Visual quality improvement in refractive surgery
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GENERAL INTRODUCTION
1.1 WHY DO PATIENTS SEEK REFRACTIVE SURGERY?

Refractive surgery is the procedure by which a refractive error, such as myopia, hyperopia, or astigmatism is treated. The procedure utilizes a variety of technical possibilities to achieve the goal of emmetropia. Patients who seek a refractive procedure are motivated to undergo an elective procedure that will enhance their vision without the need for optical correction. The procedure should be as short, safe, and as accurate as possible. The side effects are well known; surfing the web a large number of sites will be found which contain information about the complications and potential dangers of refractive surgery. Still, in the majority of cases the outcomes are acceptable to excellent, and most patients gain the spectacle freedom they were seeking, with high satisfaction in terms of improved uncorrected vision, recreation, and comfort.

Does patient satisfaction correlate with visual quality? This depends on the definition used. Patient satisfaction with visual quality basically depends on patient expectations, and patient experience with vision. Patients may have such a gradual deterioration of visual acuity, that for example they may have a Snellen vision that is not sufficient to drive a car, but may not have yet noticed this. The other extreme are people with severe complaints despite the fact that there is no corroboration on objective testing such as recurrent testing of Snellen acuity, wavefront measurement, contrast sensitivity, and straylight. Subjective visual quality is determined by a plethora of physical phenomena as well as psychological phenomena.

1.2 INTRODUCTION TO REFRACTIVE SURGERY

1.2.1 History of refractive surgery

Refractive surgery has been around since Schiotz noted that one could change the form of the cornea with incisional surgery in 1885. Lans demonstrated that incisional or thermal surgery could reshape the cornea, and with it the refraction, but had poor long-term outcomes. Nowadays refractive surgery is a combination of different techniques that enable us to change refractive errors in the eye.

Techniques commonly utilized are corneal laser surgery, implant lenses, conductive keratoplasty techniques (in which the cornea is heated in a ‘controlled’ manner, which induces a surface change), or any combination of the current techniques.

1.2.2 Aims of refractive surgery

The aim is to achieve a certain refractive goal. This may be a refraction of plano (0 Diopters (D)) to have a good unaided distance vision. This may also be a refractive error that is on purpose left undercorrected between -1.5 D and -2.00 D to have a reading acuity in a presbyopic eye (age related farsightedness, in which accommodation is not sufficient for near vision any longer). The aim may also be certain multifocality, such as with multifocal implant lenses, but also other modalities that achieve monovision try to attain this, such as intra-corneal inlays, or intrastromal femtosecond treatments like
Intracor, in which the corneal shape is changed with different modalities in order to achieve multifocality of some sort.

1.2.3 Technologies in refractive surgery

The surgical modalities in use are the excimer laser, the femtosecond laser, conductive keratoplasty, scleral imbrication, various types of keratotomy procedures, be it T-cuts or radial cuts or opposing clear cornea incisions, placement of intra-ocular lenses in the anterior chamber, or in the posterior chamber, and refractive lens exchange. Slowly but surely cataract surgery is moving in the direction of refractive surgery, because of the possibility of achieving accurate refractive results and achieving a high rate of spectacle independence for the patients. The quality of cataract surgery is improved by implementing the successes of refractive surgery; this creates a win-win situation.

The techniques used in this thesis are: Laser assisted sub-epithelial keratomileusis (LASeK), Laser in-situ keratomileusis (LASIK), Photorefractive Keratectomy (PRK), cataract surgery, refractive lens exchange (RLE), and bioptics.

In corneal laser surgery laser energy is used to ablate corneal tissue to change the curvature of the cornea. In myopia we want to flatten the corneal curvature, by centrally ablating tissue. In hyperopia the cornea is steepened by peripheral removal of tissue with the laser ablation. The ablation pattern (diameter and depth) are determined by the laser nomogram used.

In LASIK and PRK the corneal epithelium is removed and the laser beam is applied to the Bowmans membrane, which is ablated, together with the stromal tissue underneath it. The ablated area is then rinsed with balanced salt solution. In PRK a bandage contact lens is applied directly over the ablated cornea. In LASEK the preserved and removed epithelium is repositioned over the ablated cornea, and then a bandage contact lens is applied.

In LASIK a hinged flap is cut into the cornea. The diameter and the depth of the flap are determined by the instruments used. Microkeratomes are mechanical devices that cut the flap and have set depths of cutting. Femtosecond lasers allow for tailor made forms of the flap. The flap is lifted away from the stroma, and the laser ablation is applied directly to the deeper stroma. After the ablation the corneal flap is replaced and properly appositioned. In this method the incisional surface is very small, and patient comfort is rapidly improved, vision is restored within a very short time period.

In cataract surgery and RLE the crystalline lens is removed and an intraocular lens (IOL) is implanted in its stead. These implants can be of different materials, and may have one or more foci. The dioptric strength of the implant is determined after biometry of the eye. In cataract surgery and RLE it is possible to achieve a plano refractive outcome, that is, reduce the patients’ dependence on visual aids.

Bioptics is the situation in which there is a residual refractive error, which is disturbing to the patient, and can be corrected with corneal laser surgery.

There are other techniques, like intracorneal stromal rings and phakic IOLs, that all address a refractive error. These techniques are beyond the scope of this thesis.
1.2.4 Reasons for having a refractive procedure

The top five reasons to have refractive surgery were described by Khan-Lim et al. The main reason for having refractive surgery was the freedom from glasses or contact lenses. Think of walking in the rain with your glasses, or changing your contact lenses in the windy desert. The subsequent reason was contact lens intolerance, often seen after years of intensive wear of soft contact lenses. Discomfort caused by glasses or contact lenses was another reason; this can be caused by the weight of the glasses on the nose and ears, or by the manipulation of the eyes in order to wear contact lenses. Cosmetic reasons are in the fourth place. Interestingly in my practice this is a rarely mentioned cause. The fifth reason is sporting activities, like in contact sports. This is also true for professional activities which might be better and more safely performed without optical correction, like in the commercial (naval) professions, military, fire brigade, or the police.

1.2.5 Tailor-made treatment

Different treatment modalities can treat different refractive errors. The treatment should be tailored to the wishes of the patient on the one hand, and the physical properties of the patient and the eye on the other hand. The expectations of the patient should match the technological possibilities. This needs to be determined pre-operatively. Each treatment has its own safety profile, and this needs to be discussed with the patient pre-operatively in order for the patient to give consent.

The following paragraphs will describe the technologies and science that are relevant to the studies. The common denominator is that, wavefront technology, visual acuity testing, contrast sensitivity, straylight, and patient satisfaction, together lead to the outcomes in refractive surgery.

Figure 1: Time line of development of corneal refractive surgery techniques.
Table 1: Treatment modalities in refractive surgery

<table>
<thead>
<tr>
<th>Treatment modality</th>
<th>Refractive error treated</th>
<th>Preferred age group</th>
<th>Technology</th>
</tr>
</thead>
<tbody>
<tr>
<td>LASIK</td>
<td>Myopia, hyperopia, astigmatism, some presbyopia</td>
<td>Accommodating patients, or monovision in the presbyopic patient</td>
<td>Excimer laser, Femtosecond laser</td>
</tr>
<tr>
<td>LASEK</td>
<td>Myopia, hyperopia, astigmatism, some presbyopia</td>
<td>Accommodating patients, or monovision in the presbyopic patient</td>
<td>Excimer laser</td>
</tr>
<tr>
<td>Keratotomy</td>
<td>Astigmatism on steep axis</td>
<td>Any age</td>
<td>Incisional</td>
</tr>
<tr>
<td>Conductive keratoplasty</td>
<td>Mild hyperopia and presbyopia</td>
<td>Presbyopes</td>
<td>Radiowaves</td>
</tr>
<tr>
<td>Intracor</td>
<td>Presbyopia</td>
<td>Presbyopes and hyperopes up to +1.25 D</td>
<td>Femtosecond intracorneal</td>
</tr>
<tr>
<td>Intracorneal inlays</td>
<td>Presbyopie</td>
<td>Presbyopes and hyperopes up to +1.25 D</td>
<td>Intracorneal incision and implant</td>
</tr>
<tr>
<td>Phakic IOL*, angle supported</td>
<td>Myopia</td>
<td>Accommodating myopes</td>
<td>Intraocular lens</td>
</tr>
<tr>
<td>Phakic IOL*, iris enclavated</td>
<td>Myopia, astigmatism, hyperopia</td>
<td>Accommodating patients</td>
<td>Intraocular lens</td>
</tr>
<tr>
<td>Phakic posterior chamber IOL*</td>
<td>Myopia, hyperopia, astigmatism</td>
<td>Accommodating patients</td>
<td>Intraocular lens (ICL type)</td>
</tr>
<tr>
<td>Cataract surgery</td>
<td>Any refraction</td>
<td>Patients with visual loss from cataract</td>
<td>Intraocular lenses</td>
</tr>
<tr>
<td>Refractive lens exchange (RLE)</td>
<td>Hyperopes, myopes with an axial length under 25 mm</td>
<td>Patients &gt; 40 years old, motivated by their wish of freedom from optical correction</td>
<td>Intraocular lenses (monofocal, multifocal, refractive, diffractive, toric, combined toric with refractive, bifocal)</td>
</tr>
<tr>
<td>Bioptics</td>
<td>Residual refractive error after lens implantation for cataract or RLE</td>
<td>Any age</td>
<td>Excimer laser, Femtosecond laser</td>
</tr>
</tbody>
</table>

