OUTCOME AND COMPLICATIONS OF PHOTOREFRACTIVE KERATECTOMY FOR MYOPIA AND ASTIGMATISM

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Declaration

This work contains no material which has been accepted for the award of any other degree or diploma in any university or tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except were due reference has been made in the text or publication.

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Michael Goggin

Preface

The following are publications on material described in this thesis, listed by date of publication.

Goggin M, Algawi K, O'Keefe M. Astigmatism following photorefractive keratectomy for myopia. J Refract Corneal Surg 1994; 10: 540–544.

Algawi K, Agrell B, Goggin M, O'Keefe M. Randomized clinical trial of topical sodium hyaluronate after excimer laser photorefractive keratectomy. J Refract Surg 1995 11: 42–44.

Algawi K, Goggin M, O'Keefe M. Stereopsis and accommodation following photorefractive keratectomy for myopia. Eur J Implant Refract Surg 1995; 7: 150–153.

Goggin M, Algawi K, O'Keefe M. The complications of excimer laser photorefractive keratectomy for myopia in the first year. Eur J Implant Refract Surg 1995; 7: 154–159.

Goggin M, Foley-Nolan A, Algawi K, O'Keefe M. Regression after photorefractive keratectomy for myopia. J Cataract Refract Surg 1996; 22:194–196.

Goggin M, Kenna P, Lavery F. Haze following photorefractive and photoastigmatic refractive keratectomy using the Nidek EC5000 vs the Summit Excimed UV200. J Cataract Refract Surg 1997; 23: 50–53

Goggin MJ, Kenna PF, Lavery FL. Photoastigmatic refractive keratectomy for compound myopic astigmatism with a Nidek laser. J Refract Surg 1997; 13: 162–166.

Goggin M, Lavery F. Holmium laser thermokeratoplasty for the reversal of hyperopia after myopic photorefractive keratectomy. Br J Ophthalmol 1997; 81: 541–543.

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Section I

Aims

To describe the outcome of photorefractive keratectomy (PRK) for myopia and astigmatism in terms of

a. the refractive outcome (addressing its accuracy)

b. the visual outcome (addressing its safety)

To describe the effect on binocular vision of staged bilateral treatment.

To describe the complications of PRK.

To describe therapeutic measures to treat hyperopic eyes following over-correction of myopia by PRK, a common complication.

To asses the ability of topically applied hyaluronic acid to effect epithelial healing following PRK.

Section II

Introduction

2.1 History and development of refractive surgery

Refractive surgery is surgery with the primary intent of altering the refractive status of the eye. Since the chief function of the eye is to act as an optical instrument, it is not surprising that many surgical interventions on the eye may result in an alteration to its optical function even if that is not the primary intent. Scleral encirclement for retinal detachment surgery may induce significant myopia, external plombage for the same purpose may induce astigmatism and the use of silicone oil may alter markedly the eyes refractive state because of its high refractive index (Okada et al, 2000; Weinberger et al, 1999; Grimm et al, 1997; Larsen et al, 1979). Squint surgery may induce astigmatism by altering the forces governing the shape of the anterior ocular surface (Hainsworth et al, 1999; Nardi et al, 1997; Denis et al, 1995). Since the cornea is the most powerful optical element in the eye, surgery on this structure can have extensive refractive effect. It is because of this that the cornea is the primary target for many refractive surgery techniques, such procedures being termed keratorefractive procedures. Keratorefractive procedures are more commonly performed than any other form of refractive surgery. Such surgery is commonly employed following penetrating keratoplasty. Penetrating keratoplasty can have unpredictable refractive effects that may need to be addressed surgically after the graft is fully established as a clear structure (The Australian Corneal Graft Registry, 1999). These refractive effects can be reduced using incisions and sutures in the graft, host or the graft-host junction. Cataract surgery, though its primary purpose is to remove the opaque crystalline lens, is a very powerful refractive

procedure. With the appropriate choice of intra-ocular lens it has become possible to address pre-existing myopia, hyperopia and even presbyopia (Leyland et al, 2001).

Surgery on the globe, with a refractive effect, can be placed on a spectrum of "refractive intent". At one end are the procedures that have a refractive effect that is coincidental and often unwanted and at the other are the procedures that are purely refractive in intent. In the middle are those procedures with refractive effects that are desired and largely controllable such as cataract surgery and penetrating keratoplasty.

Refractive surgery predominantly uses the cornea to produce the required effect and this form of surgery was first explored in the 19th century by Lans and others (Lans, 1898). The formation of a corneal scar was found to alter corneal shape and so alter refraction. Sato altered the corneal shape by placing incisions in the posterior corneal surface in a radial manner to flatten the central cornea and reduce myopia (Sato, 1953). These procedures were carried out before the vital place of the corneal endothelium was fully understood and resulted in the loss of corneal clarity in many cases (Yamaguchi, 1982). Further development of this technique lead to the placement of anterior radial incisions to approximately 90% of the corneal mid-peripheral depth to allow flattening of the central, optically active cornea and the correction of at least low levels of myopic spherical error. This technique is known as radial keratotomy (Fyoderov, 1980; Durnev, 1976; Fyoderov et al, 1979; Bores et al, 1971). By the placement of grouped incisions, transverse incisions or arcuate incisions it is also possible to reduce astigmatic errors (Fedorov et al, 1979). The effect of these techniques rests on the physics of a dome with a fixed base (the limbus). The intraocular pressure causes the gaping of the

incisions. When placed radially in the mid-periphery of the cornea the resultant expansion of that part of the dome leads to a flattening effect centrally and the reduction of myopia. With time the gaping incisions fill with corneal stromal tissue as healing progresses. Arcuate incisions, concentric with the limbus, also in the mid-periphery lead to an expansion in the vicinity of the wound and a flattening of the incised meridia, maximal at the centre of the incision. This leads to a flattening along that meridian and, when placed on the steepest corneal meridian, a decrease in corneal astigmatism. The power change induced is inversely proportional to the distance of the incision from the corneal intercept of the visual axis and proportional to its arc length. Because no corneal tissue is lost with these techniques, displacement of tissue in one meridian leads to an opposite displacement on the orthogonal meridian. In other words, any flattening on the surgical meridian is accompanied by a steepening at 90° to it at a ratio of approximately 1:1 (a 1:1 "coupling effect") so no overall spherical effect is achieved (Thornton, 1990; Duffey et al, 1988). Usually, the incisions are placed in pairs on opposite sides of the same meridian to ensure symmetrical corneal expansion and avoid irregular astigmatism. Transverse cuts (on a straight line in the corneal mid-periphery, not concentric with the limbus) have, by comparison with an arcuate cut concentric with the limbus, a radial component (the ends of the incisions are further from the visual axis than the centre). Consequently they have less astigmatic effect and some spherical effect (Seiler et al, 1987). They are slightly easier to perform and so have achieved a degree of popularity.

Incisional keratorefractive techniques all suffer from poor predictability by comparison to more recently introduced techniques, inherent long-term weakening of the tensile

strength of the cornea and long-term variations in the result (Kemp et al, 1999; Waring et al, 1994). Though effective for many low errors, they have been largely superseded by other techniques particularly by use of the excimer laser.

Excimer lasers were developed for industrial applications. However, the remarkable lack of collateral damage to surrounding structures makes them ideal for the alteration of corneal shape in a predictable manner (Ozler et al, 1992; Marshall, Trokel, Rothery, Krueger et al, 1988; Aron-Rosa et al, 1987). The non-thermal ablation of tissue to such a high tolerance allows the accurate reshaping of the anterior corneal surface required for refractive correction. Furthermore, the shape change is not substantially altered by the subsequent healing response (Piebenga et al, 1993; Tengroth et al, 1993; McDonald et al, 1990). Though initially used to perform incisions in the cornea as a "laser knife", these devices were modified to ablate wide areas of surface tissue. To this end, the beam profile was widened and homogenised to ablate to limited depth over a wide area. The interposition of diaphragms and slits allowed for the alteration of beam shape to treat spherical and regular astigmatic errors. Such beams are difficult to produce and subsequent development has been towards reduction of beam diameter and rapid manoeuvring of the beam to perform ablations wide enough for acceptable optical results. The use of narrow beams may allow for more variability of treatment, specifically targeting optical irregularities, but generally increases the treatment duration. Addition of devices to "track" the eye may compensate for this lengthening since the effect of longer treatment duration may be reduced ability of the patient to maintain voluntary fixation of the eye (McDonald et al, 1999) though this problem seems, with experience, to be largely theoretical (Mrochen et al, 2001; Tsai et al, 2000).

Initial development of the excimer techniques was toward ablation of tissue from the corneal surface immediately beneath the corneal epithelium. This meant that Bowman's membrane was ablated. This technique was termed "photorefractive keratectomy". Initial concerns that ablation of this structure might have long-term adverse effects have not been substantiated (Stephenson et al, 1998). However, initial experiences with more recent longer-term confirmation, suggested that this technique was not stable with higher myopic corrections. It appeared that significant healing with tissue replacement took place after such treatments with consequent regression of optical effect. The placement of effect in the deeper stroma was not associated with the same vigorous healing response and a further development of the technique capitalised on this (Van Gelder et al, 2002). The fashioning of a flap of anterior corneal tissue was added to the procedure and the ablation was carried out in the stromal bed thus uncovered. This technique was termed laser in-situ keratomileusis (LASIK) (Pallikaris et al, 1990).

The anterior flap was originally completely removed form the eye and some surgeons attempted to ablate the posterior surface of the flap (Burrato et al, 1993), but this technique is now generally practiced using a hinged flap, left attached at one side, and in the exposed stromal bed not the posterior flap surface. With the separation of a portion of the anterior stromal tissue in the flap from the rest of the stroma, the residual tissue in the bed following ablation must be in excess of a safe amount so as not to interfere with the post-operative tensile strength of the cornea. The exact measure of tissue required for this is a matter of continuing debate but is generally accepted as in the region of 250 μ (the flap being 150 μ to 200 μ, depending on the cutting device used) (Probst et al, 1998). The limiting factor for the power of correctable error, by this method, is, therefore, the pre-operative corneal tissue thickness. With normal corneal

thickness, the limit of correctable errors tends to be approximately 10 D to 12 D. Clear lens extraction with insertion of a low powered intra-ocular lens is an alternative for myopic patients with insufficient corneal tissue.

The application of these laser techniques continues to develop rapidly. The most recent development has been in the area of detecting fine variations in the refractive error known as optical aberrations and the use of this information in a tailored treatment plan for selected patients. This technique development is called "wavefront directed treatment" since the aberrations are manifest as deviation of the eye's wavefront from planar on the assumption that a planar wavefront is the ideal (a fact still in dispute).

For those cases deemed to be unsuitable for excimer laser surgery, a number of other strategies have been developed. Furthermore, some alternative methods of intervention have been developed for those suitable for excimer laser treatment, but which may avoid some of the pitfalls of laser intervention. The major contraindication to the LASIK procedure is if the corneal thickness does not allow for sufficient tissue ablation of a sufficiently wide treatment zone. In such cases, surgery may be undertaken to insert a suitable correction in the form of an intraocular lens placed either in the angle of the anterior chamber (Baikoff et al, 1998), in the ciliary sulcus (Rosen et al, 1998) or supported by the iris (Fechner et al, 1998) – a phakic intra-ocular lens (IOL). Alternatively, the clear crystaline lens may be removed and an intra-ocular lens placed in the retained capsular bag (Colin et al, 1994). Phakic intra-ocular lenses have been developed that may correct for astigmatism, when placed in the correct meridian

and retained there (the matter of migration of the lens has not yet been fully settled at the time of writing). Similar lenses are in development for the aphakic state.

The chief concerns for phakic IOLs are, for those placed in the sulcus, pupil blockage requiring an iridotomy pre or per-operatively, and pigment dispersion predisposing to glaucoma, perhaps for the patient's lifetime. For those lenses placed in the angle, cases must be specifically chosen with sufficient anterior chamber depth to avoid endothelial damage over the long-term. Intra-ocular intervention in high myopes carries an increased risk of retinal hole formation and retinal detachment, in a population already pre-disposed to such conditions (Colin et al, 1999). Intra-ocular intervention carries risks of infective endophthalmitis and choroidal haemorrhage with possible catastrophic consequences. However, for those patients unsuitable for laser correction, these forms of intervention may be their only means of achieving good unaided visual acuity.

