LONG-TERM RESULTS OF PHAKIC REFRACTIVE LENSES FOR CORRECTION OF MYOPIA AND HYPEROPIA

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To my Marko and our Anton and Edvin
ABSTRACT

The phakic refractive lens (PRL) is a silicone lens implanted into the posterior chamber to correct myopia and hyperopia. At the beginning of 2002, when the PRL was introduced at St. Erik Eye Hospital, there had been no reports published on this lens model and therefore the pilot studies of myopic and hyperopic eyes were conducted to investigate the surgical outcome.

In the first study, the first 20 consecutive cases with PRL implantation were followed for 1 year after surgery. The visual acuity results were comparable to other refractive methods and demonstrated high safety and efficacy indexes. The mean distance between the posterior surface of the PRL and the anterior lens surface decreased significantly in all eyes during the 1-year follow-up. The retroillumination photographs revealed slight rotation of the PRL in most eyes. The endothelial cell count decreased significantly 1 week after surgery without changes thereafter indicating that the difference in cell density was caused by surgical trauma and not the PRL. Few complications were observed. Increased intraocular pressure (IOP) related to pupillary block developed in two eyes (1 myopic and 1 hyperopic) during the first postoperative days. A myopic eye developed corticosteroid-induced high IOP 1 week postoperatively, which resolved after discontinuation of the steroid drops. One hyperopic eye unexpectedly developed myopia after PRL implantation. The PRL was exchanged with success. Iris transillumination defects were noticed in a hyperopic eye 1 year postoperatively. No ongoing inflammation, lens opacification or glaucoma was found.

The second study was a prospective 2-year follow-up study of the same myopic and hyperopic population as in the first study. A parallel substudy was designed to evaluate the precision of the analytical methods used in the main study. Ninety-five percent of eyes had an uncorrected visual acuity (UCVA) of 0.5 or better even though the PRL with its floating design did not correct astigmatism. In 65% of cases the best-corrected visual acuity (BCVA) improved over the preoperative level. Fifteen eyes (75%) were within ±0.5 diopter (D) of the desired refraction and all eyes (100%) were within ±1.0 D. During the first year, the distance between the PRL and the anterior lens surface decreased 59% but stabilized without changes during the second year. Fifteen PRLs (75%) rotated 10 degrees or more during the first follow-up year and three PRLs (15%) between 1 and 2 years. These study parameters, the rotation of the PRL and distance measurements, indicated stabilization of the PRL position in the posterior chamber 1 year after implantation. Endothelial cell count measurements 1 week after surgery showed 8.4% endothelial cell loss with slight recovery at 1 year without significant changes at 2 years. No PRL-induced lens opacification or inflammation was seen. The study showed excellent visual outcomes in myopic and hyperopic eyes with PRL implantation without serious intra- or postoperative complications.

Evaluation of the precision of the laser flare meter and Scheimpflug method showed relatively high random errors, 17% and 10%, respectively. The endothelial cell
count, however, showed low random error (2.8%) and indicated that this method is a reliable indicator for evaluation of the corneal endothelium.

In the third study, the movement of the PRL was evaluated in relation to the behavior of the crystalline lens and the pupil during accommodation in three groups: eyes with PRL 101, PRL 100, and PRL 200. The effect of accommodation was studied with optical coherence tomography (OCT). To evaluate the precision of Visante OCT, we conducted a double-independent measurement study, which showed a random error of 5% in the measurements between the PRL and the anterior lens surface. This result indicated that Visante OCT is sufficiently accurate and reliable to allow an analysis of distances in the anterior segment. Fifty-two patients were examined at least 1 year after PRL implantation using the Visante OCT. During accommodation, significant forward movement of the anterior lens surface and the PRL was observed in each group. Although the PRL moved anteriorly with accommodation with all three lens models, the space between the PRL and the crystalline lens was preserved only with PRL 100, and the space decreased significantly with the other two models. With the PRL 101, the baseline distance between the PRL and the anterior lens surface was significantly smaller in older eyes, indicating a decreased posterior chamber depth with aging of the lens. In three myopic cases, the PRL touched the anterior lens surface at baseline and two of them developed lens opacification. Both eyes had PRL 101 model. During accommodation, an additional implant in the PRL 101 and in the PRL 100 groups came in contact with the crystalline lens. In hyperopic eyes, there was no contact with the crystalline lens at baseline. During accommodation, the PRL 200 was in contact in three cases. This study showed that the PRL and the anterior lens surface moved forward during accommodation, and in most cases there was no mechanical contact with the anterior lens surface during accommodation.

The fourth study was conducted to evaluate the surgical outcome and adverse events associated with PRL implantation in hyperopic eyes. The results showed excellent predictability with all eyes within ±1.0 D of the attempted refraction. There was no gain in BCVA and three eyes (7.5%) lost two lines of corrected visual acuity. The initial endothelial cell loss postoperatively was -4.6% and remained stable thereafter. The mean IOP remained unchanged during the entire follow-up period. The most frequent complication was development of postoperative pupillary block in seven eyes (17.5%). Two eyes with severe glare and one eye with unexpected myopia and discomfort underwent PRL explantation. Unexpected postoperative myopia was treated with PRL exchange in two eyes and with laser epithelial keratomileusis (LASEK) in one eye. No PRL-induced glaucoma or cataract developed. The study showed high refractive stability and predictability at the 1-year follow-up. There was no gain in corrected visual acuity. Despite two iridotomies performed 2 weeks preoperatively, the main complication was early pupillary block.
LIST OF PUBLICATIONS

I. Koivula A, Petrelius A, Zetterström C.
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Phakic Refractive Lens: Two-year Results.
Journal of Refractive Surgery (In press)

III. Koivula A, Kugelberg M.
Optical Coherence Tomography of the Anterior Segment in Eyes with Phakic
Refractive Lenses.
Ophthalmology [Epub ahead of print].

IV. Koivula A, Zetterström C.
Phakic Refractive Lens for Correction of Hyperopia.
(Submitted)
CONTENTS

1 Introduction .................................................................................................................. 1
  1.1 Background............................................................................................................. 1
    1.1.1 Prevalence of refractive errors................................................................. 1
    1.1.2 Refractive surgery ....................................................................................... 2
  1.2 PRL ....................................................................................................................... 6
    1.2.1 History .......................................................................................................... 6
    1.2.2 PRL design .................................................................................................... 7
  1.3 PRL Implantation .................................................................................................. 8
    1.3.1 Indications .................................................................................................... 8
    1.3.2 Contraindications ......................................................................................... 8
    1.3.3 Preoperative evaluation ................................................................................. 9
    1.3.4 Surgical procedure ......................................................................................... 9
    1.3.5 Complications ............................................................................................... 10
    1.3.6 Surgery in hyperopic eyes .......................................................................... 13
  1.4 Methods ............................................................................................................... 14
    1.4.1 Visual acuity ................................................................................................ 14
    1.4.2 Intraocular pressure ..................................................................................... 14
    1.4.3 Laser flare meter .......................................................................................... 14
    1.4.4 Corneal endothelial cell count ...................................................................... 15
    1.4.5 Scheimpflug images ..................................................................................... 15
    1.4.6 Retroillumination photographs .................................................................... 15
    1.4.7 Optical coherence tomography ................................................................... 15

2 Aims .............................................................................................................................. 17

3 Material and Methods ................................................................................................. 18
  3.1 Patients and methods (I) ....................................................................................... 18
    3.1.1 Patients ......................................................................................................... 18
    3.1.2 Inclusion criteria ........................................................................................ 18
    3.1.3 Exclusion criteria ........................................................................................ 18
    3.1.4 Follow-up ..................................................................................................... 18
    3.1.5 Statistical analysis ......................................................................................... 18
  3.2 Patients and methods (II) ...................................................................................... 19
    3.2.1 Patients ......................................................................................................... 19
    3.2.2 Follow-up ..................................................................................................... 19
    3.2.3 Analysis of the follow-up methods ............................................................... 19
    3.2.4 Statistical analysis ........................................................................................ 19
  3.3 Patients and methods (III) ..................................................................................... 19
    3.3.1 Study design ................................................................................................ 19
    3.3.2 Visante OCT as an analytical method .......................................................... 19
    3.3.3 Main outcome measures .............................................................................. 20
    3.3.4 Statistical analysis ......................................................................................... 20
  3.4 Patients and methods (IV) ..................................................................................... 20
    3.4.1 Patients ......................................................................................................... 20
    3.4.2 Inclusion criteria ........................................................................................ 20
    3.4.3 Exclusion criteria ........................................................................................ 20
    3.4.4 Arcuate keratotomy ...................................................................................... 20
3.4.5 Follow-up ................................................................. 21
3.4.6 Statistical analysis ............................................. 21

4 Results and Discussion ......................................................... 22
4.1 Visual outcome (I, II, IV) ................................................... 22
  4.1.1 Safety ................................................................. 22
  4.1.2 Efficacy ............................................................. 23
4.2 Predictability (I, II, IV) ..................................................... 24
4.3 Intraocular pressure (I, II, IV) ........................................... 24
4.4 Endothelial cell density (I, II, IV) ..................................... 25
4.5 Inflammation (I, II) ......................................................... 26
4.6 PRL rotation (I, II) .......................................................... 26
4.7 Distance between the PRL and the anterior lens surface (I, II, III) 27
4.8 Change in pupil size (III) .................................................. 30
4.9 Complications ............................................................... 30
  4.9.1 Lens opacification (I, II, III, IV) ................................. 30
  4.9.2 Pupillary block (I, II, IV) .............................................. 31
  4.9.3 Iris transillumination defect (I, II, IV) ......................... 32
  4.9.4 Overcorrection of hyperopia (I, II, IV) ....................... 32
  4.9.5 Halos and glare (I, II, IV) ........................................... 33
4.10 Analysis of follow-up methods (II, III) ............................ 33

5 Conclusions ................................................................. 34

6 Acknowledgements .......................................................... 35

7 References ................................................................. 37
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AC</td>
<td>Anterior chamber</td>
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<tr>
<td>AC PIOL</td>
<td>Anterior chamber phakic intraocular lens</td>
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<tr>
<td>ALS</td>
<td>Anterior lens surface</td>
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<tr>
<td>AS-PRL</td>
<td>Anterior surface of the phakic refractive lens</td>
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<td>BCVA</td>
<td>Best-corrected visual acuity</td>
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<td>D</td>
<td>Diopeter</td>
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<td>ETDRS</td>
<td>Early Treatment of Diabetic Retinopathy Study</td>
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<td>ICL</td>
<td>Implantable contact lens</td>
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<tr>
<td>IOL</td>
<td>Intraocular lens</td>
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<td>IOP</td>
<td>Intraocular pressure</td>
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<tr>
<td>LASEK</td>
<td>Laser epithelial keratomileusis</td>
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<tr>
<td>LASIK</td>
<td>Laser in situ keratomileusis</td>
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<tr>
<td>logMAR</td>
<td>Logarithm of the minimum angle of resolution</td>
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<tr>
<td>Nd:YAG</td>
<td>Neodymium-yttrium aluminium garnet</td>
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<td>OCT</td>
<td>Optical coherence tomography</td>
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<tr>
<td>OVD</td>
<td>Ophthalmic viscosurgical device</td>
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<tr>
<td>PC</td>
<td>Posterior chamber</td>
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<tr>
<td>PC PIOL</td>
<td>Posterior chamber phakic intraocular lens</td>
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<tr>
<td>PIOL</td>
<td>Phakic intraocular lens</td>
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<tr>
<td>PMMA</td>
<td>Polymethyl methacrylate</td>
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<tr>
<td>PRK</td>
<td>Photorefractive keratectomy</td>
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<tr>
<td>PRL</td>
<td>Phakic refractive lens</td>
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<tr>
<td>PS-PRL</td>
<td>Posterior surface of the phakic refractive lens</td>
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<tr>
<td>SE</td>
<td>Spherical equivalent</td>
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<tr>
<td>UBM</td>
<td>Ultrasound microscopy</td>
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<tr>
<td>UCVA</td>
<td>Uncorrected visual acuity</td>
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<tr>
<td>WTW</td>
<td>White to white (corneal diameter)</td>
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1 INTRODUCTION

