Turning the tide for gas permeable contact lenses

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Abstract

Gas permeable (GP) lens materials and design technology have advanced in recent years and GP lenses are recognised as providing the wearer with a reduced risk of serious sight-threatening complications, better vision and better long-term comfort. Yet despite these advantages, GP lens prescribing in the UK remains in decline. This thesis investigates how the decline might be addressed by studying the influence of prescribing habits, fitting strategies and lens surface treatments.

Initially a questionnaire was designed to investigate practitioner attitudes and behaviour toward GP lenses, and to ascertain whether eye care practitioner (ECP) reservations were responsible for prescribing decline. This survey found that, despite ECP awareness of the advantages of GP lenses, the challenges of reduced initial comfort and increased time required in fitting, results in significant negative practitioner attitudes. In an effort to address the reservations discovered, an investigation of topical anaesthetic (TA) instillation prior to GP fitting was performed in a large case-control study. The results demonstrated that this practice has no negative clinical impact on the ocular surface, marginally improves patient comfort at fitting, and significantly reduces patient anxiety prior to successive GP lens insertion.

The remainder of this thesis presents the results from a longitudinal study where groups of neophyte and soft lens wearers were fitted with GP lenses for three months; with and without plasma surface treatment (PST). Subjects were monitored and lenses harvested for surface analysis using atomic force microscopy. Examination of GP lenses demonstrated that PST produces smoother surface topographies, prior to and following wear, but this difference reduces after three months wear. Subjects previously wearing soft lenses report lower levels of comfort than neophytes, and PST does not seem to enhance the experience for either group in this cohort.

In summary, this thesis presents important findings about the influence of initial comfort on patient anxiety and practitioner attitudes towards GP lens fitting, and gives important insights into the impact of plasma treatment on comfort and performance over the first three months of lens wear.

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Abbreviations

ANOVA	Analyses of variances
AFM	Atomic force microscopy
ATR	Attenuated total reflection
BOZR	Back optic zone diameter
BVP	Back vertex power
CCLRU	Cornea and Contact Lens Research Unit
CL	Contact lens
CLO	Contact lens optician
CLDEQ	Contact Lens Dry Eye Questionnaire
CS	Contrast sensitivity
CSLM	Confocal scanning light microscopy
CVK	Computerised videokeratography
DEQ	Dry Eye Questionnaire
DK	Oxygen permeability
e	Eccentricity
EEG	Electroencephalograph
ECP	Eye care practitioner
FDA	Food and drug administration
FS	Fluorescein sodium
GOC	General optical council
GP	Gas permeable
GPC	Giant papillary conjunctivitis
HEMA	2-hydroxyethyl methacrylate
HVID	Horizontal visible iris diameter
IOL	Intraocular lens
IR	Infrared
ISPM	Interferential shifting phase microscopy
LM	Light microscopy
MK	Microbial keratitis
PMMA	Polymethylmethacrylate
PST	Plasma surface treatment
RA	Average roughness

1. Introduction and review of the literature

1.1 Introduction

Despite their many advantages, gas permeable (GP) lens prescribing in the UK and worldwide has been gradually declining over the past four decades. GP lenses offer the safest form of contact lens vision correction because they pose the least risk of a wearer developing the most serious ocular condition, microbial keratitis (Stapleton et al., 2008; Forister et al., 2009). Also, GP lenses provide excellent optical correction, often superior to that with other lens types (Ziel et al., 1990a; Bennett and Hom, 2004). This is particularly evident in eyes with irregular or scarred corneal surfaces where the GP lens 'masks' the irregularity (Griffiths et al., 1998; Looi, Lim and Tan, 2002; Margolis, Perez and Thakrar, 2007). Continuing improvements in soft lens designs and a belief that GP lenses are only fitted in complex cases may be two contributory factors in GP prescribing decline. Other factors may include negative practitioner attitudes towards GP lenses, such as concerns regarding initial and adapted comfort, and also a perceived difficulty and increased chair time needed to fit GP lenses compared with other lens types.

There are various possible approaches to encourage continued or increased GP fitting. Practitioner attitudes towards GP lenses and the skills needed to successfully fit them could be addressed in education; fitting practices such as the use of fitting sets, topical ocular anaesthetic and specialised fitting equipment or techniques may be influential in fitting success, in addition to the development of material treatments and designs to improve comfort. Any strategy to increase endorsement of the GP contact lens option amongst today's practitioners must be evidence-based, and this thesis presents some of the substantiation for continued GP presence in the contact lens field.

This PhD initially reviews current literature to ascertain whether GP lenses are fit for the modern contact lens practice, then goes on to investigate practitioner attitudes relating to GP lenses. In response to these findings, specific areas surrounding GP practice, and in particular, the fitting of GP lenses were selected for further study. The work aimed to discover whether existing soft lenses and non-contact lens wearers can be successfully fitted with GP lenses. Finally, the effect of plasma surface treatment was investigated to see whether it impacts comfort and performance of GP lens wear.

Also, the lens surface itself is examined to discover how surface treatment impacts the lens surface appearance.

1.2 The development of contact lenses

The first documented concept of contact lenses was attributed to Leonardo da Vinci in 1508. Da Vinci illustrated a man leaning over a glass bowl filled with water, and this is often interpreted as neutralisation of the cornea by contact with the water (Phillips and Speedwell, 1997) (Figure 1.1). However, more recent examination of da Vinci's original manuscripts suggests that his drawings are actually mirrors, and therefore he has been wrongly credited with the first contact lens theory (Heitz, 2003).

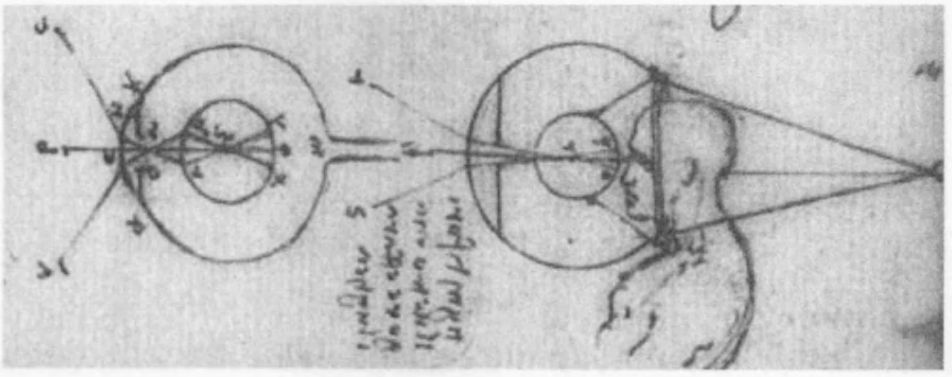


Figure 1.1 Codex D, folio 3 by Leonardo da Vinci (Phillips and Speedwell, 1997).

During the 17th and 18th Centuries, scientists performed experiments and produced theories about neutralisation of the corneal power. In 1637, Rene Descartes described a fluid-filled tube, with a glass lens at the distal end, that would be placed against the cornea to provide an image of the retina (Bennett and Weissman, 2005). Much later, in 1801, Thomas Young discovered the refractive effects of the cornea by neutralising the dioptric power with a contact lens and auxiliary lens combination (Bennett and Weissman, 2005). In 1827, George B Airy investigated ocular astigmatism and developed a theory from which he was able to produce a theoretical correction using a back surface toric lens (Phillips and Speedwell, 1997). Airy also collaborated with John Herschel, a mathematician and astronomer, who was interested in astigmatism and corneal irregularity (Bowden and Gasson, 2004). Herschel suggested, in 1845,

correcting 'very bad cases of irregular cornea' by using 'some transparent animal jelly contained in a spherical capsule of glass', and then went on to suggest whether 'an actual mould of the cornea might be taken and impressed on some transparent medium', although there is no evidence that he actually did this (Phillips and Speedwell, 1997).

The late 19th Century produced a wave of developments. In 1887, Fredrich A Müller and Albert C Müller, ocular prosthesis manufacturers in Germany, produced the first scleral lens from a blown glass shell for a patient who had skin cancer (Bennett and Weissman, 2005). The cancer had resulted in the destruction and removal of the right lower lid and the temporal part of the upper lid. The glass shell encased the cornea, but did not touch it, and trapped fluid to prevent desiccation of the cornea. The shell was transparent and permitted the patient to see through it. The patient was reported to wear the shell successfully day and night for many years. Around the same time, in 1888, Adolf Fick experimented with making moulds of rabbit corneas and human cadaver eyes to construct glass shells for six patients with corneal opacities (Efron and Pearson, 1988). However, Fick was unable to achieve the same success as the Müllers. In 1889, August Müller, a student at the University of Kiel, produced his thesis entitled "Spectacle lenses and corneal lenses", in which he reported his attempts to correct his own myopia with a corneal lens – the first time this name was applied to such a 'contact' lens.

By the beginning of the 20th Century, lens choices were limited to the Müllers' blown glass lenses or to Carl Zeiss' ground glass lenses. The former were more comfortable and could be worn for long periods of time, but lacked the optical quality of the Zeiss lenses. In any case, the lenses were principally provided for therapeutic needs and not for cosmetic, refractive wants. For this, it was not until the 1930's when the first commercial, hand-blown, glass, scleral contact lenses were made by Adolf Wilhelm Mueller-Welt, who supplied them to German officers during World War II (Mueller-Welt, 2005).

By the 1930s, Germany was no longer alone in scleral contact lens development, which was taking place in various parts of the world simultaneously. This included the development of eye impression techniques (e.g. Josef Dallos in London, Theodore

E Obrig in New York, CL Stevens in New York), the transition from glass to plastic materials (e.g. William Feinbloom in New York, Dr Istvan Györffy in Budapest, CW Dixey and Sons Ltd in the UK), and the modification of lens designs (e.g. Prof Leopold Heine in Kiel, Josef Dallos in Budapest, Theodore E Obrig in New York). The plastic materials that superseded glass were initially resins derived from oil seeds or cellulose in cotton, and from the petrochemical industry (Bennett and Weissman, 2005). The most important of these new materials was polymethylmethacrylate (PMMA), developed by Crawford and Hill in 1931 (Bennett and Hom, 2004). This material was light-weight, chemically stable, cost-effective to produce, easy to manufacture, although virtually impermeable to oxygen diffusion (Phillips and Speedwell, 1997).

So far, lens designs had been full clearance scleral lenses, but after World War II there was a rapid series of developments in corneal lenses. The first corneal lens was made, in 1946, by Kevin Tuohy when he accidentally cracked the central corneal portion away from the outer scleral zone to produce a perfect disc (Rosenthal, 2009). A patent for this mono-curve corneal lens was granted in 1950 (Phillips and Speedwell, 1997). George Butterfield modified Tuohy's design, in 1950, to produce a bicurve corneal lens with a reduced diameter (9.5mm) and thickness (0.2mm) (Phillips and Speedwell, 1997). The design was further modified and produced by both lathe-cutting and moulding techniques in the UK and Germany. In 1952, Dickinson (UK) produced a design which was much smaller than the original Tuohy design (9.5mm diameter) which was called the 'Microlens' (Bowden and Gasson, 2004). Due to its small diameter it had the ability to correct up to 4D of corneal astigmatism (Phillips and Speedwell, 1997).

Both Tuohy and Dickinson's lens designs were simple monocurves, which produced apical touch and caused corneal erosions. Further development by Norman Bier in 1955 introduced the 'Contour Principle' lens, which had multiple back surface curves. These additional curves in the lens periphery allowed the lens to align with the central cornea and to provide a 1.25mm band of edge clearance at the periphery (Norman, 1957). Bier also observed that flatter corneas required an increased degree of lens flattening to match the peripheral cornea, and he developed fitting sets in which the appropriate peripheral flattening increased with increasing back optic zone radius

(BOZR) (Norman, 1957). However, this system was complicated, and instead was replaced, from 1960, by fitting sets with standard peripheral flattening.

1.3 Modern GP lenses

By the end of the 1960's lens design had advanced significantly toward the narrow peripheral zone multicurve or aspheric corneal designs that are common today, and experimentation had also begun with designing bifocal contact lenses and using flat-fitting lenses to reduce or eradicate myopic spectacle prescriptions (Bennett and Weissman, 2005).

However, the continuing problem lay with the available lens materials. Rigid lenses were still made from polymethylmethacrylate (PMMA), which had excellent optical clarity, machinability, wettability, stability and durability, but it was non-permeable to oxygen (Hom and Bennett, 1997). This led to various problems associated with a lack of corneal oxygen supply, including corneal endothelial changes, corneal oedema and warpage, and corneal exhaustion syndrome (Stocker and Schoessler, 1985; Holden, 1989; Sweeney, 1992; Jupiter and Karesh, 1999).

During the 1970's, chemists discovered that the inclusion of silicone and fluorine components to rigid lenses polymers produced a gas permeable (GP) rigid lens material (Bennett and Hom, 2004). This was an extremely important development as the gas permeable lens material was able to provide sufficient oxygen to meet the cornea's needs (Bennett and Hom, 2004). The first such material, developed in 1971 by Norman Gaylord, was a silicone/acrylate combination, marketed as 'Polycon'. In 1979, cellulose acetate butyrate (CAB) was the first gas permeable material to be approved by the US FDA, but it was dimensionally unstable, difficult to manufacture and its oxygen permeability, although better than PMMA, was still poor. In 1975, Polymer Technology was established in Boston USA to develop oxygen permeable contact lens materials. Their first lens was the Boston I material, and they followed this with further materials (II, III and IV), which incorporated silicone and fluorine. The Boston IV material is still widely used today.

These improvements in GP materials have continued to the present day. The latest advance is the Menicon Z material which has a "hyper-oxygen transmissibility", permitting GP lens wear to move from conventional daily wear to extended overnight wear (FDA approved in 2002). For GP lens design, with these advances in oxygen permeability, the last remaining issue was to improve initial lens wear comfort. Lens design has returned to its roots in scleral lenses to meet this challenge, with the introduction of large diameter corneal and semi-scleral designs, such as the SoClear lens design.

1.4 The arrival of soft contact lenses

The first soft contact lenses were introduced in the early 1960's. Professor Otto Wichterle and Drahoslav Lim, working at the Institute of Macromolecular Chemistry in Prague, developed a new hydrogel polymer called 2-hydroxyethylmethacrylate (pHEMA, Hydron), which was transparent, absorbed up to 40% of its weight in water and had good mechanical properties. At his home, Prof Wichterle experimented in transforming this material into a suitable shape for a contact lens, using his son's construction set to assemble a prototype centrifugal casting machine. His work led, in 1964, to the first soft lenses, the Geltakt lens and the SPOFA-Lens, manufactured by Protetika in Czechoslovakia. In 1964, Wichterle's patent was sold and eventually purchased by Bausch & Lomb, who then produced the Soflens using a spun-cast method to produce the contact lens. The lens was marketed in 1971 after receiving approval as a 'drug' from the Food and Drug Administration (FDA) (Bennett and Weissman, 2005).

Initially, soft contact lenses (SCLs) were conventionally worn for any length of time (typically longer than six months) on a day wear only basis, and the lens changed when the lens performance deteriorated due to age, deposition or damage (Hom and Bennett, 1997). However, as manufacturing methods improved, soft contact lenses underwent a dramatic change. In 1976, the first toric soft lenses manufactured by CIBA Vision were approved. In 1977, the first aspheric soft bifocal contact lens, called the "Alges" (a centre-near design), was produced by Barnes-Hind. In 1980, disposable lenses were first considered following work on soft lens surface deposits, concluding that an inexpensive, disposable lens should be manufactured for weekly or

fortnightly replacement (Tripathi, Tripathi and Ruben, 1980). However, manufacturing tolerance meant that this ideal could not be realised until 1995, when Vistakon released the "1-Day Acuvue" lens. The advantages of disposable lenses are reduced maintenance, better compliance and physiological advantages for the eyes (Hom and Bennett, 1997).

The most dramatic transformation in soft lens design has been the development of silicone hydrogel materials in the late 1990's, which has permitted overnight and extended wear for soft lenses. Initial attempts at extended wear in the early 1980's, using high-water content hydrogel materials, were not successful, since the oxygen transmissibility of the hydrogels was insufficient to maintain adequate corneal oxygenation during overnight eyelid closure. However, just as combining silicone with PMMA extended the oxygen transmissibility of GP lens materials, the same has been done with pHEMA. The first silicone hydrogel lenses (Night and Day, CIBA Vision; Purevision, Bausch & Lomb) were introduced in 1999 for 30 nights continuous wear, and since then further generations of silicone hydrogels have been developed that have refined the materials available.

1.5 The effect of technology developments on prescribing rates between GP and soft lenses

The historical roots of GP lenses in scleral lens design and in the development of rigid gas permeable materials gave GP lenses a head-start over soft lenses in addressing many of the issues associated with successful contact lens wear. Current GP lenses provide stable, clear vision, good comfort with long wearing times, low risks of infection, ease of care and handling, and good manufacturing quality (McMahon, 2003; Bennett and Hom, 2004). Their principal disadvantage is the inferior initial wear comfort, in comparison with soft lenses.

Soft lenses are much larger in diameter than GP lenses, and they cover the entire cornea and stretch onto the bulbar conjunctiva. In contrast to GP lenses, their material is soft and flexible meaning that they are immediately comfortable when worn (Gasson and Morris, 1998). This comfort was for a long time the main advantage of

soft lenses over GP lenses, even as both lens materials and designs developed during the 1970's and 1980's. Indeed, 5 years after the introduction of soft lenses, Atkinson predicted their success and a consequent decline in GP lens prescribing. At that time, he reported that soft lenses already made up 50% of contact lens fits recorded in the UK (Atkinson, 1976), and by 1991 this had increased to 61% of lens fits (Pearson, 1998).

Yet in the early 1990's, GP lenses were still gaining a sizeable proportion of the contact lens market. Since then, this proportion has decreased as the enormous investment in soft lens design, materials and manufacturing, alongside huge advertising budgets by large multi-national companies, has greatly expanded the contact lens market, principally into soft lens wear, to the loss of GP lens wear.

These changes can be followed through a series of surveys conducted over the last 15 years. In 1996, a survey designed to investigate prescribing trends was randomly distributed to 1000 UK eye care practitioners (ECPs) who were asked for details about 10 consecutive contact lens fits (Morgan and Efron, 2006). This survey has since been distributed annually, both in the UK and internationally, to monitor contact lens prescribing trends (Morgan et al., 2002; Morgan and Efron, 2006; Morgan et al., 2006). In 1996, 23% of new contact lens fits were GP, indicating a marked reduction in GP prescribing between 1991 and 1996, and in subsequent publications of the survey results a steady decline in rigid lens prescribing has been recorded. By 2007, just 3% of new fits were GP, although 16% of refits were GP (Morgan, 2007). This may indicate that GPs are often refitted to existing GP wearers or in cases where soft lens fitting was unsuccessful.

A similar market trend has been observed in the USA. In 1975, approximately 2 million patients wore soft contact lenses, but within 15 years this number rose to 21.8 million, accounting for 76% of all contact lens wearers (McMahon and Zadnik, 2000). The decline in GP lens popularity in America continued, reducing from 24% of all fits in 1990 to 8% of fits in 2005 (Morgan et al., 2006). An independent survey by Barr reported 16% GP fits in 2000, which would appear to correlate with the trends described by Morgan et al. (Cheung, Cho and Edwards, 2002).

In an international survey, (Morgan et al., 2006) reported a large variation in contact lens markets around the world. In Russia, Sweden and Norway, GP lens fitting accounted for ≤2% of lens wearers; yet in Germany, the Netherlands and Japan, GP lenses prescribing accounted for ≥20% of contact lens wearers (Morgan et al., 2006). Wide variation between countries is also observed for soft contact lenses. These differences may be attributed to variability in continuing contact lens education standards, lens marketing strategies, inter-country culture and lifestyle differences. For example, it is hypothesised that existing GP patients may not attend optometric practice as frequently as soft contact lens wearers, perhaps not until a problem arises, when they seek an optometric consultation. This may artificially reduce the perceived GP contact lens population.

In response to the international results produced by Morgan et al, Eef van der Worp made some comments on why he feels GP lens fitting remains high in the Netherlands (Van der Worp, 2003). He attributes GP lens success to a strong support network, which includes contact lens associations, practitioners, ophthalmologists, and contact lens companies, with technical excellence and a willingness to invest in the GP lens market. In Dutch, the literal translation of 'rigid' lenses is 'stable' lenses and this may help give the patient a more favourable impression of the lens type. Education in the Netherlands is also technically orientated; following qualification as an optician, a further 2 year part-time training course in contact lens fitting is required. This may mean that Dutch practitioners have a greater interest in the technical aspects of fitting contact lenses than an average UK practitioner. In teaching clinics, 50% of patients examined wear GP lenses, so clinicians gain practical experience while they train. Van der Worp suggests that it is the contact lens fitter/optometrist who controls the market, and if they find fitting these lenses rewarding, then the statistics will reflect this (Van der Worp, 2003).

Morgan et al's international survey reported that, in many countries, the type of GP lens supplied is often for a 'complex fit' requiring a toric, multifocal, orthokeratology or extended-wear lens (Morgan et al., 2006). A Canadian survey reports an increase in GP lenses for extended wear from 0.7% to 30.6% between 2000 and 2006. Almost half of GP lenses fitted in Canada were spherical; however, 18.6% were toric, 19.5% multi-focal and 6.6% were for orthokeratology (Woods et al., 2007). Some countries

with low figures for GP lens prescribing have a relatively high proportion of orthokeratology fitting, for example, Australia and Belgium (Morgan et al. 2006). These figures appear to support the hypothesis that GP lens fitting is becoming a specialist skill area and GP lenses are only adopted for difficult cases (Efron, 2001).

1.6 Comfort with contact lens wear

Comfort is a particularly important issue for both contact lens wearers and contact lens practitioners, because it would appear that initial comfort with GP lenses is a deterrent to fitting or being fitted. Conversely, SCLs have good initial comfort, but generally comfort-related issues are cited as the primary reason for contact lens dissatisfaction and discontinuation (Richdale et al., 2007).

1.6.1 GP lens wear comfort

GP lenses are generally considered to be less comfortable than soft lenses due to their higher modulus of elasticity creating more mechanical impact on the ocular structures (Fonn, Gauthier and Pritchard, 1995), particularly the eye lids (Bennett, 1999). However, once adapted to GP lenses, they are perceived to be as comfortable as soft lenses (Morgan, Maldonado-Codina and Efron, 2003).

When a GP lens is initially placed on the eye most patients report ocular discomfort, because the lens moves on the cornea and the lids sense this movement (Bennett, 1999). Lid architecture, led tension, blink rate and blink action are factors which may contribute to the movement and fit of the GP lens (Carney et al., 1996), and these, combined with the lens dynamics, influence patient comfort (Carney et al., 1997). Soft lenses are initially more comfortable than GP lenses, because soft materials have a reduced modulus of elasticity compared to GP lens materials, and soft lenses have generally larger diameters which extend beyond the limbus, thus leading to less lid sensation (Phillips and Speedwell, 1997).

One significant reason for lens discontinuation, cited by contact lens wearers in general, is subjective dryness (Richdale et al., 2007). A study comparing extended GP and soft lens wearers found that the experienced GP lens wearers reported less

dryness than the soft lens wearers (Maldonado-Codina et al., 2005a). Often symptoms of ocular dryness do not correlate well with signs or diagnostic tests, therefore contact lens related dryness relies more on patient reports or dry eye questionnaire responses, rather than objective tests which may be unreliable (Nichols, 2006). Soft lens materials are water-based, and these dehydrate during lens wear, perhaps contributing to the dryness sensation (Pritchard and Fonn, 1995).

Initial discomfort with GP contact lenses may deter patients and practitioners from selecting this lens type (Fujita et al., 2004). A study aiming to predict GP daily wear success found that approximately 50% of drop-out subjects cited unacceptable adapted comfort as the reason for discontinuation, and the authors suggested that new lens designs or other strategies should be employed to improve comfort during the adaptation period (Polse et al., 1999). One controversial technique to improve initial comfort is topical anaesthetic use during GP fitting (Bennett, 1999). This is discussed further in Section 1.10.7.

One further issue for GP lens wear relates to tear exchange under the lens. While this is a positive for corneal health, since it allows improved oxygen supply to the cornea underlying the contact lens and the exchange of nutrients and waste products in the tear film, it also permits foreign bodies (e.g. dust particles) to become trapped beneath the lens. This can cause acute, short-lived discomfort which is alleviated once the foreign body is removed (Fonn et al., 1995).

1.6.2 Soft lens wear comfort

Many SCL wearers experience discomfort when wearing their lenses, as discussed earlier, this is the principal reason for discontinuation of lens wear or reduction in wearing schedule (Richdale et al., 2007). It is impossible to quantify the exact number of patients who have stopped wearing lenses, however, in the USA 73% patients are reported to have stopped wear due to discomfort and 50% patients in the UK ceased CL wear, citing the same problem (Pritchard, 2001). It has also been reported that a large number of wearers discontinue CL wear for periods of time before restarting CL wear again (Weed, Fonn and Potvin, 1993). A second study suggests there are

approximately 2.1 million CL drop-outs in the UK, indicating that there are a large number of discontented or failed contact lens wearers in the UK (Morgan, 2001).
The primary symptom reported in SCL wearers is dryness (Nichols et al., 2002). SCL wearers are reported to be 12 times more likely to experience dryness symptoms than clinical emmetropes (Nichols and Sinnott, 2006). Contact lens induced dry eye (CLIDE) can cause ocular discomfort and may occur as a result of worsening pre-existing dry eye or dry eye being induced in otherwise asymptomatic patients. The symptoms include dryness, irritation, burning, stinging, foreign body sensation, visual blurring, or general discomfort (Fonn, Situ and Simpson, 1999). The causes of dryness are complex and multi-factorial. SCL material parameters such as water content, ionicity, oxygen permeability, refractive index and modulus all influence comfort and CLIDE. Dehydration of a hydrogel lens affects the fit of the lens, as the lens parameters are altered and this results in reduced oxygen transmissibility (Pritchard and Fonn, 1995). The tear film interaction with the lens and ocular surface, poor tear quality, lens deposition or adverse reaction to contact lens solutions all contribute to dry eye and lid disease.

1.6.3 Comparison of GP and SCL wear comfort

A study by Fonn and Holden reported superior comfort with GP lenses in an extended wear study comparing subjects wearing a GP lens in one eye and a hydrogel soft lens in the other eye (Fonn and Holden, 1988). A later study recruited neophyte subjects to compare a soft and a GP lens worn simultaneously during a six-month study period. Subjects reported no statistically significant difference in adapted comfort, using visual analogue scales (VAS), over the third to sixth months of wear (Fonn et al., 1995). However, at the end of the study, subjects were asked to choose which lens was more comfortable during the study, and the soft lenses were favoured. Limitations to this study were its size, 27 subjects were recruited, but only 16 subjects completed the study (dropouts did not cite contact lens related issues as the reason); also the study ran over a relatively short time scale.

Further studies reported no significant difference in frequency of symptoms between adapted soft and GP lens wearers. These included a study comparing different forms of optical correction, including spectacles, soft contact lenses and GP contact lenses

(Vajdic et al., 1999), and studies comparing clinical performance of GP and soft hyper-transmissible lenses in extended wear (Morgan et al., 2003).

Some reports suggest that patients can achieve comfort with a hyper-transmissible GP lens, equivalent to a hyper-transmissible soft lens, after only 8 days, provided a planned wearing schedule is followed (Fujita et al., 2004). Fujita et al. reported an average adaptation time of 23 days, ranging from 2-84 days (Fujita et al., 2004), indicating that adaptation is variable and must depend on a variety of factors, including subject personality, ocular design and lens fit.

In Fujita et al.'s study, patient adaptation to GP lenses was monitored using visual analogue scales (VAS) completed by the patient at various stages during initial lens wear (Jones, 2003). It appears that early evaluation of comfort may prevent wasted practitioner efforts to improve initial comfort for those patients who ultimately will not adapt to GP lens wear.

1.7 Ocular surface sensation

1.7.1 Ocular anatomy

The anterior segment of the eye consists of the lens, iris, cornea, conjunctiva, tear film and eyelids. Contact lens wear is affected by and in turn affects the cornea, conjunctiva, tear film and eyelids, Figure 1.2.

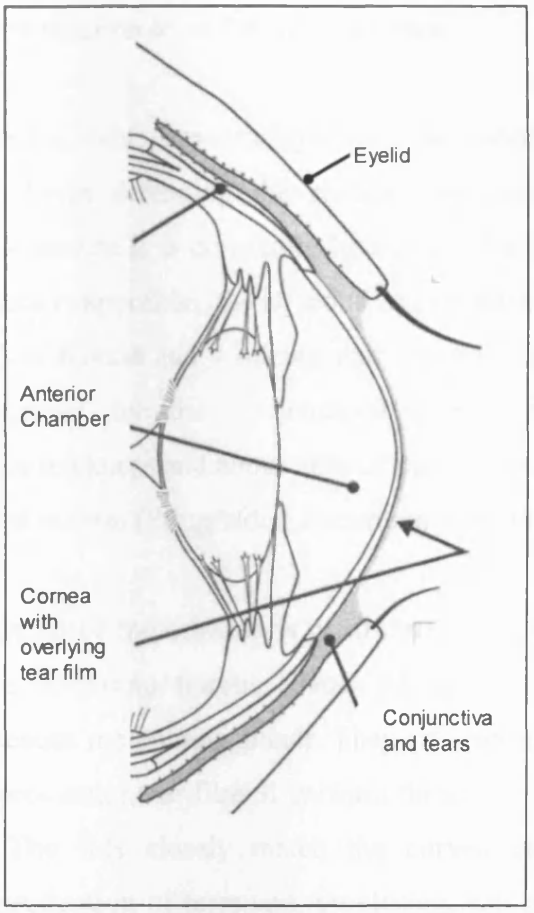


Figure 1.2 Anterior segment diagram adapted from Doughty (1999).

The cornea is the transparent, avascular surface at the anterior eye. It permits light rays to enter the eye, via the pupil to form an image on the retina. The corneal surface must be smooth and regular to optimise visual function and avoid light scattering of incident rays.

The average cornea is 11.7mm in horizontal diameter with a mean central thickness 0.54±0.03mm (Doughty and Zaman, 2000). The corneal surface is spherical in the central 3mm, but flattens progressively toward the periphery giving it an elliptical shape. The cornea protects the eye and is also responsible for 70% of the eye's refractive power. The cornea is made up from five layers; the epithelium, Bowman's layer, the stroma, Descemet's membrane and the endothelium.

The conjunctiva is a mucous membrane, it is continuous with the cornea and may be divided into the bulbar portion which covers the anterior sclera and a palpebral or

tarsal portion which lines the tarsal plate of the eyelids. The conjunctival glands or goblet cells secrete the mucoproteins found in the tears.

The tear film provides a stable, smooth layer over the cornea. Tears aid optics, and have a protective role in defending the cornea from bacterial micro-organisms, bathing the cornea to ensure it is constantly hydrated. The tears consist of an outer oily layer which reduce evaporation, the aqueous layer produced by the lacrimal gland and accessory glands of Krause and Wolfring, and a mucoid layer at the base covering the epithelium, secreted by the conjunctival goblet cells. Tear volume is approximately 7μm in thickness and about 90% of this volume is contained in the tear prism along the eyelid margin (Pflugfelder, Beuerman and Stern, 2004).

The eyelids are made up of the orbicularis oculi muscle behind which lies the tarsal plate which consists of dense fibrous tissue. Along the eyelid margins are the openings of the sebaceous meibomian glands. They are appropriately shaped to ensure the production of a pre-ocular tear film of uniform thickness, to produce a transparent refracting surface. The lids closely match the curved corneal surface and are responsible for the production of tears and, by closing, can provide a protective role (McGowan, Lawrenson and Ruskell, 1994).

1.7.2 Corneal and conjunctival sensation

1.7.2.1 Innervation of the ocular surface

The cornea is the most densely innervated epithelial surface in the body (Pflugfelder et al., 2004). The precise number of nerve endings is not yet known, however it is estimated to be between 315,000 and 630,000 (Muller et al., 2003). Animal model studies have shown that receptive field sizes are large and overlap extensively, giving a large amplification effect, but reduce the ability to localise sensations (Tanelian and Beuerman, 1984; Belmonte et al., 1991; MacIver and Tanelian, 1993b). Comparatively, the conjunctival innervation is sparse and sensitivity decreases on departure from the limbus (Lawrenson and Ruskell, 1993). Consequently, conjunctival mechanical sensitivity is lower than that of the cornea (Boberg-Ans, 1955). The eye lid margin has also been found to be more sensitive to mechanical stimulation than the conjunctiva (Norn, 1973; McGowan et al., 1994).

Innervation is supplied by the ophthalmic branch, which is served by the trigeminal nerve. The ophthalmic nerve branches into the frontal, lacrimal and nasocillary nerves. The long ciliary nerve penetrates the posterior eye and then passes between the sclera and choroid to supply the cornea (Muller et al., 2003). The conjunctiva is innervated by various sensory branches of the trigeminal nerve; the lacrimal nerve and the infratrochlear division of the nasociliary branch of the ophthalmic nerve (Burton, 1992).

The corneal nerve architecture begins with a circular limbal plexus with radial branches extending into the central cornea. *In vivo* confocal microscopy has discovered that these leashes insert predominantly in the 6-12 (o'clock) direction, but do not traverse the entire cornea, and loop back before reaching the corneal apex (Muller et al., 2003). The remaining leashes enter the cornea radially from the limbus from opposing sources i.e. 5-11, 7-1 etc (Muller et al., 1997). The nerves lose their myelination as they progress through the corneal stroma toward the apex. As they do so, they branch repeatedly sending fibres anteriorly to penetrate Bowman's layer at about 400 sites across the peripheral and central cornea (Muller, Pels and Vrensen, 1996). The nerve fibres branch again, and bend and run beneath the basal epithelial cell layer where they further divide and interconnect with peripheral nerves to also form a sub-basal epithelial plexus beneath Bowman's layer (Schimmelpfennig, 1982).

There are two types of nerve fibre; myelinated Aδ and unmyelinated C fibres. Myelinated Aδ fibres are small and straight, they run parallel and deeper within the basal cell layer and have high conduction velocity (mean 6m/s). They are thought to supply polymodal nociceptors and to respond to mechanical simuli (MacIver and Tanelian, 1993a; MacIver and Tanelian, 1993b; Muller et al., 2003). Unmyelinated C fibres are large, beaded and conduct at a lower velocity (2 m/s), running upward from the epithelial plexus towards the surface. They respond to thermal and/or chemical stimuli. Many of them have also been found to be polymodal and to respond to near-noxious mechanical stimuli (Tanelian and Beuerman, 1984; Belmonte et al., 1991; Gallar et al., 1993; Muller et al., 1996).

The conjunctival fibres are unmyelinated and terminate beneath the epithelium in the substantia propria, as free nerve endings, although, occasional fibres seem to pass into the basal lamina and terminate within the epithelium (Ruskell, 1985).

1.7.2.2 Eyelid sensation

The eyelids have high sensitivity levels; they are highest at the marginal angle. This is thought to be due to the distribution of sensory terminals including both corpuscular (specialised) nerve endings and free (unspecialised nerve endings) (McGowan et al., 1994). Eyelid sensitivity varies between individuals, but generally the inferior lid is more sensitive than the superior (McGowan et al., 1994).

1.7.3 Effect of contact lens wear on corneal sensitivity

Contact lens wear produces both short-term and long-term changes in corneal sensitivity. The studies on short-term changes relate only to PMMA and low water-content soft lens wear. PMMA wear produces a reduction, on average, of about 110% in the corneal sensitivity of an adapted lens wearer, over a 12 hour wearing period (Millodot, 1976). Soft lens wear (38% water content) produces a similar effect, although the drop is about half that produced by PMMA lenses. Examination of a higher water content lens also found a reduction in sensitivity, although the magnitude was less (Millodot, 1976). Following 8 hours contact lens wear, sensitivity significantly recovered within the first hour after lens removal. Complete recovery took longer and was related to duration of contact lens wear (Knoll and WIlliams, 1970; Millodot, 1975; Tanelian and Beuerman, 1980). For soft lens wearers, recovery of the majority of sensitivity occurs within one hour of lens removal (Millodot, 1974; Larke and Hirji, 1979; Velasco et al., 1994).

Millodot also assessed the effect of long-term PMMA lens wear on the sensitivity of subjects who had worn lenses from between 1 to 22 years. He found a gradual decline, commencing after the first few years of wear. Those subjects with the longest wear time (17-22 years) had a three-fold reduction in their sensitivity, although they remained asymptomatic. After discontinuation of wear, recovery took place over many months, rather than overnight. It appears that the greater the number

of years of wear, the longer it takes to recover (Millodot, 1978ba; Tanelian and Beuerman, 1980).

An independent comparison of adapted GP and soft lens wearers, found that both groups have reduced corneal sensitivity, compared with non-lens wearers, but there was no difference according to lens type (Murphy et al., 1999).

1.7.4 Possible mechanisms of long-term contact lens wear induced corneal surface sensitivity loss

There are three possible reasons why the sensitivity loss occurs: sensory adaptation to mechanical stimulation, metabolic impairment of the cornea affecting the nerves and corneal acidosis suppressing nerve function.

Evidence shows that lenses which produce less mechanical stimulation may give rise to a smaller decrease in corneal sensitivity (Lowther and Hill, 1968; Morganroth and Richman, 1969; Polse, 1978; McGowan et al., 1994). However, there are three clear reasons this may be incorrect: (i) when the eyes are closed overnight, sensitivity declines as a result of the lower oxygen pressure at the corneal surface and not as a result of any mechanical stimulation (Millodot and O'Leary, 1979); (ii) the cornea will have a reduction in sensitivity if exposed to reduced partial atmospheric pressure, again without any mechanical action (Millodot and O'Leary, 1980); (iii) the influence of lens oxygen permeability (Bergenske and Polse, 1987). Two experiments illustrate this effect - in the first experiment, subjects were fitted with a PMMA lens in one eye, and a GP lens in the other. After a three month period of wear a reduction in sensitivity was measured in the PMMA fitted eye, while practically no change occurred in the GP fitted eye (Millodot and Henson, 1979). A second experiment compared the effect of three types of rigid contact lenses, each with a different oxygen permeability, and concluded that epithelial oxygen availability was directly related to changes in corneal sensitivity (Millodot, 1994).

The cornea requires oxygen to maintain its integrity and to prevent infection, and it derives most of its oxygen supply from the atmosphere (Gardner et al., 2005). Contact lens wear creates a potential barrier between atmospheric oxygen and the

cornea. Oxygen is available at the cornea either by transport of oxygen through the contact lens material or by the pumping of tears beneath the contact lens during blinking (Gasson and Morris, 1998).

Oxygen permeability (Dk) is the rate of oxygen flow under specified conditions through a unit area of contact lens material of unit thickness when subjected to unit pressure differences (Phillips and Speedwell, 1997). Dk is determined by D: diffusion, this is the rate molecules can pass through the material, and K: solubility, this is governed by the number of oxygen molecules held in the polymer (Bennett and Hom, 2004). Dk increases with increasing temperature (Morris, 2004) and is measured in Fatt units (Morris, 2004).

Oxygen transmissibility (Dk/t) denotes permeability related to the thickness (t) of the contact lens (Fink, Mitchell and Hill, 2006). Dk/t of a contact lens determines how much oxygen is available to the cornea during contact lens wear. This is important because hypoxia causes changes to the structure and function of the cornea (Holden and Mertz, 1984). A minimum Dk/t value of 24.1 units is required in a contact lens to avoid corneal swelling during daily wear (Fink et al., 2006), however oxygen supply and corneal demand cannot be determined by Dk/t alone, because the characteristics of the contact lens system, the tears and the cornea all influence the oxygen flux of the cornea (Bennett and Hom, 2004).

From these experiments we can draw the conclusion that the corneal sensitivity reduction in long-term contact lens wear is mediated by a change in the oxygen supply to the cornea, and not simply by any mechanical adaptation. However, the pathway of how a reduced oxygen pressure affects the corneal nerves is not clear, although interference in the production of the neurotransmitter acetylcholine has been proposed. The corneal epithelium has the highest concentration of acetylcholine of any tissue in the body (Mindel and Mittag, 1977), and recently a sympathetic nerve supply has been found in the cornea (Ueda, del Cerro and LaCascio, 1989; Lind and Cavanagh, 1993; Marfurt and Ellis, 1993). Pesin and Candia proposed that acetylcholine plays a role in the regulation of Na+ and Cl- transport, both of which are important in the production of nerve impulses (Pesin and Candia, 1982). If this theory is correct, then we can explain the changes in sensitivity associated with contact lens

wear as being caused by an interference in the synthesis of acetylcholine (perhaps through acetyltransferase, an enzyme used to synthesise (Mindel and Mittag, 1978; Millodot and O'Leary, 1979; Millodot, 1994).

The third possible pathway of sensitivity reduction concerns an alteration in the pH of the cornea. The pH of the body is closely regulated at 7.4, and even a change of 0.05 can produce severe complications. The stromal pH is usually maintained at 7.54, but closed eye wear of a PMMA lens can lead to a decrease of pH to 7.01. This reduction is caused by respiratory acidosis due to hypercapnia (accumulation of carbon dioxide), which in turn leads to a depression of nerve function (Brennan and Bruce, 1991).

The actual reduction in sensitivity is probably a combination of these three influences, although the mode of interaction remains unclear, and will be different for PMMA, GP and soft lenses. The corneal nerve function of PMMA lens wearers will be affected by both mechanical and metabolic effects. GP lens wearers will be affected by a mechanical effect, but not significantly by the metabolic effect since the high oxygen transmissibility and tear exchange will ensure a good oxygen supply to the anterior cornea. Soft lens wearers should not be affected much by the mechanical effect, but will not have as good an oxygen supply as the GP lens wearers, and so will experience a reduction in nerve function due to the metabolic effect.

A reduced corneal sensitivity could be detrimental to the long-term health of the cornea, since the eye relies on the corneal nerves to detect foreign bodies that could damage the ocular surface. Paradoxically, the reduction in corneal sensitivity may improve contact lens wear comfort to some extent, while, at the same time, the risk of an undetected foreign body on the ocular surface is increased. The offending particle can then become trapped under the lens, prolonging the period of ocular insult. It is essential, therefore, that the corneal nerve function is minimally affected by contact lens wear.

There are various possible causes of initial discomfort with GP lenses including lens interaction with the lid and corneal sensitivity. SCL comfort is initially good, but tends to deteriorate with wear and much of this discomfort is thought to be due to lens

dehydration, tear lens interactions and possibly lens-lid interaction also. Investigation into corneal sensitivity has confirmed that a reduction in ocular sensitivity does not necessarily produce improved comfort. Therefore various controllable factors such as lens design, lens materials and fitting techniques, should be manipulated to produce optimum comfort.

1.8 Factors affecting comfort and performance

1.8.1 Lens design

The interaction of the lens with the eye is dependent on a number of lens design parameters, and it is these that influence the resulting comfort and performance of the lens.

1.8.1.1 Edge shape and design

A GP lens may be of a multi-curve or an aspheric design. Centrally, the lens radius is selected to align the lens with the corneal curvature. This will leave only a very thin (0.2μm) layer of tears separating the two surfaces. The aspheric shape of the cornea means that it flattens towards the periphery. Therefore, the curvature of the lens must alter with increasing diameter, to match this change and to maintain a good tear flow under the lens. The distance between the edge of the lens and the cornea is termed the edge clearance (La Hood, 1988).

A study investigating edge design on comfort reported that a rounded, anteriorly positioned lens edge provides the most comfortable lens edge (La Hood, 1988). Also, the results suggest that the interaction of the lens edge with the eyelid is more important in determining comfort than the edge effects on the cornea (Bennett and Grohe, 1995). A factor in minimising comfort-related problems would be careful verification of the lens edge, however it has been reported that fewer than 50% of ECPs do this routinely (Fink, Hill and Carney, 1993).

1.8.1.2 Diameter

Lens diameter affects the tear pump efficiency; smaller diameter lenses have better tear pump efficiency than larger ones (Gardner et al., 2005). The tear pump was critical in PMMA lens wear as it was the only method of oxygen delivery to the cornea. However, in modern, highly oxygen permeable lenses, the tear pump is only of mild benefit for oxygenation, though it is important for removal of debris and metabolic waste (Hazlett, 1997).

Larger diameter GP lenses are known to be more comfortable than small diameter lenses (Edrington, 2004), due to decreased lid-lens interaction (Edrington, 2004). An increased overall diameter, now possible due to greater oxygen transmissibility, enhances lens centration and is often advantageous in irregular corneas, e.g. pellucid marginal degeneration (Cornish and Sulaiman, 1996).

1.8.1.3 Centre thickness

Central thickness is an important parameter; a contact lens should be as thin as possible to aid oxygen transmissibility, however a lens that is too thin will have too much flexure resulting in instability and reduced comfort (Gardner et al., 2005). Now that highly permeable materials are available, it has been demonstrated that moderately increasing lens thickness to optimise lens design has little effect on the clinical response, as the transmissibility levels are still sufficiently high (Bennett and Hom, 2004). However, if the lens is too thick, its mass may result in an inferior-fitting position (Jones, 2003).

1.8.2 Materials

A contact lens material should provide sufficient oxygen to the cornea, be biocompatible and durable, require minimum care, and correct refractive error to give stable vision (Morris, 2004). Various material properties determine whether a material is satisfactory for contact lens use, these include permeability to oxygen, wettability, modulus of elasticity, and deposit resistance (Morris, 2004). Oxygen permeability, and its effect on corneal sensation, has already been considered in Section 1.7.4.

1.8.2.1 Wettability

Wettability describes the ability of fluids to spread and remain over the surface. When considered in relation to contact lens wear, good lens surface wettability enables the tear film to spread over, and remain on, the anterior lens surface, aiding lens wear comfort and stability of vision (Port, 2004). Various factors influence the wettability of a surface, and these should be considered when measuring the wettability of a contact lens surface, as defined by the wetting angle. These include preparation of the surface, temperature, humidity, lens age, manufacture method and surface modification, including cleaning solution, surface treatment or coating, polishing and roughness (French, 2004).

Various techniques for measuring *in vitro* lens wettability exist, these include the sessile drop technique, the captive bubble technique and the Wilhelmy balance method (Holly, 1981). However, these measurements do not accurately predict how a lens will perform on the cornea. After a period of wear, deposits from the tear film may bind to the lens surface, interrupting the pre-lens tear film and reducing wettability (French, 2004).

In vivo wettability is examined using a slit-lamp to investigate pre-lens tear layer thickness, lens drying and uniformity of the tear film on the lens (French, 2004). GP lens design aims to improve the hydrophilicity of the lens surface to increase wettability and improve initial comfort (Mengher et al., 1985; Guillon and Guillon, 1989; Loveridge, 1993). *In vivo* estimates commonly involve projection of a grid image onto the pre-lens tear film, or observation of an interference pattern of the tear film covering the lens (Tonge et al., 2001). The time taken in seconds for this projected pattern to break or distort is termed the pre-lens non-invasive break-up time and is used to provide a means of monitoring surface wettability (Franklin, 2003).

1.8.2.2 Modulus of elasticity

Toughness or modulus of elasticity is the ability of the lens to resist flexure; an important characteristic of a smooth refracting surface which can mask some degree of corneal irregularity, provide excellent visual clarity and prevent lens fracture during patient handling (Bennett and Weissman, 2005). It is controlled by the type,

amount and manner in which cross-linking agents are used to stabilise the polymer chains (Jones, Woods and Efron, 1996).

1.8.2.3 Deposition

Tear proteins, lipids, mucins and other contaminants from air or finger transfer, can deposit on a contact lens surface, Figure 1.3. The type, quantity and rate of deposition depend on the lens material, tear film composition and individual predisposition to protein adhesion (Phillips and Speedwell, 1997).

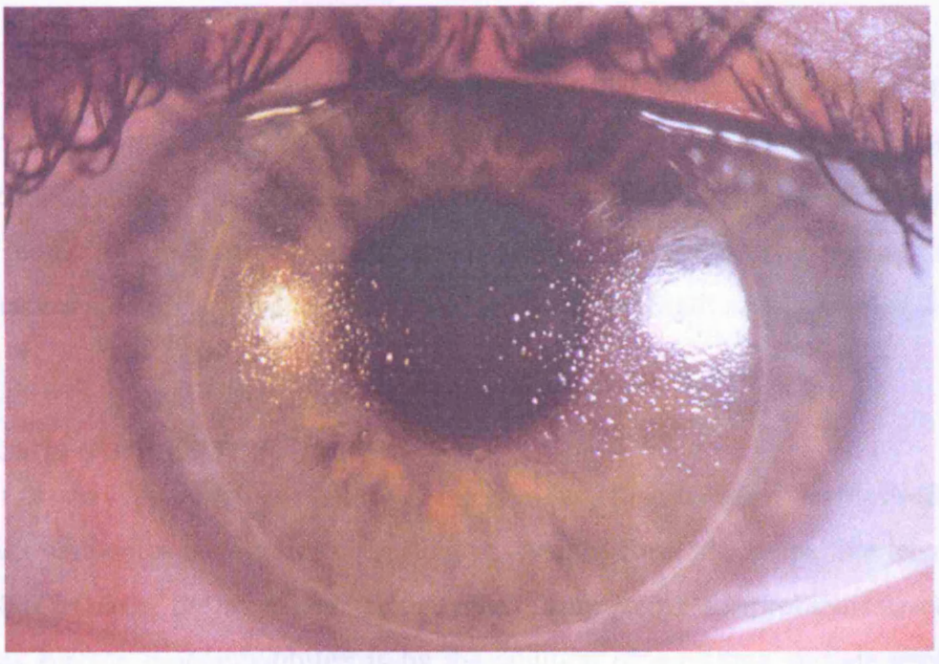


Figure 1.3: Lipid deposits on the anterior surface of a GP lens (Phillips and Speedwell, 1997).

There is conflicting evidence on whether protein deposition affects lens comfort, though deposits may be a cause of contact lens related drying (Phillips and Speedwell, 1997). Ninety percent of protein deposition is lysozyme; a tear protein, which in its natural state helps provide defence against pathogens. However, in its denatured state on the contact lens surface it may cause immunological responses (Senchyna et al., 2004; Sindt and Longmuir, 2007). Historically, GP lenses deposit fewer proteins than soft lenses, because the lens surface is less charged and the material is less porous (Morris, 2004). However, the addition of methacrylic acid increased the negative charge on the lens surface, and this attracted protein deposition. The inclusion of

fluorine reduced protein deposits, but led to more lipid collection (Bontempo and Rapp, 1997). Lipid deposition reduces the hydrophobicity of the lens surface, again allowing protein to bind (Sindt and Longmuir, 2007).

Lipids may also adhere to hydrophobic areas on the lens surface. Lipids are produced from the secretions of the meibomian glands and make up part of the tear film. There are over 45 different lipids and they vary between individuals (Lorentz and Jones, 2007) probably due to diet, medication, age, gender and environment. Studies of silicone hydrogels have shown that surface-treated lenses show improved wettability after several days of exposure to lipids (Lorentz, Rogers and Jones, 2007).

Deposition of micro-organisms including bacteria and fungi can lead to corneal inflammation or infection (Sindt and Longmuir, 2007). A careful choice of contact lens cleaning solution is important as efficacy, cytotoxicity and biocompatibility factors should all considered (Martins et al., 2009). Also rubbing and rinsing contact lenses has been demonstrated to remove surface deposits (Sindt and Longmuir, 2007).

1.8.3 Lens surface modification

Often it is very difficult to produce a material which combines the desired bulk properties with adequate surface characteristics needed for a biocompatible lens (Chu et al., 2002). One of the ways manufacturers have approached the problems associated with lens surface biocompatibility is by the addition of a plasma surface treatment (PST). Plasma treatment alters the superficial polymer surface without significant effects to the remainder of the material (Loverage, 2004). It is thought that PST smoothes the surface topography of the lens and consequently improves biocompatibility, maximises initial wettability and potentially improves lens performance, allowing longer wearing periods with superior comfort (Chu et al., 2002).

1.8.3.1 Applications in general medicine and specifically ophthalmic materials

Biocompatibility, good mechanical performance and chemical barrier behaviour have meant that a polymer film has been utilised for many technical applications. This

includes the automotive, electrical, medical, sport/leisure and aeronautics sectors (Young and Tapper, 2007). Industries have focused on surface modification to enhance surface properties, while retaining the bulk material properties. Chemical, thermal and electrical treatments have been used to alter wettability or change surface topography. However, in recent years, plasma treatments have been used because they offer high technological efficiency with low waste generation.

Examples of applications of plasma-surface modified biomaterials are given in Table 1.1 (Sanchis et al., 2008; Martins et al., 2009).

Table 1.1 Examples of plasma surface treatments in medicine.

Blood-compatible surfaces	Vascular grafts, catheters, stents, heart-valves, membranes, filters, biomolecules immobilised on surfaces
Non-fouling surfaces	Intraocular lenses (IOLs), contact lenses, wound healing, catheters, biosensors
Tissue engineering and cell culture	Improved wettability of cell membranes, antibody production, assays, vascular grafts
Sterilisation of surgical tools and devices	Cutting tools of surgeon, tweezers
Biosensors	Biomolecules immobilised on surfaces
Barriers coatings	Drug-release, gas-exchange membranes, device protection, corrosion protection, reduction of leaches (e.g. additives, catalysts, plasticisers etc)

Phacoemulsification cataract extraction involves the use of artificial, soft intraocular lenses (IOL) which can be implanted, folded, into eyes through a 3mm incision, to then unfold within the lens capsule with rapid patient recovery (Yao et al., 2006). The replacement IOL is most commonly made from silicone however, silicone attracts surface deposition which could potentially increase the risk of endophthalmitis (ocular inflammation), capsular opacification and visual acuity loss (Huang et al., 2007).

Surface modification of the IOL using a plasma technique improves biocompatibility and reduces the risk of post-operative complication, in particular endophthalmitis (the most serious complication) (Chu et al., 2002).

1.8.3.2 Plasma source and plasma-surface modification techniques

Plasma is a gas made up of a proportion of ionised and non-ionised particles. It is electrically conductive and has properties unlike solid, liquid or gas, and therefore it may be described as a fourth state of matter (Liston, Martinu and Wertheimer, 1994). It has no definite shape or volume unless enclosed in a container. In the influence of a magnetic field it may form structures such as filaments, beams and double layers (Young and Tapper, 2007).

Many plasma sources exist. The most common are gaseous, metallic and laser-based plasma sources, which may divided into two types of plasma: high temperature and low temperature. High temperature is most familiar as lightning of high voltage arcs. Low temperature plasma is used on flat screen televisions or neon signs (Yao et al., 2006).

Low temperature plasma is useful for CL modification. It may be created at atmospheric temperature (corona discharge) or at reduced pressure (radio frequency glow discharge) (Chu et al., 2002). Glow discharge is the most widely used for plasma surface treatment (PST) of lenses as it enables a large volume of stable plasma to be produced (Chu et al., 2002). The radio frequency (rf) dischargers may be divided into two types; capacitive coupling and inductive coupling, dependent on the method of rf power to load coupling. The electrodes can be situated within the discharge tube, however when the electrodes are external to the glass discharge tube impurities in the plasma process are reduced (Young and Tapper, 2007). The typical set-up for creation of glow discharge is shown in Figure 1.4.

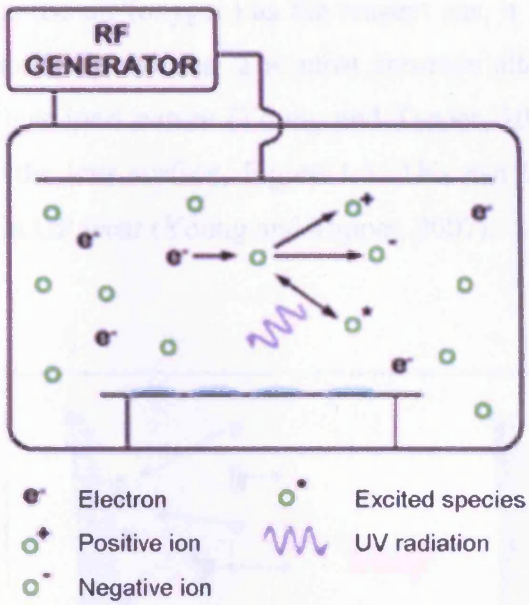


Figure 1.4 Radio frequency glow discharge set-up adapted from (Young and Tapper, 2007).

The chamber is evacuated and the process gas is introduced at low pressure (between 10-3 and 100 Torr) (Ren et al., 2008; Yin et al., 2008; Ren et al., 2009a; Yin et al., 2009). Application of high frequency radio waves ionises the gas into a charged species (ions), radicals and electrons, all of which are highly reactive. A surface placed into the plasma will be bombarded by these highly reactive particles; the resulting effects depend on type of reagent gas, treatment time, pressure and power (Liston et al., 1994).

1.8.3.3 Plasma surface modification effects

Plasma processing can add a thin deposition to the surface of the material, etch or remove surface material or modify the surface, whereas surface modification does not significantly add or remove material at the surface, but changes the superficial layers of the material (Ru and Jie-rong, 2006). Surface properties include wettability, adhesion, adsorption, chemical reactivity and sensitivity to light (Liston et al., 1994; Ren et al., 2008; Yin et al., 2008; Ren et al., 2009a; Yin et al., 2009).

The main effects of plasma modification are:

- Cleaning of organic contaminants from the surface.

Many PST techniques use air (oxygen) as the reagent gas, it is possible to use other gases, though this can be hazardous. The most common alternatives to air are the noble gases due to their inert nature (Young and Tapper, 2007). Oxygen plasma is effective at cleaning the lens surface, Figure 1.5. This can lead to improved initial wetting and comfort in GP wear (Young and Tapper, 2007).