Two concerns regarding the use of excimer laser ablation for correction of myopia have been the irreversible nature of the intervention and the inclusion of the visual axis and the surrounding area in the ablation. Should, for instance, scarring occur in this area permanent visual impairment may result. For some low errors, insertion of circular or semi-circular rings of polymethyl methacrylate (PMMA) – corneal ring segments – into the corneal mid-stroma at a 5 to 6 mm optical zone diameter will result in reasonably predictable refractive correction while avoiding the central optical zone (Twa et al, 1999). Since they can be removed this represents at least a partially reversible procedure. Tracks in the corneal mid-periphery are left behind after removal so the procedure is not fully reversible.

Refractive surgery is a rapidly developing field and techniques are being developed and modified so rapidly that assessment in research published in the peer reviewed literature is slow to catch up. It is necessary, however, for those involved in this kind of surgery to continue to put these techniques to the scrutiny that such research requires since commercial concerns may drive such endeavours to the detriment of patients.

2.2 An outline of excimer laser production and delivery technology

Using the lasing medium of a mixture of argon and fluoride gasses, the excimer laser produces laser light of 193 nm wavelength in the far ultraviolet range. Pumping of such a medium produces an "excited dimer" of argon and fluoride (an "excimer"). Subsequent decay of this dimer results in the laser emission.

In the instruments available for refractive correction, as the technique was initially developed, the beam of excimer energy produced was up to 5 mm wide and of a uniform energy profile described as a "top hat" configuration. This was engineered to allow uniform tissue ablation over a relatively wide area. The exact targeting of the beam was achieved by the opening of diaphragms of various designs in the beam path or by the use of non-ablatable mobile masks. By narrowing the beam to a slit or even a spot and moving it to the required locations on the target tissue, subsequent developments have eased the requirement for a wide uniform beam with some possible advantages in tissue relaxation time.

In its simplest form, for the treatment of simple myopia, the corneal ablation required was achieved by the stepwise opening of a circular diaphragm during laser delivery to the cornea centred on the visual axis as represented by the entrance pupil. This method achieved central corneal ablation with greater tissue removal centrally than peripherally in a stepwise manner as dictated by the desired correction. Myopic astigmatic corrections have been achieved by the application of laser energy to the cornea via an expanding slit, by the use of oval rather than circular diaphragms, with the use of ablatable masks or by the selective ablation of tissue using a mobile small spot of laser energy. Hyperopic corrections can be achieved by the selective ablation of corneal tissue in the mid-periphery causing steepening of the cornea in the region of the visual axis.

Initially, ablations were carried out on the corneal stroma and Bowman's membrane via a defect created in the corneal epithelium by various mechanical means – "photorefractive keratectomy" (PRK) (Bende et al, 1990; Seiler, Kriegerowski et al, 1990; Seiler, Kahle et al, 1990). Subsequent development of the technique has involved the cutting of a hinged corneal flap, including the anterior 120 to 180 μ of the corneal stroma and epithelium, and delivery of laser energy to the deeper corneal stroma, with subsequent replacement of the flap – "laser in-situ keratomileusis" (LASIK) (Pallikaris et al, 1991, Pallikaris et al, 1994, Pallikaris et al, 1990). This technique has enabled the treatment of larger errors with more stable outcome due to the absence of the vigorous healing response, tissue replacement and refractive regression seen with deep corneal ablations carried out on the corneal surface (Pallikaris et al, 1994, Pallikaris et al, 1997). This alteration of the healing response is probably consequent on the separation of

epithelial healing from the stromal healing response. This thesis addresses only the PRK technique, now mostly reserved for lower myopic corrections and ablations of small amounts of tissue.

2.3 The corneal tissue response to excimer laser irradiation

The high-energy interaction of the excimer laser energy with corneal tissue in characterised as a "photoablation". Molecular bonds are disrupted. Tissue is converted into a sub-atomic plasma and driven off the remaining tissue. There is little or no thermal effect and the remaining tissue is largely undamaged. Subsequent healing events are determined by the relative separation of healing epithelium and healing stroma / Bowman's layer (Fagerholm, 2000). In PRK the stroma, once epithelial healing has taken place, commences to remodel as after any injury, but with a relatively muted inflammatory response. Clinically, the most obvious event is the production of an anterior subepithelial haze attributed to the formation of glycosaminoglycans. This process is most obvious at 1 to 3 months and resolves in almost all cases between 6 months and a year (Goggin et al, 1997). Deposition of new collagen occurs during the first 6 months and some regression of refractive effect can be observed. Initial ablations are usually augmented to allow for this, in excess of the ablation dictated by the refractive effect as predicted by the Munnerlyn formula (Munnerlyn et al, 1988). The final refractive effect is clinically evident to the patient from approximately 1 month, with subsequent healing having little impact on their routine unaided visual acuity in most cases.

Epithelial closure over the approximately 8 mm defect occurs on day 2 to 5 post-operatively (Algawi et al, 1995). With closure comes a lessening of post-operative pain and the start of visual rehabilitation. Useful distance vision is established as a routine after 5 to 10 days. Initial hyperopia may limit some presbyopic patients, but, as mentioned above, this reverses in the first month. In common with any epithelial trauma, the epithelium may take some time to re-establish a full complement of hemi-desmosomal connections to the underlying healing stroma and patients are subject to some symptoms of epithelial instability in the first few months following treatment – tenderness of the ocular surface and transient morning discomfort (Seiler, Kriegerowski et al, 1991).

2.4 The optical and biological principles of myopic PRK

The anatomical substrate of myopia is the mis-match of ocular axial length with the refractive power of the cornea and lens, the total focal power of the refracting surfaces being too great for the axial length. The principal of treatment is the flattening of the central cornea to reduce the refractive power of the anterior corneal surface. Using the excimer laser, this is achieved by the ablation of tissue from the corneal stroma after removal of the corneal epithelium sufficient to allow the appropriate alteration of anterior surface curvature. The amount of tissue to be removed, expressed in microns, can be calculated from the "Munnerlyn Formula" (Munnerlyn et al, 1988).

$$\frac{(\text{Optical zone diameter in mm})^2 \times \text{Required correction in dioptres}}{3}$$

At the time of printing, the usual optical zone is between 6 and 7.5 mm for myopic correction. In five of the studies presented in this thesis the optical zone used was 5 mm, limiting the applicability of the data to current practice (Goggin et al, 1994; Algawi, Agrell et al, 1995; Algawi, Goggin et al, 1995; Goggin 1995; Goggin, 1996). Regular astigmatism can also be treated by selective ablation, in a "cylindrical" or oval pattern centred on the steepest axis (refractive or keratometric or some other compromise site where a difference exists) (Taylor et al, 1994).

Following ablation, epithelial cover is usually re-established within three days. Subsequent re-establishment of epithelial connections to the stromal substrate may take up to 6 months, during which time the epithelium may be unstable with symptoms similar to recurrent erosion syndrome (Goggin et al, 1995; Gartry et al, 1992; Seiler et al, 1994). Anterior stromal healing takes place over the next 3 to 6 months. During that period stromal replacement leads to some regression of effect necessitating slight over-treatment as a routine. The anterior stroma undergoes all the changes characteristic of corneal healing with collagen breakdown, the formation of glycosamino-glycans, and subsequent reformation of mature collagen (Essepian et al, 1994; Lohmann et al, 1991; Power et al, 1995). This process is manifest clinically by the transient formation of sub-epithelial haze, visible in the first 3 to 6 months following treatment (Lohmann et al, 1991).

The formation of a flattened area in the central 7 to 8 mm of the cornea, of course, leaves an untreated peripheral cornea. This leads to an increase in spherical aberration as an unavoidable optical side effect (Hersh et al, 1996). This can contribute to some

alterations in optical quality, particularly with ablations for larger errors. Patients may notice a decrease of contrast sensitivity particularly with dark adaptation, an effect presumably contributed to by the enlarging entrance pupil in reduced illumination (Haw et al, 2000; Bullimore et al, 1999; Schlite et al, 1997). Other symptoms may include glare and halos, also due, in part, to conversion of prolate asphericity to an oblate pattern (Niesen et al, 1997). Forward light scatter may also contribute (Lohmann et al, 1992; Lohmann et al, 1991). The creation of a more natural pattern by treatment directed by analysis of the wavefront emerging from the eye, in the future, may reduce these symptoms. Such treatments are under investigation at the time of writing. Decentration of ablation, failure of homogeneity of the laser beam or variation of the healing response over the treated area may cause irregularity of the refracting surface and alter visual quality (Alio et al, 2000; Smolek et al, 1998; Lin, 1994; Pender, 1994). Failure of the normal healing response can lead to a number of post-operative complications. Excessive stromal remodelling may cause anterior stromal opacification or "scarring" (Kremer et al, 1999; Steinert, 1997; Meyer et al, 1996; Fantes et al, 1991). Failure of epithelial anchoring can cause epithelial instability (Puk et al, 1996; Goggin et al, 1995).

2.5 Research strategy

The matters addressed below are, firstly, the outcome of photorefractive keratectomy (PRK) for myopia from the point of view of individual eyes. Photorefractive keratectomy for the correction of spherical myopic refractive errors, particularly those less than 6.00 D, has been shown to be safe and effective (Gartry et al, 1992; McDonald

et al, 1991; McDonald et al, 1990). With advances in the delivery of excimer laser energy to the cornea, sphero-cylindrical ablations are possible. Reports of the outcome of such ablations in animals and humans have been published (Shieh et al, 1992; McDonnell et al, 1991; Taylor et al, 1993; Kim et al, 1994; Campos et al, 1992). The refractive and visual acuity outcome of eyes undergoing photoastigmatic refractive keratectomy (a PRK treatment that includes a treatment for astigmatism) with a minimum of 12 months follow-up using the Nidek EC 5000 excimer laser are presented

Subsequently, the effects on binocular vision of uniocular treatment and later treatment of the other eye are addressed. The effects and complications of excimer laser photorefractive keratectomy have been documented (Puliafito et al, 1985; Marshall et al, 1986; Marshall, Trokel et al, 1988(a); Seiler, Kahle et al, 1990; McDonald et al, 1990; McDonald et al, 1991; Sher, Chen et al, 1991; Wilson et al, 1991; Gartry et al, 1992; Shieh et al, 1992; Seiler et al, 1994). It is a safe, effective and predictable tool in treating mild to moderate myopia (Sher, Chen et al, 1991; Gartry et al, 1991; Sher, Bowers et al, 1991; Kochevar et al, 1991). The anterior part of the cornea is flattened by excimer laser PRK to reduce the refractive power and to correct myopia. By reducing the myopia the accommodation required to see near objects clearly is increased in the uncorrected eye. Myopic spectacle lenses exert a prismatic "base in" effect on convergence. This reduces the requirement for convergence when viewing a near object. It is possible that treating myopia with excimer laser PRK may produce asthenopic symptoms due to the increased accommodation and convergence required. In addition, the accompanying increased convergence may lead to latent or even manifest convergent strabismus. Furthermore, stereopsis may be compromised by the

aniseikonia resulting from uniocular PRK and spectacle correction of the fellow myopic eye. This prospective study was conducted to evaluate the effect of PRK for myopia on accommodation, stereopsis and ocular alignment.

Thereafter, the commoner complications of PRK are addressed by examining the overall complications in a cohort of treated eyes with subsequent descriptions of individual complicating entities (overcorrection and epithelial healing).

Because the correction of myopia with spectacles or contact lenses is largely free of side effects, it is essential that any surgical or laser procedure designed to achieve similar optical results must be as free of complications as these methods. It is clear, however, that contact lenses in particular, are not completely free of sight-threatening complications (Dart, 1993).

The literature contains many descriptions of the optical, topographical and visual outcome of photorefractive keratectomy (PRK) (McDonald et al, 1990; McDonald et al, 1991; Sher, Chen et al, 1991; Gartry et al, 1992; Wilson et al, 1991; Shieh et al, 1992; Klyce et al, 1993), and there are many reports of the common complications of corneal ablation, such as subepithelial haze and refractive regression. There are a number describing the non-refractive complications of PRK (Seiler et al, 1994; Gartry et al, 1991).

Below, the complications that occurred in 161 eyes undergoing spherical PRK for myopia are described, with particular reference to the less-commonly described complications. The degree of satisfaction with the procedure (whether complicated or

uncomplicated) recorded by the first 50 patients with 1 eye treated, 1 year following laser therapy, is also described.

The healing process following photorefractive keratectomy for myopia dictates the final refractive error. Considerable variation in the error occurs in the early recovery period (Sher, Chen et al, 1991; Gartry et al, 1992). A proportion of eyes undergoes a variation of the astigmatic element of their refractive error following spherical excimer photorefractive keratectomy for myopia. Here are described 36 eyes out of 60 in which either a spherical refractive error before laser was replaced with a new astigmatic error, or an astigmatic error underwent a change of power and /or axis, by 6 months after a spherical ablation.