1.1 BACKGROUND

Almost 10 years ago, Tobias Neuhann wrote in his Journal of Refractive Surgery editorial: “Excimer lasers are used today practically all over the world to treat refractive errors. This provides us with a wealth of data and findings that must be analyzed, presented, interpreted, and discussed. One major finding is already certain: the absolute and indisputable necessity of refractive surgery. Even those who are skeptical about refractive surgery must accept this. Patients simply do not care about the ethical or other misgivings of ophthalmologists. People who suffer from refractive errors seek and desire a treatment. By definition, they are patients and not clients. We should not ignore this, but rather accept it; in fact, they are calling on us to help them.”(Neuhann 1998)

Refractive surgery, as all branches of medicine and surgery, is a dynamic process with advancement of knowledge leading to constant improvement in standards of care. Refractive surgery continues to evolve: it remains one of the fastest changing fields in medicine. Over the years, refractive surgeons have experienced a significant change in every aspect of refractive surgery, including patient selection, diagnostic tools, microkeratomes, refractive lasers, and refractive lenses. Patient selection has changed from correction of only myopia to include hyperopia, astigmatism, and presbyopia.

1.1.1 Prevalence of refractive errors

Mild-to-moderate hyperopia can be overcome by accommodation in youth and early adulthood, with the result that low degrees of hyperopia often are unnoticed until the onset of presbyopia in mid-adulthood. Myopia results in blurred vision at all ages. Blurred vision from refractive error can be relieved in most cases by neutralizing the refractive error with spectacles, contact lenses, or refractive surgery (Figure 1).

In Scandinavia, Fledelius estimated that the frequency of myopia in the general population was between 25% and 30% and about in 25% of cases myopia begins during adulthood (Fledelius 2000). The cause of this type of myopia is unclear, although some evidence supports an environmental influence linked to a greater amount of near work.

Comparison of prevalence rates of refractive errors among young (20-25 years) and middle-aged (40-45 years) adults in Norway showed that most subjects in both age groups were emmetropic: 51.8% of young and 52.3% of middle-aged adults. The prevalence of myopia (defined as spherical equivalent [SE] ≤ -0.5 D) was 35.0% in the young adult group and 30.3% in the middle-aged adult group. The proportion of people with high myopia (<-5.0 D) was similar in both age groups, with 2.8% among young and 3.3% among middle-aged adults. Hyperopia (defined as SE ≥ +0.50 D) increased significantly with age from 13.2% among young adults to 17.4% among the middle-aged (Midelfart et al. 2002).
In the Western European population of persons 40 years and older for the year 2000, an estimated 11.6% had hyperopia of $\geq +3.0$ D (21.6 million persons), 26.6% had myopia of $\leq -1$ D (49.6 million persons), and 4.6% (8.5 million persons; 17.1% of all persons with myopia) had myopia of $\leq -5.0$ D (Kempen et al. 2004). The prevalence of hyperopia was observed to be progressively higher with increasing age and the prevalence of myopia of -1 D or less tended to be substantially lower for individuals older than the younger age groups. Similarly, myopia of -5.0 D or less was strongly associated with age, with the highest prevalence in the youngest strata (ages 40-49 years) (Kempen et al. 2004).

### 1.1.2 Refractive surgery

Why would somebody undergo refractive surgery? Many individuals are uncomfortable with their refractive error and poor uncorrected visual acuity (UCVA). Although external aids in the form of spectacles or contact lenses are acceptable to many, several factors are instrumental in the search for a permanent solution to refractive errors. The most frequently claimed reason in people with high myopia is that with spectacle correction the viewed objects are minified, and with high myopia and hyperopia the peripheral fields are severely distorted by spectacles. In addition, contact lens intolerance, occupational requirements, sporting and other leisure interests, physical problems wearing glasses, and a psychological (self-image) desire to achieve visual freedom are the other reasons patients cite for wanting to undergo refractive surgery (Rosen and Gore 1998).

Currently, there are three general approaches to correct a refractive defect:

1. corneal refractive surgery
2. crystalline lens surgery
3. implantation of an intraocular lens (IOL) in the anterior (AC) or the posterior chamber (PC).

In any case, the main goal of refractive surgery is the attainment of the smallest residual refractive error that preserves vision quality with the same visual capacity.

#### 1.1.2.1 Corneal refractive surgery

Corneal refractive surgery might be divided into three types:

1. Incisional and thermal corneal surgery
2. Corneal ablation surgery
   a. Surface ablation
   b. Lamellar laser refractive surgery
3. Additive refractive keratoplasty

Corneal refractive surgery, except for intracorneal lenses, attempts to modify the anterior curvature of the cornea to obtain its effect. Radial keratotomy was the keystone of corneal refractive surgery to correct myopia (Fyodorov and Durnev 1979) but resulted in instability of the corneal dome (Waring et al. 1991). In thermal corneal surgery, the anterior corneal curvature is modified by thermal induced shrinkage of collagen fibers in the cornea, and the collagen shrinkage steepens the cornea. The method should be reserved for mild hyperopia in patients over 40 years (Sher 2001).
The first prototypic excimer laser system was debuted at the American Academy of Ophthalmology (AAO) in 1987 and it generated great interest in alternatives to radial keratotomy. In 1988, McDonald and colleagues (Waring et al. 1991) performed the first successful excimer laser photorefractive keratectomy (PRK) on a seeing human eye with myopia. In the early 1990s, Pallikaris and colleagues (Pallikaris et al. 1990) and Buratto and colleagues (Buratto et al. 1993) independently described a technique that combined two existing technologies: the microkeratome and the excimer laser. Pallikaris coined the term laser in situ keratomileusis (LASIK) for this new technique, which has become a widely used refractive technique worldwide.

Three methods of surface ablation are currently in use: PRK (Tengroth et al. 1993, Hamberg-Nystrom et al. 1996), laser epithelial keratomileusis (LASEK) (Claringbold 2002, Camellin 2003) and epi-LASIK ablation (Pallikaris et al. 2003, Pallikaris et al. 2005). These methods differ in the manner in which the epithelial layer is handled. However, the ablation of the most anterior portion of the corneal stroma is the same for all procedures. The ablation in particular, through Bowman’s layer leads to a wound-healing response that might result in stromal haze and scarring (Fagerholm 2000). Recovery after surface ablation is both slower and more painful than after LASIK (Tomas-Barberan and Fagerholm 1999, Shortt and Allan 2006, O'Doherty et al. 2007).

LASIK is a lamellar laser refractive surgery in which the excimer laser ablation is done under a partial-thickness lamellar corneal flap. Until recently, the lamellar flap could only be made with a microkeratome that cut the lamellar flap to depths of 100 to 200 μm. A femtosecond laser provides more accuracy in flap thickness (Kezirian and Stonecipher 2004) and flap creation is less dependent on the corneal curvature. Compared with surface ablation, LASIK results in earlier and faster improvement of UCVA, and results in no haze and less postoperative discomfort (Kato et al. 2007). With LASIK, however, the risks of flap-related complications and corneal thickness limitations may be associated with the creation of the lamellar flap (Fagerholm et al. 2004, Rao et al. 2004).

It is easier to flatten the cornea permanently for myopia than to steepen it centrally for hyperopia. In contrast to myopic excimer laser surgery, a hyperopic ablation profile is a peripheral annular ablation around the central optical zone, which produces steepening (Haw and Manche 2000). This requires larger ablation diameter than for myopic corrections. Centration is more critical and decenteration are less forgiving in hyperopic ablations, whether PRK or LASIK. Decentrations may be induced by smaller corneas of hyperopic eyes and larger ablations (O'Brart 1999).

Additive refractive keratoplasty refers to a procedure in which a foreign material, either biological or synthetic, is added to the corneal tissue to modify the ocular refractive condition. Intracorneal ring segments and inlays are reversible methods that are under development. One of the important advantages over corneal laser procedures is that intracorneal ring segments spare the visual axis. There is essentially no risk of the development of central corneal haze or scarring. No corneal tissue is removed. However, intracorneal ring segments cannot correct more than -4 D of myopia without substantially increasing ocular spherical aberration (Malecaze et al. 2002). Synthetic stromal inlays or intracorneal implants are implanted within the cornea at a depth between 36% and 60% of the corneal thickness to correct hyperopia. However, a variety of complications occurring postoperatively following implantation of the implant has limited its use in refractive surgery (Alio 2004).
1.1.2.2  Crystalline lens surgery

Clear lens extraction has been recognized since 1708, when Boerhave described the possible good results of lens extraction in myopic patients (Seiler 1999). One hundred fifty-five years later, Von Graefe warned about the increased risk of retinal detachment with this type of procedure. After the invention of sterilization in 1889, Fukala reported lens extractions through a discission of the anterior capsule in myopic eyes and has been considered the creator of clear lens extraction (Seiler 1999).

This procedure has been called clear lens extraction by some and refractive lensectomy by others. The current approach is the substitution of the natural lens with an IOL of proper dioptic power. The predictability and stability of the results, comparable to those observed after IOL implantation at the time of cataract surgery, are the main advantages of this technique (Packer et al. 2002, Leyland and Zinicola 2003). Conversely, this technique to correct refractive error must be considered with caution because it might increase the risk of retinal detachment in patients with moderate and high levels of myopia, among other complications (Colin et al. 1999). For some hyperopic patients, while retinal detachment is not a major concern, they often have a shallow anterior segment with little room in the anterior or the posterior chamber for a phakic lens, and refractive lensectomy may be the only surgical alternative (Kolahdouz-Isfahani et al. 1999). However, young patients undergoing this procedure must be aware of the consequent loss of accommodation (Fink et al. 2000). In fact, the current use of multifocal IOLs and the emergence of early accommodative IOLs as refractive surgical techniques now are directed to presbyopia (Fernandez-Vega et al. 2007).

1.1.2.3  Phakic intraocular lens surgery

The third general approach in refractive surgery is placing an intraocular lens in the phakic eye. This definition includes any lens located between the cornea and the anterior surface of the crystalline lens, which is left undisturbed inside the eye. Corneal procedures have the advantage of preserving the human lens but there are limits to the range of correction at the corneal plane. With the most popular refractive surgical procedure, LASIK (Duffey and Leaming 2005), keratectasia is a significant issue and provides a certain myopic limit (Seiler et al. 1998, Pallikaris et al. 2001), whereas the difficulty in producing added corneal power creates a limit on the hyperopic side (Zadok et al. 2003, Varley et al. 2004).

