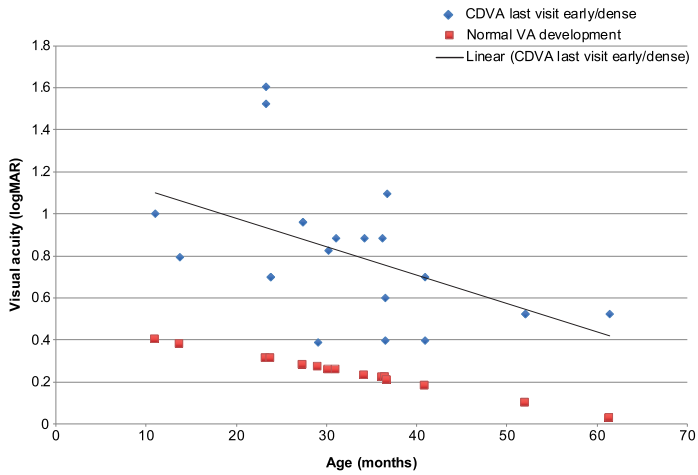

Figure 15. Visual acuity (VA) at the last visit in the early surgery group (blue squares), with a regression line showing development. Normal values calculated from The Multiethnic Pediatric Eye Disease Study (Pan et al. 2009) CDVA= corrected distance visual acuity.

The time interval after surgery to glaucoma diagnosis was 15 ±8.4 weeks, equal to early-onset in some studies (Lambert et al. 2013) but short time to glaucoma-onset compared with other studies (Chen et al. 2004) (Chak et al. 2008). Cataract surgery and first surgery for glaucoma were both conducted within half a year. For 6/15 of the glaucoma group, one procedure seemed to be enough for pressure control in the comparatively short follow-up period. In two eyes (1.8%) one or two drainage tube devices (Molteno tubes) had to be implanted to control pressure. Surgery before 5 weeks of age seemed to trigger early-onset glaucoma while surgery after that period was associated with a lower risk of SG.

The eyes that did develop glaucoma were to a much higher extent eyes with comorbidity. An important finding of this study is that eyes with comorbidity are quite numerous in this child cataract cohort (19.3%). These children also developed glaucoma to a higher extent and 81.8% of the children who developed glaucoma either had systemic disease or had ocular comorbidity, compared with 11%% of children without comorbidity. The percentage of eyes with comorbidity that did develop glaucoma was 57.1% while only 3.4% of children without comorbidity developed glaucoma. There was no significant difference between glaucoma rate in unilateral compared with bilateral cases which might be expected if only ocular comorbidity is at risk. Only one case developed glaucoma after surgery later than 12 weeks of age. This differs from studies in which glaucoma is common during the first 7 months (Chen et al. 2004; Chak et al. 2008) (Haargaard et al. 2008) One explanation for this discrepancy may be efficient screening in our population, with early detection of and surgery for dense cataracts with more comorbidity. Indeed, the median age at surgery was 4.4weeks in the comorbidity group while it was 3.2 years in the group without comorbidity. If the discrepancy is indeed due to good screening, this demonstrates that the status of the eye is important for the risk of developing SG.

With surgery after 5 weeks of age but before 2 years of age the glaucoma rate dropped to less than 7%. With a similar glaucoma rate as in a previous study with aphakia at our Department (Magnusson et al. 2000) and low rates of SG if surgery is performed after 5 weeks of age, the IOL used seems unlikely to negatively affect the risk of early-onset glaucoma, at least not after 5 weeks of age.

3.4.5 PAPER V

Paper V is a registry-based study using PECARE data on glaucoma incidence and onset of SG during the first 8 years (2007-2014) with a mean follow-up of 3.31 ±1.77 years. In the cohort of 207 children (and 288 eyes), 38.9% were below 1 month and 58.3% were under 3 months of age at the time of surgery, therefore being younger compared with cataract children in most studies. (Plager et al. 2014) (Solebo et al. 2015) (see Figure 16). The majority of the eyes with surgery before 3 months of age were defined as dense (155/168, 92.3%) In coherence with other studies, the glaucoma rate was high in these cases and 79 eyes of 57 individuals were registered with postoperative glaucoma.