Although final refraction in about 85% of eyes having photorefractive keratectomy is within 1.00 diopter (D) of the desired refraction (Epstein, Fagerholm et al, 1994) some eyes experience regression to moderate myopia (Tengroth et al, 1993). This regression most often occurs in highly myopic eyes (Heitzmann et al, 1993). The treatment and outcome in 23 eyes that showed myopic regression after PRK are described.

Also addressed is sub-epithelial haze. Sub-epithelial haze is an almost universal occurrence following photorefractive keratectomy and photoastigmatic refractive keratectomy (PARK) (Epstein, Fagerholm et al, 1994). It is an established cause of decreased contrast sensitivity in conditions of reduced illumination and contributes to complaints of poor night vision following excimer surface ablations of the cornea (Lohmann, Fitzke et al, 1993). It is usually transient, maximal at 3 to 6 months

following treatment, and gone by 1 year. Subepithelial haze is a manifestation of the healing response, which alters collagen formation in the anterior stroma (Marshall, Trokel, Rothery, Krueger, 1988; Essepian et al, 1994). Smoother ablations excite less stromal reaction than rougher ablations (Fantes et al, 1990; Gipson, 1990; Gaster et al, 1989). One strategy to smooth the ablated surface is the use of a scanning delivery system. This system is present in the Nidek EC 5000 (Obata et al, 1994) but not in the Summit ExciMed UV200. A retrospective study was carried out to determine whether this delivery system difference led to a difference in the clinical manifestation of moderate or severe haze in the first year.

Laser thermal keratoplasty (LTK) is a technique to increase central corneal curvature for the correction of hyperopia and astigmatism. It is derived from work carried out initially by Lans at the end of the nineteenth century (Lans, 1898). By heating the corneal stroma to approximately 60°C, collagen shrinkage can be induced (Seiler, Matallana et al, 1990; Stringer et al, 1964) and placement of a ring of such burns about an appropriately chosen central optical zone can increase the curvature of the central cornea in a predictable manner while inducing peripheral flattening (Kohnen et al, 1996). This can be achieved by the absorption of the infrared light (2100 nm wavelength) produced by the focused holmium:YAG laser beam in the corneal stroma.

Over-correction following myopic photorefractive keratectomy, with a target of emmetropia, leaving a spherical equivalent of greater than 1.0 D of hyperopia occurs in approximately 1% of eyes treated (Epstein, Fagerholm et al, 1994). Low hyperopic refractive errors are tolerated by younger patients, but less so by those approaching the

age of symptomatic presbyopia. This study analysed the efficacy, safety, and 1 year stability of outcome of LTK carried out on 11 eyes with persistent symptomatic hyperopia following PRK for naturally occurring myopia.

Sodium hyaluronate (Healon, Pharmacia, Monrovia, Calif.) is a sterile non-pyrogenic viscoelastic preparation of highly purified non-inflammatory, high molecular weight sodium hyaluronate. It is a transparent, viscous solution which has been used in intraocular surgery for more than 23 years. Several surgical methods have been used to correct myopia during the past 4 decades (Barraquer, 1981; McDonald et al, 1985; Waring et al, 1985), including excimer laser photorefractive keratectomy (Burrato et al, 1992). However, the epithelial defect resulting from this procedure causes severe pain in most patients. Pain is a common complication of surgical procedures for myopia (Rashid et al, 1989).

Sodium hyaluronate has been reported as efficacious, in combined surgical and drug therapy, in promoting healing of the cornea in the treatment of severe eye burns (Reim, 1986; Reim, 1989; Reim, 1990). The positive effect of sodium hyaluronate on epithelial healing in corneal alkali wounds in rabbit eyes was confirmed in another study (Chung et al, 1989). Topical sodium hyaluronate application during penetrating keratoplasty has been suggested to promote epithelial healing (Reed et al, 1987). Nishida et al demonstrated that sodium hyaluronate stimulates corneal epithelial migration in cultured rabbit cornea. The study described below was conducted to investigate whether topical sodium hyaluronate application, following photorefractive keratectomy for myopia, has an effect on postoperative pain and epithelial healing.

Section III

Methods

3.1 Outcome of photorefractive keratectomy for myopia

One hundred and sixty consecutive eyes underwent photoastigmatic refractive keratectomy for primary myopic astigmatism, using the Nidek EC 5000, between April 1994 and June 1995. A retrospective analysis, of this population was performed. Early experience with this laser device demonstrated a consistent under-correction of the cylinder using the ablation algorithms programmed into the device's on-board computer. In light of this experience, and in discussion with the users, the manufacturers recommended a 25% addition to the cylinder power for ablation. All eyes in this study were treated in this manner. There were insufficient data at 1 year after the treatment on 67 eyes (36 defaulted on follow-up and in 31, examinations were not carried out sufficiently close to the first anniversary of the photoastigmatic refractive keratectomy procedure to be considered a true assessment of the outcome). During the first year, two eyes had a supplementary "mini-radial keratotomy" for residual spherical error that may have affected the remaining astigmatism, a third eye had arcuate keratotomy for residual astigmatism and a fourth eye had supplementary photoastigmatic refractive keratectomy for residual myopic astigmatism. These four eyes were also excluded, leaving 89 eyes in 81 patients, 43 males and 38 females, with a mean age of 34 years (range 20–60 years) for analysis at 1 year.

All eyes were examined fully before laser surgery, including videokeratography, keratometry, and manifest refraction. The refraction used to plan the ablation was the

subjective refraction, providing the spectacle-corrected visual acuity following at least 2 weeks free of contact lens use. The mean spherical equivalent refraction, at the spectacle plane, was –5.68 D (SD 2.67) with a mean cylinder power of –1.40 D (SD 0.75; range –0.50 to –5.00 D). The aim of treatment in all eyes was zero refractive astigmatism. A residual spherical error of –0.50 D was targeted in the non-dominant eye in pre-presbyopic patients, to delay symptoms of presbyopia. Thirty eight eyes had a baseline spherical equivalent refraction greater than 6.00 D of myopia and 51 eyes, 6.00 D or less of myopia.

Ablations were done according to a standard protocol. For the correction of the sphere, 0.25 D was subtracted from the subjective refraction in any patient over 35 years old, because of an empirical observation of the tendency of those patients to be overcorrected. No correction for hyperopic shift induced by the toric ablation was made. The cornea was anaesthetised using topical proxymetacaine 0.5%. At the slit-lamp, the corneal limbus was marked at either end of the horizontal meridian. The patient was then placed under the laser operating microscope, a speculum inserted, and the two limbus marks aligned with the horizontal orientation mire in the microscope to ensure proper orientation of the eye for the toric ablation. The pupil was constricted before surgery with pilocarpine 2%. The ablation, following removal of the central 7.5 mm of epithelium, was centred on the visual axis-determined by observation, preoperatively, of the position of the corneal light reflex in the entrance pupil using a direct ophthalmoscope and the position of the laser instrument fixation device reflex. The standard program of ablation on the Nidek EC 5000 is sequential. It ablates the required spherical correction first, then the cylindrical element. The cylindrical

ablations are achieved by a scanning laser delivery system through an expanding slit and the spherical ablations through an expanding diaphragm. Ablations are carried out using a central optical zone and a peripheral transition zone. All eyes had a peripheral transition zone of 7 to 7.5 mm and a central optical zone of 5.5–6.5 mm. The laser energy was between 125 mJ and 175 mJ with a pulse repetition rate of 30 Hz.

After excimer ablation, fucidic acid (1%) was instilled, the eye padded for 24 hours and fucidic acid (1%) used twice a day until epithelialization was established (usually within 72 hours). Follow-up examinations were performed 2 days, 2 weeks, and every month until 6 months, and then at 1 year. The manifest subjective refraction giving the best spectacle-corrected visual acuity was recorded at each visit. Topical medications were restricted to copious tear film supplementation from the time of cessation of the topical antibiotic in those eyes with less than –6.00 D of preoperative myopia, and fluorometholone 0.1% drops three times a day in those eyes with a preoperative spherical equivalent refraction greater than –6.00 D, for the first month in most eyes. All medications were ceased by 3 months. These 89 eyes were followed for, a minimum of 12 months.

3.2 Photorefractive keratectomy and binocular vision

Twenty-one patients, 11 females and 10 males, with a mean myopic refractive error of –3.80 D (range –1.5–6.00 D), underwent excimer laser PRK for myopia for their first eye with a target of emmetropia. The mean age was 25.95 years (range 20–33 years).

A detailed history regarding asthenopic symptoms was taken, visual acuity testing, automated and subjective refraction, cover test and assessment of extraocular muscle movements were carried out preoperatively and at each postoperative visit. Amplitude of accommodation, near and distant stereopsis, AC/A ratio and ocular alignment were assessed preoperatively and at 3 and 12 months postoperatively. Nine patients had treatment of their second eye between 6 and 9 months following their first PRK and the same assessments were carried out at 3 months after the second treatment. Amplitude of accommodation (AA) was measured using the RAF near point rule with full spectacle correction. The mean preoperative AA was 10.04 D (range 8–13 D). Near stereopsis was measured using Titmus Stereo Test. Mean pre-laser near stereopsis was 52 seconds of arc (range 40–140). Distant stereopsis was measured using the disparate circles of the Mentor B-Vat stereo test (Zanoni et al, 1991). Mean distant stereopsis was 143 second of arc (range 30–240). AC/A ratio was assessed using the heterophoria method (Parks, 1982).

The data analysis was performed using the Epi Info software program and the comparison of results were carried out using the Fisher exact method. A figure of $P = \text{or} < 0.05$ was regarded as statistically significant.

Table 1. Subject characteristics

Number of patients	Length of study	Myopia treated	Age	Stereopsis
21 patients (Male 11 Female 10)	Mean: 13 months Range: 9–16 months	Mean: –3.80D Range: –1.50 to –6.00D	Mean: 25.95 years Range: 20–33 years	Near: Titmus Stereo Test Distant: B VAT Mentor Stereo test

3.3 The complications of photorefractive keratectomy

One hundred and eighty eight consecutive eyes in 140 patients (59 males and 81 females) undergoing PRK for myopia were prospectively followed for 1 year to record complications occurring during that period. Of these 140 patients, 8 underwent the procedure to aid their participation in recreational sport and 6 to gain access to, or remain in employment requiring a specified level of unaided visual acuity. The rest simply wanted to be rid of their optical crutch or reduce their dependence on it. Data on the l-year review of 27 eyes was not available due to failure of patients to attend at the appropriate appointment for 21 eyes, inadequate records on 5 eyes and an inability to examine 1 further patient who became acutely psychotic shortly before his 1 year review date. This left a study population of 161 eyes, in 119 patients (50 male and 69 female) with completed follow-up data at 1 year. Their mean age was 31 years (SD 8.14), and the range 20–61 years.

All patients were counselled regarding the likely change in the nature of their vision, the implications of presbyopia in the emmetropic eye, the comparability of contact lens corrected vision and uncorrected vision following laser and, because of the youth of this technique, the lack of knowledge of the long-term outcome. Furthermore, the statistical likelihood of achieving good unaided visual acuity was put before them and comment invited.

All patients underwent a full pre-laser ophthalmic examination including retinoscopy, automated refraction and videokeratography. This latter technique was used to exclude patients with minor degrees of keratoconus, provide baseline topographical

measurements for those undergoing PRK and similar measurements for those ceasing contact lens wear for a period before PRK (Wilson et al, 1994). No patients with known ocular surface disorders, keratoconus (even in its presymptomatic form, as demonstrated by videokeratography) or collagen vascular disorders were treated. All procedures were carried out by 1 operator, according to a standard protocol using the Summit Technology ExciMed UV200LA argon fluoride system to carry out spherical ablations in 143 eyes (88.8%) with low to moderate myopia (6 D or less) and 18 highly myopic eyes (11.2%) (Table 2).

Table 2. Range of pre-PRK refractive errors

Low myopes	(–1.25 to –6 D)	143 eyes (88.8%)
High myopes	(–6.25 to –12.5 D)	18 eyes (11.2%)
		n =161 eyes

Seven eyes (4.3%) had greater than 1 D of cylinder before laser. All patients were treated under topical anaesthetic (amethocaine) and had pilocarpine 1% instilled before laser therapy. No patients required sedation. Following patient fixation training, the corneal epithelium was removed, using a Beaver blade, over a central 7 mm diameter circular area. Pulsed laser was then applied to a central 5 mm diameter zone, the number of pulses dependent on the degree of myopia. Thirty eyes received topically applied hyaluronic acid and 30 a placebo, immediately following photoablation, as part of a controlled, double-blind trial reported below (Algawi et al, 1995).