*) IOL = intra-ocular lens

1.3 WAVEFRONT TECHNOLOGY, WAVEFRONT GUIDED TREATMENTS, AND HIGHER ORDER ABERRATIONS

1.3.1 Wavefront technology and higher order aberrations

Light can be described in several ways. In classical geometrical optics, light rays that come from infinity are considered to be linear bundles of light, and the refraction is measured in spheres and cylinders. In physical optics light is considered a wave, and lights spreads in a spherical way in all directions. A wavefront of light comes into the eye, and every plane the wave encounters can change the direction and speed
of the wave and thus the shape of the wavefront. As such, light that was in phase within the wavefront can become out of phase, or aberrated. This can be measured by aberrometers. (See figure 2)

Spectacles can correct up to the second order aberrations, that is spheres and cylinders, all the higher order aberrations represent irregular astigmatism. Historically, irregular astigmatism used to be a refractive error that could not really be measured,

Figure 2: A wavefront aberration is the deviation of the wavefront measured in an optical system when compared to the reference wavefront of an ideal optical system. In the Hartman Shack aberrometer a wave of light is projected with a laser and recorded through an array of lenslets, and the light returning from the optical system being measured is compared to the perfect optical system. The differences are measured and mapped out: the difference between the ‘perfect eye’ and the actual measurement are the higher order aberrations.
and was treated empirically with rigid gas permeable (RPG) contact lenses. We now know that irregular astigmatism is caused by higher order aberrations (HOA). Smirnov was the first to measure HOAs with a psychophysical method in 1961. In 1994 the first optical measurement of aberrations of the human eye were done using a Hartmann-Shack sensor. Using adaptive optics the correction of the HOA led to better optical quality in normal eyes. Mrochen et al were the first to publish the use of wavefront technology in refractive surgery. It was shown that even normal eyes with good uncorrected visual acuity had some form of irregular astigmatism, these are the HOA. These HOA depend on factors like blinking, tearfilm stability, ageing, and accommodative state.

Aberrometry today plays a role in refractive surgery, in getting ‘supervision’, but also diagnostic in forms of irregular astigmatism, and in the design of implant lenses and contact lenses. The HOA can be expressed as the total root mean square error (RMS), a set of coefficients from Zernike terms (Figure 3), Strehl ratio, point spread function, modulation transfer functions, and more coefficients. The HOA representation as RMS is numeric, and can be specific to a certain aberration, like coma or spherical aberration, or it can be in the form of a color map. The RMS gives the clinician an indication of the clinical effect the HOA have on the patients’ vision. In figure 5 we see a translation to the point spread function which may better illustrate the visual disturbance the patient may see at different pupil diameters. This enhances the clinicians capability of understanding the clinical implication of the HOA.

Each refractive component of the eye can contribute to the HOA: the tearfilm, the anterior cornea, the posterior cornea, the crystalline lens, and even vitreous turbidity, and retinal thickness.

1.3.2 Wavefront technology in refractive surgery

In standardized keratorefractive excimer laser procedures, the sphere and the cylinder are treated. The treatment of these refractive errors induces a change in the form of the cornea, and in some cases causes irregular astigmatism, HOA. The goal of wavefront based refractive surgery is to reduce existing aberrations, and possibly to reduce induction of aberrations. As a result we expect better unaided visual acuity,
contrast acuity and fewer side-effects in terms of night vision problems.\textsuperscript{13, 15-16} In wavefront treatments, we can treat the total of the HOA, but then again, new HOA are induced.\textsuperscript{15, 17} The treatment of HOA can result in overcorrections.\textsuperscript{15, 18} In state of the art laser treatments, wavefront-guided, or customized treatments are performed – these take into account the most important of the HOA and the effect that their treatment might have on the postoperative refraction and HOA. In this way visually disturbing HOA are removed, the effect of the treatment of HOA is predicted and corrected for in the ablation profile.\textsuperscript{10}

1.4 CONTRAST SENSITIVITY

1.4.1 Quality of vision, snellen visual acuity, contrast sensitivity, wavefront technology, and straylight
Quality of vision is difficult to define, and harder to measure in a repeatable and standardized manner. The Snellen acuity test tests spatial-resolving ability under high contrast circumstances. It is very sensitive to defocus, astigmatism, and HOA. Contrast sensitivity test is more dependent on the whole visual system depending on the precise version of the test, from the cornea, through the retina, and the visual pathways to the visual cortex, i.e. the whole physiological system.\textsuperscript{19} Aberrometry measures the optical quality in terms of spatial distortion of the wavefront. Straylight is another aspect of optical quality, measuring the optical quality of the eye due to light scattering dominating from 1 degree away from the center of the point spread function.
1.4.2 Background to contrast sensitivity testing

There are many factors in visual performance that relate to contrast sensitivity. If contrast sensitivity is lost, this may impair function like reading, finding objects, mobility, and driving. However, contrast sensitivity testing is always supplementary to visual acuity testing.

Visual acuity, as measured under high contrast condition is but one way to describe visual quality. This is actually a spatial resolving power of vision, in which the smallest target is seen at high contrast. Campbell and associates found in the 1960-ies that for sinusoidal gratings humans see medium resolution targets best as compared to low or high resolution targets. This is called the contrast sensitivity function. Figure 6 shows the kind of gratings used for contrast sensitivity testing. A lot of contrast sensitivity tests have been invented, and attempts have been made to chart the differences in contrast sensitivity in different disease states, however no specific defect for a specific disease has been found. There are conditions like ageing, cataract, and other pathologies, in which we know that contrast sensitivity is decreased, but the testing for contrast sensitivity has little diagnostic value. The use of contrast sensitivity has played a role in the screening for glaucoma, but the low sensitivity and specificity of these tests have impeded the implementation of contrast sensitivity tests in clinical practice.

The main problem with contrast sensitivity is that it is subjective and rather inaccurate. It complements other measurements of vision, like visual acuity and straylight, but has little added value. Relevant to refractive surgery we know that refractive multifocal IOL’s cause a decrease in contrast sensitivity, especially under...
twilight conditions. This reduced contrast is because of the fact that there are 2 foci, of which one is in focus, and the other acts like a disturbing light screen and reduces contrast.

Contrast refers to the amount of lightness or darkness an object has in its surroundings. There are a lot of tests that were developed that test contrast sensitivity, since interest in this began in the 1960s.

Contrast sensitivity is defined as the inverse of the contrast value at threshold. Contrast sensitivity is plotted on a chart in which the x axis is the spatial frequency, and the y axis is contrast sensitivity in log scale. Spatial frequency is specified in cycles per degree (cpd), which corresponds to the spatial frequency of the sine wave grating in terms of size, using cycles per degree of visual angle as the unit. Maximal contrast sensitivity function is at 3 to 6 cpd. The curve of contrast sensitivity is bell shaped. At the high frequency end, where contrast sensitivity is lowest, 100% contrast is needed, it corresponds to visual acuity. Figure 6 shows a typical contrast sensitivity curve.

The complexity of different targets in day to day situations, and facial recognition have been studied. Military situations have also been extensively studied. Road safety has been a major subject of testing contrast sensitivity function. One study showed that patients with visual acuity of 0.5 or worse due to cataracts, as a result of improved contrast sensitivity after cataract surgery, had half the rate of motor vehicle accidents, when compared to those who did not have surgery and still had their own crystalline lens. This was not corroborated by later studies.

The clinical use of contrast sensitivity can be in detection and monitoring of disease, and in gauging the effects of therapeutic intervention. The therapeutic intervention can be in the form of drugs, or new IOL technology, or even refractive surgery.

Several contrast sensitivity tests have been used: the Regan chart, and the Pelli-Robson chart, the Holladay Contrast Acuity Test, and grating charts propagated by different researchers.

Astigmatism, spherical blur, higher order aberrations, light scatter, and the retina-brain system may cause disturbance of contrast sensitivity. As a result contrast testing.

Figure 6: The contrast sensitivity curve (yellow line) is shown here superimposed upon a grating chart illustrating the gratings being used for contrast sensitivity testing. Contrast sensitivity = 1/threshold value for contrast visibility. To the left side contrast sensitivity is plotted on the vertical axis, on the right side the corresponding percentage contrast is plotted. The curve illustrated that Snellen acuity corresponds to the highest contrast (100%).
1.4.3 Contrast sensitivity testing in clinical practice
The clinical use of contrast sensitivity can be in detection and monitoring of disease, and in gauging the effects of therapeutic intervention. The therapeutic intervention can be in the form of drugs, or new IOL technology, or even refractive surgery.

Several contrast sensitivity tests have been used: the Regan chart, and the Pelli-Robson chart, the Holladay Contrast Acuity Test, and grating charts propagated by different researchers.

Astigmatism, spherical blur, higher order aberrations, light scatter, and the retina-brain system may cause disturbance of contrast sensitivity. As a result contrast testing, wavefront measurements, and straylight measurements complement each other, and enable the diagnosis of which element of the visual pathway causes a decrease in contrast. In the clinical situation the information obtained from contrast sensitivity testing is usually redundant, and not cost effective.

1.5 STRAYLIGHT IN REFRACTIVE SURGERY

1.5.1 History and development of the concept of straylight
By definition of the Commission Internationale d’Éclairage (CIE) straylight is disability glare. Disability glare occurs when visibility is reduced when there are glaring light sources in the field of view. Straylight predicts the loss of retinal image contrast as a result of intraocular scatter. The first measurements of straylight in humans were done in the 1920-ies and 30-ies by Luckiesh, Holladay, and Stiles. Later studies resulted in the introduction of a straylight parameter. For a long time there was a discussion whether disability glare is an optical or a neuronal phenomenon.