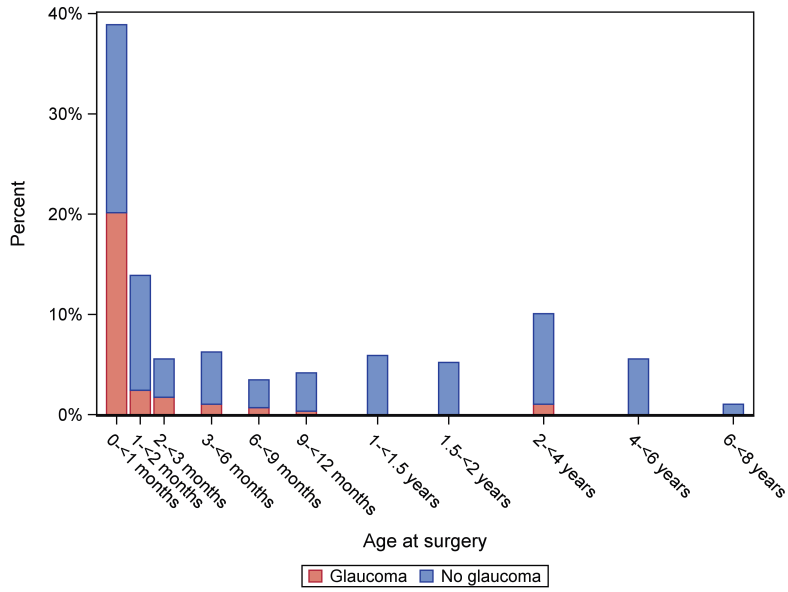

Figure 16. Distribution of age at cataract surgery and glaucoma rate.

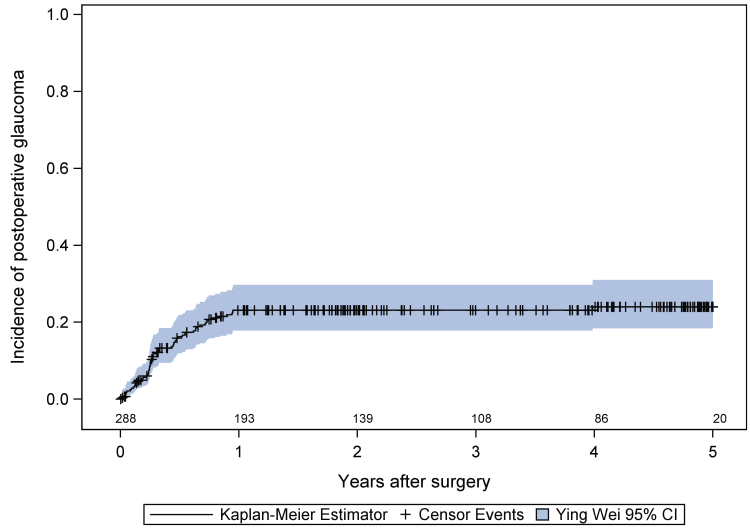

Figure 17. Incidence of postoperative surgical treated glaucoma together with 95% confidence interval in PECARE (Kaplan-Meier).

In a registry-based study, the registry record sometimes raises questions. Some of the registered glaucoma cases had neither any surgery for glaucoma nor pharmacological treatment registered. A more certain fact in this respect, especially among the young children studied here, is surgically treated glaucoma. The rate of surgically treated glaucoma in the registry was 64 eyes of 49 individuals. The cumulative incidence of surgically treated glaucoma was 23.7%, a comparatively high rate in a paediatric cohort, closer to that of infantile cohorts (Vishwanath et al. 2004) The glaucoma rate in children with surgery later than 3 months and the late-onset glaucoma rate were lower than expected and the cumulative rate 1 year after surgery was between 0.2% and 1.3%, which is low. With the cumulative progression rate, a final 10-year rate will be around 30% (Figure 17), - close to the figure reported in an earlier study on SG in Denmark (Haargaard et al. 2009).

This paper is a report on the glaucoma incidence in Sweden which has had a good screening programme for the early detection of cataract in newborn babies. The incidence has previously been validated in the register and 75% of the cataracts are found and have had surgery before 3 months of age (Magnusson et al. 2013). The early operations consist of dense cataracts with known poor prognosis if left un-operated. This is also reflected in the results of this study with a comparatively large number of early-onset SG.

Many similar studies on infantile cohorts have a substantial contribution of glaucoma from surgery after the first year (Watts et al. 2003) (Chak et al. 2008). In the present study the number of cataract surgeries after the initial 3 months is fairly low; hence, glaucoma after surgery is rare in the period after 3 months. Secondary glaucoma after congenital cataract surgery has been reported to have a bimodal onset with an early-onset and a late-onset (Mills & Robb 1994) (Kang et al. 2006). Other reports have found a more constant increase over the years (Ruddle et al. 2013) Whether early surgery triggers the glaucoma that will develop anyhow in the future, or whether the early-onset glaucoma is different and adds to the total glaucoma rate is too early to tell. The follow-up time in the study was comparatively short with regard to this question.

3.5 DISCUSSION OF METHODS AND MATERIALS

3.5.1 PAPER I

The strength of this paper is the established values and validation of values by re-testing. A single erroneous value will not affect the results of the study. A limitation of the paper is the small number of cases with aberrant growth included in the study.

3.5.2 PAPER II

The strength of Paper II is the small number of methods used and the consistency with regard to this decision in order to have large enough numbers for comparison of results. This makes it possible to compare methods and results with similar studies at a general level.