Post-laser management consisted of routine reviews on the first post-laser day, at 1 week, 1, 3, 6 and 9 months, 1 year and 2 years. The exact topical drug regime used in

the post-laser period varied somewhat, but, following 1 day's double padding and oral analgesia, it usually consisted of topical Maxitrol ointment (dexamethasone 0.1%, neomycin sulphate 0.35% and polymyxin B sulphate 6000 IU/g) 4 times/day for 1 week. This was replaced (after 1 week) by dexamethasone 0.1% drops, fluorometholone 0.1% drops or betamethasone 0.1% drops administered 3–4 times/day on an empirical basis in the absence of a substantial consensus in the literature, at that time, regarding the optimal regime following PRK. From 3 weeks on, the steroid dose and the potency of the particular topical steroid preparation used were varied according to the refraction at each visit. If regression of the early hyperopic shift occurred more rapidly than usual (e.g. regressing to less than 1 D of hypermetropia within the first month), then, though the eyes had not yet become myopic, the steroid regime was augmented by increasing dose, frequency or potency of the agent, or both. Regression into the myopic range (at any time) was aggressively treated with dexamethasone 0.1% drops applied as often as 8 times a day and reduction of the intraocular pressure (IOP) by as much as 30% using topical medications. With this method regression could be reversed and, if it subsequently recurred, the regime was reapplied. Intraocular pressure was measured at each visit and pressures over 21 mmHg (as a result of steroid response) treated with topical anti-hypertensives. Topical therapy was ceased in most patients during the third month. This drug regime was standard at the time of this study, but is seldom used at the time of writing.

All complications occurring during or after excimer laser PRK were recorded. At 1 year following PRK, the first 50 consecutive patients treated (28 male and 22 female), all with only 1 eye treated, filled out a questionnaire concerning their overall satisfaction

with the procedure, their current use of optical correction and whether they had achieved their original goal in undertaking the treatment. This sub-group consisted of 38 eyes (76%) of 6 D of myopia or less, and 12 eyes (24%) of greater than 6 D. Satisfaction was recorded on a graded scale of 0–10, 0 representing complete dissatisfaction and 10 total satisfaction. This questionnaire is reproduced in Table 3.

Table 3. Patient outcome questionnaire

Reason for undertaking treatment:
Has that goal been achieved (Y/N/Partially): Do you ever use correction now (Y/N):
If Yes, Current use of glasses ( )
or contact lenses ( ) please tick one or
put 1 for most frequently used and 2 for less frequently used.

for driving	(Y/N):	
for TV	(Y/N):	
for reading	(Y/N):	
for work	(Y/N):	type of work:
for pastimes	(Y/N):	type of pastime:
socially	(Y/N):	

Satisfaction with outcome:
Please mark on scale 0 = totally dissatisfied to
10 = completely satisfied.

0—1—2—3—4—5—6—7—8—9—10

3.4 Astigmatism following photorefractive keratectomy

Sixty eyes in 52 consecutive patients were followed up for 6 months or more following excimer laser photorefractive keratectomy for myopia using a Summit Technology ExciMed UV200LA argon fluoride laser system with one operator. This instrument produces pulsed laser radiation at a wavelength of 193 nm and a fluence of 180 mJ/cm^2 at the corneal surface. The patient's fixation was ensured by the use of a single light emitting diode (LED) fixation lamp coaxial with the laser beam.

All eyes had automated and subjective non-cycloplegic refraction before treatment. For those using contact lenses, a period of at least one week following removal of contact lenses was allowed to elapse before final measurements were taken. In only 17 eyes was contact lens wear constant before the treatment. Contact lens use was intermittent or non-existent (usually due to intolerance) in all others. Most eyes also had a corneal topographical map constructed using an EyeSys Laboratories corneal topography system. The mean age of the patients was 31 years (±8.38), range 20–61 years. The mean sphere was –4.73 diopters (D) before laser, range –12.5 D to –1.25 D. The mean cylinder, before laser, was 0.40 D, range 0.00 D to 3.50 D.

No eyes with ocular surface disorders or collagen vascular disorders were treated.

All eyes were treated under topical anaesthetic (amethocaine) and had pilocarpine 1% instilled before laser therapy. Sedation was not required in any case. Following patient fixation training, the corneal epithelium was removed, using a Beaver blade, over a central 5- to 6-millimeter diameter circular area. Pulsed laser was then applied to a

central 5-millimeter diameter zone, the number of pulses dependent on the amount of myopia. No complications of the treatment were encountered.

Following treatment, all eyes had Maxitrol ointment instilled (dexamethasone 0.1%, neomycin sulphate 0.35% and polymyxin B sulphate 6000 IU/g) and a double pad applied for at least 24 hours. Twenty-nine eyes received topical hyaluronic acid (Healon) at the same time as the Maxitrol and 31 did not. All eyes were reviewed on the first post-treatment day, at 1 week, and 1 month following laser treatment and subsequently attended at monthly intervals, when they were examined, had non-cycloplegic retinoscopy and /or automated refraction, and a manifest refraction was carried out. Spectacle-corrected and unaided visual acuity was assessed. A topographical map of the cornea was constructed at the 3 and 6-month reviews, using a video-keratoscope, to double check the optically measured change in corneal topography and confirm central placement of the laser therapy. A change in cylinder was deemed to have occurred only if the difference in measurements for spectacle-corrected visual acuity was 0.50 D and/or 10° or greater, because of the difficulty in establishing reproducible results between observers below this level. Following laser, all eyes were continued on topical Maxitrol ointment four times a day. This was usually changed, after 1 week, to dexamethasone 0.1% drops, fluorometholone 0.1% drops, or betamethasone 0.1% drops administered three to four times a day on an empirical basis in the absence of a substantial consensus in the literature regarding the optimal regime following photorefractive keratectomy at that time. Intra-ocular pressure (IOP) was measured at each visit and pressures over 21 mmHg (as a result of corticosteroid response) were treated with topical antihypertensives. Eyes regressing in the first

All procedures were carried out according to a standard protocol. Before surgery, pilocarpine 1% was instilled in the eye to be treated. Topical anaesthesia (amethocaine) was used in all cases, and no patient required supplemental sedation. After patients learned how to fixate on the laser light, the corneal epithelium was removed with a Beaver blade over a central 7-mm diameter circular area. Pulsed laser was then applied to a central 5 mm diameter zone.

Examinations were conducted 1 day; 1 week; 1, 3, 6, and 9 months; and 1 and 2 years postoperatively. Follow-up data from 18 months to 2 years were available for 12 eyes in the regression group and 54 eyes in the no regression group.

The postoperative topical drug regime varied slightly. In general, it comprised 1 day of double patching of the treated eye and oral analgesics followed by topical neomycin, polymyxin B sulphate, and dexamethasone (Maxitrol) three times a day for 4 days. No topical medications were used during the subsequent month. After that time, topical steroids were administered in selected cases according to the refraction at each visit. If regression of the early hyperopic shift occurred fairly rapidly (i.e. regressing to less than 1.00 D of hyperopia within the first month), fluorometholone 0.1% drops or betamethasone 0.1% drops four times a day for 1 month then twice a day for 2 weeks were prescribed, even though the eyes were not yet myopic. Myopic regression at any time was aggressively treated with dexamethasone 0.1% drops applied as often as eight times a day. Topical therapy was discontinued in most patients during the third month. In the eight eyes without stable reversal of regression, it was continued intermittently for between 5 and 46 weeks before being abandoned.

Five of the 23 eyes that regressed developed increased intraocular pressure (IOP) of greater than 21 mmHg and were treated simultaneously with topical antihypertensive agents. Seven other eyes, not "steroid responders", also received topical antihypertensives to lower IOP by as much as 30% from the baseline value.

3.6 Haze following photorefractive keratectomy

Between July 1990 and April 1994, PRK was performed on 726 consecutive eyes using the Summit ExciMed UV 200. The mean pre-treatment spherical equivalent myopic error was 4.47 diopters (D) ±1.82 (SD) (range 1.00 to 11.25 D). Between August 1993 and July 1995, PRK and PARK were performed on 494 consecutive eyes using the Nidek EC5000. Mean pre-treatment spherical equivalent myopic error was 4.58 ± 2.48 D (range 14.00–0.75 D). These means did not differ significantly (P = 0.56, Kruskal-Wallis test). All treatments were carried out on naturally occurring myopia in normal eyes. The mean optical zone diameter was 4.83 ± 0.33 mm (range 3.0–5.0 mm) in eyes treated with the Summit system, which did not have the facility to ablate transition zones. The mean optical zone was 5.47 ± 0.27 mm (range 4.0–6.0 mm), with a mean transition zone of 6.96 ± 0.15 mm (range 6.0–7.5 mm), in eyes treated with the Nidek system. The difference in optical zone sizes was significant (P = 0.004, Kruskal-Wallis test). This suggests that ablations with the Nidek would be generally deeper than those for equivalent refractive errors with the Summit. At 1 year postoperatively, there were no statistically significant differences between the two groups in the percentage of eyes achieving 6/12 or better unaided visual acuity, the

percentage falling within 1.0 D of the planned postoperative refractive error, and the percentage losing two or more lines of best corrected acuity (Table 4). The degree of haze on an established six point scale (0, 0.5, 1, 2, 3, and 4) (Fantes et al, 1990) was judged at the slit-lamp at the 3, 6, and 12 month visits. All treated eyes have passed the first anniversary of their treatment but 252 (51.0%) in the Nidek group and 324 (44.6%) in the Summit group defaulted on the 1 year follow-up visit.

Table 4. Visual and refractive outcomes at 1 year postoperatively

Outcome	Summit Group Number of eyes	%	Nidek Group Number of eyes	%	P-value
Visual					
6/12 or better unaided	348 (n = 378)*	92.1	185 (n = 209)*	88.5	0.2**
Loss of 2 or more lines of best corrected visual acuity	5 (n = 402)	1.2	2 (n = 242)	0.8	0.47***
Refractive					
Within 1.0 D of desired refractive error	350 (n = 402)	87.1	204 (n = 242)	84.3	0.39**

* Excludes eyes in which target spherical equivalent was greater than –0.75 D
** Yates corrected chi-square test
*** Fisher's exact test

3.7 Holmium laser thermal keratoplasty following photorefractive keratectomy

Eleven consecutive eyes in 11 patients (10 female, one male) aged between 25 and 69 years (mean 40 years) underwent LTK using the Technomed Holmium 25, contact holmium:YAG laser system between March and October 1995. This system produces a laser light in the infrared range (2100 nm wavelength) and has a pen-shaped handpiece delivery system that is applied to the cornea. The radiation is focused by a sapphire lens in the handpiece tip. Twenty-five pulses were delivered, each of 1.0 ms duration, 20-mJ energy, and at a pulse frequency of 15 Hz, at each burn site. These settings were used in all cases. All 11 eyes had undergone PRK (three using the Summit ExciMed UV200 and eight using the Nidek EC5000) for naturally occurring myopia between 7 months and 3 years (mean 17 months) before undergoing LTK. The mean spherical equivalent before PRK was –6.08 D (SD 1.67 D) and all eyes were normal at this time. The best corrected and unaided Snellen acuities before PRK are shown in Table 13 (page 71). The mean spherical equivalent before LTK was +2.06 D (SD 1.02 D, range +1.00 D to +4.75 D) based on a non-cycloplegic refraction since this most closely approximates the patient's day-to-day refractive error.

Four eyes each had an unsuccessful trial of epithelial debridement in the interval between PRK and LTK, leaving unaltered refractive errors.

The treatment was applied under topical anaesthetic using amethocaine 1% (tetracaine), centred on the visual axis using the fixation device in the Nidek EC5000 excimer laser delivery system. The target in all cases was emmetropia. The burn sites were marked on the corneal epithelium, the diameter of the optical zone being determined by the

desired refractive result and the burns were all applied in a circular pattern. Four burns were applied to one eye with a +1.0 D error, eight burns to a further eight eyes with errors between +1.25 D and +2.25 D, and 16 burns to a further two eyes, one with a sphere equivalent of +2.625 D and a second with +4.75 D. One eye, initially receiving eight burns for a sphere equivalent of +2.25 D, had a further eight applied 2 months later because of an inadequate response to the first treatment. When four or eight burns were applied they were all placed equidistant from each other on the circumference of the circular 9-mm optical zone. If 16 burns were required, eight were placed at the 8 mm zone in one ring and the rest were placed at the 9 mm zone, each immediately peripheral to a burn in the inner ring – that is, in a radial pattern.

Topical fucidic acid 1% suspension (Fucithalmic) was applied for 48 hours postoperatively. The patients were allowed to use topical amethocaine 1%, as required for the first day, and the eyes were examined at 48 hours, 1 week, 1 month, 3 months, 6 months, and a year. No other medications were used. A non-cycloplegic refraction and unaided and best-corrected acuities were recorded at each visit. No complications occurred during the treatments or in the follow up period.

