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The Impact of Soft CL Wear on Corneal Curvature and Thickness and on the Outcomes of Refractive Laser Surgery

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Abstract

Introduction: Soft CL (SCL) wear can alter the cornea and have significant effects on vision quality (Hardten and Gosavi, 2009; Pflugfelder et al., 2002; Ryan and Jacob, 1996; Tseng et al., 2007). This may have implications for visual outcomes following corneal refractive surgery (CRS) (Tang et al., 2005). The time required for resolution of these SCL-induced changes can vary (González-Méijome et al., 2003a; Hashemi et al., 2008; Ng et al., 2007; Nourouzi et al., 2006; Schornack, 2003; Wang et al., 2002b). Despite this, current guidelines relating to cessation of SCL wear prior to CRS vary greatly, and are lacking in relation to the criteria required to achieve stability of measurements (FDA, 2014; Royal College of Ophthalmologists, 2011).

Purpose: To examine the influence of SCL wear on cornea structure, the corneal epithelium and endothelium and the outcomes of CRS.

Methodology: The cornea and CRS outcomes were compared between patients who wore SCLs (n = 179) against a non-CL wearing control group (NCL) (n= 148).

Results and conclusion: SCL wear had a significant effect on corneal curvature (mean anterior inferior tangential radii SCL 7.77mm, NCL 7.90mm, p = 0.04). Peripheral endothelial cell density (SCL = 3109 cells/mm^2, NCL = 2935.08 cells/mm^2, p = 0.03), mean endothelial cell area (SCL = 322.25 cells/mm^2, NCL = 346.92 cells/mm^2, p = 0.00) and coefficient of variation of cell size (SCL = 29.13, NCL = 25.63, p = 0.00) were significantly affected by SCL wear. Six weeks following LASIK central epithelial thickness was significantly thicker in the SCL group (59.65 ±6.20µm) compared with the NCL group (54.42 ±8.12µm, p = 0.04) whereas the epithelial thickness in the nasal periphery was significantly thinner in the SCL group (59.52 ±7.01µm) compared with the NCL group (65.83 ±9.16µm, p = 0.03). Although 24 hours was insufficient for resolution of these changes, 2 weeks SCL cessation was sufficient. Previous SCL wear had no negative impact on visual outcomes following CRS compared with a NCL control group, regardless of previous SCL cessation time prior to CRS (all p values > 0.05).

Declaration

I certify that this thesis, which I now submit for examination for the award of Doctor of Philosophy (PhD), is entirely my own work and has not been taken from the work of others, save and to the extent that such work has been cited and acknowledged within the text of my work.

This thesis was prepared according to the regulations for postgraduate study by research of the Dublin Institute of Technology and has not been submitted in whole or in part for another award in any other third level institution.

The work reported on in this thesis conforms to the principles and requirements of the DIT's guidelines for ethics in research. DIT has permission to keep, lend or copy this thesis in whole or in part, on condition that any such use of the material of the thesis be duly acknowledged.

Signature _____ Date 4th January 2016

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Go raibh míle maith agaibh go léir!

Abbreviations list

ANOVA	Analysis of variance
BCSVA	Best corrected spectacle visual acuity
BFS	Best fit sphere
CCT	Central corneal thickness
CL	Contact lens
COR	Coefficient of repeatability
CRS	Corneal refractive surgery
CSF	Contrast sensitivity function
D	Dioptres
DK/t	Oxygen transmissibility
DW	Daily wear
EW	Extended wear
FDA	Food and drug administration
FFK	Forme fruste keratoconus
G1SiHy	Generation one silicone hydrogel
G2SiHy	Generation two silicone hydrogel
G3SiHy	Generation three silicone hydrogel
ICC	Intra-class correlation coefficient
ICT	Inferior corneal thickness
LASEK	Laser epithelial keratomileusis
Laser	Light Amplification by the Stimulated Emission of Radiation
LASIK	Laser in situ keratomileusis
LOA	Limits of agreement
LogMAR	Logarithm of the minimum angle of resolution
mm	Millimetres
MMC	Mitomycin-C
NCL	Non-contact lens
NCT	Nasal corneal thickness
OCT	Optical coherence tomography
POTF	Pre-ocular tear film
PRK	Photorefractive keratectomy
RR	Relative repeatability
SAI	Surface Asymmetry Index
SCL	Soft contact lens
SCT	Superior corneal thickness
SD	Standard deviation
SEAL	Superior epithelial arcuate lesion
SiHy	Silicone hydrogel
SimK	Simulate keratometry
SRI	Surface Regularity Index
TCT	Temporal corneal thickness
TL	Thinnest pachymetry location
TMS-1	Topographic Modelling System
UDVA	Unaided distance visual acuity
US	Ultrasound
UK	United Kingdom
UV	Ultraviolet
VA	Visual acuity
VAR	Visual acuity rating
WT	Wearing time