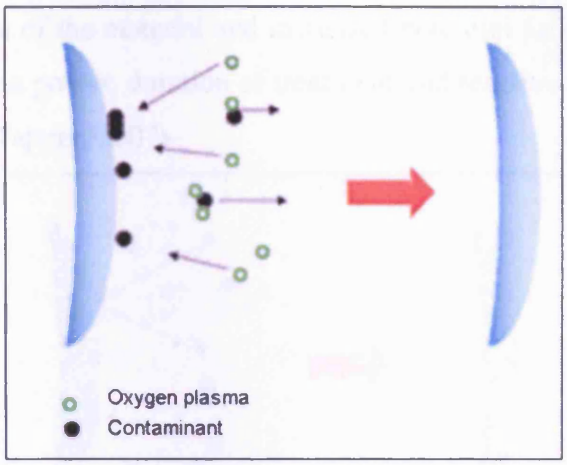


Figure 1.5 Oxygen plasma removes contaminants from the lens surface, adapted from (Young and Tapper, 2007).

- Altering surface characteristics

Plasma may bind and chemically alter the surface, this process is called functionalisation. Oxygen plasma binds to the surface to form molecular structures that may enhance wetting, Figure 1.6.

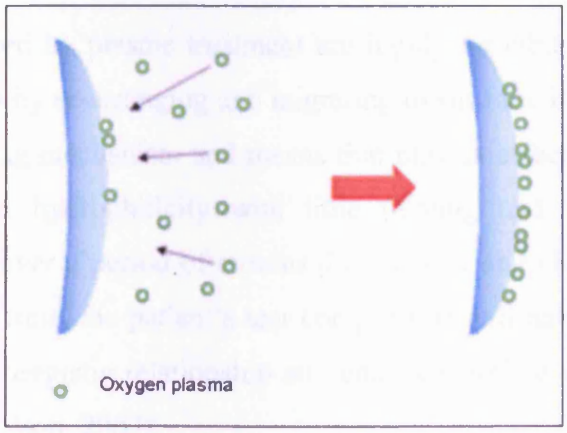


Figure 1.6 Plasma may bind and chemically alter the surface in a process called functionalisation, adapted from (Young and Tapper, 2007).

- Cross-linking of near surface molecules.

This increases cohesive bonds and strengthens the surface layer (Ren et al., 2008; Yin et al., 2008; Ren et al., 2009a; Yin et al., 2009).

Over-oxidation or etching is an unwanted result, caused by plasma reacting with the materials surface to remove the weak boundary layer, Figure 1.7. This causes an increase in the surface area and the material may appear hazy with flaky patches. It results in degradation of the material and increased potential for deposition. Research has shown that plasma power, duration of treatment and reactive agent require careful control (Young and Tapper, 2007).

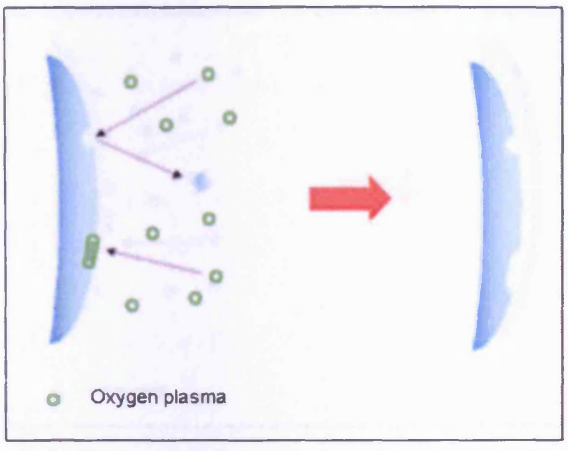


Figure 1.7 Plasma etching or over oxidation of lens surface, adapted from (Sanchis et al., 2008).

1.8.3.4 Lifespan and limitations of plasma treatment

Polar groups produced by plasma treatment are highly unstable and tend to reach a more stable situation by re-arranging and migrating toward the internal bulk material. This is the main aging mechanism and means that plasma effects are not permanent, resulting in reduced hydrophilicity with time (Young and Tapper, 2007). The treatment wears off over a period of months due to wear and cleaning, however it is thought that, by this time, the patient's tear components will have interacted with the lens to produce a synergistic relationship and enhance surface wettability (Nicolson and Vogt, 2001; Nicolson, 2003).

1.8.3.5 Plasma treatment of soft lens surfaces

Silicone hydrogel (SH) lenses were designed to give high oxygen permeability, however the silicone component is hydrophobic and therefore not biocompatible with the eye. This led to the surface plasma treatment of SH lenses to improve wettability and overall clinical performance (Subbaraman et al., 2006). Treatment of SH materials added a thin layer of plasma to completely alter the surface from the bulk material, Figure 1.8. Studies on deposition of plasma treated SH lenses have shown that plasma treatment technique reduces lysozme deposition (Young and Tapper, 2007).

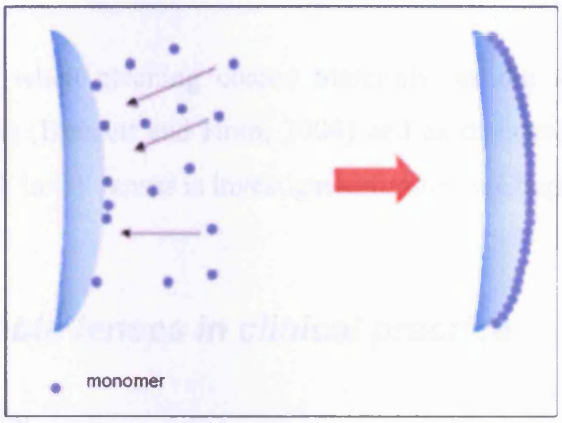


Figure 1.8 Plasma treatment to add a thin deposition to alter surface from bulk material adapted from (Young and Tapper, 2007).

1.8.3.6 Plasma surface treatment of GP lenses

Following the success of plasma treatment in soft SH materials, PST of GP lenses is now under investigation (Port and Loveridge, 1986). Only one manufacturer reported earlier use of PST, to enhance GP lens performance for overnight wear (Port and Loveridge, 1986). Also, this study reported no influence of PST on oxygen transmissibility (Young and Tapper, 2007).

Following the manufacturing process, a residue sometimes remains on a GP lens surface or, if the lens is handled prior to insertion to the eye, oils may adhere to the lens surface. This may produce a poorly wetting GP lens, leading to reduced vision and comfort. It is suggested that PST may improve lens comfort and vision (Yin et al., 2008). Also, the process reduces surface roughness and minimises the adhesion of

microbes, such as pseudomonas (Schafer, 2006). Although PST is not essential to GP success, the potential to improve initial comfort and wettability is very appealing (Young and Tapper, 2007). Figure 1.9 shows an example of the change in wetting angle achieved by PST of a GP lens.

Figure 1.9 Contact angle measurement of a GP before and after PST from (Bennett and Weissman, 2005).

Caution is required when cleaning coated materials, as the surface may be less resistant to scratching (Bennett and Hom, 2004) and as discussed earlier, PST has a limited life span. PST in GP lenses is investigated further in Chapters 5 and 6.

1.9 Gas permeable lenses in clinical practice

1.9.1 Visual acuity

Visual acuity, for patients with spherical refractive errors or low corneal astigmatism, is objectively and subjectively superior in spherical GP lens wear compared with spherical SCL wear. The anterior surface of the GP lens presents a spherical, optically smooth surface to the incident light, while, at the same time, the posterior surface combines with a tear lens to remove any irregularities or astigmatism in the cornea from the optical path, so creating an optically superior refractive surface (Snyder, Wiggins and Daum, 1994; Choi et al., 2007). Since soft lenses drape over the corneal surface, they cannot create a tear lens and so transfer through any corneal irregularity or astigmatism to the anterior surface of the contact lens. To correct corneal astigmatism with a soft lens, a toric lens must be used. When this is done, visual acuity levels become more even between GP and soft lenses. One study which compared spherical GP lenses with toric hydrogel lenses found that the GP lenses were subjectively superior for clarity of vision (Hong, Himebaugh and Thibos, 2001). However, this study found no significant statistical differences in threshold visual acuity, visual comfort and quality or stability of vision.

In-vivo, objective measures of enhanced visual performance revealed differences between rigid and soft lenses (Hong et al., 2001). Rigid lenses appeared to reduce asymmetric aberration, spherical aberration and wavefront variance resulting in superior optical performance compared with soft lenses (Hong et al., 2001). However, the author commented that neutralising corneal aberrations may have an adverse effect by exposing lenticular aberrations (Hong et al., 2001). Hence, there is some controversy over the effect of rigid lenses on optical aberrations and also on how directly aberration affects visual acuity (Choi et al., 2007).

A study amongst Chinese patients found superior visual acuity and contrast sensitivity results in the mid-high order spatial frequencies in subjects corrected with rigid lenses, when compared with spectacles or SCL correction (Qu et al., 2003). A study by Ziel reported better contrast sensitivity in all spatial frequencies with rigid lens wear between the initial and 6 month visits, though the reasons for this are unclear. It was suggested that contrast sensitivity measurement may be the best predictor for visual function in contact lens wear (Ziel et al., 1990b). Conversely, SCL wearers have been shown to have reduced contrast sensitivity in the mid and high spatial frequencies (Wachler et al., 1999).

GP lenses offer a wide selection of multifocal designs for presbyopic patients. It has been suggested that GP multifocal lens options may provide superior correction than soft multifocal designs (McMahon, 2003). A recent study assessed the visual performance of subjects wearing a variety of presbyopic corrections, including GP multifocal contact lenses, soft bifocal contact lenses, GP monovision lenses and multifocal spectacles. The results indicated that GP multifocals provided the best binocular high and low contrast acuity, and the least monocular disability glare in the contact lens wearing group (Rajagopalan, Bennett and Lakshminarayanan, 2006). Studies investigating GP multifocals have reported success rates of over 75 percent, with one (Woods et al.) reporting 86 per cent success (Hansen, 1996; Byrnes and Cannella, 1999; Woods et al., 1999; Anderson, 2003).

Patients who have scarred or irregular corneas due to pathology, trauma, corneal graft or idiopathic causes may benefit from GP contact lens correction. As described earlier, the rigid nature of the GP material means that it can mask underlying corneal

irregularity. For example, keratoconus is a progressive condition characterised by the gradual conical-shaping of the cornea. This can lead to irregular, distorted vision and eventually may require corneal transplant. GP lenses are regularly fitted to patients with keratocous. The majority of keratoconic patients can be successfully fitted and achieve good visual acuity delaying the need for surgery (Fowler, Belin and Chambers, 1988)

1.9.2 Complications associated with gas permeable lenses

Contact lens wear is known to be a factor in several eye conditions. Many of these minor complications can be managed by community eye care practitioners (ECPs), while the more severe require hospital treatment.

1.9.2.1 Dryness with GP wear

Dryness associated with GP wear differs from soft lens dryness in manifestation, aetiology and severity. Generally in GP wear symptoms are associated with peripheral corneal desiccation (3 & 9 o'clock staining), Figure 1.10 (Schnider, Terry and Holden, 1997). The amount of staining can vary from superficial epithelial stippling to intense staining defect with dellen formation. Various sources may be responsible for development of peripheral corneal dessication. The most common reason is thought to be due to a bridging effect; the lens edge bridges the superior lid away from the cornea at the 3 and 9 o'clock zones. The gap created is not sufficiently wetted by the tears and so this area develops corneal staining(Van der Worp et al., 2003).

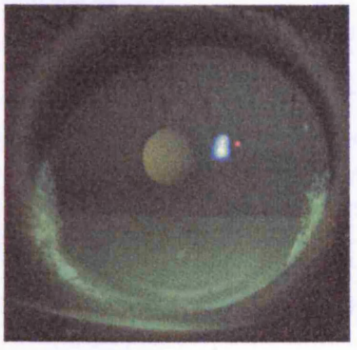


Figure 1.10 Peripheral corneal desiccation.

Management of this condition can sometimes be problematic. In general, alteration to lens parameters such as edge lift or edge thickness, alteration of the lens fit (to ensure centration, movement and encourage lid attachment) or provision of tear supplements are required (Van der Worp et al., 2003; Van der Worp et al., 2008).

1.9.2.2 Ptosis with long-standing GP wear

Prolonged use of GP lenses is associated with an acquired ptosis in some wearers. Although the aetiology is not entirely understood, it is hypothesised that lens removal by placing a finger at the outer canthus, pulling the lid laterally and then giving a sharp blink may cause levator aponeurosis dehiscence (Jupiter and Karesh, 1999; Thean and McNab, 2004). Incidence is low, though it is possible that sub-clinical ptosis may be present binocularly in many long-standing GP lens wearers (Bennett et al., 1998b).

1.9.3 Infection with GP wear

Microbial keratitis (MK) is a rare, but sinister, complication of contact lens wear, and is therefore well-documented in the literature. MK is an acute corneal inflammation, commonly caused by bacterial infection, though fungi and acanthamoebae can sometimes be attributed (Millis, 2005). An example of MK is shown in Figure 1.11

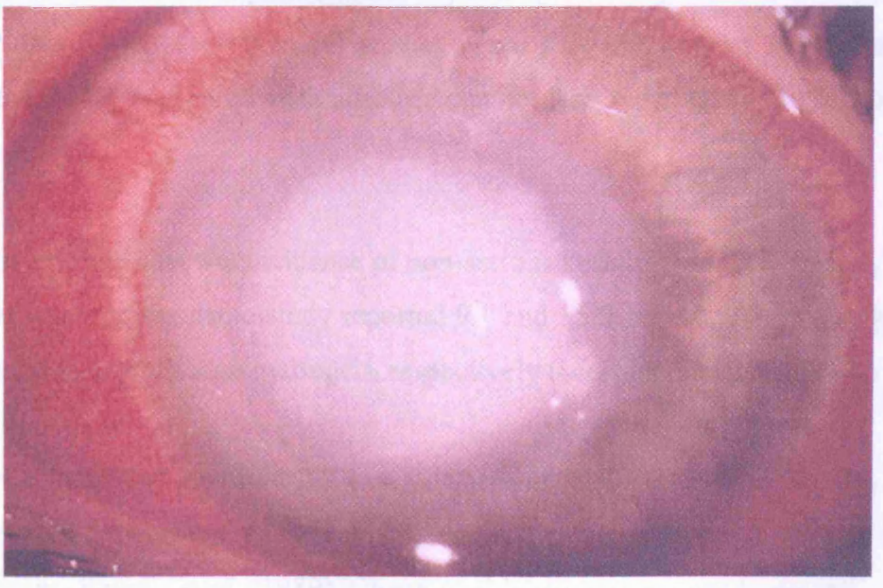


Figure 1.11 Contact lens-related microbial keratitis, presented at five days without treatment, from Phillips and Speedwell (1997).

There is large variation in the rate of corneal incidents associated with different contact lens materials and modalities of lens wear. Knowledge of contact lens risk factors and rate of infection incidence is required when fitting patients with contact lenses. Overnight wear of CLs is reported to be the biggest risk factor for the development of MK (Stapleton et al., 2008). Males are four times more likely to experience a corneal event than females (Morgan et al., 2005a), smoking increases risk by 35%, though general health problems and compromised ocular health may increase risk of contact lens associated events (Efron and Morgan, 2006). There may be a link between factors such as occupation and hobbies, i.e. swimming, and incidence of keratitis (Efron and Morgan, 2006). Bacterial contamination in contact lens wear may be attributed to lens material, unhygienic hands or biofilm in the lens case (McLaughlin et al., 1998; Ladage et al., 2001b). Care systems also influence infection rates (Phillips and Speedwell, 1997). Rigid lens multipurpose solutions have been shown to achieve and maintain antimicrobial efficacy, required by the FDA over a 12 week period (Boost, Cho and Lai, 2006), whereas studies of soft lens multi-purpose solution have shown that efficacy reduces below the FDA guidelines over the same storage period (Leung, Boost and Cho, 2004).

1.9.3.1 Incidence of infection

The incidence of keratitis reported varies depending on study methodology, size and classification of MK. However, all studies agree that GP contact lenses have the lowest rate of MK compared with all other contact lens types (Dart, 1993; Cheng et al., 1999).

It has been reported that the incidence of non-serious keratitis in GP wear is 5.7 cases per 10,000 wearers, the same study reported 9.1 and 55.9 per 10,000 for day wear of daily disposable and silicone hydrogels, respectively (Morgan et al., 2005b).

Morgan et al. (2005b) reported 2.9 cases of serious MK per 10,000 wearers. Other studies reported a lower rate of microbial keratitis; 1.0-1.1 cases per 10,000 wearers in GP daily wear (Poggio et al., 1989). Cheng et al.'s study was very large; 639,000 GP wearers, as it involved the entire contact lens wearing population in the Netherlands. A smaller, American study reported a slightly higher incidence of keratitis in GP lens

wear at 4.0 cases per 10,000 wearers (Stapleton et al., 2008). The most recent and largest prospective population-based surveillance study of MK incidence reported 1.2 cases of both presumed and severe MK per 10,000 wearers (Poggio et al., 1989; Cheng et al., 1999; Seal et al., 1999; Lam et al., 2002; Morgan et al., 2005b).

The incidence of MK is generally reported to be higher in all SCL wearing modalities compared with GP lenses. Daily-disposable (DD) hydrogel lenses have the lowest incidence of MK within the SCL group. The reported incidence of MK in DD hydrogel wear ranges from 2.7-4.9 cases per 10,000 wearers (Poggio et al., 1989; Cheng et al., 1999; Seal et al., 1999; Lam et al., 2002; Morgan et al., 2005b). The largest and most recent study, reported 2.0 cases of presumed MK per 10,000 DD wearers and 0.5 cases of severe MK per 10,000 (Stapleton et al., 2008). Severe MK was defined based on the location, treatment and vision loss incurred. The reduced incidence of MK with DD wear is thought to be due to elimination of the storage case and consequently reduced potential for contamination by gram-negative bacteria (McLaughlin et al., 1998; Keay et al., 2005).

It was predicted that the development of silicone hydrogel materials with higher oxygen transmissibility would considerably reduce the incidence of microbial keratitis (Ren et al., 1999; Willcox and Holden, 2001). However, the rate of presumed MK is 11.9 per 10,000 with daily wear soft silicone hydrogel (SH) lenses. These figures indicate that silicone hydrogel materials have not reduced the rate of serious infection as anticipated.

1.9.3.2 Pathogenesis of infection

Pseudomonas aeruginosa is the most common bacterial agent associated with the development of microbial keratitis in contact lens wearers (Ren et al., 1999; Willcox and Holden, 2001). A contact lens on the cornea can cause various changes to the corneal surface, including a reduction in the rate of epithelial shedding (Ren et al., 1999). Binding of bacteria to corneal epithelial cells is required to initiate infection (Nilsson 2002; Ren et al. 1999) (Ren et al., 1999), and increased bacterial binding occurs with contact lens wear (Ren et al., 1999), thus the risk of infection is heightened with contact lens wear (Ladage et al., 2001b).

The increase in binding sites on the corneal epithelium during contact lens wear appears to be caused by oxygen deprivation (Ren et al., 1999). Ren predicted that if contact lens permeability increased to a critical level, then the lens would no longer *damage* the corneal surface and the risk of infection would be the same as in non-wearers (Ren et al., 1999). Indeed, the rate of infection is reduced with high permeability soft contact lenses (Nilsson, 2002), yet even premium soft contact lenses still have higher rates of corneal binding of bacteria than rigid lenses, and so it can be concluded that oxygen permeability is not the sole contributory factor in contact lens infection.

Therefore it can be concluded that GP materials not only provide excellent oxygen permeability but, do *not* reduce the rate of epithelial shedding or increase pseudomonas aeruginosa binding to epithelial cells (Ren et al., 1999; Ladage et al., 2001b). These differences in lens-eye interaction are believed to explain the low incidence of MK with GP wear.

A study investigating sub-clinical inflammation of the conjunctivia, found that levels were lower in the GP wearing group compared with the SCL group (Pisella et al., 2001). This finding may be explained by the diameter difference; soft lenses extend onto the conjunctiva whereas the GP lens is smaller and covers only part of the cornea. This reduced corneal coverage means atmospheric oxygen is available at the limbal zone and peripheral cornea, resulting in less corneal infiltrates, sterile ulcers and irregular staining patterns compared to soft lenses.

Further lens parameters which may affect the rate of infection include lens surface treatments, rigidity and wettability of the material, and it is these factors which help to account for the difference in infection rates between rigid and soft lens types (Ladage et al., 2001b; Willcox and Holden, 2001; Schein et al., 2005).

1.9.4 Myopia control

Young myopes have a 78.9 - 80% success rate with rigid lens wear (Bennett and Hom, 2004; Walline et al., 2004). There are many advantages in fitting a highly

myopic child with contact lenses, these include reduction in distortion and prismatic effects and relief from cosmetic and comfort issues related to spectacle wear (Garriott, 1999). Fitting young myopes with rigid lenses has also led to reports that rigid lenses may slow or halt myopic development during adolescence (Baldwin et al., 1969; Goss, 1982; Khoo, Chong and Rajan, 1999).

In 1990, a longitudinal study monitoring myopic progression in children aged 8-13 years, fitted with either rigid contact lenses or spectacles, demonstrated a statistically significant reduction in myopic progression (0.16D per year) in children wearing rigid contact lenses compared to children wearing spectacles (Perrigin et al., 1990). However, measurement of corneal curvature indicated that corneal flattening in contact lens wear accounted for less than half of this effect (Perrigin et al., 1990). In contrast, other studies have found that myopia can increase with rigid lens wear (Baldwin et al., 1969), or that rigid lens wear has no effect on myopic progression in children (Katz et al., 2003).

A study by Walline aimed to eradicate study design problems affecting reliability. Walline's study compared the effect of rigid gas-permeable and soft contact lenses in young myopes over a 3 year period; it reported a significant reduction in myopic progression in the rigid lens group: 0.40 Dioptre difference in refractive error progression during the first year and 0.23 Dioptre difference in the following 2 years. Corneas wearing soft contact lenses steepened more than those wearing rigid lenses during the study. There was no significant difference in axial growth of eyes with different lens type. The report concluded that myopic development was statistically, significantly slowed with rigid lens wear. However, this impact on myopic progression may be less significant in clinical terms (Walline et al., 2004).

1.9.5 Extended wear and orthokeratology

The increased oxygen permeability of contact lenses allowed the extended wear oxygen criteria set by Holden and Mertz to be achieved (Holden and Mertz, 1984). Extended wear of GP lenses is reported to have no incidence of MK with GP lenses (Morgan et al., 2005a; Morgan et al., 2005b). However, the incidence of microbial

keratitis is between 18-25.4 cases per 10,000 wearers when soft SH lenses are used on an extended wear basis, (Cheng et al., 1999; Morgan et al., 2005b; Schein et al., 2005; Stapleton et al., 2008).

A study comparing performance of GP and soft hyper Dk contact lenses in extended wear reported similar visual acuity and adapted comfort levels for the lens types. Subtle differences in physiological responses were observed: corneal staining was greater in GP wearers, though this was present both before and after extended lens wear (Maldonado-Codina et al., 2005b). The study concluded that GP lenses are successful and safe as an extended wear option.

Orthokeratology (OK) employs a specially designed-reverse geometry rigid contact lens which temporarily reshapes the cornea during overnight wear, resulting in the reduction or elimination of refractive error, providing improved unaided vision (Mountford, Rushton and Dave, 2004; Swarbrick, 2006). Generally OK is used to treat myopia up to 4 Dioptres, though it can treat astigmatism and hyperopia to some degree, and treatment of presbyopia is currently being developed (Swarbrick, 2006; Gifford and Swarbrick, 2008). OK causes central epithelial thinning and mid-peripheral epithelial and stromal thickening, the cellular mechanisms involved are under investigation, though the corneal effects are reversible (Mountford et al., 2004).

OK is reported to have good levels of patient satisfaction compared to alternative lens modalities (Swarbrick, 2006). Figures show that OK prescribing has become more frequent in Canada over recent years; it accounted for 2.5% of all fits in 2006 and almost half of rigid lens fits were with OK lenses (Morgan et al., 2006; Woods et al., 2007). In the UK, OK accounted for 1 % of all fits in 2006 (Morgan et al., 2006).

In Hong Kong, since the introduction of OK in 1997, there has been much interest in this treatment, because 70 % of the adolescent population is myopic. However, a survey found that practitioners are concerned about the risk of complications and patient compliance, and also whether claims regarding myopia control are founded (Cheung et al., 2002).

There is no data on the exact frequency of MK with overnight OK. Overnight wear of contact lenses increases the risk of infection, but it is not known whether OK represents a greater risk than other forms of overnight contact lens wear (Walline et al., 2005). A review of 50 cases of MK, reported 60% of affected patients were aged 15 or under, current research is interested in whether children and are at increased risk of contact lens related MK (Watt and Swarbrick, 2005). The same review reported 90% of cases were of Asian ethnicity. While OK practice in countries such as China, Taiwan and Hong Kong is now under tighter regulation, it is not clear whether this cohort is predisposed to MK (Watt and Swarbrick, 2005).

Myopia control with OK is currently being investigated and results are not yet conclusive, though pilot studies have demonstrated variable amounts of myopia control in adolescents (Reim, Lund and Wu, 2003; Cheung, Cho and Fan, 2004; Cho, Cheung and Edwards, 2005; Walline et al., 2005). One possible explanation is that OK changes the aberrations experienced in the peripheral visual field and this influences the development of refractive error (Swarbrick, 2006). Further studies are required to investigate myopic control with OK.

1.10 GP lens fitting techniques

1.10.1 Patient selection and evaluation

Gas permeable lenses may be fitted to healthy corneas and, as described in Section 1.4.1, may also be beneficial for scarred or irregular corneas. A thorough patient history should first be taken to determine if the patient is suitable for GP lens wear. Patient motivation is important as it influences the probability of successful GP fitting. Practitioner communication, verbal and non-verbal has been demonstrated to impact on long-term fitting success (Bennett et al., 1998b). Therefore, GP lenses should be presented in a favourable, but realistic, manner as patients will tolerate initial lens awareness if the benefits have been explained and they expect a period of adaptation before reaching optimum comfort (Benoit, 1996).

GP lenses tend to be suited to full time or frequent use, whereas soft, disposable options are better suited to intermittent wear or for sporting use (Yamane, 1990). GP

lenses may require increased patient motivation levels, because initially fitting and adaptation to GP lenses may be more arduous than SCL fitting.

1.10.2 Anterior eye health assessment

Tear film and slit-lamp bio-microscopy examination should be undertaken to evaluate the integrity of the tears, eyelids, conjunctiva and cornea prior to lens fitting (Gasson and Morris, 1998).

The cornea, conjunctiva and eyelids should be assessed for any significant defect, infection or inflammation. Contact lens fitting is contra-indicated until any such findings are resolved (Bennett and Hom, 2004). Clear note taking is essential to allow an accurate record of the examination and, to assist the lens fitter, different grading scales have been produced that allow the assessment of specific ocular signs according to set visual standards.

1.10.2.1 Grading scales

A quantitative measure of the ocular surface findings is useful in evaluating health status and aids comparison of ocular surface changes between visits. Many grading scales are available, based on a description, photograph or painted illustration of a progressive change in a specific ocular appearance or condition. The first example for ocular hyperaemia came from pioneering work by McMonnies and Chapman-Davies, in the 1980s, who developed a 6-grade scale of an irritated, hyperaemic eye and its gradual return to baseline level (McMonnies and Chapman-Davies, 1987ab). Currently, the Efron grading scales and the Cornea and Contact Lens Research Unit (CCLRU) grading scales (Figure 1.13) are most prevalent in optometric clinical practice (Terry et al., 1993; Efron, 1997; Efron, Morgan and Katsara, 2001). Both are 5-grade scales, although the CCLRU scale does not show grade 0 (normal). Interpolation of the scales into 0.1 decimal intervals increases the sensitivity of the scale (Bailey et al., 1991; Efron et al., 2001). The main grading items used reflect the parameters of interest in assessment of the 'normal' eye – ocular redness, corneal staining, palpebral conjunctiva redness/roughness.

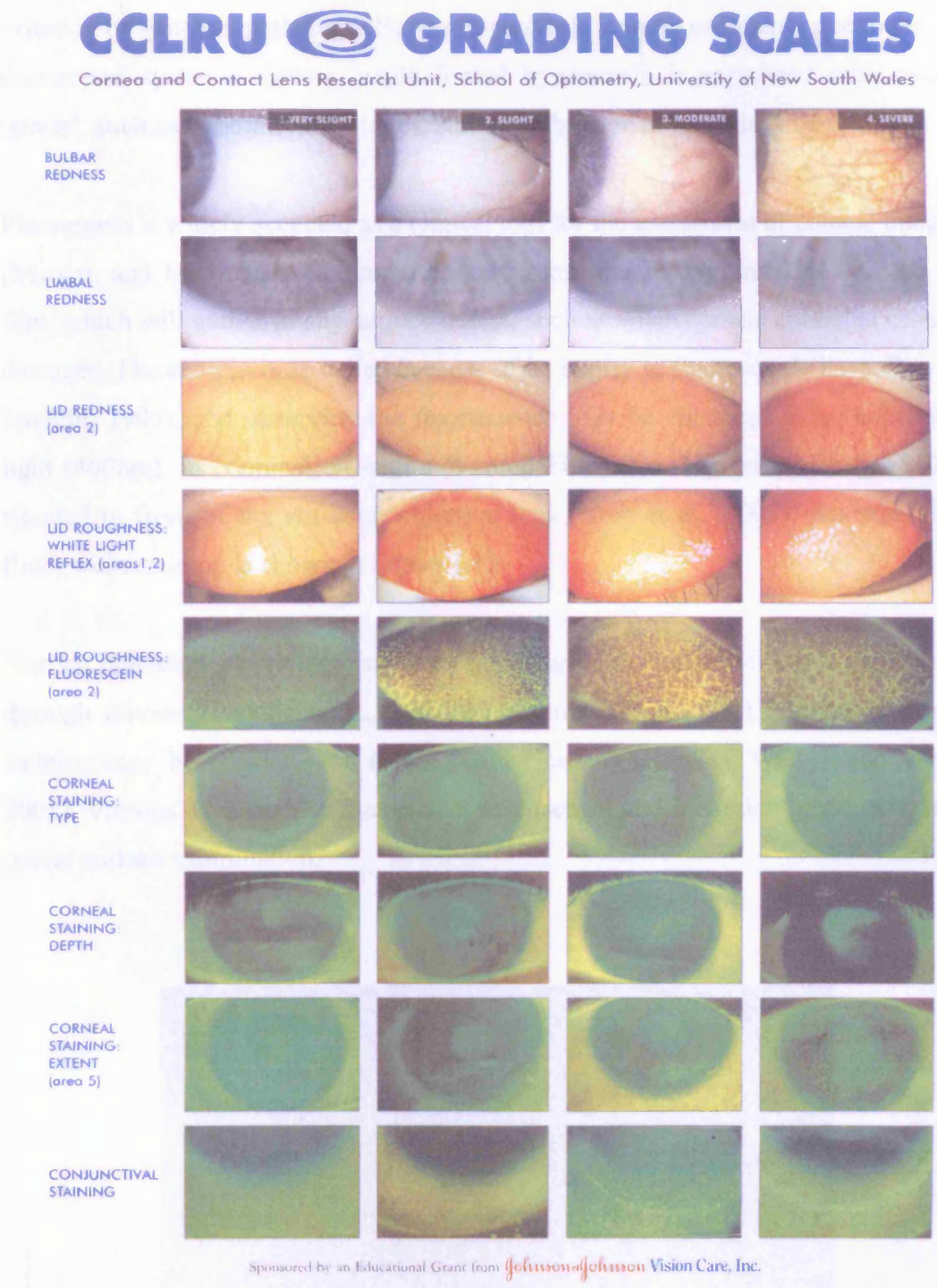


Figure 1.12 The CCLRU grading scales.

1.10.2.2 Ocular surface assessment

Assessment of bulbar conjunctival or limbal hyperaemia is commonly used as a measure of ocular health. Hyperaemia is due to an increase in the volume of blood to

the anterior sclera, bulbar conjunctiva and limbal vessels in response to inflammation, irritation or systemic pathology. Bulbar hyperaemia is more commonly due to general ocular and systemic factors, while limbal hyperaemia is associated with corneal 'stress', such as keratinise, infiltrates, staining, abrasion or hypoxia (Efron, 2004).

Fluorescein is widely accepted as a clinical tool for the assessment of corneal integrity (Morgan and Maldonado-Codina, 2009). It is an orange dye, instilled into the tear film, which will gather in any surface defect, such as when corneal epithelial cells are damaged. Fluorescein is so called because of its ability to fluoresce (Wilson, Ren and Laurent, 1995), and observing the fluorescence may be enhanced using cobalt blue light (460nm), in conjunction with a Wratten Filter (No. 12), transmitting >510nm, situated in front of the slit-lamp objective lens (Isreb et al., 2003). An example of fluorescein staining is shown in Figure 1.13.

Normal epithelial physiology involves shedding of epithelial cells and replacement through mitosis (Ladage et al., 2001a; Yamamoto et al., 2001); therefore corneal staining may be present even in the healthy cornea (Dundas, Walker and Woods, 2001). Various dyes such as fluorescein, rose Bengal and lissamine green exist to aid ocular surface examination.

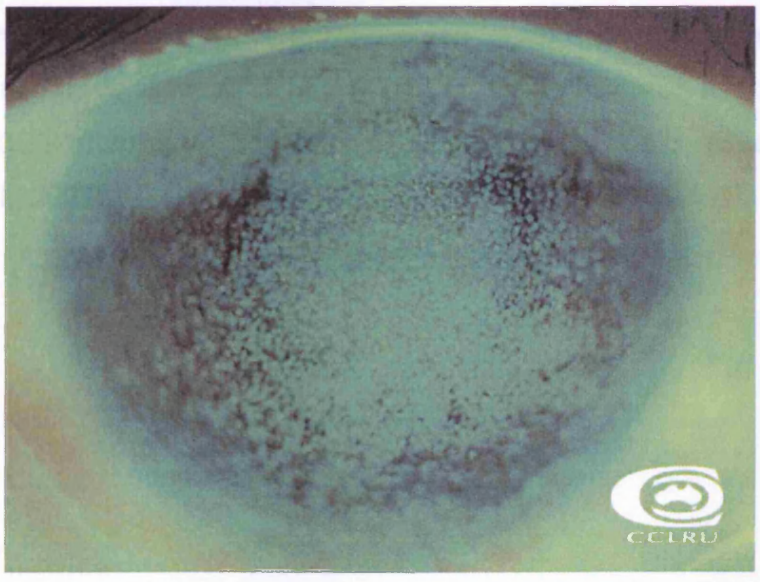


Figure 1.13 Corneal staining produced using sodium fluorescein, from CCLRU.

1.10.2.3 Tear break-up time

The integrity of the tear film may be assessed by measuring the length of time following a regular blink until the tear film develops a break. This is called the tear break-up time (TBUT). The classical theory suggests that tear break-up occurs when lipid, which is hydrophobic in nature, migrates to the deeper mucous layer of the tear film and compromises the hydrophilicity of the epithelial surface. Tears then recede from this area and a dry spot forms (Holly, 1981). Alternative theories regarding the process responsible for TBUT propose rupture of the mucous layer or disturbance of the superficial epithelial glycocalyx (Efron, 2004). TBUT on the surface of a contact lens will differ because the tears on the surface thin due to evaporation, at the same time as surface tension forces draw tears to the meniscus at the lens edge. In addition, the presence of any surface deposits will further reduce pre-lens TBUT.

Tear break-up time may be measured in a number of ways. The traditional method involves instillation of sodium fluorescein stain into the tear film, followed by slit-lamp observation of the tear break-up. This is an invasive method, and the fluorescein is thought to interfere with the measurement by destabilising the tear film (Mengher et al., 1985). A non-invasive technique involves the use of the Tearscope Plus^{TM} (Keeler Ltd, Windsor, UK). An illuminated black and white grid pattern is projected onto the tear film, and the reflection is viewed using the slit-lamp bio-microscope eyepieces or with an attachable magnification lens. The patient is instructed to blink and then hold their lids open. The time taken from eye opening to when the grid pattern begins to distort is the non-invasive break-up time (NIBUT). Tolerant contact lens wearers have a median NIBUT of 20secs, whereas for intolerant wearers this is reduced to 13secs (Glasson et al., 2003).

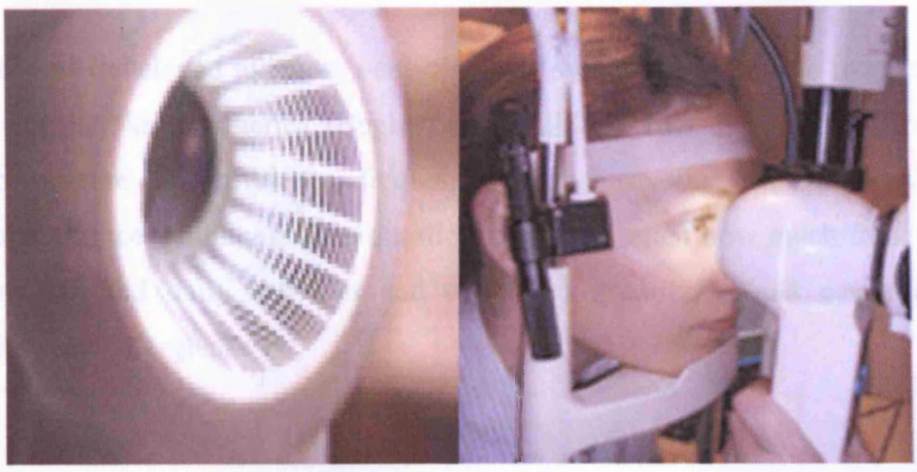


Figure 1.14 The Tearscope Plus™ (Keeler Ltd, Windsor, UK), showing the internal illumination with projection grid inserted (left), and the instrument in position on a slit-lamp bio-microscope for observing the tear film (right).

1.10.2.4 Symptom questionnaires

Contact lens dry eye is a very common clinical problem though it is poorly understood. Symptoms of dryness may cause patients to reduce wearing time or stop wear completely (Pritchard, Fonn and Brazeau, 1999). A variety of questionnaires have been designed to predict contact lens success in neophyte wearers and also to diagnose dryness in CL wearers (Begley et al., 2000). Two questionnaires were selected for use later in this research; neophyte patients completed the Dry Eye Questionnaire (DEQ) and existing SCL wearers completed the Contact Lens Dry Eye Questionnaire (CLDEQ). These questionnaires were selected because they have demonstrated an ability to evaluate dry eye in CL practice, and are easily understood to patients (Begley et al., 2002; Nichols et al., 2002).

The CLDEQ consists of 36 questions specific to symptoms of contact lens related dry eye. Literature and clinical review surrounding dry eye in CL wear help to derive the constructs of the questionnaire. There are nine sub-categories: discomfort, dryness, vision changes, soreness and irritation, grittiness and scratchiness, foreign body sensation, burning, photophobia and itching. The questionnaire asks about frequency of symptoms followed by diurnal intensity variation. The scoring algorithm categorises respondents into either asymptomatic or symptomatic CL wearers (Nichols et al., 2002; Nichols, Mitchell and Nichols, 2004).

The DEQ was developed to assess ocular surface symptoms in mild to moderate dry eye patients in North America (Begley et al., 2001). This questionnaire included scales to measure the prevalence, frequency, diurnal severity, and intrusiveness of nine ocular surface symptoms. The questionnaire also asked how much these ocular symptoms affected daily activities and contained questions about computer use, medications and allergies.

1.10.3 Diagnostic fitting

Keratometry measures corneal curvature over the central 3mm annulus of the cornea and measurements are used to determine required lens BOZR (Gasson and Morris, 1998). The contact lens covers a much larger area of the cornea and therefore keratometry provides a guide for the initial central base curve (Van der Worp, 2008).

Anatomical measurements include horizontal visible iris diameter (HVID), which assists in lens diameter selection (Gasson and Morris, 1998). Vertical palpebral aperture (VPA) measurement will influence the lens-lid interaction, and may guide on lens diameter selection and lens edge-lift design. The measurement of the habitual and maximum pupil diameter will determine the required optical zone diameter (Bennett and Hom, 2004). Baseline refraction should be recorded so that the appropriate GP lens power can be selected.

Using these measurements, diagnostic GP fitting can be completed. Insertion of trial lenses is then required to assess which lens best fits the cornea (Bennett and Hom, 2004). The first lens is selected using the keratometry results to determine the BOZR, the HVID to determine the TD, and the over-refraction to determine the lens power. This lens is placed on the eye and the fit observed. The lens fitter judges whether the fit is appropriate and may choose to place further lenses of different BOZR, edge clearance, TD or lens power to reach the best fit and optical correction for the patient. To assist the fitter, manufacturers have produced 'fitting sets' of their lenses, which comprises a series of lenses, usually of fixed diameter and standard dioptric power (-3D), but with a progressive range of BOZR. This process may be time-consuming for both the patient and practitioner, but it allows the eye care practitioner to evaluate the

lens-cornea fitting relationship and make necessary changes to obtain a good fit (Bennett, 1998).

1.10.3.1 Fitting sets and vCJD

In June 1999 the UK Department of Health stated that contact lenses should be for single patient use. This was confirmed by the Medical Devices Agency, and subsequently legislated for by the General Optical Council. Only 'special complex diagnostic lenses' could be exempt from this rule (Macalister and Buckley, 2002). This caused much change for UK ECPs who used diagnostic GP fitting. The reason for this change in contact lens practice was cited as a remote theoretical risk of cross-infecting patients with variant Creutzfeldt-Jakob disease (vCJD) (Macalister and Buckley, 2002).

vCJD is a human prion disease, which is neuro-degenerative in nature (Macalister and Buckley, 2002). A prion is an unusual, transmissible agent. Normally, prion proteins are found on many cell surfaces across the body, but in prion disease the amino acid chain is distorted causing insolubility and resistance to protease breakdown, causing accumulation in the central nervous system. It is proposed that this accumulation causes symptoms, which include dementia, ataxia, muscle spasm and visual disturbance (Weber et al., 1997). There are various different human prion diseases, these include Kuru; transmitted by ingestion of infected human brain tissue; classical CJD, usually caused by gene mutations; and inherited forms; Gerstmann-Straussler-Scheinker disease and fatal familial insomnia, and vCJD, transmitted by ingestion of meat infected with bovine spongiform encephalopathy (BSE) prions (Macalister and Buckley, 2002).

There is a theoretical possibility that if prions are released from the corneal epithelium, they could adsorb to the surface of a contact lens (Sweeney et al., 2003), and remain on the contact lens surface in a potentially active state, despite cleaning and disinfection procedures. In theory, provided a sufficient prion level is present, introduction of the lens to a different eye could allow transmission of vCJD (Macalister and Buckley, 2002).

Two percent sodium hyper-chlorite may be used to reduce the infectivity of GP trial lenses in the UK (Hogan, 2003). More recently, it has been confirmed that there is no threat of transmission of prion disease by use of contact lens reuse. However, guidelines on disinfection of lenses after use are still stringent to ensure no transmission of other microbes or pathogens between patients (Buckley, 2010).

1.10.4 Empirical fitting

In the late 1980s, computerised videokeratography (CVK), or topographers, became available. The CVK technology generated many data points across the cornea and then created a detailed corneal contour map (Nosch et al., 2007). Most topographers are based on a Placido disc reflection system using the tear-film boundary as a mirror (Van der Worp, 2008). This enables quantitative topographical information of the central cornea to be obtained. A limitation of CVK, as with the keratometer, is that only the central 6-8mm of the cornea can be mapped (Van der Worp, 2008). Secondly, a well-wetting anterior surface is essential and several measures must be taken to avoid artefacts.

CVK can also suggest GP parameters and simulate fluorescein patterns; however, it cannot visualise lid effects or lens flexure (Szczotka, Capretta and Lass, 1994). Despite reports that CVK is useful in lens selection for 'normal' corneas (Szczotka, 2003), the use of this technology is not common practice in the UK private sector. This may be due to the instrumentation costs and/or the limitations of static fitting. CVK is successful and efficient in fitting lenses in complex cases with corneal irregularity (Nosch et al., 2007).

1.10.5 Optimum fitting criteria

Whether the first lens chosen for the patient is derived from diagnostic or from empirical fitting, the most important factor when evaluating the lens-cornea fitting relationship, is the fluorescein pattern (Bennett and Hom, 2004). This may be done using a slit-lamp or hand-held Burton UV lamp. When assessing a lens fit various factors are assessed (Gasson and Morris, 1998).

- Centration of lens in primary gaze
- Movement on blink and on excursions

- Fluorescein pattern

Optimum fitting, according to Gasson and Morris (1998), is considered to be:

- Central lens position, not crossing limbus
- Lens should drop slowly over the cornea following blink

And the fluorescein pattern should be:

- Central apical clearance with a fine layer of fluorescein (across about 7.0mm)
- Mid-peripheral alignment fit, diameter 1.5mm
- Edge clearance, about 0.5mm

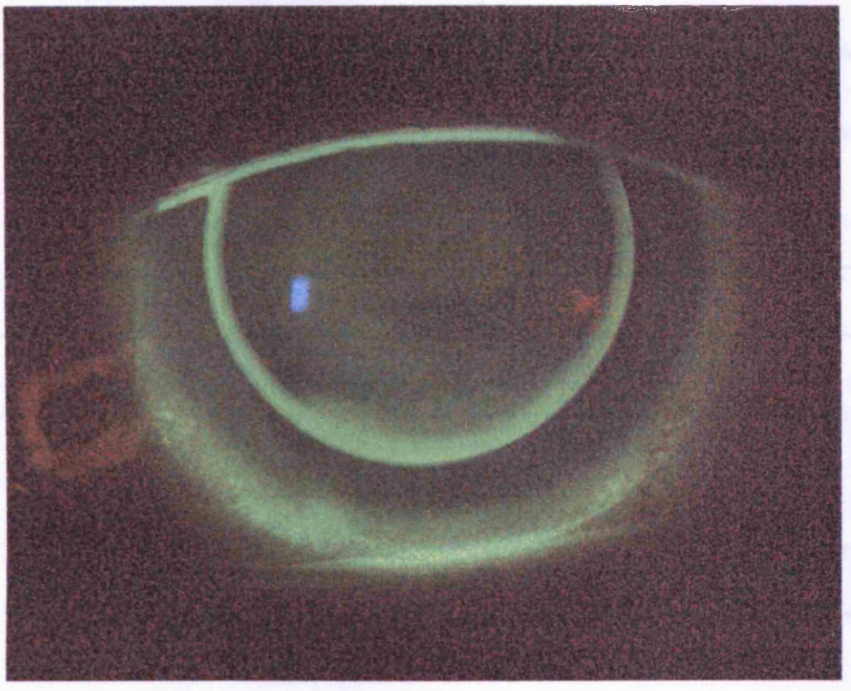


Figure 1.15 A fluorescein pattern illustrating an alignment fit.

Based on these assessments, the practitioner would judge the GP fit as optimal or acceptable, sub-optimal but still acceptable, or unacceptable. Alternatively, fits can be judged as steep, flat or toric. If the fit is not acceptable then the appropriate alternative lens specification is ordered to improve the fitting, i.e. steepen or flatten BOZR. There are other methods of grading a fit such as using a verbal scale (Table 1.2) or using numeric codes (Table 1.3) to describe the fit (Van der Worp et al., 2002).

Table 1.2 Interpretation of fluorescein patterns adapted from (Bennett, 1995).

Parameter	Appearance	Management
Base curve radius	Steep: green appearance centrally	Flatten BOZR
	Flat: black appearance centrally	Steepen BOZR
Optical zone	Large: green appearance centrally	Reduce optical zone/flatten BOZR
	Small: black appearance centrally	Increase optical zone/steepen BOZR
Intermediate	Steep/narrow: gray appearance in mid-periphery	Flatten/widen curves
	Flat/wide: green appearance signifies excessive edge lift	Steepen/narrow curves
Peripheral curves	Steep/narrow: gray appearance in mid-periphery	Flatten/widen curves
	Flat/wide: green appearance signifies excessive edge lift	Steepen/narrow curves

Table 1.3 Grading of tear layer thickness under GP lens(Van der Worp et al., 2002).

Grade	Outcome
+2	Rejected: thick
+1	Sub-optimal: thick
0	Optimal
-1	Sub-optimal: thin
-2	Rejected: thin

1.10.6 'Chair time' and skill required to fit GP lenses

Practitioners may perceive they spend a longer time fitting and dispensing a GP lens compared with SCL fitting. In some cases this will be true, because there is a greater possibility to vary the parameters of GP lenses than with soft lenses to achieve an optimum lens-cornea fitting relationship. SCL materials match the shape of the cornea due to their inherent flexibility, meaning there is less opportunity for practitioner manipulation, often allowing immediate supply from waiting stocks (Efron, 2005).

Since fitting sets are no longer generally used, GP trial lenses must be ordered specifically for each patient, making fitting a more time-consuming process. Practitioners may perceive GP lens fitting as more skilful than soft lens fitting and this may deter GP fitting in a busy practice with increasingly demanding patients.

In a letter to Clinical and Experimental Optometry in 1999, Don Ezekiel suggested that the profession may be becoming de-skilled in GP lens fitting (Ezekiel, 1999). If practitioners are not regularly using and improving their GP lens fitting skills, then it seems logical to suggest they will gradually be lost. However, Efron argues that the skill requirements are simply changing over time to meet different clinical needs (Efron, 2000).

A survey investigating education of GP lenses to optometric students in the UK, in the 1990s, found that there was no shortfall in the educational standards in this area (Pearson, 1998). However, this survey was completed before the vCJD effect on GP fitting, and student practical experience may now be more limited because there are fewer GP lens wearers in a typical patient cohort, resulting in fewer patients available to attend university clinics (Efron, 2005). It can therefore be surmised that newly qualified optometrists may feel a lack of confidence or experience to fit and care for GP lens patients (Efron, 2000).

1.10.7 Topical anaesthetic

Topical ocular anaesthetics have been available since the 1930s (Shafi and Koay, 1998) and they are commonly used in optometric practice to temporarily block

transmission of nerve impulses along sensory fibres and so remove the sensation of pain (Hopkins and Richard, 2007). They are used in a variety of procedures including contact tonometry, gonioscopy, scleral contact lens fitting and certain diagnostic dry eye tests (Lawrenson et al., 1998).

Anaesthetic use in GP fitting results in enhanced initial comfort (Bennett et al., 1998a) and may reduce patient anxiety about initial lens comfort (Schnider, 1996). This is shown to reduce the number of patient drop-outs and enhance perception of the adaptation process (Bennett et al., 1998a), thus reducing negative reports about initial GP comfort and increasing patient success with GP lenses.

Practitioners may feel encouraged to fit GP lenses if initial comfort is improved with anaesthetic, particularly in patients perceived to be sensitive or anxious about initial lens comfort (Schnider, 1996). A clinical study which investigated 20 neophyte subjects, apprehensive about trialling GP lenses, reported minimal lens awareness, lacrimation, and a minor increase in blink rate with anaesthetic, whereas the control group reported significant lacrimation and blepharospasm (Schnider, 1996).

The use of anaesthetic will reduce the chair time required in GP fitting as reflex lacrimation and blepharospasm are lessened; allowing more immediate, accurate lens fit assessment (Bennett et al., 1998a). This is advantageous to both patient and practitioner. TA use in GP fitting is further discussed and investigated in Chapter 4.

1.11 Aims and hypotheses for this PhD

1.11.1 Aims and objectives

Reviewing the literature indicates that GP lenses offer a safe, effective, comfortable contact lens option, yet, over the past three decades there has been a downward trend in GP prescribing in the UK. It is likely that much of the change in prescribing trends is due to the attitudes and opinions of the prescribing practitioner. Poor initial comfort in GP wear is often cited by patients and practitioners as a disadvantage with this lens type (Bennett et al., 1998a; Bennett et al., 1998b). Comfort in contact lens

wear is critical because dissatisfaction in this area is cited as the chief reason for contact lens discontinuation (Richdale et al., 2007). Although comfort in adapted GP wearers is generally very good (Fonn et al., 1995), poor initial comfort in GP wear may have led to the misperception that adapted comfort is also poor. Contact lens manufacturers continually strive toward improved comfort levels with lens. One method used to enhance comfort is the modification of the lens surface with plasma treatment.

This PhD aims to:

a) Investigate ECP views and practices relating to contact lenses, with particular emphasis on GP contact lenses;

b) Investigate the use of topical anaesthetic (TA) prior to GP lens fitting, to ensure this does not cause any adverse ocular surface response;

c) Patient anxiety and perception of comfort during GP fitting (with TA) and dispensing (without TA) will be investigated;

d) Plasma surface modification will be investigated to establish whether initial and adapted comfort and performance are improved;

e) Demonstrate that both neophyte and existing successful soft lens wearers can be successfully fitted with GP lenses;

f) Compare surface topography of plasma treated and untreated lenses after wear.

1.11.2 Hypotheses

- Use of topical anaesthetic in GP fitting will not cause adverse ocular surface response;
- Use of topical anaesthetic in GP fitting will improve patient's first experience of GP lens wear and reduce anxiety about proceeding with GP wear;
- Neophyte and SCL wearers can be successfully fitted with GP lenses;
- Plasma surface treatment of a GP will improve initial and adapted comfort and performance;
- Worn plasma treated lenses will have smoother topographies than untreated lenses;
- GP surface topography will correlate well with on-eye comfort i.e. smoother lenses will be more comfortable when worn.

2. A survey of UK practitioner attitudes to the fitting of GP lenses

2.1 Introduction

Despite soft lens developments, GP lenses were and are still one of the safest lens types available. As noted in Section 1.9.3, reviewing the incidence of MK associated with different lens types shows GPs to have the lowest risk associated with lens wear. There are many other advantages associated with GP lenses including visual acuity, irregular cornea fitting (e.g. keratoconus and orthokeratology). Yet, it is clear that rigid lens prescribing is, at best, static or in decline in the UK (as discussed in Section 1.5). Figure 2.1 demonstrates the gradual decline in GP prescribing in the UK over the last decade.

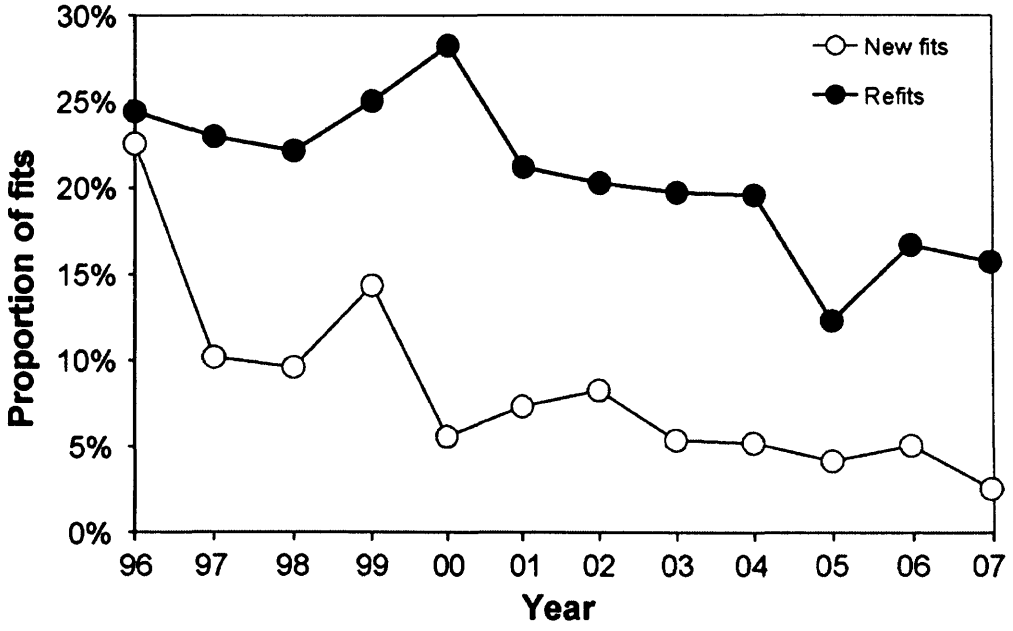


Figure 2.1 Proportion of GP lens new fits or refits as a proportion of the total numbers of contact lens fitting/refitting in the UK (reproduced from Morgan and Efron (2008b)).

This decline may be logically attributed to a variety of factors, including perceived GP disadvantages such as initial discomfort, increased 'chair time', and the additional practitioner skill required to fit and manage such patients. At the same time, major investment has been made in developing and promoting new soft lens materials and designs.

However, there is no published evidence regarding eye care practitioner (ECP) attitudes to contact lens prescribing or, specifically, any misgivings about GP lenses, and without an understanding of ECP attitudes to GP lenses, it is not possible to hypothesise what part ECPs, and indeed, their experience and environment, have played in the decline of GP prescribing. Thus, it is not known whether contact lens prescribing trends are associated with ECP's experience level or interest, or whether practice type influences ECP fitting habits. Quality and availability of equipment varies between practices, and this might influence the quantity and type of contact lens practice. Some practitioners are under pressure to examine and dispense increasing numbers of patients per session; this may lead to prescribing habits that are perceived to require the least consultation time. Practitioners may be biased toward a particular company or contact lens brand; they may be affected by personal contact lens experiences, good or bad, or anecdotal feedback about lenses. As yet, no published evidence to support these ideas exists in the literature. This knowledge could provide powerful tools in education of ECPs.

2.1.1 Aims and Hypotheses

The aims of this study were to investigate:

a) survey a large number of UK-based ECPs in order to observe their current practice and attitudes;
b) whether practitioners find GP fitting demanding and time consuming;
c) practitioner opinions regarding patient ocular health and comfort with GP wear;
d) whether practitioners consider TA use customary and acceptable practice in GP fitting.

ECPs are reluctant to fit GP lenses for a variety of reasons, because they may believe that:

- the challenge and time involved in GP fitting is more demanding than for soft contact lens fitting;
- patient eyes are healthier in soft contact lenses;
- specialist equipment is required for successful GP fitting;
- initial and adapted comfort in GP wear is less good compared to soft contact lenses;
- topical anaesthetic in GP fitting is not customary practice in the UK.