Phakic IOLs (PIOLs) allow correction outside the limits of the corneal refractive surgery (Sanders and Vukich 2003). The insertion of an implant in a phakic eye preserves accommodation and is reversible. Current IOL choices include AC PIOLs, angle-supported or iris-fixated models, and PC PIOLs, sulcus-fixated or free-floating models.

Historically, the idea of curing refractive problems by means of built-in or integrated additional optics (built-in glasses or contact lenses) sounds logical; however, even the great surgeons of our time failed initially with this approach that dates back to the late 1950s. Despite the well-known setbacks of Strambelli (Strambelli 1954), Barraquer (Barraquer 1959), and Choyce (Choyce 1966), individual scientists never allowed the idea of PIOL implantation to die. Three different scientists pursued three different anatomic concepts for PIOLs at roughly the same time: Baikoff saw a solution in the angle-supported anterior chamber lens (Baikoff and Joly 1990); Fechner
developed another solution in the modification of Worst’s iris fixated lobster claw IOL (Fechner et al. 1989, Fechner and Worst 1989); and Fyodorov implanted a silicone lens into the posterior chamber (Fyodorov et al. 1991) (Figure 2).

The Baikoff design, angle-supported PIOLs evolved from 4-point fixation poly(methyl methacrylate) (PMMA) versions (Baikoff and Joly 1990) to three-point PMMA versions, and then to foldable IOLs to decrease induced astigmatism. The PMMA versions failed basically due to endothelial cell loss, pupil ovalization, and induced astigmatism. To overcome these problems, the material was changed from PMMA to hydrophilic acrylate or hydrophobic acrylate. However, severe complications such as endothelial decompensation (Coullet et al. 2007) and pupil ovalization (Leccisotti 2005) after implantation of an anterior PIOL have resulted in several European countries having recalled these lenses for the correction of refractive errors (Kohnen 2007).

The iris-fixated PIOL for the correction of myopia was introduced in 1986 as a rigid single-piece PMMA model with a 5.0- or 6.0-mm optic (Fechner et al. 1989, Fechner and Worst 1989). The iris-fixated PIOL has been implanted for more than 20 years through a 5.0- to 6.0-mm incision. The goal of reducing surgically induced astigmatism was achieved with the development of the foldable iris-fixated model with silicone optic and PMMA haptics introduced in 2003. The foldable design makes implantation possible through a 3.2-mm incision. However, this PIOL may be associated occasionally with recurrent intraocular inflammation (Tahzib et al. 2006), enhanced iris dispersion with posterior synechiae (Koss et al. 2007), and lenticular glistering (Cisneros-Lanuza et al. 2007).

The posterior chamber PIOLs to correct myopia was introduced first by Fyodorov in 1986 (Fyodorov et al. 1991). The first-generation Fyodorov PC PIOL was a one-piece silicon lens fixated by a haptic in the PC. In 1990, this lens was replaced by a second-generation model. Using
knowledge of the early model of silicon posterior PIOL designs as a basis, two manufacturers, i.e., Medennium Inc., Irvine, CA, USA and Staar Surgical Co, Monrovia, CA, USA, currently are researching and marketing posterior PIOL designs (Figure 3).

The implantable contact lens (ICL) (Staar Surgical Co) has undergone many modifications in design since 1993 (Assetto et al. 1996). The latest model, V 4, developed in 1999, made significant improvement in the amount of vaulting over the anterior lens capsule from the previous model (Sanders and Vukich 2002).

The lens has a one-piece plate design with a rectangular shape, 7.5 to 8.0 mm wide, available in four standard overall lengths: 11.5 to 13.5 mm for myopic lenses and 11.0 to 13.0 mm for hyperopic lenses to adapt to eyes of different sizes. The diameter of the optic zone is 4.65 to 5.5 mm in the myopic lenses, based on the desired dioptric power, and 5.5 mm for hyperopic ICLs. Available powers for myopic lenses range from -3.0 to -22.0 D and from +3.0 to +20.0 D for hyperopic lenses (Lackner et al. 2003).

The lens is introduced by means of a Staar microinjector. The proximity of the ICL to the crystalline lens, a dynamic phenomenon, has been postulated to be a risk factor for cataract development, which has been the main problem with this lens, and a greater vault would be expected to decrease ICL-crystalline lens contact (Sanders and Vukich 2002, Lackner et al. 2003, Sanders et al. 2003, Sarikkola et al. 2005). However, it is also possible that interference with lens nutrition instead of IOL contact of the crystalline lens may be the cause of cataract (Olson et al. 2005).

The main differences between the ICL and the phakic refractive lens (PRL) are the lens material and lens dynamics. The ICL is made of a collamer; which is hydrophilic acrylic with some cross-linked porcine collagen (Olson et al. 2005). The PRL is made of hydrophobic silicone and rests on the zonulas and floats in the PC, whereas the ICL is fixated and supported in the ciliary sulcus. Cataract formation has been reported less frequently with the PRL (Hoyos et al. 2002, Pallikaris et al. 2004). However, rotation of the PRL in the PC excludes the possibility for cylinder compound whereas the ICL has the toric alternative for myopic eyes (Sanders et al. 2007).

1.2 PRL
1.2.1 History
To reduce the incidence of potential problems with phakic AC lenses, especially such sequelae as lens contact with the corneal endothelium and pupil ovalization, Fyodorov and co-workers (Fyodorov et al. 1991, Fyodorov et al. 1993) introduced a PC PIOL made of silicone to be inserted between the iris and the crystalline lens. Fyodorov performed the first implantation of this silicone design IOL in a phakic eye to correct high-degree myopia in August 1986. The first models were pupil-fixated lenses (mushroom lenses) that were implanted in the former Soviet Union until 1990 (Wiechens et al. 1997). These lenses were designed to be fixated in the ciliary sulcus, but because the optic had the shape of a collar-button with a small diameter (3.2 mm in the
first model) and protruded into the AC, the pupil could not constrict anterior to the lens optic. The optic and haptics were connected by a bridge through the pupillary opening.

This Fyodorov IOL was modified to correct high myopia (Fechner et al. 1996). The modified IOL, the Chiron-Adatomed silicone lens, had a single-piece plate design with plano haptics, and also was made of silicone. With a wide range of powers (up to -25.0 D), the characteristic features were the long overall length (up to 12.5 mm) and a larger optic diameter (5.5 mm) (Erturk and Ozcelik 1995). In some diopteric ranges, the optic edge around its circumference was very thick (up to 1.1 mm). This lens was withdrawn from the market because of anterior lens fibrotic opacities in the contact zones with the thick edges of the IOL (Marinho et al. 1997, Brauweiler et al. 1999, Fechner 1999, Menezo et al. 2001).

The latest version of these lenses is the PRL (Figure 4), now marketed by Zeiss-Meditec (Jena, Germany), formerly by Ciba Vision (Salt Lake City, UT, USA) and IOLTech (La Rochelle, France), after the commercial rights were purchased in 2000 from the developer, Medennium International Vision (Cincinnati, OH, USA) (Lovisolo and Reinstein 2005). The current design has been manufactured since 1995 worldwide, and sold on the European market since 2000. The clinical department of the PRL distributor estimates that more than 5500 PRLs have been implanted worldwide until 2004 and thereafter more than 2800 PRLs have been sold in Europe only. The current data are incomplete and do not reflect the actual number of implants worldwide (Fresnais Laetita, Product Manager, Zeiss-Meditec, personal communication, October 2007).

Figure 4. The PRL for myopic and hyperopic eyes.

Myopic model

Hyperopic model

1.2.2 PRL design

The PRL is available in myopic and hyperopic models and is manufactured by Medennium Inc. Irvine, California, USA. According to the manufacturer, it is made from a highly purified, optically clear silicon elastomer, with a refractive index of 1.46 and a specific gravity of 0.99.

The overall lens shape is designed to conform to the natural shape of the PC of the human eye. A major feature of this lens is reported to be the hydrophobic nature of its material, which, in association with aqueous fluid dynamics, should prevent contact of the lens with the AC of the crystalline lens: The IOL would “float” on the natural lens, and no contact with this ocular structure would be observed even during accommodation. Because no real fixation is achieved
with this lens, rotation and lens positioning at different meridians during the postoperative period can be expected to occur.

The PRL has spherical, thin, flexible haptics, which are frosted to reduce the incidence of postoperative halos or glare (Figure 5). The haptics rest on the zonulas.

The refractive range of the myopic implant is -3.0 to -20.0 D and that of the hyperopic design is +3.0 D to +15.0 D. Both are available in increments of 0.5 D. There are two different sizes of myopic PRL depending on the white-to-white (WTW) diameter of the cornea: model PRL 101 with a length of 11.3 mm for WTW over 11.3 mm and model PRL 100 with a length of 10.8 mm for WTW between 10.5 to 11.3 mm. Hyperopic PRL is manufactured only in one size with an overall length of 10.6 mm (model PRL 200). The central optic zone is biconcave or concave convex. The optic size of the hyperopic PRL is 4.5 mm and for the myopic models 4.5 to 5.0 mm depending on the dioptic power.

The PRL neutralizes only the spherical compound and not the cylinder and the surgical goal is to neutralize the spherical correction. The clinical department of the PRL distributor calculates the PRL power needed corresponding to the preoperative refraction using the following data: refraction, keratometry, AC depth, WTW diameter, and desired target postoperative refraction.

1.3 PRL IMPLANTATION

1.3.1 Indications

The PRL is designed for the surgical correction of moderate to high myopia between -3.5 to -27.0 D and hyperopia between +3.0 to +11.5 D corresponding to available PRL power. Phakic IOL implantation is generally performed in patients older than 20 years who have stable refraction; the refraction might not be stable in younger patients. The upper age limit might be pre-presbyopic, although this could be seen as a relative recommendation. Especially in highly myopic eyes with increased risk for retinal complications in intraocular surgery, PRL implantation can be considered before clear lens extraction if the crystalline lens is clear (Sanders 2003). To maintain the safety of the corneal endothelium, the AC depth should be at least 3.0 mm including the cornea and endothelial cell density greater than 2000 cells/mm². Increased intraocular pressure (IOP) may imply insufficient aqueous flow and therefore the preoperative IOP should not exceed 25 mmHg.

1.3.2 Contraindications

A general contraindication to PRL implantation is a history of ocular pathology, including nanophthalmos, conditions associated with impaired corneal endothelium, glaucoma and pigment dispersion syndromes, pseudoexfoliation of the lens capsule, ocular manifestations of diabetes, the presence of lens opacities (or early cataract formation in a previously operated fellow
eye), and history of uveitis. Dystrophies causing abnormal corneal shape (e.g., keratoconus) are not corrected by a PRL. Pupil size is a critical factor in refractive surgery. However, the impact of large pupils in dim light as a reason for halos and glare is debated (Pop and Payette 2004, Villa et al. 2007). In general, PRLs are best avoided in patients who have large pupils in dim light.