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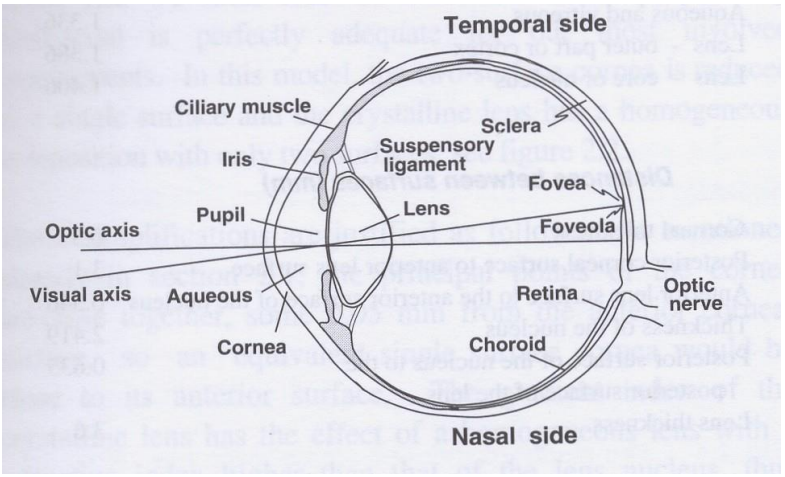
1 CHAPTER ONE: THE CORNEA AND REFRACTIVE ERROR

1.1 The anterior segment of the eye

The anterior segment of the eye includes the tear film, sclera, conjunctiva, limbus, cornea, anterior chamber, iris and crystalline lens (Figure 1-1). Soft CL (SCL) wear can result in changes to the anterior segment including changes to corneal shape, hydration levels and sensitivity to stimuli (Alba-Bueno et al., 2009; Schornack, 2003). These effects may be attributed to the mechanical effect of wearing the SCL or the reduction of oxygen transmission to the corneal layers (Jones and Jones, 2001).

Figure 1-1: Schematic drawing of the human eye



(Tunnacliffe 1993)

1.1.1 Pre-ocular tear film

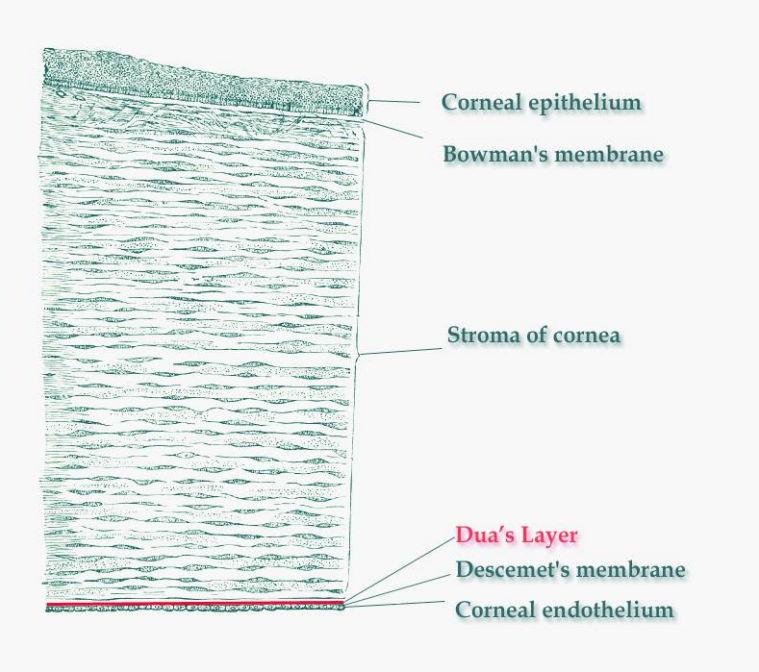
The pre-ocular tear film (POTF) is composed of 3 layers (mucus, aqueous and lipid) (Klyce, 2000). In order to function as a refractive surface, it must be smooth and transparent (Doshi, 2004). The POTF nourishes the corneal epithelium by providing essential oxygen and nutrients, and also contains antibacterial proteins, which protect