2.2 Methods

2.2.1 Questionnaire design

Since no existing survey was available to obtain the desired information, a questionnaire was designed for this purpose. Initially a review of the relevant literature was undertaken; focus group meetings, involving researchers and community ECPs, and interviews were held to acquire relevant information. The information was collated to produce a pilot questionnaire; this was completed by a random selection of optometrist colleagues (n=10). The pilot results were assessed to identify unnecessary items and the questionnaire was gradually refined to the final format.

The final questionnaire comprised twenty questions and is shown in Figure 2.2. Questions 1-9 asked for general information about the ECP, including job description, length of time qualified, relative amounts of general optometric work and contact lens work, practice type and equipment available. The remaining 11 questions asked the ECP to consider a statement with respect to contact lenses in general and then with respect to GP lenses specifically. A Likert-type response scale was employed. This provided the respondent with a 7 point response scale to indicate level of agreement or disagreement with a statement (Likert, 1932). Psychometricians advocate seven or nine point scales as they produce better internal reliability than those with fewer categories (Masters, 1974). ECPs were asked to indicate their level of agreement or disagreement with each statement by circling the appropriate number on a scale, ranging from 0 (strongly disagree) to 6 (strongly agree). A score of 0, 1 or 2 was considered to indicate disagreement, 3 indicated neither agreement or disagreement, and a score of 4 or more indicated agreement with the statement. Finally, the ECP was invited to add his or her own comments about contact lens fitting in the UK.

A

Contact Lens Questionnaire

If you do not fit contact lenses, please pass this questionnaire to a colleague who does.

1) What is your job description?
- ☐ Optometrist
- ☐ Contact lens optician

2) How long have you been qualified? .....years

3) What type of practice do you work in? (Please tick all appropriate answers)
- ☐ Multiple
- ☐ Own franchise
- ☐ Independent
- ☐ Hospital
- ☐ Other (Please specify) .....

4) What City/Town do you work in? .....

5) How many days do you work as a clinician each week? .....days

6) Approximately how many patients do you see each day? .....patients

7a) Approximately how many contact lens patients do you see? .....week/ month/quarter
(delete as appropriate)

b) How many rigid gas permeable (RGP) lenses do you fit? .....week/ month/quarter
(delete as appropriate)

c) How many RGP aftercares do you do? .....week/ month/quarter
(delete as appropriate)

d) How many soft contact lenses do you fit? .....week/ month/quarter
(delete as appropriate)

e) How many soft contact lens aftercares do you do? .....week/ month/quarter
(delete as appropriate)

8a) If you fit RGPs, do you use anaesthetic during fitting? (Please tick all appropriate answers)
- ☐ Always
- ☐ Sometimes
- ☐ Never

b) If yes, what type and concentration of anaesthetic do you use?.....

9) What equipment do you have in your practice? (Please tick all appropriate answers)

☐ Slit lamp	☐ Keratometer
☐ Auto-refractor	☐ Topographer
☐ Radiuscope	☐ V-gauge
☐ Focimeter	☐ Burton lamp

B

In the following questions, please choose and circle the most appropriate answer.

	Strongly Agree						Strongly Disagree
10) I relish the challenges of fitting:							
a) Contact lenses generally	6	5	4	3	2	1	0
b) RGP lenses	6	5	4	3	2	1	0
11) A slit lamp and keratometer are sufficient kit for successfully fitting:							
a) Contact lenses generally	6	5	4	3	2	1	0
b) RGP lenses	6	5	4	3	2	1	0
12) A topographer is advantageous in fitting:							
a) Contact lenses generally	6	5	4	3	2	1	0
b) RGP lenses	6	5	4	3	2	1	0
13) It is time-consuming to fit:							
a) Contact lenses generally	6	5	4	3	2	1	0
b) RGP lenses	6	5	4	3	2	1	0
14) Poor initial comfort discourages me from fitting:							
a) Contact lenses generally	6	5	4	3	2	1	0
b) RGP lenses	6	5	4	3	2	1	0
15) It is clinically acceptable to use topical anaesthetic during RGP lens fitting:	6	5	4	3	2	1	0
16) Now that fitting sets are not commonly used, I fit fewer RGP lenses:	6	5	4	3	2	1	0
17) I frequently recommend:							
a) Contact lenses generally	6	5	4	3	2	1	0
b) RGP lenses	6	5	4	3	2	1	0
18) Anterior eyes are generally healthy in established:							
a) Contact lens wearers	6	5	4	3	2	1	0
b) RGP lens wearers	6	5	4	3	2	1	0
19) Patients report good comfort levels once adapted to:							
a) Contact lenses generally	6	5	4	3	2	1	0
b) RGP lenses	6	5	4	3	2	1	0
20) RGP lenses are becoming obsolete:	6	5	4	3	2	1	0

Figure 2.2 The ECP Contact Lens Questionnaire; A: first page and B: second page.

2.2.2 Subject recruitment

Ethical approval for the study was obtained from the School of Optometry and Vision Sciences Ethical Committee, Cardiff University. The General Optical Council (GOC) was asked to supply the contact details of 1000 randomly selected ECPs from their optometrist and contact lens optician (CLO) registers and the questionnaires were posted to them in April 2007. Each questionnaire was accompanied by a cover letter explaining the purpose of the study and inviting ECPs to complete the questionnaire and return it to the investigator in a stamped, addressed envelope provided.

2.2.3 Statistics

Data produced from Likert response scales are considered to be ordinal and therefore non-parametric statistics were employed for analysis. Results were tabulated within SPSS (version 16) and examined using statistical tests, including Wilcoxon Rank, Mann-Whitney test and Pearson Chi Square. Significance was set at the 0.05 level.

2.3 Results

2.3.1 Demographic information

Demographic information relating to questionnaire responses is found in Table 2.1 and Figure 2.3. Responses from ECPs not involved in contact lens fitting were excluded from the contact lens fitting statistics, but their subjective responses were included in the remaining opinion-based analyses. The number of ECP responses used in analysis for each question is given in Tables 2.2-2.4. Contact lens opticians (CLOs) accounted for 4.4% of our respondents, which is somewhat less than the anticipated 10.7% on the GOC registers (as of January 2010).

Table 2.1 Questionnaire response information.

Questionnaire responses	**N**	**%**
Questionnaires posted	1000	100
Completed questionnaires	451	45.1
Not returned	530	53.0
Blank questionnaires returned	19	1.9
Respondent Demographics		
Optometrists	431	95.6
CLO	20	4.4
Practitioners seeing CL patients	434	96.4
Practice Type		
Multiple	192	42.6
Franchise	18	4.0
Independent	183	40.6
Hospital	5	1.2
Mixed	52	11.5
Practitioner details	**Median, range**	
Patients seen per day	15 (3-40)	
Number days worked per week	5 (1-7)	
Average length qualified (years)	7 (0-64)	

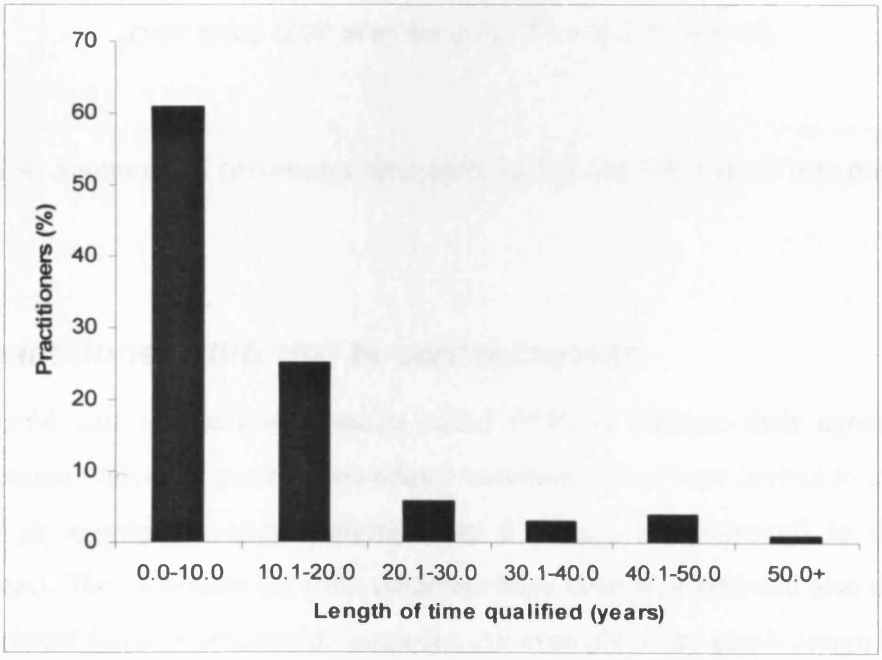


Figure 2.3: Distribution of experience amongst practitioners who responded to the survey (n=451).

2.3.2 Frequency of contact lens practice

The average number of contact lens patients seen per quarter showed large variance amongst ECPs (130, 0-2275; median, range). Predictably, CLOs tended to see many more contact lens patients than the optometrists, as their clinical time is dedicated solely to contact lens work. Approximately 89% of all contact lens appointments were devoted to soft contact lens work and 11% to GP work (Figure 2.4).

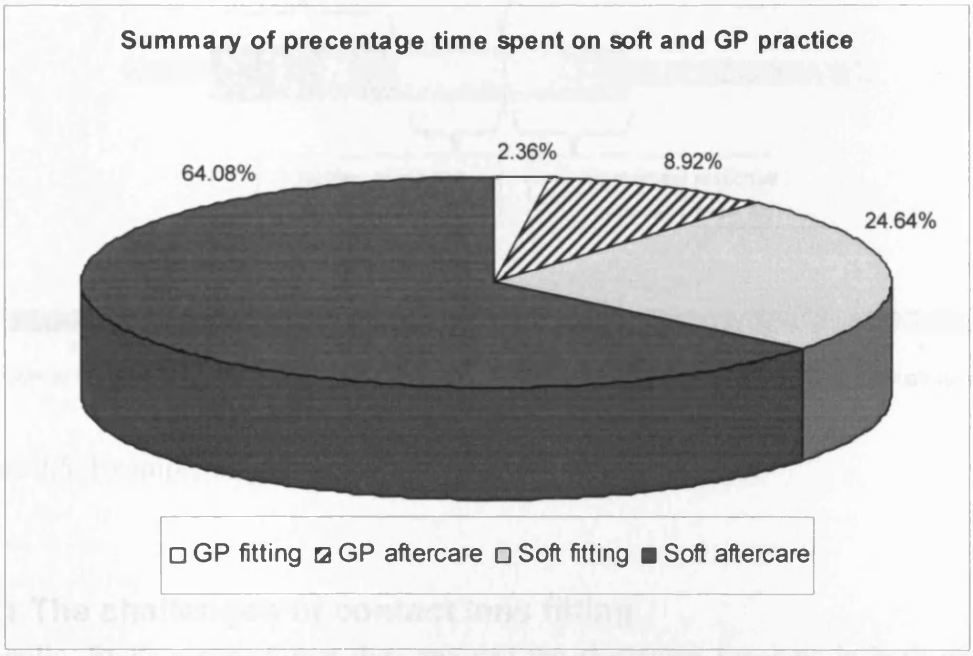


Figure 2.4: Summary of percentage time spent on soft and GP contact lens practice.

2.4 Practitioner attitudes to contact lenses

The second part of the questionnaire asked ECPs to indicate their agreement or disagreement with each contact lens related statement. They were invited to do this by circling an appropriate score ranging from 0 (strong disagreement) to 6 (strong agreement). The responses for each statement have been tabulated and also displayed in a graphical form for illustration purposes. An example of the graph design is shown in Figure 2.5.

Considering the statement: '*xxxxxxxxxx*'

% of respondents expressing agreement = sum of percentage scores for categories 4, 5 and 6.

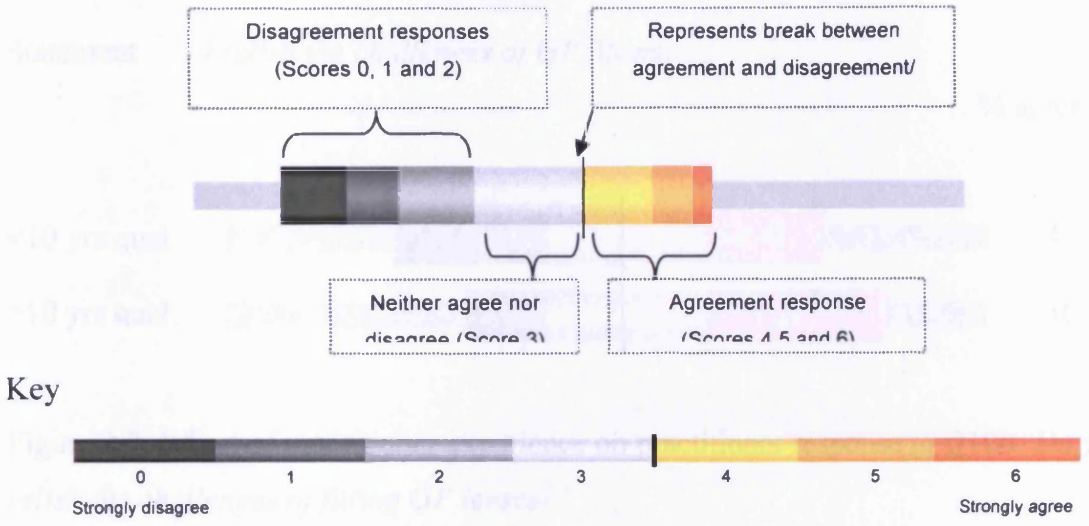


Figure 2.5: Example of presentation of results

2.4.1 The challenges of contact lens fitting

Generally, ECPs reported that they enjoyed the challenges involved in both general lens fitting and specifically GP fitting (Figure 2.6, Table 2.2). However, when analysed, the ECP's responses were more positively skewed towards general CL fitting compared with GP fitting (Wilcoxon Rank $p<0.05$).

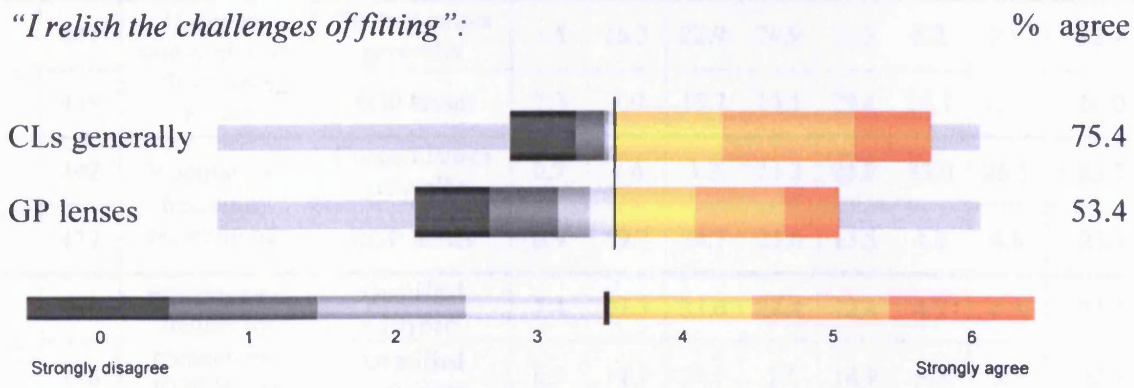


Figure 2.6: Percentage practitioner responses to Q10a and b *'Do you relish the challenges of fitting contact lenses?'*

More experienced ECPs, those qualified for 10 years or more, tended to respond more positively to the statement *'I relish the challenges involved in GP fitting'* compared to the less experienced ECP (qualified less than 10 years) (Wilcoxon Rank, $p<0.05$) (Figure 2.7, Table 2.2).

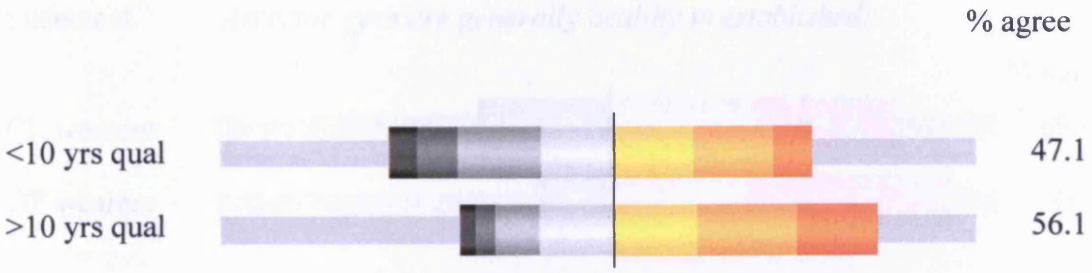


Figure 2.7: Effect of practitioner experience on practitioner response to Q10b *'Do you relish the challenges of fitting GP lenses?'*

Table 2.2: Summarised data showing ECP responses to attitude-related questions

Q	N	Statement		0	1	2	3	4	5	6	% Agree
				Disagreement → Agreement (%)							
10	438	I relish the challenges of fitting:	Contact lenses generally	1.1	1.1	6.8	15.5	25.6	31.1	18.7	75.4
	436		RGP lenses	5.5	7.3	16.1	17.7	18.8	21.3	13.3	53.4
10	254	I relish the challenges of RGP fitting:	Qualified <10years	6.6	9.3	19.5	17.5	18.7	19.1	9.3	47.1
	176		Qualified >10 years	4.0	4.6	10.3	17.8	19.5	24.1	19.5	56.1
13	441	It is time-consuming to fit contact lenses	Contact lenses generally	7.5	16.3	22.9	20.9	21.3	8.2	2.9	32.4
	439		RGP lenses	2.3	3.9	13.7	14.1	29.4	24.1	12.5	66.0
17	442	Practitioners frequently recommend:	Contact lenses generally	0.7	1.6	3.2	11.3	23.8	33.0	26.5	83.3
	437		RGP lenses	6.9	19.7	24.7	25.6	13.5	4.8	4.8	23.1
17	255	Practitioners frequently recommend RGP lenses	Qualified <10years	7.4	23.3	23.6	24.4	12.4	4.7	4.3	21.4
	176		Qualified >10 years	6.3	14.9	25.9	27	14.9	5.2	5.7	25.8
20	257	RGP lenses are becoming obsolete	Qualified <10years	6.2	11.2	14.2	15.8	25.0	18.8	8.8	52.6
	180		Qualified >10 years	13.0	9.6	18.1	19.2	19.8	15.8	4.5	40.1

2.4.2 Eye health in contact lens wear

ECPs generally agreed with the statement that the anterior eyes are healthy in both the general contact lens wearing population and the GP wearing population. Significantly more ECPs agreed that anterior eyes are healthy in GP wearers than in a general CL wearing cohort (Wilcoxon Rank, $p<0.05$) (Figure 3.8, Table 3.3).

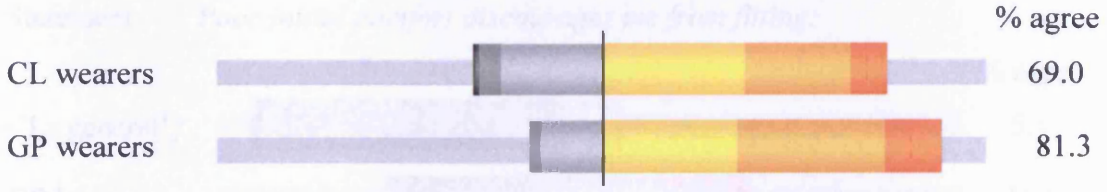


Figure 2.8: Percentage practitioner responses to Q18a and b '*Do you feel that the anterior eyes are healthy in established contact lens wearers?*'

Table 2.3 Summarised data showing ECP responses to health and comfort-related questions.

Q	N	Statement		0	1	2	3	4	5	6	% Agree
				Disagreement → Agreement (%)							
14	436	Poor initial comfort discourages me from fitting:	Contact lenses generally	29.8	33.0	22.2	9.6	2.1	2.8	0.5	5.4
	435		RGP lenses	9.2	14.0	18.4	17.2	17.0	17.0	7.1	41.1
15	432	It is clinically acceptable to use anaesthetic during RGP fitting:		15.0	11.8	17.6	25.2	16.2	9.0	5.1	30.3
18	438	Anterior eyes are generally healthy in established:	Contact lenses generally	0.2	1.1	5.0	24.7	34.0	26.3	8.7	69.0
	439		RGP lenses	0.2	0.7	2.7	15.0	32.3	35.8	13.2	81.3
19	444	Patients report good comfort levels once adapted to:	Contact lenses generally	0.0	0.0	0.2	5.0	18.0	52.0	24.8	94.8
	437		RGP lenses	0.0	0.0	1.1	8.9	27.0	46.0	16.9	89.9

2.4.3 Effect of initial discomfort on contact lens fitting

Initial discomfort in lens fitting was not found to discourage ECPs from fitting contact lenses generally. However, ECP responses for the same statement with respect to GP fitting were significantly different, indicating that reduced initial comfort with GP lenses does significantly discourage (some) ECPs from fitting this lens type (Wilcoxon Rank, $p<0.05$) (Figure 2.9, Table 2.3).

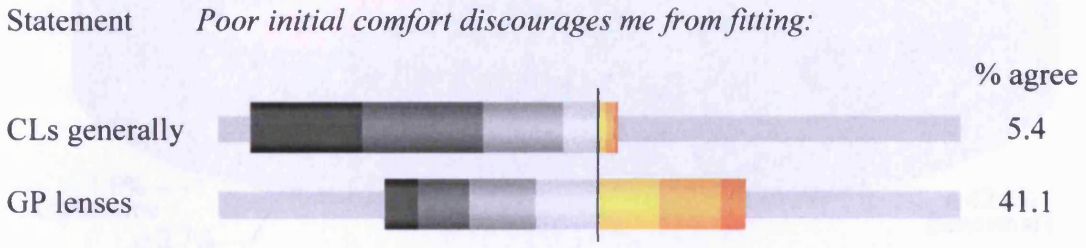


Figure 2.9: Percentage practitioner response to Q14a and b '*Does poor initial lens comfort discourage you from contact lens fitting?*'

2.4.4 Use of topical anaesthetic for gas permeable lens fitting

Predominantly, UK ECPs do not use topical anaesthetic (TA) when fitting GPs: 12.4% of ECPs use TA some of the time when they fit GP lenses, and just 1.4% of ECPs routinely use TA for fitting. Statistically, there was no correlation between ECP experience when comparing those qualified for more than or less than ten years, in terms of topical anaesthetic use (Pearson Chi Square, $p=0.512$) (Figure 2.10).

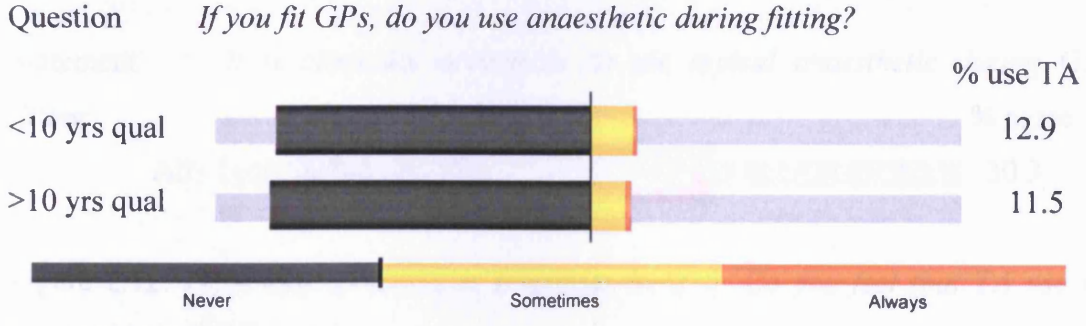


Figure 2.10: Percentage practitioner responses to Q8a '*Do you use TA during GP fitting?*'

Of ECPs that use TA, proxymetacaine is the most common drug selection, used by 51.8% of those ECPs, followed by benoxinate, used by 42.6% of ECPs (Figure 2.11).

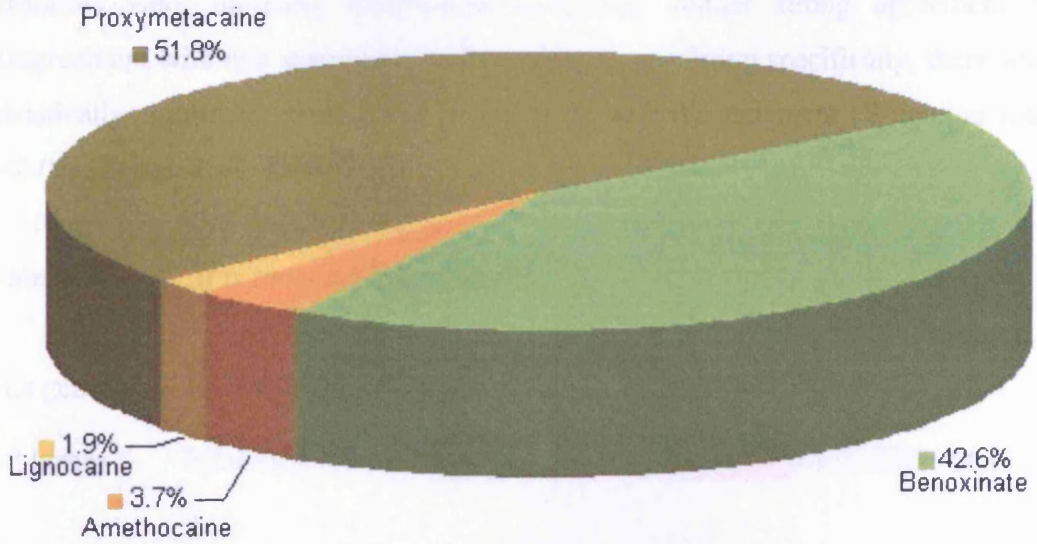


Figure 2.11: Percentage practitioner responses to Q8b '*What is your preferred topical anaesthetic agent?*'

2.4.5 Attitudes toward use of topical anaesthetics during contact lens fitting

The questionnaire also asked about ECP opinion regarding the use of topical anaesthetics (TA) during routine GP fitting. ECP responses regarding TA use were varied (Figure 2.12, Table 2.3). Approximately 25% of ECPs neither agreed nor disagreed with a statement describing TA use as acceptable. 15% of ECPs strongly disagreed with TA use for routine fitting, and only 5% strongly agreed with its use.

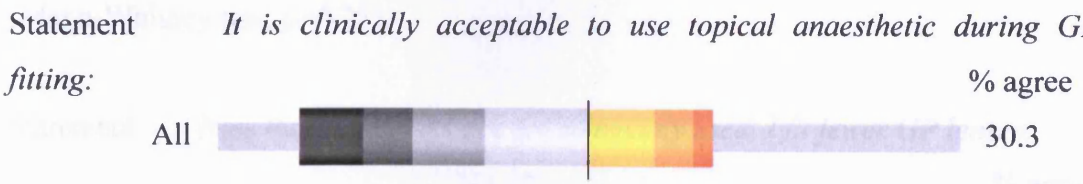


Figure 2.12: Percentage practitioner responses to Q15 '*Do you feel that TA use is acceptable in GP fitting?*'

2.4.6 Time required to fit contact lenses

When asked whether contact lens fitting, in general, is time-consuming, ECP responses were normally distributed, indicating neither strong agreement nor disagreement with this statement. With respect to GP fitting specifically, there was a statistically significant skew toward agreement with the statement (Wilcoxon Rank, $p<0.05$) (Figure 2.13, Table 2.2).

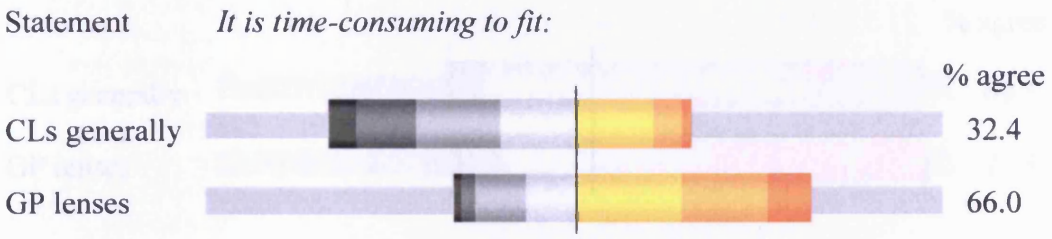


Figure 2.13: Percentage practitioner responses to Q13a and b '*Do practitioners find contact lens fitting time consuming to fit?*'

2.4.7 Use of trial lens sets in GP fitting

ECPs were asked whether the withdrawal of trial lens sets traditionally used to aid GP fitting had influenced the fitting rate of GP lenses. This meant that ECPs who qualified after 1999 (n=377) would not have been exposed to regular fitting set use, therefore their responses have been excluded to produce the second graph (Figure 2.14). Remaining ECP opinions were varied, indicating neither strong agreement nor disagreement with the statement (Table 2.4). Comparison of responses indicated no significant difference between ECPs qualified before and those qualified after 1999 (Mann-Whitney test, $p=0.25$).

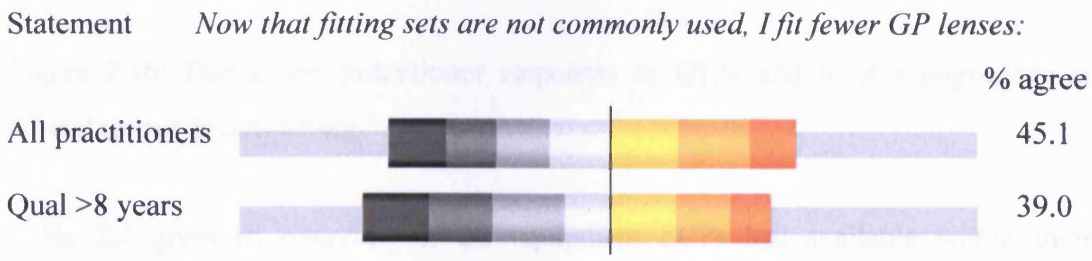


Figure 2.14: Percentage practitioner, qualified more than 8 years, responses to Q16 '*Does the discontinuation of fitting set use mean reduced GP fitting?*'

2.4.8 Equipment for contact lens fitting

ECPs strongly agreed that a slit-lamp and keratometer are sufficient for successful GP fitting. However, ECP agreement was statistically weaker with respect to application of a slit-lamp and keratometer for general contact lens fitting (Wilcoxon Rank, $p<0.05$) (Figure 2.15, Table 2.4).

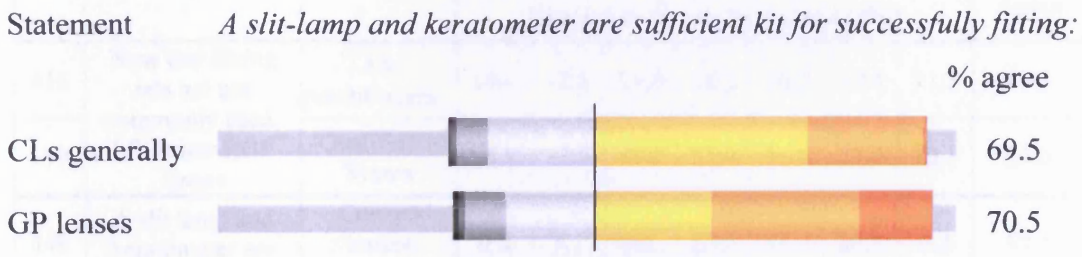


Figure 2.15: Percentage practitioner responses to Q11a and b '*A slit-lamp and keratometer are sufficient for successful lens fitting?*'

When asked whether a topographer would be advantageous for contact lens fitting, Figure 2.16 and Table 2.4 indicate that ECP responses for contact lenses generally were normally distributed, while responses for GP fitting were positively skewed indicating statistically stronger agreement with this statement (Wilcoxon Rank, $p<0.05$).

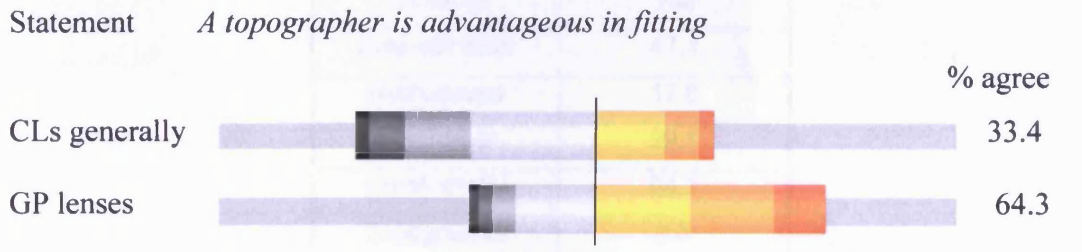


Figure 2.16: Percentage practitioner responses to Q12a and b '*A topographer is advantageous in lens fitting?*'

Table 2.4 gives an overview of the equipment ECPs had available within their practice. Although ECPs generally believed a topographer would be advantageous in GP fitting, the results demonstrate that just 9.6% of ECPs have a topographer

available to them in practice. Equipment such as a radiuscope and v-gauge, associated with GP work, do not appear to be standard practice equipment.

Table 2.4 Summarised data showing ECP responses to equipment-related questions.

N	Statement		0	1	2	3	4	5	6	% Agree
			Disagreement → Agreement (%)							
416	Now that fitting sets are not commonly used, I fit fewer RGP lenses	All practitioners	14.4	12.3	13.0	15.1	16.3	17.5	11.3	45.1
179		Qualified > 8years	15.9	15.9	17.4	11.6	15.9	13.0	10.1	39.0
440	A slit lamp and keratometer are sufficient kit for successfully fitting:	Contact lenses generally	0.5	1.1	6.6	22.3	44.5	24.8	0.2	69.5
438		RGP lenses	1.1	1.4	8.2	18.7	24.4	30.8	15.3	70.5
400	A topographer is advantageous in fitting	Contact lenses generally	3.8	9.5	18.5	35	19.3	9.8	4.3	33.4
403		RGP lenses	2.7	4.2	6.2	22.6	26.6	23.6	14.1	64.3

Table 2.5 Equipment available in practice.

Equipment	Practices with equipment (%)
Slit-lamp	100
Auto-refractor	47.4
Radiuscope	17.8
Focimeter	99.1
Keratometer	99.1
Topographer	9.6
V-gauge	13.6
Burton lamp	74.2

2.4.9 Adapted comfort in contact lens wear

ECPs agreed that patients report good comfort levels in both adapted GP and general CL wearers (Figure 2.17, Table 2.3). However, ECPs believe more firmly that patients in the general CL wearing population experience good comfort compared with those in the GP cohort (Wilcoxon Rank $p<0.05$).

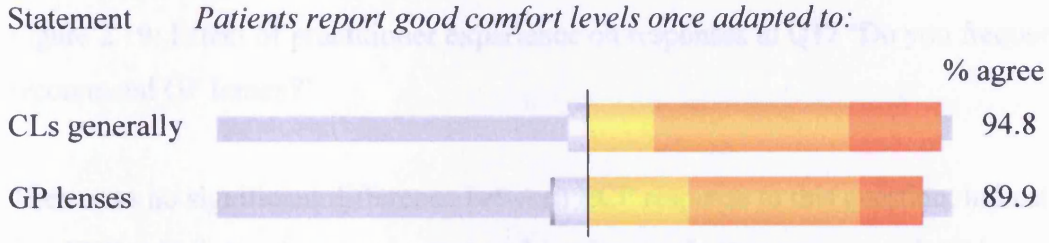


Figure 2.17: Percentage practitioner responses to Q19a and b '*Patients report good comfort levels once adapted to lenses*'.

2.4.10 Practitioner contact lens recommendations

Despite ECP opinion that GP wearers generally have 'healthier anterior eyes' than other lens wearing cohorts, negative ECP perceptions toward GP fitting appears to result in a significantly lower frequency of GP recommendations to patients (Wilcoxon Rank, $p<0.05$), shown in Figure 2.18. However, Table 2.2 indicated that more experienced ECPs tend to recommend GPs more frequently than less experienced ones, although this is not statistically significant.

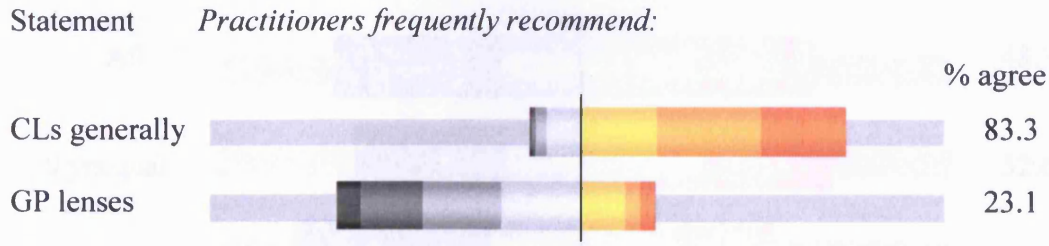


Figure 2.18: Percentage practitioner responses to Q17a and b '*Do you frequently recommend lenses?*'

Practitioners frequently recommend GP lenses:

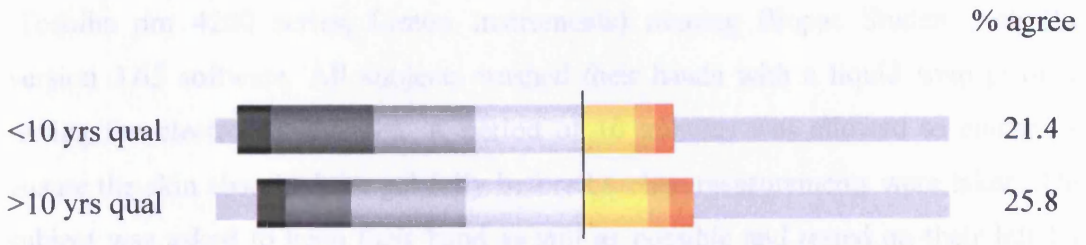


Figure 2.19: Effect of practitioner experience on responses to Q17 'Do you frequently recommend GP lenses?'

There was no significant difference between ECP response to this question, indicating that ECP experience does not impact on how frequently they recommend GP lenses to patients (Figure 2.19).

2.4.11 GPs are becoming obsolete

Finally, ECPs were asked whether they agree that GP lenses are becoming obsolete. Approximately half of young ECPs (qualified less than 10 years) felt that this statement was true; while more experienced ECPs (qualified longer than 10 years) were somewhat more optimistic, with only 40% agreeing that GPs are becoming obsolete (Figure 2.20 and Table 2.2).

GP lenses are becoming obsolete:

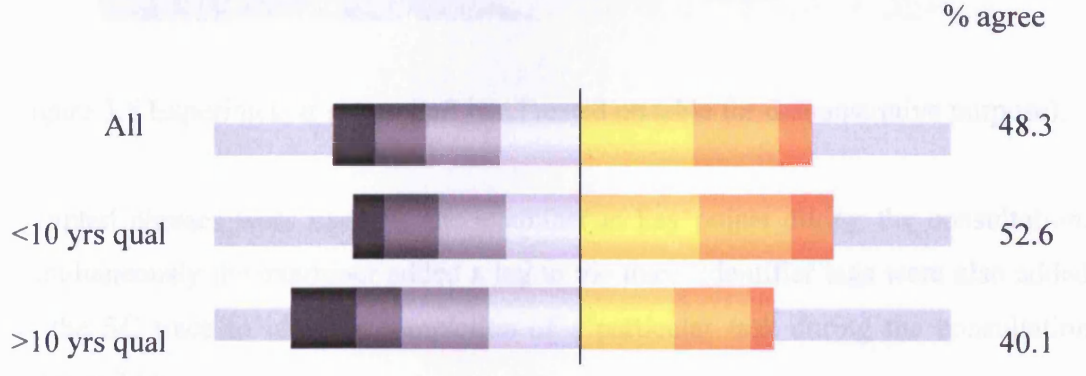


Figure 2.20: Percentage practitioner responses to Q20 '*Are GPs becoming obsolete?*'

2.5 Discussion

The use of GP lenses in UK contact lens practice has undergone a gradual decline over the past decade, even though GP lenses can give superior clinical outcomes compared with alternative soft or silicone hydrogel lenses (Ziel et al., 1990a; Qu et al., 2003; Bennett and Hom, 2004). This survey has confirmed that GP contact lens practice makes up only a small part of UK contact lens practice (11%). This is supported by reports in the literature, which indicate a steady decline in GP prescribing in favour of soft lenses (Morgan et al., 2002; Morgan and Efron, 20062008ab; Morgan, 2009ab). One explanation may be that developments in soft lens designs and materials (material permeability, deposit resistance, wettability, improved toric and presbyopic options) have led ECPs to believe that GP lenses have been 'superseded'. However, a clearer understanding of practitioner attitudes toward GP lenses may provide clearer understanding of why GP prescribing is in decline.

This survey has allowed the examination of several factors that may play a part in the prevalence of GP prescribing. The idea that GP fitting is more demanding in time, clinical skill and equipment than soft lens fitting is supported by the results. Most ECPs perceive GP fitting to be more time consuming than general contact lens fitting, even though they appear to enjoy the challenge. Despite this, less than one quarter of the sample would frequently recommend GP lenses to their patients. It would seem that the technical challenge of fitting the lenses is not a major factor in the decline of GP fitting, at least with experienced ECPs.

The survey found that ECPs who trained or qualified after 1999 held different attitudes to their longer practicing counterparts. In June 1999, the UK Department of Health stated that contact lenses should be for single patient use only, due to the remote theoretical risk of cross-infecting patients with variant Creutzfeldt-Jakob disease (vCJD) (Macalister and Buckley, 2002). Up until that time, ECPs were able to use fitting sets to efficiently assess the best fit before ordering the final specification lens. From the survey results, ECPs qualified for less than 10 years were less interested in the fitting challenge – less than half of this group enjoyed fitting GP lenses, and they were more likely to think GPs were becoming obsolete.

Generally, ECPs qualified longer than 10 years tended to hold more positive attitudes toward GP lenses, compared with those qualified for a shorter period. This suggests that the more recently qualified have not had the same experience during their education, and in their early, qualified years, in fitting GP lenses, as those who trained and qualified before 1999. It has been reported that there is no shortfall in the education of GP fitting in UK optometry schools; however, there may be a lack of practical experience available to early career ECPs because there are now fewer GP lens wearers in a typical patient cohort, resulting in fewer patients available to attend clinics (Efron, 2005).

Most ECPs surveyed felt that specialist equipment was not essential for GP fitting, although many agreed that instrumentation such as a topographer would be beneficial to the fitting process. Published literature supports practitioner belief that topography may aid GP fitting, however clinical judgement remains a mandatory element in successful fitting (Postma, Postma and Schnider, 1993; Szczotka et al., 1994; Bufidis, Konstas and Mamtziou, 1998).

Respondents demonstrated that TA use during GP fitting is not customary practice in the UK. Previous research has shown the use of TA during fitting to be safe and effective in improving initial comfort and long-term patient success in GP wear (Bennett et al., 1998a). The results represent an important finding because initial lens discomfort is cited by ECPs as a disincentive to GP prescribing. A second advantage of TA use is that it reduces lacrimation and blepharospasm, allowing prompt fit assessment following insertion, and thus a shortened fitting process (Bennett et al., 1998a). This is potentially of significant benefit to UK practitioners because, as discussed earlier, ECPs find GP fitting takes longer than alternative lens types. Practitioner opinion regarding the acceptability of using TA in contact lens fitting is varied, and only 1 in 3 of those surveyed believe it is safe practice.

The survey gave practitioners the opportunity to propose that initial and adapted comfort issues deter ECPs from GP fitting. Comfort is a particularly important issue for both contact lens wearers and contact lens ECPs, because comfort-related issues are cited as the primary reason for contact lens dissatisfaction and discontinuation (Richdale et al., 2007). The results from the survey reveal an interesting paradox in

practitioner views. Although ECPs indicated that poor initial comfort with GP lenses discourages them from fitting this lens type, they acknowledged that adapted GP wearers generally experience good comfort levels. Such adapted lens wear comfort has been confirmed in previous research, with no differences between a cohort of adapted GP and soft lens wearers reported (Morgan et al., 2003). These findings would support the supposition that compromised initial comfort is a factor in reduced GP fitting statistics. They also indicate that it is the reservations of the practitioner regarding comfort which affects subsequent advice and lens options presented to the patient. This is reflected in the results of this study, which show GP lenses are not frequently recommended to patients by ECPs.

Despite some negative attitudes surrounding GP lenses, this survey found that ECPs believe patients are more likely to have a healthy anterior eye when wearing GP lenses compared with contact lenses generally. This belief is in line with current education and research which reports that GP lenses have statistically lower average number of complications compared with soft lenses (Stapleton et al., 2008; Forister et al., 2009).

There is a risk of bias in this survey, since the ECPs who completed and returned the questionnaire may be those with an interest or bias toward contact lens practice. This may be reflected in the response from ECPs who positively supported the statement that they relish the challenges involved in fitting all types of contact lenses. However, even when practitioner responses were compared between lens types, ECPs responded significantly more positively with respect to general fitting over GP fitting. In the survey, ECPs were asked to report their approximate frequency of fitting and aftercare consultations. The accuracy of response is dependent on each practitioner's reliability in reporting the type and quantity of contact lens consultations – possible incorrect reporting of these statistics may have influenced the accuracy of the results.

Orthokeratology lens fitting is a specialised form of GP fitting. In the UK, in 2008, less than 1% of all fits in UK were with orthokeratology lenses. This type of fitting, and other more specialised GP fitting such as post-graft and keratoconic fitting, was beyond the focus of this study. However, it would be interesting to further investigate patient selection as it may be observed that practitioners select GP lenses for specialist

cases or when a problem solving lens is required. In a letter to Clinical and Experimental Optometry in 1999, Don Ezekiel suggested that the profession may be becoming de-skilled in the area of rigid lens fitting (Ezekiel, 1999). His view would seem logical, if ECPs are not regularly using and improving their rigid lens fitting skills, they will gradually be lost. Efron argues that the skill requirements are simply changing over time to meet different clinical needs (Efron, 2000). Therefore GP prescribing will not disappear completely, but it may become an activity for an elite speciality group of practitioners.

To exert influence on these 'negative' practitioner attitudes toward GP prescribing, three areas need to be addressed. Firstly, for those ECPs who qualified after 1999 in the UK, some additional training may be of help in developing their clinical skills in GP fitting. Similarly, contact lens training institutions should review their GP training provision to ensure it provides those in training with the opportunity to develop their practical skills. Secondly, the use of topical anaesthetic in aiding the initial comfort experience during GP lens fitting should be investigated amongst a UK cohort to confirm whether there is a long-term benefit to the patient in comfort and that no adverse clinical reactions are produced. Thirdly, alternative GP lens designs, such as large diameter lenses, should be investigated as this may improve lens wear comfort while still providing the benefits of GPs for ocular health (Bennett, 1999).

2.6 Conclusions

UK contact lens ECPs are aware of the benefits that GP lenses provide in terms of ocular health and optical correction. While they accept they take longer to fit, they enjoy the challenge of the fitting, which suggests that they are not grossly lacking in clinical skill, nor do they feel hindered by lacking any specialist equipment. However, they are unhappy with initial patient comfort, and are not yet prepared to use topical anaesthetics during initial fitting. As a consequence, ECPs believe that GP lenses are becoming obsolete. Undoubtedly the initial comfort of soft lenses has a large role to play, but negative practitioner attitudes toward various aspects of GP fitting means fewer recommendations to patients and reduced GP prescribing.

3. Investigation of the effect of topical anaesthetic use prior to GP lens fitting

3.1 Introduction

3.1.1 General introduction

The decline in gas permeable (GP) prescribing is well documented. In Chapter 2 a contact lens questionnaire was designed and implemented to investigate practitioner attitudes and practices relating to GP lenses. One finding was that initial discomfort with GP lenses discourages practitioners from recommending this lens type to patients. Secondly, practitioners reported that the use of topical anaesthetic (TA) to aid fitting is not common practice in the UK. Further, practitioner opinion regarding the acceptability of TA use during GP fitting was divided. The outcomes of this questionnaire highlighted the need for an investigation of the safety and merit of TA during GP fitting to aid initial comfort experience.

TA use in GP fitting has been demonstrated to enhance initial patient comfort (Bennett et al., 1998a), and may also reduce patient anxiety about initial lens comfort (Schnider, 1996). If initial comfort is improved with TA, particularly in patients perceived to be sensitive or anxious, practitioners may feel encouraged to consider GP lenses as a potential option (Schnider, 1996).

Use of TA may make the first GP experience more comfortable, however some clinicians argue that this makes the second visit, without TA, a worse experience. Therefore, the use of TA may unhelpfully mislead the patient. Published literature shows that use of TA results in less patient dropouts following the fitting phase (Bennett et al., 1998a), however an insight into patient experience over the fitting phase would be advantageous. This study was designed to investigate the use of TA during GP lens fitting.

3.1.2 Chemical composition of anaesthetic

The TA molecule consists of an aromatic residue and an amino group, linked by an alkyl chain; either ester or amide, Figure 3.1 (Lawrenson et al., 1998). This linkage determines how the drug is metabolised. Local anaesthetics with ester linkages have a

short duration of action, because an ester linkage is easily hydrolysed compared to an amide linkage, which is more resistant to hydrolysis (Lawrenson et al., 1998).

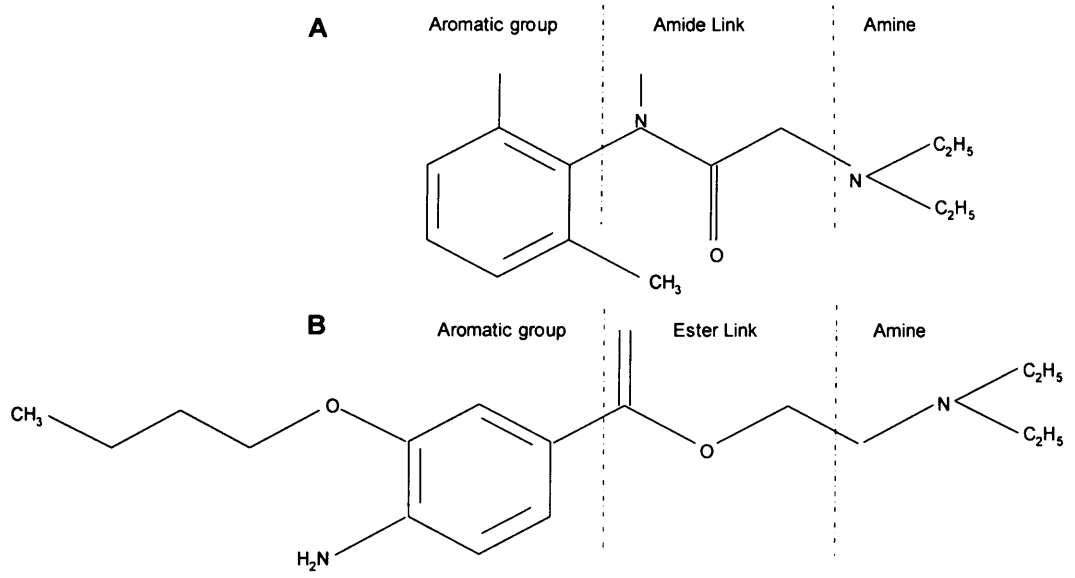


Figure 3.1 Molecular structure of anaesthetics; A: an amide linkage and B: an ester linkage, adapted from Lawrenson et al., 1998.

TAs are weak bases which can exist alternately in ionised (water-soluble) and non-ionised (lipid-soluble) form. The non-ionised form can absorb across the tears and through the cornea, whilst the ionised form is responsible for the anaesthesia effect. The pH of the drop affects the proportion of the non-ionised drug available for absorption at the cornea. Decreasing the pH, within limits, will increase the non-ionised proportion. However, the more that pH deviates from physiological pH 7.4, the more the drop will irritate the eye on instillation (Millis, 2005). Solubility and stability of the drug will also be altered by pH variation (Lawrenson et al., 1998).

3.1.3 Mechanical action of topical anaesthetics

Local anaesthetics affect the epithelial ion transport system of the cornea, causing a temporary block in the conduction of action potentials along nerve fibres, and preventing the sensation of pain in a localised area (Hopkins and Richard, 2007). It is suggested that anaesthesia inhibits the short-circuit current across the cornea by reducing the chloride permeability of the corneal cells (Schoen and Candia, 1979).

3.1.4 Anaesthetic selection

The coca plant was traditionally used for its anaesthetic properties in Peru; cocaine was first isolated in 1860 and used as a local anaesthetic in 1884. However, it has many undesirable effects including mydriasis, epithelial desquamation and increased corneal permeability; also it is an addictive compound (Lyle and Page, 1975; Boljka, Kolar and Vidensek, 1994).

The ideal anaesthetic would take effect promptly, provide adequate duration and depth of anaesthesia, cause no ocular irritation, and no systemic or corneal toxicity (Sun, Hamilton and Gimbel, 1999). Various topical anaesthetics are available to optometrists for professional use; the most significant difference between them is the amount of discomfort on instillation (Hopkins and Richard, 2007).

The anaesthetic pH affects the comfort on instillation; the lower the pH, the more acidic the drug and the more it stings on instillation (Shafi and Koay, 1998; Millis, 2005). Even if the anaesthetic agent is diluted by the tears, the effect is small due to the relatively large volume of anaesthetic instilled in one drop (Lawrenson et al., 1998). Proxymetacaine has been shown to sting least compared to other anaesthetics including amethocaine, oxybuprocaine (Lawrenson et al., 1998; Shafi and Koay, 1998; Hopkins and Richard, 2007) and amethocaine and lidocaine (Hopkins and Richard, 2007). Duration of stinging with proxymetacaine is shorter than amethocaine and oxybuprocaine (Lawrenson et al., 1998; Shafi and Koay, 1998): proxymetacaine stings for 3.2 seconds, compared with 22.1 seconds for amethocaine (Shafi and Koay, 1998) and 7.2 seconds for oxybuprocaine (Emmerich, Carter and Berens, 1955). This may be attributed to the slightly less acidic formulation for proxymetaciane compared to the other agents (Lawrenson et al., 1998).

Osmolarity is similar for the three preparations, indicating that it is unlikely that this component affects instillation comfort (Lawrenson et al., 1998). Structurally, proxymetacaine is an ester of meta-aminobenzoic acid, while amethocaine and oxybuprocaine are esters of para-aminobenzoic acid. It is unclear whether this difference contributes to comfort differences.

Due to its mild sting, proxymetacaine is the most commonly used agent for ocular anaesthesia (Hopkins and Richard, 2007). It is a synthetic topical anaesthetic, available in unit dose form, in 0.5% solution. Anaesthesia onsets 6-20 seconds post-instillation (Hopkins and Richard, 2007), though accuracy of onset time measurement is poor because drug-induced stinging may be present following instillation. One minute after instillation, complete anaesthesia is achieved (Lawrenson et al., 1998), and lasts approximately 15 minutes (Hopkins and Richard, 2007), though recovery varies greatly between subjects. The return of sensation varies between 8 and 32 minutes, and after 45 minutes all subjects return to baseline sensitivity (Lawrenson et al., 1998).

3.1.5 Adverse reactions to local anaesthetic

Following anaesthetic instillation, the eye is potentially at risk of damage due to decreased corneal sensitivity, reduced blink rate and abnormal drying of the cornea. Patients should be warned against excessive eye rubbing and of the risks of foreign body injury (Lyle and Page, 1975).

Ocular side-effects following instillation of one drop of anaesthetic are possible, though reactions are generally mild and reversible within three hours (Boljka et al., 1994). Toxic side-effects of anaesthetics can cause damage to the epithelium, including deposits on cell membrane or microvilli and loss of microvilli in epithelial cells. This damage to the microvilli leads to desquamation of the epithelial cells and interrupts contact between microvilli (Boljka et al., 1994). One reason for anaesthetic toxicity is a change in pH (Boljka et al., 1994), and pH-adjusted preparations may reduce the possibility of corneal toxicity (Sun et al., 1999). Local anaesthetics cause delayed healing of the corneal epithelium because epithelial sliding or motility is inhibited (Rosenwasser et al., 1990). Repeated instillation of anaesthetic can increase the risk of defects in the epithelium or keratitis (Rosenwasser et al., 1990).

An acute epithelial allergic reaction is rare, but can develop as a diffuse keratitis. The cornea becomes oedematous, conjunctival vessels become congested, and patients report photophobia and blurred vision (Lyle and Page, 1975). Treatment is not usually required and the cornea generally returns to normal within one hour.

There have been no reported systemic toxic reactions from anaesthetic used for topical anaesthesia in the eye (Lyle and Page, 1975). However, anaesthetics can produce a toxic effect if anaesthetic is injected into a blood vessel, or topical application is made to a large mucosal surface e.g. nasal or oral mucosa (Norden, 1976).

Anaesthetics can also cause a systemic allergic reaction, generally in patients pre-disposed to allergies. This type of reaction requires prior sensitisation and involves histamine release, causing various effects including oedema, itchiness and breathing difficulties (Lyle and Page, 1975). Severe allergic response is rare and anaphylactic reaction is even less common (Lyle and Page, 1975).

3.1.6 Anxiety and contact lenses

Anxiety is the adaptive response to a threat, for example, in response to clinical procedures (Shute, 1986). Anxiety is known to influence patient success with contact lenses (Hewett, 1984; Hutchison, 2001). It has been suggested that patients may not try contact lenses because they are anxious about having them placed on their eyes (Hutchison, 2001).

3.1.6.1 Subjective measurement of anxiety

Visual analogue scales (VAS) ask the patient to rate their experience or feelings by marking a scale. Usually this is a horizontal line with a word descriptor at each end (Crichton, 2001). They are a time-efficient and simple way of eliciting a valid, reliable subjective assessment of an attitude or characteristic (Price et al., 1983), such as comfort or anxiety level.

Van der Worp et al., (2009) used VAS to measure ocular comfort in GP lens wearers to investigate the inter-relationships between signs of corneal staining and contact lens comfort. VAS is most effective when looking for change within the same individual over time (Crichton, 2001), however care must be taken in the interpretation of results because VAS feedback is highly subjective, making comparison between individuals less reliable. VAS aims to ascertain a subject's

position within a continuous sensation spectrum, but this is not truly possible because humans can only discriminate between approximately seven categories (Miller, 1956). This means that respondents mentally break the scale down into several discreet parts, therefore, scores should not be interpreted as a linear scale (Straube and Campbell, 2002). Instead, it is suggested they should be analysed by rank ordering of scores (Crichton, 2001).