Limiting factors of the study are the different causes and severity levels of glaucoma; the problems in defining the endpoint and success rate; the lack of papilla analysis and visual field analysis and different methods for pressure measurements intraoperatively and postoperatively; as well as pressure and VA levels obtained by different observers using different methods; and inter-observer variation; and measure faults. The primary glaucoma group had cataract as a complication, with a calculated rate of 21%. The SG group had other surgeries apart from glaucoma procedures, which were difficult to count as complications; however, more surgical procedures have demonstrated increased risks of low success (Kargi et al. 2006). The follow-up from the first

surgical event is good, but some children have had a short time since their last surgical event.

3.5.3 PAPER III – IV

Just as the case in Paper II, the number of eyes/children is the strength of the study (Kim et al. 2012) (Lambert et al. 2001) Vasavada (Vasavada et al. 2004). The two groups among the early surgery group gave the opportunity to compare results regarding VA development in an infantile cohort together with a group of older children with developmental cataract.

Limitations are: lack of a reference group (similar to Paper II), And that the follow-ups were performed at different sites by different observers; as well as the different methods for pressure measurement; VA-testing differences; and different routines for testing refraction.

Moreover, there is a selection bias in the methods used. There was no comparison with other methods used. There is also a selection bias in Papers III and IV as not every patient was included; the studies included only those with a primary BiL-IOL implant. The not included cases may have been further cases with comorbidity.

3.5.4 PAPER V

The strength of this study is the number of children from a defined geographic area, which made it possible to collect a large enough cohort with a rare condition such as paediatric cataract. More than one centre with different methods for surgery is included.

Regarding limitations, this study differs from the previous studies in the thesis in that it is registry-based. To be able to compare visual development with other children at a specific age, the time of glaucoma onset is specified within a year. We have used a statistical tool- imputation- to calculate the time of glaucoma onset. Imputation means that a certain event is set to have happened randomly between the last observation without the event and the first observation with the event. In this study the method seemed good enough, with figures close to the onset time actually measured in a subgroup of the cohort, the study in Paper III. If, however, as in the case of visual development, there is a window for successful treatment of chamber angle deficiencies, the data have to be more specific. For the subgroup “surgically treated glaucoma” the time is obtainable but this still leaves the not surgically treated glaucoma children without data on onset time.

4 MAJOR CONCLUSIONS

- Calculating the rate of refractive growth is a sensitive and feasible means of detecting glaucoma after cataract surgery in infants.
- The SG rate in a Swedish cohort subjected to cataract surgery between 2002 and 2010 (13.8%) was similar to the rate in other cohorts of paediatric cataract surgery.
- Glaucoma surgery with angle surgery as first and implantation of a glaucoma drainage device as second line of treatment seems to adequately lower pressure in most eyes with SG.
- The rate of secondary cataract formation, and VAO after primary BiL-IOL implantation is low in a paediatric cohort (4.6%).
- The results regarding VA after cataract surgery were comparatively good in a short-range follow-up, bearing in mind the young age of the cohort.
- Ocular and systemic comorbidity was high in this cohort of paediatric cataracts. Bilateral cataract children have coexisting systemic disease in 54.5% of cases. Unilateral cataracts have ocular comorbidity in 35%.
- Surgery during the first weeks of life seems to improve VA.
- Surgery during the first weeks of life increases the rate of SG.
- With the current methods used, surgery after 5 weeks seems to reduce early-onset SG development.
- In Sweden, the incidence of surgically treated SG after cataract surgery in a cohort consisting mainly of infants below 3 months of age is 23.7% in a 3-year follow-up. The annual increase is about 1%.

5 GENERAL DISCUSSION OF FINDINGS

Some prerequisites are essential for evaluation of cataract surgery in children. Early diagnosis of children with congenital and early developmental cataract is crucial for timing of treatment. Screening gives the possibility to choose the most opportune timepoint for surgery. The aim of surgery is primarily good vision but the stability of the condition is also important. Early surgery increases the chance of good visual development. Surgery within 3 weeks of birth has the possibility of not affecting visual development from either a cortical or a VA point of view. Postponing surgery to 6 weeks of age in our cohort rendered a loss in VA at the age of 3 years, as shown in Paper IV, which was an expected finding according based on previous studies. Severe amblyopia and nystagmus are at this point less likely to affect final VA. In the short perspective of these studies and with these methods, amblyopia seems to be the limit of VA development.

Early surgery also increases the risk of early-onset SG. Studies elsewhere and in this thesis have confirmed this. What "early surgery" means, in weeks or months, with regard to glaucoma is not as evident. Depending on the perspective, range from 2 weeks to 2 years have been used. Previous studies proposed that inflammation and substances from LECs and vitreous chemicals were the cause of early-onset glaucoma (Asrani et al. 2000) and VAO. From this perspective, the idea of blocking LECs (Kappelhof et al. 1987) and vitreous contact with anterior chamber fluid seemed a valid way to limit the problem of glaucoma as well as VAO. At the time some studies supported this by showing a lower rate of SG with a primary implantation of an IOL (Lundvall & Zetterstrom 1999; Asrani et al. 2000; O'Keefe et al. 2001). The reduced rate of glaucoma seemed not to affect the VAO rate, which was even higher among the pseudophakic eyes (Astle et al. 2009) (O'Keefe et al. 2001). Postponing surgery is not a cure to SG but it decreases the rate of early glaucoma development wright (Wright et al. 1992) Glaucoma will develop as a consequence of paediatric cataract surgery but the rate in an infantile compared with a paediatric cohort will approximately double from 10-20% (Magnusson et al. 2000) to 20-30% (Vishwanath et al. 2004; Kirwan et al. 2010; Ruddle et al. 2013). This is evident in the short run. With long-term studies the rate of glaucoma increases and once having had cataract surgery in childhood means a life-long risk of glaucoma (Ruddle et al. 2013).