1.3.3 Preoperative evaluation
Before PRL implantation, a general preoperative examination should include assessment of the UCVA, spectacle-corrected visual acuity with manifest refraction and cycloplegic refraction in hyperopic eyes, keratometry, corneal topography, slit-lamp microscopy, applanation tonometry, dilated funduscopy, and biometry. In eyes with pathological myopia, a posterior segment evaluation should be performed to document and treat if necessary any retinal pathology that may lead to retinal detachment.

Patient lifestyle, vocation, and hobbies also might affect the selection for surgery, and the choice of vision correction modality. Considering the limitations of the surgery, patients who can tolerate zero risk to vision or need perfect stereopsis (and who presently have good vision and stereovision with other forms of correction) for their jobs or hobbies might not be good candidates for refractive procedures.

In eyes with pre-existing astigmatism, an arcuate keratotomy can be performed at least 1 month before PRL implantation. The keratotomies are placed on the steep axis of the corneal astigmatism (Lindstrom et al. 1994).

Before PRL implantation, two neodymium-yttrium aluminium garnet (Nd:YAG) laser iridotomies, placed 90 degrees apart, are performed in the peripheral iris (single burst 3-10 mJ) to avoid the possibility of pupil block after PRL implantation. These generally measure 250 to 500 μm in diameter and are located superiorly in order to be covered by the upper eyelid (Figure 6). Iridotomies should be performed at least 1 to 2 weeks preoperatively. One surgical, peripheral iridectomy also can be performed intraoperatively. The choice of anesthesia can vary from general anesthesia to sub-Tenon’s and topical anesthesia.

Figure 6. Two iridotomies in the superior iris covered by the upper eyelid.

1.3.4 Surgical procedure
A combination of cyclopentolate 0.75% and phenylephrine 2.5% is applied 3 times 30 minutes before surgery or 150 μl of cyclopentolate 0.1%, phenylephrine 1.5%, and lidocaine 1% is administered intracamerally (Lundberg and Behndig 2003, Behndig and Eriksson 2004) at the beginning of the procedure to obtain good pupil dilation. The incision for implantation of a PRL
can be a self-sealing, clear corneal tunnel of 3.2 x 1.5 mm. Intraoperatively, care is taken to prevent the surgical instruments from touching anatomic structures such as the corneal endothelium, the crystalline lens capsule, or the iris diaphragm. The use of an ophthalmic viscosurgical device (OVD) is important for protecting adjacent tissues and allowing the lens to unfold in a controlled manner (in our case injection of an OVD that is not too heavy; sodium hyaluronate 1.34% [Biocorneal®, Corneal, Paris, France]).

The PRL is inserted with a forceps specially designed for this lens (Dementiev implantation forceps, Figure 7). Once the lens unfolds slowly in the AC, the haptics initially lie anterior to the dilated pupil. Each haptic corner then is placed gently behind the iris through the pupil with a long spatula or an intraocular hook without placing pressure on the crystalline lens and without decentering the optic.

Figure 7. The PRL implantation forceps to insert the PRL into the anterior chamber through 3.2 mm incision. After the PRL has introduced into the anterior chamber, it unfolds and the PRL lies anterior to the dilated pupil.

When proper horizontal PRL orientation is verified, a miotic agent, acetylcholine chloride (Miochol®, Novartis Pharma Stein AG, Stein, Switzerland) is injected that causes the pupil to constrict and traps the lens in the PC. The remaining OVD then is irrigated out of the AC. At the end of surgery, 1 mg of cefuroxime sodium (Zinacef®, Baxter Healthcare Corporation, Deerfield, IL) is injected into the AC (Montan et al. 2002). Corneal wounds can be closed by stromal hydration without using a suture.

The suggested postoperative treatment includes 0.1% topical dexamethasone eye drops three times daily for 1 week with dose tapering over 3 weeks. Cyclopentolate 1.0% is prescribed twice daily for 2 days to prevent elevated IOP related to retained OVD.

1.3.5 Complications

The PC PIOL is a potentially reversible procedure but one in which the possibilities of complicating cataract formation, pigment dispersion, and pupil block glaucoma coexist. Like all refractive surgical procedures, whether corneal or lenticular, it is invasive and therefore carries small but definable general risks such as inflammation and infection.

1.3.5.1 Cataract formation

The possibility of crystalline lens damage and cataracts formation is probably the most controversial issue of PC PIOL implantation (Werner et al. 2001). The anterior subcapsular opacification (Figure 8) has been described as typical form of an posterior PIOL-induced cataract (Fink et al. 1999, Arne and Lesueur 2000, Gonvers et al. 2003, Sanchez-Galeana et al. 2003). In the normal, undisturbed lens, the epithelium is confined to the anterior surface and to the equatorial region and equatorial lens bow (Blumenthal et al. 1991). The epithelium of the crystalline lens consists of a sheet of anterior epithelial cells (A-cells) that are in continuity with
the cells of the equatorial lens bow (E-cells). The primary type of response of these A-cells to any stimulus is to proliferate and form fibrous (Font and Brownstein 1974). The A-cells lining the anterior capsule are the cells of origin of anterior subcapsular cataract (Apple 2000). The second zone is a continuation of the anterior lens cells around the equator, forming the equatorial lens bow (E-cells). In sharp contrast to their precursors (A-cells), mitoses, cell division, and multiplication in this region are quite common. New lens fibers are continuously produced in this zone throughout life (Apple 2000).

A primary risk factor for lens opacification seems to be direct mechanical contact with the anterior lens surface (Sanders and Vukich 2002, Gonvers et al. 2003). Therefore, the distance between the posterior PIOL and crystalline lens seems to be important when evaluating different models of PIOLs (Baikoff et al. 2004). In accommodation, the anterior lens surface moves forward and assumes a more rounded shape (Brown 1973). Fechner and colleagues suggested that pressure from the posterior PIOL on the anterior surface of the crystalline lens may be caused by constant or intermittent contact from increased crystalline lens curvature during accommodation (Fechner 1990, Fechner 1999). It can be assumed that in eyes with an implanted PC PIOL, the PIOL moves closer to the crystalline lens during accommodation, especially in nonpresbyopic eyes (Baikoff et al. 2004), since with increasing age the maximum possible change in lens movement declines (Koretz et al. 1997). However, the crystalline lens grows throughout life approximately at the same rate as the AC depth decreases, i.e., 13 μm annually (Koretz et al. 1997). Such growth may be responsible for reduction of the space between the crystalline lens and the phakic IOL.

Nevertheless, other factors may be involved in cataractogenesis. The crystalline lens ideally should not be touched at all during phakic IOL implantation. However, accidental contact with the anterior lens capsule can occur during injection of OVD, phakic IOL injection or insertion, haptics placement behind the iris, and IOL rotation (Pallikaris et al. 2004, Sarikkola et al. 2005). Pressure applied on the phakic lens should be reduced to a minimum, if necessary, for IOL positioning. Anterior capsule trauma, even when unnoticed, can lead to proliferation of epithelial subcapsular cells (A-cells), which can provoke crystalline lens opacities months later. A possible effect of the Nd:YAG laser used to make iridotomies in the preoperative or postoperative period cannot be ignored, although this therapy is not directly related to the surgical procedure.

Additionally, contact between the IOL and the crystalline lens in the midperiphery may block normal circulation of the aqueous humor. A pool of aqueous stagnation can cause in part metabolic changes and alteration of crystalline lens nutrition. To clarify the cause of secondary cataract after ICL implantation, Fujisawa et al studied aqueous circulation in the space between the ICL and crystalline lens in porcine eyes (Fujisawa et al. 2006). When an ICL similar to the human eye was inserted into porcine eyes, anterior subcapsular opacities developed in all cases during the 3-month follow-up. No direct contact was observed between the ICL and crystalline lens at any time. The results suggest that the ICL altered...
the circulatory dynamics of the aqueous humor, probably because of poor circulation on the anterior surface of the crystalline lens, and resulted in cataract. There are structural and functional differences between human and porcine eyes, and results cannot be extrapolated directly to human eyes. However, the findings are interesting and could partly explain the difference in cataract incidence between ICL and PRL.

1.3.5.2 Inflammation

Like all intraocular procedures, posterior PIOL implantation carries general risks such as inflammation and infection. The study of Jimenez-Alfar-o and associates showed a constantly elevated flare at all time points, which indicates continuous disruption of the blood-aqueous barrier and subclinical inflammation of the anterior segment. After phacoemulsification with IOL implantation, anterior segment inflammation measured with the laser flare meter usually returns to preoperative values 1 year postoperatively. Therefore, the constantly elevated flare values in these patients can reasonably be attributed to the presence of the phakic lens (Jimenez-Alfar-o et al. 2001). The mechanisms may include constant friction between the posterior iris surface and the phakic lens or between the haptic and the ciliary sulcus. The flare values observed with iris-fixated or angle-supported AC PIOLs were more elevated than the values observed with the ICL in the study of Jimenez-Alfar-o and associates. The subclinical inflammation may have repercussions not only on the crystalline transmittance but also on the corneal endothelium. Subclinical inflammation may cause metabolic disturbances of the crystalline lens, resulting in cataract formation.

1.3.5.3 Pupillary block glaucoma

Complications also can include pupillary block glaucoma (Figure 9) owing to functional closure of the laser iridotomies (Rosen and Gore 1998, Pesando et al. 1999, Sarikkola et al. 2005). The IOP can increase in the immediate postoperative period because of residual OVD, postoperative inflammation, and steroid drug treatment (Hoyos et al. 2002, Pallikaris et al. 2004).

Figure 9. A schematic representation of an eye that shows pupillary block induced by a posterior PIOL. If the iridotomies do not facilitate sufficient aqueous outflow, the pupil is occluded by the posterior PIOL with a large volume of aqueous trapped between the PIOL and the crystalline lens.

1.3.5.4 Pigment deposits

Fine pigment deposits can be seen on the lens surface in the postoperative period. This seems to be more frequent when Nd:YAG laser iridotomies are performed. Pigment deposition did not seem to impair the image quality of the lens (Jimenez-Alfar-o et al. 2001). Another concern is
possible pigmentary dispersion syndrome resulting from contact between the iris and the posterior PIOL (Brandt et al. 2001). This syndrome is characterized by deposition of pigment in the trabecular meshwork on the corneal endothelium (forming the Krukenberg spindle) and on the anterior lens capsule, as well as radial, slit-like, transilluminating defects of the iris (Abela-Formanek et al. 2001). Although all patients in the series of Jimenez-Alfaro and coworkers had contact between the ICL and the posterior surface of the iris, no patient had pigmentary dispersion (Jimenez-Alfaro et al. 2001). Davidorf and associates believe that pigment dispersion on the ICL surface is surgically related, because the amount of pigment in that series appeared not to progress (Davidorf et al. 1998).

1.3.5.5 Glare and halos

Subjective edge glare and halos have been reported by many surgeons. Because the optic size of the posterior PIOLs varies between 4.5 to 5.5 mm, patients whose pupils enlarge beyond that size in dim light may be subject to minor halos or night glare, phenomena that would also trouble a patient if the lens optics were decentered. Some surgeons do not consider implanting phakic lenses if the pupillary diameter in dim conditions is 7 mm or larger. Night halos appear to be less frequent than might be expected with PC PIOLs, possibly because the lenses are behind the pupil, thus increasing the effective optic zone (Werner et al. 2001). Even large iridectomies can increase the risk of light scattering through the iridectomy and cause glare, especially if the iridotectomy is visible and not covered by the upper eyelid.