against infection (Kaufman and Alm, 2002). The POTF can be depleted with SCL wear resulting in corneal damage and changes in visual acuity (VA) and contrast sensitivity function (CSF) (Alonso-Caneiro et al., 2009; Guillon and Maïssa, 2005; Nichols and Sinnott, 2006; Ruben et al., 1976).

1.1.2 The cornea

The cornea is an avascular structure, which forms a robust outer barrier, protecting the inner structures of the eye. The cornea obtains nutrients through diffusion from the POTF, aqueous humour and the limbus (Yeniad et al., 2003). Along with the POTF, it provides two thirds of the refractive power of the visual system, focusing light on the retina (Klyce, 2000; Mejía-Barbosa and Malacara-Hernández, 2001; Rabinowitz, 2006). For an image to focus on the retina, the cornea must have the correct curvature and refractive index. Each layer of the cornea has its own refractive index (epithelium: 1.404, stromal anterior surface: 1.380 and posterior surface: 1.373) which contributes to corneal refractive power (Patel et al., 1995). However, a standard corneal refractive index of 1.3375 can be taken which accounts for both the front and back corneal surface (Mejía-Barbosa and Malacara-Hernández, 2001). The cornea is comprised of 6 layers: the epithelium, Bowman's membrane, the stroma, Dua's layer, Descemet's membrane and the endothelium (Dua et al., 2013).

Figure 1-2: Diagram of human corneal layers



Sourced from Gray's Anatomy / Sci-News.com (Mizuno, 2013)

1.1.2.1 The epithelium

The epithelium is the outermost layer of the cornea (Figure 1-2). The position of the epithelium and the associated differences in refractive index between it and the POTF, mean that the epithelium plays the largest role in light scatter induced by SCL wear (Wang et al., 2004a). The epithelium is coated by the POTF and measures approximately 50µm thick (Edelhauser and Ubels, 2003; Holladay, 2008a; Knox Cartwright and Hull, 2008). It's function is to form a protective barrier, to prevent micro-organisms within the POTF penetrating to the stromal level; this prevents infection in the eye. Prolonged periods of SCL wear can result in the erosion of discrete areas of epithelial cells (Liesegang, 2002). This can result in a loss of epithelial integrity, which could provide a possible route for fungal, viral or bacterial infection (Egorova et al., 2008; Larke, 1997a). Reduction of epithelial thickness, found with long-term SCL wear, is inversely related to the oxygen transmissibility (DK/t) of the

SCL (González-Pérez et al., 2003; Holden et al., 1985; Sweeney, 2003). DK/t is calculated from the oxygen permeability (DK) of the SCL material and the thickness (t) of the SCL. The units for DK/t are (cm/sec)($ml O_2$/ml x mmHg). Recovery of epithelial thickness can take up to 1 month to resolve following cessation of SCL wear (Holden et al., 1985). Additionaly, the epithelial barrier function reduces with extended wear (EW) of both high and low DK/t SCL materials (Lin et al., 2003). It is not known if this is due to corneal hypoxia or mechanical trauma or both. Daily wear (DW) of hydrogel SCLs can result in an increase in epithelial cell size compared with both NCL subjects and those wearing high DK/t SiHy CLs (Stapleton et al., 2001). A healthy epithelium is essential for corneal healing after CRS. Following PRK and LASEK the epithelial cell layer must regenerate following its complete (PRK) and temporary (LASEK) surgical removal. An intact epithelium is necessary in order to reduce stromal haze following LASIK (Nakamura et al., 2001). Although the role of therapeutic bandage SCLs in epithelial healing and recovery times following CRS has been explored (Eliaçık et al.; Plaka et al.), the role of prior SCL wear in the healing process following CRS has not been previously investigated.