Not every paediatric cataract needs early surgery or even surgery at all. Small size cataracts and changes in the crystalline lens often do better without surgery (Bradford et al. 1992). Cataracts scheduled for early surgery are therefore not

only found early but are also denser, meaning more advanced changes in the lens. It would be strange if these changes were exclusively confined to the lens. Mesenchymal cells responsible for development of the anterior segment (McMenamin 1989) as well as foetal vessel remnants exist not only within the lens and developmental changes are to be found in other structures in the anterior segment as well (Goldberg 1997). With better possibilities to examine genomic information more cataracts are classified as syndromal (Gillespie et al. 2014).

In Paper V the incidence of glaucoma with surgery before 1 month of age was high, which is consistent with other studies (Chen et al. 2004) (Comer et al. 2011)In contrast to other studies (Chak et al. 2008) very few new glaucoma cases appeared after this initial cluster. This can be explained by early surgery. It may however, also be explained by comorbidity. If comorbidity is the reason, the cause of glaucoma is a combination of early surgery and changes in the development of the chamber angle. Development of the chamber angle continuous after birth by the posterior sliding of structures (Anderson 1981). Normally at time of birth, the uveal meshwork has reached the level of the scleral spur. The normal growth of the cornea is known to be substantial during the first 2 months in life (Inagaki 1986). Microcornea increases the risk of glaucoma after cataract surgery in infants (Wallace & Plager 1996). An underdeveloped anterior segment seems to contribute to glaucoma. If time alone would be the cause, glaucoma would disappear after a certain time when the eye is large enough, which seems not to be the case in cohorts where screening is not undertaken or surgery is postponed (Wright et al. 1992). If congenital cataracts are operated on later, glaucoma occurs at higher age (Haargaard et al. 2008; Comer et al. 2011).

Do these changes in the anterior chamber vanish with age? Probably not. A recent study reports that the canal of Schlemm has a smaller horizontal diameter in eyes after lensectomy in children compared with normal eyes many years after surgery (Daniel et al. 2019). While accommodation and contraction of the ciliary muscle normally enhances the outflow of fluid from the anterior chamber (Inomata et al. 1972; Inomata et al. 1972), less happens in eyes after lensectomy (Daniel et al. 2019). This means that eyes after lensectomy, in general have a defect that may promote glaucoma.

In Paper II, the results after treatment of SG showed that 70% of the cases needed one or two pressure-lowering procedures and among those only treated once the follow-up time was almost 7 years. The first and second procedure in glaucoma secondary to cataract is usually a trabeculotomy. The mechanism of action was thought to be the removal of thickened membranes in the trabecular

meshwork or reopening the collapsed canal of Schlemm (Hoskins et al. 1984). Although the mechanism is not fully understood the site of action and the absence of visible fistulation may indicate that the solution is long-lasting for these eyes, similar to results in congenital glaucoma cases (Haas 1968; de Silva et al. 2011). Still, a number of cases will be resistant to treatment and continue to progress (de Silva et al. 2011). Just as is the case with congenital cataract, early surgery for glaucoma has better prognosis than late surgery. The highest rate of success in congenital glaucoma surgery is between 2 months and 1 year with rates of 80-90%. Before and afterwards success rates are somewhat lower but children up to the age of 3 still have a reasonably good chance of success (Haas 1968; deLuise & Anderson 1983). The majority of the children in the cohorts in Papers III-V had their first glaucoma surgery procedure in this period. Whether early surgery triggers glaucoma into early-onset, glaucoma that will develop eventually anyway or if early surgery leads to additional glaucoma cases is not possible to answer from these studies, but the Kaplan-Meier curves in Paper V may indicate, in this fairly short perspective, a low increase more than 1 year after surgery.

Early diagnosis and treatment may enhance the success rate in paediatric glaucoma. The subject of Paper I is refractive growth, a method for quick and more certain diagnosis of glaucoma secondary to aphakia. Problems of diagnosis of glaucoma in the age group 1-4 years where corneal oedema is not necessarily present have made some suspect that undetected glaucoma may account for lower reported incidence in this age group (Vishwanath et al. 2004). With the rebound tonometry, it is less likely to miss suspiciously high pressures (Dahlmann-Noor et al. 2013). Instead, the false high IOPs will become a problem (Flemmons et al. 2011). Refractive growth will increase the possibility to sort out damaging IOP levels.