1.5.2 Clinical value of straylight
Clinically straylight may produce complaints of hazy vision, loss of contrast and color saturation, difficulties with recognizing objects against light, and halos around bright light sources. Straylight has a negative effect on contrast sensitivity. Straylight and glare are the result of forward scatter, while the slit-lamp image relies on backscatter. So, in the patient with good Snellen acuity, and a normal slit-lamp examination, forward scatter can still cause clinically significant glare complaints, which we cannot diagnose using the traditional modalities. Therefore it can be concluded that straylight measurements significantly complement the clinical tests.

The point spread function (PSF) (see figure 7) describes the response of an imaging system to a point object. The point spread function enables us to understand the quality of the retinal image. Small changes in the PSF may cause severe visual disturbances. The PSF has a spatial domain, which is the horizontal axis, which is the angle of the visual input. It has a very steep peak with a very wide spread. (See figure 7). The tip of this peak is the 1 min of arc in which we test visual acuity. Clinically this can be in Snellen acuity charts, or with wavefront aberrometry, measuring HOA. The peak is around 1 min of arc or 0.02 degree. The vertical axis is the intensity domain. It is...
logarithmic, and we see that the intensity is highest at the center at 0 degrees, and quickly decreases as it spreads out to 90 degrees. We measure visual acuity at the center core of the PSF. Contrast sensitivity is measured in a wider area of this core up to 0.3 degrees or 3 cpd, which is a little bit spread form the core. Straylight is measured more than 1 degree away from the central core of the PSF. Straylight does not contribute to VA or to HOA. The functional importance of straylight is in its relation to disability glare and visual complaints related.

The clinical importance in measuring straylight is that it correlates weakly to visual acuity, and can explain visual complaints that are not measured by spatial resolution such as Snellen visual acuity testing. The Snellen acuity, which tests high contrast small degree spatial resolution vision, can be very high, while the other aspects of the point spread function, that is straylight cause visual disability. This is explained by the fact that part of the light from the image of interest comes to a focused image, while part of the light is dispersed and forms a homogenously dispersed background. The severity of this loss of contrast depends on the illuminance ratio between the background and the image. For example when driving at night with oncoming traffic, this may cause blinding.

There are many different tests for glare. According to the CIE definition glare disability is straylight. Actual glare tests come however in many forms. The relationship with the CIE definition is often unclear. The simplest glare test is a pen light, this is a cheap test, in which Snellen acuity is measured, while the patient is blinded by the light source form the penlight, but inaccurate because of pupil miosis and lack of
Another glare test is with the brightness acuity tester. It is practical, but the validity of this test has been questioned. There are several other commercial devices which combine visual acuity testing with glare testing. From the available literature it is clear that most of these devices are not valid in testing for glare. Many glare tests show improving function under different conditions. The only device that excelled in evidence for validity and reliability in clinical tests, is the straylight meter. Clinical experience is still limited, but is rapidly expanding. The straylight meter has developed from the direct compensation method to the compensation comparison method. This change in methodology has enabled the development of a computerized test based on the psychophysical well-established forced choice principle. The patient looks in the device and is offered a flickering light ring. This light is scattered and perceived as a faint flicker in the center of the ring. A counterphase light is then presented, and this can silence the straylight flicker. The alternate forced choice help determine the amount of compensation light needed, and also the reliability of the test outcome. The test has an estimated standard deviation (ESD), which is an internal check for reliability of the measurement. A reliable test has to have ESD of less than 0.08 to 0.12 log units depending on the application.

Clinically straylight in early cataract is important: the patient may be visually impaired, but pass all the spatial visual acuity tests. In our day to day life, this means there are quite a lot of drivers who should not be driving, based on their straylight measurements. As in all clinical tests, there needs to be a clear cut off between normal and abnormal and a low risk for false positives, that is classifying people as having disability glare based on the test results, while they actually are not visually impaired by glare. In order to have a straylight meter that gives reliable and repeatable results, that could, for example serve in regulations of drivers licenses, it was concluded that a forced choice test would contribute to this.

For normal eyes, subtle anatomic factors that influence straylight measured, are the pupil size, the color of the iris, the translucency of the sclera and eye-walls, the vitreous cavity and its contents, and the retina. It has been suggested that eyes with a longer axis, that is myopic eyes, have more straylight. Age is really important factor that goes with increased straylight. This is strongly correlated with cataract formation. It has been shown that the reliability of straylight measurements is not influenced by the patients age, and that corneal light scatter is constant with age. In the normal young eye the cornea contributes about 1/3 of the total straylight, the lens contributes another 1/3. The iris, sclera, and retina contribute the remaining 1/3. Clinical situations in which disability glare is relevant are corneal opacities, be it by dystrophies, scars, contact lens wear or resulting from corneal refractive surgery. In cataracts, or in pseudophakia glare is a known symptom. Myopia in itself is a reason for increased straylight. Rozema et al ascribed this to the possibility that most myopes were contact lens wearers, and van der Meulen et al showed contact lens wear is related with an increase in straylight. Vitreous disturbances are potentially important (paper in preparation). In lamellar corneal transplantation procedures
pre-operative straylight level was predictive for surgical outcome. (IJE van der Meulen, submitted paper).

In cataracts disability glare is increased.\textsuperscript{39-40, 54} In pseudophakia with monofocal lenses straylight is often reduced to levels of younger people.\textsuperscript{39, 55} Straylight in pseudophakia is related to the size of the capsulorrhexis and amount of anterior capsular polishing.\textsuperscript{56} Pseudophakic patients seem to have higher straylight values under scotopic circumstances, mostly related to the size of the capsulorrhexis.\textsuperscript{56-57} Straylight is also increased in posterior capsular opacification (secondary cataract) that may occur post-operatively and is often alleviated by doing a YAG capsulotomy.\textsuperscript{55}

Nightvision problems and glare have been shown to cause a decrease in contrast sensitivity in the first generation multifocal diffractive intraocular lenses.\textsuperscript{28, 58-60} However, straylight correlated more with older age than with the monofoality or multifocality of the IOL.\textsuperscript{60} Aspheric and spheric IOLs also do not show a difference in straylight.\textsuperscript{61} This is not surprising, as we know that the higher order aberrations are on a different part of the point spread function than the straylight. These results were corroborated in studies with newer design multifocal lenses that are of refractive and diffractive design, and of different materials (silicone or acrylic materials).\textsuperscript{62-64} Subjective reporting of glare experienced under all light conditions and at night is no reliable predictor for disability glare (straylight) measured.\textsuperscript{63}

1.5.3 Straylight in refractive surgery

In refractive surgery forward and backward scatter have been studied. To organize these data, one must take into account the development and different techniques in refractive surgery. Current modes of corneal refractive surgery are mainly by ablating tissue, be it on the surface like in PRK and LASEK, or after a flap is cut, as in LASIK.

Radial keratotomy for myopia is a technique in which radial incisions are made into the peripheral and mid-peripheral cornea, at 85-90\% depth of the cornea. These incisions heal and fill with plugs of epithelial cells, which cause the incisions to gap and thus change the corneal curvature. Actually we purposefully induce scarring in the cornea. Some of these scars can be in the pupillary opening, in mydriasis, like in night-vision conditions and causing complaints of glare and glare disability. In the PERK study (Prospective Evaluation of Radial Keratotomy study) no significant increase of subjective glare complaints was found.\textsuperscript{65} Decreased contrast was found in cases the incisions where within the central clear zone.\textsuperscript{66} Veraart showed that with the direct compensation method straylight was increased after radial keratotomy.\textsuperscript{67} The increase in straylight was related to the pupil diameter and not to the number of incisions.\textsuperscript{67}

Also in excimer-laser assisted refractive surgery we may expect an increase in straylight. In surface ablations we expect tissue response with changes in cellular structure and organization.\textsuperscript{68-70} In LASIK the stroma of the cornea is cut, the corneal lamellar structure is disrupted, and after excimer tissue ablation the tissue surfaces are disrupted. So, also in LASIK we expect cellular and fibrillar changes.\textsuperscript{68-70}

In photorefractive keratectomy (PRK), one would expect an increase in straylight, as the healing process within the cornea may contribute to this increase. In PRK an increase
in straylight was found. This was time related, and decreased to pre-operative levels, except in eyes which developed severe haze. Harrison et al found that straylight did not increase at 1 month post PRK. The fact that there was no increase in straylight was attributed to a larger treatment zone of 6 mm, compared to a treatment zone of 5 mm in Veraarts’ study. Schallhorn showed straylight to be significantly increased at 1 month, and decrease to pre-operative levels at 3 and 12 months. He concluded that glare disability was transient. Only in an individual case was straylight increased in such a way, that the patient rejected treatment of the other eye. In other studies straylight was shown to initially increase and later decrease to pre-operative levels.