3.8 Sodium hyaluronate following photorefractive keratectomy

Forty eyes of 40 patients with myopia, 17 men and 23 women were recruited. Their ages ranged from 21 to 53 years (mean, 31 years). All patients were white except for one Asian. The distribution between treatment of right and left eyes was equal.

Each patient was given, prior to inclusion in the study, full and adequate verbal and written information regarding the objective of the study and possible risks involved. The patients were informed of their right to withdraw from the study at any time. Written informed consent was obtained from each patient prior to treatment.

Each patient was allocated for application of sodium hyaluronate (10 mg/mL sodium hyaluronate) or placebo (sodium hyaluronate buffer) after photorefractive keratectomy, according to a randomization computer program. Sodium hyaluronate (10 mg/mL) was dissolved in sodium hyaluronate buffer. The syringes were filled with either solution and were marked with patient numbers to be issued consecutively. All syringes were packed in a similar manner. Neither the operator nor the observer had access to the randomization list.

Seven millimetres of epithelium concentric with the constricted pupil was scraped using a beaver knife. All eyes were treated using 193-nanometer Summit Technology ExciMed UV 200 argon fluoride excimer laser. The diameter of the treatment zone was 5 mm with fluence of 180 mJ/cm^2 and repetition rate of 10 Hz. A small amount of the test product was applied immediately after the laser treatment to the centre of the cornea followed by the routine application of Maxitrol (dexamethasone 0.1%, neomycin sulphate 0.35% and polymyxin B sulphate 6000 IU per gram) eye ointment. A double eye pad was then placed over the treated eye.

The systemic analgesic, Solpadeine (paracetamol 500 mg, codeine phosphate 8 mg and caffeine 30 mg), was given postoperatively. Patients were advised to take analgesic

tablets as needed and were also prescribed a sedative, Dalmane 30 mg (flurazepam), to be taken at night time.

The patients were assessed at 1, 2, 5, and 7 days postoperatively. At each visit, the patients were asked to reveal the degree of pain experienced which was recorded on a five-point scale (none, very mild, mild, moderate, or severe).The Haag Streit 900 slit-lamp microscope was used to measure the diameter of the residual unhealed area of epithelium at each visit. The length of slit beams, at two directions, was measured using the incorporated beam length measure. This was compared to the area initially denuded at the time of treatment, which was usually 7.0 mm centrally placed over the entrance pupil.

Maxitrol ointment was applied topically to the treated eye by all patients four times per day during the first week. Case Report Forms were computer-processed using a VAX-computer from Digital Equipment. The treatments were compared using Wilcoxon's rank sum test for categorical data, chi-square for binary data, and t-test for continuous data.

Section IV

Results and Discussion

4.1 Outcome of photorefractive keratectomy for myopia: Results

One year after photoastigmatic refractive keratectomy on 89 eyes, the mean spherical equivalent refraction was –0.44 D (SD 0.87 D). Seventy-one eyes (79.8%) had a spherical equivalent refraction within 1.00 D of the target refraction and 79 eyes (89%) achieved 6/12 or better uncorrected visual acuity. Of the 51 eyes with a preoperative spherical equivalent refraction of –6.00 D or less, 45 eyes (88.5%) were within 1.00 D of the target refraction and 26 (68.4%) of the 38 eyes with a preoperative spherical equivalent refraction greater than –6.00 D achieved this correction. A correction index gauging the effect of the spherical equivalent correction achieved can be derived by dividing the achieved spherical equivalent change by the targeted spherical equivalent change, i.e. by comparing the attempted versus the achieved correction at the corneal plane. The mean value was 1.04. The ideal index would be 1, indicating a 4% trend toward over-correction. Of the low to moderate myopes (preoperative spherical equivalent refraction of –6.00 D or less), 50 of 51 eyes (98%) achieved 6/12 or better uncorrected and of the high myopes (preoperative spherical equivalent refraction of greater than –6.00 D), 29 of 38 eyes (76%) achieved 6/12 or better, uncorrected. Four of 89 eyes (4.5%) lost more than two lines of spectacle corrected visual acuity with nine eyes (10%) gaining Snellen acuity of at least one line when preoperative spectacle corrected visual acuity was compared with postoperative uncorrected visual acuity.

The mean postoperative cylinder power was –0.36 D (SD 0.28; range 0 to –1.25 D). However, because of the variation of axis from that present before surgery, this figure needs further elucidation. Vector analysis using the Alpins method (Alpins, 1993) and the Alpins Statistical System for Ophthalmic Refractive Surgery Techniques (ASSORT) software, was carried out to evaluate the efficacy of the toric ablations. The mean magnitude of error (surgically induced astigmatism vector magnitude minus the targeted induced astigmatism vector magnitude) was –0.10 D (SD 0.27) – a small under-correction (the optimal value is 0, where surgically induced astigmatism vector magnitude equals targeted induced astigmatism vector magnitude). The mean angle of error (derived from the angle between the surgically induced astigmatism vector and the targeted induced astigmatism vector) was 0.73° (SD 10.91, range –61° to +24° where negative values indicate that the surgically induced astigmatism vector lies further clockwise than the targeted induced astigmatism vector and positive values if the surgically induced astigmatism lies further counter-clockwise). The mean difference vector magnitude, i.e. the amount of dioptric correction still to be induced to reach the target, was 0.35 D (SD 0.27). Once again the optimum value is 0. The mean angle of correction (the angular separation between achieved and targeted astigmatism axes (optimum value, 0) was –0.12° (SD 46.71). The ratio of the amount of correction achieved to the amount attempted (surgically induced astigmatism magnitude divided by the targeted induced astigmatism magnitude) is the correction index. The inverse of this index is called the coefficient of adjustment. The mean coefficient of adjustment was 1.11 (SD 1.33), again indicating under-correction. Finally, the mean index of success (the magnitude of the difference vector over the magnitude of the targeted

keratectomy carried out using other excimer laser instruments (Taylor et al, 1993; Kim et al, 1994).

This study did not divide the study population into groups on the basis of the power of the preoperative cylinder (low, moderate or high errors) because there were only 9 eyes with greater than 2.00 D of astigmatism. Several publications have relied on cylinder subtraction methods to analyse the results of toric ablation, despite the limitations of such methods (Alpins, 1993; Gallinaro et al, 1996; Kremer et al, 1996; Niles et al, 1996). This limits comparison of results with those presented here. All measures of vector power indicate a constant under-correction despite the routine addition of 25% to the cylinder power for ablation. The mean coefficient of adjustment was 1.11. This is a measure of the adjustment required to improve future surgery on the basis of those eyes analysed. It suggests that the algorithms used in this study be adjusted upward by 11% for our study eyes to overcome the under-correction. This would be the equivalent of adding 39% to the algorithms resident in the device, since the eyes studied all had 25% added to the resident algorithms in the treatments they received. The demonstration of under-correction in cylinder power and the accuracy of the axis of the correction is consistent with other publications (Taylor et al, 1993; Kim et al, 1994, Gallinaro et al, 1996; Kremer et al, 1996). The mean angle of error was 0.73°. That this angle is so close to zero implies only that there were equal numbers and magnitudes of clockwise and counter-clockwise vector misalignments since clockwise misalignments are given a negative value and counter-clockwise misalignments, a positive value in the Alpins method (Alpins, 1993). This fact is important – implying no constant error in either

direction. How much variation in misalignment occurred is better expressed by the standard deviation of this variable (10.91°), still a relatively small value.

One eye was excluded because the patient underwent an arcuate keratotomy 9 months after photoastigmatic refractive keratectomy for 3.00 D of residual astigmatism (refraction; +2.25 / –3.00 x 20°). Before surgery, the refractive error was –6.75/–0.5 x 120°. The induction of astigmatism following PRK has been described (Goggin et al, 1994). The exclusion of this eye induces a bias in the results, but because the cylinder outcome at 1 year was altered by the procedure before that time, inclusion would be invalid. The fact that this exclusion was applied to only one eye limits the bias in a study population of 89 eyes. Furthermore, two eyes were excluded because they had mini radial keratotomy for residual spherical myopia within the first year and one had a repeat photoastigmatic refractive keratectomy for myopic astigmatism. Table 5 below contains the relevant result data calculated from only those eyes included in the study in one column and the same variables calculated from the relevant data from all eyes, including the eyes excluded from the study, with the assumption that measurements carried out immediately before the supplementary treatment would have been stable to 1 year. Variations are small.

Table 5. Refractive and visual acuity outcomes 1 year after photoastigmatic refractive keratectomy

	Excludes four eyes that had supplementary treatment before 1 year	Includes four eyes that had supplementary treatment before 1 year
Parameter	**Percent of eyes (n)**	
All eyes within 1.00 D of target	79.8 (71)	77.4
Eyes (–6.00 D or less) within 1.00 D of target	88.5 (45)	84.9
Eyes (more than –6.00 D) within 1.00 D of target	68.4 (26)	67.5
All eyes with 6/12 or better uncorrected visual acuity	89 (79)	84.9
Eyes (–6.00 D or less) with 6/12 or better uncorrected visual acuity	98 (50)	94.3
Eyes (more than –6.00 D) with 6/12 or better uncorrected visual acuity	76 (29)	72.5
All eyes that lost two or more lines of spectacle-corrected visual acuity	4.5 (4)	4.3
All eyes that gained two or more lines of spectacle corrected visual acuity	10 (9)	10.75
Mean postoperative cylinder power (D)(SD)	–0.36 (0.28)	–0.40 (0.39)
Mean magnitude of error (D)(SD)	–0.10 (0.27)	–0.10 (0.29)
Mean angle of error (°)(SD)	0.73 (10.91)	–0.06 (14.4)
Mean difference vector magnitude (D)(SD)	0.35 (0.27)	0.39 (0.39)
Mean coefficient of adjustment (SD)	1.11 (1.33)	1.12 (1.38)
Mean index of success (SD)	0.23 (0.09)	0.25 (0.1)

The l-year uncorrected visual acuity of photoastigmatic refractive keratectomy for primary myopic astigmatism is as good as that reported for PRK in eyes with little or no astigmatism and, from this perspective, seems an effective treatment for these errors (Taylor et al, 1993; Goggin et al, 1994; Epstein, Fagerholm et al, 1994). The alignment of the correction is adequate. However, the algorithms for the Nidek EC5000 needs to be altered to allow for the consistent under-correction of cylinder power.

4.3 Photorefractive keratectomy and binocular vision: Results

No patients complained of asthenopia or presbyopic symptoms. All the patients could read N5 unaided. Three patients (14.28%) had asymptomatic persistent reduction of the amplitude of accommodation (AA) of ≥ 2 D (mean = 3.0 D). One of these 3 patients underwent PRK for the second eye. This did not improve the AA. Near stereopsis was reduced by a mean of 88 seconds of arc in 11 patients (52.3%) at the 3 months visit (range 10–360). Four of these (36.3% of those affected) regained their preoperative near stereopsis spontaneously by the end of the study follow-up period. An additional 4 patients (36.3% of those affected) regained their preoperative near stereopsis 3 months following treatment of the second eye (Table 6).

Table 6. Results – near stereopsis

Mean pre-laser stereopsis = 52 second/arc (range 40–140 second/arc) n = 21
52% (11 eyes) stereopsis reduced by a mean of 88 second/arc (range 10–360 second/arc) Time: 3 months post-laser
36% of affected eyes (n = 4) recovered pre-laser stereopsis without PRK in the 2nd eye Time: 1 year post-laser
36% of affected eyes (n = 4) recovered pre-laser stereopsis 3 months following PRK in the 2nd eye

Distant stereopsis was reduced by a mean of 103 seconds of arc (range 60–180) in 8 patients (38%) at the 3 months postoperative visit. Only those who underwent PRK in the second eye (3 patients) recovered their preoperative distant stereopsis (Table 7). The number of patients who recovered distant stereopsis following treatment in the second eye was significantly higher than those who recovered it spontaneously (P = 0.01, tailed value). There was no such significant difference for near stereopsis. No change in AC/A ratio, ocular alignment, or movements was noted in any case.