1.3.5.6 PIOL decentration and luxation in the vitreous

A decentered posterior PIOL generally arises from an inadequate lens length. Decentration may also lead to monocular diplopia. There are some reports of serious complications with PRL dislocations into the vitreous cavity and subluxation, suggesting that PRL rotation causes excess pressure against the zonules (Eleftheriadis et al. 2004, Martinez-Castillo et al. 2004, Hoyos et al. 2005, Donoso and Castillo 2006). The distributor of the PRL has reported problems in Italy and Spain with 11 PRL luxations into the vitreous cavity up to 2004 and three cases from 2004 to the present (2 cases in 2005 and 1 in 2006, all in Italy) (Fresnais Laetita, Product Manager, Zeiss-Meditec, personal communication, October 2007).

1.3.5.7 Retinal detachment

The patient population undergoing refractive surgery is largely myopic and as such is particularly vulnerable to posterior segment pathology. PIOL implantation in myopic eyes is associated with the risk of retinal detachment that ranges from 0.8% to 4.8% (Ruiz-Moreno et al. 2006). A dilated fundus examination is an integral part of optimum clinical care in patients who undergo refractive surgery, and shared preoperative assessment by a retinal specialist is advisable in those with a predisposing retinal pathology (Brady et al. 2007).

1.3.6 Surgery in hyperopic eyes

Preoperative UCVA plays a significant role in the motivation to undergo refractive surgery; a 30-year old myopic patient is more likely to seek corrective surgery than a 30-year old patient with hyperopia. Since refractive surgery is performed less frequently in hyperopic eyes compared with
myopic, the surgical outcome and adverse effects of PIOLs in hyperopic eyes are not that well documented in the literature (Sher 2001).

Hyperopic eyes often have relatively smaller anterior segments, which may require more careful IOL insertion to avoid contact with the corneal endothelium (Davidorf et al. 1998). Hyperopic eyes with a central AC depth of 3.0 mm or less are an important contraindication to PIOL implantation to avoid postoperative pupillary block and to maintain a safe distance from the corneal endothelium. In addition, Davidorf and colleagues reported that the incidence of pupillary block glaucoma in hyperopic eyes was more than double the incidence of pupillary block they observed in a previous series of ICL implantations in myopic eyes (Zaldivar et al. 1998). Pupillary block glaucoma, related to functional closure of the iridotomies or retention of an OVD, seems to be particularly important with hyperopic eyes (Pesando et al. 1999).

According to Rosen and Gore (Rosen and Gore 1998), an intraoperative surgical iridectomy at a location away from possible occlusion by the PIOL is important to minimize the risk of pupillary block, particularly in small eyes with hyperopia and eyes with brown irides.

Pesando and coworkers implanted ICLs in 59 hyperopic eyes with a follow-up of 6 to 10 years. The postoperative refraction was within ±1.00 D in 96% of the eyes. According to those authors, the refractive predictability appeared better for hyperopia than for myopia using the ICL (Pesando et al. 1999, Pesando et al. 2007).

1.4 METHODS

1.4.1 Visual acuity

The visual acuity was tested using the Early Treatment of Diabetic Retinopathy Study (ETDRS) acuity charts in all the studies with modification in the study IV, in which the ETDRS logarithm of the minimum angle of resolution (logMAR) acuity charts was used. The safety index was defined as the ratio of the mean postoperative BCVA over the mean preoperative BCVA and the efficacy index as the ratio of the mean postoperative UCVA over the mean preoperative BCVA, respectively (Koch et al. 1998).

1.4.2 Intraocular pressure

Goldman applanation tonometry was used to measure IOP at the follow-up visits.

1.4.3 Laser flare meter

The protein concentration in the AC flare was measured using the Kowa FM-500 laser flare meter (Figure 10). The laser flare meter measures indirectly aqueous protein concentrations in the AC by measuring light scattered from protein (Sawa et al. 1988). All eyes had pupils dilated with topical 0.5% tropicamide. Ten sequential scans were averaged. Flare values were expressed as photon counts per millisecond (ms).

Figure 10. Examination with Kowa-500 laser flare meter.
1.4.4 Corneal endothelial cell count

The Topcon SP 1000 specular microscope and IMAGEnet systems were used for counting corneal endothelial cell density (Figure 11). Cell morphologic indices were not studied. On the basis of about 100 identified cells taken from the recorded picture of the endothelium, the computer traced the cellular outlines while the investigator corrected false readings (semiautomated method). The software performed the final calculation and the values were expressed as cells/square millimeter (cells/mm²).

1.4.5 Scheimpflug images

Images of the anterior segment were made using a Nidek EAS-1000 Anterior Eye Segment Analysis System through a dilated pupil. After the photography, the measurement of the distance (in millimeters) between the posterior surface of the PRL (PS-PRL) and the anterior lens surface was repeated three times and averaged to obtain final results for distance (Figure 12). The disadvantage of the Scheimpflug method is the need for pupil dilation to obtain images of the entire surface of the crystalline lens and stimulation of the fellow eye to study accommodation of the eye under observation.

1.4.6 Retroillumination photographs

The retroillumination photographs were taken after pupil dilatation with tropicamide 0.5% to illuminate at least one edge of the PRL for comparison between the different follow-up examinations. The edges of the PRL were projected over each other to determinate possible degrees of rotation (Figure 13).

1.4.7 Optical coherence tomography

Optical coherence tomography (OCT) uses low-coherence interferometry to provide in vivo cross-sectional images of tissue structures. OCT was developed initially for retinal imaging, using a near-infrared 800-nm wavelength (Hee et al. 1998). For anterior segment imaging, a longer
wavelength of 1300 nm allows greater penetration through high light-scattering tissues, such as the limbus and sclera, and makes it possible to visualize angle structures (Radhakrishnan et al. 2001). The technique works by splitting the light source into a reference and a measurement beam. The measurement beam from the ocular structures interacts with the reference light reflected from the reference mirror causing interference.

In study III, evaluation of different distances in the anterior segment and the horizontal diameter of the pupil was performed with Visante OCT (Zeiss, Jena, Germany). The patient fixates on a target that is adjustable with positive or negative lenses, which are located within the OCT device, allowing compensation for spherical ametropia (Figure 14). It is also possible to defocus the target with negative lenses to induce physiologic accommodation in the examined eye.

After acquiring the scan, software in Visante OCT automatically finds the anterior and posterior corneal surfaces. The investigator may apply additional measurement overlays for analysis (Figure 15).

**Figure 14.** Scanning with Visante OCT. The patient is asked to focus on a central target internal to the OCT device. After the scanning in the non-accommodated state the eye is stimulated with negative lenses to achieve accommodation. The eye can be scanned several times at different degrees of accommodation.

**Figure 15.** Visante OCT image of a myopic PRL before and after the measurement overlays are applied for analysis.
2 AIMS

1. To evaluate the surgical outcome and adverse events associated with correction of myopia and hyperopia with a PRL (I, II, IV).
2. To investigate the dynamics of the PRL in relation to the behavior of the crystalline lens and the pupil (I, II, III).
3. To determine the random errors and evaluate the precision of the analytical methods used in the trials (II, III).
3 MATERIAL AND METHODS

3.1 PATIENTS AND METHODS (I)

3.1.1 Patients

Twenty eyes of 20 patients (11 women, 9 men) with a median age of 31 years (range, 23-43 years) were included. Fourteen eyes were myopic with a median spherical equivalent (SE) refraction of -9.19 D (range, -6.88 to -17.63) and six eyes were hyperopic with a median SE of +6.13 D (range +3.25 to +8.63 D). The local ethics committee provided approval of the study protocol. The patients were informed about the details of the study and they provided informed consent.

3.1.2 Inclusion criteria

The inclusion criteria were patient age between 20 and 45 years, UCVA less than 0.5 in Snellen visual acuity, BCVA of the fellow eye better than 0.1, stable myopia between -3.5 and -27.0 D or hyperopia between +3.0 and +11.5 D corresponding to the available PRL power, a normal anterior segment with an AC depth of at least 3.0 mm including the cornea, endothelial cell density greater than 2500 cells/mm², and an IOP less than 20 mm Hg. Only one eye of each patient was included in the study to avoid bias.

3.1.3 Exclusion criteria

Patients were excluded if they had regular astigmatism of 3.0 D or higher, cataract, corneal pathology, a narrow angle or glaucoma, a history of anterior or posterior segment inflammation, diabetes, infections, or retinal pathologies.

3.1.4 Follow-up

All patients were scheduled for follow-up visits on 1 day, 1 week, 3 months, and 1 year postoperatively. The follow-up examinations were completed in all cases. The visits involved a detailed ophthalmologic examination including manifest refraction, slit-lamp microscopy, applanation tonometry, laser flare measurement, Scheimpflug slit images through a dilated pupil to evaluate the distance between the PRL and the crystalline lens, and retroillumination photographs to evaluate the PRL rotation in the PC. The endothelial cell density was measured preoperatively, and at 1 week and 1 year postoperatively. Safety and efficacy indexes were evaluated based on the UCVA and the BCVA.

3.1.5 Statistical analysis

Statistical analysis was performed using Friedman 2-way analysis of variance (ANOVA) by ranks with multiple comparisons (Siegel S. 1988). The level of significance was P<0.05.

3.2 PATIENTS AND METHODS (II)

3.2.1 Patients

In the primary study, the study population and the inclusion and exclusion criteria were the same as in study I. In the parallel sub-study “analysis of the follow-up methods”, 20 eyes other than
those in the primary study were included. These eyes met the inclusion criteria as in the primary study and they also had undergone surgery to implant a PRL.

### 3.2.2 Follow-up

The patients were scheduled for a follow-up visit 2 years after PRL implantation and the follow-up was completed in all cases. The visit involved a detailed ophthalmologic examination including manifest refraction, slit-lamp microscopy, applanation tonometry, laser flare measurement, Scheimpflug slit images in dilatation, retro-illumination photographs, and endothelial cell count. The crystalline lens was clinically assessed by slit-lamp, retro-illumination photographs, and Scheimpflug images to analyze lens transparency. Safety and efficacy indexes were evaluated in the same manner as in study I.

### 3.2.3 Analysis of the follow-up methods

To evaluate the precision of the analytical methods used, double-independent measurements of laser flare meter, endothelial cell count, and determination of the distance between the PRL and the crystalline lens with Scheimpflug images were performed on 20 eyes after PRL implantation and they were not included in the primary study. All the measurements were done by the same investigator (M.T.).

### 3.2.4 Statistical analysis

Statistical analysis was performed by Friedman 2-way ANOVA by ranks with multiple comparisons. The level of significance was $P < 0.05$.

### 3.3 PATIENTS AND METHODS (III)

#### 3.3.1 Study design

The study population included 52 patients (52 eyes) with myopia and hyperopia. The PRLs were implanted between April 2002 and May 2005. The inclusion criteria included a minimum of 1 year after PRL implantation. Only one eye of each patient was enrolled in the study to avoid bias. An eye was excluded if any refractive surgery was combined with PRL implantation. The study had a cross-sectional design in which all patients were scanned with the Visante OCT only once without follow-up and the association between the distance PRL-anterior lens surface and lens opacification was investigated. The local ethics committee approved the study. All patients were provided with written and oral explanations of the study, and they all provided their consent.