The State and Trait Anxiety Questionnaire takes better account of the facts that anxiety levels appear to vary between individuals, and both internal and external forces may influence anxiety levels (Spielberger, 1966; Spielberger, Gorsuch and Lushene, 1983). Spielberger and Smith, (1966) suggested that 'trait' anxiety refers to a person prone to anxiety, while 'state' anxiety is a transient anxiety experience. He also suggested that many factors influence the anxiety process including trait anxiety, past learning and memory, and sensory and cognitive feedback (Spielberger, 1966). Trait anxiety may be dependent on heredity, via the physiological system, along with visceral brain function, which is responsible for emotional processing (Eysenck, 1967).

The Spielberger State-Trait Inventory (STAI) (Spielberger et al., 1983) incorporates two 20-item question sets measuring state and trait anxiety. The items are generic and the STAI has been used to measure anxiety in many healthcare studies (Cruise et al., 1997; Farmer et al., 2003; Sari et al., 2005). The full STAI is lengthy and has therefore been shortened to a 6-item state scale (Marteau and Bekker, 1992), which has also been successfully used in healthcare studies (Maissi et al., 2004; McManus et al., 2005; Robb et al., 2006). It has good internal reliability and strong correlation with the full STAI (Cronbach alpha 0.82, r=0.95) (Marteau and Bekker, 1992). Court et al., (2009) produced a shortened version of the trait anxiety scale which was validated for optometric patients.

3.1.6.2 Objective measurement of anxiety

Anxiety or stress produces physiological changes to the body which can be quantifiably measured. One method of stress or arousal measurement is skin conductance (SC). SC shows the emotional state reflected by changes in the

sympathetic nervous system. Sympathetic activation causes release of acetylcholine, which acts on the muscarinic receptors leading to sweat production and a skin conductance increase (Storm, 2008). SC has been used as a tool for monitoring post-operative pain in medicine (Ledowski et al., 2007). It has been found to be better than alternative objective methods including heart rate, blood pressure and electroencephalograph (EEG) at detecting pain (Storm, 2008). SC was used in a study which evaluated patient anxiety during a soft contact lens fit procedure (Court, Greenland and Margrain, 2008). However, no investigation of anxiety during GP fitting, specifically with and without TA, has been reported.

3.1.7 Aims and objectives

a) To investigate the effect of TA use on ocular surface signs during GP fitting, compared to a placebo drop (saline);

b) To investigate the impact of TA use on both subjective and objective measures of patient anxiety during GP fitting;

c) To investigate the impact of previous TA use (during lens fitting) on the second patient experience with GP lenses (where no drops are applied).

3.1.8 Hypotheses

- Subjects in whom TA is instilled prior to GP fitting subjectively find GP lenses more comfortable that those who receive a placebo drop (saline);
- Subjects in whom TA is instilled are less anxious during the fitting process, than those receiving a placebo drop;
- Instillation of TA does not cause significant increases in hyperaemic or corneal response to GP insertion;
- At a return visit, subjects who have previously received TA at Visit 1 are less anxious prior to their second GP trial compared with those who receive a placebo drop at Visit 1.

3.2 Methods

3.2.1 Subjects

Forty seven subjects from staff and students within Cardiff University were recruited. Subjects attended for two study visits;

- Visit 1 mimicked a GP contact lens fitting. Either TA or placebo drops were instilled;
- Visit 2 mimicked a GP contact lens collection. No drops were instilled.

Twenty-nine subjects were neophyte and 19 had experience of or were current soft contact lens wearers. Subjects were randomly assigned to group A or B and either received TA 0.5% proxymetacaine (minim: Chauvin Pharmaceuticals, Romford, Essex, UK) or placebo drop; 0.9% saline (minim; Chauvin Pharmaceuticals, Romford, Essex, UK). Figure 3.2 shows the cohort sub-division. Informed consent was obtained and ethical permission for the study was obtained from the School of Optometry and Vision Sciences Ethical Committee. Subjects were excluded if they had worn GP contact lenses before, suffered from any ocular condition including dry eye or any systemic condition known to affect the tear film or cornea, were taking any medication known to affect the tear film or cornea, or were pregnant or breast-feeding. All procedures conformed to the tenets of the Declaration of Helsinki.

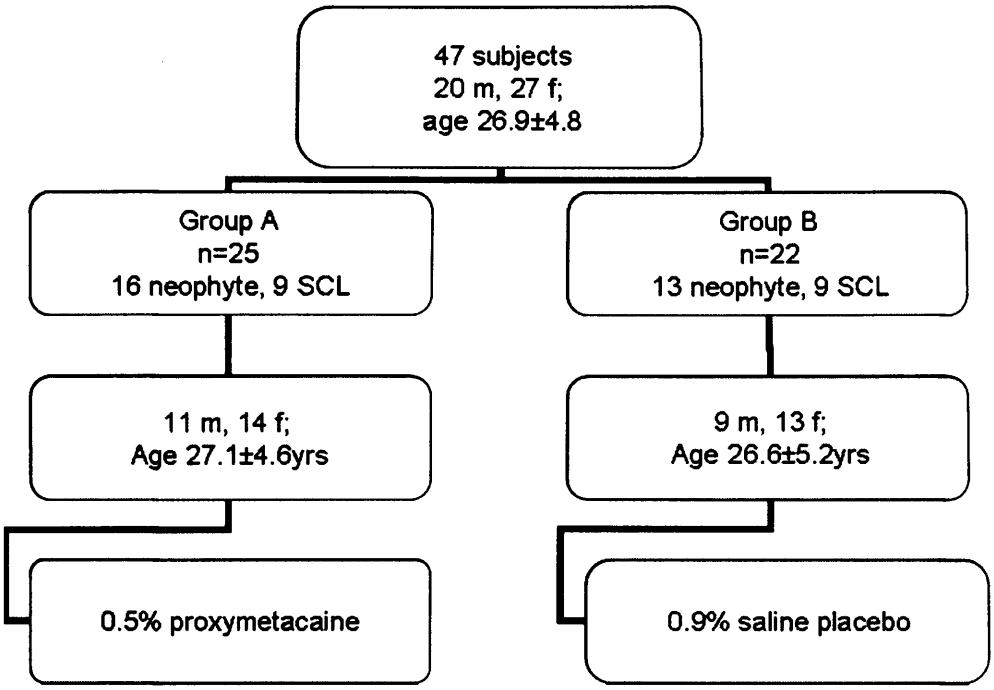


Figure 3.2 Flow chart to show cohort division.

3.2.2 Visit 1

3.2.2.1 Assessment of anxiety prior to lens fitting

Prior to lens fitting, anxiety was assessed in two ways: using a *visual analogue scale (VAS)* and a *'state-trait' questionnaire*. Figure 3.3 demonstrates the VAS used and Figure 3.4 shows the shortened version of the State and Trait questionnaires.

How anxious do you feel about having lenses on your eyes today?

NOT AT ALL *ANXIOUS* — VERY *ANXIOUS*

Figure 3.3 Anxiety visual analogue scale.

SELF-EVALUATION QUESTIONNAIRE: Part 1 (State)

	NOT AT ALL	SOMEWHAT	MODERATELY SO	VERY MUCH SO
1. Right now I feel calm	1	2	3	4
2. Right now I am tense	1	2	3	4
3. Right now I feel upset	1	2	3	4
4. Right now I am relaxed	1	2	3	4
5. Right now I feel content	1	2	3	4
6. Right now I am worried	1	2	3	4

SELF-EVALUATION QUESTIONNAIRE: Part 2 (Trait)

	ALMOST NEVER	SOMETIMES	OFTEN	ALMOST ALWAYS
1. Generally I feel like a failure	1	2	3	4
2. Generally I am "calm, cool, and collected"	1	2	3	4
3. Generally I feel that difficulties are piling up so that I cannot overcome them	1	2	3	4
4. Generally I am happy	1	2	3	4
5. Generally I feel secure	1	2	3	4
6. I get in a state of tension or turmoil as I think over my recent concerns and interests	1	2	3	4

Figure 3.4 Shortened version of Spielberger State-Trait questionnaire.

Respondents are asked to complete Part 1 (State) by circling the appropriate number to the right of the statement to indicate *'how you feel right now'*. Part 2 is completed to indicate how subjects feel generally.

3.2.2.2 Skin conductance recording

This study utilised a standard objective technique for recording anxiety or arousal. SC was measured by attaching two silver-silver chloride electrodes (coated with electrode gel) to the pads of the index and middle finger of the subject's left hand. Signals from the electrodes were amplified (x2000) and low pass filtered (0-35Hz) using a

physiological amplifier (Biopac MP30, Linton Instruments) connected to a laptop PC (Toshiba pro 4200 series, Linton Instruments) running Biopac Student Lab Pro version 3.65 software. All subjects washed their hands with a liquid soap prior to having the electrodes attached. A period of 10 minutes was allowed to elapse, to ensure the skin absorbed the gel fully before baseline measurements were taken. The subject was asked to keep their hand as still as possible and rested on their left leg throughout the consultation.

The contact lens trial was then conducted, and SC was recorded continuously throughout.

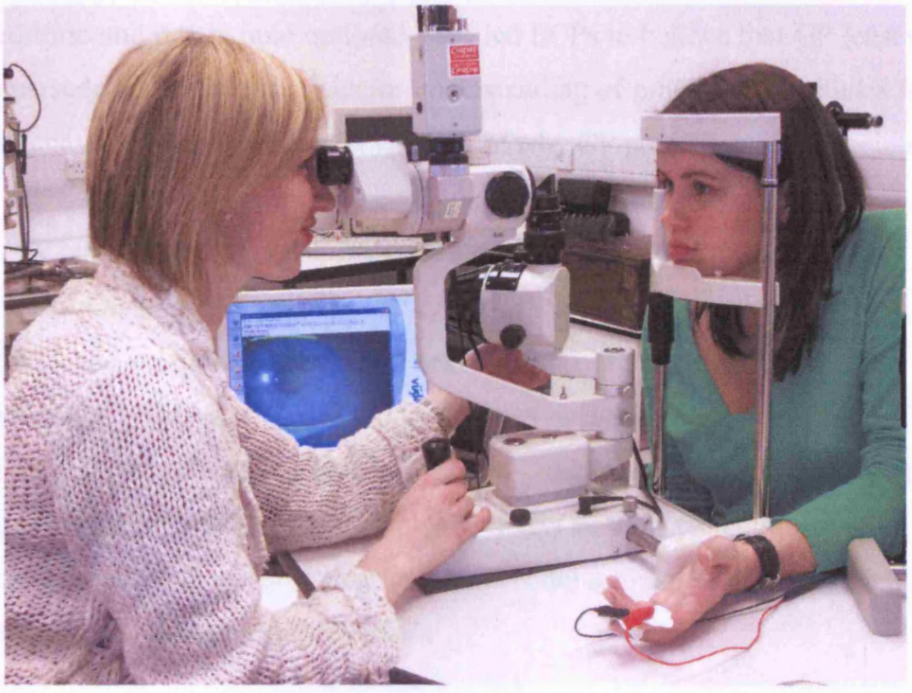
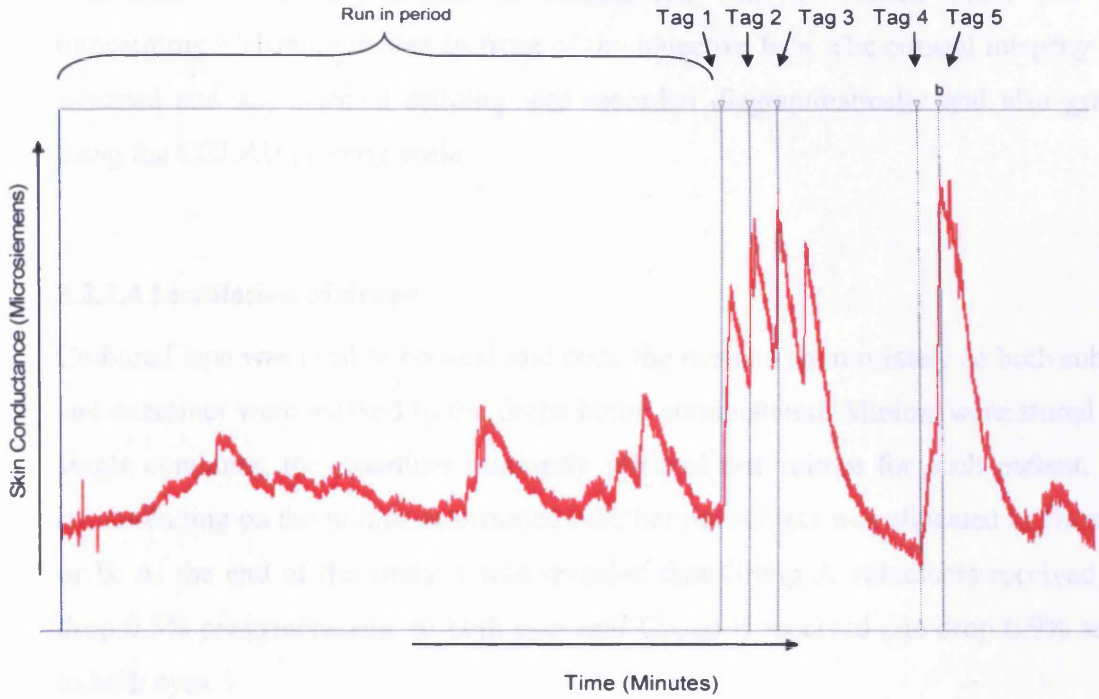


Figure 3.5 Experimental set up (left hand rested on table for demonstrative purpose).

Scripted phrases were used by the examiner at key points during the consultation; simultaneously the examiner added a tag to the trace. Identifier tags were also added to the SC trace to identify completion of a particular task during the consultation (Figure 3.6).



Tag 1 Examiner says 'I'm going to put a drop into your eyes now'.

Tag 2 Examiner says 'I'm now going to insert the lenses to your eyes'

Tag 3 Completion of lens insertion

Tag 4 Examiner says 'I'm now going to remove the lenses from your eyes'

Tag 5 Completion of lens removal

Figure 3.6 Typical example of raw skin conductance trace.

3.2.2.3 Anterior eye assessment

Corneal topography of both eyes was measured using the Keratron Scout topographer KS-1000 (Optikon, Rome, Italy). A slit-lamp (Sl-8Z; Topcon, Japan) was used to assess the health of the anterior eye. Initially, white light assessment allowed grading of conjunctival and limbal hyperaemia according to the Cornea and Contact Lens Research Unit (CCLRU) grading scale.

A Fluorescein sodium (FS) sterile ophthalmic strip (Chauvin Pharmaceuticals, Romford, Essex, UK) was wetted with non-preserved 0.9% saline (Oxysept Saline; Allergan/Advanced Medical Optics, Marlow, Buckinghamshire, UK) and FS instilled to the inferior tarsal conjunctiva. Tear film fluorescence was enhanced with cobalt

blue light transmitting 460nm in conjunction with a Wratten Filter (No 12) transmitting >510nm situated in front of the objective lens. The corneal integrity was assessed and any corneal staining was recorded diagrammatically and also graded using the CCLRU grading scale.

3.2.2.4 Instillation of drops

Coloured tape was used to conceal and code the minims appropriately so both subject and examiner were masked to the drops being administered. Minims were stored in a single container; the examiner randomly selected one minim for each patient. The colour coding on the minim determined whether the subject was allocated to Group A or B. At the end of the study it was revealed that Group A volunteers received one drop 0.5% proxymetacaine to both eyes and Group B received one drop 0.9% saline to both eyes.

3.2.2.5 Contact lens trial

Based on keratometry measurement, appropriate gas permeable contact lenses were selected from a fitting set (Quasar, No.7 Contact Lens Laboratory, Hastings, UK.) Lens diameter varied with lens BOZR (Table 4.3) and back vertex power -3.00 Dioptres. The required lenses were cleaned and rinsed using Boston Advance 2-step system (Baush & Lomb, Surrey, UK). Approximately one minute after TA instillation, a pair of lenses was applied with the patient adopting slight downward gaze. Lens position and movement was assessed once the lenses were settled and tearing/blepharospasm had subsided (typically 10 minutes). The fitting conclusion was drawn following instillation of FS to the superior conjunctiva. Lenses were subsequently removed by the examiner, by placing mild pressure on the lid margins.

3.2.2.6 Final eye assessment

Changes in conjunctival and limbal hyperaemia were graded and recorded. Also any alteration in corneal staining was noted and graded. (Further FS was instilled at this stage only if required, as successive FS instillation is known to increase corneal staining (Josephson and Caffery, 1988).

3.2.2.7 Comfort visual analogue scale

Following completion of the contact lens fitting the SC electrodes were removed. Subjects then completed a further VAS to indicate how comfortable they felt the lenses had been on their eyes, (Figure 3.7).

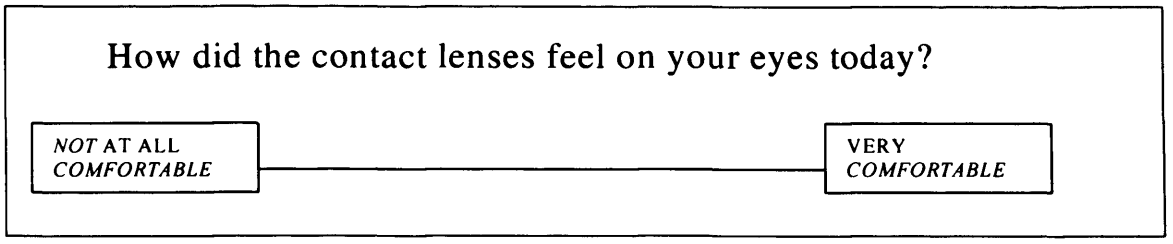


Figure 3.7 Comfort visual analogue scale.

3.2.3 Visit 2

Subjects returned for a second session one week later to simulate the typical scenario in clinical practice for lens collection. The sequence of events was as follows:

1) Assessment of anxiety prior to lens fitting;
2) Skin conductance recording. SC tag 1 was omitted and tags 2-5 were inserted onto the SC trace as in Visit 1;
3) Anterior eye assessment;
4) No drops were instilled prior to lens insertion in either group;
5) Contact lens trial (both eyes);
6) Final eye assessment;
7) Comfort visual analogue scale.

3.3 Results

3.3.1 Ocular surface results

Interpolation of the CCLRU grading scale produces an approximate interval scale and it has been argued that parametrical statistical tests may be applied to such data (Barbeito and Simpson, 1991). Both parametric and non-parametric tests were performed on this data; only the parametric results are reported as the outcomes were similar. Statistically, no significant difference was found between right and left eyes

for hyperaemia or corneal staining ($0.28<p<0.89$, Paired T-tests), therefore only right eye data are presented.

3.3.1.1 Visit 1

At Visit 1, no significant difference was found in baseline ocular surface appearance (hyperaemia, staining) between Groups A and B ($0.27<p<0.97$; Independent t-tests). Following GP insertion, conjunctival and limbal hyperaemia, and corneal staining had significantly increased in both groups when compared with their baseline measures; (Table 3.1 and Figure 3.8).

Table 3.1 Grading measurements at Visit 1.

		Pre-GP grading	**Post-GP grading**	**Difference in grading Pre- & Post-GP**	**Difference between Groups A & B**
		Mean±SD	Mean±SD	Mean±SD (Paired t-test)	Mean±SD (Independent t-test)
Conjunctival hyperaemia	Group A	1.84±0.28	2.08±0.43	0.25±0.25 ($p<0.05$)	0.10±0.64 ($p=0.15$)
	Group B	1.78±0.26	1.93±0.34	0.15±0.16 ($p<0.05$)	
Limbal hyperaemia	Group A	1.59±0.42	1.91±0.50	0.26±0.56 ($p<0.05$)	0.01±0.14 ($p=0.93$)
	Group B	1.52±0.28	1.78±0.40	0.27±0.26 ($p<0.05$)	
Corneal staining	Group A	0.19±0.27	0.63±0.66	0.44±0.56 ($p<0.05$)	0.17±0.16 ($p=0.30$)
	Group B	0.28±0.49	0.55±0.66	0.27±0.54 ($p<0.05$)	

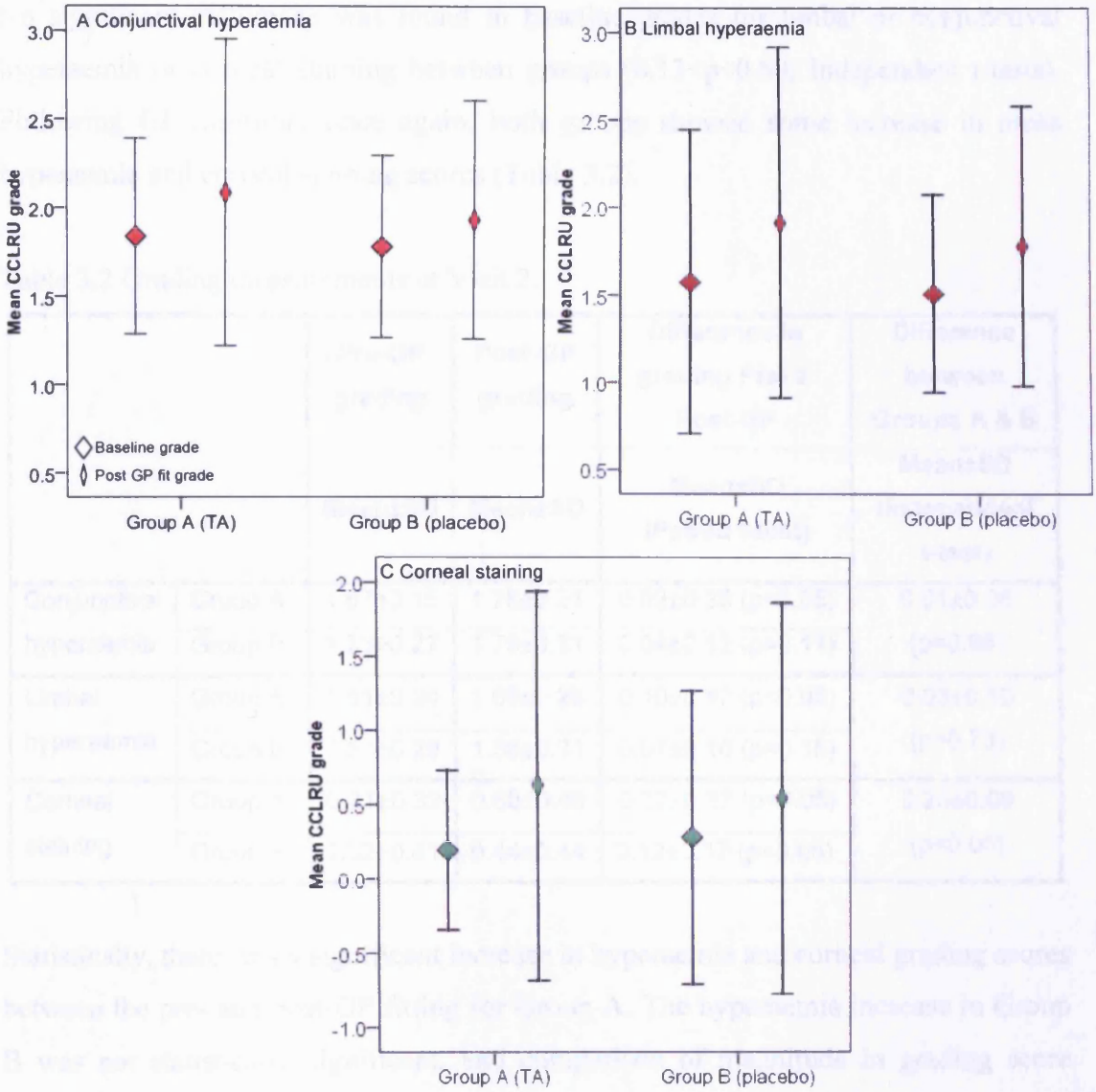


Figure 3.8 Error plots showing mean and two standard deviations in CCLRU grading scores pre- and post- GP fitting at Visit 1. A: Conjunctival hyperaemia, B: Limbal hyperaemia and C: Corneal staining.

Comparison of magnitude of change in CCLRU grading pre- and post-GP fitting revealed no significant differences between Group A and B for hyperaemia or corneal staining. Likewise, no statistical difference was found between final CCLRU scores for Groups A and B, Table 3.1.

3.3.1.2 Visit 2

No significant difference was found in baseline grades for limbal or conjunctival hyperaemia or corneal staining between groups ($0.13<p<0.60$; Independent t-tests). Following GP insertion, once again, both groups showed some increase in mean hyperaemia and corneal staining scores (Table 3.2).

Table 3.2 Grading measurements at Visit 2.

		Pre-GP grading	Post-GP grading	Difference in grading Pre- & Post-GP	Difference between Groups A & B
		Mean±SD	Mean±SD	Mean±SD (Paired t-test)	Mean±SD (Independent t-test)
Conjunctival hyperaemia	Group A	1.67±0.15	1.78±0.21	0.03±0.36 ($p<0.05$)	0.01±0.08 ($p=0.86$)
	Group B	1.73±0.27	1.78±0.31	0.04±0.12 ($p=0.11$)	
Limbal hyperaemia	Group A	1.51±0.34	1.69±0.26	0.10±0.42 ($p<0.05$)	0.03±0.10 ($p=0.73$)
	Group B	1.51±0.29	1.56±0.31	0.07±0.16 ($p=0.15$)	
Corneal staining	Group A	0.31±0.32	0.68±0.49	0.37±0.37 ($p<0.05$)	0.25±0.09 ($p<0.05$)
	Group B	0.32±0.41	0.44±0.44	0.12±0.17 ($p<0.05$)	

Statistically, there was a significant increase in hyperaemia and corneal grading scores between the pre- and post-GP fitting for Group A. The hyperaemia increase in Group B was not statistically significant, and comparison of magnitude in grading score change between groups revealed that there was no significant difference in amount of hyperaemic response between Groups A and B; Table 3.2 and Figure 3.9. Following GP fitting, corneal staining was significantly increased in both groups; however there was a significantly greater corneal response in Group A than Group B.

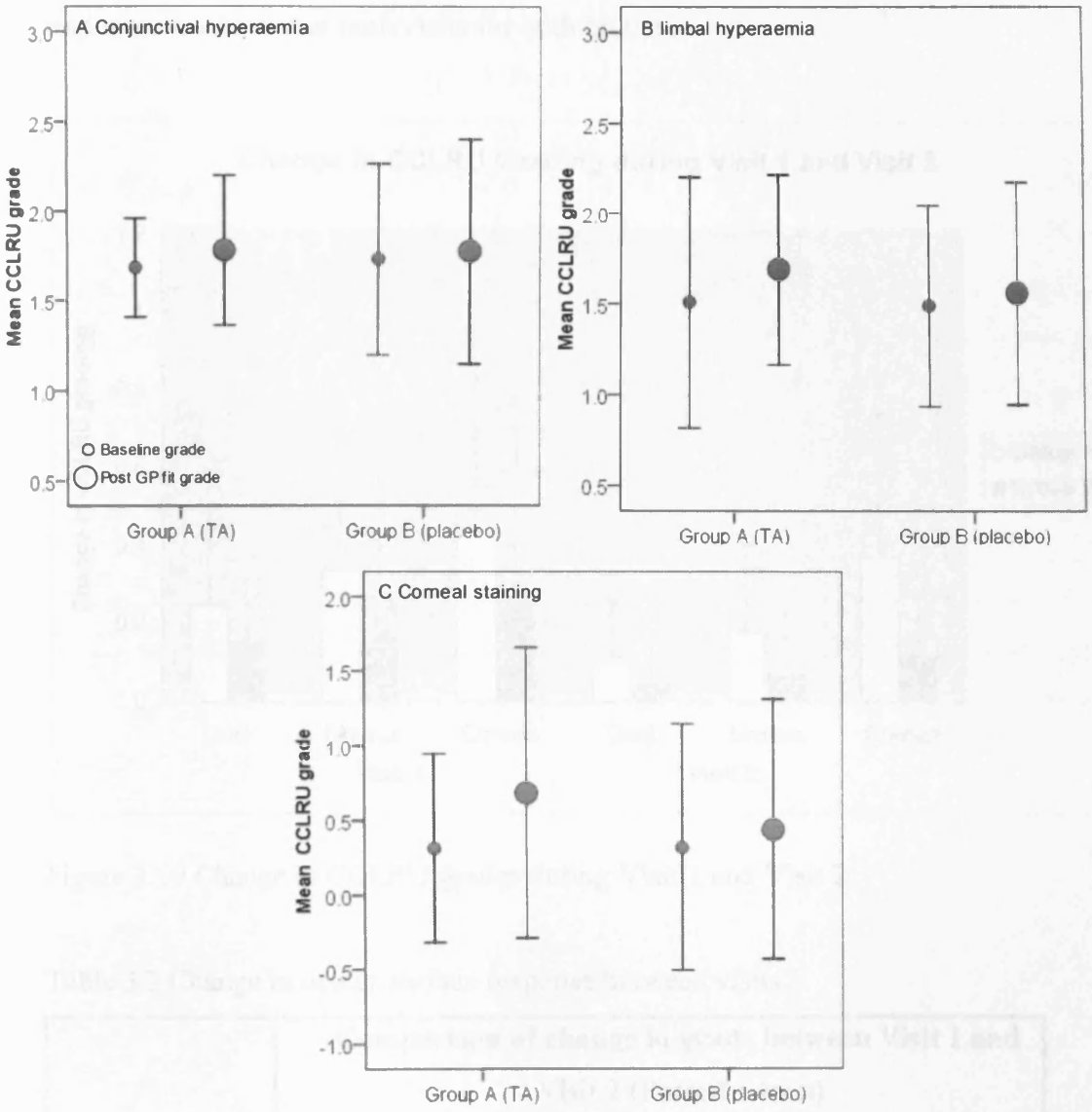


Figure 3.9 Error plots showing mean and two standard deviations CCLRU grading scores pre- and post-GP fitting at Visit 2; A: Conjunctival hyperaemia, B: Limbal hyperaemia and C: Corneal staining.

3.3.1.3 Ocular surface results summary

Figure 3.10 shows the change in CCLRU grade during the GP fitting at Visits 1 and 2. Ocular surface responses in Group A were larger than Group B at both visits. However, they were only significantly greater at Visit 2, despite no drops being instilled. Comparison of ocular surface response between the two visits indicated that

hyperaemia response was significantly reduced at Visit 2 (Table 3.3). Staining response was similar at both visits for both groups.

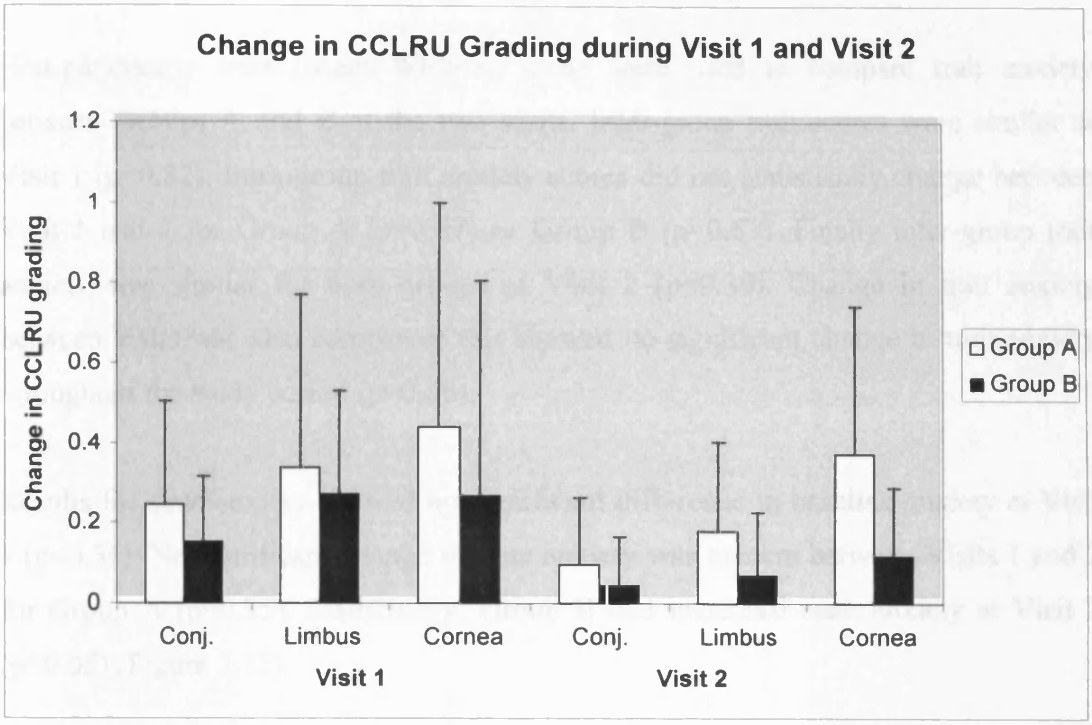


Figure 3.10 Change in CCLRU grades during Visit 1 and Visit 2.

Table 3.3 Change in ocular surface response between visits.

	Comparison of change in grade between Visit 1 and Visit 2 (Paired t-tests)			
	Group A		Group B	
Conjunctival hyp.	-0.24±0.35	p<0.05	-0.11±0.14	p<0.05
Limbal hyp.	-0.27±0.50	p<0.05	-0.18±0.23	p<0.05
Corneal staining	-0.09±0.60	p=0.46	-0.16±0.51	p=0.17

3.3.2 Psychological effects

3.3.2.1 State trait questionnaire

Internal reliability of the short version state and trait questionnaires was assessed using Cronbach alpha. This ensures that the questionnaire demonstrated internal consistency producing results that are correlated to one another (Bland and Altman,

1997). The Cronbach alpha values for this analysis were: Visit 1, state anxiety α=0.97 Visit 2, state anxiety α=0.99. This indicates a high degree of consistency (making comparison of state anxiety results statistically reliable).

Non-parametric tests (Mann-Whitney tests) were used to compare trait anxiety between Groups A and B at the two visits. Inter-group trait scores were similar at Visit 1 (p=0.82). Intra-group trait anxiety scores did not statistically change between Visit 1 and 2 for Group A (p=0.97) or Group B (p=0.63). Finally inter-group trait anxiety was similar for both groups at Visit 2 (p=0.39). Change in trait anxiety between visits was also compared; this showed no significant change in trait anxiety throughout the study period (p=0.56).

Results for state anxiety showed no significant difference in baseline anxiety at Visit 1 (p=0.56). No significant change in state anxiety was evident between Visits 1 and 2 for Group A (p=0.35). Statistically, Group B had increased state anxiety at Visit 2 ($p<0.05$) (Figure 3.11).

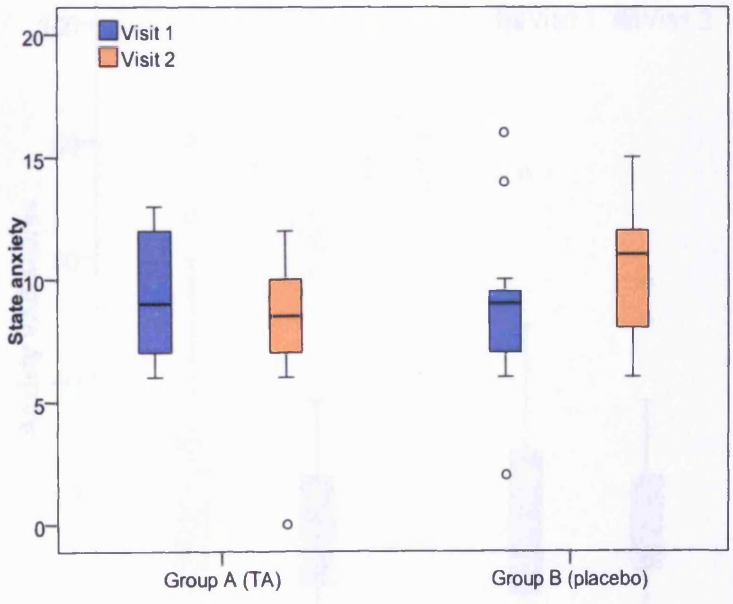


Figure 3.11 A box plot showing median and range state anxiety scores for Group A and Group B at Visit 1 and Visit 2. (Whiskers represent 10^{th} and 90^{th} percentiles).

3.3.2.2 VAS anxiety

There was no significant difference between Group A and B anxiety scores at Visit 1. At Visit 2, Group A were significantly less anxious about lens insertion. Whereas, Group B were marginally more anxious at visit 2, though this finding was not statistically significant. Comparison of mean change in anxiety over the two visits, between groups, was not significant (Table 3.4 and Figure 3.12).

Table 3.4 VAS anxiety results for Groups A and B at each visit.

VAS scores (%)		Group A (TA)	Group B (placebo)	Difference between A&B Mann-Whitney test
Visit 1	Median	13.57	9.29	p=0.33
	Range	0.00-84.29	0.00-74.29	
Visit 2	Median	10.71	17.14	p=0.31
	Range	0.00-35.71	0.00-55.71	
Change between visits, within groups Wilcoxon Rank test		p<0.05	p=0.94	

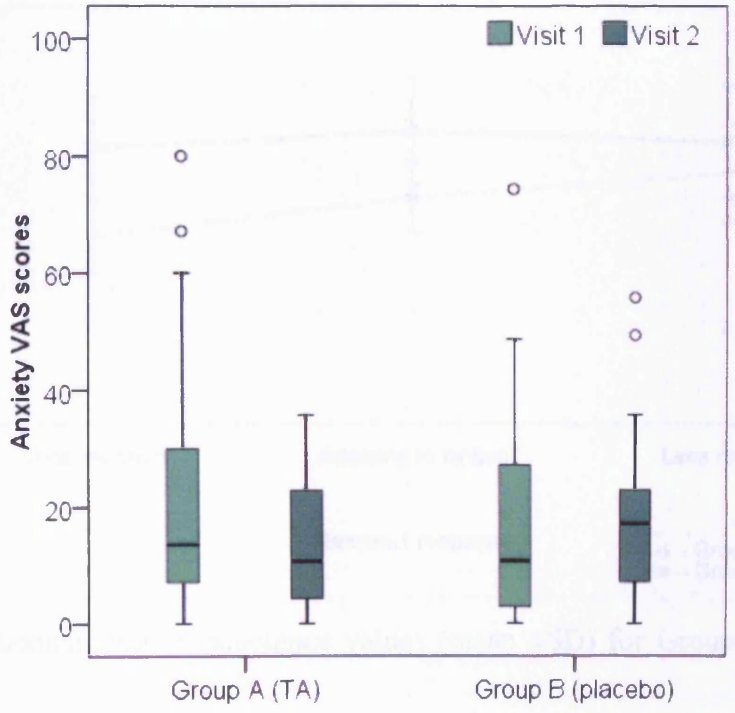


Figure 3.12 A box plot showing median and range of VAS anxiety scores prior to GP insertion at Visit 1 and Visit 2.

3.3.2.3 Skin conductance

Absolute SC values do not allow comparison of SC between individuals. Therefore, SC values recorded during the 'run-in period' (from start of trace until insertion of drops) were averaged and subtracted from subsequent recordings to normalise the data for all subjects. During the study, tags were added to the trace to identify the start and finish of particular events, e.g. lens insertion. SC response occurs with a latency of approximately 1-3 seconds following a stimulus (Dawson, Schell and Filion, 2000) making it difficult to directly link a response to a particular event, so for this reason the tags were helpful in marking periods of interest. This meant that information from the trace, such as mean response and maximal response, was determined within these periods of interest. Maximal response was selected as the key result for analysis in the following results because this gave the subject's peak arousal or anxiety experienced within each period. There appears to be a trend of heightened anxiety in Group B throughout compared with Group A; Figure 3.13.

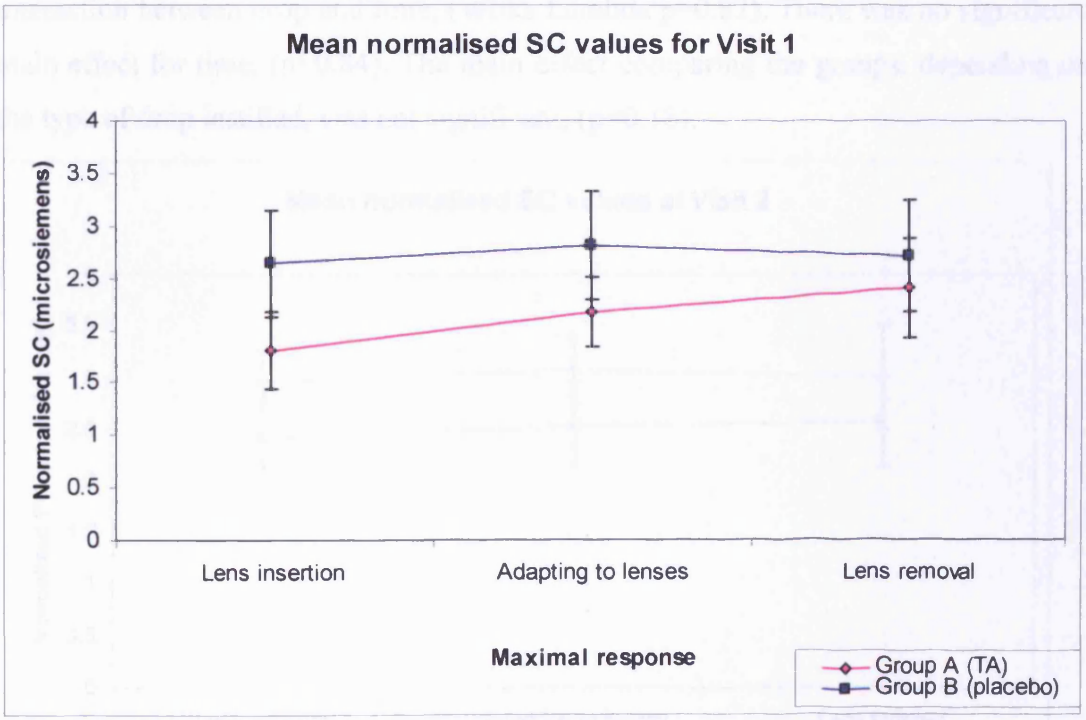


Figure 3.13 Maximal skin conductance values (mean ±SD) for Groups A and B at Visit 1.

A mixed, between-within subjects analysis of variance was conducted to assess the impact of two different interventions (effect of drops) on subjects' maximal SC

response across three time periods (lens insertion, adaptation to lenses and lens removal). There was no significant interaction between drop and time, (Wilks Lambda p=0.97). There was no significant main effect for time, (p=0.97). The main effect comparing the groups, depending on the type of drop instilled, was not significant (p=0.64).

A one-way repeated measures ANOVA was conducted to compare maximal SC responses over time first for Group A and then for Group B. There was no significant effect of time; (p=0.78 Group A, p=0.98 Group B).

Figure 3.14 shows that at Visit 2, Group B SC values were lower than Group A. Though, statistically, there was no significant difference between Group A and Group B scores at this visit.

A mixed, between-within subjects analysis of variance indicated no significant interaction between drop and time, (Wilks Lambda p=0.82). There was no significant main effect for time, (p=0.84). The main effect comparing the groups, depending on the type of drop instilled, was not significant, (p=0.18).

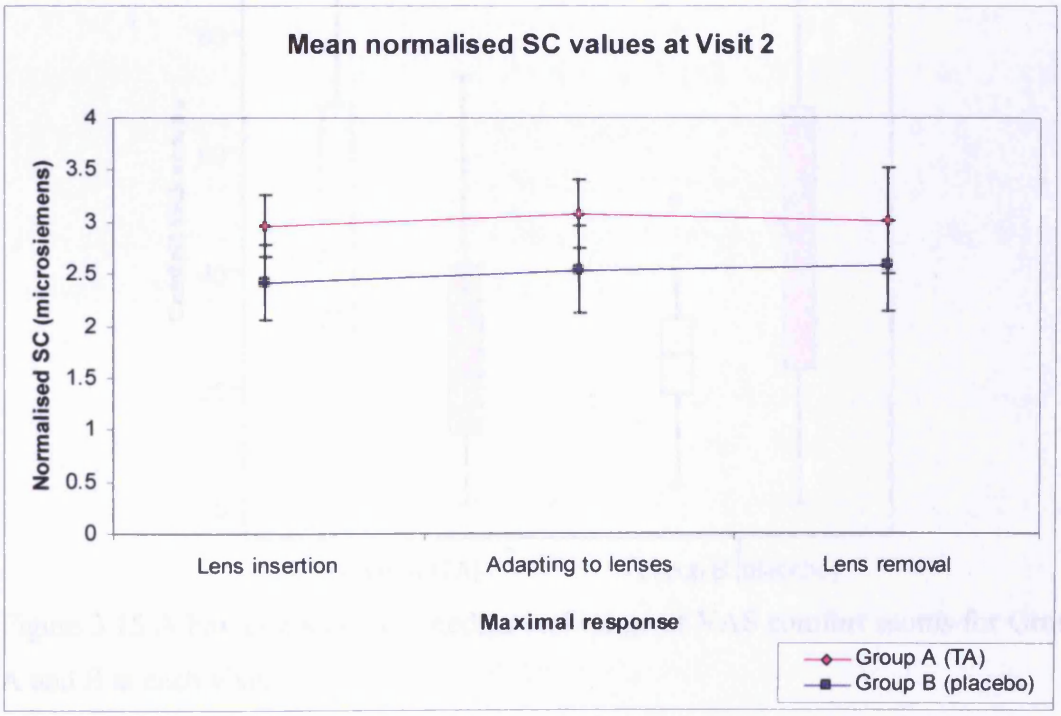


Figure 3.14 Maximal skin conductance values (mean ±SD) for Groups A and B at Visit 2.

3.3.2.4 VAS comfort

At Visit 1, initial GP comfort scores were higher in Group A compared with Group B, though this difference was not statistically significant. At Visit 2, comfort scores significantly decreased in Group A and increased in Group B; Table 3.5 and Figure 3.15.

Table 3.5 VAS comfort results for Group A and B at each visit.

VAS scores (%)		Group A (TA)	Group B (placebo)	Difference between A & B Mann-Whitney test
Visit 1	Median	28.57	26.79	p=0.25
	Range	2.86-100.00	2.86-97.86	
Visit 2	Median	22.86	58.57	p=0.12
	Range	0.00-100.00	0.00-98.57	
Change between visits, within groups Wilcoxon Rank test		p<0.05	p<0.05	

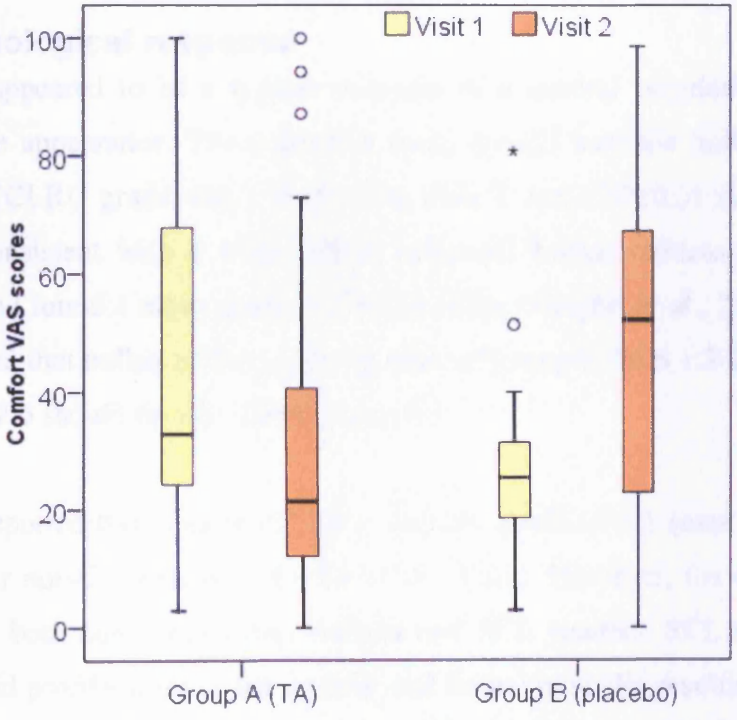


Figure 3.15 A box plot showing median and range of VAS comfort scores for Groups A and B at each visit.

3.3.3 Summary of results

- GP lens trial at Visit 1 was associated with small increases in hyperaemia and corneal staining, but there was no difference associated with TA use;
- At Visit 2, increases in staining and hyperaemia were observed, however hyperaemic responses were significantly less than at Visit 1. Corneal staining also tended to be less, though this difference was not statistically significant;
- There was no statistical difference in measured anxiety during lens adaptation with use of TA drops compared with the placebo drops;
- VAS scores indicated that subjects who received TA during Visit 1 were significantly less anxious at Visit 2;
- At Visit 2, comfort appears slightly reduced for subjects who had received TA at their first visit, and significantly increased for subjects who had received a placebo drop.

3.4 Discussion

3.4.1 Physiological response

This cohort appeared to be a typical example of a normal population in terms of ocular surface appearance. The collective mean (n=47) baseline bulbar conjunctiva hyperaemia CCLRU grade was 1.81±0.27 at Visit 1 and 1.70±0.21 at Visit 2. These results are consistent with a study which measured bulbar redness in 121 healthy individuals and found a mean grade 1.93±0.32 units (Murphy et al., 2007). The same study indicated that bulbar redness grading normally ranges from 1.3-2.6, and a grade of more than 2.6 should be considered abnormal.

It has been reported that a mean CCLRU staining grade of 0.1 (max 0.5) should be anticipated for non-CL wearers (Dundas et al., 2001). However, the cohort reported here included both non-contact lens wearers and SCL wearers. SCL wear alters cell exfoliation and proliferation in the corneal and limbal epithelia resulting in increased staining (Ren et al., 1999; Ladage et al., 2001b). This study found mean baseline corneal staining grade 0.23±0.39, which was marginally higher than the Dundas et al. (2001) study for non-wearers, and marginally less than the mean Grade 0.5 reported in a study of asymptomatic hydrogel CL wearers (Begley et al., 1996).

Most eye care practitioners (ECPs) would accept that slight increases in ocular surface hyperaemia occur when contact lenses are first applied. Due to inter-subject variability, measurement of change in bulbar redness is more meaningful than absolute values; a change of 0.4 units should be considered clinically significant (Murphy et al., 2007). The results here indicate that the mean increase in hyperaemia grades during the GP trial were small (less than one quarter of a CCLRU grade), but statistically significant. Importantly, the study demonstrated that use of TA did not promote significantly more hyperaemia in this cohort.

This study found less than 0.1 difference in mean corneal staining grade (post-GP wear) between the placebo and TA group. Although mean change in corneal staining grade was larger in the TA group, this difference was not statistically significant. Similar studies have also reported no significant increase in corneal staining with TA use compared with a control drop (Sturrock and Nunn, 1979; Boljka et al., 1994). Although, it should be noted that corneal assessment did not take place immediately following lens application in the Bennett et al. study (1998a).

This result is perhaps surprising given that most optometrists will anecdotally report a reluctance to use TA due to its 'toxic effect'. Yet, UK practitioners routinely instil TA prior to clinical techniques such as Goldman applanation tonometry (Murphy et al., 2007). Clinicians are aware of the potential risks associated with TA use but consider that the benefits of producing corneal anaesthesia outweigh them. Indeed, TA is known to be mildly toxic to the corneal epithelium (Josephson and Caffery, 1988). One study investigating corneal staining reported 17.6% of eyes stained with fluorescein at baseline measurement, but following TA instillation 60% eyes stained with fluorescein (Ramselaar et al., 1988). However, it is likely that the preservative (0.01%, benzalkonium chloride) accompanying the TA in that study was responsible for the staining increase. Research has reported that sequential instillation of TA was not responsible for increased epithelial permeability, but the addition of preservatives significantly increases corneal permeability (Rosenwasser et al., 1990). Preservative-free TA minims (0.5%, proxymetacaine) were used in this study to reduce the risk of ocular surface response associated with preservative. Repeated use of TA can delay wound healing or cause keratitis (Lawrenson et al., 1998), but only one drop of TA was used in this study.

At Visit 2, the results indicated that corneal staining was increased in all subjects following GP insertion; the mean grade increase was not clinically significant for either group (Schlenker and Leary, 1982). Hyperaemia increase was statistically more significant in Group A than Group B. A possible explanation for these findings might be that the Group B hyperaemic reaction was conditioned by an improvement in comfort experience at the second exposure to GP lenses. Meanwhile, subjects in Group A, who received TA at Visit 1 experienced a reduced level of ocular comfort at Visit 2, and therefore responded as if they were naïve to GP lenses. An alternative explanation might be that while baseline hyperaemia grades were greater in Group B than Group A ($p=0.06$), the mean increase in redness was small and similar (<0.05) for both groups.

3.4.2 Physiological response

Measured trait anxiety at the start of each visit (although not expected to change between visits) confirmed an even distribution of tendencies toward anxiety in both groups, i.e. there was no skew in either group towards very sensitive individuals. State anxiety refers to the transient or current level of anxiety experienced by the subject. Variations in volunteer personality types and extraneous factors, which might have influenced state anxiety levels, may produce the wide variation observed in results prior to the first-time lens trial. Importantly, both measures of anxiety (state anxiety and VAS) were not significantly different between Groups A and B at Visit 1. Presumably both groups were naïve to GP lenses and masked at to whether they would receive TA or placebo drops.

At the return visit, subjects who had previously received TA at the fitting visit, showed less anxiety when measured with the VAS, but no significant change in state anxiety scoring. It may be that the state score was affected by extraneous stress factors and this masked the reduction in anxiety relating specifically to GP insertion. Conversely, the placebo group state anxiety scores showed a significant increase at Visit 2 implying that their negative experience at Visit 1 caused them to feel more anxious in anticipation of GP insertion for the second time. However, this was not the case for their anxiety VAS responses, which showed no significant change from Visit

1. This is perhaps because subjects were no longer naïve to GP lenses and knew what to expect (i.e. no fear of the unknown as at Visit 1). Social anxiety research indicates that within a formal encounter people generally want to make a good impression and want to avoid appearing foolish (Margrain, Greenland and Anderson, 2003). Therefore an alternative explanation may be that subjects were too embarrassed to admit to feeling anxious at the prospect of second-time GP discomfort experience, a condition more easily expressed on a simple VAS.

During lens fitting, subjects who had received TA appeared less 'aroused' during the adaptation period than the placebo group. This seems a logical finding as Group A subjects were anaesthetised and therefore experienced better comfort, and consequently reduced stress levels. Apart from reduced corneal sensitivity, other factors which may affect stress levels during adaptation to lenses might have included change in vision due to power of trial lens (-3.00 Dioptres), acceptability of the lens fit and individual lid architecture or tightness. However, the effects of these factors should have been equal for both groups.

At Visit 2, SC appeared somewhat heightened in the anaesthetic group because they now experienced the full sensation of the GP lens, whereas Group B had lower SC response as they experienced an improved level of comfort at second exposure to GP lenses. However, statistically there was no difference in the results for the two groups.

Electrodermal activity is the most widely accepted measure of arousal or anxiety, and SC is the best objective measurement of electrodermal activity (Court et al., 2008). Previous research has investigated SC during soft contact lens fitting and reported characteristic anxiety fluctuations during the consultation. Specifically, heightened stress response during lens insertion and lens removal was reported (Carney et al., 1997; Bennett, 1999). Visual inspection of each trace produced by subjects in this study found heightened SC response during lens insertion and removal. However, this research was specifically interested in alterations to the SC response due to the use of TA during GP fitting. The trends shown in the results indicate that there may be a reduction in anxiety with TA, however the results were not statistically significant. Trends may become significant with increased sample size.

Comfort levels appeared to be improved in the group that received TA prior to initial lens fitting, but this was not significantly better than the placebo group. This lack of statistical significance may be because there was a wide variation in comfort scores and the sample size. If the cohort had been larger, it is likely that this trend would have shown statistical significance. It may be that the superior palpebral conjunctiva is less well anaesthetised due to application of the drop to the inferior palpebral conjunctiva. This is supported by the ideas that comfort during GP wear may be more directly linked to sensitivity of superior tarsal plate and position of lens margin in relation to superior lid (Bennett et al., 1998a).

Different methods of TA insertion during GP fitting may affect patient experience. When fitting children Walline et al. (2001) suggested putting a drop of TA on the back surface of the GP lens. This way the TA and lens are inserted in a single procedure, rather than two separate, potentially stressful, events. Future research might investigate the impact of instilling TA direct to the superior palpebral conjunctiva in terms of GP comfort.

As anticipated, subjects reported a relative decrease in comfort at their return visit when TA was not used. However, comparison of comfort VAS scores at Visit 2 found no significant difference in comfort between the two groups ($p=0.12$).

3.4.3 General discussion

The findings from this study indicate that TA is beneficial in reducing both objective anxiety measurements during adaptation to GP lenses and self-reported anxiety prior to second-time lens insertion. This concurs with a study which reported reduced drop-out rates in first-time wearers fitted with use of TA at fitting and dispensing visits (Schnider, 1996). A similar study fitted apprehensive patients using TA and reported superior comfort, less alteration to blink rate and less tearing compared with a control group. Furthermore, 50% of subjects felt confident about wearing GP lenses following fitting with TA compared with 20% of control subjects (Schnider, 1996). This study also reported the use of TA to significantly reduce time for GP stabilisation on eye. GP stabilisation time, blink rate or lacrimation were not measured during this investigation. Effect of TA on GP stabilisation time might be of interest as the time

needed to fit GP lenses is perceived to be greater than that for soft lens fitting. Use of TA to shorten fitting appointments might be a further indication for TA use in GP fitting.

In this study, the use of TA during GP fitting has been demonstrated to be a clinically safe practice with potential patient benefits including improved first-time GP wear comfort, reduced anxiety during adaptation and reduced anxiety prior to second-time GP wear. The disadvantages of TA use may be the reduced comfort during second-time GP wear when no TA is administered. However, in some patients, particularly those who are apprehensive prior to GP trial, use of TA may be an appropriate and beneficial practice.