Table 7. Results – distant stereopsis

Mean pre-laser stereopsis = 143 second/arc (range 30–240 second/arc) n = 21
38% (n = 8) stereopsis reduced by a mean of 105 second/arc (range 60–180 second/arc) Time: 3 months post-laser
37.5% (n = 3) recovered pre-laser stereopsis 3 months following PRK in the 2nd eye
62.5% (n = 5) persistent reduced stereopsis 1 year post laser (without PRK in the 2nd eye)

4.4 Photorefractive keratectomy and binocular vision: Discussion

Accommodation and convergence are closely linked since both are concerned with viewing objects closer than optical infinity. Initiation of accommodation is usually accompanied by stimulation of convergence. AC/A ratio is usually constant for each person. However, there is some "elasticity" or relative convergence. This elasticity is encountered in subjects with refractive errors or heterophorias. A myope, for example, must converge without accommodation when viewing an object at the far point of the eye. This same myope should exert convergence in excess of accommodation to have a clear binocular vision of near objects. This is called positive relative convergence (Parks, 1982). Correction of myopia necessitates more accommodation to see near objects clearly. Myopic spectacle lenses exert a prismatic "base in" effect on convergence. This reduces the requirement for convergence when viewing a near object. One may speculate that treating myopia with excimer laser PRK may produce asthenopic symptoms due to increased accommodation. In addition, increased convergence may lead to latent or even manifest convergent strabismus. In this study, relatively young patients (20–33 years) were selected. This was intended to avoid the age-related reduction in AA (Duane, 1922). Despite the reduction of the AA of ≥ 2 D in 3 patients, no asthenopic or presbyopic symptoms were reported and patients could read the smallest print in the reading text test (N5) unaided. The possible explanation of this reduction in AA is latent hypermetropia. Cycloplegic refraction, which was not performed in our study, would have confirmed this possibility. Despite the fact that performance using the RAF rule could be reduced in cases of defective convergence (Cashell et al, 1980), this was not detected in any of our patients when tested for ocular alignment. Stereopsis, defined as blending the two slightly disparate uniocular images

into 1 solid image with depth, is the most acute form of binocular vision. Stereopsis may be compromised by the expected aniseikonia (Tychesen, 1992) following uniocular correction of myopia and spectacle correction of the second myopic eye. Von Noorden suggested that uniocular stereoscopic clues gradually dominate the binocular stereoscopic clues (Von Noorden, 1985). This may be the reason why our patients have not complained of binocular disturbances following unilateral PRK. In this study, 11 patients had a reduction of the near stereopsis of greater than or equal to 10 second of arc. Four patients restored their preoperative near stereopsis without treating the second eye. This may well be attributed to the monocular clues the Titmus Stereo Test offers (Marsh et al, 1980; Kohler et al, 1973). Perhaps using the major amblyoscope or TNO (Okuda et al, 1977) stereotests would have given more informative stereoacuity because these 2 tests lack the uniocular clues the Titmus stereo test offers. The recovery of near stereopsis did not show any statistically significant pattern, with or without treatment.

With planned post-operative monovision (1 eye corrected for near vision and the other for distance, in the presbyopic population), as long as stereoacuity reduction is kept below 50 seconds of arc, patients tend not to develop asthenopia (Jain et al, 1996). This is also the case when induced anisometropia is low (1.25 D) (Wright et al, 1999). However, long-standing anisometropia may adversely affect steroacuity, measured even with full correction of the anisometropia, implying continued susceptibility of the binocular visual system to binocular disparity (Fawcett et al, 2001).

Distant stereopsis was reduced in eight patients. Whilst treating the second eye has restored the preoperative levels of distant stereopsis, no improvement was documented

in those with only 1 eye treated. It would have been interesting to test for stereopsis using a contact lens in the untreated eye instead of spectacle correction. Unfortunately that was not possible due to contact lens intolerance in some patients as well as the technical difficulties of obtaining the suitable contact lens for a "once only" use. The consistency of the distant stereopsis at all visits may be attributed to the lack of uniocular clues in the Mentor B-Vat stereo test (Zanoni et al, 1991).

This study showed that distant stereopsis was significantly improved following the second PRK in all those patients with an initial reduction in stereopsis. In addition, despite objective reduction of AA in three patients, no asthenopic or presbyopic symptoms were reported. This work confirms the safety of excimer laser photorefractive keratectomy for myopia in areas of binocular function.

4.5 The complications of Photorefractive keratectomy: Results

One hundred and eighty eight consecutive eyes were treated over a 20-month period, of which 161 were available for analysis. The complications that arose can be divided into an "early" group (those that did not persist to the 1 year review) and a "late" group (persisting to 1 year). Thirty-six of the 161 eyes (22.4%) had some form of early complication after laser. A list of these appears in Table 8. The most frequently occurring problems were those associated with the use of topical medications in the immediate post-laser period. This was found in 33 eyes (20.5%). In 19 of these eyes (11.8%) the corneal epithelium underwent changes characteristic of drug toxicity (SPE

Two further eyes (1.2%) developed recurrent erosions in the early post-laser period (within 6 weeks). Both settled with conservative management, using topical lubricants. Though no other patients developed frank epithelial erosion, at the 1 year post-laser review in 48 eyes (29.8%) symptoms of discomfort on waking and/or corneal tenderness were reported (see Table 9). None of these patients had any of the signs of failure of epithelial anchorage or were disturbed by their symptoms.

Table 9. Late non-refractive complications (persisting to 1 year)

Complication	Number of eyes
Subepithelial haze	96 (59.6%)
trace	78 (48.4%)
grade 1	13 (8.1%)
grade 2	5 (3.1%)
Pain on waking and/or tenderness	48 (29.8%)
Glare	3 (1.9%)

One patient developed a 3 mm ptosis following the procedure that necessitated a Gavaris procedure. This patient also developed irregular astigmatism, limiting the visual outcome but still achieved 6/12 Snellen visual acuity without correction at 1 year (the best corrected vision was 6/9 at that time, using +0.75 DC at 90°). This patient's case was complicated by the presence of an atypical multi-system disorder, probably of auto-immune origin, admitted by the patient only after treatment. This consisted of cerebrovascular accidents occurring on 2 occasions, coeliac disease and mild hypothyroidism.

Amongst the 161 eyes, only 4 (2.5%) underwent early complications directly attributable to the excimer ablation, other than the almost universal early occurrence of

subepithelial haze, i.e. 1 eye with a split in Decemet's membrane, 1 with ptosis and irregular astigmatism and 2 with recurrent erosions. All other complications, in the first 6 months, were due to topical medications or were refractive in nature.

Table 9 lists the non-refractive complications persisting to 1 year, the "late" complications. Subepithelial haze was noted in 96 eyes (59.6%). In 78 (48.4%) this was recorded as "trace". Thirteen eyes (8.1%) had grade 1 haze and 5 (3.1%) grade 2 (Fantes et al, 1990). Sixty-five eyes (40.4%) showed no haze.

Glare and other "edge effects", such as reduced acuity with reduction of illumination, are common in the post-laser period. However, patients seldom complain of them unless questioned specifically. At the 1 year review, only 3 patients out of 161 (1.9%) complained of glare severe enough to interfere with daily life. One of these patients describes difficulty driving at night and another will not undergo PRK in the second eye for fear of inducing the same symptoms in that eye.

With regard to the visual outcome, at 1 year, 155 (96.3%) achieved 6/12 Snellen acuity, or better, without correction. One hundred and forty-seven eyes (91.3%) were within 1 D of the desired final refraction. Fluctuations in the cylindrical element of the refraction occurred during the healing period, and these are reported below. When surveyed at 1 year, 39 patients (78% of the sub-group consisting of the first 50 consecutive eyes, in 50 patients, treated) regarded that their original goal in undergoing the treatment (whatever that may have been) had been achieved in full. A further 8 (16%) said that their goal had been achieved in part, and 3 (6%) that it had not been achieved. With regard to the satisfaction score (on the 0–10 scale described above) 24 patients (48%) scored 10, 12 (24%) scored 9 and 8 (16%) scored 8.

The rest of the scores are shown in Table 10. Three patients (6%) scored less than 7 (the same 3 that had not achieved their prelaser goal). One of these had 4.5 D of hypermetropia at 1 year, another 3 D of myopia, and 1 had 1 D of myopia while retaining 1 D of with-the-rule astigmatism present before PRK. This last patient achieved 6/9 unaided but had reverted to full time contact lens use, while the 2 former patients achieved 6/36 and 6/60 unaided. In response to the question "do you ever use correction now?" (i.e. 1 year after PRK), 11 patients (22%) replied in the affirmative. Nine used spectacles, 1 had reverted to contact lens use and 1 used both. Of these 11 patients, 8 had residual myopia, 1 residual hypermetropia, 1 was using spectacles for presbyopia, having been rendered emmetropic and 1 was the patient mentioned above using a contact lens to correct pre-existing astigmatism and low myopia. Computerised videokeratography demonstrated, post-laser, that the mean decentration of the ablation zone was 0.38 mm and that in only 1 case did this exceed 0.5 mm (measuring 0.93 mm).

Table 10. 1 year post-PRK patient satisfaction rating

Rating	Number of patients
0	1 (2%)
1	1 (2%)
3	1 (2%)
7	3 (6%)
8	8 (16%)
9	12 (24%)
10	24 (48%)
	n=50

By linear graded scale where 0 = totally dissatisfied;
10 = completely satisfied.

4.6 The complications of photorefractive keratectomy: Discussion

Few studies have specifically enumerated the complications associated with PRK (Seiler et al, 1994; Gartry et al, 1991; Seiler et al, 1992), though many suggest that there are no "significant" complications (Fantes et al, 1990; Brancato and Tavola, 1993; Salz et al, 1993; Weinstock et al, 1993). In this series, just under a quarter of eyes receiving PRK for myopia underwent early complications of their treatment. These relatively frequent complications in the post-laser period, if not addressed, could lead to long-term loss of vision (e.g. endothelial decompensation associated with a split in Decemet's membrane). However, 94% appeared satisfied with the outcome of their procedure at 1 year. The 1 year outcome, as measured by unaided visual acuity (96.3% seeing 6/12 or better) or final refractive error (91.3% within 1 D of the intended result) compares favourably with other published results (Sher, Chen et al, 1991; Gartry et al, 1992; Brancato and Tavola, 1993; Salz et al, 1992; Salz et al, 1993).

The occurrence of steroid related raised IOP at a rate of just over 9% over a treatment period of about 3 months, is expected. The use of topical steroids in the post-laser period was controversial (Gartry, Kerr-Muir, Lohmann et al, 1992; Machat, 1993; Tuft et al, 1993) and is now less frequently or intensively practised. Routine, early use of a combined preparation of dexamethasone, neomycin and polymyxin leads to epithelial toxicity of the cornea in 12% of patients. This is, of course, an avoidable complication.

The occurrence of a break in Decemet's membrane in the post-laser period, though it caused no adverse effect on vision in the long term (achieving 6/9 unaided acuity at 1 year and maintaining a clear cornea), is some cause for concern. This complication

Despite these complications, it is worth noting that visual and optical function of the series of patients assessed at 1 year was good (96.3% seeing 6/12 or better and 91.3% within 1 D of the intended refraction) and 94% achieving their pre-laser goal fully or in part (Kahle et al, 1992). The 6% (3 patients out of 50) who did not achieve their goal all underwent refractive complications of PRK. One failed to demonstrate early, healing-induced, regression from hypermetropia to emmetropia, the second showed vigorous regression into myopia, and the third finding the lack of correction for a pre-existing low astigmatism sufficiently troublesome to warrant a return to contact lens wear. A further 7 patients with residual myopia were using either contact lenses or spectacles, part time. Interestingly, all of these said they had achieved their therapeutic goal, partially or completely, implying that their pre-PRK expectations were realistic. It is also worth noting that, other than sub-epithelial haze which occurs almost universally in the early post-treatment period, only 4 eyes in 161 (2.5%) underwent early complications directly attributable to PRK, none of which altered the visual outcome. Late non-refractive complications are more common, but are generally benign also (haze, minor ocular discomfort and glare). Photorefractive keratectomy appears to be safe when compared with constant contact lens use (Dart, 1993), and in particular is safer than extended wear contact lens use (MacRae et al, 1991).

The pre-laser assessment described above allows selection of those eyes most likely to respond well to PRK, i.e. with low myopia, low regular astigmatism and free of irregular astigmatism. Along with the physical assessment, it is good practice to counsel the patients, as described, to ensure that their expectations are realistic. By this

means, and with frequent follow-up by experienced personnel it may be possible to minimise the occurrence of complications.

4.7 Astigmatism following photorefractive keratectomy: Results

Sixty consecutive eyes in 52 patients (26 male, 26 female) were assessed at 3 and 6 months following spherical excimer laser photorefractive keratectomy. Of these, 36 (60%) eyes had a change in the astigmatic element of their refraction at the 6-month review. The change could be categorised in one of four ways: a change from a spherical refraction before laser to an astigmatic refraction after laser (12 eyes, 20%), an increase in the power of a pre-existing cylinder after laser (4 eyes, 6.7%, two of which also had a change of axis), a decrease of the pre-existing cylinder power (12 eyes, 20%, 10 to zero and the remaining two with a change of axis), or a change of cylinder axis without a change in power (8 eyes, 13.3%, 5 without a change of rule and 3 with a change of rule). The mean power change (in 28 eyes) was 0.75 D (range 0.50 D to 1.75 D) by cylinder subtraction. The axis of new cylinders was predominantly with-the-rule (8 out of 12), 2 others being against-the-rule and 2 oblique.