In LASIK an increase in post-operative straylight would be expected, based on the incisive effect of cutting the LASIK flap, and the misalignment of the corneal collagen lamellae. Beerthuizen et al reported the first study on straylight after LASIK. At 1 month he did not find increased straylight in eyes that had either LASIK or PRK. The study did show that under individual circumstances straylight was increased. This was mostly related to microstriae or debris in LASIK, and haze in PRK. Vignal et al. studied straylight in PRK and LASIK. They showed that straylight was overall within the normal range in 79% of treated eyes, compared to 86% of untreated controls. This is the first study in which increased straylight was correlated to patient subjective glare complaints. In our study on myopic subjects we demonstrated that straylight actually improved in both LASIK and LASEK. This is possibly related to a change in corneal thickness. Contact lens use can increase straylight, especially the use of hard contact lenses. It was suggested that contact lens use pre-operatively may account for some of the decrease, but by protocol patients do not wear their contact lenses pre-operatively, for 2 weeks in the case of soft contact lenses, and for 10-14 weeks in the case of hard contact lenses.

Another study has shown straylight to decrease after LASIK by 0.11 log units, at 2 weeks post-operatively, but the decrease at 6 months of 0.06 log units was no longer statistically significant. Another study was done comparing straylight in eyes treated contra-laterally with LASIK and PRK. Also here no increase was found in straylight in both groups, up to 12 months. Rozema related a post-operative decrease in straylight after LASEK for myopia to pre-operative increased straylight from contact lens wear. With proper adherence to removal of contact lenses before measuring eyes for excimer laser refractive surgery (prevention of treating warpage related changes) one does not expect a pre-operative increase in baseline straylight alone from the wear of contact lenses. Maybe the fact that all these patients are myopic plays a more significant role after all.

The discussion whether straylight decreases or increases after uneventful excimer laser corneal surgery is not over yet. It is my understanding, that up to now all data point to the effect that modern laser treatment does not increase straylight. Straylight is increased only if there is a specific cause for increasing glare in the eye, in the form of flap striae or debris under the flap in LASIK, or haze and scarring in LASEK and PRK, and causes that have yet to be elucidated. There is a good correlation between post-operative complaints of patients and increased straylight. The relation between...
backscatter slitlamp findings and straylight is problematic – we don’t always have clinical findings that correlate.

Statements that night vision is severely impaired after corneal laser surgery, and hence should not be done, are contrary to the findings, both clinically, and also contrary to satisfaction analysis of patients. This is reminiscent of the dilemmas on compromise. \(^{82}\) Maybe a compromise of having better uncorrected visual acuity, at the possible price of some side-effects in some of the people treated, some of the time, is acceptable. These side effects may be disturbing only under very specific condition may be a good trade–off for some people, and not for other. This is where free choice after good informed consent comes into play.

1.6 QUALITY OF VISION AND PATIENT SATISFACTION

1.6.1 Concepts of quality of vision and correlation to patient satisfaction

For most ophthalmologists the standard used for assessing visual acuity is some sort of a visual acuity card, be it the Snellen chart, the ETDRS chart, or any variant thereof. A visual acuity under high contrast conditions may not always predict the quality of vision in terms of straylight, contrast acuity and sensitivity. Quality of vision measured by questionnaires give an impression of quality of vision as subjectively experienced by the patient. This can be quantified in QALY “quality adjusted life years” which tries to give a numerical equivalent to perceived quality of life.

Patient satisfaction responds not only to the surgical and numerical outcomes, but also to quality of life, and function as seen by the patient after surgery. Measuring patient satisfaction is problematic, because perception of quality of vision by the patients is subjective and influenced by the personality of the patient, levels of expectations, and surrounding factors, like information on internet sites, the “grape-vine” and other lay-talk. It has even been shown that patients who are dissatisfied with vision after LASIK, still would recommend having LASIK, so reported satisfaction is not necessarily a sufficient measure of quality of vision. \(^{83}\)

One definition of patient satisfaction is the difference between the pre-operative expectation of the outcome and the actual post-operative outcome. This can be managed by communication: usually this is summarized as “under-promise and over-deliver”. Refractive surgeons manage their patients’ satisfaction actively. \(^{1}\) This process was learned through study of patient satisfaction. \(^{84}\) Refractive surgeons also learn to translate patient complaints into diagnostic and therapeutic solutions towards those complaints. \(^{85}\)

1.6.2 Patient satisfaction questionnaires and their validity

There are different questionnaires for quality of vision. Some of these questionnaires like the “Activities of Daily Vision” and the VF-14 are specific for cataract patients. \(^{86}\) These questionnaires do not answer the specific demands of refractive surgery
patients. Some questionnaires incorporate a global yes or no, and some questionnaires ask about aspects of the surgery – the procedure itself, the recovery, and the visual outcome and possible side effects. The NEI VFQ 25 questionnaire was developed to answer many questions about many ocular situations in a validated manner, but also in a manner that it is still applicable in the clinical setting. The assessment of the success of refractive surgery was basically only evaluated in terms of clinical criteria. In the mid-nineties the first articles that specifically mentioned patient satisfaction started to appear. Questionnaires were formulated by clinicians, and the process of validation of their content came later. All the questionnaires also have different levels of sensitivity and specificity to the problem being assessed. Questionnaires for cataract surgery and spectacle freedom are used in different settings, and then used, usually in a non-validated manner for assessment of visual function after implantation of multifocal IOLs. Another questionnaire developed was the Refractive Error Correction Quality of Life Questionnaire (RQL). This was developed after the NEI VFQ 25 was found to be insufficient in answering quality of vision issues in refractive surgery. Recently, the validity of this questionnaire was tested. Ongoing insight into patient satisfaction measuring methods has shown that the modality tested, should be uni-dimensional. That is, one cannot derive one score, from more than one modality. In the case of the NEI VFQ 25 the modalities tested are visual function and quality of life, and these cannot be reported in a single score.

The newest validated quality of vision questionnaire is a questionnaire that was validated for different types of surgery (from refractive surgery to cataract) and includes scales for frequency, severity, and how bothersome a symptom is. Some factors could be specifically linked to lower satisfaction after LASIK: increasing age of the patient, or flatter pre-operative curvatures, the need for enhancement procedures, and night vision problems. These night vision problems can affect night-driving. Some of the night vision complaints are caused by higher order aberrations, which may influence quality of vision. Newer diagnostic and interventional technology appears to improve these outcomes. For example: the larger optical zones used to prevent halos. As such, patient satisfaction and complaints can be analyzed and translated into technical and clinical improvements.

The most important factor that came out of these questionnaires is that the magnitude in terms of visual acuity and contrast sensitivity of the improvement after surgery is not a measure of its success. The functional improvement, as perceived by the patient, can be a measure of success of surgery.

Outcomes of satisfaction questionnaires are even influenced by where the questionnaire is filled out, at the clinic or at home, or by the non-responders. So, the major obstacle remains, that satisfaction is a psychological phenomenon that is hard to gauge, and it has proven difficult, to say at least, to capture all modalities of quality of vision and refractive surgery in one single questionnaire. In my opinion, the use of objectively measurable parameters such as visual acuity, refractive error, and straylight allow for objectivation of the deviation are preferable to patient satisfaction questionnaires with their myriad confounding factors.
1.7 OUTCOMES IN CORNEAL LASER SURGERY

1.7.1 Outcomes of standard laser treatment with first generation lasers

Conventional or standard laser treatment refers to the ablation of the sphero-cylindrical correction with the laser according to Munnerlyn’s formula. Conventional laser treatment of myopia induces positive spherical aberration proportional to the amount of myopia treated. Outcomes of standard treatment for low to high myopia from early studies are summarized in table 2 and 3. Standard (or conventional) treatments have been reported to reduce contrast sensitivity.

1.7.2 Results with wavefront guided lasers and their relation to improved technologies

With the advent of wavefront-guided laser treatment we see an overall improvement in percentages gaining uncorrected distance acuity of 0.5, 1.0 or better, improved contrast sensitivity.

Table 2: Outcomes of uncorrected visual acuity early studies on corneal laser surgery.

<table>
<thead>
<tr>
<th>Authors - year</th>
<th>myopia</th>
<th>% 1.0 or better</th>
<th>% 0.5 or better</th>
<th>Refraction within 1.0D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seiler112, 1991</td>
<td>-4.50 ± 1.00 D</td>
<td>48</td>
<td>96</td>
<td>92</td>
</tr>
<tr>
<td>MacDonald113, 1989</td>
<td>-2.3 to -5.0 D</td>
<td>28</td>
<td>86</td>
<td>57</td>
</tr>
<tr>
<td>Salz114, 1992</td>
<td>-1.75 to -5.00</td>
<td>42</td>
<td>92</td>
<td>92</td>
</tr>
<tr>
<td>Sher115, 1991</td>
<td>-4.00 to -12.00</td>
<td>19.3</td>
<td>45</td>
<td>55</td>
</tr>
<tr>
<td>Gimbel115, 1993 (first eyes)</td>
<td>-5.62 ± 1.63</td>
<td>67.2</td>
<td>96.2</td>
<td>43</td>
</tr>
<tr>
<td>Gimbel115, 1993 (2nd eyes after nomogram adjustment)</td>
<td>-4.96 ± 1.48</td>
<td>73.1</td>
<td>92.3</td>
<td>45.2</td>
</tr>
</tbody>
</table>

Table 3: Outcomes of standard ablations for myopia with LASIK and PRK.