Early surgery affects the rate of VAO. The normal growth of the lens during the first months of life makes the proliferation level of LECs very high. Methods for cataract removal either focus on removing all cells (lensectomy) or seal the anterior and posterior capsule together. Despite development this seal is not able to completely block proliferation of LECs (Kappelhof et al. 1987; Apple et al. 1992). With the introduction of IOLs in children a defect was introduced in the seal, which resulted in an increased rate of VAO (Plager et al. 2014; Solebo et al. 2015). Two solutions emerged; optic capture, where the defects in adhesions were limited to the IOL haptics (Gimbel & DeBroff 1994) ; and the BiL-IOL, where the adhesions were theoretically sealed in a groove in the rim of the IOL (Tassignon et al. 2002). We have shown a low rate of VAO of 4.6% with the use of BiL-IOL in children and even in infants below 3 months of age, which even exceeds results of aphakia in this cohort of

unselected children eligible for BiL-IOL implantation. There were a total of 10.1% of BiL-IOL-specific complications, such as luxation, refractory change and deposits, but the re-operation rate was still low compared with results using other IOLs in children (ref).

The CDVA was good with early surgery. Visual development benefits from surgery by 3 weeks of time even compared with 6 weeks. Poorer VA outcome in eyes with glaucoma, as previously reported (Chen et al. 2004; Kirwan et al. 2010)was not seen. Severe amblyopia and nystagmus are less likely to affect final VA. In the short perspective of these studies and using these methods, amblyopia - not glaucoma seems to limit VA development.

Early screening and identification of cataracts in need of surgery will make it possible to optimize timing of surgery. From a developmental point of view regarding cortical pathways and VA development, surgery performed before 3 weeks of age seems to be optimal and the results may be somewhat less satisfactory if postponed even to the sixth week. Glaucoma after surgery is much more frequent during the first 4-5 weeks. Cataract surgery after 5 weeks of age with the BiL-IOL technique has a low rate of SG. This makes the optimal time for surgery 5-6 weeks of age for a child with a dense cataract if early-onset glaucoma is to be lowered substantially.

The use of a primary BiL-IOL implantation does not seem to affect glaucoma rate after 5 weeks of age and with a VAO rate equal to or lower than that of aphakia, BiL-IOL as a choice seems as good as aphakia during the first 3 years, provided the ocular measures allow implantation, and may even prove to be better, with less need for a secondary intervention in the long term.

Glaucoma surgery targeting a known defect in primary congenital glaucoma seems to have similar pressure-lowering effects in treatment of SG after surgery for cataract. Glaucoma diagnosed and treated with angle surgery during the first year in life may have a better prognosis than late-onset glaucoma; regarding the life expectancy of a child it is still not evident what is the optimal strategy.

6 FUTURE PERSPECTIVES

Congenital cataract and childhood glaucoma are rare conditions in children.

Two of the studies in this thesis includes comparisons of results of child cataract surgery at 3 and 6 weeks of age with a primary BiL-IOL implant. Cataract surgery in infants today is usually postponed until after 4-6 weeks of age and the percentage of primary IOL implants is decreasing, mainly because of the number of adverse events resulting in retreatments reported in the IATS and ioLunder2 studies (Solebo et al. 2018; Poole et al. 2019). The majority of adverse events are VAO. The BiL-IOL concept offers an intraocular state without a break in the capsular integrity resembling that of aphakia and as far as we know these promises are still valid. The incidence of VAO with the BiL-IOL is similar to results in aphakia as reported in the studies of this thesis and elsewhere (Van Looveren et al. 2015; Solebo et al. 2018).

If a primary IOL is to be inserted when is then the optimal time to perform the procedure? Surgery during the first 4 weeks of life provided excellent VA outcome (Birch et al. 2009). In the study of Paper IV, VA levels indeed seem to be higher if surgery was performed at 3 weeks of age compared to at 6 weeks. Unfortunately, this comes at a cost of increased risk of SG in accordance with other studies (Vishwanath et al. 2004; Chak et al. 2008). To postpone surgery until after 5 weeks of age seems judging from these studies to be the right decision; the final VA may become somewhat inferior but the rate of early-onset SG would be reduced.

The anterior chamber is not fully developed at birth (Anderson 1981). Surgery during the first month may affect developing structures and be a cause of glaucoma secondary to cataract surgery. But what if secondary glaucoma is not a complication that may arise after bad-timing of surgery or from surgical trauma, but a condition occurring in a certain number of eyes with congenital or developmental cataract due to the condition itself? This is a possible explanation if congenital cataract is not an isolated finding but part of a syndrome, caused by genetic variation/mutations (Gillespie et al. 2014). Long-term studies indicate that this may be the case since the number of eyes with glaucoma is increasing over time regardless of the timing of surgery (Haargaard et al. 2008; Ruddle et al. 2013).