An astigmatic change in corneal topography was significantly associated with the existence, before laser, of an astigmatic refractive error ($P = 0.0004$, Yates corrected chi square test). Those with an astigmatic error, before laser, had a relative risk of this sort of change of 2.29 (Taylor Series 95% confidence interval, 1.43 to 3.67) and, consequently, the mean cylinder power before laser in the group that underwent a

change (0.58 D) was significantly higher than the mean in those who did not (0.13 D) (P = 0.0004 Kruskal-Wallis test).

The mean sphere, before laser, was higher in the group that underwent change (–5.22 D versus –4.00 D), but this did not achieve statistical significance, with P = 0.071 (Kruskal-Wallis test). A summary of the refractive errors before, and at 6 months after photorefractive keratectomy in the group that underwent change, appears in Table 11.

Astigmatic change was not significantly associated with regression of the refractive error into the myopic range, the degree of anterior stromal haze after laser (grade 2: Fantes et al, 1990) or less in all but one case where grade 3 was noted), the sex or age of the patient, the side undergoing photorefractive keratectomy, constant contact lens use before laser or padding of the eye for more than one day. There was no significant difference in the amount of laser delivered to each group and the mean spherical error following laser of the two groups did not differ significantly.

Table 11. Refractive error (D) in 36 eyes before and at 6 months after photorefractive keratectomy (PRK)

Before PRK			6 months after PRK		
Sphere	Cylinder	Axis	Sphere	Cylinder	Axis
Eyes with new cylinders					
–8.50	+0.00		0.00	+1.25	100*
–7.50	+0.00		0.00	+1.00	180*
–3.25	+0.00		0.00	+1.00	100*
–7.00	+0.00		–1.50	+1.00	55*
–2.75	+0.00		–0.25	+0.75	75
–6.0	+0.00		0.00	+0.50	90
–2.00	+0.00		+0.25	+0.50	90
–5.50	+0.00		0.00	+0.50	60
–3.00	+0.00		+0.25	+0.50	105
–4.25	+0.00		+0.00	+0.75	160
–3.25	+0.00		–0.25	+0.50	90
–4.00	+0.00		–0.50	+0.50	90
Eyes with decrease in power					
–5.5	+1.00	90	–0.75	+0.00*	
–5.50	+1.00	90	0.00	+0.00*	
–7.25	+1.00	90	0.00	+0.00*	
–5.25	+1.00	90	0.00	+0.00*	
–4.25	+0.50	70	0.00	+0.00	
–2.00	+0.50	90	0.00	+0.00	
–5.50	+0.75	90	0.00	+0.00	
–2.50	+0.50	60	+0.75	+0.00	
–3.00	+0.50	90	0.00	+ 0.00	
–8.25	+1.25	90	+1.25	+0.75	75
–2.25	+0.50	90	0.00	+0.00	
–12.50	+3.50	80	–2.00	+3.00	110
Eyes with increase in power					
–5.50	+0.50	90	–2.25	+2.25	110*
–5.50	+0.50	180	–1.00	+1.00	180
–3.00	+0.50	90	0.00	+1.00	90
–6.75	+0.75	90	+2.50	+1.25	180
Eyes with change of axis without change of power of 0.50 diopters or more					
–6.75	+0.75	90	–0.75	+0.75	80
–9.50	+1.50	60	– 1.50	+1.75	75
–2.75	+0.50	90	–0.75	+0.75	100
–4.00	+1.00	90	0.00	+1.25	80
–3.25	+0.50	90	0.00	+0.50	180
–5.50	+1.00	90	–1.50	+1.25	75
–4.50	+0.50	180	+0.50	+0.75	160
–10.25	+0.75	90	–0.50	+0.50	170

* Eyes with a change in cylinder power of 1.00 diopter or more.

Table 12 contains a summary of the variables described above. Significance was measured by the chi square test for categoric variables, the ANOVA test for comparison of means in normally distributed data, and the Kruskal-Wallis test for non-parametric data.

Table 12. List of variables assessed for association with astigmatic change following photorefractive keratectomy

Variable	P value	Relative risk where applicable (95% confidence limits)
Sex	NS	
Age	NS	
Side treated	NS	
Existence of cylinder before laser	0.0004	2.29 (1.43 to 3.67)
Greater mean cylinder before laser	0.0004	
Constant contact lens use before laser	NS	
Mean sphere before laser	NS	
Mean laser dose	NS	
Hyaluronic acid use after laser	NS	
Regression	NS	
Degree of stromal haze after laser	NS	
Pad for > 1 day	NS	
Mean sphere after laser	NS	

Significance measured by chi square test for categoric variables, ANOVA test for comparison of means and Kruskal-Wallis test for non-parametric data. NS = not significant.

Centration of the ablated zone was assessed by videokeratography, measuring the distance between the centre of the treated zone and the centre of the entrance pupil. The centre of the treated zone was established, where the flattened area was not circular, by finding the intersection of the shortest and longest diameters of the flattened area. The mean decentration in the group undergoing change at 6 months was 0.384 mm, the mean

in the group where change did not occur was 0.382 mm. This difference was not significant. The maximum decentration that occurred was 0.93 mm in one case.

Comparison of refractive errors before and at 3 and 6 months after photorefractive keratectomy reveals that of the 36 eyes that had astigmatic change at 6 months by comparison with their examination before photorefractive keratectomy, 21 (58%) had change occurring both in the first 3 months and between 3 and 6 months.

With regard to the unaided visual acuity after laser, in this series 33 eyes achieved 6/12 or better in the group with astigmatic change (91.7%, n = 36) and 22 (91.7%, n = 24) in the group without change, at 6 months. If those eyes with a myopic error before laser treatment of greater than 6.00 D are excluded, all those in the group with astigmatic change achieved 6/12 or better, and all but one achieved 6/12 or better in the group without change. In the former group, 12 reached the same level of acuity as their spectacle corrected acuity before laser, and 11 in the latter. These differences are not statistically significant.

Following photorefractive keratectomy, because of the variety of pharmacological regimes used after the first week, it was not possible to assess their role on an individual basis in the processes described. However, a proportion of eyes, both with and without astigmatic change, had ceased receiving medication between 1 and 3 months following photorefractive keratectomy. Once again, there was no significant difference between the two groups in this regard. Six eyes, three eyes in each group, demonstrated a rise in IOP in response to topical corticosteroid. Of the 29 patients who received topical

hyaluronic acid immediately after laser, 17 had a change in the cylindrical element of their refractive error, and of the 31 who did not receive it, 19 had such a change. This difference is not significant.

4.8 Astigmatism following photorefractive keratectomy: Discussion

The healing process taking place in the anterior corneal stroma dictates the final refractive error following photorefractive keratectomy. Stabilisation of this process has been noted from as early as 2 months following treatments for those with lower refractive errors (McDonald et al, 1991). It has been our observation that a considerable proportion (60%) of patients following routine application of excimer laser photorefractive keratectomy for myopia, by a standard technique (and achieving good ablation centration), have a change in the cylindrical element of their manifest refraction during the first 6 months. This observation is directly contrary to previous publication (McDonald et al, 1991; McDonald et al, 1990). Early publications would suggest that at 6 months these changes are likely to be stable (Sher, Chen et al, 1991; Gartry et al, 1992; Wilson et al, 1991), however, the authors have observed change after this time.

Three eyes undergoing photorefractive keratectomy, exposed preoperatively to paraformaldehyde, have had an increase in astigmatism reported following laser. The change was attributed to corneal remodelling following the chemically induced keratitis (Pallikaris et al, 1992). The findings reported in this study would suggest that at least some of the change may have occurred even without exposure to formaldehyde.

from standard of laser fluence or beam profile leading to "astigmatic" ablation, the astigmatic change would most likely have been stable from the time of treatment. However, in 58% of the eyes that underwent such change this change was a continuous process during the follow-up period.

Furthermore, routine beam profile analysis by polymethylmethacrylate (PMMA) block and gelatin film ablation (as recommended and assessed by the laser system manufacturer), carried out each time the laser system was switched on, revealed no such variation. During the period of the study, a maximum of five treatments was carried out before the beam profile was re-assessed.

Manipulation of the factors that affect healing will be necessary to refine and improve the visual outcome in photorefractive keratectomy.

Several agents are available to manipulate these processes-the most commonly used are corticosteroids. The advent of topically applied cyclo-oxygenase inhibitors may, in the future, allow more selective inhibition of prostaglandin activity. These more selective agents may have different effects on the processes compared to corticosteroids and these differences need to be investigated.

In summary, a series of eyes demonstrating changes of the cylindrical element of their refractive error at 6 months following photorefractive keratectomy for myopia are presented. This represented over half those treated over the same period. The only significant correlate was the presence of a cylindrical refractive error before laser. The

(Morlet et al, 1993; Brancato, Corones et al, 1993; Lohmann and Marshall, 1993). Why do topical steroids reverse refractive regression in some eyes and not in others? Is response dependent on the types of collagen individual eyes produce while healing? Does a change in the water content of the stroma or of another intercellular matrix component contribute to regression, or does it result from topographic changes alone? Without an understanding of these mechanisms, treatment of refractive regression can only be empirical.

4.11 Haze following photorefractive keratectomy: Results

In the Summit group, data were obtained on 692 eyes at 3 months, 612 at 6 months, and 402 at 1 year, and in the Nidek group, 456 eyes at 3 months, 379 at 6 months, and 242 at 1 year. At 3 months, 82 eyes (11.8%) in the Summit group and 15 eyes (3.3%) in the Nidek group had grade 1 or 2 haze. This difference was significant (P = 0.0000006, Yates corrected chi-square test) with a relative risk of 3.6 (95% Taylor Series confidence limits, 2.1 to 6.17). No eye in either group had grade 3 haze. At 6 months, 58 eyes (9.5%) in the Summit group and 6 (1.6%) in the Nidek group had grade 1 or 2 haze. This difference was also significant (P = 0.0000017, Yates corrected chi-square test) with a relative risk of 5.62 (95% confidence limits, 1.73 to 18.28). Again, no eye had grade 3 haze at this point. At 1 year, 28 eyes (7.0%) in the Summit group had haze of grade 1 or greater (25 with grade 1, 2 with grade 2, and 1 with grade 3); only 3 eyes (1.2%) (all with grade 1) in the Nidek group were in this category. This was also

included, except at 1 year at which time no eyes in the Nidek group were observed with these grades and the very few seen with the Summit system failed to yield a statistically significant difference. There were no eyes with grade 2 or greater in the Nidek group after the 3 month examination, and grade 4 was not seen at any time following treatment with either system.

Unfortunately, many patients defaulted on the 1 year follow-up visit, leaving approximately half the treated eyes available for analysis. This probably reflects the private practice setting of the study. Since haze can contribute to glare and reduced contrast sensitivity and since it is not an unreasonable supposition that most patients who default are satisfied with their results, the high default rate suggests that this study may overestimate the prevalence and severity of haze at 1 year. The default rates for the 3 and 6 month visits, when haze is more severe and more prevalent, were considerably smaller (mean 12.8%).

The effect of ablation diameter on the degree of haze is unsettled. In this study population, the maximal ablation diameter was 7.5 mm for the Nidek EC5000 and 5.0 mm for the Summit ExciMed UV 200. Furthermore, the mean optical zone diameter was significantly larger in the Nidek group eyes, with commensurately greater ablation depth. Reports suggest that a difference is present only in the first 3 months (with the wider ablation causing less haze) (Kalski et al, 1996) or that there is no difference (O'Brart et al, 1996). In this study, differences were demonstrated up to 1 year, i.e. 9 months after one would expect the effects of simple diameter variation to have resolved.

In conclusion, these observations tend to confirm that the smooth ablations produced by a scanning delivery system, in contrast to the fixed-beam system in the ExciMed UV 200 device, excite a less vigorous healing response as manifested by the degree of haze. Whether this observed difference affects the post-laser contrast sensitivity of patients has not been determined. This would require a randomised study with measurements taken during the observation periods described since haze is a transient phenomenon.