<table>
<thead>
<tr>
<th>Authors/Year</th>
<th>myopia</th>
<th>% 1.0 or better*</th>
<th>% 0.5 or better*</th>
<th>Refraction within 1.0D</th>
<th>% of eyes with 2 lines lost**</th>
</tr>
</thead>
<tbody>
<tr>
<td>El Danasoury, Fernandez, 2000, Tole118, 2001</td>
<td>-2 to -6</td>
<td>67-86%</td>
<td>93-100%</td>
<td>94-100%</td>
<td>2.1%</td>
</tr>
<tr>
<td>Hersh119, 1998, Kawesh120, 2000, Pallikaris121, 1994</td>
<td>-6 to -12</td>
<td>26-71%</td>
<td>55-100%</td>
<td>41-96%</td>
<td>0-4.5%</td>
</tr>
<tr>
<td>Hersh119, 1998, Kawesh120, 2000, Pallikaris121, 1994</td>
<td>-12</td>
<td>26-65%</td>
<td>32-65%</td>
<td>Up to 27%</td>
<td></td>
</tr>
</tbody>
</table>

* uncorrected distance visual acuity, ** best corrected distance visual acuity
Table 4: Outcomes of wavefront excimer laser treatments.

<table>
<thead>
<tr>
<th>Authors/Year</th>
<th>Mean myopia ± SD</th>
<th>% 1.0 or better*</th>
<th>% 0.5 or better*</th>
<th>Refraction within 0.5D</th>
<th>% of eyes with 2 lines lost**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Awwad et al126, 2004</td>
<td>-3.59 ± 1.54 (LADARvision 4000) -3.62 ± 1.46 (VISX S4)</td>
<td>NR</td>
<td>98</td>
<td>98</td>
<td>0</td>
</tr>
<tr>
<td>Durrie and Stahl127, 2004</td>
<td>-4.66 ± 1.73 (LADARvision 4000) -4.382 ± 1.71 (VISX S4)</td>
<td>93</td>
<td>100</td>
<td>83</td>
<td>0</td>
</tr>
<tr>
<td>Pop and Payette134, 2004</td>
<td>-4.0 (Nidek 5000-CATz)</td>
<td>92</td>
<td>100</td>
<td>85</td>
<td>0</td>
</tr>
<tr>
<td>Aizawa et al125, 2003</td>
<td>-7.30 ± 2.72</td>
<td>77.9</td>
<td>96.5</td>
<td>77.3</td>
<td>4.5</td>
</tr>
<tr>
<td>Venter129, 2005</td>
<td>-3.72 ± 1.96</td>
<td>100</td>
<td>88</td>
<td>92</td>
<td>4</td>
</tr>
</tbody>
</table>

* uncorrected distance visual acuity, ** best corrected distance visual acuity.

rates of reaching target refraction, and also decreased rates of loss of lines of CDVA (Table 4).122 For the first time there is a report that post-operative UDVA is better than pre-operative CDVA.123

Have treatments improved? The above tables show that from the very first publications of excimer laser treatments, predictability and visual acuity outcomes greatly improved.84, 95, 113-114, 124 13-15, 18, 85, 116-121, 125-132 How have lasers improved over the years? The very first lasers were mostly broad-beam lasers, in which the cornea was ablated in a single pass. Problems then were caused by the ablated tissue which interfered with the rest of the laser beam application causing central islands. Cyclotorsion in supine position interfered with the effectiveness of astigmatic corrections.133-134 Centration of the treatment on the papillary axis or the center of the pupil have long been topics of discussions. Centration, especially with the newer ablation profiles that are wavefront-guided or optimized are very sensitive to centration on the visual axis.135 Newer laser systems, especially those with custom-capability have sophisticated eye-track systems. The tracking systems are usually a combination of passive trackers, that stop the laser ablation beam if the eye deviated from the operative field, and active eye-tracker systems, with infra-red cameras, which adjust the movement of the laser beam with the eye-movement of the patient.137 Parallax, that is the curvature with which the laser beam arrives at the ocular surface, is not corrected for, and this may change the effectiveness of the laser pulse, hence good fixation and centration remain the mainstay of a well applied laser treatment.138 Newer lasers using flying spots and smoother ablation profiles cause less haze and also less regression.139-140 Wavefront guided or wavefront optimized nomograms are based on wavefront measurements of the patients’ eyes. Wavefront ablation nomograms can also help save tissue, because less tissue is needed per diopter of defocus.130 This effect may be related to the specific laser used.
Wavefront-guided treatments had comparable predictability and safety to standard laser treatments, but patient satisfaction, specifically with night vision and night vision with glare was improved. Higher order aberrations are still being induced, but in much less amounts than with conventional laser nomograms. This effect is more pronounced if the pre-operative HOA are higher. Most adverse events remained the same as they were mostly related to microkeratome and flap events, and not inherent to problems with the laser ablation profile. Data on accuracy of the treatment can be inferred from the retreatment rates, but these are not complete in most studies on standard treatments and on wavefront guided treatments. Contrast sensitivity was unchanged or slightly improved in all these studies, which is not surprising as we know that low contrast visual acuity is significantly correlated with HOA.

1.7.3 Improving outcomes by reducing side effects of wavefront based ablations

Recently more studies have shown that outcomes with the newer lasers are more accurate and reproducible (Table 5). Supervision defined as 2.0 Snellen acuity (or 20/10) is not reported often. Wavefront optimized ablations are wavefront guided ablations, in which an attempt is made to preserve the cornea asphericity. It was found that for eyes with HOA of over 0.35 microm the wavefront guided ablation had a better result, than the wavefront optimized. The average cornea is prolate (spheroid in which the polar axis is greater than the equatorial radius), but the normal range is between mild oblate (spheroid in which the polar axis is shorter than the radius of the equatorial circle) to moderately prolate. Even when trying to preserve the prolate shape of the cornea by using optimized ablation profiles, all treated eyes have a tendency toward an oblate shift. In a retrospective study of 160 eyes treated with an optimized ablation, post-operatively all eyes were between prolate and mildly oblate. However, there was no significant correlation between contrast sensitivity function and visual acuity and the corneal shape. They showed, that spherical aberration was the greatest predictor for contrast and glare abnormalities. Other studies comparing wavefront guided versus optimized treatments, have come to the conclusion that wavefront guided treatments decrease HOA and are associated with better contrast sensitivity.

Millions of patients have been treated, mostly satisfactory with cornea laser surgery. The discussion about which ablation profile is best is not completely clear. Most improvements in technology arrived more or less simultaneously: iris registration technology, eye-tracker technology, ablation profile technology, it is very hard to discern, but there seems to be limited evidence that wavefront ablations achieve better outcomes.
Table 5: Results of wavefront guided treatments.

<table>
<thead>
<tr>
<th>Author / year</th>
<th>LASER</th>
<th>FU in mths</th>
<th>N= Eyes</th>
<th>Pre-op SE</th>
<th>Post-op SE</th>
<th>±0.5D UCDA &gt; 1.0</th>
<th>UCDA &gt; 1.0 Gain of UCVA Lines (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee¹⁴⁹ 2006</td>
<td>VISX S4 CustomVue</td>
<td>6</td>
<td>104</td>
<td>-4.08±0.31</td>
<td>-0.44±0.31</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>Awwad¹²⁶ 2004</td>
<td>VISX S4 CustomVue</td>
<td>3</td>
<td>50</td>
<td>-3.59±1.55</td>
<td>-0.14±0.29</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LADAR 4000 Custom Cornea</td>
<td>50</td>
<td>50</td>
<td>-3.16±1.63</td>
<td>-0.04±0.24</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>Nuijts¹³⁰ 2002</td>
<td>Technolas 217z</td>
<td>6</td>
<td>6</td>
<td>-3.88±1.92</td>
<td>-0.06±0.41</td>
<td>92</td>
<td>67</td>
</tr>
<tr>
<td>Kim¹⁵ 2004</td>
<td>Technolas 217z</td>
<td>3</td>
<td>24</td>
<td>-3.27</td>
<td></td>
<td>93</td>
<td>67</td>
</tr>
<tr>
<td>Brint¹³² 2005</td>
<td>LADAR 4000 Allegretto Wave</td>
<td>30</td>
<td>30</td>
<td>-3.67</td>
<td></td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>Slade¹⁴ 2004</td>
<td>Alcon Custom cornea</td>
<td>1</td>
<td>25</td>
<td>-3.41</td>
<td>-0.12±0.31</td>
<td>92</td>
<td>76</td>
</tr>
<tr>
<td></td>
<td>VIXS CustomVue</td>
<td>25</td>
<td>25</td>
<td>-3.34</td>
<td>-0.40±0.40</td>
<td>72</td>
<td>56</td>
</tr>
<tr>
<td>Kohnen¹²⁸ 2004</td>
<td>Technolas 217z Zyoptix 3.17</td>
<td>12</td>
<td>97</td>
<td>-5.22±2.07</td>
<td>-0.25±0.43</td>
<td>77</td>
<td>83</td>
</tr>
<tr>
<td>Subbaram¹³¹ 2007</td>
<td>Technolas 217z APT</td>
<td>1</td>
<td>175</td>
<td>-4.89±2.06</td>
<td>-0.11±0.34</td>
<td>92</td>
<td>93</td>
</tr>
<tr>
<td>Mrochen¹³ 2000</td>
<td>Wavelight Allegretto</td>
<td>1</td>
<td>3</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Lapid-Gortzak¹⁸ 2008</td>
<td>Technolas 217z APT</td>
<td>3</td>
<td>64</td>
<td>-3.77±1.57</td>
<td>0.03±0.16</td>
<td>95</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td>LASEK 36 lasik</td>
<td>36</td>
<td></td>
<td>-3.03±1.47</td>
<td>0.04±0.36</td>
<td>93</td>
<td>21</td>
</tr>
</tbody>
</table>

1.8 Cataract Surgery and Refractive Lens Exchange

1.8.1 Refractive lens exchange

Refractive lens exchange is the technique in which the lens preferably in presbyopic patients is removed and replaced by an intra-ocular lens. Since the advent of multifocal IOLs this can be offered as an elective refractive procedure.¹⁵⁰ Patients opt for a form of freedom from spectacles for far and near vision. The outcomes in terms of unaided distance acuity need to be optimal. Residual refractive error need to be treated using methods available for refractive correction.¹⁵¹

In hyperopic patients this technique is least controversial as these patients have a relative lower risk of retinal complications than myopes. Corneal surgery and phakic...
implantation surgery are less effective in treating hyperopic errors, because of the anatomic restrictions. Refractive lens exchange may solve the refractive error in a safe and predictable manner. 152

1.8.2 Effect of refractive lens procedures on conventional cataract surgery
On the one hand, one could state that the advent of refractive lens procedures has increased the demand for optimal refractive outcomes. On the other hand, the fact that the outcomes in refractive lens procedures are constantly being improved has also caused the demand for better outcomes in cataract surgery to increase. Basically, cataract surgery can no longer be seen as the removal of the cataractous lens and replacement with an artificial clear lens, but also as a refractive procedure, in which one strives for the optimal refractive outcome.