Angle chamber glaucoma surgery in congenital glaucoma has the most favourable outcome if performed during the first year of life (Haas 1968), and the effect in quite a number of cases seems to last (de Silva et al. 2011). May

it even be an advantage of early-onset of glaucoma, having a more favourable outcome of surgery, as opposed to late-onset glaucoma which may be more difficult to treat?

With the current knowledge, postponing surgery to 6 weeks or later is the strategy at Sahlgrenska University Hospital. If long-term results of the present cohorts will show an increase in SG rate it will indicate that this was the right decision. If, however, the progression rate stays within the prognostic limits of study V and the rate at 10 years of age ends up between 25-30%, the SG rate is similar to that of most studies and postponing surgery made no difference.

In the present studies comorbidity rates are high which is a common finding in a cohort of children with congenital cataract. These eyes are already affected by one developmental defect, cataract, and may also exhibit other changes.

Children with rare conditions like congenital cataract and coexisting developmental changes benefit from a treatment regimen with few methods because this enable the surgeons to attain adequate experience. The methods used should therefore have an equal potential in similar conditions. A variety of methods make the evaluation of results difficult. But even with a strict treatment regimen, evaluation of outcome is challenging. Comparison of treatment regimens will benefit from cooperation between centres. Registries are example of such cooperation and the PECARE is the result of such a cooperation in Sweden. In a registry, different treatments can be compared without reducing the number of patients for each contributing centre. One of the papers of this thesis reports on prospectively gathered data from the PECARE, a unique national based cohort of child cataract surgery in Sweden. A European registry of child cataract surgery project (EuReCCa) has started within the EUREQUO, (European Registry of Quality Outcomes for Cataract and Refractive Surgery) and collaboration will hopefully make it possible to compare different treatment regimens which should be beneficial for the progress of knowledge for children with cataract.

In mean time the main questions for the future remain:

- At what age should surgery be performed?
- Is primary IOL implantation beneficial in infants?
- What is the visual and refractive outcome of children with early surgery in week 3 compared to week 6 in the age when visual development has reached a more mature state?

- What is the success rate of glaucoma surgery for secondary glaucoma?

- Will the rate of glaucoma in PECARE continue to increase or will the prognosis hold for the future?

7 ETHICAL CONSIDERATION

At the time this study was performed, primary IOL implantation in children was not as much discussed as it is today. Several studies have reported the use of IOLs in children and, apart from rates of PCO that seemed high, no contraindications in general have been shown. The BiL-IOL has been used in children and seems to have better results regarding VAO compared with other IOLs. Intraocular lenses also seem to have a protective effect against glaucoma. We need to decide what is more important - VA or complication rates?