4.13 Holmium laser thermal keratoplasty following photorefractive keratectomy: Results

Table 13 contains the refractive and vision outcome for each eye at 1 year. The mean spherical equivalent was +0.511 D (SD 0.551 D) at that time. Ten of the 11 eyes were seeing 6/12 or greater, unaided (91%) and nine were within 1.0 D of the target sphere equivalent (82%). Recovery of unaided acuity occurred during the first week in four cases and the first month in the rest. The two eyes greater than 1.0 D from the target both demonstrated regression into substantial hyperopia and had the largest hyperopic errors before LTK. One eye lost greater than one line of best corrected vision (9%) going from 6/5 to 6/7.5 and one gained a line (9%), from 6/12 to 6/7.5.

Table 13. Refractive and visual outcome at 1 year

Patient no.	Pre PRK SE (D)	Pre-LTK			No. of burns	1 year		
		SE (D)	VA unaided	VA best corrected		SE (D)	VA unaided	VA best corrected
1	–7.75	+4.75	6/36	6/5	16	+1.125	6/9	6/5
2	–6.5	+2.625	6/36	6/6	16	+1.50	6/12	6/6
3	–4.25	+2.25	6/12	6/6	8	–0.375	6/9	6/7.5
4	–8.25	+2.125	6/24	6/12	8	0	6/7.5	6/7.5
5	–5.5	+2.125	6/18	6/6	16	+0.25	6/6	6/6
6	–6.75	+2.00	6/7.5	6/5	8	+0.75	6/9	6/7.5
7	–7.00	+1.75	6/24	6/6	8	+0.875	6/18	6/6
8	–7.375	+1.50	6/18	6/5	8	+0.25	6/6	6/6
9	–3.625	+1.25	6/12	6/5	8	+0.75	6/9	6/6
10	–3.375	+1.25	6/12	6/4	8	0	6/5	6/5
11	–6.5	+1.00	6/9	6/5	4	+0.625	6/5	6/5

SE = sphere equivalent; PRK = photorefractive keratectomy; LTK = laser thermal keratoplasty

Table 14 lists the refractive errors over the follow up period.

Table 14. Stability of refractive outcome

	Sphere equivalent (D)		
Patient no.	At 3 months	At 6 months	At 1 year
1	+1.125	+0.125	+1.125
2	+0.375	0	+1.50
3	DNA*	+0.50	–0.375
4	0	+0.50	0
5	–0.125	–0.125	+0.25
6	+0.625	+0.625	+0.75
7	+0.75	+0.75	+0.875
8	+0.25	+0.125	+0.25
9	+0.125	+0.875	+0.75
10	+0.375	+0.625	0
11	DNA	+0.25	+0.625
Mean	+0.389	+0.386	+0.523
SD	0.392	0.328	0.553

*DNA : did not attend for follow up visit

It can be seen that the two eyes demonstrating the greatest regression (patients 1 and 2) regressed during the second 6 months after treatment. Comparison of the mean sphere equivalents for each follow up date demonstrates no significant difference between 3 and 6 months (P = 0.909, Kruskal-Wallis test), 6 and 12 months (P = 0.548, Kruskal-Wallis test), or 3 and 12 months (P = 0.593, Kruskal-Wallis test). No complications occurred during the follow up period and gradual resolution of the "stress lines", seen running between laser burns in the peripheral cornea in the first few months after treatment, was noted, even in cases where the therapeutic effect was stable. The burns themselves became difficult to discern over the second 6 months.

4.14 Holmium laser thermal keratoplasty following photorefractive keratectomy: Discussion

Significant over-correction (greater than 1.0 D) following myopic PRK occurs in approximately 1% of eyes (Epstein, Fagerholm et al, 1994). This can be symptomatic because of anisometropia with an untreated fellow eye or even a successfully treated fellow eye. In those patients of an age susceptible to symptomatic presbyopia, it can be particularly problematic. The mean age of the patients in this study was, not surprisingly, 40 years at the time of their treatment.

Current keratorefractive techniques available for the correction of hyperopia include holmium: YAG laser thermal keratoplasry, hyperopic PRK (Dausch et al, 1993), hyperopic LASIK, and intrastromal refractive implants (Barrett GD, at thc 1995 International Society of Refractive Keratoplasty meeting, San Francisco, CA, USA).

For those eyes with hyperopia following photorefractive keratectomy, simple removal of the corneal epithelium (with or without the use of a postoperative soft contact lens) was considered anecdotally among refractive surgeons as a possible method of stimulating wound healing to try and reduce over-correction (Gordon, 1994). More formal study of this technique has been disappointing (Gauthier et al, 1996) showing no effect on hyperopic errors. Our limited experience of the technique, in this study, would tend to agree with this conclusion.

Holmium: YAG laser thermal keratoplasty has been studied for naturally occurring hyperopia with limited success. Regression of effect from 1 to 2 months, postoperatively, "appears to be the rule" (Durrie et al, 1994). In this study of a small number of eyes with hyperopia induced by PRK, LTK appears considerably more successful; 91% of eyes had 6/12 unaided visual acuity at 1 year and 82% were still within 1.0 D of the target refraction (emmetropia in all cases). Because of the relative rarity of this condition, the numbers of eyes available for study is small. Substantial regression occurred in those eyes with the largest pre-treatment hyperopic errors (both greater than 2.5 D). Because the regression was in relatively few eyes and was relatively mild (the greatest 1 year error being 1.5 D of hyperopia), comparison of the mean spherical equivalents at 3, 6 and 12 months showed no significant difference. These results compare favourably with those published for PRK for low to moderate myopia (Epstein, Fagerholm et al, 1994). Furthermore, early recovery of unaided visual acuity occurs after this treatment (within the first months in all cases and the first week in a third of cases). Most regression of effect in this study occurred in the second six

months after treatment. Perhaps the absence of Bowman's membrane after PRK alters the anterior corneal response to LTK.

LTK for hyperopia, persisting after PRK for myopia, appears on the basis of this study, to be a useful, stable, and safe method of correcting low errors. The long-term stability of the results will need to be observed further.

4.15 Sodium hyaluronate following photorefractive keratectomy: Results

Most of the patients reported having moderate to severe pain at day 1, and none-to-mild pain at the day 2 visit. None of the patients had pain at the day 7 visit (Tables 15 and 16). Six patients, two in the control group and four in the sodium hyaluronate group, received additional analgesic medication during the follow-up study period. There was no statistical difference regarding pain at any of the postoperative visits.

Table 15. Postoperative pain in the sodium hyaluronate group (number of eyes)

Pain	Day 1	Day 2	Day 5	Day 7
None	0	6	17	20
Very mild	0	5	0	0
Mild	5	6	0	0
Moderate	8	3	0	0
Severe	7	0	1	0

Table 16. Postoperative pain in the control group (number of eyes)

Pain	Day 1	Day 2	Day 5	Day 7
None	0	8	16	16
Very mild	0	5	2	1
Mild	1	6	0	0
Moderate	12	0	0	0
Severe	7	1	0	0

The median percentage of epithelium regrowth (per-operative defect diameter versus post-operative defect) was 50% at the first postoperative visit and 100 at the third visit in the two groups. The estimated percentage of epithelial healing was not significantly different between the two groups at any of the visits.

At the third postoperative visit (5 days after laser surgery), four patients, two in the sodium hyaluronate group and two in the control group, failed to attend. Seven days after laser surgery, three patients in the control group did not attend.

No adverse event occurred during the 1-week follow-up period.

4.16 Sodium hyaluronate following photorefractive keratectomy: Discussion

Pain occurring after photorefractive keratectomy is a significant side effect in most patients (Gartry et al, 1991; Seiler, Kahle et al, 1990; Seiler, Wollensak et al, 1991). It starts 2 to 3 hours after treatment, reaches a peak at 12 hours, and abates over a 24-hour

hyaluronate) was produced in the corneal stroma during healing. Experimental work by Molander et al (Molander, Ehinger et al, 1993; Molander, Lindquist, Lind et al, 1993; Molander, Lindquist, Stenvi et al, 1993) showed in rabbits that endogenous hyaluronate (sodium hyaluronate) increased significantly in the corneal tissue following extracapsular lens extraction, anterior segment trauma and radial keratotomy. These findings suggest a possible role of endogenous sodium hyaluronate in the healing of corneal tissue. Vinciguerra et al (Vinciguerra et al, 1991) used topical 0.4% hyaluronic acid routinely in the immediate period following photorefractive keratectomy. In the study by Reim and Saric (Reim 1986) antibiotic drops were applied to the chemically burned rabbit eye followed by sodium hyaluronate application. In our study, sodium hyaluronate was applied first to the laser-treated cornea followed by the application of Maxitrol ointment. This combination of sodium hyaluronate and ointment created a thick smear which perhaps did not allow for optimal penetration of the sodium hyaluronate. This lack of penetration could have contributed to our negative findings. Pain resulting from photorefractive keratectomy remains a universal problem despite the thousands of patients treated and the various local and systemic medications used.

spontaneously by the end of the study follow-up period and another third 3 months following treatment of the second eye. Distant stereopsis was reduced by a mean of 103 seconds of arc (range 60–180) one third of the patients studied. Only those who underwent PRK in the second eye recovered their preoperative distant stereopsis. No change in AC/A ratio or ocular alignment was noted in any case. Significantly greater numbers of patients recovered distant stereopsis following treatment of the second eye than recovered it spontaneously (P = 0.01, tailed value). There was no such significant difference for near stereopsis.

These results indicate that binocular function is disturbed in half those undergoing PRK for myopia for their first eye, as would be expected. Despite this, no patients complained of asthenopia or reduced binocular function. Treatment of the fellow eye restored near and distant stereopsis in all cases studied.

Complications occurring following photorefractive keratectomy for myopia are listed above. In 161 eyes studied, 22.4% had early complications of their procedure. These were most commonly caused by the use of routine post-laser medications. Furthermore, only 6% of 50 patients surveyed, failed to achieve their original aim (wholly or in part) in undergoing the treatment. In no case was the visual outcome compromised by non-refractive complications. It is notable that PRK appears, on these figures, safer than extended wear soft contact lens use.

Astigmatism following photorefractive keratectomy for myopia has been reported as stable as early as 2 to 3 months. A spherical photorefractive keratectomy was carried

out and the manifest refraction of the eyes was followed for 6 months. In over half the eyes presented above there are variations in the cylindrical component of their refraction at 6 months after laser treatment. This observation implies meridional variability in the healing process of the anterior cornea following photorefractive keratectomy.

The effect of topical steroid treatment in eyes that show refractive regression after photorefractive keratectomy to correct myopia was explored. Topical steroid treatment was given to reverse the regression. Refraction and uncorrected visual acuity before and after treatment were measured. Refractive regression after PRK for myopia was permanently reversed in some eyes; final stable refraction was close to the intended value in about half.

To determine the prevalence of moderate to severe subepithelial haze following photorefractive keratectomy for myopia and to compare the prevalence in eyes treated with the Summit ExciMed UV 200 and the Nidek EC5000, a retrospective study of 726 consecutive eyes treated with the Summit system and 494 consecutive eyes treated with the Nidek system with similar mean preoperative refractive errors and outcome was carried out. At 3 months, 11.8% in the Summit group and 3.3% in the Nidek group had grade 1 or 2 haze ($P = 0.0000006$). At 6 months, 9.5% and 1.6%, respectively, had grade 1 or 2 ($P = 0.0000017$). At 1 year, 7.0% in the Summit group had grade 1, 2, or 3, whereas only 1.2% in the Nidek group were in this category (all with grade 1) ($P = 0.0019$), showing that, in the first postoperative year, moderate and more severe haze was significantly less prevalent in eyes treated with the Nidek EC5000 than in those treated with the Summit ExciMed UV200.

Over-correction following myopic photorefractive keratectomy, with a target of emmetropia, leaving a spherical equivalent of more than 1.0 D of hyperopia is of the order of 1%. The study presented above analyses the efficacy, safety, and 1-year stability of outcome of laser thermal keratoplasty (LTK) carried out on eyes with persistent symptomatic hyperopia following photorefractive keratectomy (PRK) for myopia. With ten of the 11 eyes treated seeing 6/12 or greater, unaided (91%) and nine within 1.0 D of the target sphere equivalent (82%), LTK appears safe, predictable, and stable for low errors followed for 1 year.

Finally a randomized clinical trial of topical sodium hyaluronate after excimer laser photorefractive keratectomy showed no effect on pain or corneal epithelial healing.

This dissertation outlines the outcome of photorefractive keratectomy (PRK) for myopia and astigmatism in terms of the refractive outcome showing it to be acceptably accurate and its visual outcome showing it to be acceptably safe. It also confirms the presumed effect on binocular vision of staged bilateral treatment. Following a description of the complications of PRK there is a description of therapeutic measures used to treat the common complication of hyperopia following over-correction of myopia, and the failure of effect of one suggested method of influencing healing following PRK.

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