3.5 Conclusions

Use of TA did not adversely increase ocular surface hyperaemia or corneal staining response during GP lens fitting. At the second visit, the ocular redness response to GP lenses was reduced, irrespective of previous drop experience (TA or placebo). Comfort at initial fitting was marginally improved with TA, although it was worse at the dispensing visit. Patients who received TA during fitting had significantly reduced subjective anxiety (VAS) prior to lens collection, indicating this practice may minimise drop-out rates. In summary, use of TA in GP fitting has been demonstrated to be clinically safe practice that may enhance first GP experience, especially in anxious patients, hopefully reducing later drop-out rate.

4. Comfort and performance in GP lens wear: A longitudinal study

4.1 Introduction

This Chapter investigates whether GP lenses are a viable lens of first choice for the average subject, or whether GP lenses should be reserved for fitting to subjects with more specialised requirements. A cohort of subjects with no prior contact lens experience (neophytes) or existing soft contact lens SCL wearers were fitted with GP lenses in a three month daily wear study.

It has been confirmed that initial comfort in GP lens wear is a challenge to practitioner fitting and may also dissuade patients from trying GP lenses. Attempts to improve initial comfort by plasma surface treatment (PST) of GP lens surface has been reported to enhance surface properties and is becoming a routine practice (Schafer, 2006; Young and Tapper, 2007). It has been suggested that initial comfort and overall performance is improved with PST, however little literature exists to demonstrate these findings. Therefore the work will also investigate the effects of PST of GP lens surfaces in terms of subject comfort and lens performance.

4.1.1 Aims and objectives

The aims of this study were:

a) To fit GP lenses based on topography, using fit simulation technology;
b) To fit half the cohort with plasma treated lenses and the remainder with untreated lenses;
c) To monitor their ocular health and comfort during three months of GP wear.

4.1.2 Hypotheses

- Both neophyte subjects and existing SCL wearers can be successfully fitted with GP lenses. Once adapted to contact lens wear, all subjects report good comfort levels;
- Topography and fit simulation technology will result in (good) fitting success;
- Subjects fitted with plasma treated GP lenses will experience
    - Greater initial and long term comfort than untreated lens wearers
    - Better stability of vision than subjects wearing untreated lenses;

- Less clinical signs of disruption to the anterior ocular surface, in particular the corneal epithelium, compared with subjects wearing untreated lenses.

4.2 Methods

4.2.1 Study design and subject selection

The study aimed to recruit volunteers to be fitted with and wear GP lenses on a full time, daily-wear basis during a 3 month longitudinal study. Subjects were sub-divided depending on history; non-wearer or existing SCL wear, and then according to the lens type fitted; plasma treated or untreated lenses. This is displayed in Figure 4.1.

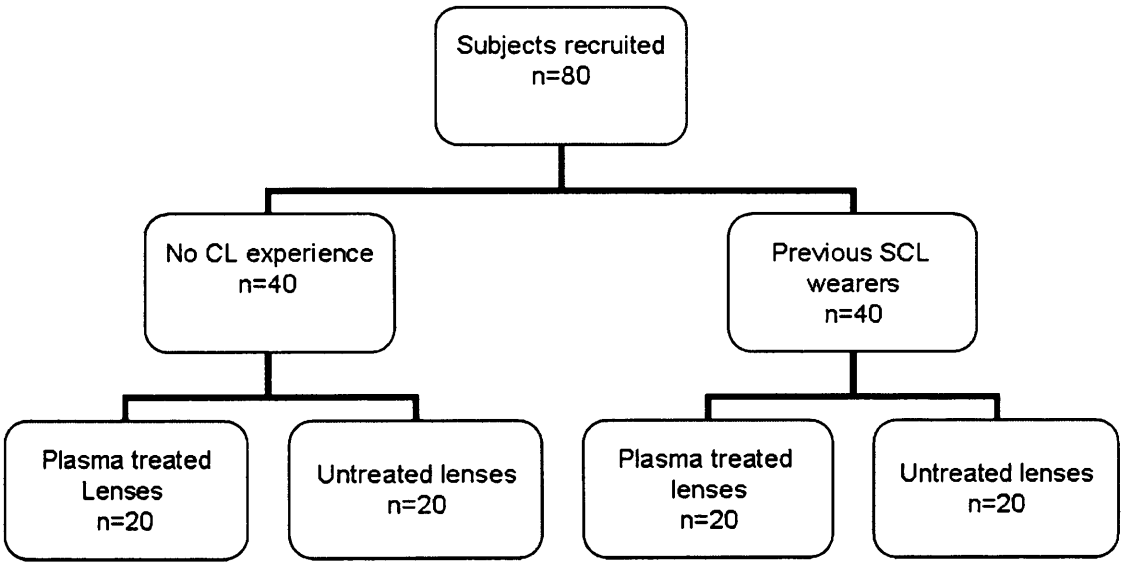


Figure 4.1 Experimental design showing cohort sub-divisions.

Subjects aged between 18-44 years were recruited from staff and students within Cardiff University. Subjects were excluded if they:

- Had worn GP contact lenses within the last five years;
- Had a history of any ocular or systemic condition known to affect the tear film or ocular surface;
- Were taking any medication known to affect the tear film or ocular surface;
- Were pregnant or breast-feeding;
- Had a score ≥2.5 on any of the Cornea and Contact Lens Research Unit (CCLRU) graded items;

- Had not had an eye examination within the previous 12 month period.

Ethical approval for this study was obtained from the School of Optometry and Vision Sciences Ethical Committee, Cardiff University. All procedures conformed to the tenets of the Declaration of Helsinki.

Subjects were excluded or withdrawn if a suitable fit could not be achieved by following the protocol given in section 4.2; or if ocular surface signs indicated that they should not continue with lens wear. Subjects could withdraw voluntarily from the study at any time without reason.

Subjects attended the laboratory at least five times during the study, plus any additional visits as necessary:

1) Initial assessment and lens selection
2) Dispensing/collecting visit
3) Review at 1 week
4) Review at 1 month
5) Review at 3 months

4.2.2 Subject suitability and contact lens selection

Optimum refraction was measured using trial lenses and visual acuity (VA) and contrast sensitivity (CS) measured with the Test Chart 2000 (Thompson, Hertfordshire, UK). Slit-lamp biomicroscopy was then used to assess whether the subject was suitable for contact lens fitting. Investigations included tear quality and tear break-up time with the Tearscope Plus^{TM} (Keeler, Windsor, UK) and instillation of fluorescein to check corneal integrity and record baseline ocular surface appearances using the CCLRU Grading Scale.

Topography was performed on both eyes with the Keratron Scout Topographer KS-1000 (Optikon, Rome, Italy). This was followed by measurement of the vertical palpebral aperture height, horizontal visible iris diameter and pupil sizes (at different ambient and scotopic illumination levels) for each eye.

Subjects were asked to complete the following questionnaires:

- State and Trait Spielberger Anxiety Index (shortened forms);
- Contact Lens Dry Eye Questionnaire (CLDEQ) (if SCL wearer) or Dry Eye Questionnaire (DEQ) (if neophyte).

The contact lens of choice was an aspheric GP lens (Quasar, No.7 Contact Lens Laboratory Ltd, Hastings, UK) with 10mm diameter as standard. A consistently larger diameter lens was chosen as larger diameter lenses are reported to enhance subject comfort (discussed in Section 1.8.1.2.) and also to aid centration of aspheric lens designs (Gasson and Morris, 1998). Plasma treatment was applied to the GP surface using low pressure argon plasma.

Topography information was recorded by Keratron Scout software (Optikon, Rome, Italy) and this was then transferred to the i-Link software package (No 7 Contact Lens Laboratories, Hastings, UK). The i-Link software allows simulation of the fluorescein fitting pattern. The flattest keratometry reading is used as a first lens selection criteria, within the software, and the user specifies which diameter is required.

Optimal simulated fitting was considered to be:

- Central apical clearance with a 2-5μm layer of fluorescein (across about 7.5mm)
- Mid-peripheral alignment fit, diameter 2.0mm
- Even edge clearance, about 0.5mm

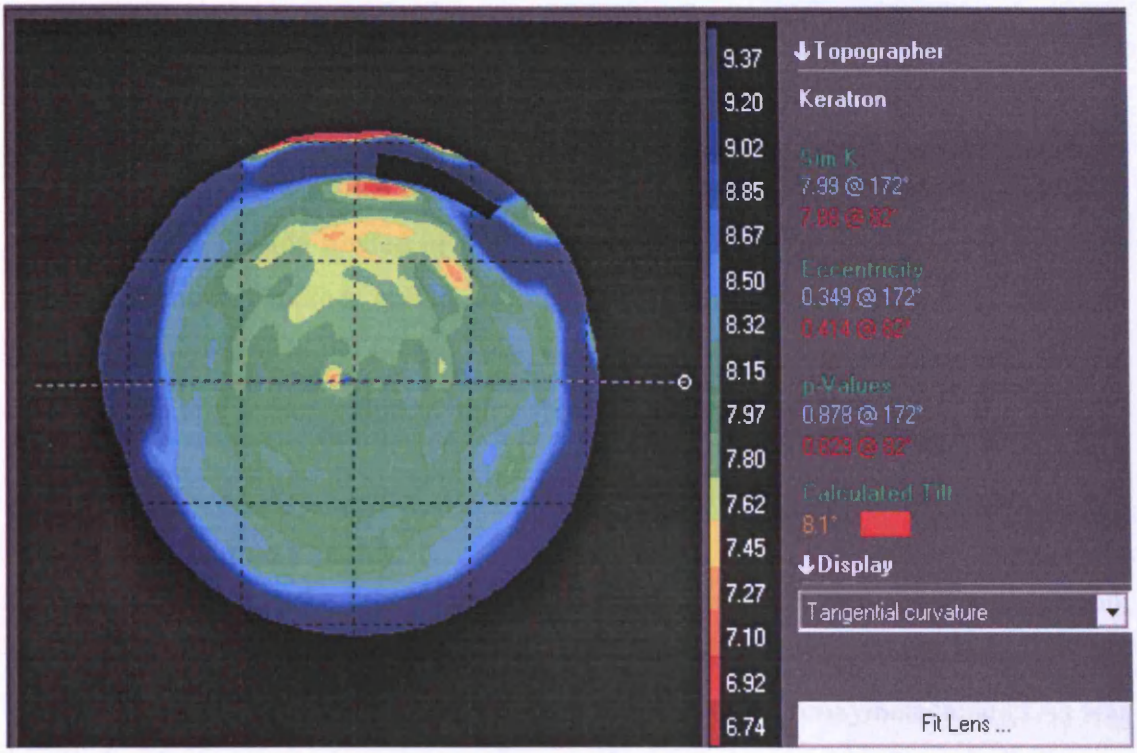


Figure 4.2 i-Link image

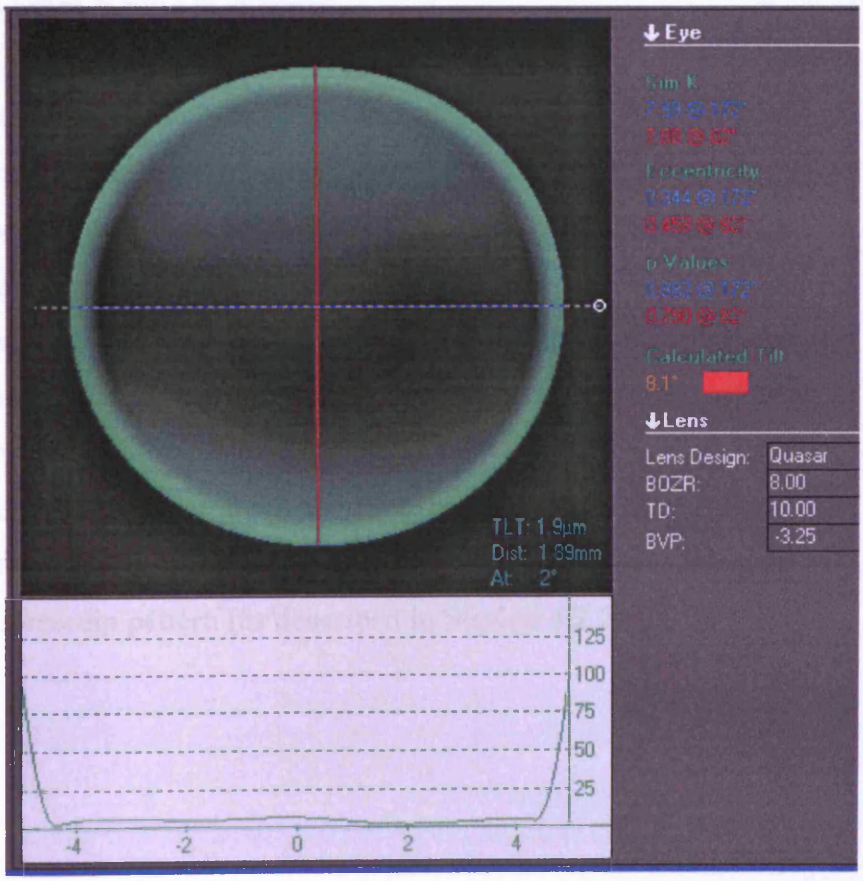


Figure 4.3 Tear layer profile and simulated fluorescein pattern

The best simulation lens fit and the back vertex power were determined using the iLink and trial lenses were ordered. Orders were sent using email, via an independent party (project supervisor). In this way, the investigator remained masked to the selection of subjects assigned to treated or untreated lenses. Each order was randomly allocated to the plasma treated or untreated group before the order was forwarded to the manufacturer. Another colleague received the orders and checked the contents before handing them to the investigator, so as not to reveal lens specifications via the delivery note and preserve this masking throughout the study.

4.2.3 Lens fit assessment

Lenses received from the laboratory were cleaned with Menicare solution (Menicon, Japan) and prepared for use. Slit-lamp examination was performed to ensure no change to ocular health prior to lens trial. One drop 0.5% proxymetacaine (TA) was instilled to both eyes to improve ocular comfort (as presented in Chapter 4). Lenses were placed on the eyes and ten minutes was allowed for subjects to adapt to the lenses and reflex tearing to subside.

Slit-lamp assessment was used to assess:

- Centration of lens in primary gaze;
  The lens must be central to ensure optimal optical performance.
- Movement on blink and on excursions;
  The lens should move on blink and excursions, but this movement should be smooth and of moderate pace, and the lens should not override the limbus in any direction.
- Lid interaction, i.e. inter-palpebral or lid attached fit;
  Either is acceptable, a note should be made of lid-lens interaction.
- Fluorescein pattern (as described in Section 4.2.2).

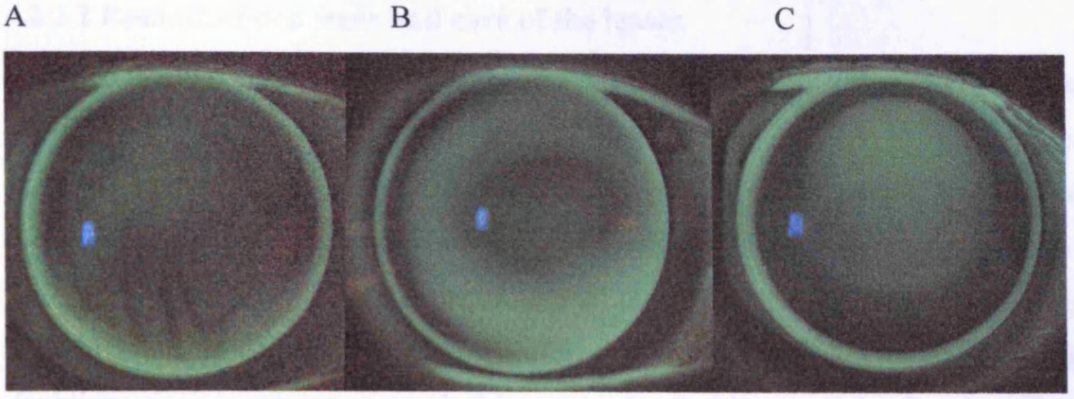


Figure 4.4 Examples of fluorescein patterns; A: Alignment fit (interpalpebral), B: Flat fit and C: Steep fit.

Based on these assessments, the practitioner judged the GP fit as clinically acceptable or unacceptable, using the descriptors; steep, flat or toric. If the fit was not acceptable then the appropriate alternative lens specification was ordered to improve the fitting, i.e. steepen or flatten back optic zone radius (BOZR). The subject was then asked to return for another visit to collect their contact lenses. (A total of three fitting attempts was permissible, however if a successful fit was not achieved by this time, then the subject was excluded from the study.)

If lens fit was acceptable, VA was measured and an over-refraction procedure performed to ensure the optimum back vertex power (BVP) prescribed.

4.2.3.1 Visual analogue scales

Prior to lens insertion a visual analogue scale (VAS) was completed to indicate how anxious subjects felt about lenses on their eyes (Figure 4.5).

How anxious do you feel about having lenses on your eyes today?

NOT AT ALL *ANXIOUS* — VERY *ANXIOUS*

Figure 4.5 Anxiety VAS, completed prior to insertion.

4.2.3.2 Recommended wear and care of the lenses

Provided the lens fit and BVP were acceptable, the subject was instructed in lens care, and lens insertion and removal. All subjects were given the same solutions (Menicare and Progent, Menicon, Japan). Care instructions for all subjects were; daily rub and rinse the lenses after wear and rinse prior to insertion. Weekly, the lenses were to be soaked in Progent for 10-30 minutes followed by a thorough rub, rinse and overnight soak in Menicare solution. Wearing times were to be gradually increased using a doubling principle (1hour on day 1, 2 hours on day 2, 4 hours on day 3 etc) until a full wearing schedule was achieved (at least 8 hours, 5 days per week). Written care instructions including emergency contact details, were issued along with the contact lenses. A follow up appointment was planned for 1 week 7±3 days.

4.3.3 Problems with fitting

Other studies using topographical devices to aid GP fitting have reported good success rates. However, this study found that the choice of fixed lens design and fixed total diameter posed a series of fitting problem in the initial subjects recruited to the study. It appeared that adopting a large diameter philosophy to fit everyone was not appropriate.

Twenty subjects were recruited to the study and fitted using the protocol described.
For nine subjects the initial lens fit produced a three-point-touch fluorescein pattern similar to the one shown in Figure 4.6. This pattern showed approximately 0.3-0.5mm edge clearance, 0.0-0.75mm mid-peripheral touch and then a large area of clearance across the central zone. However, apically/ infero-apically there is a dark area indicating central corneal touch. This fit was considered unacceptable.

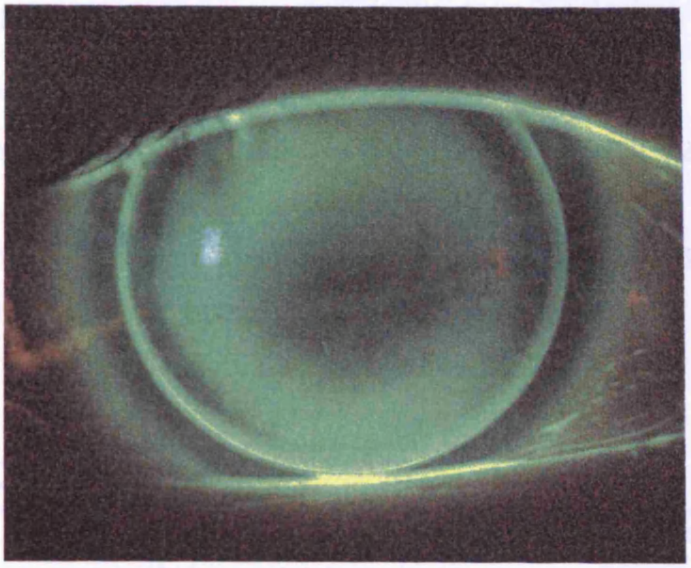


Figure 4.6 Three-point touch fluorescein pattern.

Table 4.1 Breakdown of initial 20 fit outcomes.

Subjects	Fit Assessment	Action	Outcome
9	Three-point touch	Refit; unsuccessful	Excluded
7	Acceptable, alignment	No action	Included
1	Toric, required amendment	Toric flange	Included
2	Steep, required amendment	BOZR flattened	Included
1	Flat, decentred, required amendment	BOZR steepened	Included

Table 4.1 shows the breakdown of initial fit outcomes. Once the fitting problem became apparent, it was decided that the lens fitting protocol must be amended. This would ensure that more subjects could be fitted with optimum or acceptable GP lenses and consequently participate in the study. Subjects who had already embarked on the study and achieved acceptable fits using the original fitting protocol were retained and continued on the study. Subjects with the three-point-touch lens fits were excluded from the study. Possible reasons for these findings will be presented and discussed later in this Chapter.

4.2.4 Protocol amendment

4.2.4.1 Lens fitting

The protocol was amended to use trial lens fitting sets at the initial assessment visit, rather than the iLink software fitting package. The lens selected was based on simulated keratometry readings obtained during topography. The BOZR selection followed the No. 7 Quasar fitting guide; Table 4.2. and Table 4.3 shows the corresponding fitting set parameters associated with each BOZR.

Table 4.2 No. 7 Quasar fitting guide for initial BOZR selection

0.00 to 1.50 D Cyl	Select lens on flattest K/nearest steeper lens
1.50 to 3.00D Cyl	Select 0.10 steeper than the flattest K.
Over 3.00D Cyl	Consider Quasar Toric

Table 4.3 Fitting set lens parameters

BOZR (mm)	TD (mm)	BVP (D)
7.4-7.6	9.2	-3.00
7.7-8.2	9.6	-3.00
8.3-8.5	10.0	-3.00

Reverting to the more traditional method of GP lens fitting also allowed further optimisation of both BOZR and TD at the collection visit as necessary. The criteria for acceptable lens fit were the same as that used in initial fitting series.

4.2.4.2 Revised aims and objectives

The revised aims of the study were:

a) To fit neophyte and existing SCL wearers with GP lenses;
b) To fit half the cohort with plasma treated lenses and the remainder with untreated lenses;
c) To monitor their ocular health and comfort during 3 months of GP wear.

4.2.4.3 Hypotheses

- Both neophyte subjects and existing soft lens wearers can be successfully fitted with GP lenses. Once adapted to contact lens wear, all subjects report good comfort levels;
- Subjects fitted with plasma treated GP lenses will experience
    - Greater initial and long term comfort than untreated lens wearers
    - Better stability of vision than subjects wearing untreated lenses;
    - Less clinical signs of disruption to the anterior ocular surface, in particular the corneal epithelium, compared with subjects wearing untreated lenses.

4.2.5 Follow-up visits

4.2.5.1 One week follow-up

Subjects were invited to attend their first follow-up appointment at 7±3 days post-collection. The following were recorded at this visit:

- History and symptoms
    - Handling issues
    - Wearing schedule during past week
    - Wearing schedule today
- VAS regarding comfort and vision were completed (Figure 4.7).

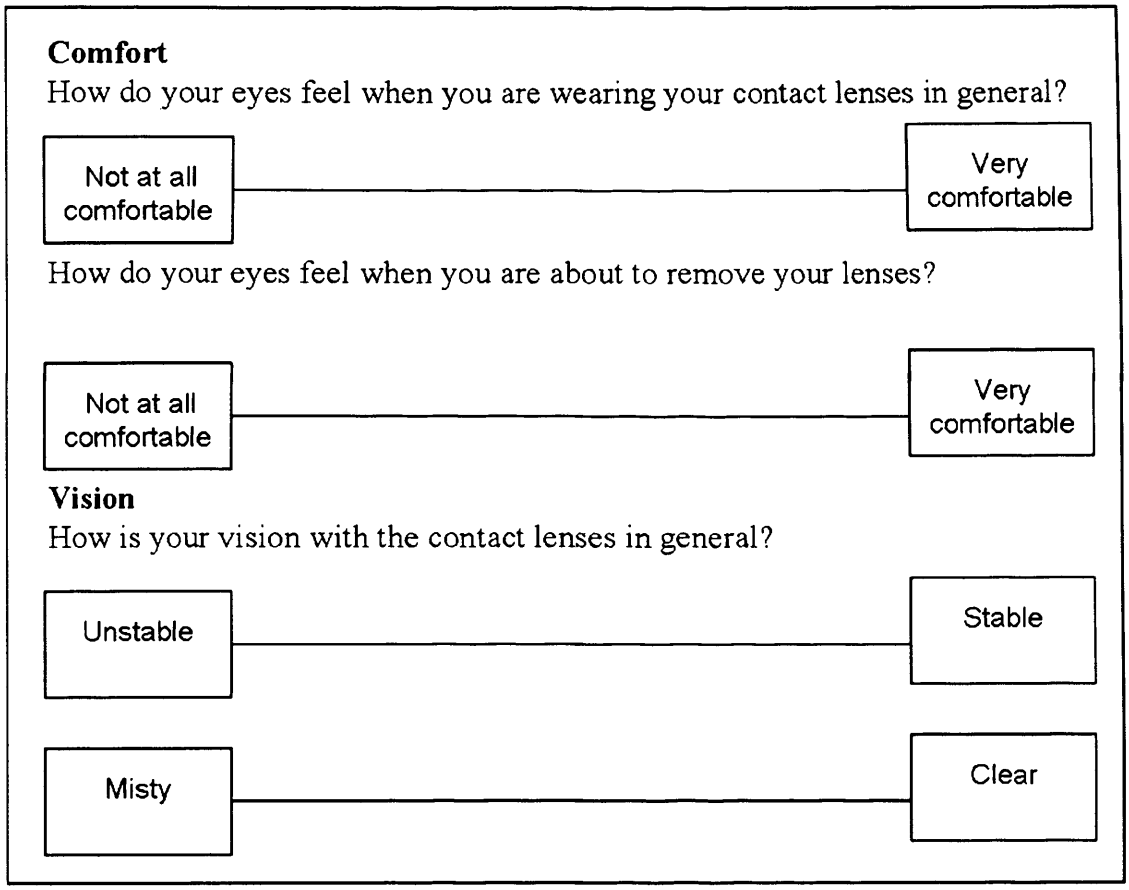


Figure 4.7 VAS to investigate subjective comfort and vision with GP lenses

- VA and CS were measured (Test Chart 2000);
- Lens surface was assessed with the slit-lamp, using white illumination;
- Lens fit assessed;
    - The slit-lamp was used to first asses the dynamic fit and interaction of lid with lens as described in Section 4.2.3. Fluorescein was instilled and the fit was assessed using the criteria from Section 4.2.2;
    - A fit conclusion was drawn, if unacceptable, amendment to fit was made as appropriate;
- Lenses were removed;
- Anterior surface assessment;
    - This was performed using the slit-lamp. CCLRU grading scales were used to grade limbal hyperaemia, conjunctival hyperaemia. (Tarsal changes were measured from one month onwards);
    - Fluorescein was instilled to grade corneal staining;

- Other aspects of anterior ocular health were recorded and monitored during the study, e.g. eyelids and lashes, estimated tear meniscus height, tarsal hyperaemia, conjunctival staining with fluorescein. However, only the key measures (hyperaemia and staining) were investigated and presented in this study;

- Topography was measured, both eyes, with Keratron Scout KS-1000 (Optikon, Rome, Italy).

4.2.5.2 One month follow-up

As at one week follow up; replacement lenses or modifications as necessary.

4.2.5.3 Three months follow-up

As at one week follow-up.

Subjects were then asked whether they would like to continue with GP lens wear.

4.3 Results

As in Chapter 3, parametric statistics have been employed for analysis of the CCLRU grading scale results. It has been proposed that interpolation of the grading scales produces an approximate interval scale and therefore parametrical statistical tests may be applied to such data (Barbeito and Simpson, 1991). VAS data was analysed with non-parametric tests as these data are considered to be ordinal.

4.3.1 Demographic results for entire cohort

In total, eighty seven subjects were recruited for the study. Table 4.4 shows the biometric information for the entire cohort initially recruited to the study. Figure 4.8 shows details of the subjects as they progress through the study to completion or until discontinuation.

Table 4.4 Biometric information.

Total number of subjects recruited	87
Gender (male/female)	32/55
History (neophyte/SCL)	33/54
Mean age ± SD; range (yrs)	29.0 ± 7.15; 19-44
Mean sphere ± SD; range (DS)	-3.11 ± 2.46; -10.00 to +2.25
Mean cylinder ± SD; range (DC)	-0.78 ± 0.58; 0 to -3.00
Mean VPA ± SD; range (mm)	11.1 ± 1.26; 8.0 to14.0
Mean HVID ± SD; range (mm)	11.5 ± 0.35; 10.0 to 12.5
Mean pupil ± SD; range (mm)	3.98 ± 0.58; 3.0 to 6.0
Mean keratometry value ± SD; range (mm)	7.77 ± 0.24; 7.30 to 8.46 (Horizontal) 7.61 ± 0.47; 7.08 to 8.30 (Vertical)

Figure 4.8 Study subjects who completed or dropped out of the study

4.3.2 Comparing the subjective properties of the cohorts

4.3.2.1 Anxiety tendencies

The anxiety levels between both sets of groups; neophyte and SCL, and plasma treated and untreated groups were compared to establish that groups were adequately matched in this respect. The internal reliability of the short version state and trait questionnaires was good with Cronbach alpha measured at α=0.73, as described in Section 3.3.2.1. The groups were subsequently compared to examine any differences in state and trait anxiety before commencing the study. Comparison of subjects assigned to plasma treated and untreated lens wear demonstrated no statistically significant difference in trait and state anxiety tendencies (Mann-Whitney tests p=0.40, p=0.20, respectively). There were also no significant differences in state and trait anxiety tendencies between the subjects who were new to contact lenses generally and those who had worn soft contact lenses previously (Mann-Whitney Tests, p=0.55, p=0.17 respectively).

4.3.2.2 Dry eye tendencies

Results from the CLDEQ and the DEQ questionnaires indicated there was no significant association between neophyte and SCL groups and dry eye (Figure 5.9) (Chi-square test, p=0.67, Phi= -0.05).

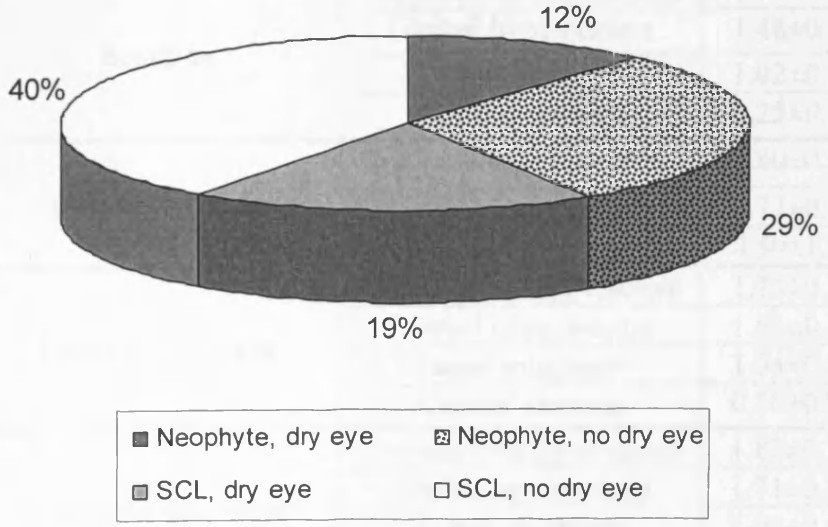


Figure 4.9 A pie chart showing percentage of dry eye subjects in neophyte and SCL groups.

4.3.2.3 Changes in visual function and anterior surface

The main results for visual function for the entire cohort throughout the study are shown in Table 4.5. There was a reduction in VA comparing optimum spectacle correction with GP correction; however CS measures were unchanged. Mean Ocular surface values during the study for the entire cohort are shown in Table 4.6.

Table 4.5 Visual function measures for the entire study cohort during the study.

	Visual acuity (logMAR)	**Contrast sensitivity (logMAR)**
Baseline (n=78)	-0.071±0.08	1.14±0.19
At lens collection (78)	-0.033±0.10	Not measured
1 week (n=70)	-0.048±0.09	1.15 ±0.10
1 month (n=43)	-0.040±0.10	1.14±0.10
3 months (n=28)	-0.039±0.09	1.17±0.10

Table 4.6 Anterior surface CCLRU grades for the entire cohort at each stage of the study.

	CCLRU grades	**Mean±SD**
Baseline	Conjunctival hyperaemia	1.71±0.20
	Limbal hyperaemeia	1.48±0.45
	Tarsal roughness	1.02±0.54
	Corneal staining	0.25±0.38
1 week GP wear	Conjunctival hyperaemia	1.80±0.24
	Limbal hyperaemeia	1.72±0.33
	Corneal staining	0.50±1.26
1 month GP wear	Conjunctival hyperaemia	1.74±0.22
	Limbal hyperaemeia	1.63±0.35
	Tarsal roughness	1.04±0.57
	Corneal staining	0.30±0.29
3 months GP wear	Conjunctival hyperaemia	1.83±0.24
	Limbal hyperaemeia	1.71±0.30
	Tarsal roughness	1.03±0.46
	Corneal staining	0.32±0.31

As the sample size reduced at each stage of the study, the results are now presented at each time point with comparisons between groups, neophyte and SCL, and plasma treated and untreated, in the cohort.

4.3.3 Comparison of results at one week

Only subjects who completed the study to one week or longer are presented (n=70).

4.3.3.1 Visual function in neophytes and SCL groups at one week

Baseline visual function measures (with trial spectacle lenses) were not statistically different in the neophyte group compared with previous SCL wearers (Independent t-tests, $0.22<p<0.78$).

Both the neophyte and SCL groups showed a small average decrease in VA at one week follow up, which was statistically significant for the neophyte group (Table 4.7). CS remained stable (Table 4.7). Statistical comparisons of mean change between groups for VA and CS were insignificant (Independent t-tests, p=0.10 p=0.67, for VA and CS, respectively). Subjective responses using VAS showed that the neophyte group reported better visual stability and clarity compared with the SCL group. However, these differences were not statistically significant (Mann-Whitney test, p=0.46 (stability) and p=0.57 (clarity), Figure 4.10).

Table 4.7 Absolute visual function measures at one week (paired t-tests)(n=70).

	Neophyte			SCL		
	Baseline	**1 week**	**p value**	**Baseline**	**1 week**	**p value**
Visual acuity (logMAR)	-0.09±0.08	-0.03±0.08	p<0.05	-0.07±0.09	-0.05±0.08	p=0.27
Contrast sensitivity (logMAR)	1.17±0.08	1.16±0.10	p=0.63	1.16±0.16	1.15±0.11	p=0.64

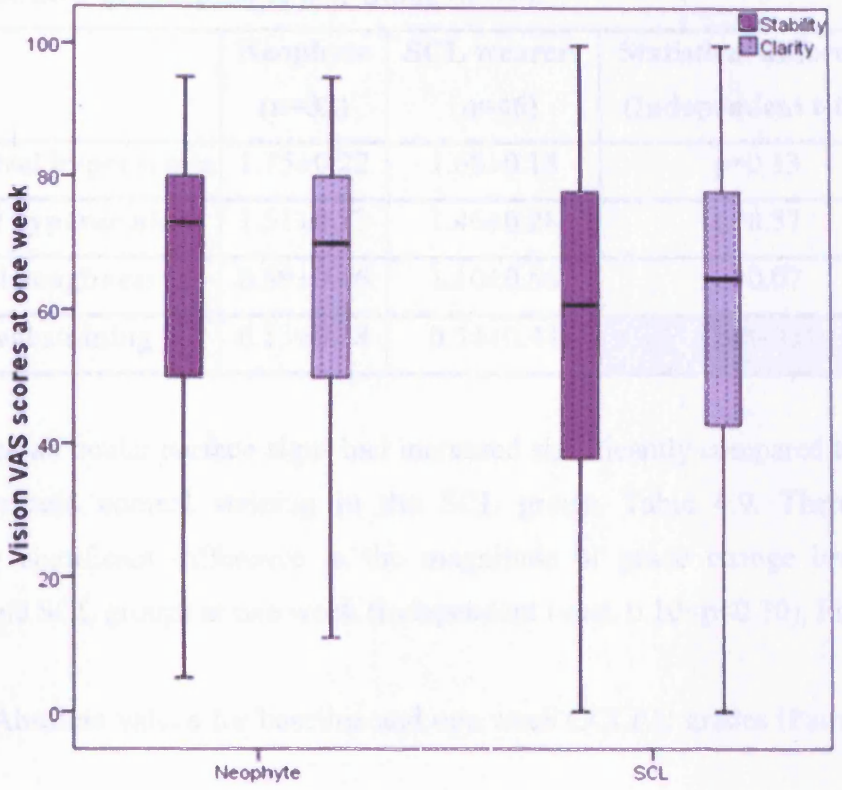


Figure 4.10 A box plot showing median, lower and upper quartiles and range of VAS results for visual stability and visual clarity at one week in the neophyte and SCL groups (0=Unstable, 100=Stable; 0=Misty, 100=Clear) (n=70).

4.3.3.2 Ocular surface grading in neophytes and SCL groups at one week

No statistical differences were evident between right and left eye grades for hyperaemia, tarsal roughness or corneal staining grades, and therefore only right eye data are presented (Paired t-test, $0.19 < p < 0.71$). Results are summarised in Table 4.8. No significant difference was observed for conjunctival or limbal hyperaemia. However, soft lens wearers had significantly more staining at baseline than non-lens wearers. Tarsal roughness was greater in the SCL group; though, this difference was outside statistical significance.

Table 4.8 CCLRU grades prior to lens fitting (n=70).

	Neophyte (n=32)	SCL wearers (n=46)	Statistical difference (Independent t-test)
Conjunctival hyperaemia	1.75±0.22	1.68±0.18	p=0.13
Limbal hyperaemia	1.51±0.33	1.46±0.28	p=0.57
Tarsal roughness	0.89±0.46	1.10±0.56	p=0.07
Corneal staining	0.13±0.18	0.34±0.44	p<0.05

At one week all ocular surface signs had increased significantly compared to baseline measures except corneal staining in the SCL group; Table 4.9. There was no statistically significant difference in the magnitude of grade change between the neophyte and SCL groups at one week (Independent t-test, 0.10<p<0.30), Figure 4.11.

Table 4.9 Absolute values for baseline and one week CCLRU grades (Paired t-tests), (n=70).

CCLRU grading	Neophyte			SCL		
	Baseline	One week	p value	Baseline	One week	p value
Conjunctival hyperaemia	1.75±0.22	1.85±0.22	p<0.05	1.68±0.18	1.77±0.20	p<0.05
Limbal hyperaemia	1.51±0.33	1.75±0.34	p<0.05	1.46±0.28	1.59±0.38	p<0.05
Corneal staining	0.13±0.18	0.39±0.32	p<0.05	0.34±0.44	0.41±0.52	p=0.45

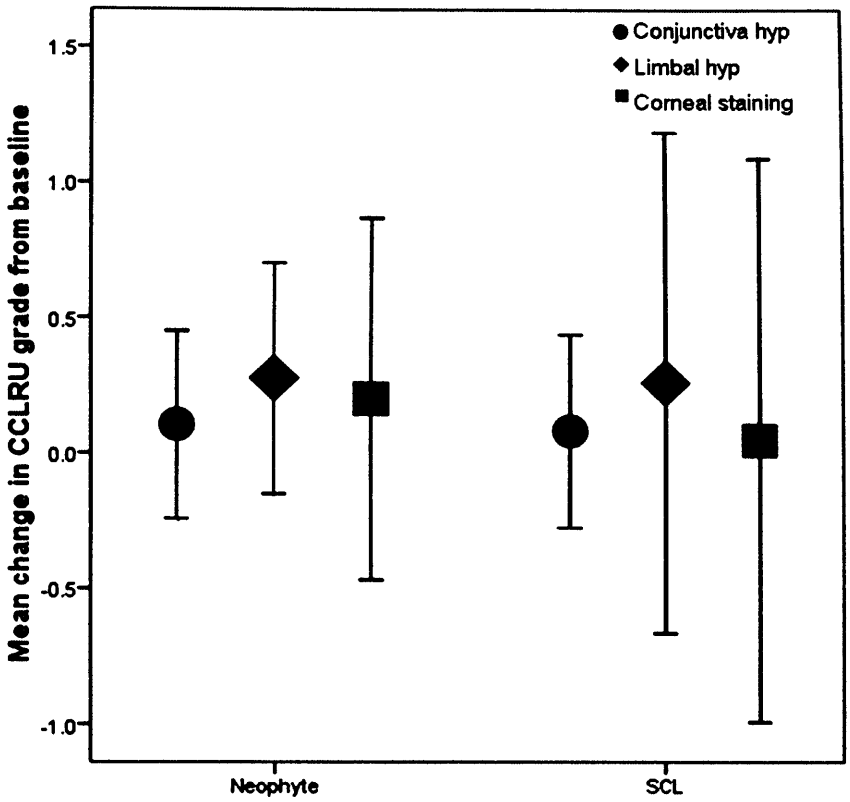


Figure 4.11 Difference plot showing mean change (+/-SD) for ocular surface grading (CCLRU) in neophyte and SCL groups after one week of GP lens wear (n=70).

4.3.3.3 Subjective comfort in neophyte and SCL groups at one week

VAS comfort (absolute) scores at one week indicated that the neophyte group were significantly more comfortable with GP lenses generally than the SCL group (Mann-Whitney test, $p<0.05$), Figure 4.12. The difference in end-of-day comfort was not statistically significant between the two groups (Mann-Whitney test, $p=0.40$).

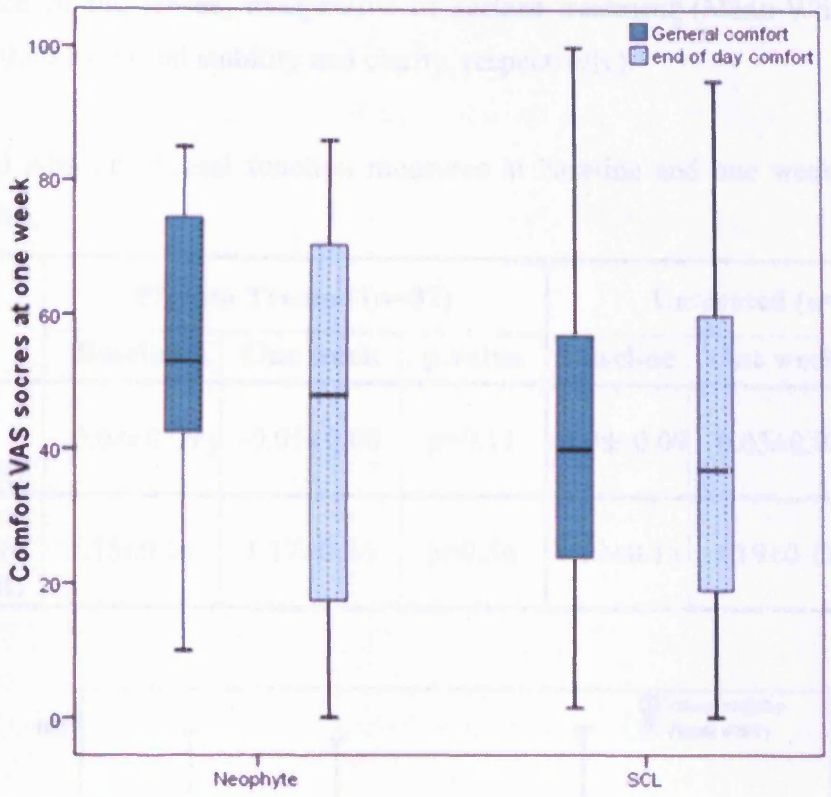


Figure 4.12 A box plot showing median, lower and upper quartiles, lower and upper quartiles and range of VAS results for general comfort and end-of-day comfort at one week in Neophyte and SCL groups (0=Not at all comfortable, 100=Very comfortable) (n=70).

4.3.3.4 Visual function in plasma treated and untreated groups at one week visit

There was no difference in VA and CS in subjects fitted with plasma treated or untreated lenses at the baseline visit (Independent t-tests, p=0.78, p=0.99 respectively). Table 4.10 indicates that VA was significantly worse at one week (compared with baseline) in the untreated lens wearing group. The other measures showed no significant change from baseline, indicating there was no significant difference.

Comparison of magnitude of change in VA between the neophyte and SCL groups was not significant (Independent t-test, p=0.30). Likewise, comparison of magnitude of change in CS between groups found no significant difference (Independent-test, p=0.094). Figure 4.13 demonstrates that there was no difference in subjective visual

performance of the lenses, irrespective of surface treatment (Mann-Whitney tests, p=0.44 p=0.40 for visual stability and clarity, respectively).

Table 4.10 Absolute visual function measures at baseline and one week (Paired t-tests) (n=70).

	Plasma Treated (n=32)			Untreated (n=38)		
	Baseline	**One week**	**p value**	**Baseline**	**One week**	**p value**
Visual acuity (logMAR)	-0.08±0.09	-0.05±0.08	p=0.11	-0.08±0.09	-0.03±0.08	p<0.05
Contrast sensitivity (logMAR)	1.15±0.14	1.17±0.36	p=0.56	1.19±0.13	1.19±0.11	p=0.11

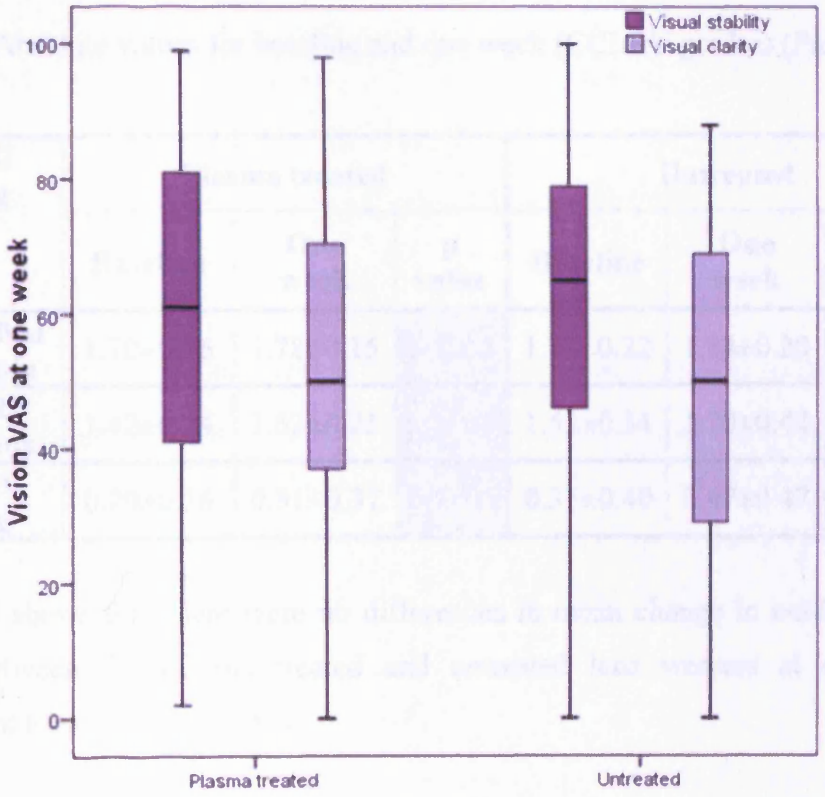


Figure 4.13 A box plot showing median, lower and upper quartiles and range of VAS results for visual stability and visual clarity at one week in plasma treated and untreated groups (0=Unstable, 100=Stable; 0=Misty, 100=Clear) (n=70).

4.3.3.5 Ocular surface findings in plasma treated and untreated groups at one week

Baseline CCLRU ocular surface grades were similar for subjects subsequently ascribed to plasma treated and untreated GP wear (Table 4.11). All grades significantly increase from baseline measures at one week; Table 4.12.

Table 4.11 CCLRU grades prior to lens fitting (n=70).

CCLRU grading	Plasma treated (n=32)	Untreated (n=38)	Statistical difference (Independent t-test)
Conjunctival hyperaemia	1.70±0.16	1.73±0.22	p=0.39
Limbal hyperaemia	1.42±0.24	1.52±0.34	p=0.14
Tarsal roughness	0.95±0.52	1.04±0.53	p=0.46
Corneal staining	0.20±0.36	0.31±0.40	P=0.20

Table 4.12 Absolute values for baseline and one week (CCLRU grades) (Paired t-test) (n=70).

CCLRU grading	Plasma treated			Untreated		
	Baseline	One week	p value	Baseline	One week	p value
Conjunctival hyperaemia	1.70±0.16	1.78±0.15	p<0.05	1.73±0.22	1.84±0.20	p<0.05
Limbal hyperaemia	1.42±0.24	1.62±0.25	p<0.05	1.52±0.34	1.70±0.44	p<0.05
Corneal staining	0.20±0.36	0.31±0.37	p<0.05	0.31±0.40	0.47±0.47	p<0.05

Figure 4.14 shows that there were no differences in mean change in ocular surface findings between the plasma treated and untreated lens wearers at one week (Independent t-test, $0.36<p< 0.82$).

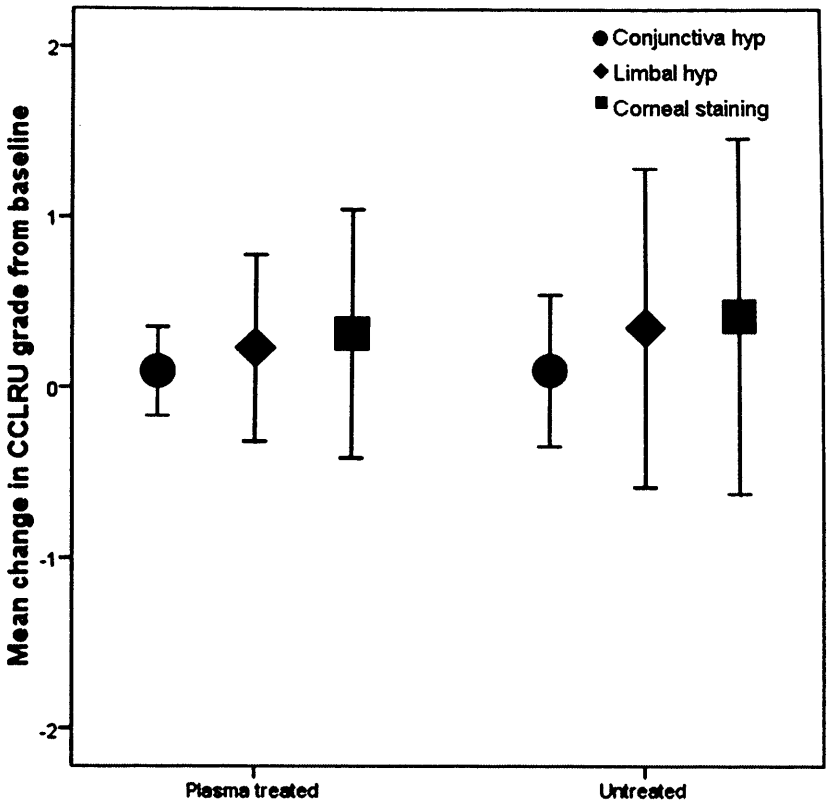


Figure 4.14 Error plot showing mean change (+/-SD) for ocular surface CCLRU grading in plasma treated and untreated groups at one week(n=70).

4.3.3.6 Subjective comfort in plasma treated and untreated groups at one week

Median comfort was marginally higher in the untreated lens wearing group during general wear; however, this finding was not statistically significant (Mann-Whitney test, p=0.55). At one week, subjective end-of-day comfort was significantly better in the untreated group; (Mann-Whitney Test, p=0.035), (Figure 4.15).

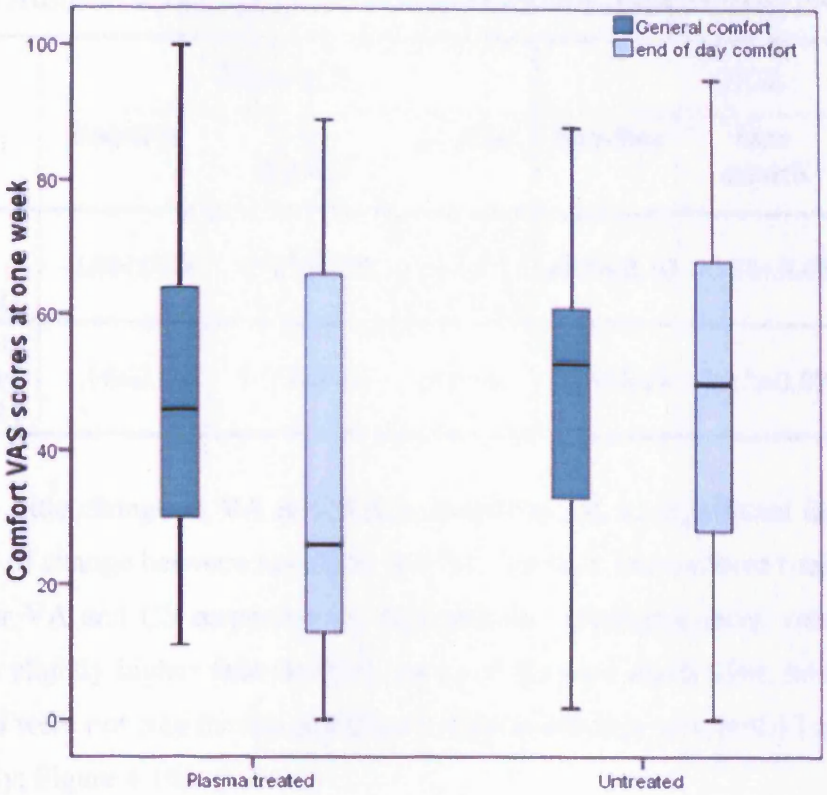


Figure 4.15 A box plot showing median, lower and upper quartiles and range of VAS results for general comfort and end-of-day comfort at one week in plasma treated and untreated groups (0= Not at all comfortable, 100=Very comfortable) (n=70).

4.3.4 Comparison of results at one month

Data from subjects who completed the study to one month (n=43) or longer are presented.

4.3.4.1 Visual function in neophyte and SCL groups at one month

Table 4.13 shows baseline and one month visual function measures for the neophyte and SCL groups. At one month, VA was significantly worse (than baseline) in the neophyte group.

Table 4.13 Absolute visual acuity and contrast sensitivity (Paired t-tests) (n=43).

	Neophyte			SCL		
	Baseline	**One month**	**p value**	**Baseline**	**One month**	**p value**
Visual acuity (logMAR)	-0.08±0.08	-0.03±0.08	p<0.05	-0.09±0.10	-0.05±0.08	p=0.10
Contrast sensitivity (logMAR)	1.16±0.09	1.13±0.11	p=0.46	1.16±0.18	1.15±0.09	p=0.63

There was little change in VA or CS from baseline and no significant difference in magnitude of change between neophyte and SCL groups (Independent t-tests, p=0.99, p=0.79, for VA and CS respectively). Subjectively, neophytes rated visual stability and clarity slightly higher than the SCL group at the one month visit, however these differences were not statistically significant (Mann-Whitney test, p=0.13 and p=0.51, respectively; Figure 4.16).

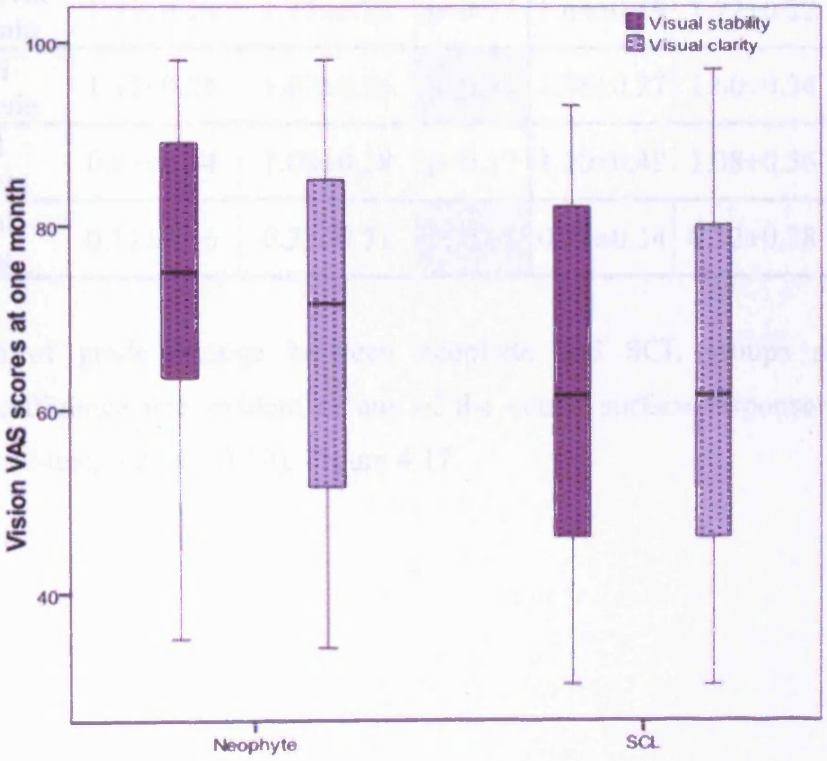


Figure 4.16 A box plot showing median, lower and upper quartiles and range of VAS results for general comfort and end-of-day comfort at one month in neophyte and SCL groups (0=Unstable, 100=Stable; 0=Misty, 100=Clear) (n=43).

4.3.4.2 Ocular surface grading in neophytes and SCL groups at one month

There was no significant difference in any aspect of ocular surface response to GP wear between the neophyte and SCL groups (Independent t-test, 027<p<0.79). Table 4.14 shows absolute values for baseline and one month grades compared using paired t-tests. Limbal staining is significantly higher than at baseline for both neophyte and SCL groups. The neophyte group showed a significant increase in corneal staining compared with their baseline measure, however, the SCL group had significantly more staining than the neophytes at baseline; and therefore showed no increase in staining (from their baseline measure) at one month GP wear. Neither conjunctival nor tarsal grades were significantly increased in either group.

Table 4.14 Absolute CCLRU grades at baseline and one month (Paired t-tests)(n=43).