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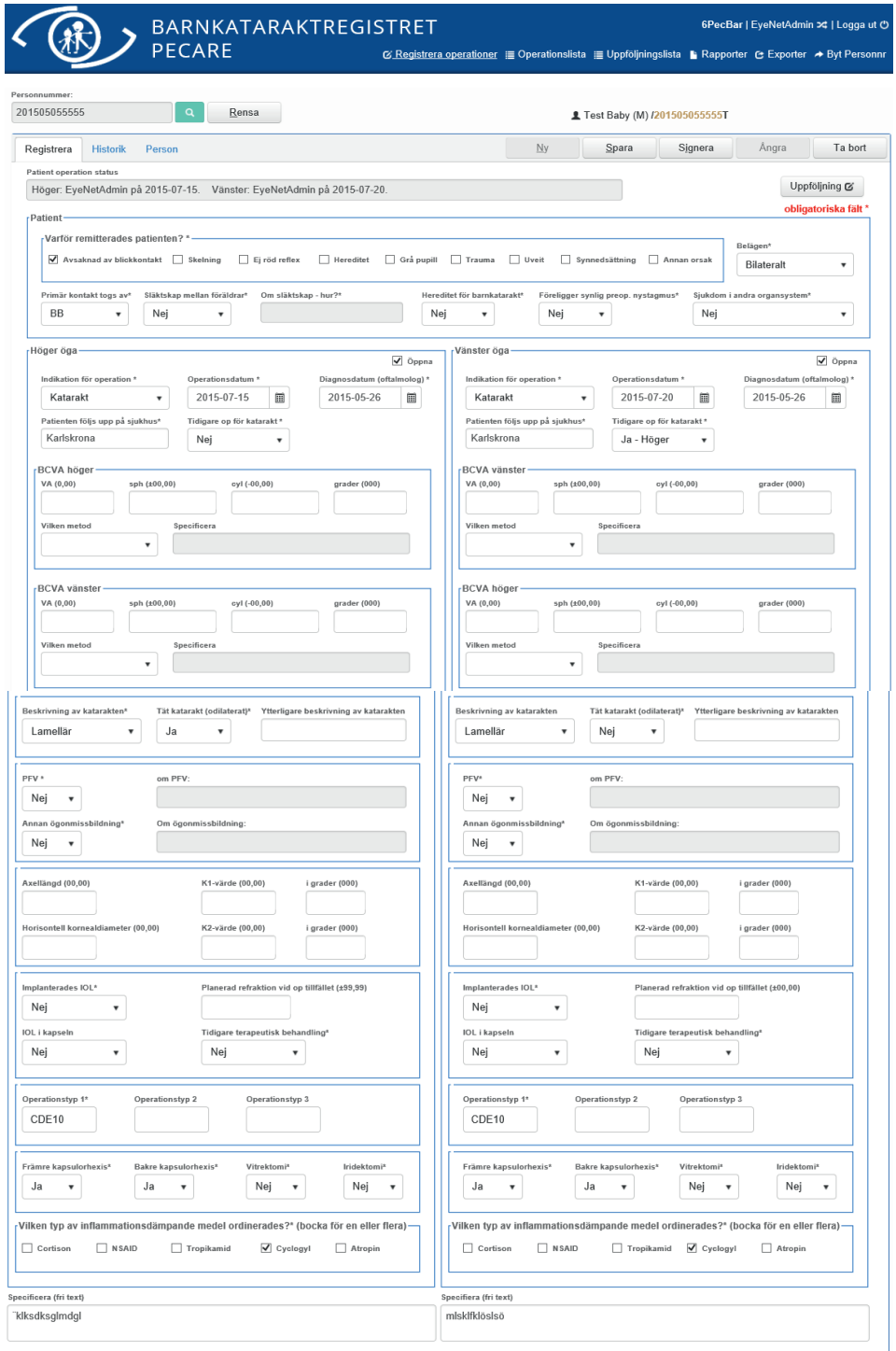
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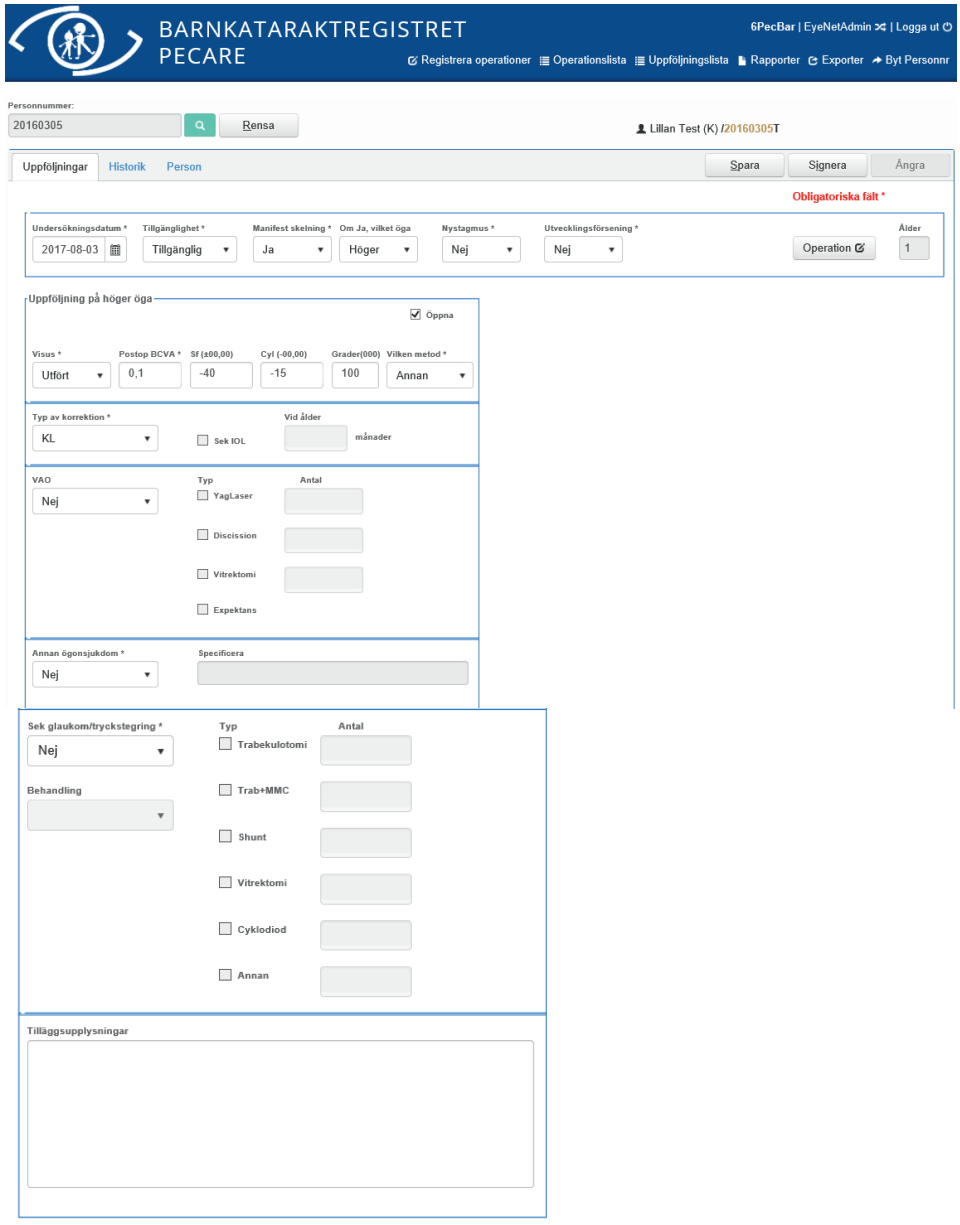
Höger öga
Öppna
Indikation för operation *
Katarakt
Operationsdatum *
2015-07-15
Diagnosdatum (oftalmolog) *
2015-05-26
Patienten följs upp på sjukhus*
Karlskrona
Tidigare op för katarakt *
Nej
BCVA höger
VA (0,00)
sph (±00,00)
cyl (-00,00)
grader (000)
Vilken metod
Specificera
BCVA vänster
VA (0,00)
sph (±00,00)
cyl (-00,00)
grader (000)
Vilken metod
Specificera
Vänster öga
Öppna
Indikation för operation *
Katarakt
Operationsdatum *
2015-07-20
Diagnosdatum (oftalmolog) *
2015-05-26
Patienten följs upp på sjukhus*
Karlskrona
Tidigare op för katarakt *
Ja - Höger
BCVA vänster
VA (0,00)
sph (±00,00)
cyl (-00,00)
grader (000)
Vilken metod
Specificera
BCVA höger
VA (0,00)
sph (±00,00)
cyl (-00,00)
grader (000)
Vilken metod
Specificera
Beskrivning av katarakten*
Lamellär
Tät katarakt (odilaterat)*
Ja
Ytterligare beskrivning av katarakten
PFV *
Nej
om PFV:
Annan ögonmissbildning*
Nej
Om ögonmissbildning:
Axellängd (00,00)
K1-värde (00,00)
i grader (000)
Horisontell kornealdiameter (00,00)
K2-värde (00,00)
i grader (000)
Implanterades IOL*
Nej
Planerad refraktion vid op tillfället (±99,99)
IOL i kapseln
Nej
Tidigare terapeutisk behandling*
Nej
Operationstyp 1*
CDE10
Operationstyp 2
Operationstyp 3
Främre kapsulorhexis*
Ja
Bakre kapsulorhexis*
Ja
Vitrektomi*
Nej
Iridektomi*
Nej
Vilken typ av inflammationsdämpande medel ordinerades?* (bocka för en eller flera)
Cortison
NSAID
Tropikamid
Cyclogyl
Atropin
Specificera (fri text)
´klksdksglmdgl
Beskrivning av katarakten
Lamellär
Tät katarakt (odilaterat)*
Nej
Ytterligare beskrivning av katarakten
PFV*
Nej
om PFV:
Annan ögonmissbildning*
Nej
Om ögonmissbildning:
Axellängd (00,00)
K1-värde (00,00)
i grader (000)
Horisontell kornealdiameter (00,00)
K2-värde (00,00)
i grader (000)
Implanterades IOL*
Nej
Planerad refraktion vid op tillfället (±00,00)
IOL i kapseln
Nej
Tidigare terapeutisk behandling*
Nej
Operationstyp 1*
CDE10
Operationstyp 2
Operationstyp 3
Främre kapsulorhexis*
Ja
Bakre kapsulorhexis*
Ja
Vitrektomi*
Nej
Iridektomi*
Nej
Vilken typ av inflammationsdämpande medel ordinerades?* (bocka för en eller flera)
Cortison
NSAID
Tropikamid
Cyclogyl
Atropin
Specifiera (fri text)
mlsklfklöslsö