#### 3.3.2 Visante OCT as an analytical method

To evaluate the precision of Visante OCT, a double-independent measurement study was conducted. Twenty-two eyes of 12 patients underwent scanning of the anterior segment; the scans were repeated after an interval of 5 minutes. The investigator evaluated the distances from the PS-PRL to the anterior lens surface and from the anterior surface of the PRL (AS-PRL) to the posterior corneal surface before the patient underwent a new scan. The second scan was analyzed later without knowledge of the results of the first scan.
3.3.3 Main outcome measures

Manifest refraction was tested before the OCT scans were performed to compensate for spherical ametropia during scanning. After scanning, the crystalline lens was examined after the pupils were dilated using tropicamide 0.5% to determine the presence of lens opacification. Baseline measurements were performed in the non-accommodated state at the horizontal meridian. All examinations were performed in a room with dim illumination. The eye was stimulated with negative lenses to achieve accommodation. The target was slowly defocused in -0.25 D increments until it was subjectively blurred and could no longer be focused (push-up method). The mean lens power added before blurred vision was achieved was -4.6 D (range, -1.25 to -13.0 D).

3.3.4 Statistical analysis

Confidence intervals, based on the t-distribution, were calculated for differences in mean results. The differences were statistically significant when the confidence intervals did not include zero. Results are expressed as mean ± 95% confidence interval based on a significance level of $P<0.05$. Regression analysis was used to determine regression equations.

3.4 PATIENTS AND METHODS (IV)

3.4.1 Patients

The study population included 40 consecutive eyes of 25 patients with hyperopia independent of the degree of astigmatism. A certain degree of amblyopia was observed in 12 eyes (30%). The local ethics committee approved the study. All patients provided informed consent after the study was explained fully.

3.4.2 Inclusion criteria

The inclusion criteria were patient age between 20 to 45 years, hyperopia corresponding to an available PRL power, a normal anterior segment with an AC depth of at least 3.0 mm including the cornea, an endothelial cell density greater than 2000 cells/mm², and IOP below 25 mmHg.

3.4.3 Exclusion criteria

Patients were excluded if they had a narrow angle or glaucoma, infections, and a history of anterior or posterior segment inflammation. In addition, those who did not undergo one of the postoperative follow-up visits were excluded.

3.4.4 Arcuate keratotomy

The PRL with its floating design cannot correct astigmatism. In cases of astigmatism of 2 D or greater with a substantial effect on visual outcome, an arcuate keratotomy with a 7-mm-diameter clear zone (Lindstrom et al. 1994) was performed preoperatively in nine eyes (22.5%). The mean time between the relaxing keratotomies and the PRL surgery was 2.4 months (range, 1.0-4.6 months). Only a moderate effect was gained in eyes with lower hyperopia and no effect in eyes with hyperopia over 10 D.
3.4.5 Follow-up

The patients were scheduled for follow-up visits at 3 months and 1 year postoperatively. The first six patients (six eyes) had the first postoperative examination at 1 week instead of 3 months. The visits involved a detailed ophthalmologic examination including manifest refraction, slit-lamp microscopy, applanation tonometry, and measurement of the endothelial cell count.

3.4.6 Statistical analysis

Each patient was the subject in the statistical analysis and not the eye because in some cases both eyes were included in the analysis. Statistical analysis was performed by a mixed effects model. The level of significance was less than 5% ($P<0.05$). Statistical analyses were performed by SAS 9.1.3 Proc Mixed (Cary, NC).
4 RESULTS AND DISCUSSION

4.1 VISUAL OUTCOME (I, II, IV)

4.1.1 Safety

Safety was evaluated by measurement of the BCVA. The safety index (I, II) was 1.13 at 1 year and 1.2 at 2 years. At 1 year, 3 eyes (15%) and at 2 years five eyes (25%) gained two or more lines of BCVA. All eyes were myopic. No eye lost two or more lines of BCVA (Figure 16).

At 1 and 2 years, 80% of eyes had a BCVA of 1.0 or better (93% of myopic and 50% of hyperopic eyes), an improvement over the baseline level in myopic eyes. There was no change in the hyperopic eyes. All the eyes had a BCVA of 0.5 or better at 1 year that did not change at 2 years.

The 1-year follow-up in 40 hyperopic eyes showed a safety index 0.89. No eyes gained two or more lines. Two eyes (5.0%) lost two lines of BCVA. The mean BCVA decreased from 1.03 preoperatively to 0.93 at 3 months ($P<0.05$) without a change at 1 year ($P>0.05$). At 1 year, 17.5% of eyes had a BCVA of 1.0 or better and 65% had 0.5 or better.

The BCVA increased significantly in myopic eyes with excellent visual outcome and safety results. However, in the hyperopic eyes, the BCVA decreased postoperatively, and even though the clinical relevance of this decrease can be discussed, the result showed no postoperative gain in BCVA in hyperopic eyes. Limited improvement in BCVA also has been reported in studies with other hyperopic PIOLs (Davidorf et al. 1998, Bartels et al. 2006). This could be explained by a smaller image size with corrected refraction closer to the nodal point of the eye and elimination of the spectacle-induced magnification experienced by patients with hyperopia preoperatively. In high myopia, the spectacle correction minifies the image, which is eliminated after refractive surgery resulting in gains of lines of vision (Langenbcher et al. 2007). Preoperative contact lens-corrected visual acuity compared with postoperative spectacle-corrected visual acuity might provide a more realistic evaluation of the safety index and a comparison between hyperopic and myopic eyes (MacRae 1998).

Figure 16. Percentage of eyes gaining and losing lines of BCVA 2 years postoperatively (study II).

At 1 and 2 years, 80% of eyes had a BCVA of 1.0 or better (93% of myopic and 50% of hyperopic eyes), an improvement over the baseline level in myopic eyes. There was no change in the hyperopic eyes. All the eyes had a BCVA of 0.5 or better at 1 year that did not change at 2 years.

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4.1.2 Efficacy

The efficacy index (I and II) was 0.89 at 1 year and 0.91 at 2 years (Figure 17). The UCVA was 1.0 or better in 50% of eyes (64% of myopic and 17% of hyperopic) at 1 year and in 40% (50% of myopic and 17% of hyperopic) at 2 years. All myopic eyes had an UCVA of 0.5 or better. In hyperopic eyes, the UCVA was 0.5 or better in 67% of eyes at 1 year and 83% of eyes at 2 years.

In 40 hyperopic eyes (IV), the efficacy index was 0.70 at 1 year. The UCVA was 1.0 or better in seven eyes (17.5%), 0.50 or better in 26 eyes (65%), and less than 0.5 in seven eyes (17.5%). In the last group, the mean preoperative BCVA was 0.6±0.19 (range, 0.32-0.8). The mean astigmatism was -1.9±0.61 D (range, -1.0 to -2.5 D) compared with the astigmatism in the other eyes -0.96±0.65 (range, ±0.0 to -2.5 D).

The efficacy index showed slight undercorrection corresponding to uncorrected astigmatism. However, UCVA showed excellent outcomes especially in myopic eyes in which all eyes had an UCVA of 0.5 or better even though the PRL with its floating design cannot correct astigmatism. In cases of astigmatism with a substantial effect on visual outcome, there are other options complementary to PRL. One of these is bioptics in which the PIOL is combined with a corneal laser procedure (Zaldivar et al. 1999, Sanchez-Galeana et al. 2001). PRL implantation followed by LASIK or LASEK enhancement could provide more precise results and produce the parallel treatment of preexisting and surgically induced astigmatism. However, combining corneal and intraocular surgeries exposes patients to complications from both techniques. The toric ICL can solve some problems in the myopic eyes, because it remains rotationally stable after surgery (Gimbel and Ziemba 2002). Unfortunately, there is no toric hyperopic PC PIOL currently commercially available.

In the study of 40 hyperopic eyes, the fact that 30% of eyes had different levels of amblyopia certainly had a substantial effect on the postoperative visual outcomes.

Figure 17. The efficacy index during the 2-year follow-up period.
4.2 PREDICTABILITY (I, II, IV)

The change in SE refraction in studies I and II showed that 15 eyes (75%) were within ±0.5 D of the desired refraction and all eyes (100%) were within ±1.0 D at the 1- and 2-year visits. Eighteen eyes (90%) were within ±1.0 D of emmetropia at 1 and 2 years postoperatively. The study population of 40 hyperopic eyes showed even more precious predictability (Figure 18).

Thirty-five eyes (87.5%) were within ±0.5 D of the desired refraction and all eyes (100%) were within ±1.0 D. At 1 year postoperatively, 87.5% (35 eyes) were within ±1.0 D of emmetropia.

The current standard-of-care precision in refractive surgery is ±1.0 D from the attempted refraction (Lovisolo and Reinstein 2005). In cases of residual refractive error in the form of pure spherical ametropia after PRL implantation, the PRL was exchanged for the right power as we did in two hyperopic cases with primary overcorrection postoperatively. After replacement of the PRL in these eyes, all cases were within ±1.0 D of the desired refraction and the refraction remained stable during the follow-up period. These results are better compared with other studies of the PRL and the ICL (Davidorf et al. 1998, Fink et al. 1999, Hoyos et al. 2002, Pallikaris et al. 2004, Sarikkola et al. 2005).

4.3 INTRAOCULAR PRESSURE (I, II, IV)

In the mixed myopic and hyperopic study population (I, II), the mean IOP was 16±1.8 mmHg (range, 13-21 mmHg) preoperatively, 16±2.0 mmHg (range, 13-20 mmHg) at 1 year and 16±3.0 mmHg (10-22 mmHg) at 2 years.
One hyperopic and one myopic eye developed pupillary block 2 and 4 days after surgery, respectively. In both cases the IOP was normalized with complementary Nd:YAG-iridotomies and medication. A myopic eye developed corticosteroid-induced high IOP of 49 mmHg 1 week postoperatively that resolved after discontinuation of the steroid drops.

In the hyperopic study population, there was no difference in the mean IOP values between visits ($P>0.05$). The mean IOP was 15.5±3.2 mmHg (range, 8-24 mmHg) preoperatively and 15±3.3 mmHg (range, 8-26 mmHg) at 1 year. Seven eyes (17.5%) developed pupillary block by a mean of 6 days postoperatively (range, 1-15 days) and were treated successfully with Nd:YAG-iridotomies and medication.

The IOP was stable and no long-term changes or glaucoma was observed, which confirms the results in the other PRL studies (Pallikaris et al. 2004, Donoso and Castillo 2006). However, the most frequent complication was early postoperative pupillary block in one myopic and seven hyperopic eyes. This is discussed further in the chapter 4.9 on complications.

### 4.4 ENDOTHELIAL CELL DENSITY (I, II, IV)

The mean changes in endothelial cell count (studies I and II) were -247 cells/mm² (range, -1288 – 160 cells/mm²) (-8.4 %) 1 week after surgery, -203 cells/mm² (range, -767 – 176 cells/mm²) (-7.1%) 1 year postoperatively, and -228 cells/mm² (range, -899 – 173 cells/mm²) (-7.7%) 2 years postoperatively. Friedman 2-way ANOVA showed statistical significance between visits preoperatively and at all postoperative visits ($P<0.05$). However, there was no change in the endothelial cell density between 1 week and 1 year or 2 years postoperatively ($P>0.05$).