CCLRU grade	Neophyte			SCL		
	Baseline	One month	p value	Baseline	One month	p value
Conjunctival hyperaemia	1.71±0.16	1.77±0.22	p=0.17	1.64±0.19	1.72±0.22	p=0.07
Limbal hyperaemia	1.45±0.28	1.67±0.36	p<0.05	1.36±0.27	1.60±0.34	p<0.05
Tarsal roughness	0.89±0.44	1.00±0.58	p=0.12	1.10±0.49	1.08±0.56	p=0.83
Corneal staining	0.11±0.16	0.27±0.31	p<0.05	0.27±0.34	0.32±0.28	p=0.45

Comparison of grade change between neophyte and SCL groups showed no significant difference was evident in any of the ocular surface responses measured (Independent t-test, 0.27<p<0.79), Figure 4.17.

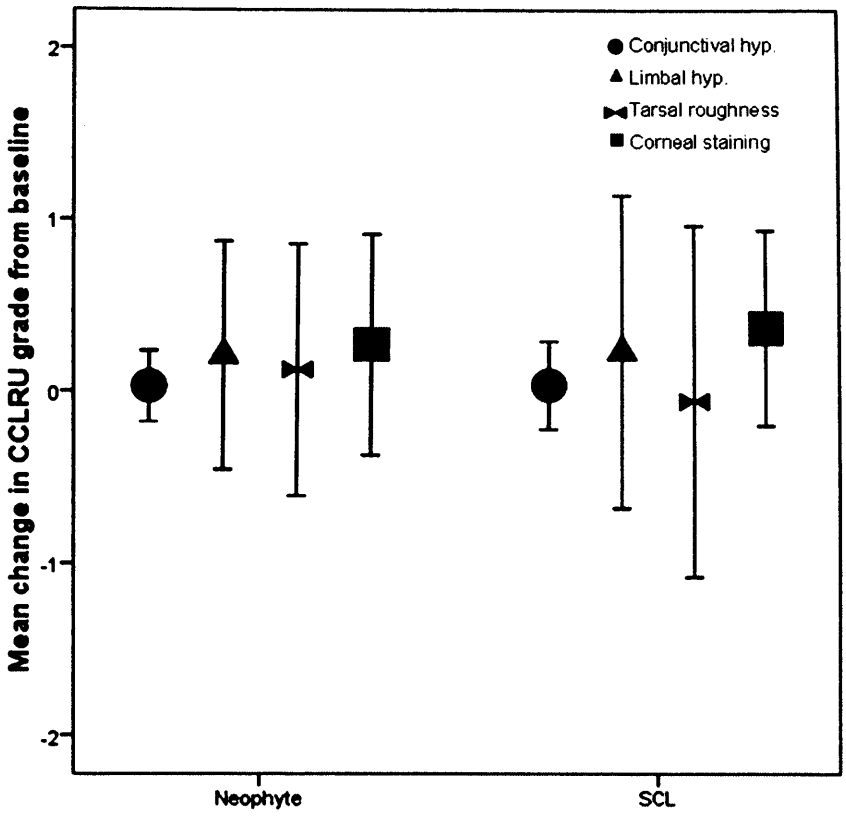


Figure 4.17 Difference plot showing mean change (+/-SD) for ocular surface CCLRU grading in neophyte and SCL groups at one month GP wear (n=43).

4.3.4.3 Subjective comfort in neophyte and SCL groups at one month

Figure 4.18 shows subjective (absolute scores) comfort at one month, results indicated that the neophyte group experienced better general and end-of-day comfort in comparison with the SCL group (Mann-Whitney Test, $p<0.05$).

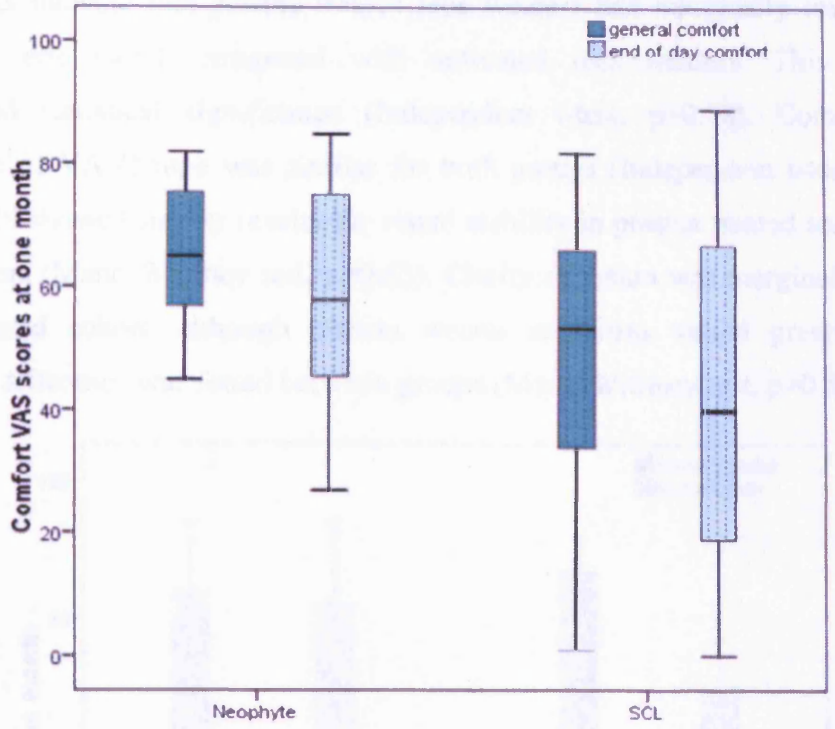


Figure 4.18 A box plot showing median, lower and upper quartiles and range of VAS results for general comfort and end-of-day comfort at one month in neophyte and SCL groups (0=Not at all comfortable, 100=Very comfortable) (n=43).

4.3.4.4 Visual function in plasma treated and untreated groups at one month

Table 4.15 shows that no difference in VA was found between baseline measurements (with optimum spectacle correction) and treated GP lenses at one month, whereas VA was significantly worse (than baseline) in the group wearing untreated lenses. One month CS results were similar to baseline measures for both groups.

Table 4.15 Absolute VA and CS measures at baseline and one month. (Paired t-test) (n=43).

	Plasma Treated			Untreated		
	Baseline	**1 month**	**p value**	**Baseline**	**1 month**	**p value**
Visual acuity (logMAR)	-0.09±0.09	-0.05±0.08	p=0.08	-0.08±0.09	-0.03±0.12	p<0.05
Contrast sensitivity (logMAR)	1.14±0.17	1.16±0.11	p=0.60	1.19±0.12	1.12±0.10	p=0.06

The results indicate that plasma treated lens wearers had marginally improved CS results at one month compared with untreated lens wearers. This difference approached statistical significance (Independent t-test, p=0.08). Comparison of magnitude of VA change was similar for both groups (Independent t-test, p=0.37). Figure 4.19 showed similar results for visual stability in plasma treated and untreated lens wearers (Mann-Whitney test, p=0.63). Clarity of vision was marginally better in the untreated cohort, although plasma wearer responses varied greatly, and no statistical difference was found between groups (Mann-Whitney test, p=0.89).

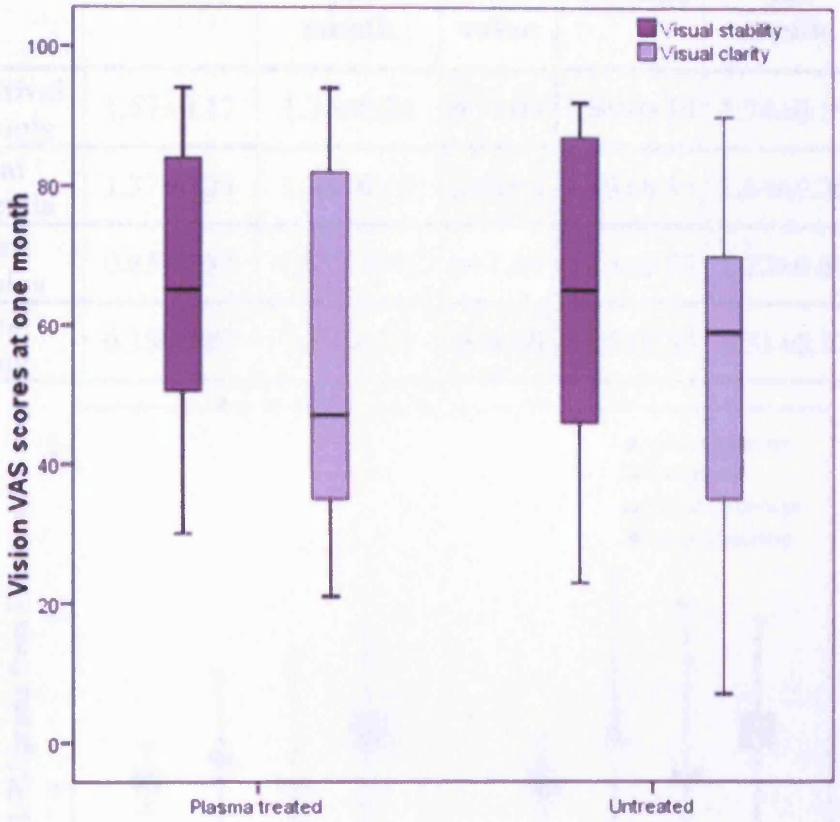


Figure 4.19 A box plot showing median, lower and upper quartiles and range of VAS results for general comfort and end-of-day comfort at one month in plasma treated and untreated groups (0=Unstable, 100=Stable; 0=Misty, 100=Clear) (n=43).

4.3.4.5 Ocular surface findings in plasma treated and untreated groups at one month

Table 4.16 indicates that there was a greater increase (from baseline measures) in absolute grades for conjunctival hyperaemia and corneal staining with plasma treated lenses. Both groups showed significant increases in limbal hyperaemia scores and

both had no significant change in tarsal roughness. However, comparison of grade change between the plasma treated and untreated groups for all ocular surface assessments, at one month, found no significant differences (Independent t-test, $0.43<p<0.92$), (Figure 4.20).

Table 4.16 Absolute CCLRU grades at baseline and one month (Paired t-tests) (n=43).

CCLRU grading	Plasma Treated			Untreated		
	Baseline	One month	p value	Baseline	One month	p value
Conjunctival hyperaemia	1.67±0.17	1.76±0.26	p<0.05	1.69±0.19	1.74±0.19	p=0.26
Limbal hyperaemia	1.37±0.22	1.65±0.37	p<0.05	1.43±0.33	1.64±0.35	p<0.05
Tarsal roughness	0.85±0.52	0.85 ±0.46	p=1.00	1.13±0.39	1.22±0.61	p=0.43
Corneal staining	0.15±0.23	0.29±0.29	p<0.05	0.25±0.33	0.31±0.32	p=0.48

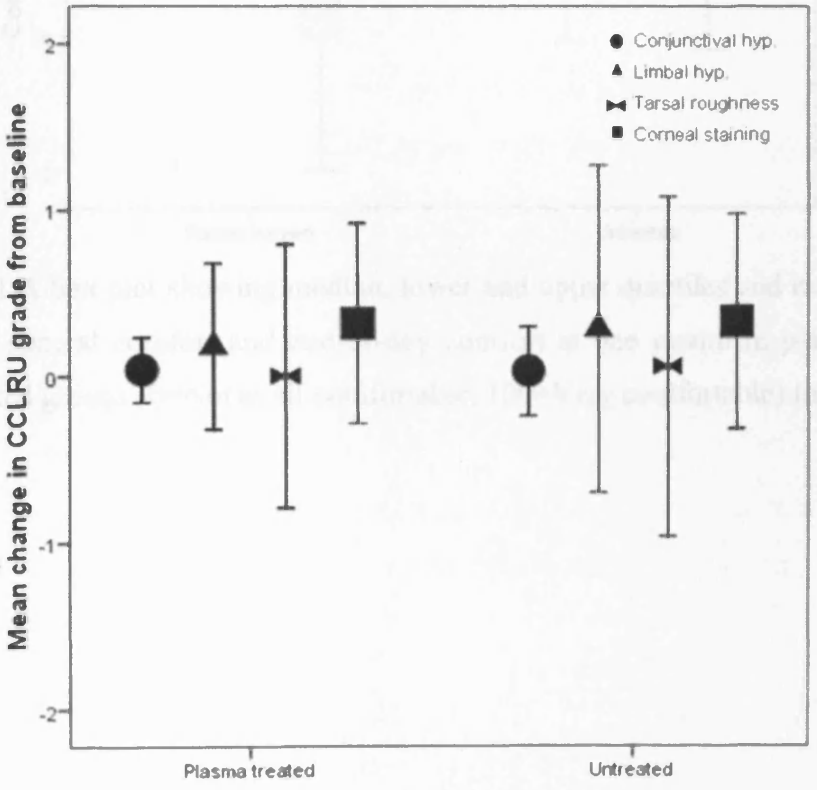


Figure 4.20 Difference plot showing mean change (+/-SD) for ocular surface CCLRU grading scores in plasma treated and untreated groups at one month of GP lens wear (n=43).

4.3.4.6 Subjective Comfort in plasma treated and untreated groups at one month

Untreated lens wearers reported marginally better subjective general comfort and moderately better end-of-day comfort than plasma treated wearers. These differences were not statistically significant; (Mann-Whitney test, p=0.31 and p=0.09, respectively), (Figure 4.21).

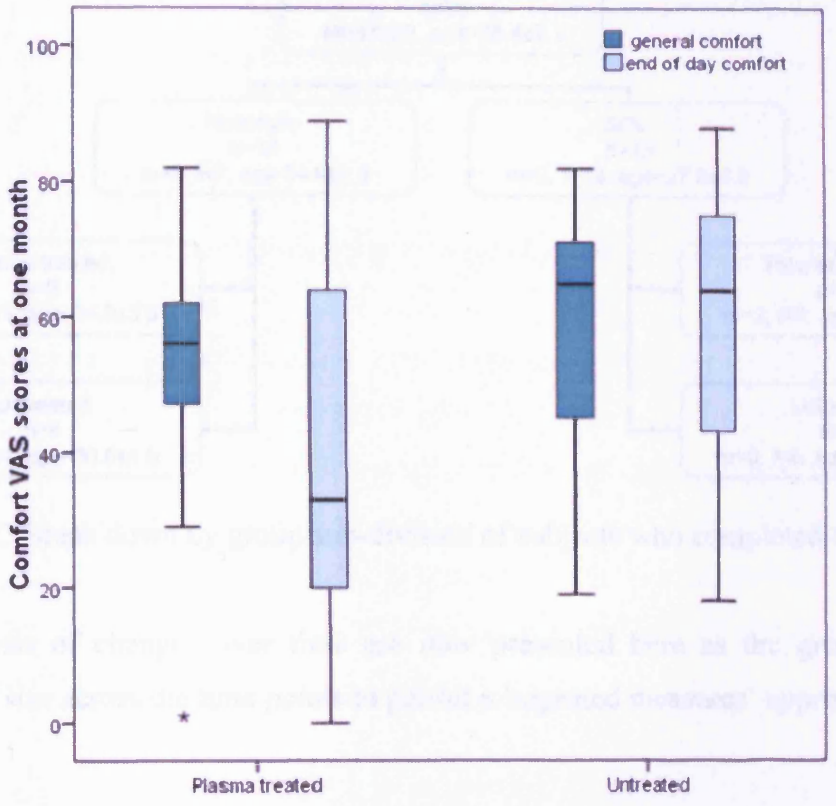


Figure 4.21 A box plot showing median, lower and upper quartiles and range of VAS results for general comfort and end-of-day comfort at one month in plasma treated and untreated groups (0=Not at all comfortable, 100=Very comfortable) (n=43).

4.3.5 Comparison of results at three months

The sub-division of the subjects who completed the study is shown in Figure 4.22. When questioned, 68% (n=19) wanted to continue with GP wear following the study.

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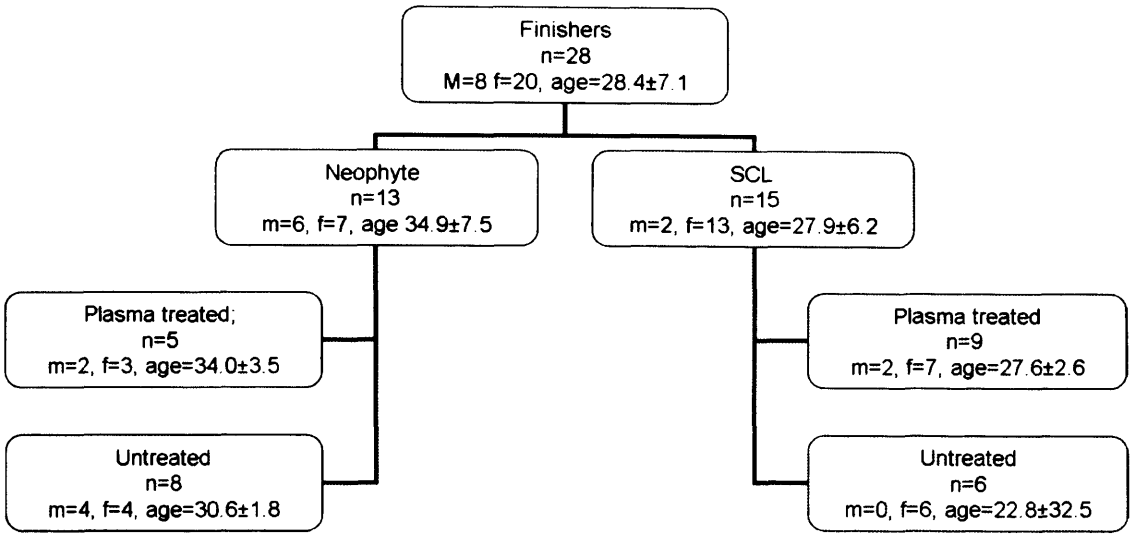

Figure 4.22 Break down by group sub-division of subjects who completed the study.

The analysis of changes over time are now presented here as the groups are of consistent size across the time points to permit a 'repeated measures' approach.

4.3.5.1 Visual function in neophyte and SCL groups at three months

No differences in baseline visual function measures were evident between neophyte and SCL groups (Independent t-test, p=0.23 and p=0.78, for CS and VA respectively).

Comparison of change within groups indicated that there was no significant change in VA or CS measures at 3 months, from baseline, in either neophyte or SCL group (Table 4.17).

Table 4.17 Absolute visual function measures at baseline and 3 months (Paired t-tests) (n=28).

	Neophyte (n=13)			SCL (n=15)		
	Baseline	**3 months**	**p value**	**Baseline**	**3 months**	**p value**
Visual acuity (logMAR)	-0.09±0.08	-0.07±0.08	p=0.49	-0.08±0.11	-0.06±0.09	p=0.35
Contrast sensitivity (logMAR)	1.18±0.09	1.19±0.10	p=0.89	1.16±0.18	1.18±0.09	p=0.10

Initially, VA with GP correction was marginally worse than baseline spectacle correction, however this improved with adaptation. A mixed between-within ANOVA for VA indicated that there was no interaction effect between time and grouping ($p=0.68$); the effect for time was statistically significant ($p<0.05$) and there was a large effect size (0.27). The effect of group was not statistically significant ($p=0.68$), suggesting that patient CL history did not impact on visual acuity results during the study (Figure 4.23 A). CS was marginally better in neophyte group than SCL group, but using ANOVA, neither time ($p=0.51$) nor group ($p=0.37$) was significant and no interaction effect was found ($p=0.80$), (Figure 4.23 B).

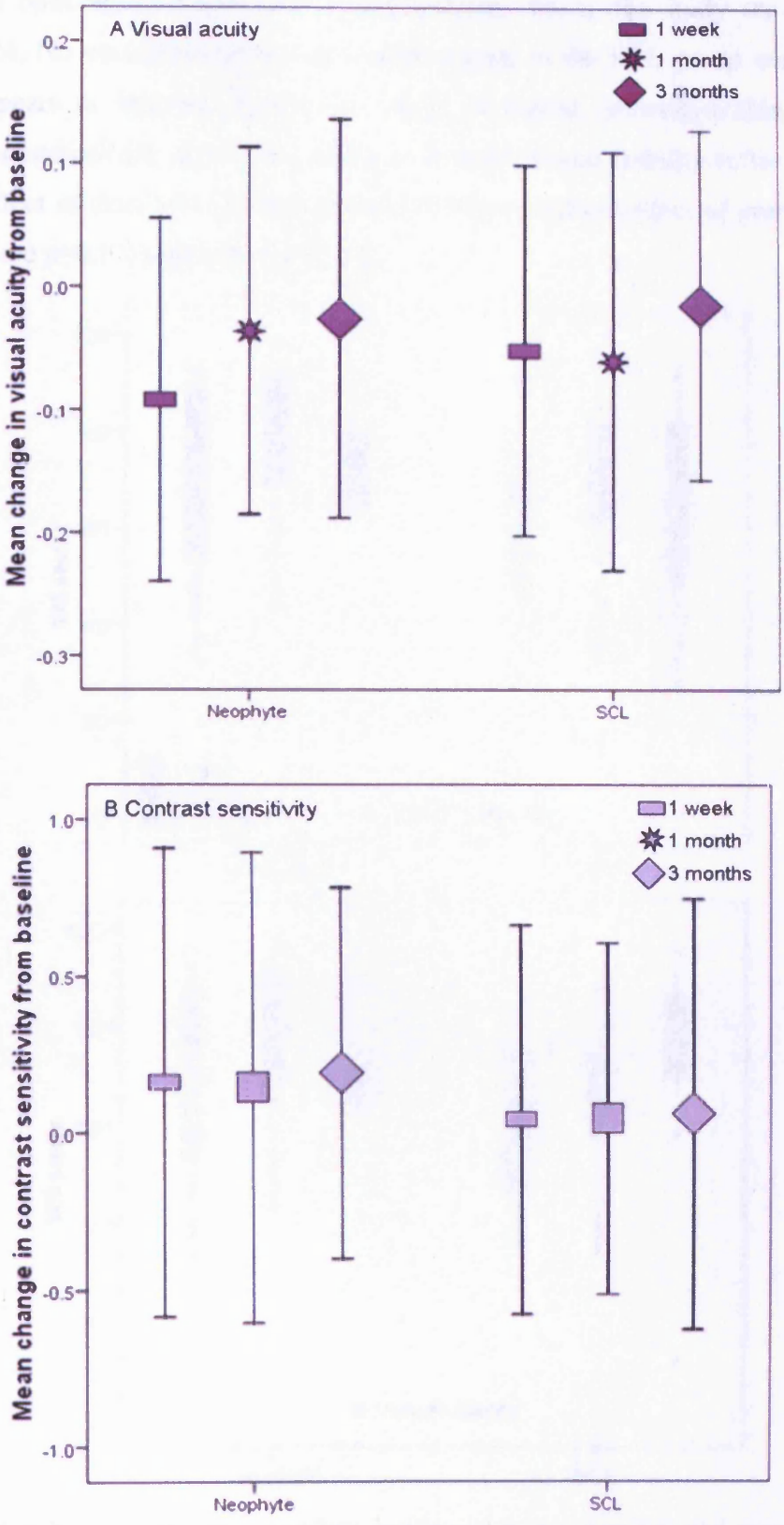

Figure 4.23 Error plot showing mean change (+/-SD) in visual function for neophyte and SCL groups, A: Visual acuity and B: Contrast sensitivity (n=28).

Subjective opinions of vision clarity and stability during the study are shown in Figure 4.24. No consistent trend was visible except in the SCL group where visual clarity appears to improve during the study. A mixed, between-within ANOVA revealed no statistically significant changes in either visual stability (effect of group p=0.24; effect of time p=0.13; interaction p=0.96) or clarity (effect of group p=0.31; effect of time p=0.17; interaction p=0.16).

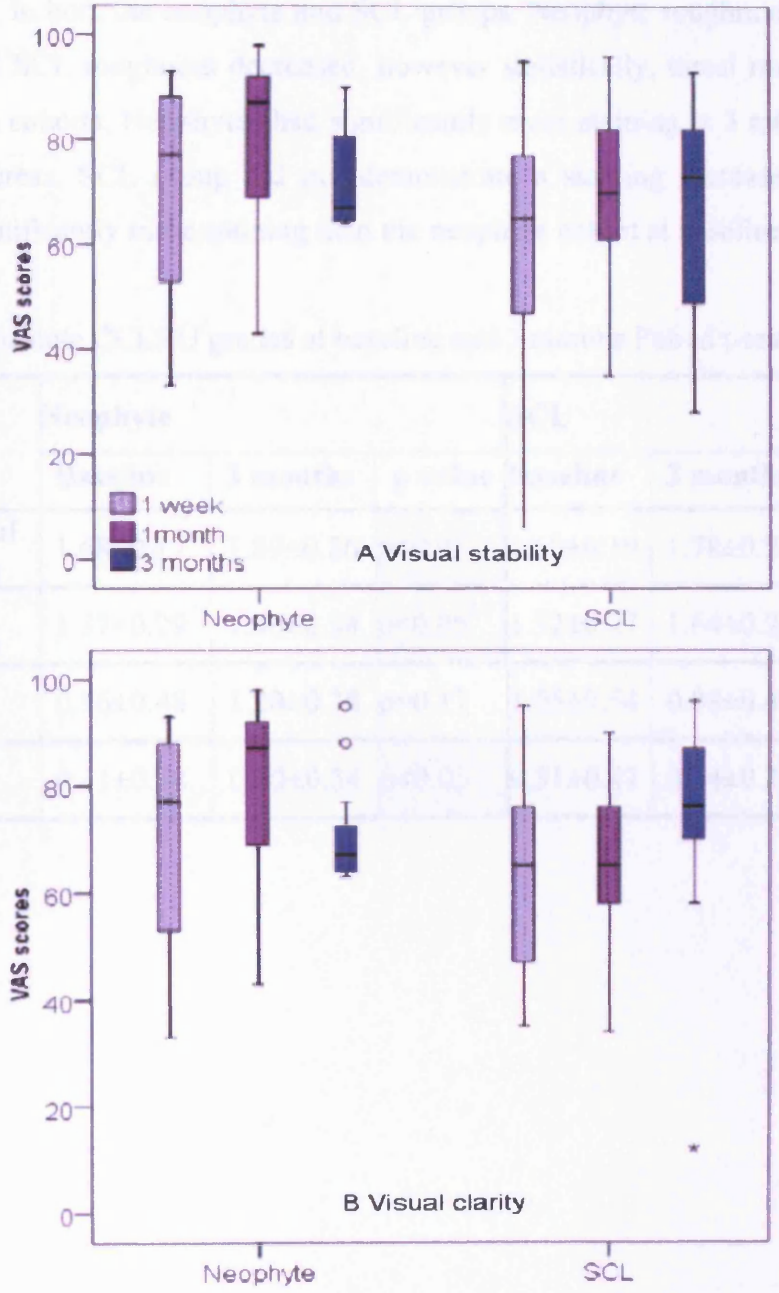

Figure 4.24 A box plot showing median, lower and upper quartiles and range of VAS results for A: visual stability and B: visual clarity in neophyte and SCL groups (0=Unstable, 100=Stable; 0=Misty, 100=Clear) (n=28).

4.3.5.2 Ocular surface findings in finisher, neophyte and SCL groups at three months

Baseline surface grading scores were similar for neophytes and SCL groups in the finisher cohort (Independent t-tests, $0.23<p<0.64$).

Table 4.18 shows that hyperaemia was significantly greater at 3 months, compared with baseline, in both the neophyte and SCL groups. Neophyte roughness marginally increased and SCL roughness decreased, however statistically, tarsal roughness was stable in both cohorts. Neophytes had significantly more staining at 3 months than at baseline, whereas, SCL group did not demonstrate a staining increase. (The SCL group had significantly more staining than the neophyte cohort at baseline.)

Table 4.18 Absolute CCLRU grades at baseline and 3 months Paired t-tests (n=28).

CCLRU grading	Neophyte			SCL		
	Baseline	3 months	p value	Baseline	3 months	p value
Conjunctival hyperaemia	1.68±0.17	1.89±0.26	p<0.05	1.60±0.19	1.78±0.21	p<0.05
Limbal hyperaemia	1.37±0.29	1.80±0.34	p<0.05	1.32±0.27	1.64±0.26	p<0.05
Tarsal roughness	0.96±0.48	1.20±0.38	p=0.17	1.05±0.54	0.88±0.49	p=0.18
Corneal staining	0.11±0.18	0.40±0.34	p<0.05	0.31±0.47	0.24±0.25	p=0.64

Figure 4.25 indicates a small increase in corneal staining (compared with baseline), for both groups, that appeared to remain consistent throughout the study. Statistically, there was no interaction between time and grouping (p=0.28), and the effects of time and group were not significant for corneal staining (p=0.74 and p=0.79, respectively).

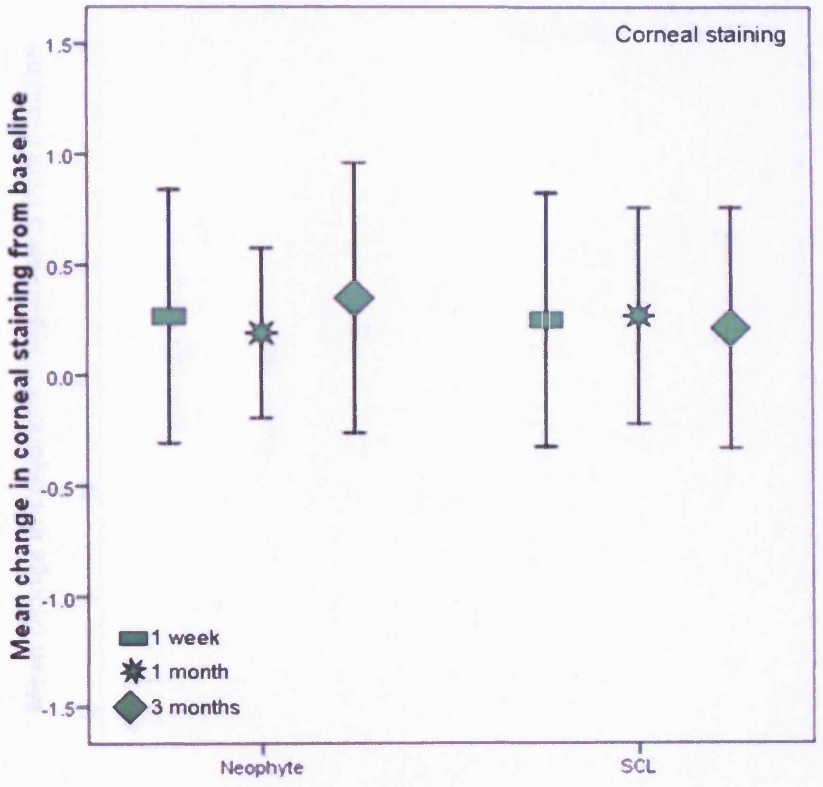

Figure 4.25 Difference plots showing mean change (+/-SD) for ocular surface CCLRU corneal staining grade in neophyte and SCL groups (n=28).

Figure 4.26 demonstrates the marginal increase in conjunctival hyperaemia for both groups throughout the study. There was no interaction effect (p=0.65), and the effects of time and grouping on conjunctival hyperemia were not statistically significant (p=0.12 and p=0.67, respectively).

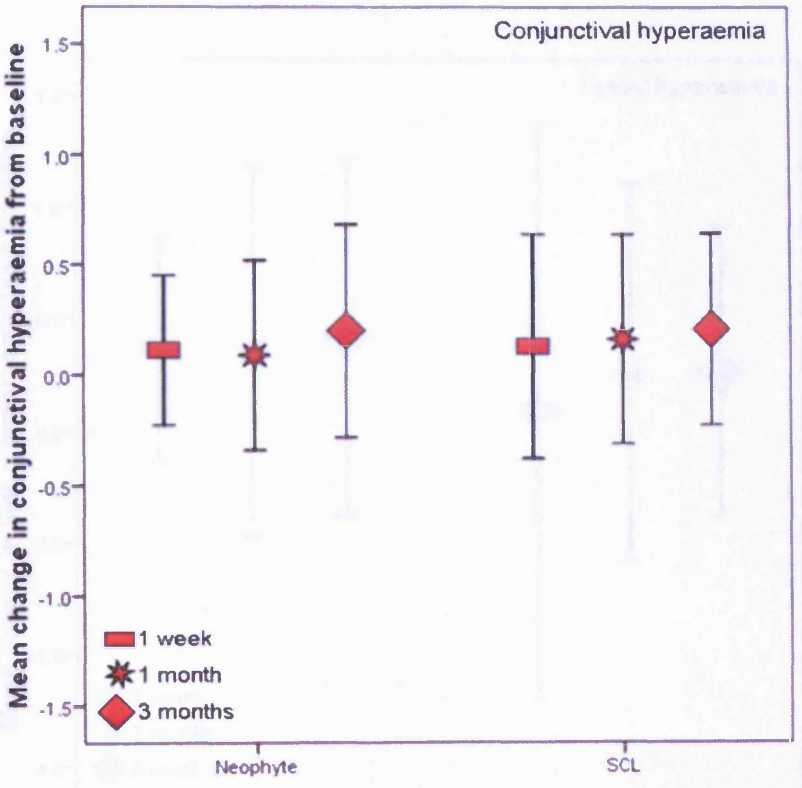

Figure 4.26 Difference plots showing mean change (+/-SD) for ocular surface CCLRU conjunctival hyperaemia grade in neophyte and SCL groups (n=28).

Results for limbal hyperaemia (Figure 4.27) were more varied; generally, neophytes exhibited a greater initial increase in limbal hyperemia compared to baseline than SCL wearers, but the change over time was not significant (p=0.34). Statistically there was no interaction effect (p=0.50), and there was no effect for grouping (p=0.24).

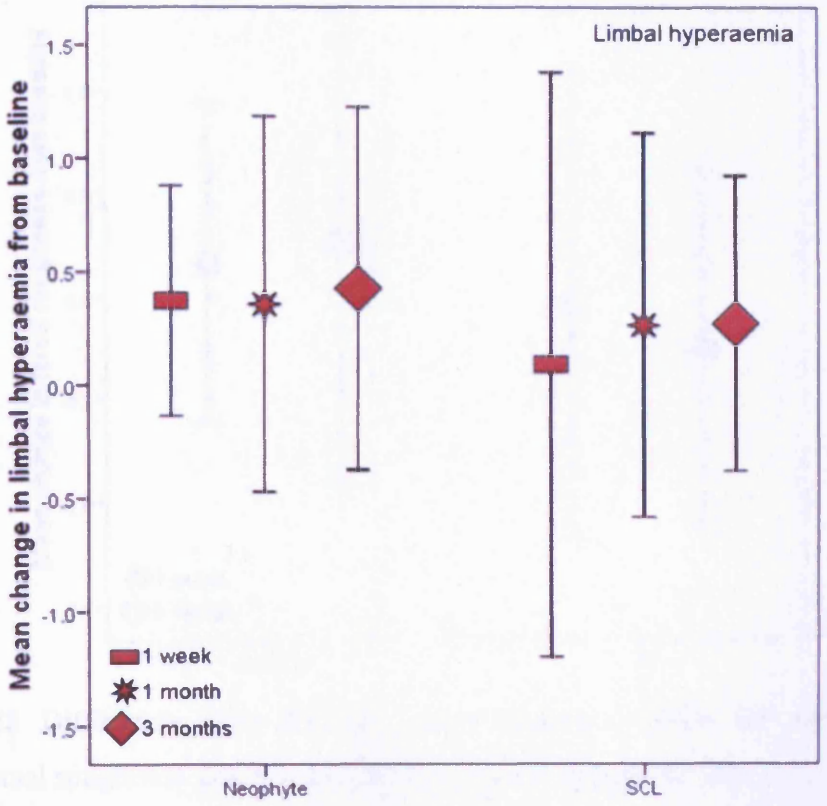

Figure 4.27 Difference plots showing mean change (+/-SD) for ocular surface CCLRU limbal hyperaemia grade in neophyte and SCL groups (n=28).

Figure 4.28 shows that although neither group had a statistical change in tarsal roughness grade, comparison of the change in roughness for SCL and neophyte groups resulted in a statistically significant difference between groups at 3 months (Independent t-test, $p<0.05$). (Tarsal roughness was not recorded at 1 week.)

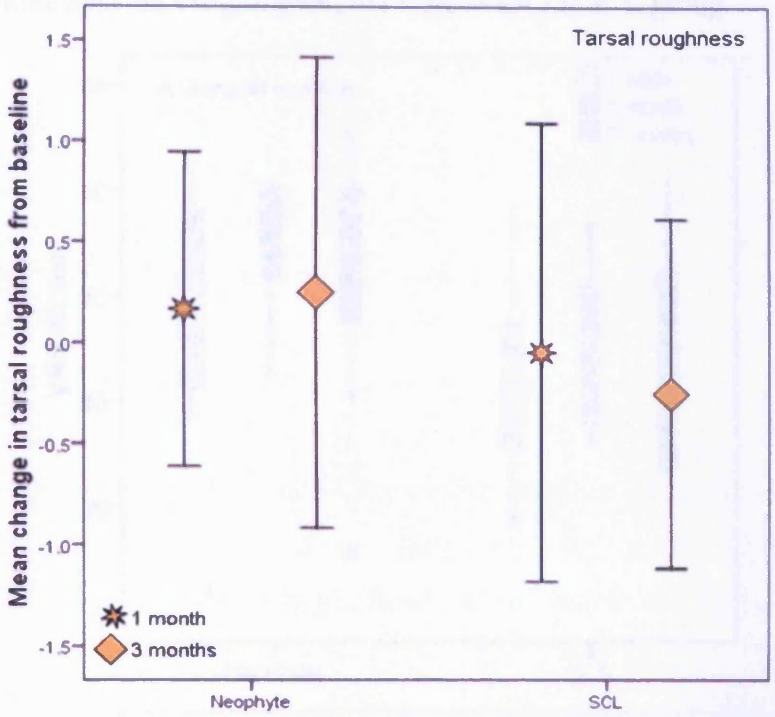

Figure 4.28 Difference plots showing mean change (+/-SD) for ocular surface CCLRU tarsal roughness grade in neophyte and SCL groups (n=28).

4.3.5.2.1 Corneal topography

Corneal topography was measured prior to GP fitting (baseline), and was also measured at each follow up visit. Repeated corneal curvature measurement found no significant interaction effect ($p=0.51$), the effect of time was insignificant ($p=0.97$) and there was no between subjects effect ($p=0.76$).

4.3.5.3 Subjective comfort in finisher, neophyte and SCL groups at three months

The neophyte group reported better comfort (Figure 4.29 A) throughout the study compared with the SCL group. There was no statistical interaction effect ($p=0.70$), time influence was outside statistical significance ($p=0.07$), however, there was a significant effect for group ($p<0.05$). This indicates that subject experience (neophyte or previous SCL wear) influenced GP lens wear comfort.

End-of-day comfort is shown in Figure 4.29 B. The neophyte scores were generally stable throughout the study. The SCL group appears to have improved comfort at one month visit, but this is reduced by the 3 month visit. There was a statistical interaction effect ($p<0.05$) which makes analysis of individual effects invalid, i.e. for neophytes the effect of time appears insignificant, but significant for SCL group.

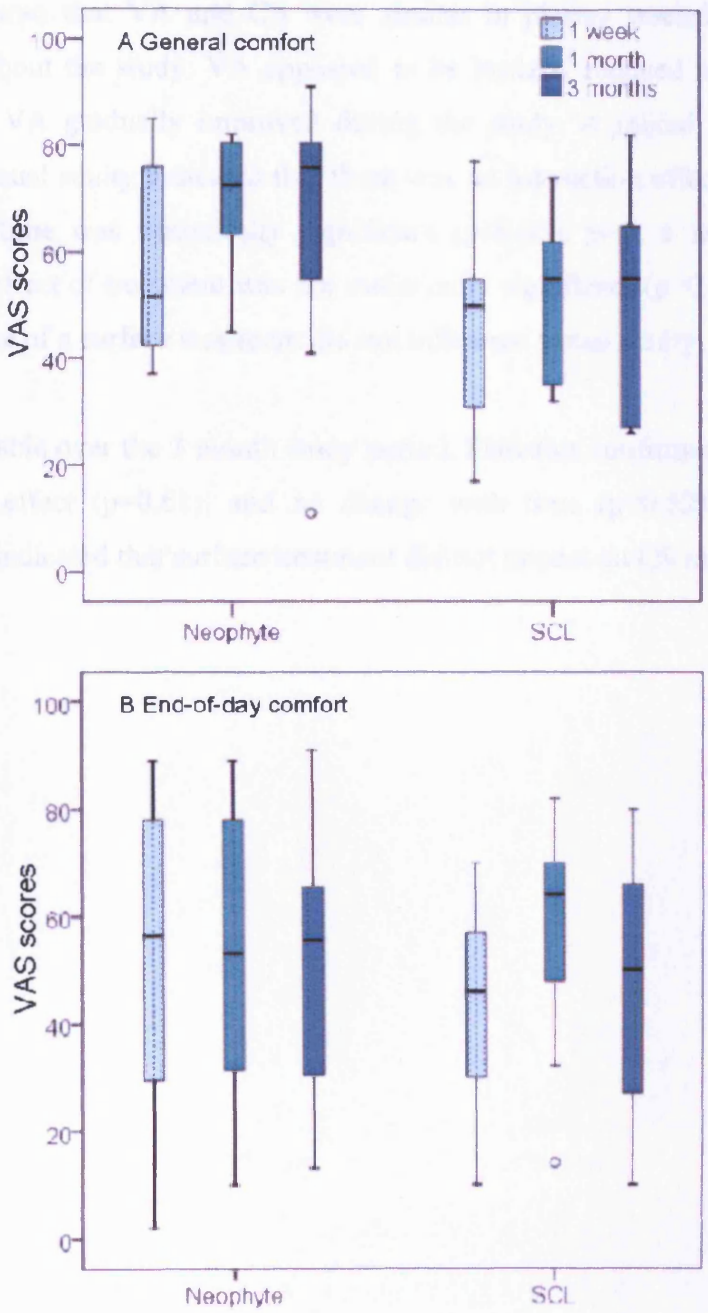

Figure 4.29 A box plot showing median, lower and upper quartiles and range of general comfort VAS results in neophyte and SCL groups; A: General comfort and B: End-of-day comfort (0=Not at all comfortable, 100=Very comfortable) (n=28).

4.3.5.4 Visual function in plasma treated and untreated groups at three months

No statistical difference was evident between plasma treated and untreated groups for visual function at baseline measurement (Independent t-tests, $p=0.36$ (CS) and $p=0.57$ (VA)).

Figure 4.30 shows that VA and CS were similar in plasma treated and untreated wearers throughout the study. VA appeared to be initially reduced at the one week visit, however VA gradually improved during the study. A mixed between-within ANOVA for visual acuity indicated that there was no interaction effect ($p=0.61$), and the effect for time was statistically significant ($p<0.05$), with a large effect size ($p=0.28$). The effect of treatment was not statistically significant ($p=0.15$), suggesting that the presence of a surface treatment did not influence visual acuity.

CS appeared stable over the 3 month study period. Statistics confirmed that there was no interaction effect ($p=0.61$), and no change with time ($p=0.52$) and treatment ($p=0.92$). This indicated that surface treatment did not impact on CS results.

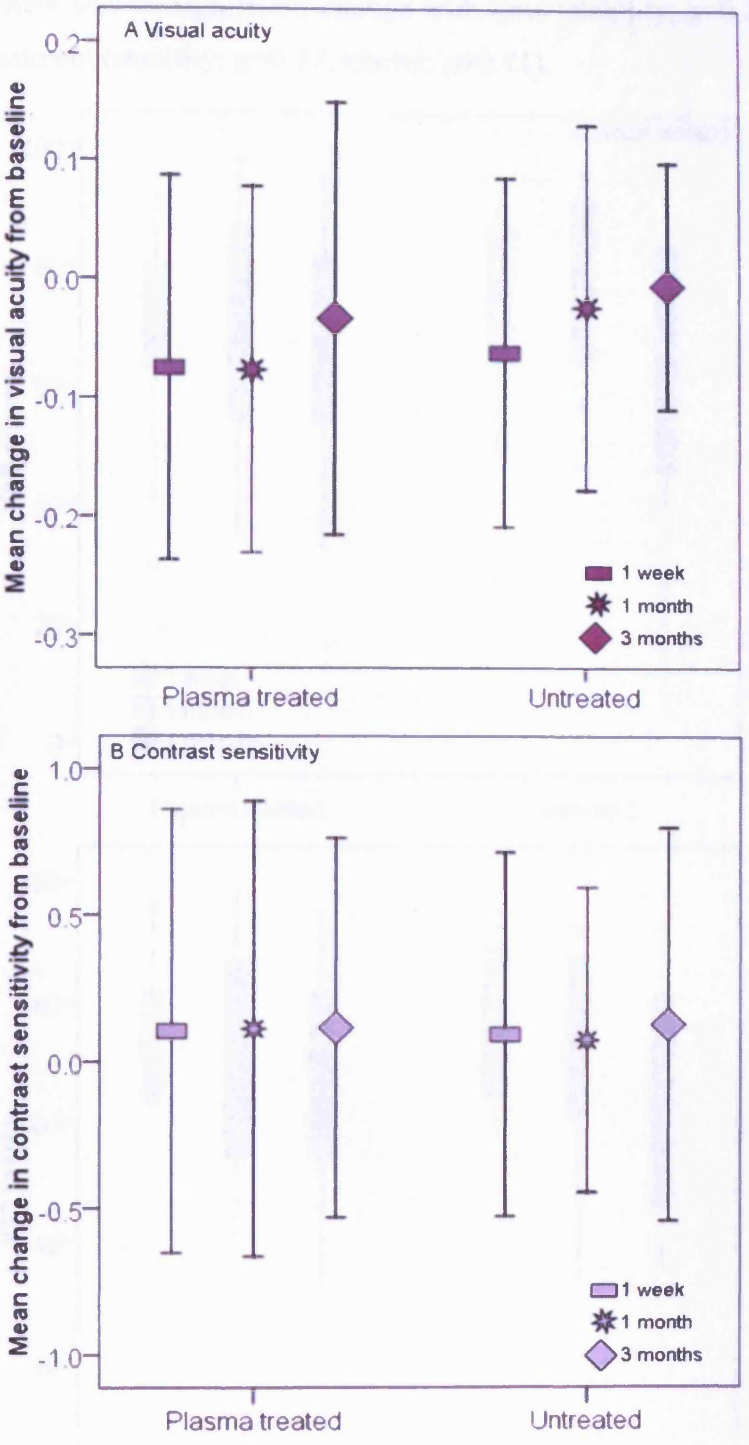

Figure 4.30 Error plot showing mean change (+/-SD) in visual function for plasma treated and untreated groups A: Visual acuity and B: Contrast sensitivity (n=28).

Subjective visual stability and clarity were similar in both treated and untreated lens groups and showed no obvious trend; Figure 4.31 A and B. Statistical analysis showed no interaction effect between treatment and time (stability; p=0.45, clarity;

p=0.31), and there was no significant change with time (stability; p=0.12 and clarity; p=0.13), or treatment (stability; p=0.57, clarity; p=0.71).

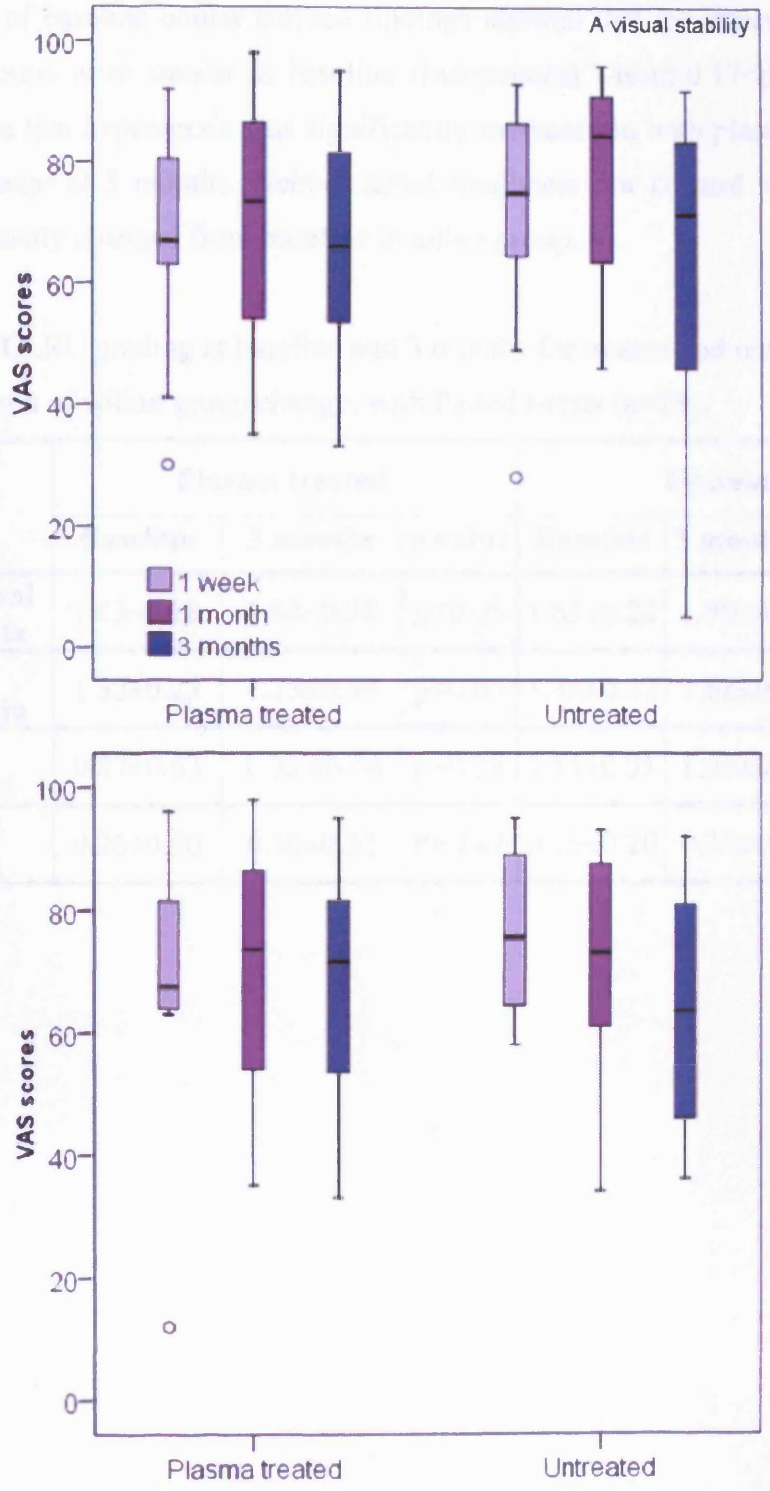

Figure 4.31 A box plot showing median, lower and upper quartiles and range of VAS results for A: visual stability and B: visual clarity in plasma treated and untreated groups (0=Unstable, 100=Stable; 0=Misty, 100=Clear) (n=28).

4.3.5.5 Ocular surface findings in plasma treated and untreated groups at three months

Comparison of baseline ocular surface findings showed that the plasma treated and untreated groups were similar at baseline (Independent t-tests $0.17<p<0.76$). Table 4.19 indicates that hyperaemia was significantly increased in both plasma treated and untreated groups at 3 months. Neither tarsal roughness nor corneal staining grades were significantly changed from baseline in either group.

Table 4.19 CCLRU grading at baseline and 3 months for treated and untreated groups, and comparison of within group change, with Paired t-tests (n=28).

CCLRU grading	Plasma treated			Untreated		
	Baseline	3 months	p value	Baseline	3 months	p value
Conjunctival hyperaemia	1.63±0.18	1.88±0.28	p<0.05	1.65±0.20	1.80±0.18	p<0.05
Limbal hyperaemia	1.32±0.23	1.75±0.39	p<0.05	1.36±0.32	1.68±0.19	p<0.05
Tarsal roughness	0.87±0.63	1.00 ±0.44	p=0.39	1.14±0.31	1.05±0.50	p=0.57
Corneal staining	0.26±0.50	0.30±0.31	P=0.82	0.16±0.20	0.33±0.31	p=0.08

Figure 4.32 shows marginally increased corneal staining during the study, in both plasma treated and untreated groups. There was no interaction effect (p=0.45), no change over time (p=0.78), and there was no significant effect associated with plasma treatment (p=0.64). This implied that surface treatment did not affect the staining response.

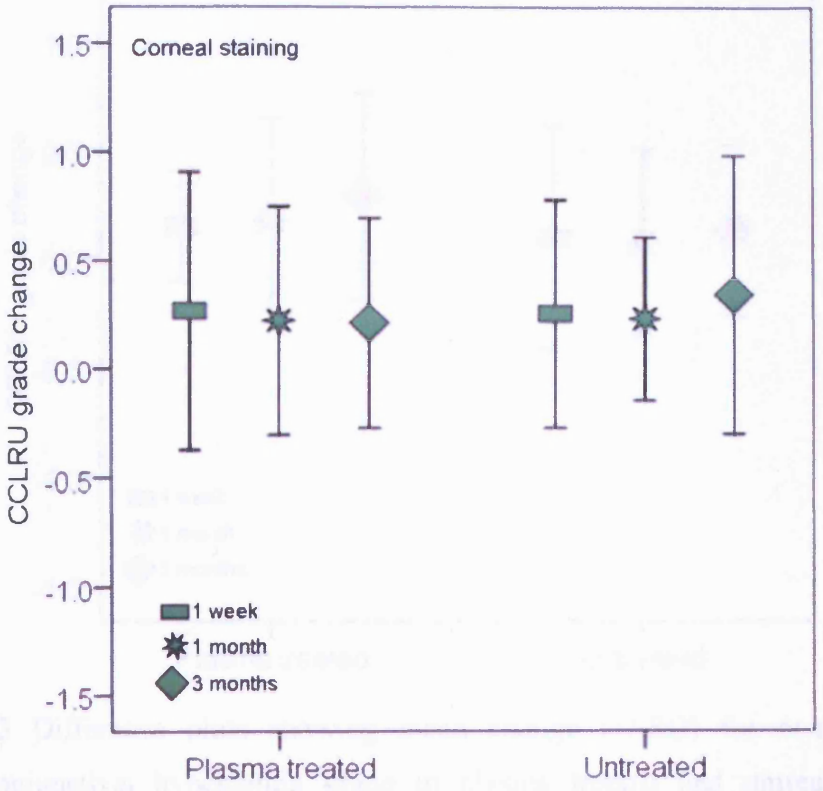

Figure 4.32 Difference plots showing mean change (+/-SD) for ocular surface CCLRU corneal staining grade in plasma treated and untreated groups (n=28).

Figure 4.33 shows a small increase in conjunctival hyperaemia throughout the study, irrespective of surface treatment. Statistically there was no interaction effect (p=0.52), no influence of time on the result (p=0.09) or effect of treatment (p=0.21).

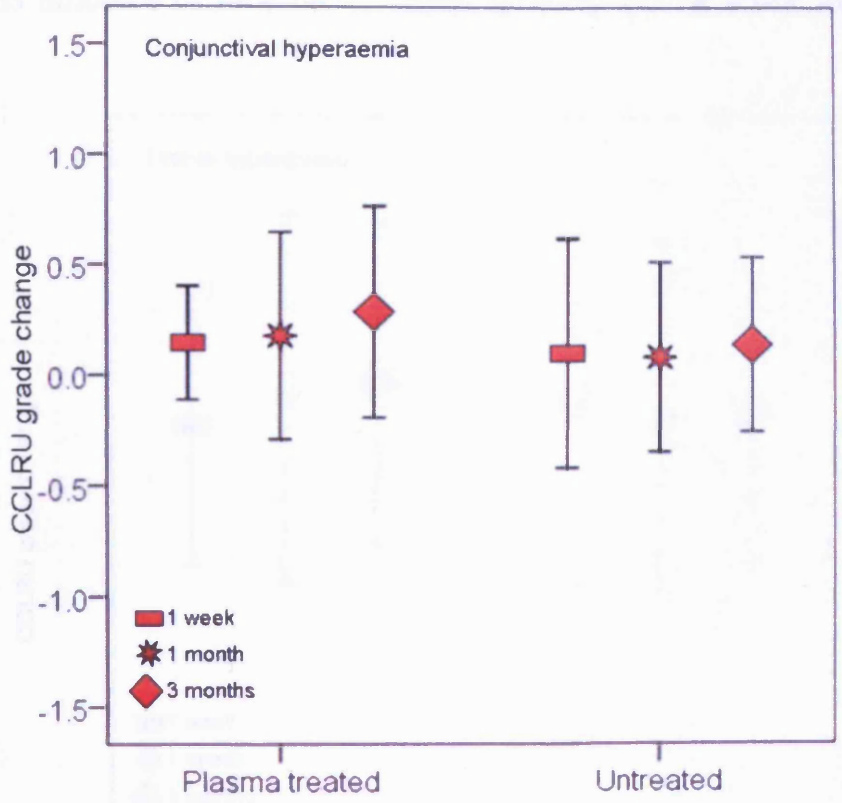

Figure 4.33 Difference plots showing mean change (+/-SD) for ocular surface CCLRU conjunctival hyperaemia grade in plasma treated and untreated groups (n=28).

Figure 4.34 indicates gradually increasing limbal hyperaemia in the plasma treated wearing group throughout the study. The untreated wearers' limbal hyperaemia appears stable during the study. Statistical analysis indicated no interaction effect (p=0.45), no influence of time on the result (p=0.78) and no effect for treatment (p=0.64).