BARNKATARAKTREGISTRET
PECARE
6PecBar | EyeNetAdmin | Logga ut
Registrera operationer
Operationslista
Uppföljningslista
Rapporter
Exporter
Byt Personnr
Personnummer:
20160305
Rensa
Lillan Test (K) /20160305T
Uppföljningar
Historik
Person
Spara
Signera
Ångra
Obligatoriska fält *
Undersökningsdatum *
2017-08-03
Tillgänglighet *
Tillgänglig
Manifest skelning *
Ja
Om Ja, vilket öga
Höger
Nystagmus *
Nej
Utvecklingsförsening *
Nej
Operation
Ålder
1
Uppföljning på höger öga
Öppna
Visus *
Utfört
Postop BCVA *
0,1
Sf (±00,00)
-40
Cyl (-00,00)
-15
Grader(000)
100
Vilken metod *
Annan
Typ av korrektion *
KL
Sek IOL
Vid ålder
månader
VAO
Nej
Typ
Antal
YagLaser
Discission
Vitrektomi
Expektans
Annan ögonsjukdom *
Nej
Specificera
Sek glaukom/tryckstegring *
Nej
Typ
Antal
Trabekulotomi
Behandling
Trab+MMC
Shunt
Vitrektomi
Cyklodiod
Annan
Tilläggsupplysningar