Were, until recently, decreased visual acuity coupled to patient complaints was the indication to perform a lens procedure, we now know, that visual quality also depends on objective visual quality parameters such as straylight, which when increased, can be a viable clinical indication to perform cataract surgery even when Snellen acuity is 1.0 or better. Amesbury et al showed in their study that patients who were operated for cataract with a 20/20 (1.0) visual acuity based on subjective complaints of glare and questionnaire results, had improved post-operative results based on subjective criteria, even though their pre-operative visual acuity of 20/20 is generally considered good vision. 153 We clearly see that the attention to indications for cataract surgery is shifting: a decreased visual acuity is an arbitrary and insufficient descriptor of visual disability. Straylight is a complementary descriptor of visual quality. With increased straylight, even in the absence of decreased visual acuity, there is an indication for performing a lens procedure; with the new development of straylight measurement this aspect of visual function should be added as an objective criterion in the clinical setting in cases were patient complaints do not correspond to visual acuity.

1.8.3 Multifocal intraocular lenses
Until recently, implant lenses were monofocal lenses. In these lenses there is one focus, set at the focal plane of the IOL used. Most patients need additional correction in glasses or contact lenses to be able to read or see at intermediate or far distances, because mainstream cataract surgery has the alleviation of the lens opacity as its goal, and the refractive outcome is secondary. Multifocal lenses have more than one focus, and thus enable both far and near vision without the need for additional optical correction. There are different designs of multifocal lenses. Those can be made of different materials including silicone, acrylic hydrophobic materials, to acrylic hydrophilic lenses, and combinations of material in between. The most commonly used are of the type in which refractive or diffractive rings within the optic divide the light for vision to a distance vision focus and a near vision focus. The distance between the different rings and the form of the rings on the optic can be different. IOL’s with rings, which alternate distance and near vision in their correction, are called
refractive multifocal lenses. When the difference in the near and far foci is achieved by using diffraction, the lens becomes a diffractive IOL. When the rings have decreasing effect from the center to the periphery of the lens these lenses are called apodized lenses. This principle allows for better differentiation of the near and far foci, and as a result less light is lost to the near focus in case of low light conditions. They are not effectively multifocal lenses, but they do have 2 main foci, which makes them actually bifocal with little depth of field. Theoretically and clinically diffractive IOLs perform better for near than refractive IOL, while the distance vision is comparable.

These lenses give side effects as a result of the existence of a secondary focus in the optic. The secondary focus causes a ‘blur circle’ on the retina. This may cause complaints of a shade or a blur and may cause complaints of seeing ‘halos’ and other dysphotopsias. The success of these lenses lies in the motivation of the patient to be spectacle independent, and the ability to resist the side effects of these lenses.

Other types of lenses are those that mechanically change as a result of an accommodative effort. For example double hinged lenses, in which the optic is monofocal but is supposed to move with the capsular bag during an accommodative effort after the crystalline was removed. Other lenses are designed with two optics in which the compression at the equator of the lens capsule moves the 2 optics apart during accommodation and thus the focal length is changed, and between 4 and 7 D of accommodation can theoretically be achieved. The clinical outcomes of single and dual optic pseudo-accommodative IOL’s is controversial. In the FDA studies lenses like the Crystalens (Bausch and Lomb) model AT-45 IOL showed some improvement of near visual acuity. Patel et al showed that there was almost no effect on near visual acuity with this lens. Most studies show that the accommodation span of these lenses is clinically not sufficient. However Leydolt has shown that motivation for intermediate visual acuity can give a pseudoeffect in achieving that visual acuity, even when the patient has a monofocal IOL.

1.8.4 Results with multifocal IOLs
The most studied and up to now clinically effective lenses are of the refractive and diffractive type. Their use has been proven to be effective and safe.

However, patient satisfaction clearly depends on outstanding refractive results post-operatively. Patient selection, astigmatism control, careful biometry, and precise IOL calculation are factors that enhance patient outcomes. Steinert has shown that bilateral implantation with the Array multifocal implant as opposed to unilateral implantation of a multifocal IOL, increases the percentage of reading without glasses from 53-58% to 81%.

Primary outcomes after multifocal lens implantation are the distance uncorrected and corrected visual acuity, the near visual acuity, and spectacle independence. Secondary outcome measures are the depth of field, contrast sensitivity, glare, subjective assessment of quality of life or visual function, and surgical complications.

In the 1990-ies the first generation of multifocal diffractive IOL’s caused side effects in significant numbers. Second generation multifocal diffractive IOL’s
have better results, and may sometimes outperform refractive IOL's for near visual
tasks. Still, success of multifocal implants is probably mostly related to motivation
of the patient. Newer lenses have modifications in their form, such as aspheric
prolate anterior surface, lens edge changes, and placement of the diffractive rings on
the posterior surface, which may reduce spherical aberrations, and improve mesopic
contrast sensitivity. Multiple studies have shown that multifocal IOL's produce a
higher quality of life, spectacle independency in a high percentage of patients, with
acceptable unwanted photic phenomena, and also lower contrast sensitivity.

1.8.5 The future of multifocal IOLs and cataract surgery
The demand for refractive lens surgery will, in my opinion, increase because of
increasing demands for spectacle freedom, and with increasing public knowledge of
what can be achieved with cataract and refractive surgery. Refractive surgery will cause
technical improvements to be implemented in cataract surgery. Again, the benchmark
will, in my opinion, move away from posterior capsular break, and gross complications,
to outcomes in terms of refractive outcomes and patient satisfaction.

In medical indication in cataract surgery until now, patient complaints of decreased
vision, coupled to decreased visual acuity is the most widely accepted indication to
perform cataract surgery. Advances in understanding, that increased straylight with age
is mostly related to the development of cataract, and that this can occur with a visual
acuity of 1.0, will most probably also lead to a change in indication to perform cataract
surgery, based on the addition of this new objective parameter for visual quality.

1.9 OUTCOMES IN BIOPTICS

1.9.1 Definition and practice of bioptics
The term bioptics is used for different types of refractive combined procedures. The
term most probably stems from doing two refractive (optical) procedures consecutively
in a single eye. In 1995 Maloney published the results of PRK in a few eyes that
had residual myopia after cataract surgery, within a larger study of the results of
PRK in myopia. The term was coined in 1999 by Zaldivar to describe the use of an
additional refractive procedure on the cornea after target refraction was not achieved
with a phakic lens implantation. Some define bioptics when the LASIK flap is cut
before the lens procedure and lifted when the enhancement is needed. Since, it
has been expanded to the definition in which we now use it, which more broadly
encompasses any refractive surgery procedure in which more than one type of surgical
technique is used. Bioptics is also a solution in those cases in which the magnitude
of the refractive error exceeds the corrective range of any of the existent refractive
procedures. The second procedure extends the corrective measure to the one that
is necessary to achieve target refraction. The combined procedure can include a
phakic lens implantation which includes an expected or unexpected residual error
which can then be corrected in the corneal plane with any of the above mentioned
technologies. The procedure can include LASIK with incisional corneal astigmatic corrections, or a combination with phakic IOL implantation with LASIK and PRK. The combination of refractive lens exchange, also known as clear lens exchange with ensuing LASIK or LASEK correction for either hyperopia or myopia. Cataract surgery with residual refractive errors and subsequent LASIK and LASEK procedures have been published. Leccisotti used bioptics to achieve 3 goals: a. treating large refractive errors by a sequential method, usually a lens related procedure followed by a corneal procedure, b. improving stability and predictability of the refractive outcomes, c. maintain a state of minimal induction of higher order aberrations, i.e. ensure that HOA stay as low as possible.

Correction of the untreated corneal astigmatism or residual refractive error enables adjustment and correction of the final outcome of these pseudophakic multifocal patients. These refractive surgery procedures give safe and predictable results. Table 6 summarizes the published results of bioptics.

1.9.2 Safety and predictability of bioptics
A major concern is that these patients tend to be older, and as such may be more prone to complications. Corneal refractive surgery, according to the literature should be performed 6-12 weeks after the lens procedure, to allow for wound and IOL stabilization, and allow subclinical corneal edema to dissipate. More epithelial defects, and more epithelial ingrowth have been observed, as has the incidence of Diffuse Lamellar Keratitis of up to 15%. Other authors reported extremely low complication rates. In our series the main adverse event has been residual refractive error or not effective enough laser treatment in about 7 %. LASIK was as safe as LASEK in our hands in the groups that we treated. Haze, which has been reported by Maloney to have been around 8% is most probably less frequent because of better ablation profiles with newer lasers.