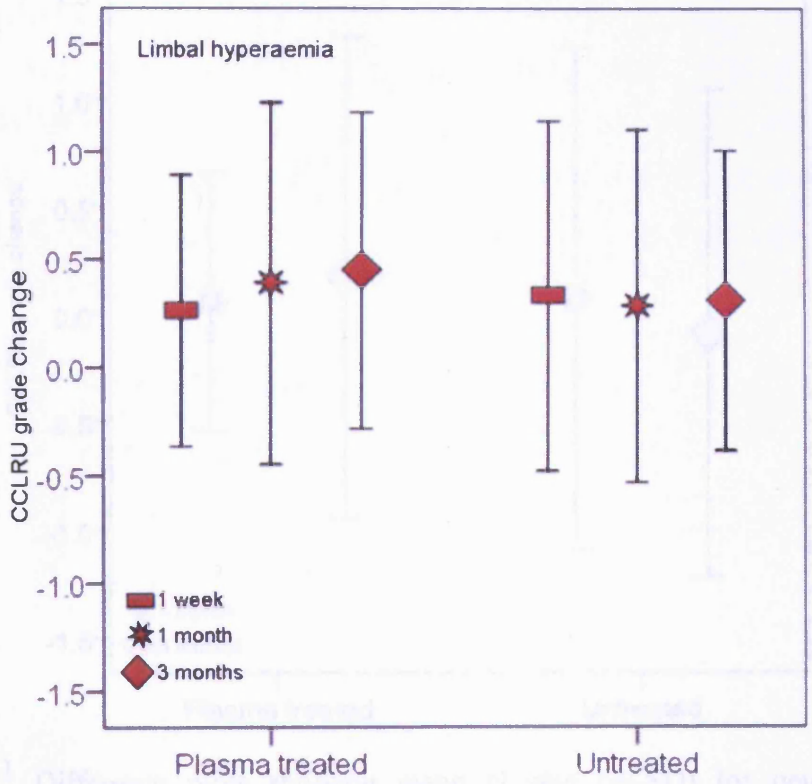

Figure 4.34 Difference plots showing mean change (+/-SD) for ocular surface CCLRU limbal hyperaemia grade in plasma treated and untreated groups (n=28).

Tarsal roughness (Figure 4.35) marginally increased in plasma treated wearers and marginally reduced in untreated wearers, but statistically there was no difference in roughness at the one or 3 month visit (Independent t-tests, p=0.94 and p=0.31 respectively).

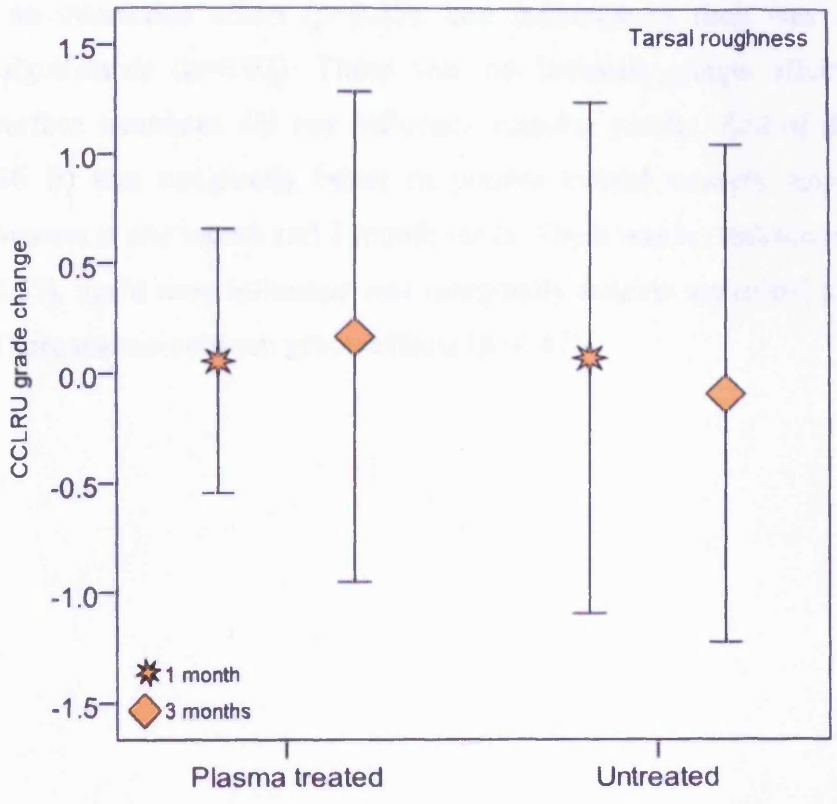

Figure 4.35 Difference plots showing mean change (+/-SD) for ocular surface CCLRU tarsal roughness grade in plasma treated and untreated groups (n=28).

4.3.5.5.1 Corneal topography

Comparison of simulated keratometry readings during the study found that corneal curvature was similar at baseline in the two groups. There was no significant interaction effect (p=0.18) the effect of time was not significant (p=0.99) and there was no between groups effect (p=0.92), indicating corneal curvature did not change irrespective of the lens surface treatment.

4.3.5.6 Subjective comfort in plasma treated and untreated groups at three months

General comfort, shown in Figure 4.36 A, indicates that both groups reported better comfort with time/adaptation but the range in response was very large. Statistically there was no interaction effect ($p=0.25$), and influence of time was approached statistical significance ($p=0.07$). There was no between groups effect ($p=0.52$), implying surface treatment did not influence comfort results. End-of-day comfort (Figure 4.36 B) was marginally better in plasma treated wearers compared with untreated wearers at one month and 3 month visits. There was no statistical interaction effect ($p=0.57$), again time influence was marginally outside statistical significance; ($p=0.06$). There was no between group effects ($p=0.42$).

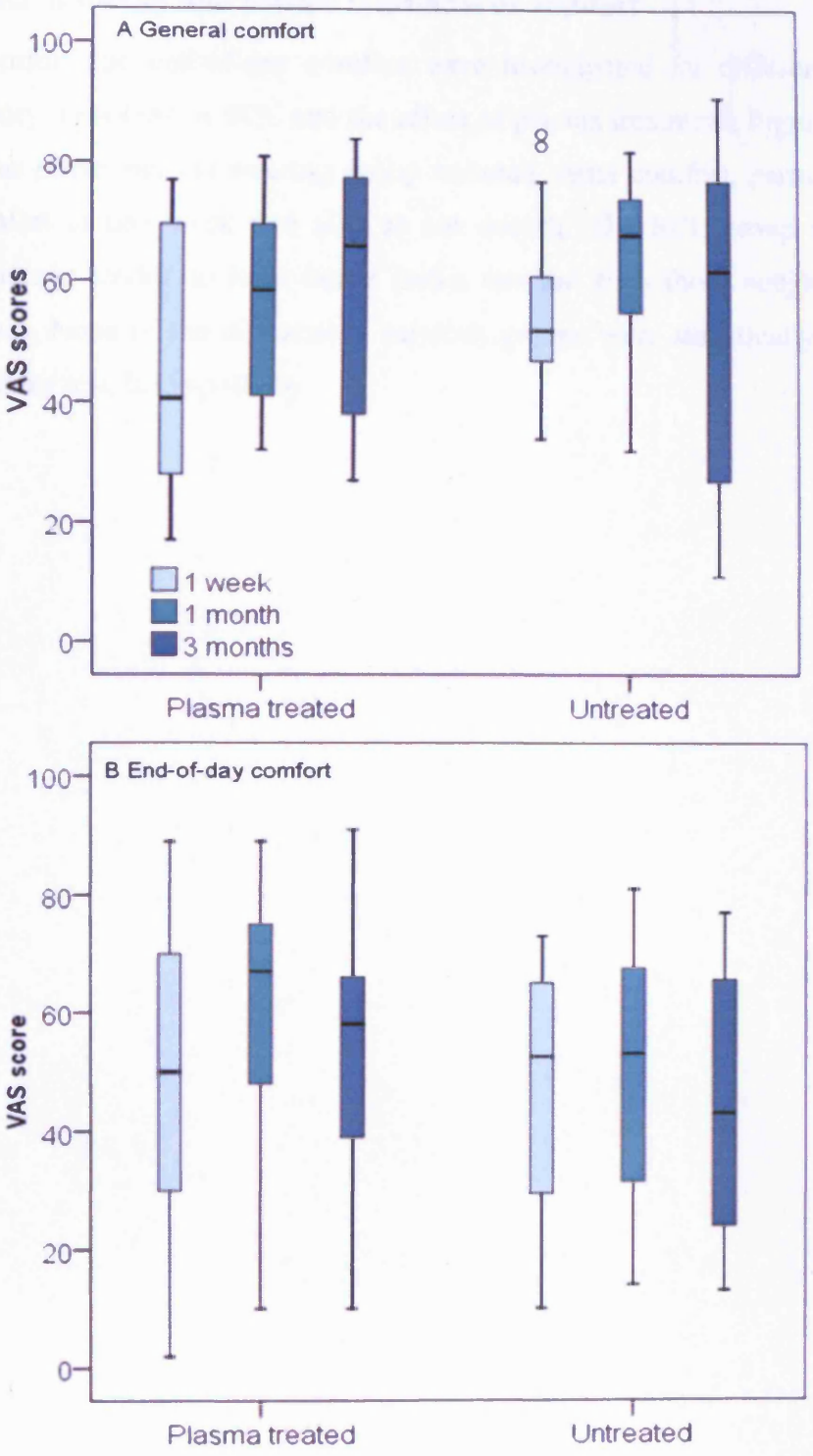

Figure 4.36 A box plot showing median, lower and upper quartiles and range of comfort VAS results in plasma treated and untreated groups; A: General comfort and B: End-of-day comfort (0=Not at all comfortable, 100=Very comfortable) (n=28).

4.3.5.7 Effect of history and plasma treatment on comfort

General comfort and end-of-day comfort were investigated for differences due to subject history; neophyte or SCL and the effect of plasma treatment; Figures 4.37 and 4.38. The neophyte, plasma wearing group reported better comfort, particularly end-of-day comfort at one week and also at one month. The SCL group without the plasma treatment tended to have better initial comfort than those subjects wearing treated lenses. None of the differences between groups were statistically significant (Mann Whitney test; $0.15<p<0.80$).

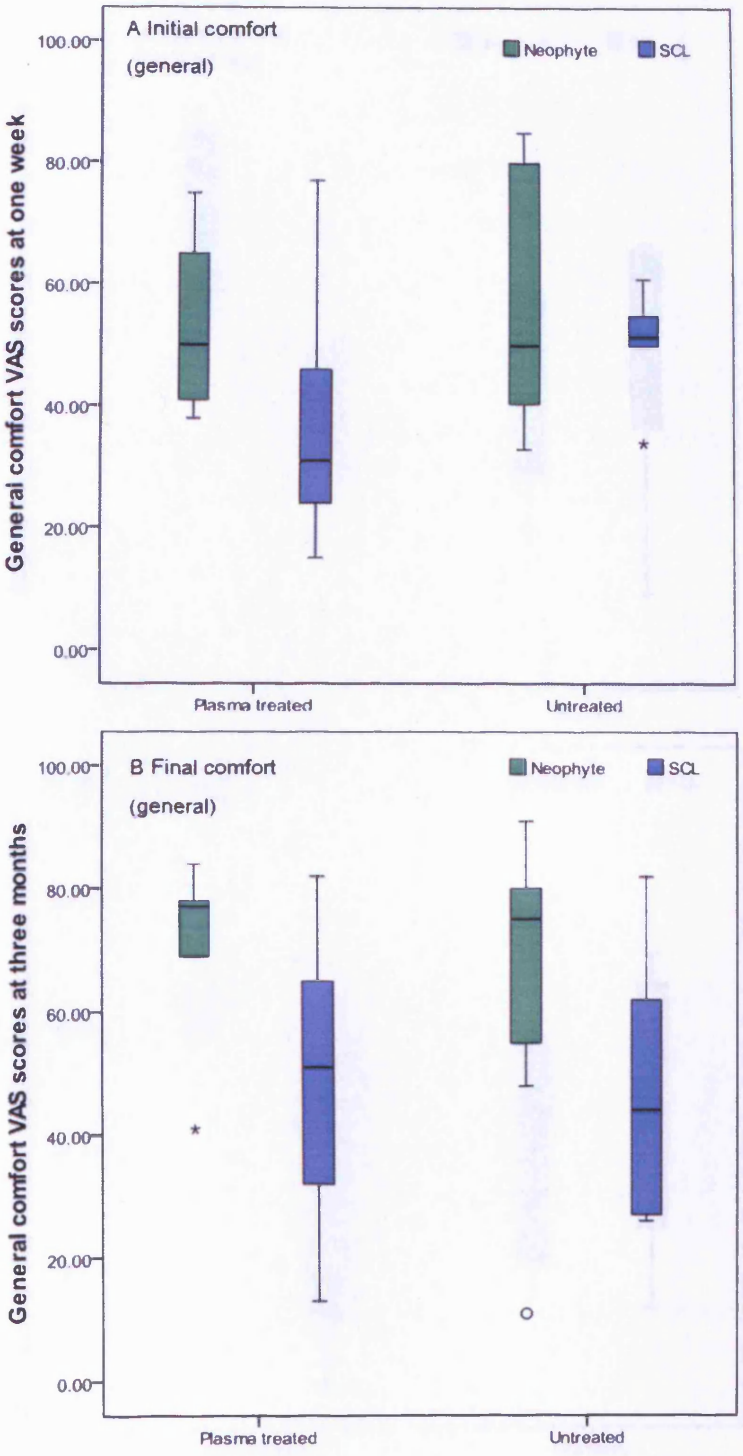

Figure 4.37 A box plot showing median, lower and upper quartiles and range of general comfort VAS results for neophyte and SCL groups wearing plasma treated and untreated lenses; A: Initial comfort B: Final comfort(0=Not at all comfortable, 100=Very comfortable) (n=28).

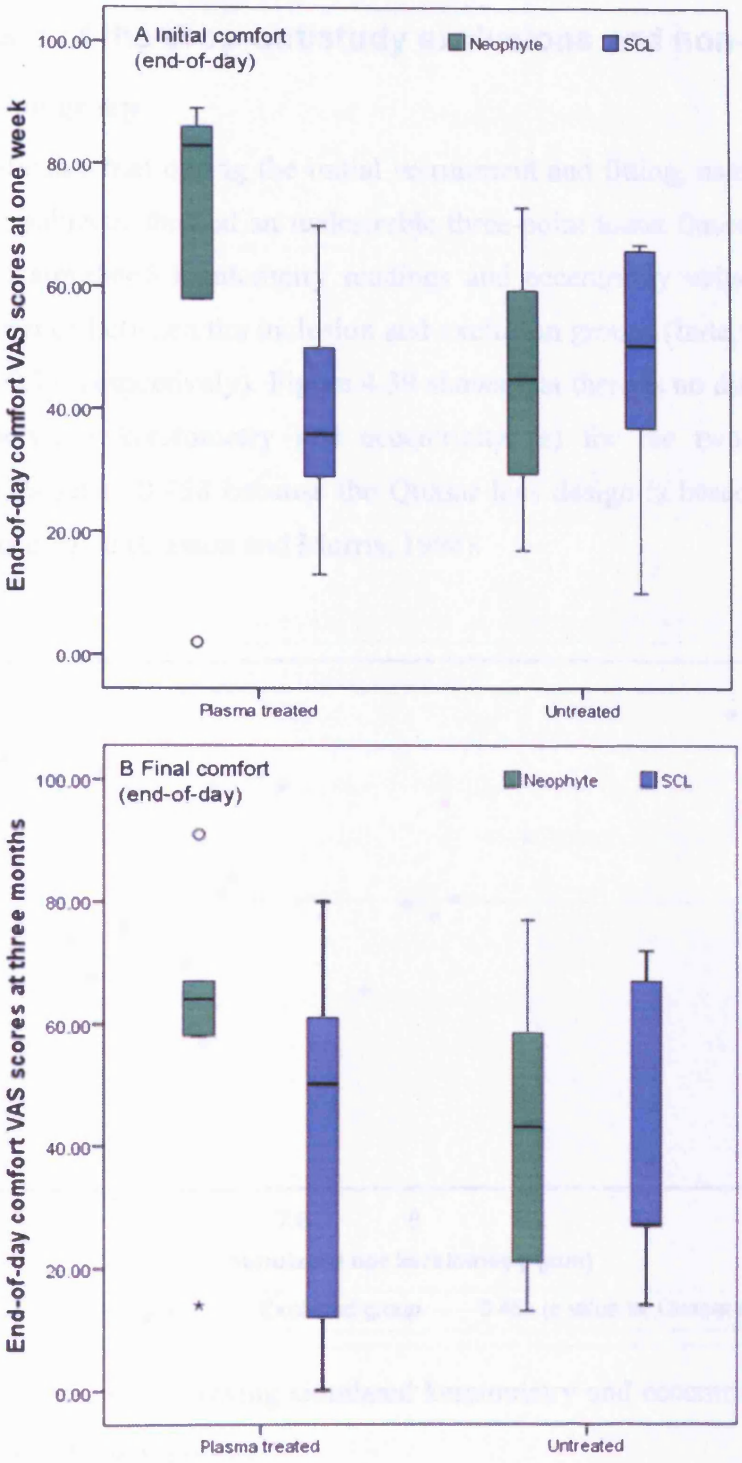

Figure 4.38 A box plot showing median, lower and upper quartiles and range of end-of-day comfort VAS results for neophyte and SCL groups wearing plasma treated and untreated lenses; A: Initial comfort B: Final comfort (0=Not at all comfortable, 100=Very comfortable) (n=28).

4.3.6 Analysis of the drop-out/study exclusions and non-finishers

4.3.6.1 Exclusion group

Section 5.4 indicated that during the initial recruitment and fitting, using the original protocol, some subjects showed an undesirable three-point touch fluorescein pattern. Comparison of simulated keratometry readings and eccentricity values showed no statistical difference between the inclusion and exclusion groups (Independent t-tests, p=0.53 and p=0.71, respectively). Figure 4.39 shows that there is no difference in the relationship between keratometry and eccentricity (e) for the two groups. The horizontal line is set at 0.458 because the Quasar lens design is based on a corneal model with this e value (Gasson and Morris, 1998).

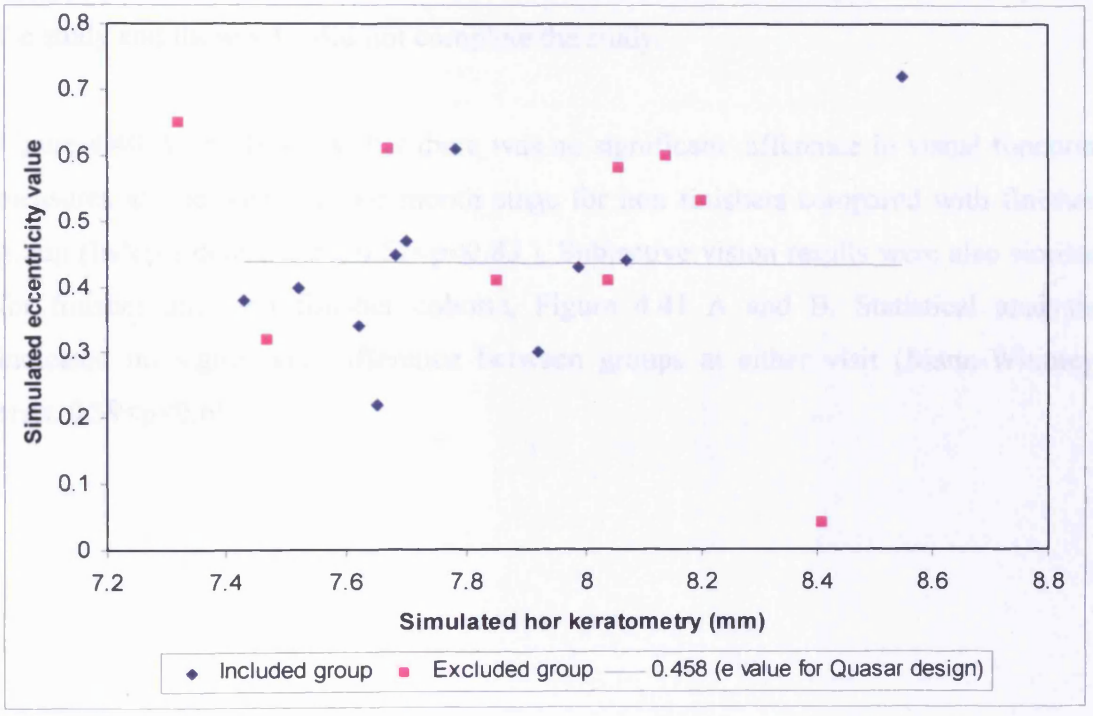

Figure 4.39 A scatter plot showing simulated keratometry and eccentricity values for the included and excluded groups

4.3.6.2 Non-finisher group

Table 4.20 indicates the reasons why subjects, fitted using the amended fitting protocol, did not complete the study.

Table 4.20 Reason for subject withdrawal or exclusion from the study

Reasons for withdrawal from study	N	Percentage of non finishers (%)
Intolerance	25	50.0
Visual acuity	4	8.0
Handling	2	4.0
Fitting	3	6.0
Ocular surface	3	6.0
Lost to follow up	13	26.0

The following sections present the differences in results from subjects who completed the study and those who did not complete the study.

Figure 4.40 A and B show that there was no significant difference in visual function measures at one week or one month stage for non finishers compared with finisher group (Independent t-tests, $0.52<p<0.83$,). Subjective vision results were also similar for finisher and non finisher cohorts, Figure 4.41 A and B. Statistical analysis indicated no significant difference between groups at either visit (Mann-Whitney tests, $0.39<p<0.68$).

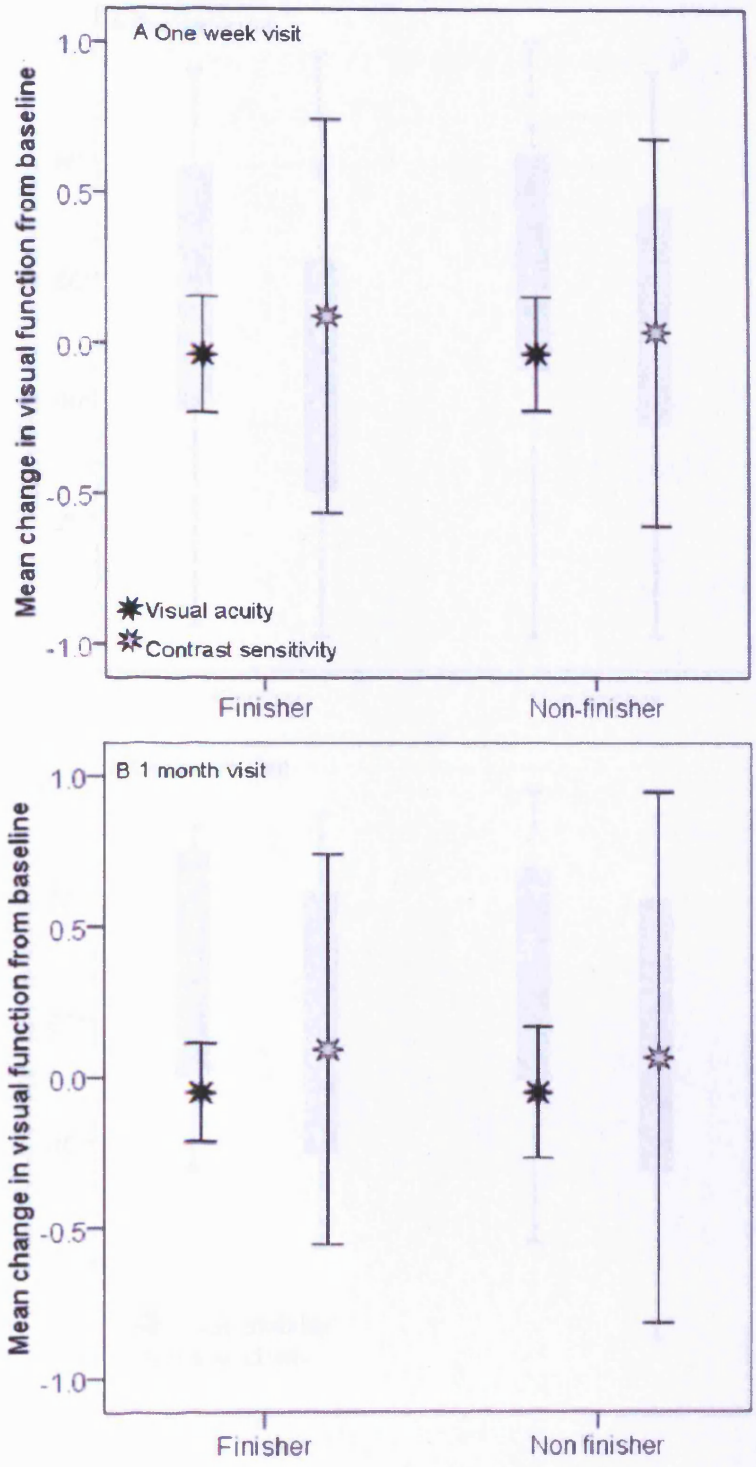

Figure 4.40 Difference plot showing mean change (from baseline measurement) (+/- SD) for visual acuity and contrast sensitivity in finisher and non finisher groups at A: One week and B: One month visit.

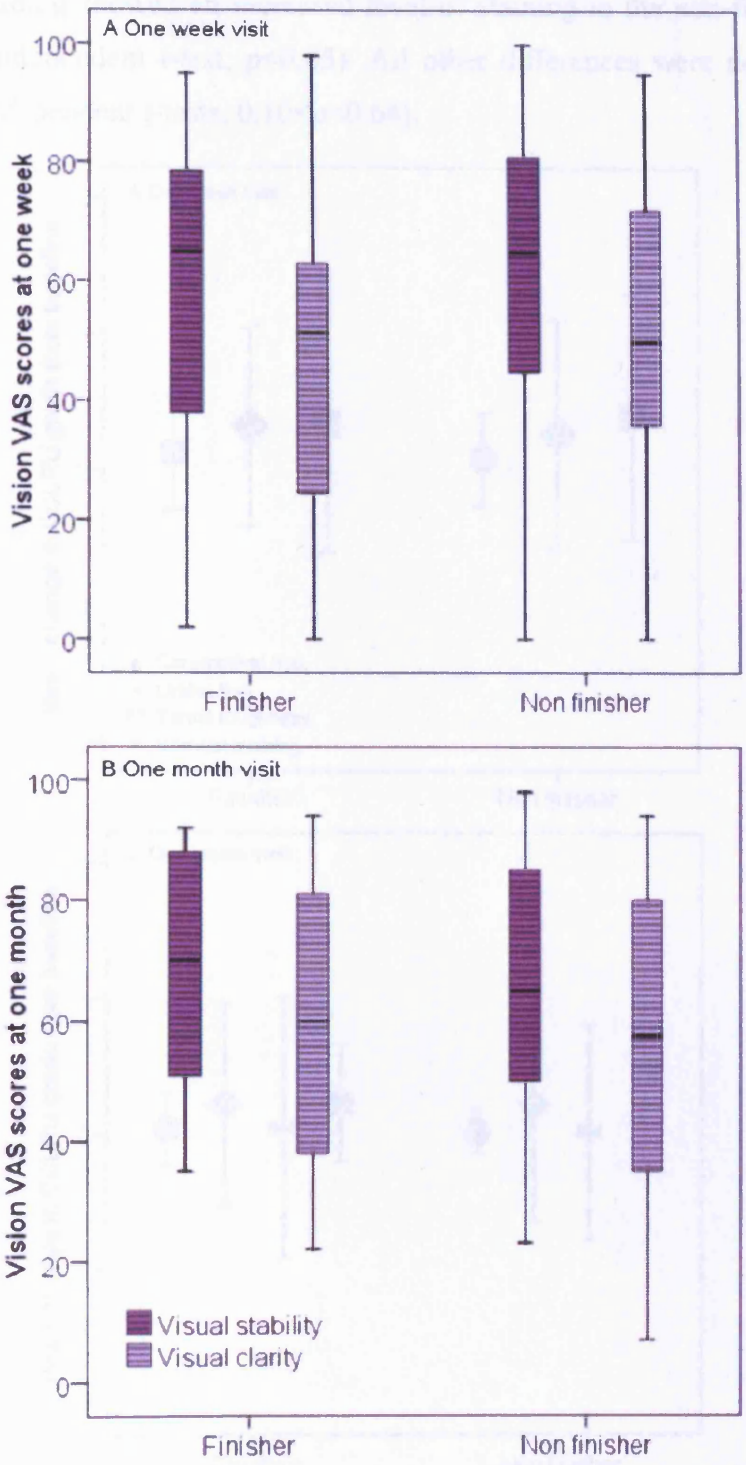

Figure 4.41 A box plot showing median, lower and upper quartiles and range of VAS results for visual stability visual clarity in finisher and non finisher groups at A: One week visit and B: One month (0=Unstable, 100=Stable; 0=Misty, 100=Clear).

Generally results for ocular surface changes with GP wear were very similar between the finisher cohort and non-finisher group, Figure 4.42. However, statistical analysis

of corneal staining showed an increased level of staining in the non-finish group at one month (Independent t-test, $p<0.05$). All other differences were not statistically significant (Independent t-tests, $0.10<p<0.64$).

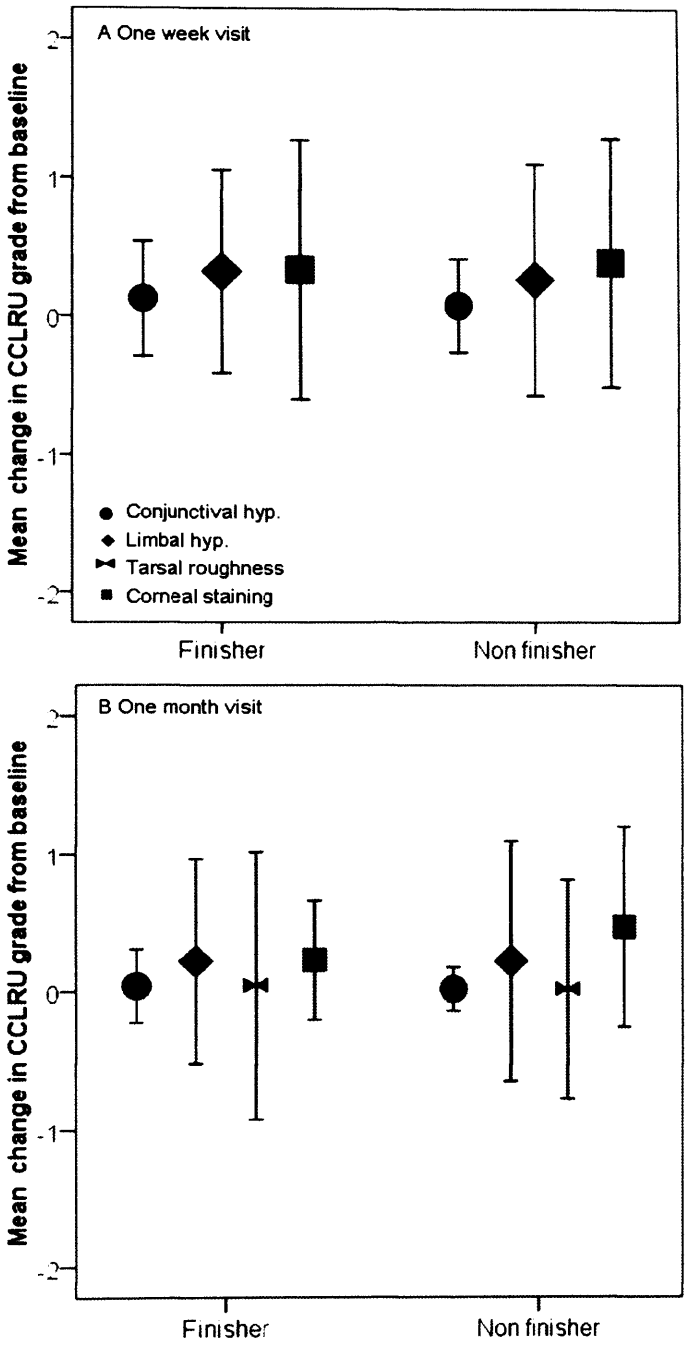

Figure 4.42 Error plot showing mean change (+/-SD) for ocular surface CCLRU grading in finisher and non finisher groups at A: One week visit and B: One month visit.

Figure 4.43 shows that subjective comfort was marginally worse in the non-finisher group, particularly for end-of-day comfort. Statistical analysis revealed no statistical

difference between finisher subjects and non-finishers ($0.16<p<0.68$, Mann-Whitney tests).

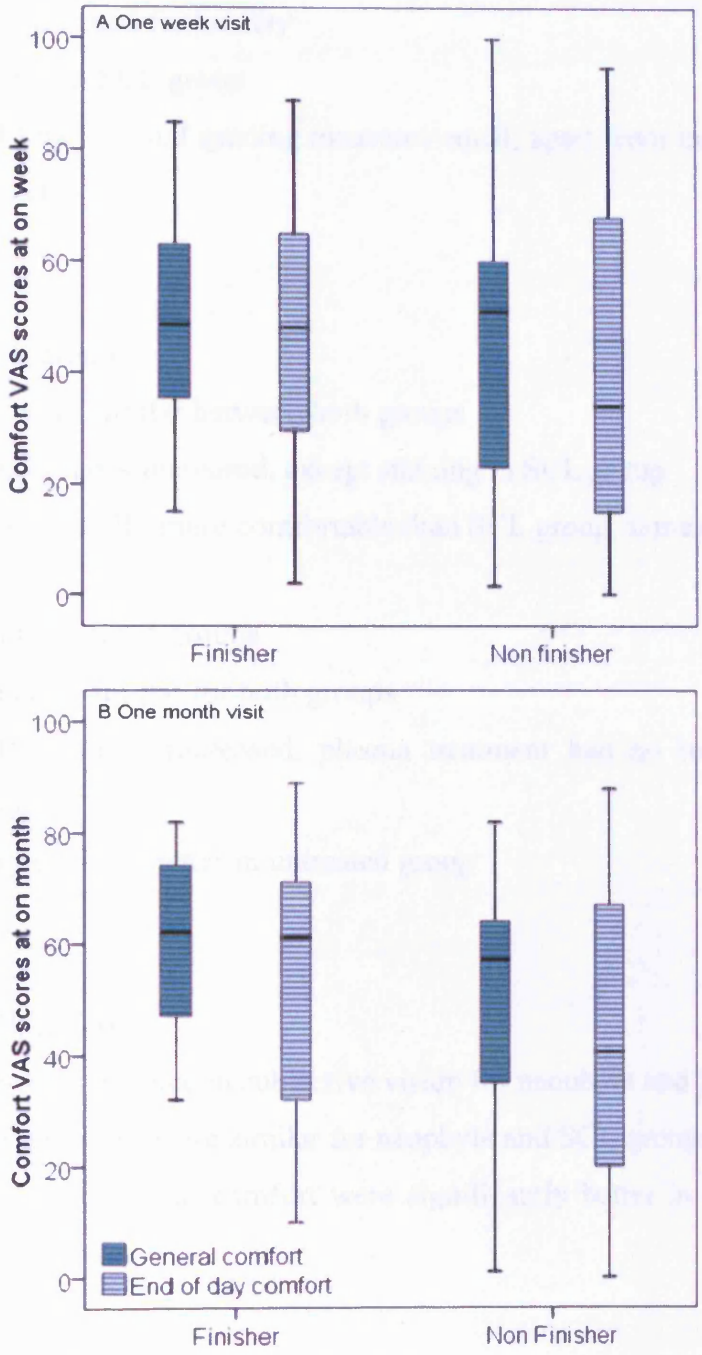

Figure 4.43 A box plot showing median, lower and upper quartiles and range of comfort VAS results in finisher and non finisher groups for general comfort and end-of-day comfort at A: One week visit and B: One month (0=Not at all comfortable, 100=Very comfortable).

4.3.7 Summary of results

Baseline

- All groups matched for anxiety
- More dry eye in SCL group
- All visual function and grading measures equal, apart from increased staining in SCL group

One week

Neophyte and SCL groups

- Visual function similar between both groups
- All CCLRU grades increased, except staining in SCL group
- Neophytes generally more comfortable than SCL group, same at end-of-day

Plasma treated and untreated groups

- Visual function similar for both groups
- All CCLRU grades increased, plasma treatment had no impact on ocular surface signs
- End-of-day comfort better in untreated group

One month

Neophyte and SCL group

- There was no difference in subjective vision for neophyte and SCL groups
- Ocular surface signs were similar for neophyte and SCL groups
- End-of-day and general comfort were significantly better in neophyte group than SCL group

Plasma treated and untreated lenses

- Visual function (CS) marginally better for plasma treated lenses, but not significantly
- Plasma treated group had marginally larger increase in ocular surface hyperaemia and staining, but no significant difference with untreated group
- No significant difference in comfort, irrespective of surface treatment

Three months

Neophyte and SCL group

- No difference between visual function in the two groups, though visual acuity did show improvement with time
- There was no difference in subjective visual performance for neophyte and SCL group
- Ocular surface similar for both groups, marginally increased grades from baseline
- Neophyte group significantly better comfort than SCL group

Plasma treated and untreated group

- Visual function measures improved throughout the study, there was no difference for treated or untreated group results
- Ocular surface redness was marginally increased in both groups. Ocular response was similar irrespective of surface treatment
- Comfort responses tended to improve with time, but there was no difference between comfort with plasma treatment
- Initially neophyte group had marginally better end-of-day comfort than SCL group, but this was not statistically significant.

4.4 Discussion

The practitioner survey (Chapter 2) indicated that ECPs are less likely to recommend GP lenses to patients than soft lenses, and it has been suggested elsewhere that GP lenses are now more often reserved for specialist cases, e.g. keratoconic patients or astigmatic corneas. Yet the practice of GP lens fitting in the UK arises from a history of lenses being designed and used for the general contact lens wearing population, when the benefits of GP lenses were recognised. In other countries, e.g. the Netherlands and Austria, GP lens fitting is still a core lens choice option for practitioners and patients. The advantages of GP lenses for ocular health are acknowledged, but comfort remains a significant issue. If GP lens fitting in the UK is to undergo a renaissance, a central feature will be the re-fitting of existing soft lens wearers into safer GP lenses. This study hypothesised that GP lenses could be successfully fitted to both neophyte and existing SCL wearers, with the help of topical anaesthetic. Successful fitting was considered to mean no clinically significant adverse ocular surface responses, acceptable comfort and visual function, and patient preference for GP lenses, after 3 months of lens wear.

4.4.1 Ocular surface response

GP lens fitting was associated with increased redness and staining, regardless of whether the subject was a neophyte or previous soft lens wearer, but the changes in ocular surface signs were small, and remained similar and clinically insignificant throughout. There were no cases of ocular infection and no patients required prescribed topical therapeutic treatment.

Ocular hyperaemic changes are generally used as a measure of the ocular response to contact lenses, as it is known that contact lenses may impact on both conjunctival hyperaemia and limbal hyperaemia (McMonnies, Chapman-Davies and Holden, 1982). Generally, bulbar conjunctival hyperaemia is thought to be due to general ocular and systemic or environmental factors, while limbal hyperaemia tends to be associated with corneal stress (Pult et al., 2008). It is clinically expected that patients wearing contact lenses may have more hyperaemia than non-wearers, however there are few figures available to quantify how much change is associated with GP wear.

McMonnies et al. (1982) investigated the vascular response to SCL and GP wear in the 1980s, however, it should be noted that a different scale was used for grading in this study. At that time, he reported a much greater limbal hyperaemic response to SCLs than GPs. In general, the change in ocular hyperaemic grade score was (0-0.25), which is less than the 0.4 grade change on the CCLRU scale considered to be clinically significant (Murphy et al., 2007). Therefore, it can be concluded that GP wear generally has no clinically significant influence on the ocular surface of participants.

Results regarding impact of GP wear on ocular surface signs indicated little difference between groups (neophyte/SCL wearer; treated/untreated). In those who completed the entire study, the only difference between groups was noted for tarsal roughness. The neophyte group showed a very slight increase in roughness with GP wear. However, the SCL group underwent a slight reduction during the study. This could imply that wearing contact lenses may generally cause increased surface roughness, but that GPs tend to impact less on tarsal roughness than soft contact lenses.

4.4.2 Lens wear comfort

As patients adapted to the GP lenses, their subjective rating of comfort increased. General comfort was better amongst naïve subjects, compared to those who had worn soft contact lenses. This may be because SCL wearers have an expectation of contact lens comfort and use their soft lens comfort experiences as a benchmark, and, inevitably, initial GP comfort is less good compared with soft comfort generally. Neophytes do not have this experience, and so they have no concept of how a lens should feel, allowing them to make a more positive comfort response.

At one week, end-of-day comfort showed less difference between the groups, which may be because the soft lens group experience is of having poorer comfort towards the end of wear and they find that GP comfort reduces less than they anticipate. In soft lens wear, dehydration of the lens may cause altered lens parameters and increased lens-lid interactions resulting in reduced end-of-day comfort (Fonn et al., 1999). However, at one week, many subjects were still adapting to GP lenses and

experience of full day wear was limited (if achieved at all), possibly making subject responses at this visit more variable.

At one month, neophyte end-of-day comfort was significantly better than the SCL group, and at three months neophytes were significantly more comfortable, in general, than the SCL group. This could be because the SCL group expectations of comfort were not met rapidly enough by GP lens wear. Adaptation time is variable between individuals, and it has been suggested to take 23±23.1 days to adapt to GP lenses (Fujita et al., 2004). If subjects require 6 weeks to adapt to lenses, then their opinion of comfort may take time to forget their SCL experience and appreciate the newly acquired end-of-day comfort. Alternatively, this may indicate that the SCL group are less tolerant to lens wear because of ocular surface changes caused by previous SCL wear. Both neophyte and SCL groups had similar baseline dryness, anxiety and ocular surface signs, but corneal staining was significantly higher in the SCL group prior to refitting with GP lenses. It is therefore possible that sub-clinical dryness, as well as the clinical signs of corneal stress, were present and pre-disposed this group to less satisfactory comfort with GP lenses. It would be interesting to investigate whether a break from SCL wear prior to GP fitting would allow the ocular surface to return to baseline/normal and thus produce different results.

Lens surface treatment appeared to not improve comfort responses at any stage of the study, irrespective of lens wear history (neophyte or SCL). On the contrary, end-of-day comfort was significantly better in the untreated group at the one week visit. The findings are surprising, since plasma treatment of GP lenses has been reported to reduce lens awareness, improve visual clarity and provide easier adaptation for new GP wearers (Schafer, 2006). It is possible that plasma surface treatment offers microscopic surface changes to the lens, but the advantages are not clinically or statistically detectable using the measures selected for this study. At one week, end-of-day comfort may be associated with several factors, including corneal sensitivity and lens adaptation, tear quality, visual acuity, lens-cornea fitting and individual patient opinion, as well as plasma treatment.

4.4.3 Visual function

Throughout this study the mean visual acuity and contrast sensitivity (CS) results with GP lens correction were not significantly different from the spectacle trial lens correction. Contrast sensitivity is important because CS measurement is thought to be the best indicator of visual function (Ziel et al., 1990a), and, at times, CS results were marginally better than spectacle acuity, though not statistically significantly. This trend is supported by another study which reported superior CS with adapted GP lens wears compared with spectacles or SCL wearers (Qu et al., 2003). The trend may have become significant if the study had continued over a longer period of time or if the cohort size had been larger.

At one week, visual function measures were similar in the neophyte and SCL groups. However, at one month, neophytes reported marginally better visual stability than the SCL group. The SCL group subjects often made the comment that they could tell the GP lens was mobile on the eye, unlike a relatively immobile soft lens. This may have resulted in less stable vision at one month compared with the neophyte group, who were unable to make the same comparison. The lens movement sensation may also have been a factor in lens wear comfort for the SCL group. Interestingly, by the three month stage, the SCL cohort reported marginally better clarity of vision than the neophyte group (though not significantly). Presumably this is in comparison to SCL correction and indicates that, once adapted to GP lenses, subjective performance was very good. Again, this is supported by Qu et al. (2003) who found that clarity of vision with GP correction is superior to that of SCL correction. At the three month stage, no difference between neophyte and SCL groups was evident. Over the course of the entire study, visual function improved for the neophyte and SCL groups, indicating a link between adaptation and visual performance.

It was anticipated that visual function might be superior in the plasma-treated cohort, however no differences were measured between subjects at one week follow-up. At one month, contrast sensitivity was marginally better for the plasma-treated wearers compared with the untreated group. This finding may be in support of plasma treatment improving visual function. However, at the three month visit, this trend had disappeared and visual function was similar for both groups. This could mean that the sample size was not sufficiently large, or that other factors related to adaptation issues

obscured the trends, or that surface treatment has no significant impact on visual function.

4.4.4 Patient preference

Successful wearers completed 3 months full-time GP wear. A greater proportion of the neophyte group completed the study; 33% compared with 28% of the SCL group. This implies that success in GP fitting was better for neophytes than existing content SCL wearers. Soft contact lens wearers were not recruited based on any existing dissatisfaction with their contact lenses - if the study had aimed to fit dissatisfied SCL patients with GP lenses this outcome might have been more positive for GP lenses. Contact lens dissatisfaction results in approximately 34% patients ceasing to wear lenses (due to discomfort), yet around 77% return to be refitted (Pritchard et al., 1999), indicating that it is not lack of patient motivation. Therefore, if GP lenses could offer improved adapted comfort, in particular end-of-day comfort, then this group of patients might become successful wearers. On a positive note, when questioned, 68% (n=19) wanted to continue with GP wear following the study.

4.4.5 Subject drop-out

Recruitment of subjects to this study was successful, but retaining patients over the three month study period was less successful. The final drop-out rate was 64.1%, which was higher than anticipated. Almost 50% of drop-out subjects cited unsatisfactory lens comfort as the reason for discontinuation. Bennett et al.(1998) recruited eighty subjects to be fitted with GP lenses and only 10 subjects dropped out of this study, but it ran for a shorter period of just one month. In comparison, at the one month stage in this study, the drop-out rate was only 44.8%. The large drop-out rate highlights the need for patient motivation and perseverance in adapting to GP wear.

Fitting GPs in a research environment may alter practitioner and patient interactions. In a clinical setting, following an eye health check, the practitioner would typically suggest an array of CL options based on the patient's visual requirements, work, lifestyle and desired modality of wear. The patient would then select the type of lens to be trialled based on safety, visual performance, convenience, costs, etc. In this research study, the practitioner only offered GP lenses, and, provided the subject met

the inclusion requirements, they were invited to be fitted with GP lenses (at no cost). The initial comfort issues and adaptation process were openly discussed. However, the practitioner may have been positively-biased regarding GP lenses and their benefits in order to attract subjects to the study. Indeed, positive practitioner attitude and verbal communication has been demonstrated to reduce drop-out rate (Bennett et al., 1998).

Motivation of the subject to complete the study may have been insufficient. Neophyte subjects had either no experience of GP lenses, or had previously tried a soft lens and been unsuccessful, perhaps due to handling difficulties, discomfort or vision-related issues. Subjects with no previous CL experience may have joined the study simply because they were offered free lenses, solutions and eye care. They may not have had sufficient motivation to actively seek a CL practitioner and be fitted with lenses earlier in their life, reflecting an underlying sensitivity about their eyes, lens handling or fear of infection. These factors may have made this group more pre-disposed to fail a GP trial.

The SCL group were generally content with their current lenses. Motivation to change to GP lenses may have been due to understanding of the positive health and vision benefits associated with GP wear. However, for many, the tangible benefit may have been the free lenses and care associated with the study. Refitting with GP lenses required time for appointments, learning to handle and care for a new type of lens, and ocular adaptation to GP lenses. For some subjects, these factors may have outweighed health, vision or cost benefits.

4.4.6 Lens diameter

Larger diameter lenses are advantageous as they promote better comfort and reduce corneal dessication (Hazlett, 1997; Schnider, Terry and Holden, 1997; Caroline and Andre, 2002). With this in mind, the initial study protocol was to fit relatively large diameter (10mm), aspheric contact lenses to every subject, but this fitting methodology was unsuccessful in achieving an optimum cornea-lens fit in many cases. Sub-optimal fitting has been demonstrated to adversely affect comfort and, if not modified, this fitting protocol would have jeopardised the validity of the study

(Van der Worp et al., 2002). Therefore, it was decided that a modified protocol, which permitted smaller diameter lenses, should be employed to ensure that an optimum lens fit was achieved for each subject.

To investigate whether there were any keratometry indicators that larger diameter lenses would fit some corneas better than others, the topography data, including simulated keratometry and eccentricity values, were analysed retrospectively. No statistical differences were found between the k or e values in the good or bad fitting groups. The k-value and e-value (eccentricity) describe the rate of flattening of a parabolic curve and are used to quantify aspheric changes across the cornea. For a contact lens, changing the e-value of the design can affect edge lift and mid-peripheral lens bearing. Higher eccentricities can create increased amounts of bearing on the apex of the cone, a feature seen with the 10mm diameter Quasar, which has an e-value of 0.458.

By adjusting the lens BOZR, the e-value of the aspheric lens design and the diameter of the lens, the fitter can control the overall fit of the lens (Indovina and Potter, 2008). However, by fixing the lens diameter, much of this control is lost – a feature expressed in the sub-optimal fitting observed in this study. To obtain optimal fitting with aspheric lens designs, the fitter must be free to modify all parameters of the lens design.

4.4.7 Final Conclusions

GP lenses can be successfully fitted to existing SCL wearers, although the drop-out rate may be high. As shown in Chapter 3, topical anaesthetic, as used in this study, can assist in overcoming the initial GP lens wearing experience, but for long-term success, educating patient expectation and motivation are important (Bennett et al., 1998b). GP lenses provide equivalent visual performance and ocular surface response to soft lenses. Research shows that large diameter GP lenses provide advantages for lens wear comfort (Hazlett, 1997; Caroline and Andre, 2002), but the fitter must be free to control all the lens design parameters, and understand how they interact.

5. Effect of plasma treatment on GP surface topography and performance

5.1 Introduction

Plasma surface treatment (PST) of GP lenses is a recent development, and is proposed as a method for improving wear comfort and resistance to deposition. PST is able to alter the superficial polymer surface without significantly affecting the remaining underlying material (Chu et al., 2002). Surface properties of the lens, including wettability, adhesion, adsorption, chemical reactivity and sensitivity to light, may be altered (Ru and Jie-rong, 2006).

In GP lenses, PST aims to remove residual spoilation from the lens manufacturing process and thereby reduce the contact angle, making the lens more wettable. It has been suggested that this may improve lens comfort and vision (Port and Loveridge, 1986; Schafer, 2006; Young and Tapper, 2007; Yin et al., 2008). Furthermore, it is thought that PST reduces surface roughness and binding of potentially sinister microbes such as pseudomonas aeruginosa (Bruinsma et al., 2003). However, no research relating GP surface quality to the performance or comfort of the lens has been performed.

5.2 Surface examination techniques for polymers

Surface properties influence the interaction of a material with a living system. Thus, it is important to adequately characterise the surface of any biomaterial (Ratner, 1983). A wide variety of methods for material surface examination exist. Analysis techniques must be very sensitive, to the order of angstroms and nanometers, so that only the most anterior layer (not the bulk material) properties are investigated (Merrett et al., 2002). Microscopy techniques for surface examination include scanning electron microscopy, transmission electron microscopy, atomic force microscopy and confocal microscopy (Merrett et al., 2002; Munk and Aminabhavi, 2002; Stuart, 2002). Spectrometry can be used to assess the amount of chemical species present by their emission or absorption of spectra. Spectroscopic techniques include x-ray photoelectron spectroscopy, Fourier-transform infrared attenuated total reflection spectroscopy, and secondary ion mass spectroscopy (Merrett et al., 2002; Munk and Aminabhavi, 2002; Stuart, 2002). Measurement of contact angles is also a useful tool

in the evaluation of surface hydrophobicity and hydrophilicity. A brief overview of various techniques will be given in the following sections.

5.2.1 Scanning electron and transmission electron microscopy

Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) have been used to investigate the surface morphology of many materials, including GP contact lenses (Merindano et al., 1998). In these techniques, a 5-10nm diameter electron beam is passed across the sample surface in synchronisation with a beam from a cathode-ray tube. The scattered electrons produced result in a signal which modulates this beam. This produces an image with a superior depth-of-field compared to that of an optical microscope. A three-dimensional (3-D) image may be obtained and magnification of up to $X2x10^5$ may be achieved (Merrett et al., 2002). Historically, a thin layer of conducting material is used to coat the sample surface, however newer SEM techniques may not require a conductive coating (Stuart, 2002). SEM is a destructive technique and therefore repeat measures on the same lens are impossible.

It has been reported that the front surface of unworn GP lenses of different materials sometimes have comparable or identical appearances when measured with SEM (Fourny, Kantelip and Amrouche, 1989). However, identical lens materials can also show different appearances (Fourny et al., 1989). This conflict may be explained by manufacturer specific finishing or polishing techniques (Merindano et al., 1998).

5.2.2 Interferential shifting phase microscopy

Interferential shifting phase microscopy (ISPM) achieves high-precision measurements of optical materials without destruction (Merindano et al., 1998). Video systems connected to a computer make data from phase-measurement extremely precise and by using phase shifting techniques a contour map of the surface is obtained (Merindano et al., 1998). ISPM of unworn GP lens surfaces has been performed to produce statistical data including root mean square roughness (RMS) and average roughness (Ra) values relating to surface roughness. Ra represents the average distance of the roughness profile to the centre plane of the surface profile. RMS represents the standard deviation for the mean surface plane. Both values are

expressed in nanometres. RMS values ranged from 7.2-14.3nm and Ra values from 5.7-11.4nm for a variety of GP lens materials (Merindano et al., 1998). The main advantage ISPM has over SEM is that it is a non-destructive technique.

5.2.3 Confocal scanning microscopy

Conventional light microscopy (LM) illuminates the in-focus and out-of–focus information points equally resulting in potential blurring and poor contrast (Stuart, 2002). Confocal scanning light microscopy (CSLM) provides blur-free optical sectioning of a specimen by eliminating out-of-focus information, through spatial filtering, using a point source of light for excitation (Merrett et al., 2002). No sample preparation is required and an image of high resolution is produced. CSLM can generate two-dimensional images by scanning points across the focal plane of the specimen, which can then be combined in depth to give detailed three-dimensional images (Merrett et al., 2002). The disadvantage of LM is that is gives qualitative rather than quantative information about the sample surface.

5.2.4 X-ray photoelectron spectroscopy

X-ray photoelectron spectroscopy (XPS) provides information about the polymer surface chemistry. An x-ray irradiates a sample, hitting the core electrons of the atoms, penetrating to a depth of 1 micrometer. When a sample is irradiated under ultra–high vacuum, photoelectrons (e) are emitted either from the core or from the valence levels (Stuart, 2002), Figure 5.1 and 5.2.

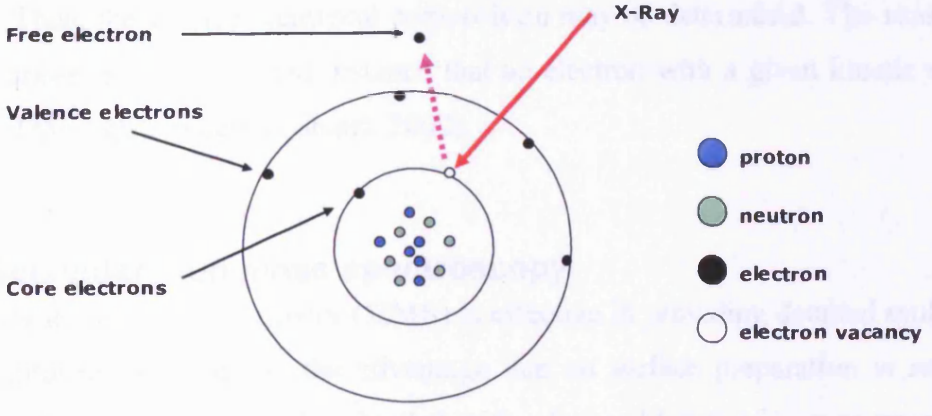

Figure 5.1 The x-ray and the atom, demonstrating that the core electrons respond well to the x-ray, adapted from Torres (2006).

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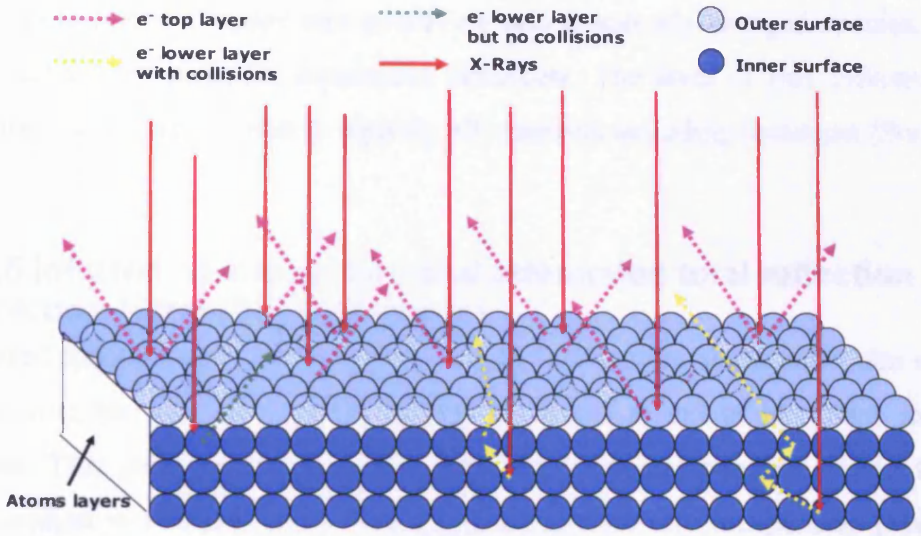

Figure 5.2 The x-ray interaction with the outer surface atom layers, adapted from Torres (2006).

On removal of the electron, a vacancy remains which can be filled by an electron from a higher level (Munk and Aminabhavi, 2002). The energy released results either in the emission of an X-ray or may be transferred to another weakly bound electron (Munk and Aminabhavi, 2002). The emitted photoelectrons are collected by a lens system and focused into an energy analyser which counts the number of electrons with a given kinetic energy.

Energies are characteristic of the atomic core levels from which the photoelectrons are emitted. Thus, the surface elemental composition may be determined. The sensitivity of XPS arises from the limited distance that an electron with a given kinetic energy can travel through a material (Stuart, 2002).