In 40 hyperopic eyes, the mean change in the endothelial cell count at 3 months was -139 cells/mm² (range, -911 to +328 cells/mm²) (-4.6%) and at 1 year -115 cells/mm² (range, -847 to +183 cells/mm²) (-3.8%) as shown in Figure 19. The endothelial cell densities at 3 months and 1 year were significantly lower than preoperatively ($P<0.01$). Between 3 months and 1 year postoperatively, the cell count increased by a mean of 25 cells/mm² (1.1%), a difference that did not reach significance ($P>0.05$).

![Figure 19](image.png)

*Figure 19.* The mean endothelial cell density in hyperopic eyes. The error bars indicate 95% confidence intervals. Endothelial cell loss was -4.6% at 3 months without a significant change at 1 year.
Surprisingly, hyperopic eyes (study IV) had lower endothelial cell loss compared with the myopic eyes. The results in hyperopic eyes were comparable to the hyperopic ICL implantations that had a -4.7% endothelial cell loss postoperatively and remaining unchanged throughout the 10-year follow-up (Pesando et al. 2007). Evaluation of the endothelial cell density in 78 myopic eyes with PRL implantation showed a -7.1% cell loss at 3 months and a -6.3% cell loss at 1 year (Koivula et al, Poster presentation, ESCR Winter Meeting, Athens, Greece, 2007), which confirms the results in the studies I and II with most myopic eyes.

However, the myopic ICL implantations have shown another pattern. The low initial endothelial cell change after surgery (-1.8 to -2.1% at 3 months) was followed by continuous cell loss -5.7 to -7.9% at 2 years and -8.9 to -12.9% at 3 years (Dejaco-Ruhswurm et al. 2002, Edelhauser et al. 2004). With a mean cell density of 3000 cells/mm² at 20 years of age, physiologic endothelial cell loss is reported to be approximately 0.6% per year (Bourne et al. 1997), indicating that continuous cell loss after ICL implantation is more than the result of aging. According to the authors, one explanation could be endothelial cell remodeling. The compensatory changes that occur in the endothelium during recovery from surgical trauma, such as the migration of cells from the central cornea to the area where the surgical trauma occurred, may account for the significant central cell loss over the first postoperative years (Dejaco-Ruhswurm et al. 2002, Edelhauser et al. 2004). In our studies, there was no continuous cell loss after 3 months, indicating that the initial loss mainly results from the surgical procedure and is not induced by the PRL.

Although the surgical maneuvers are identical in myopic and hyperopic PRL eyes, the hyperopic eyes with shallower ACs may have increased risk for contact with the corneal endothelium intraoperatively. However, the myopic cases still had increased cell loss. Can the difference in the PRL design with biconcave optics in myopic eyes increase the risk of damage to the corneal endothelium in myopic eyes at the time of surgery?

### 4.5 INFLAMMATION (I, II)

The highest average flare count was 15.6 photons/ms at 1 day after surgery compared with the mean 3.8 photons/ms before surgery. The mean laser flare returned to the preoperative level at 3 months and did not change at 1 or 2 years after surgery ($P>0.05$). Laser flare was not influenced by PRL rotation.

The laser flare measurements were as expected at the highest level 1 day postoperatively due to surgical trauma. Similar results have been found in eyes implanted with an ICL (Sarikkola et al. 2005). The laser flare findings in eyes with an ICL were compared with the control group that did not undergo surgery during 2 years. The results showed that laser flare values after ICL implantation were well within the range of normal values (Sanders 2003).

### 4.6 PRL ROTATION (I, II)

Fifteen PRLs (75%) rotated 10 degrees or more during the first follow-up year and three PRLs (15%) between 1 and 2 years. The centration of the PRL was good in all eyes. Figure 20 illustrates PRL rotation in a hyperopic eye over time.
The rotation of the PRL may indicate aqueous exchange behind the PRL. Therefore, the floating design of the PRL could be a protective factor for the crystalline lens. The retroillumination photographs showed that the PRL rotated in the PC even though the rotation was much less after the first follow-up year. In addition, the findings from the other PRL studies with ultrasound biomicroscopy (UBM) suggested that PRL rotation could indicate the right haptic position on the zonules without capturing in the sulcus (Garcia-Feijoo et al. 2003, Garcia-Feijoo et al. 2003). However, there have been some reports of serious complications with PRL luxation into the vitreous cavity, suggesting that PRL rotation causes excess pressure against the zonules (Eleftheriadis et al. 2004, Martinez-Castillo et al. 2004, Hoyos et al. 2005). Results in studies I and II cannot confirm this hypothesis. Some degree of rotation was shown in most eyes but in most cases just once between different visits. The absence of PRL decentration can be seen as an indication for right lens sizing.

4.7 DISTANCE BETWEEN THE PRL AND THE ANTERIOR LENS SURFACE (I, II, III)

Figure 21 shows the central distance between the PS-PRL and the anterior lens surface over time (I, II) measured with the Scheimpflug technique. In both myopic and hyperopic eyes, the gap decreased during the first year after surgery. The mean distance was 0.26±0.14 mm (range, 0.0 – 0.46 mm) at 1 year and 0.27±0.15 (range, 0.0 – 0.56 mm) at 2 years. A significant difference was found when comparing the 1-year and 2-year distances with 1-day distance (P< 0.05). The possible effect of accommodation was not investigated. The disadvantage of the Scheimpflug method is the need for pupil dilatation to obtain images of the entire surface of the crystalline lens and stimulation of the fellow eye to study accommodation of the eye under observation (Koretz et al. 2002).

However, the impact of accommodation seems to be essential for distance evaluation. Bäikoff and coauthors...
(Baikoff et al. 2004) showed in a case report with AC OCT that the PS-PRL touched the anterior lens surface during accommodation. Our distance measurements with OCT showed the mean baseline distance 0.35±0.18 mm (range, 0.0 – 0.80 mm) and during accommodation 0.28±0.24 mm (range, 0.0 – 0.94 mm). All eyes in the OCT study were investigated at least 1 year after PRL implantation.

The study population was divided into the groups according to the lens model. There was no significant difference in the initial PS-PRL and the anterior lens surface distance between the eyes that received the PRL 101, PRL 100, and PRL 200. During accommodation, with the PRL 200 and the PRL 101, there was a mean 84-μm decrease in the distance between the PRL and crystalline lens. The distance between the PRL 100 and crystalline lens did not change during accommodation (Table 1). The changes in the distances between the posterior corneal surface and the anterior lens surface and the anterior lens surface and the AS-PRL were significant with all PRL models (P<0.05).

<table>
<thead>
<tr>
<th>Model</th>
<th>Baseline</th>
<th>Accommodation</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRL 101 (n=31)</td>
<td>0.38</td>
<td>0.29</td>
<td>-0.084±0.044*</td>
</tr>
<tr>
<td>PRL 100 (n=10)</td>
<td>0.30</td>
<td>0.31</td>
<td>0.002±0.100</td>
</tr>
<tr>
<td>PRL 200 (n=11)</td>
<td>0.32</td>
<td>0.23</td>
<td>-0.083 ±0.074*</td>
</tr>
</tbody>
</table>

* p<0.05

**Table 1.** Mean distance between the posterior surface of the PRL and the anterior lens surface with 95% confidence interval at baseline and during accommodation.

The contact between the PRL and the anterior lens surface at baseline and during accommodation in different PRL types is shown in Table 2.

<table>
<thead>
<tr>
<th>Model</th>
<th>Baseline</th>
<th>Accommodation</th>
<th>Cataract</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRL 101</td>
<td>2</td>
<td>3 (2+1)</td>
<td>2</td>
</tr>
<tr>
<td>PRL 100</td>
<td>1</td>
<td>2 (1+1)</td>
<td>0</td>
</tr>
<tr>
<td>PRL 200</td>
<td>0</td>
<td>3 (0+3)</td>
<td>0</td>
</tr>
</tbody>
</table>

**Table 2.** The number of PRLs in contact with the anterior lens surface at baseline and in accommodation in the different PRL models. The last column shows the distribution of cases with lens opacification between the PRL models.
All cases with contact between the PRL and the anterior lens surface at baseline had continuous contact during accommodation. Of these three eyes (5.8%), two (3.8%) developed lens opacities. In a total of five cases (9.6%), the PRL touched the crystalline lens during accommodation without contact at baseline. None of these eyes developed a cataract.

In Figure 22, the distance between the PS-PRL and the anterior lens surface at baseline is plotted against patient age. The initial distance was significantly lower in older eyes implanted with the PRL 101 ($r = -0.36; P < 0.05$). There was no significant trend in eyes implanted with the PRL 100 and the PRL 200 ($r_s = -0.12$ and 0.14, respectively; $P > 0.05$).

![Figure 22](image)

**Figure 22.** Significant correlation between age and distance to the crystalline lens in PRL 101 ($P < 0.05$) but not in PRL 100 and 200.

In the development of the posterior PIOL design, a great effort has been directed toward proper vaulting of the implant because a flat design was shown to produce most of the cataracts (Sanders and Vukich 2002). Therefore, the evaluation of the distance between the posterior PIOL and the crystalline lens seems to be important when comparing different PIOL models.

The distance measurements with the Scheimpflug method showed a significant decrease in the distance between the AS-PRL and the anterior lens surface during the first follow-up year without changes at the 2-year visit, indicating a time-related interaction. This result was confirmed in a study with the ICL (Baumeister et al. 2004). The distances measured with the Scheimpflug method showed comparable results with distances during accommodation investigated with Visante OCT. However, the baseline measurements evaluated with OCT showed an increased distance between the PS-PRL and the anterior lens surface compared with the Scheimpflug technique. This finding is important because it reveals a good average safety distance between the PRL and the crystalline lens evaluated with a more precise method than the Scheimpflug method.

During accommodation, the anterior lens surface moves forward and assumes a more rounded shape (Brown 1973). We found a significant forward movement of the anterior lens surface and PRL in each group. Although the PRL moved anteriorly with accommodation with all three lens models, the space between the PRL and crystalline lens was preserved only with the PRL 100,
and the space decreased with the other two models. The smaller size and weight of the PRL 100 may account for the difference in response to accommodation.

Lens thickening with age did not decrease the baseline distance between the PRL and crystalline lens in eyes with the PRL 100 and PRL 200. However, with the PRL 101 the initial gap decreased significantly with increasing age, indicating a smaller PC depth with aging of the lens.

The measurements with the Scheimpflug method revealed contact between the PRL and the crystalline lens in two cases without lens opacifications. In the OCT study, three cases had contact at baseline and two of them had lens opacifications. No eyes with PRL touch only during accommodation had lens opacities.

4.8 CHANGE IN PU PIL SIZE (III)

Another force that pushes the posterior surface of the artificial lens toward the anterior surface of the crystalline lens is pupil constriction resulting from light as reported by Petternel et al (Petternel et al. 2004) who found a significantly reduced distance between the ICL and crystalline lens under photopic conditions with pupil constriction.