<table>
<thead>
<tr>
<th>Author / year</th>
<th>N= (eyes)</th>
<th>Surgery</th>
<th>SE Pre-op</th>
<th>SE Post-op</th>
<th>FU</th>
<th>Within 1 D</th>
<th>Within 0.5 D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zaldivar181 1999</td>
<td>55</td>
<td>LASIK</td>
<td>-2.61</td>
<td>+0.09</td>
<td>1m-4y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kim191 2005</td>
<td>19</td>
<td>LASIK</td>
<td></td>
<td></td>
<td>100</td>
<td>83.3 myopes 90.9 hyperopes</td>
<td></td>
</tr>
<tr>
<td>Ayala190 2001</td>
<td>22</td>
<td>LASIK</td>
<td>-2.90 ± 1.80</td>
<td>0.4 ± 0.6</td>
<td>12m</td>
<td>81.8</td>
<td></td>
</tr>
<tr>
<td>Norouzi197 2003</td>
<td>20</td>
<td>LASIK</td>
<td>2.19 ± 0.88</td>
<td>-0.32 ± 0.34</td>
<td>6m</td>
<td>100</td>
<td>85</td>
</tr>
<tr>
<td>Artola195 1999</td>
<td>30</td>
<td>PRK</td>
<td>-5.00 ± 2.5</td>
<td>-0.25 ± 0.5</td>
<td>12m</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>Pop189 2001</td>
<td>31</td>
<td>PRK</td>
<td>-3.78 ± 2.11</td>
<td>-2.25 ± 1.37</td>
<td>75</td>
<td>41.7</td>
<td></td>
</tr>
<tr>
<td>34</td>
<td>LASIK</td>
<td></td>
<td></td>
<td></td>
<td>83.3</td>
<td>83.3</td>
<td></td>
</tr>
<tr>
<td>Kuo192 2005</td>
<td>11</td>
<td>LASIK</td>
<td>-3.76 ± 2.50</td>
<td>-0.88 ± 1.43</td>
<td>12.2m</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
1.9.3 Outcomes of bioptics in patients with presbyopia correcting lenses

Residual refractive errors after multifocal lens implantation are the main reason for patient dissatisfaction post-operatively. There are not many studies showing data of excimer laser procedures following multifocal lens implants. In most studies the use of the ablation nomogram is not specified, and standard treatments (that is spherocylindrical treatments) as well as wavefront based treatments are used and analyzed together. Jendritza et al describes the use of wavefront treatments and concludes that it is a safe treatment for the refractive error, but that higher order aberrations do not improve. They found that wavefront could not reliably be measured. Wavefront treatment does have the advantage of iris registration and the possibility of correcting for possible IOL decentration and secondary refractive error, but the HOA mostly increased post-operatively. Table 7 summarizes the results of bioptics in multifocal IOLs.

1.9.4 Bioptics and wavefront technology

Most IOL’s change the HOA. Some HOA, like negative spherical aberration enhance depth of focus, at the cost of other aspects of quality of vision. Some IOL’s correct for spherical aberrations. Another aspect is that a wavefront guided treatment may remove HOA that actually enhance quality of vision. This is an unwanted side-effect. Another issue with wavefront measurements, is the fact that the IOL optic is 5-6 mm in diameter, depending on what kind of multifocal IOL is used. If the lens is decentered, or the pupil is wider than the optic when the measurement take place, aberrations

<table>
<thead>
<tr>
<th>Author year</th>
<th>N= (eyes)</th>
<th>Surgery</th>
<th>SE Pre-op</th>
<th>SE Post-op</th>
<th>FU Within 1 D</th>
<th>Within 0.5 D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leccisotti196 2004</td>
<td>18 Array PRK Standard</td>
<td>1.28 ±0.74</td>
<td>0.33 ±0.27</td>
<td>100</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td>Moftuoglu201 2009</td>
<td>85 ReSTOR Femto LASIK standard Wavefront</td>
<td>-0.34 ±0.9</td>
<td>-0.07 ±0.29</td>
<td>6m</td>
<td>99% 96%</td>
<td></td>
</tr>
<tr>
<td>Jendritza203 2008</td>
<td>20 Tecnis LASIK Wavefront</td>
<td>1.06 ±0.77</td>
<td>-0.03 ±0.28</td>
<td>3m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jendritza203 2008</td>
<td>4 ReSTOR LASIK Wavefront</td>
<td>0.75 ±0.56</td>
<td>0.13 ±0.22</td>
<td>3m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jendritza203 2008</td>
<td>3 ReZoom LASIK Wavefront</td>
<td>0.08 ±1.2</td>
<td>0 ± 0</td>
<td>3m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alfonso204 2008</td>
<td>53 Femto LASIK Standard</td>
<td>0.2 ±0.49</td>
<td>0.014 ±0.0170</td>
<td>6</td>
<td>100% 96.2%</td>
<td></td>
</tr>
<tr>
<td>Lapid-Gortzak199 2010</td>
<td>18 ReSTOR LASIK Standard</td>
<td>0.50 ±0.72</td>
<td>0.29 ±0.34</td>
<td>3 m</td>
<td>100% 88%</td>
<td></td>
</tr>
<tr>
<td>Lapid-Gortzak199 2010</td>
<td>27 ReSTOR LASEK Standard</td>
<td>0.34 ±0.73</td>
<td>0.21 ±0.13</td>
<td>3 m</td>
<td>100% 78%</td>
<td></td>
</tr>
</tbody>
</table>
coming from the optic edge and beyond, are translated in the treatment as HOA that are treated centrally on the cornea. We have performed wavefront guided LASIK in multifocal and monofocal IOL’s with unsatisfying results in terms of uncorrected visual acuity (UCVA) and residual refractive error, and as a result have abandoned this practice (Lapid-Gortzak, unpublished data.).

Lessicotti showed the results of PRK for residual ametropia after refractive lens exchange with the Array multifocal IOL. He showed that this was effective in treating the refractive error, but that this had no effect of dysphotopic complaints. Alfonso et al. show that standard femtoLASIK treatment for residual ametropia is safe and predictable.

1.9.5 Conclusion on bioptics
From the available literature it seems that bioptics is a viable option for residual refractive error after IOL implantation, irrespective of whether the IOL is monofocal or multifocal. The technique is still evolving in terms of indications and preferable technique utilization.

1.10. COMPLICATIONS AND MANAGEMENT OF COMPLICATIONS IN REFRACTIVE SURGERY

1.10.1 How often do complications occur in refractive surgery and what are their clinical implications?
Complications in refractive surgery are feared by both patients and surgeons. The definition of a complication from the patients’ perspective is any result that deviates from the patients expectations. From the surgeons’ point of view it is any result that fails to achieve the planned refractive target, a complication leading to severe visual loss, or chronic complaints. There are no accurate estimates of complications, because of the lack of clear and universally accepted definitions of complications. Fortunately serious side effects leading to severe visual loss are rare. There are reports from about 10 years ago that estimated the incidence of complications in LASIK to around 5%. More recent reports have shown a significant decrease in the incidence of complications to 0.02%-1.5%.

Looking at meta analysis of corneal laser surgery, we see that patient satisfaction rate for myopic LASIK is around 95.4% and for hyperopic treatment satisfaction rate is 96.3%. The 1 in 20 patients who are not satisfied, are so because they did not achieve the expected refractive outcomes or have bothersome side-effects.

The most common cause for dissatisfaction is a residual refractive error. Despite the fact that it is not a severe complication, it leads to enhancement (refractive surgeons’ euphemism for retreatments) and more prolonged recovery time till the target is achieved.

Levinson et al analyzed the reasons patients seek a second opinion after refractive surgery procedures. The foremost reasons were residual refractive error, dry eyes,
redness or pain in the eye, and glare and halo complaints.\textsuperscript{210} Note that none of these complaints are actually caused by vision threatening complications.

Severe or blinding complications occur rarely, but have a great impact on our patients.\textsuperscript{205} In LASIK these are mostly flap related; iatrogenic ectasia, infections, incomplete flap, traumatic flap problems, striae, diffuse lamellar keratitis, epithelial ingrowth and flap melts. In LASEK, PRK and surface ablations, complications are mostly related to healing and to infections. LASEK has a lower incidence of serious complications.

1.10.2 The most common complication: dry eyes
Dry eyes is the most common complication after both LASIK and surface ablation.\textsuperscript{211-212} The corneal nerves are ablated by the excimer laser. Regeneration has been shown to be aberrant, but protective function is regained. The best way to prevent this complication is by not treating patients whose tear film is insufficient. This is done by meticulous pre-operative diagnosis of the tearfilm production and function as given in treatment guidelines by peer groups.\textsuperscript{205, 213} It has been shown that the symptoms improve with time. Treatment consists of lubrication, and when necessary punctual occlusion with plugs or cautery, and sometimes by the use of Cyclosporin eyedrops or autologous serum eyedrops.\textsuperscript{214-216}

1.10.3 Complications in LASIK
Most complications are microkeratome related. These are the flap-cutting related problems, and the secondary ectasia problems. Other potentially serious complications include infection, diffuse lamellar keratitis, and epithelial ingrowth.