5.2.5 Secondary ion mass spectroscopy

Secondary ion mass spectrometry (SIMS) is effective in providing detailed molecular surface information, and has the advantage that no surface preparation is required (Stuart, 2002). The surface is bombarded with a focused beam of ions or atoms, and the energy from the incident beam is transferred to the surface zone of the material, resulting in emission of secondary particles (Stuart, 2002). Those particles around the

impact site may become ionised, and these are separated (as a function of the ratio of mass per electric charge) into positively and negatively charged species, which are detected in two different acquisition chambers. The level of flux influences surface etching. SIMS can be used to identify all elements including hydrogen (Stuart, 2002).

5.2.6 Infrared spectroscopy and attenuated total reflection Fourier transform infrared spectroscopy

Infrared spectroscopy (IR) is used to obtain information about molecular structure by measuring the frequency of IR radiation needed to excite vibrations in molecular bonds. This produces information about the chemical bonding within the sample. Preparation is minimal and instrumentation is relatively inexpensive (Merrett et al., 2002).

IR spectroscopy in attenuated total reflection (ATR) couples IR with the phenomenon of total internal reflection to restrict the analysed volume on the surface region of the sample. Information about the molecular structure of the material including inter- and intra-molecular interactions, and the orientation of molecules, can be obtained through analysis of the IR spectra (Merrett et al., 2002).

5.2.7 Contact angle methods

Measurement of the contact angle of a liquid test droplet on a surface reveals surface information inaccessible by surface spectroscopies. Several methods of contact angle measurement are documented, these include sessile drop method, captive bubble method and Wilhelmy plate method.

In the sessile drop method, a drop of water is placed on the test material and the angle of contact is measured. Angles less than 90 degrees indicate hydrophilicity. Angles greater than 90 degrees denote hydrophobicity. Drop size, purity, time of measurement and surface preparation can however, cause variability (Hom and Bennett, 1997), Figure 5.3.

The captive bubble method measures the wetting angle in a bubble chamber under controlled conditions (Poster, Gelfer and Fernandez, 1986). A test material is

immersed in saline or distilled water and an air bubble is formed. Wetting angles are much less than with sessile drop measurement (Bennett and Hom, 2004), Figure 5.3.

The Wilhelmy plate method is deduced by immersion of the test material into water. The advancing angle is measured as the solution moves over the material during immersion and the receding angle is measured as the material is withdrawn (Tonge et al., 2001), Figure 5.3.

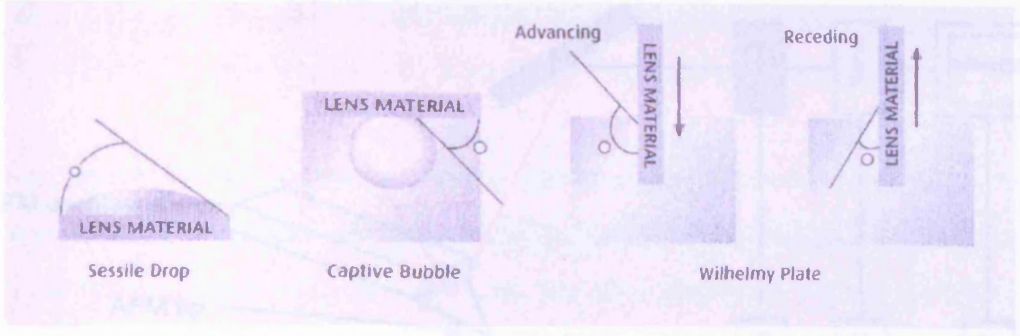

Figure 5.3 Sessile drop method, captive bubble method and Wilhelmy plate method, from Baush and Lomb materials product guide, accessed 10/04/2010 (http://www.bausch.com/en_US/ecp/visioncare/product/gpcontacts/gp_lens_materials.aspx).

5.2.8 Atomic Force Microscopy

Atomic force microscopy (AFM) maps the topography of a polymer surface using a scanning probe to create a 3D image (Stuart, 2002). It is usually performed in ambient conditions and, because no electrical surface conductivity is required, many inorganic and polymer surfaces may be studied with minimal cost and relative ease, as little or no sample preparation is required (Munk and Aminabhavi, 2002). AFM has become the most common type of scanning microscopy for polymeric biomaterials (Merrett et al., 2002).

AFM uses a fine-tipped probe which is positioned several angstroms above the surface of the sample. It measures the interaction force between the tip of the probe and the surface. The resultant force has two components: an attractive van der Waals component, typical for molecules in contact, and a repulsive component that does not allow the molecules to overlap (Munk and Aminabhavi, 2002). The probe is an

insulator and is attached to a cantilever with a reflective surface which is scanned in the x-y plane. A piezo-electric support is used to mount the sample and moves in response to surface changes sensed by the probe. The deflections are monitored by the reflected laser beam. Measurements can be made either in contact (no oscillation of the cantilever) or tapping (with oscillation of the cantilever) mode (Figure 5.4).

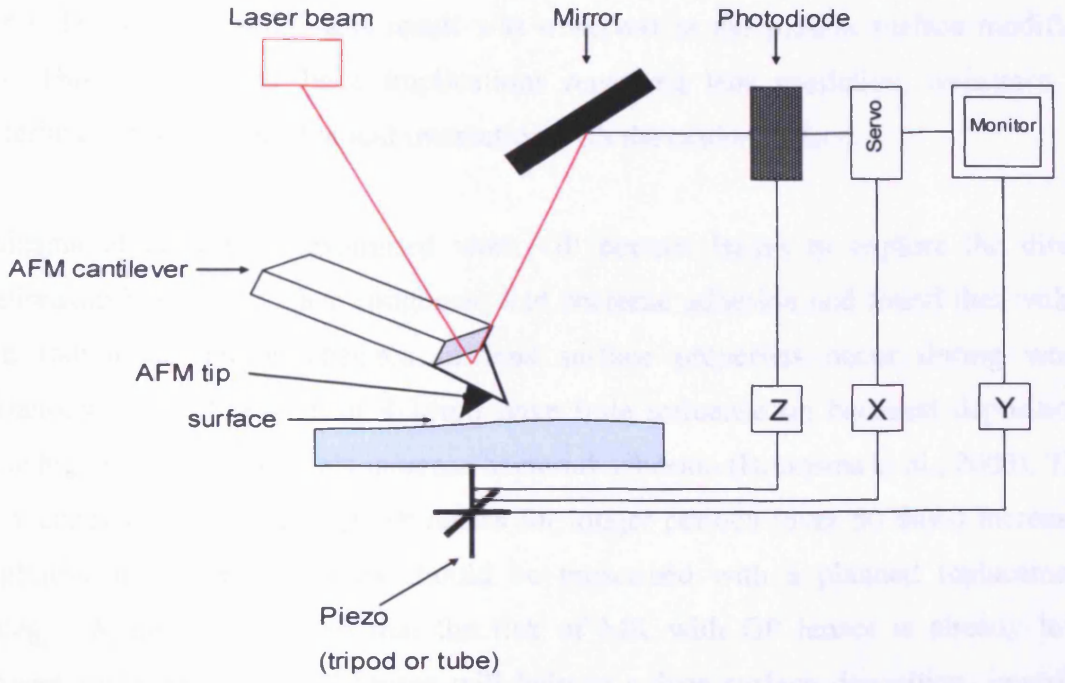

Figure 5.4 Basic AFM operation (adapted from Baguet, Sommer and Duc, (1993).

5.3 Applications of AFM

AFM is a well-established technique in flatness analysis and imaging polymer surfaces, including biopolymers (Munk and Aminabhavi, 2002). For example, chitosan membrane is biocompatible and biodegradable and has therefore received much interest as a potential material for use in biomedical applications. Oxygen plasma treatment is sometimes performed to improve surface hydrophilicity of chitosan. However, while changing the surface properties, this process also affects the surface morphology. AFM investigation showed that the surface roughness increased (from 2.7nm to 3.7nm (single measurements)) following plasma treatment, indicating the surface was etched (Wang et al., 2009).

AFM has also been used to analyse the surfaces of both GP and soft contact lenses. In soft lens studies, AFM has been described as a very powerful tool for high resolution examination of lens surface structure and identification of significant differences in worn and unworn lens morphology (Bhatia, Goldberg and Enns, 1997). More recent research has reported significant differences in AFM results when investigating surface topography of three different unworn soft lenses (González-Méijome et al., 2006). The highest roughness result was observed in the plasma surface modified lens. This finding may have implications regarding lens spoilation, resistance to bacterial adhesion or mechanical interaction with the ocular surface.

Bruinsma et al. (2003) examined worn GP contact lenses to explore the direct relationship between surface roughness and bacterial adhesion and found that within each individual, major changes in lens surface properties occur during wear. Variations in roughness from 4-14nm have little influence on bacterial deposition, while higher roughness levels increase bacterial adhesion (Bruinsma et al., 2003). The study concluded that wearing GP lenses for longer periods (over 50 days) increases roughness and, therefore, GPs should be prescribed with a planned replacement strategy. While, it is known that the risk of MK with GP lenses is already low, frequent replacement of GP lenses will help to reduce surface deposition, improve wetting and maintain an optimum visual performance, to ensure the risk of MK is kept at a minimum. It has been reported that PST wears off over a period of months. (Young and Tapper, 2007; Sanchis et al., 2008). This may cause an increase in surface roughness and physiological influence on wearing comfort. However, it has been hypothesised that patients and their tear physiology are adapted to the lens material by this point, so it is relatively unimportant (Young and Tapper, 2007).

5.3.1 Aims and objectives

The advantages of PST of contact lenses are widely published but there is no published evidence to demonstrate the topographical differences between worn, treated and untreated GP lenses. Furthermore, any correlation between patient comfort and surface roughness has not been evidenced.

AFM has been selected for use in this work because;

a) It has been demonstrated by several studies to be effective at investigating surface roughness of polymer surfaces, and specifically GP materials (Baguet et al., 1995; Bhatia et al., 1997; Bruinsma et al., 2002; Munk and Aminabhavi, 2002; Yin et al., 2008; Ren et al., 2009b);

b) It is possible to re-analyse samples;

c) It provides quantative information about the roughness or topography of the lens surface;

d) Little or no sample preparation is required (Bruinsma et al., 2003)

e) Access to this equipment was readily available at the School of Chemistry, Cardiff University.

This Chapter comprises three parts. The first involves the development of protocols for sample preparation prior to AFM. The second looks at the repeatability of AFM measurements on GP contact lenses, and the final part is an *ex-vivo* examination of factory-new and worn lenses (from established wearers). It aims to examine the relationships between plasma treatment, on lens surface topography and *in vivo* performance. In summary, the aims are:

a) To develop a protocol for sample preparation techniques prior to AFM analysis;
b) To investigate repeatability of AFM analysis;
c) To investigate unworn samples with and without plasma treatment;
d) To investigate 3 month worn lenses with and without plasma treatment;
e) To investigate any correlation between surface roughness and comfort.

5.3.2 Hypotheses

- Sample preparation protocol impacts on AFM results;
- Localised variation in surface topography will be found, but repeated measures, and adherence to stringent sample preparation protocols, will produce repeatable results;
- Samples that have under gone surface modification with plasma will have smoother topographies than untreated samples, irrespective of wear;

- There is an inverse correlation between lens comfort and topography, i.e. the smoother the lens, the better the subjective comfort.

5.4 Preliminary experiments and development of protocols

5.4.1 Introduction

Published work investigating GP surfaces using AFM described one method of sample preparation (Baguet et al., 1993). However, this method was selected by the authors for use prior to a series of different surface analyses and may not have been the best protocol for AFM specifically. In particular, the lens sample was dipped 5 times into non-preserved saline and the lens tapped on tissue paper before analysis. This may have contaminated the sample surface.

AFM will be used to measure surface topography of worn lenses. It is important that the preparation of samples is consistent and avoids degradation or surface disruption, to ensure accurate, reliable AFM results. Sample contamination could potentially lead to falsely high, surface roughness readings. Soft lenses are generally examined under aqueous buffered conditions (González-Méijome et al., 2006). However, GP lenses may be examined wet or dry. In the following series of protocols only dry sample preparation was investigated.

5.4.1.1 Aim and objective

a) To examine four different methods for sample preparation prior to AFM

5.4.1.2 Hypothesis

- Sample preparation impacts on AFM result

5.4.2 AFM methodology

The AFM (Nanoscope IIIa Dimersion 3100, Digital Instruments, Santa Barbara, CA, USA) was operated in tapping mode using an uncoated, symmetric tip of 40 nanometres (nm) (300kHz).

5.4.2.1 Quantitative topographic analysis

Root mean-square-roughness (RMS) and average surface roughness (Ra) were obtained from the roughness analysis program using Nanoscope III software (Digital Instruments, Santa Barbara, CA, USA). Both values are expressed in nanometres. These measures were specifically selected because they have been widely used in other surface roughness studies, as they give the most meaningful and reliable statistical interpretation of the surface topography (González-Méijome et al., 2006). Some earlier studies also report maximum roughness values, however reporting the peak roughness value of an area does not reflect the topography of the lens and may be unreliably high due to local imperfection or sample contaminations (Bruinsma et al., 2003).

5.4.2.2 Sample preparation

The preliminary method employed to prepare GP samples for AFM is based on work which aimed to investigate multiple surface properties of worn GP lenses (Bruinsma et al., 2003).

Worn lenses (Quasar fluorosilicone acrylate, No, 7 contact Lens Laboratory, Hastings, UK) were collected from both eyes and stored in their case filled with care solution (Menicare Plus, Menicon Japan) and directly transported to the laboratory. The lens was removed from transport containers and transferred to Menicare Plus solution in a sterile well, using sterile stainless steel tweezers. The lens remained in solution for a minimum of 5 minutes. Lenses were cut into smaller parts using a sterile surgical knife. Following removal from the lens case, lenses were dipped 5 times in 0.9% saline (non-preserved) and then excess saline was removed by gently tapping the lens edge on paper tissue, after which the lenses were allowed to air dry. Lenses were then mounted onto the platform using adhesive tape, ready for AFM.

The preparation technique was repeated using three different methodologies (Table 5.2). Each employed an alternate solution prior to lens drying; otherwise the preparation method was the same as Method 1 above. A single, worn lens was used to produce four samples, one for each method.

Table 5.2 Overview of Methods 1-4: alternative methods used to wash and dry the sample

	Lens wash preparation	Lens drying method
Method 1 (based on Bruinsma et al., 2003)	Stored in Menicare Plus solution, dipped 5 times in 0.9% saline (non-preservee)	Air dried
Method 2	Stored in Menicare Plus solution, not washed	Nitrogen hose (pressure 2 bar) until surface dry
Method 3	Stored in Menicare Plus solution, dipped 5 times in 0.9% saline (non-preserved)	Nitrogen hose until surface dry
Method 4	Stored in Menicare Plus solution, dipped 5 times in purified, distilled water	Nitrogen hose until surface dry

Surface roughness images were recorded at five locations on each sample, Figure 5.5. This technique was employed to investigate the possibility of local variation in topography within a sample. This technique was not evident in other published work (Bruinsma et al., 2003). The investigator was not masked to the preparation technique.

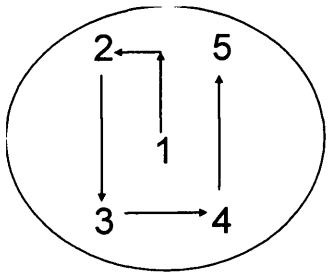

Figure 5.5 Example of surface locations (approximate) on GP lens selected for AFM analysis.

Figure 5.6 Atomic force microscope.

5.4.3 Results

The results are shown in terms of RMS and Ra for each preparation method. The median and range for each method are shown as the results were not normally distributed.

The mean values of RMS and Ra for each preparation method (1-4) in Figure 5.7 and examples of the surface images produced in two and three dimensions are shown in Figures 5.8.

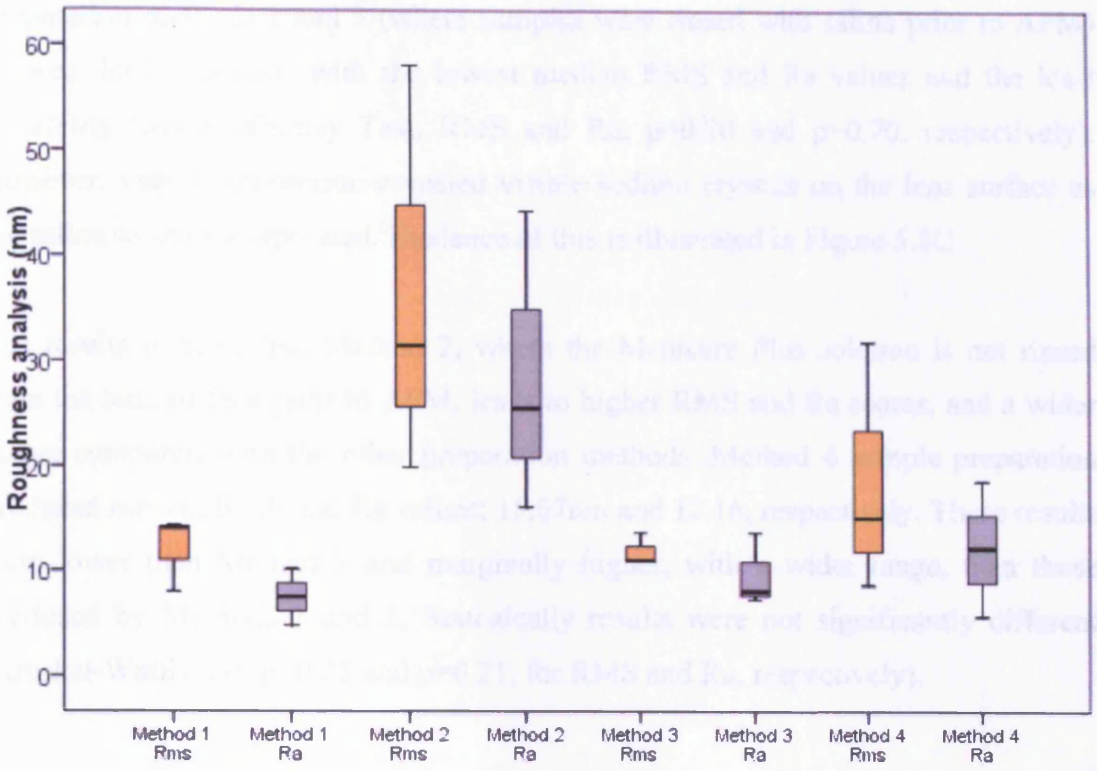

Figure 5.7 A box plot showing median and range values for surface analysis result for the four sample preparation techniques (N=1, 5 scans per sample).

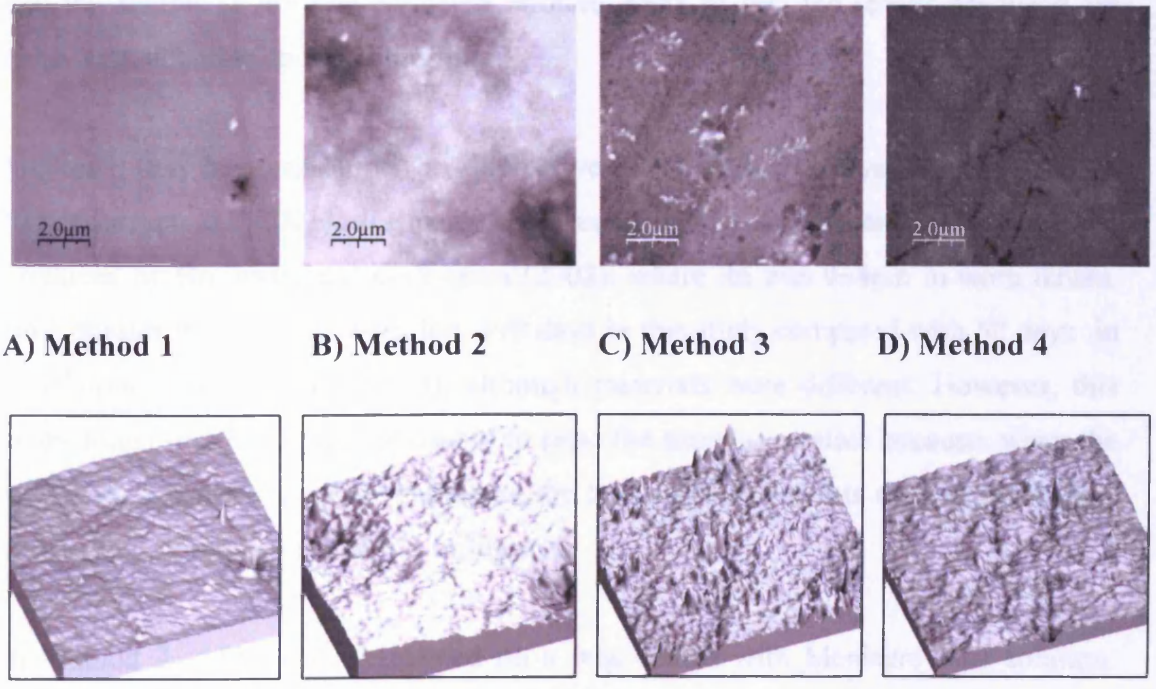

Figure 5.8 Two and three-dimensional image examples of each method.

Preparation methods 1 and 3 (where samples were rinsed with saline prior to AFM) showed similar results, with the lowest median RMS and Ra values and the least variability (Mann-Whitney Test, RMS and Ra; p=0.70 and p=0.70, respectively). However, visual comparison revealed visible sodium crystals on the lens surface as the saline solution evaporated. Evidence of this is illustrated in Figure 5.8C.

The results indicate that Method 2, where the Menicare Plus solution is not rinsed from the lens surface prior to AFM, leads to higher RMS and Ra scores, and a wider range, compared with the other preparation methods. Method 4 sample preparation produced median RMS and Ra values; 15.07nm and 12.16, respectively. These results were lower than Method 2 and marginally higher, with a wider range, than those produced by Methods 1 and 3. Statistically results were not significantly different (Kruskal-Wallis test, p=0.25 and p=0.21, for RMS and Ra, respectively).

5.4.4 Discussion and conclusions

This study indicates that the sample preparation protocol, when inspected visually, is seen to impact AFM results; however, this was not evident statistically. It is critical that the sample is not contaminated prior to AFM so that the results produced are consistent, accurate and meaningful.

Method 1 has been employed in alternative AFM surface analysis in GP research (Bruinsma et al., 2003). Ra values produced in this study are similar to those produced by Bruinsma and colleagues (2003); where Ra was 9±4nm in worn lenses. Both studies investigated worn lens (90 days in this study compared with 50 days in Brunisima et al.'s work (2003)), although materials were different. However, this study found that it was not advisable to rinse the sample in saline because, when the lens drys, sodium crystals contaminate the lens surface. For this reason, Methods 1 and 3 should both be considered unsuitable.

In Method 2, AFM was performed on a lens coated with Menicare Plus solution. Menicare Plus is a multi-purpose cleaning and conditioning agent. It contains lubricating factors which coat the lens surface to improve on-eye comfort and wetting. However, AFM investigates only the most anterior layers of the sample. This may

mean that the overlying dried lens solution masked the true lens surface, making this preparation method unsuitable prior to AFM.

In Method 4, where the lens is stored in Menicare Plus solution, rinsed in ultra-purified, distilled water and then dried with a nitrogen hose, there is the least likelihood of contamination of the sample via care solution or air-borne contaminants. This methodology is similar to that used in sample preparation in other biological AFM research (Thundat, Allison and Warmack, 1994). Air drying the sample may permit air born particles to adhere to the lens surface, therefore drying with dry nitrogen after rinsing is a superior preparation technique (Thundat et al., 1994). Interestingly, despite the lower risk of sample contamination when using Method 4, the RMS and Ra results were higher, though not significantly, than with Methods 1 and 3. The reasons for this are unclear.

Avoiding contamination during sample preparation is critical in producing reliable surface analysis results with AFM. It would appear that Method 4 preparation poses the least risk of lens contamination and should be used when preparing GP samples for AFM. This method was chosen for sample preparation in the subsequent studies described in this Chapter.

5.4.5 Conclusions

The protocol for GP lens preparation prior to AFM should be as follows:
After harvesting the lenses they should be stored in a clean case filled with Menicare Plus solution and directly transported to the laboratory. The lens should be transferred to Menicare Plus solution in a sterile well, using sterile stainless steel tweezers. The lens should be cut into smaller parts using a sterile surgical knife. The sample is then dipped 5 times in distilled, ultra-purified water and air dried with a nitrogen hose. Finally, the lens is secured onto an adhesive mount.

5.5 Repeatability of AFM for measurement of GP surface topography

5.5.1 Introduction

This study investigated the repeatability of AFM, using a consistent preparation protocol, when examining two samples of the same lens.

5.5.2 Methods

A worn GP lens (Quasar, No. 7 Contact Lens Laboratory, Hastings, UK) was collected from a subject who completed the 3 month study in Chapter 4. Two different sections of the lens were prepared for AFM using the prescribed protocol in Section 5.4.5. Five 100μm^2 areas were scanned on each lens sample, referred to as sample 1 and sample 2. A diagram shows this in Figure 5.9.

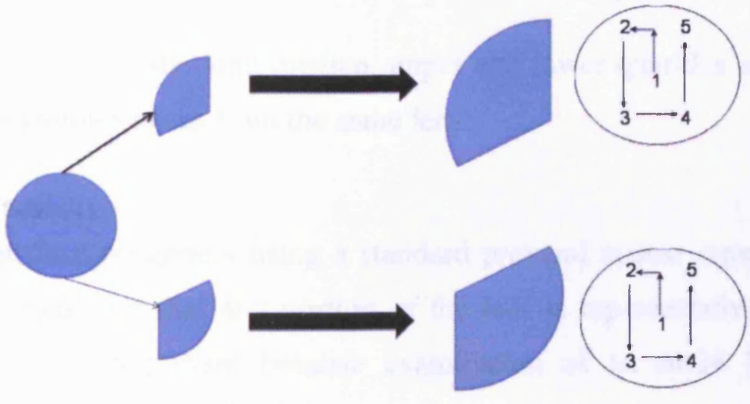

Figure 5.9 A schematic diagram showing how the lens was divided prior to examination.

5.5.3 Results

Considering the five measures on each sample, Sample 1 showed a larger range of results for RMS and Ra than Sample 2. No statistically significant difference was found between results for RMS and Ra in the two lens samples (Wilcoxon Rank test, p=0.35 and p=0.89, respectively) (Figure 5.10).

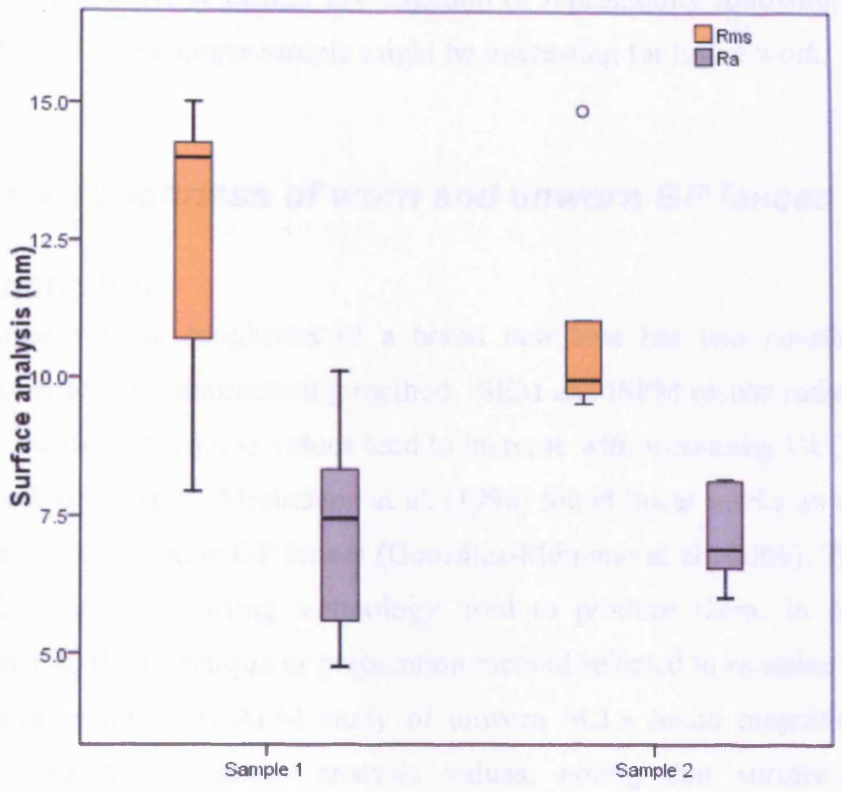

Figure 5.10 A box plot showing median, upper and lower quartiles and range AFM results for two samples taken from the same lens.

5.5.4 Discussion

Measures of surface roughness using a standard protocol appear repeatable within a single sample, implying that any portion of the lens is representative of its surface topography. This is important because examination of an entire lens surface is impractical with this method of AFM.

The results demonstrate that values for Ra and RMS vary both within-samples and between-samples. This indicates that the surface topography varies across the lens. This concurs with studies which have found that the manufacturing process is responsible for surface topography variations (Fourny et al., 1989; Merindano et al., 1998). All GP lenses are made by lathe-cut technology and variation has been attributed to linear surface scratches detected on unworn GP lenses when examined by SEM (Merindano et al., 1998).

One criticism of this study might be that it was small as it investigated only one lens at two locations with five readings at each location. Reproducibility over time was not

examined in this study. A further investigation of repeatability following prolonged storage and involving a larger sample might be interesting for future work.

5.6 Surface roughness of worn and unworn GP lenses

5.6.1 Introduction

Any measured surface roughness of a brand new lens has two possible origins: material properties or manufacturing method. SEM and ISPM results indicate that, in general, GP surface roughness values tend to increase with increasing Dk (Merindano et al., 1998). Using ISPM, Merindano et al. (1998) found linear marks on the anterior lens surface of factory-new GP lenses (González-Méijome et al., 2006). This may be explained by the lathe-cutting technology used to produce them. In addition, as previously noted, the technique or preparation method selected to examine the surface may influence results. An AFM study of unworn SCLs found magnification also significantly affects roughness analysis values, noting that surface roughness increases as observation area is increased (Young and Tapper, 2007; Sanchis et al., 2008).

GP lenses are often prescribed for full-time daily wear, often for long periods. Planned replacement after 6 or 12 months wear is common, but sometimes lenses are worn until degradation of comfort or acuity necessitates replacement. Despite cleansing and disinfection procedures, organisms and deposits adhere to lens surfaces. Wear, handling and cleansing of CLs changes the physio-chemical properties of the CL surface. The hydrophobicity, electrostatic charge and surface roughness may be altered. Plasma treatment has been suggested to reduce deposition and improve performance, however, as discussed in 5.3, it may wear off over time (Valsesia et al., 2004).

5.6.1.1 Aims and objectives

a) To examine unworn plasma-treated and unworn, untreated lens surfaces;

b) To examine surface topography of three-month worn, plasma treated and worn, untreated GP lenses using AFM.

5.6.1.2 Hypotheses

- Unworn, plasma treated lenses will have smoother topographies than untreated lenses;
- Following 3 months wear, no difference in surface topography of plasma treated and untreated lenses will be present.

5.6.2 Methods

5.6.2.1 Unworn lens samples

Four unworn lenses were examined under AFM. Two lenses had been plasma-treated and two were untreated, but they were otherwise identical (Table 5.3). Lenses were prepared using the protocol described in Section 5.4.5.

Table 5.3 Summary of nominal parameters of the GP lenses studied.

	All lenses (treated and untreated)
Manufacturer	No7 Contact Lens Laboratory
Material	Flourosilicone acrylate
Manufacturing procedure	Lathe cut
Dk	60
BOZR (mm)	7.55
TD (mm)	9.20
Rx (D)	-5.25

5.6.2.2 Worn lens samples

During the 3 month GP study in Chapter 4, subject comfort was measured using VAS. Following 3 months GP wear, 20 lenses were collected: 10 were plasma-surface-treated, 10 were untreated. The surface topography of the anterior surface of samples from each lens were evaluated with atomic force microscopy (AFM Nanoscope IIIa Dimersion^{TM} 3100, Digital Instruments, Santa Barbara, CA, US) in tapping mode at five locations, as shown in Figure 5.9, over a 100μm^2 area. The mean value of average roughness (Ra) and root mean square of roughness (RMS) values were obtained for each sample.

5.6.3 Results

5.6.3.1 Unworn lens results

Surface roughness analysis results for two factory-new untreated and two factory new, plasma-treated GP lenses are displayed in Figure 5.11 and a three dimensional image example of the lenses is shown in Figure 5.12. Results showed that untreated lenses had significantly higher mean RMS and Ra values compared with plasma treated samples, (Mann-Whitney test, $p<0.05$).

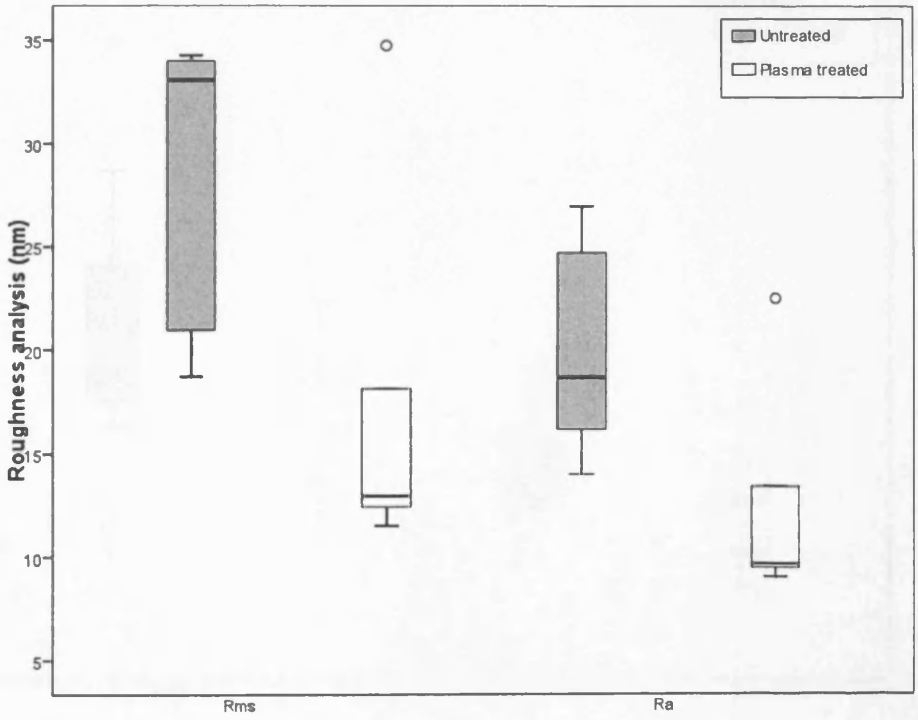

Figure 5.11 A box plot showing median and range values for surface analysis of unworn plasma treated and untreated lenses (2 lenses, 2 samples from each lens, 5 readings per sample).

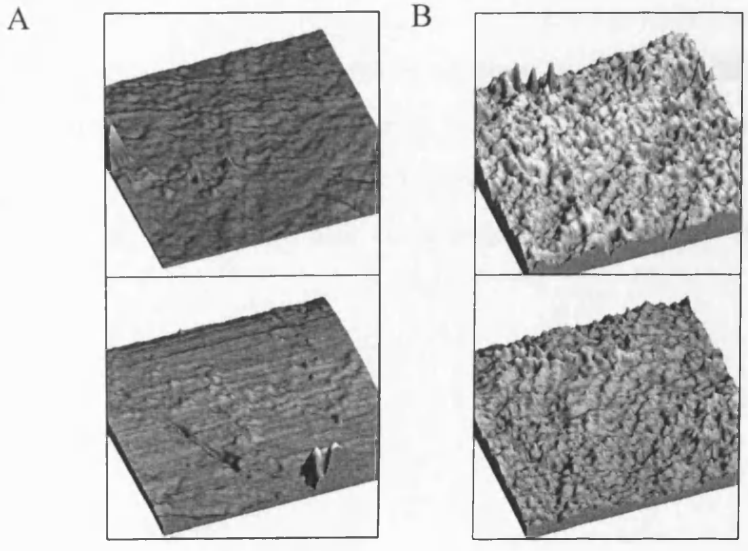

Figure 5.12 Surface appearance of unworn GP lenses (A) plasma treated (B) untreated.

5.6.3.2 Worn sample results

Median Ra values were higher in untreated lenses [12.92nm (range 11.34-26.59)] than plasma-treated lenses [11.18nm (range 7.68-15.97)]; this difference approached statistical significance (Mann Whitney test, p=0.06). Median RMS scores were significantly higher in untreated, worn samples [18.70nm (15.01-32.94)] than plasma-treated, worn samples [14.82nm (11.24-20.99)]; (Mann-Whitney test, $p<0.05$) (Figure 5.13).

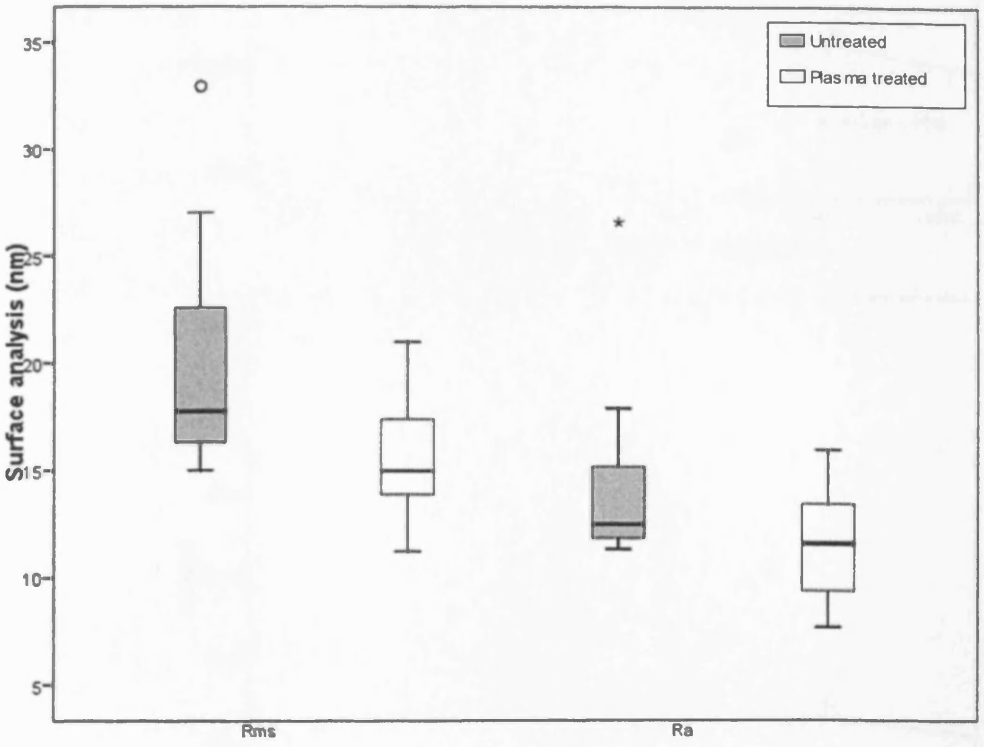

Figure 5.13 A box plot showing median and range values for surface analysis results for worn, plasma-treated and worn, untreated samples.

No correlation was found between general comfort, reported by VAS at the 3 month visit, and RMS or Ra scores (Spearmen correlation, p=0.64, R^2= 0.06, and p=0.78, R^2=0.07, respectively). This is demonstrated in Figure 5.14A and 5.14B. Also no correlation between surface treatment and roughness was evident (Pearsons correlation, p=0.36).

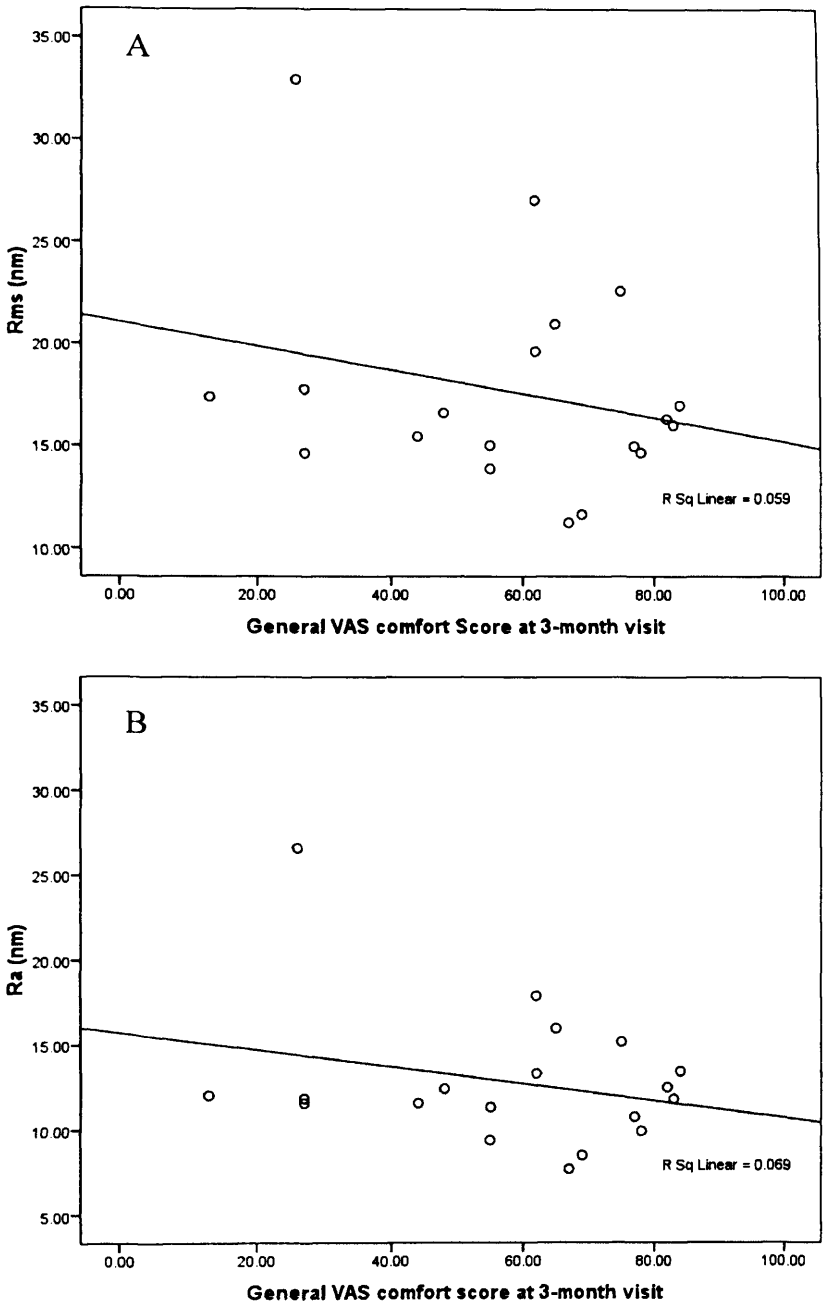

Figure 5.14 Correlation between surface roughness measured by AFM and VAS comfort after 3 months wear. A: Correlation between general comfort VAS scores (at three months GP lens wear) and RMS, and B: Correlation between general comfort VAS and RA (0=Not at all comfortable, 100=Very comfortable).

5.6.4 Discussion

The surface roughness of a device in contact with a living system will influence the biological reactivity of the device with the surface. So for a contact lens placed on the ocular surface, the lens polymer should interfere as little as possible with the epithelial surface, cornea and the conjunctiva. This is important for maintenance of ocular health and patient tolerance of the lens.

As anticipated, unworn, plasma-surface-treated GP lenses had lower Ra and RMS values compared with unworn, untreated GP lenses. This finding agrees with the findings of Valsesia et al. (2004), who investigated the surface topography and characterisation of PMMA co-polymer films, with and without plasma-surface-treatment. Since surface roughness has been found to increase bacterial adhesion and may adversely affect contact lens comfort, the findings of this study suggest that there is a clinical benefit associated with plasma treatment of GP lenses.

Plasma-treated lenses that had been worn for three months were also smoother than untreated, worn lenses. This confirms that plasma treatment of GP lenses can reduce surface roughness initially, and is maintained with lens wear.

Although the treated lenses were still smoother at 3 months than the untreated lenses, the lens smoothness had reduced somewhat. This may be for several reasons, but the most obvious and logical one is that the plasma treatment has diminished over time and lost its smoothing properties. This idea is supported by Young et al. (2007), who suggested that plasma treatments wear off with cleaning and wear. In addition, the variability of results may be due to inter-subject differences such as variation in hygiene, differences in wear schedule, lifestyle and patients' tear physiology. Where possible, these factors have been controlled; for example, patients were instructed to follow the same care procedure and use the same contact lens solutions, and all were advised to wear lenses on a full time basis for 12 weeks. However, non-compliance issues are commonplace in contact lens patients (Polse et al., 1999). The random allocation of subjects should ensure that non-compliance with lens care had a similar influence on both lens groups, but it is possible that poor lens care had less influence on the treated lens surfaces than the untreated.

Moreover, there appears to be greater variability in the surface roughness scores when lenses are untreated, both worn and unworn. It should be noted that the samples used in this study will have varied in time since manufacture, as well as on which lathe the lens was made, since it has been found that exposure to atmospheric conditions may contaminate lens surface and impact on AFM results (Shakesheff, 1995). Another possible influence on the results could be that, following lens harvesting, the lenses were stored in Menicare Plus solution for varying periods (<3 weeks) before examination with AFM.

To establish whether the results seen here are a direct result of lens aging, it would be interesting to investigate how plasma-treated lenses are affected over longer periods, e.g. six or twelve months. Also it has been indicated that solutions play a pivotal role in contact lens comfort and lens hygiene, and some solutions, when digitally rubbed onto the lens surface, may scratch or alter the plasma-treated surfaces.

5.7 Final Discussion

This chapter aimed to develop a protocol for sample preparation prior to AFM analysis and investigate repeatability of AFM analysis using the newly-designed preparation protocol. Also, it aimed to investigate the differences between surface topography in plasma-treated and untreated lenses, both worn and unworn, to examine any influence surface topography had on *in vivo* comfort.

The work was successful in designing a sample preparation protocol which produced repeatable AFM results. It confirmed the initial hypothesis that sample preparation impacts the AFM results. Thus, it is critical to consistently use a specific preparation methodology to minimise surface damage or sample contamination and to produce accurate, repeatable AFM results. The work also discovered that a previous sample preparation methodology was not acceptable, because it produced sodium chloride surface contamination as a by-product of rinsing the sample with saline (Bruinsma et al., 2002).

Untreated sample surfaces were significantly rougher than plasma treated ones. This was true for both worn and unworn lenses, confirming the final hypothesis. Interestingly, unworn, untreated lenses in this investigation had the highest roughness scores, higher than worn, untreated lenses. This may be because factory-new lenses have many surface contaminant residues from the manufacturing process, whereas worn lenses are 'cleaned' by wear and the daily cleaning regimen. However, this trend may be dampened by increasing the sample size. Local variations in topography in single samples were found, as anticipated. However, by measuring surface roughness at 5 separate areas within each sample, the median values could be calculated, which improved repeatability.

It has been suggested that contact lens plasma surface treatments age and wear off over a period of months (Sanchis et al., 2008). The results found that after 3 months wear, plasma treatment was still evident, although surface roughness scores were lower than unworn treated. The measurement of surface roughness before and after wear would allow the measurement of change in roughness over time.

It was hypothesised that comfort would be improved with reduced surface roughness, as a result of PST. However, although the surface roughness was reduced by PST, subjective comfort was not improved. This finding may be because the surface analysis results are at microscopic levels and therefore do not significantly impact on ocular comfort. Alternatively, the comfort responses may be affected by other factors such as edge finish, lens fit, tear stability, lens lid interaction or corneal sensitivity. These differences will vary between subjects, independently of surface roughness, and will impact on subjective comfort.

The preparation technique used involved cutting the lens into smaller pieces before mounting on the microscope stage. This destructive technique would currently prevent AFM measurement prior to wear. However, if a curved body or bodies were produced, it may be possible to mount the entire lens for investigation. Care would be needed in securing the lens to the mount, as use of an adhesive (as in this study) may leave residues on the back surface of the lens.

A limitation of AFM is that is does not investigate the surface chemistry. Future work might involve further analysis of the lens samples using X-ray photoelectron spectroscopy (XPS). This technique may lead to better surface characterisation and a clearer understanding of correlation between lens surface effects on lens performance following PST.

6. Final Discussion and future work

It is a fact, largely accepted in UK contact lens practice, that GP lenses have been superseded by new soft hydrogel and silicone hydrogel contact lenses, and that their usefulness is now limited to the obscure fitting requirement or 'difficult' patient. GP lenses were, at one time, the lens of first choice, but the dramatic developments in soft lens design and materials has opened up contact lens wear to a vast new population of wearers. For this, all contact lens fitters and lens wearers should be grateful, and perhaps the decline of GP lens fitting is a natural phase of obsolescence in the face of more advanced lens technology. Yet, the benefits of GP lens wear remain significant and cannot be avoided; in particular, the greatly reduced risk of serious sight-threatening complication and the appreciably better long-term comfort for many wearers.

GP lenses are not without their friends among manufacturers, fitters and patients. The belief held that GP lenses can continue to be an option for the general lens wearing population has encouraged a renaissance in GP lens design and materials, such as large diameter lenses, surface treatments, hyper-transmissible materials and aspheric designs, and attention has also turned to the education and professional development of the lens fitters themselves, to ensure that the additional fitting skills required of GP lenses is preserved and promoted among optometrists and contact lens opticians.

A discussion of whether the decline in GP lens prescribing is a 'good thing' or a 'bad thing' is not the remit of this thesis. Rather this thesis has considered how the decline might be addressed, and even reversed, by the introduction of these new GP lens design developments.

It is obvious that practitioner training and opinions are fundamental in determining prescribing habits, but this is the first work to scientifically survey a large sample of the UK profession to discover more precisely their attitudes towards GP lenses, compared to contact lenses generally. The discovery that ECPs acknowledge the safety and long-term comfort of GP lenses, but remained reluctant to fit due to initial comfort and the extra time taken provides clear indicators for key areas of improvement in education, manufacture and clinical practice. In the UK, GP trial lens fitting sets are not routinely used and empirical fitting is routine practice; if contact lens manufacturers can further develop and promote supported fitting schemes,

perhaps via the use of topography, then practitioners' perceptions of the ease of fitting could be enhanced. The level of experience that practitioners can gain in GP lens fitting post-qualification may also be a problem as the pool of patients continues to shrink and business models change, which is evident in the results that indicate that older practitioners are less intimidated by this area of contact lens practice. Looking ahead, a survey that specifically targets ECPs within five years of qualification may be useful to examine why this population appears to become de-skilled in this area.

Use of topical anaesthetic (TA) during the lens fitting process is more common in the USA than in the UK (Schnider, 1996; Bennett et al., 1998a), and traditional teaching in the UK discourages the use of TA in contact lens practice. However, if a major problem is initial lens comfort with GP contact lenses, then TA offers an opportunity to present GP lenses in a much more favourable light to the patient. The study in this thesis is the first UK investigation of the short-term effects of TA use versus a placebo in new patients during GP lens fitting. The results of the study were positive. Following TA use at the first lens fitting visit, subjective patient anxiety was significantly reduced at the second collection visit, and the subjects who received the TA tended to report a better comfort experience. Importantly, the ocular surface response was similar in the TA and placebo groups. Use of TA has been demonstrated to reduce long-term drop-out rates (Bennett et al., 1998a), but this study also found that patient retention may be improved in the short-term. Walline et al. (2001) suggested instilling the TA drop on the back (concave) surface of the contact lens, as practiced in his children study of myopia, in order to avoid having the stinging drop prior to lens insertion. Of course, this might simply make the lens insertion feel even more uncomfortable, but it is an example of the potential that TA use provides in improving comfort responses.

Since GP lens comfort is both a criticism (in the short-term) and a potential benefit (in the long-term), any developments in GP materials and design is worthy of further investigation. Larger diameter lenses have been suggested to give superior comfort (Hazlett, 1997; Caroline and Andre, 2002; Edrington, 2004), and so one aim of this research was to fit a relatively large, 10.00mm, lens diameter to the volunteer subjects. While the lens design was successful for 11 out of the 20 subjects, the high exclusion rate unexpectedly revealed a problem that exists with fitting a large

diameter, aspheric system-designed lens. While a comparative analysis between the lens and corneal eccentricity found no correlation, the restrictions that a system-designed lens places on the fitter were obvious. The clear message is that the fitter must have control over the BOZR, diameter and eccentricity value of an aspheric lens design to obtain optimum fit, and that the use of keratoscopic software to design GP lenses should not be conducted without trained input by the fitter. Indeed, it is inevitable that fitting a larger diameter lens will provide a greater challenge as there is more lens area to be matched to the individual corneal topography, and current corneal topographers are limited to obtaining information only over the central 6-8mm area of the cornea (Van der Worp et al., 2002). This also has an impact on ECP training in GP fitting, and provides an interesting aspect to the argument between empirical fitting and diagnostic fitting.

Further investigation of very large total diameter (TD) lenses, where the lens would vault over the entire cornea and limbus and extend onto the bulbar conjunctiva, would be extremely interesting. Some larger diameter lenses are available and are currently being fitted in the UK, such as the SoClear lens (No.7 Contact Lens Ltd, Hastings, UK). Comfort may be superior because this lens will stabilise and move less, the lens edge will rest on the bulbar conjunctival, which has lower touch sensitivity than that of the cornea, and the lens edge would interact less with the sensitive eyelid zone at the marginal angle. However, fitting larger lenses, despite the improvements in Dk, may result in more occlusion of the anterior surface, reducing tear exchange and could risk increasing the potential for ocular infections.

A more recent development in lens materials has been the introduction of specialised surface treatments to improve wettability, protein deposit resistance and lens wearing comfort. Plasma surface treatment (PST) was first made familiar in its use with the first generation silicone hydrogel materials, and the potential benefits have now led to it being used with GP lenses. The longitudinal study investigated, for the first time, whether plasma surface treatment of GP lenses resulted in improved comfort and performance. The results were disappointing, since no significant benefit to comfort or performance was found in subjects fitted with the plasma-treated lenses. This finding was unexpected as the literature has suggested that PST provides superior comfort and performance (Schafer, 2006; Franklin and Franklin, 2007; Young and

Tapper, 2007). Indeed, on investigation with atomic force microscopy (AFM) the worn, plasma treated lenses were found to be significantly smoother than the untreated ones. Yet, no correlation between comfort and surface topography was found in this research. This implies that there may be a measurable difference in lens performance or comfort with plasma treated lenses, but this study was not rigorous enough to detect it or was not of sufficient duration, or that the group examined were naïve to GP lenses and therefore were not sensitive to the improvement made by plasma treatment. When initial comfort was measured, many other extraneous factors may have impacted on the results obscuring any impact that PST had on early comfort or performance. Alternatively, it may be that the measures of visual function and comfort were not measured appropriately.

Despite the insignificant findings relating to comfort and performance with PST, this study was successful in being the first study to quantify the surface topography of plasma-treated GP lens surfaces using AFM. This work investigated and established the optimum lens sample preparation protocol prior to AFM analysis and, using this, discovered the significant differences in topography of 3 month worn treated and untreated lenses. Recent work has investigated the type and power of PST required to produce the optimum GP surface topography at manufacturing stage (Ren et al., 2008; Yin et al., 2008; Ren et al., 2009a; Yin et al., 2009), but, until this study, no research existed to demonstrate the impact of PST on *in vivo* lens performance and comfort. Also, the effect of time and wear on PST has not been extensively researched. It has been suggested that PST wears away over time (Young and Tapper, 2007), and while this is the first study to investigate worn, treated GP lens surfaces, the short 3 months of wear may not be long enough to allow deterioration in the surface treatment. If lens spoilage could be avoided during AFM analysis, then further research to compare before and after wear surface topography of PST lenses would provide interesting data.

To further this research on surface treatment, a comparison study between eyes or a cross-over type study would give better comparison of treated versus untreated comfort and performance. A future study of interest would be the investigation of differences in comfort and performance with plasma treatment in a group of experienced GP wearers. It is anticipated that this group might be more sensitive to

surface treatment differences because there would be fewer external variables impacting their subjective response.

There is also much future work to be done in examining lens surface topography and how it affects the lens biocompatibility with the eye. The next phase of surface analysis of treated and untreated lenses should be the use of XPS to investigate the polymer surface chemistry and how this changes with wear. Many studies have used XPS at the manufacturing stage to look at surface changes before and after PST (Ren et al., 2008; Yin et al., 2008; Ren et al., 2009a). However, XPS of worn PST lenses would provide a clearer understanding of what elements or compounds are present on the lens surface and may help to better explain on-eye performance of GP lenses.

The survey showed that, despite the advantages of GP lenses, they are reluctant to recommend GP lenses as the first choice. The limited success found in the subject cohort in this study emphasised the significant role that patient history plays in success with GP lenses. Neophytes have no prior experience and therefore accept adaptation and report better initial comfort than previous SCL wearers, whose expectations are modified by previous SCL comfort experiences. Thus, we are reminded that patient selection and motivation are important factors for GP success, irrespective of positive practitioner communication about GP lenses.

In conclusion, the question remains as to whether the future for GP lenses is to be a gradual decline or a welcome rejuvenation. This work has shown that practitioners and their attitudes toward GP lenses are, in part, responsible for the downtrend in GP prescribing in the UK, but that its recovery also lies in their education and professional development. As always, GP fitting success is dependent on the individual patient history and motivation to wear GP lenses, but this may be encouraged with the use of topical anaesthetic. The evidence from this study shows that TA may be safely used to enhance first GP experience and significantly reduce patient anxiety surrounding second-time GP wear. Plasma treatment shows much promise, and clearly results in a smoother GP lens surface topography, but future studies must be made to understand the full benefit of this smoothness on lens comfort or performance. And in the future, the promise of very large diameter GP lens

designs, combined with hyper-transmissible lens materials, suggests that there may be a renaissance for GP lenses.

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