The reduction in pupil diameter during accommodation was found in all models ($P<0.05$). There was a correlation between the reduction in pupil diameter and the reduction in the distance between the PS-PRL and the anterior lens surface during accommodation in eyes with the PRL 200 ($r = 0.67; P<0.05$) but not in eyes with the PRL 101 and PRL 100 ($r_s = 0.20$ and $-0.41$, respectively). In hyperopic eyes, this correlation confirmed the results from the study of Petternel et al., although the number of hyperopic cases was rather small. However, pupil constriction in myopic eyes, as part of the accommodative process with lens changes, did not have the same effect as pupil constriction induced by light. Even if the pupil closed in front of the PRL, it did not push the myopic PRL backward to the crystalline lens.

4.9 COMPLICATIONS

4.9.1 Lens opacification (I, II, III, IV)

Anterior subcapsular opacification was observed in two myopic eyes. No PRL removal or cataract extraction has been performed due to lens opacities.

In the first case, the mean follow-up time after the onset of lens opacification was over 3 years. The eye had gained two lines of vision over the preoperative BCVA without loss thereafter and had stable opacification. The other eye had progressive opacification and lost one line from the preoperative value during 6 months of follow-up (Figure 23).

Both cases had central contact between the PRL and the crystalline lens. However, the higher age of these patients (48 and 49, respectively), extremely high myopia (SE -17.0 and -20.25 D, respectively), and the problematic PRL exchange in the case with stable opacification cannot be overlooked. The results

Figure 23. Anterior subcapsular opacification in a myopic eye of 49-year-old man 2 years after PRL implantation detected at the time of OCT scanning.
from ICL studies indicated that mechanical contact, presbyopic age, and intraoperative trauma are associated with an elevated incidence of crystalline lens opacification (Gonvers et al. 2003, Lackner et al. 2004, Sarikkola et al. 2005). High myopia itself increases the risk for earlier cataract formation compared with emmetropic, low myopic, and hyperopic eyes (Sarikkola et al. 2005).

A 34-year-old hyperopic patient developed anterior lens vacuoles initially after surgery. The lens was clear at the 3-month follow-up visit without further complications. The obvious reason for the transient vacuoles was intraoperative trauma to the crystalline lens. In hyperopic eyes with a shallow AC, the risk of accidental contact of the anterior capsule during surgery is increased and extra care should be taken during implantation to avoid contact with the lens capsule and corneal endothelium.

4.9.2 Pupillary block (I, II, IV)

The most frequent complication was early postoperative pupillary block in one myopic and seven hyperopic eyes despite two iridotomies performed 2 weeks preoperatively. Residual OVD in the posterior chamber or incomplete iridotomies were reported to be the most common reasons for increased IOP postoperatively (Jimenez-Alfaro et al. 2001, Hoyos et al. 2002, Sarikkola et al. 2005). Pupillary block itself was reported to be the most important complication in the earlier studies with the hyperopic ICL (Rosen and Gore 1998, Pesando et al. 1999). But in recently published ICL study, this was not a problem if double peripheral Nd:YAG laser iridotomies or a classic 12 o’clock iridectomy was performed (Pesando et al. 2007).

However, ICL implantation in 61 Asian eyes with myopia showed transient rise in IOP in 26% of eyes within the 2 months postoperatively (Chang and Meau 2007). Compared to myopic Caucasian eyes, the Asian eyes have smaller WTW diameter and shallower anterior chamber, which can cause problem with ICL sizing because the recommended protocol is based on Caucasian populations. The myopic Asian eyes can be compared with Caucasian hyperopic eyes, which also have narrow iridocorneal angles. The presence of an implant can have long-term effects on the redirection of the aqueous flow. In contrary to results of Chang and Meau, our findings suggest that the risk for angle-closure glaucoma seems to increase during the first 2 weeks after surgery. Identifying eyes with a narrow iridocorneal angle could determine those needing extreme care in the creation of sufficiently large laser iridotomies or surgical iridectomy.

The difference between the PRL and the ICL is in the dynamics of the implant. The PRL floats in the posterior chamber, whereas the ICL is fixated and supported in the sulcus angle. The floating design of the PRL makes rotating the implant possible. Even if the PRL is most often implanted in the horizontal meridian (at the 3 to 9 o’clock meridian), it can easily change the meridian after the implantation and thus occlude one of the iridotomies at the superior part of the iris or even both of them if they are too close together (Hoyos et al. 2002). Even though the rotation mechanism of the PRL is the same in myopic and hyperopic eyes, the risk of pupillary block in hyperopic eyes seems to be more prominent.

Our findings suggest that if there is any doubt of penetration through the all iris layers with the initial Nd:YAG-iridotomy treatment, the patient should return for complementary treatment so that absolutely reliable iridotomies are performed before PRL implantation, particularly in small
eyes and eyes with brown irides. The distance between the iridotomies should be over 6.0 mm, which is the width of the PRL. If the laser treatment fails, the Nd:YAG-iridotomies should be combined with an intraoperative surgical iridectomy.

4.9.3 Iris transillumination defect (I, II, IV)

No pigment dispersion was found in any case even though the posterior iris surface seems to touch the anterior PRL surface. However, horizontal iris transillumination defects (Figure 24) were observed in a hyperopic eye 1 year after PRL implantation combined with pupil ovalization at 2 years and no other complications. The same kind of iris atrophy has been reported in another PRL study (Hoyos et al. 2002) as well as in myopic eyes with ICLs (Brandt et al. 2001). UBM showed iris capture and the anterior convexity of the PRL, indicating poor fit of the PRL in the posterior chamber. The patient had no complaint of glare or halos. Since the hyperopic PRL is manufactured in only one size, exchanging it for a smaller model was impossible. The patient is followed on a regular basis.

Figure 24. Transillumination defects in the iris in a hyperopic eye. The PRL has signs for oversizing for the actual posterior chamber. The patient was satisfied with the visual outcome and did not require PRL explantation.

4.9.4 Overcorrection of hyperopia (I, II, IV)

Unexpected postoperative myopia with a mean postoperative SE of -1.35 D (range, -1.35 to -1.75 D) was found in four hyperopic eyes (studies I, II and IV) with a mean preoperative SE +5.53 D (range, +3.25 - +8.75). The PRL was exchanged in two cases and in one case a LASEK enhancement was performed. These procedures changed the mean SE to -0.08 D (range, ±0.0 to -0.25 D).

In the fourth case, the patient did not desire PRL exchange or LASEK enhancement but wanted PRL explantation, after which the patient returned to spectacle use without loss in BCVA.

The refraction of a hyperopic eye can be challenging. Young hyperopes can transiently accommodate without correction while reading an eye chart but cannot maintain accommodation without asthenopic symptoms. Accommodation affects the manifest refraction, which should be combined with cycloplegic refraction before surgery, because the theoretical approach to calculating the lens power is as important as the proper surgical technique. Additionally,
preoperative contact lens-corrected visual acuity and refraction may provide more accurate results for PRL power calculation in high myopia and hyperopia than the traditional spectacle-corrected visual acuity and refraction.

In hyperopic eyes, slight postoperative hyperopia seems to be more acceptable than myopia, which must be considered in the power calculation. Young patients are used to accommodate and prefer that after surgery rather than vice versa. In the hyperopic study population, the mean patient age was comparable with that in the studies of myopic eyes. However, hyperopia becomes increasingly problematic with advancing age and patients treated for hyperopia might on average be older than myopic patients. Therefore, hyperopes approaching presbyopia do not gain any benefits if the surgery leaves them hyperopic.

4.9.5 Halos and glare (I, II, IV)

Two hyperopic eyes had severe glare and halos in dim light and night. The PRL was removed 17 and 24 months postoperatively, which resulted in symptom relief in both cases. In the study of Hoyos and associates, night halos and glare were reported in 26% of eyes, although the PRLs were well centered (Hoyos et al. 2002). The study of Pallikaris and coworkers confirmed this result: 28.5% of high myopic eyes had minor glare and halos at night. In most cases the pupil diameter was greater than 7 mm. However, these symptoms decreased 6 months after implantation (Pallikaris et al. 2004). Because the optic size of the PRL is 4.5 to 5.0 mm, patients whose pupils dilate beyond that size in dim light may be subject to halos or night glare, phenomena that also would be problematic for a patient if the lens optics were centered.

4.10 ANALYSIS OF FOLLOW-UP METHODS (II, III)

In the assessment of any new instrument, an estimate of the reproducibility is essential before further data analysis can be performed. To evaluate the precision of the instruments used in the main trials, double-independent measurement studies were conducted. Evaluation of the precision of the laser flare meter showed a random error of 17%, which was higher compared with the 12% within-subject variability in aqueous flare in normal eyes (Shah et al. 1991). The endothelial cell count, however, showed a low random error (2.8%) as a reliable indicator for the evaluation of corneal endothelium. The result was confirmed in another study with the same system as ours (Vecchi et al. 1996). The random error using the Scheimpflug method (with the EAS-1000 system in the evaluation of the distance between the PRL and the anterior lens surface) was 10%. For Visante OCT, the same study design using double-independent measurements, repeated after 5 minutes, showed a random error of 5% in the measurements between the PRL and crystalline lens and 1.25% in the measurements between the PRL and the posterior corneal surface. This result indicated that Visante OCT is sufficiently accurate and reliable to allow an analysis of distances in the anterior segment and confirmed the results of a study with Visante OCT in measurements of the AC (Koch et al. 1998). Because the PRL does not change thickness during accommodation, the mean central thickness of the PRL in each group at baseline and during maximum accommodation served as an internal control. The results were comparable to the error analysis and confirmed the accuracy of the measurements. With its high-resolution capacity, AC OCT is more precise than Scheimpflug images.
5 CONCLUSIONS

Treating high myopia and hyperopia is a more challenging task than treating patients with low ametropia. The clinical outcomes of PRL implantation are better or comparable to existing refractive surgery alternatives. PRL implantation meets the high expectations of refractive surgery and provides excellent quality of vision and corrects myopia and hyperopia with good predictability and refractive stability. The lens has a biocompatible design and material that do not induce ongoing endothelial cell loss and only induce subtle iris or lens damage resulting in less cataractogenesis than that seen with other PC PIOL models. The lens is foldable and can be implanted through a small, self-sealing incision. It is adjustable and can be exchanged. In addition, the method is reversible in contrast to techniques that permanently alter corneal tissue.

However, the PRL does not have all the ideal qualities of a PIOL. The future implant could be improved with a 7-mm diameter functional optic, which might decrease the risk for edge effects, glare, and halos. Lens design should better guarantee the free flow of aqueous and minimize the risk of pupillary block. The lens should be easy to implant to facilitate the development of fewer intraoperative complications and decrease the psychologic stress for the surgeon, which results from reports of luxation of the PRL. The ideal PIOL should not be manufactured only in negative and positive powers but also have a spherocylindrical alternative for eyes with astigmatism. In the best of worlds, the PIOL would even correct presbyopia without reducing the quality of vision. This would provide an implant with a solution for virtually every refractive problem and would be tolerated by the patient for decades, perhaps for life. The method therefore has to be refined further and studied carefully.
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7 REFERENCES