1.10.3.A Flap related problems
The flap related problems, are related to microkeratome malfunction. This causes the cut of the corneal lamella to be incomplete, or buttonholed. The literature shows that there is a learning curve in cutting flaps.\textsuperscript{207} Stulting et al reported that in the first 1000 LASIK flaps, 2.7 \% had flap-related complications.\textsuperscript{206} Gimbel et al reported that the incidence decreased from 4.5\% in the first 100 flaps cut, to 0.5\% in the last 200 cases of the first 1000 cases.\textsuperscript{207} A later study showed an incidence of 0.68\% of flap complications.\textsuperscript{217} In these cases the procedure should be aborted, the flap allowed to heal, and after that another procedure can be considered. Based on surgeons experience and preference this can be another LASIK procedure or the safer surface ablation approach.\textsuperscript{205}

1.10.3.B Secondary ectasia
Secondary ectasia occurs when the residual stromal bed is too thin, and the cornea is under biomechanical pressure, bows forward. This causes irregular astigmatism, severe visual loss, and sometimes corneal transplantation is needed to try and solve the problem. Iatrogenic ectasia is more common to LASIK. It can rarely occur in PRK and LASEK, but this has only been reported in eyes that have had a forme fruste keratoconus to begin with.\textsuperscript{218-219}
Secondary ectasia can be avoided in some cases. Accurate topography and pachymetry and analysis of these measurements can help avoid treating these patients. The use of thinner flaps may leave more residual stromal bed thickness. By calculating the minimal RSB thickness, at 300 microns instead of 250 micron, which is the minimum according to the literature. Patients at risk need to be detected pre-operatively. This pre-operative diagnosis is called forme fruste keratoconus. This is a very frustrating situation, because there are no absolute diagnosis parameters. At this point diagnosis is based on anterior and posterior corneal surface parameters, and their relative changes form the center of the cornea to the periphery coupled to a high index of suspicion. In the literature there are scoring methods for the relative risk. The relatively new process of post-publication peer review on these already published data and analysis of this literature have brought about a discussion on how to prevent secondary ectasia, at high sensitivity and specificity, without preventing refractive surgery because of false positives in our screening procedures. 220-222 Besides better understanding and diagnosis of which patient might be at risk for ectasia, moving away from LASIK technology to surface ablations, using thinner LASIK flaps, and calculating thicker stromal residual beds have been the modalities in which the prevention of secondary ectasias has developed.

1.10.3.C Infection

Infection after LASIK is a rare and sometimes severe complication. It is different from infective keratitis in non-LASIK corneas, because the flap offers physical protection to relative non-pathogenic pathogens, and this causes a more indolating infection which is hard to diagnose and eradicate. Pre-operative control of infection and sterility contribute most probably to the low incidence of infective keratitis after LASIK.

Reactivation of old infections, such as is the case in herpetic eye disease is an entirely different problem. Herpetic eye disease starts with a primary infection which is often asymptomatic.223 This explains why sometimes the patients (and their surgeons) don’t even know that they are at risk for a recurrence. The exact triggers for herpetic reactivation are unknown. Suggested triggers are stress, UV radiation, and surgical trauma. The excimer laser wavelength of 193 nm is close to the UV range, and could be such a trigger. Asbell has shown that deepithelialization of the cornea alone, like in surface ablations, is not a sufficient trigger for reactivation of herpes.223 The use of an excimer laser is, and can be suppressed by prophylactic antiviral therapy.223 Herpetic eye disease is considered a relative contra-indication for corneal refractive surgery. It encompasses the risk of reactivation of active viral replication, but also of immune-mediated keratitis which in the end leads to scarring and corneal deformation and unexpected refractive outcomes secondary to corneal irregularities224, and even corneal perforation.225 Sometimes the visual disability from an herpetic corneal scar can be very disturbing to patients. In the well-motivated patient, under maximal anti-viral prophylactic coverage, both PRK and LASIK have been shown to improve vision in terms of scar tissue removal and refractive error correction.226
1.10.3.D  **Diffuse lamellar keratitis**

Diffuse lamellar keratitis is the sterile intra-lamellar inflammation that can develop starting 8 hours after the procedure. This is mostly an acute inflammation. Some of the risk factors, like autoclave biofilm with exotoxins, powdered gloves, certain LASIK blades, meibomian gland dysfunction and its’ secretion are known. Others are not. Prevention, like with any complication is the best solution. DLK comes in 4 stages, of which stage 1-2 need thorough follow up and intervention with steroid eye-drops only, while stages 3-4 need surgical intervention in the form of flap relift, rinsing the inflammatory debris between the flaps, and reposition the LASIK flap. Untreated severe DLK may lead to crinkles in the flap and flap melt and severe visual loss, or to epithelial ingrowth.

1.10.3.E  **Epithelial ingrowth**

Epithelial ingrowth is when the corneal epithelium grows under the lamellar flap. The incidence is between 1-20% of surgeries. Most of cases are self-limiting, and need no intervention. In 1 to 1.7% epithelial ingrowth is persistent, reaches the optical axis, and may rarely cause decreased vision by direct obscuration of vision or more often decreased visual acuity secondary to flap surface deformation and irregular astigmatism. These are also the indications for surgical removal of the epithelial ingrowth.\(^\text{227-229}\) The incidence of epithelial ingrowth has decreased with better blade technology, and smoother flap edges\(^\text{227}\), but in cases of relift of flap that have been cut several years ago, the incidence may be as high as 30-40%.\(^\text{230}\) We show in our article that the effect of the epithelial ingrowth is not only on the flap surface and refractive error, but also in terms of disability glare, as measured by improved straylight after removal of epithelial downgrowth.\(^\text{231}\)

1.10.4 Complications in LASEK and PRK

1.10.4.A  **Delayed surface healing**

Delayed healing and irregular healing is sometimes seen in patients with insufficient tear secretion, overuse of topical anesthesia, use of mitomycin C.\(^\text{232}\) Diabetic patients or patients with other autoimmune disorders show more problems with delayed surface healing.\(^\text{232}\) Generally this is associated with more haze and regression and surface irregularity.

1.10.4.B  **Haze**

Haze occurs when ablation depth is deeper, in higher settings of myopia. It is known to start at around 1 month, and usually peaks by 3 months and usually abates by 6 months.\(^\text{232}\) It is dependent on the quality of the laser beam, but also on external factors like exposure to sunlight. Fibrocyte migration caused by cytokines like tumor necrosis factor alpha, and transforming factor beta, cause fibrosis and scarring.\(^\text{231}\)

1.10.4.C  **Infection**

Infectious keratitis may complicate surface ablation, especially before complete wound closure. Infection after surface ablations usually is caused by Gram positive
bacteria, Gram negative organisms, and rarely also by opportunist organisms like *Mycobacterium chelonae*. Sterile infiltrates can sometimes be seen. This is associated with the use of non-steroidal anti-inflammatory eye drops. The most important differential diagnosis of sterile infiltrates is bacterial keratitis. Infection can lead to severe visual loss and needs to be diagnosed and treated. Sterile infiltrates usually dissipate with corneal healing and use of steroid drops after the epithelium has closed.

1.10.5 Complications in refractive lens procedures
In refractive lens procedures besides the residual refractive error, glare and halo complaints, any complications associated with an intra-ocular procedure can occur, but does so rarely. The most feared complication being an endophthalmitis: this has an incidence of 0.4% after cataract surgery in the Netherlands, according to the 2009 Cataract Surgical Practice Survey. Retinal detachment is the other major threat for vision. The recent literature has shown that myopia, younger age, longer axial length of the eye, male gender, and absence of posterior vitreous detachment are risk factors for retinal detachment in this type of surgery.

1.11 AIMS OF THIS STUDY
Refractive surgery is a rapidly developing field, which encompasses many techniques that are widely practiced. Most technology is well-described in peer-reviewed literature. However there are still data missing. In this study we try to investigate several aspects of refractive surgery that are relevant in the current state of the art in this field of surgery.

The first aspect is the improvement in terms of reducing refractive error and improving Snellen visual acuity. Do wavefront optimized laser nomograms improve vision and decrease unwanted side-effects? As to bioptics: what is the minimal refractive error that can be safely treated, and is a standardized ablation or a wavefront ablation pattern the best way to achieve emmetropia?

The second aspect is investigation of quality of vision, defined by straylight. Does straylight, a parameter for quality of vision, change in corneal laser surgery? Are there differences between myopic and hyperopic treatments?

The third and last aspect in this thesis is the effect of adverse events and their treatments on Snellen visual acuity and quality of vision. Adverse events are a major concern in refractive surgery. It is impossible to broadly discuss rare events and their effect. We investigated the effect of epithelial ingrowth on straylight, and more importantly, the consequences of removal of ingrowth on straylight and visual acuity. Incidence and treatment effect of specific complications are investigated.
REFERENCES


74. Butunzer Z, Elliott DB, Gimbel HV, Simmon S. Visual function one year after excimer la-


146. Tuan KM, Chernyak D. Corneal asphericity and visual function after wavefront-guided LASIK. Optom Vis Sci 2006;83:605-10.


186. Arne JL, Lesueur LC, Hulin HH. Photorefractive keratectomy or laser in situ keratomileusis for residual refractive error after phakic intraocular lens implantation.


209. Varley GA, Huang D, Rapuano CJ, Schallhorn S, Boxer Wachler BS, Sugar A. LASIK for hyperopia, hyperopic astigmatism, and...