1.1.2.2 Bowman's layer

The second corneal layer, called Bowman's membrane is acellular. This layer is comprised of connective tissue measuring 10μm thick centrally and provides tensile strength (Kaiser et al., 2013). Bowman's membrane does not have the capability of regeneration. Therefore, following trauma or surgical removal such as with PRK/LASEK there is a permanent loss of this layer (Doshi, 2004).

1.1.2.3 The stroma

The third layer is the corneal stroma, which accounts for 90% of corneal thickness (Edelhauser and Ubels, 2003; Efron, 2007; Kaufman, 2002). The stroma is predominantly made up of collagen fibrils (Efron, 2007). The collagen fibrils in Bowman's membrane and the stroma provide most of the cornea's tensile strength (Dupps and Wilson, 2006). Corneal transparency is dependent on regular arrangement of these collagen fibrils (Meek et al., 2003). This may be disturbed with SCL wear, as increased lactic acid through SCL induced hypoxia creates an osmotic load in the stroma (Jalbert and Stapleton, 1999). In order to maintain corneal transparency, it is important that the collagen fibrils be of a uniform diameter and are distributed in a regular manner (Kaufman, 2002). This is regulated by the endothelial pump, which brings water from the aqueous into the stroma (Liesegang, 2002; Wiffen et al., 2000). Small changes in the spatial ordering of the fibrils in the cornea, or an increase in the corneal thickness through oedema, can increase light scatter and reduce VA (Bergmanson and Chu, 1982; Klyce, 1991; Meek et al., 2003; Wang et al., 2004a).

Keratocytes are the main cellular element of the stroma. Their function is to secrete the protocollagen and proteoglycan matrix. Keratocytes also have a phagocytic function during inflammation (Doshi, 2004). Over-wear of low DK/t SCLs creates an anoxic environment in the cornea. Short-term exposure to this environment can result in corneal oedema and a reduction in the number of stromal keratocytes (Kallinikos, 2004). This may impact upon corneal thickness, as the function of keratocytes is to synthesise new stromal tissue, and keratocyte loss may induce stromal thinning (Efron, 2007). Keratocytes are activated when the stroma is damaged, such as during CRS or trauma, and a portion of these cells differentiate into myofibroblasts during wound

healing (Moilanen et al., 2003). Following surgery or trauma, there is increased light scatter due to the newly formed extracellular matrix of keratocyte cells and oedema (Böhnke and Masters, 1999; Tervo and Moilanen, 2003). Following keratocyte activation, wound healing in the stroma results in the resynthesis and cross linking of collagen (Kaufman and Alm, 2002). It is hypothesised that damage to keratocytes through anoxic conditions with SCL wear may then have an effect on corneal thickness and corneal healing following CRS. This thesis proposes to explore this hypothesis.

1.1.2.4 Dua's layer

The next layer, called Dua's layer, is acellular (Dua et al., 2013). Further research is necessary to investigate the clinical relevance of this layer to SCL wear and CRS. This research is beyond the scope of this thesis, as Dua's layer cannot be seen using the Pentacam or OCT.

1.1.2.5 Descemet's layer

The next layer is Descemet's layer which is the basement membrane of the endothelium. It aids corneal resistance to pathology and trauma (Klyce and Beuerman, 1988). Folds in Descemet's membrane can occur due to significant oedema induced by over wear of low DK/t SCLs (Brooks et al., 1986).

1.1.2.6 The endothelium

The inner most corneal layer is the endothelium (Kaufman, 2002). It comprises a single layer of hexagonal cells measuring 5μm thick centrally (Knox Cartwright and Hull, 2008). The function of the endothelium is to maintain corneal clarity as it maintains

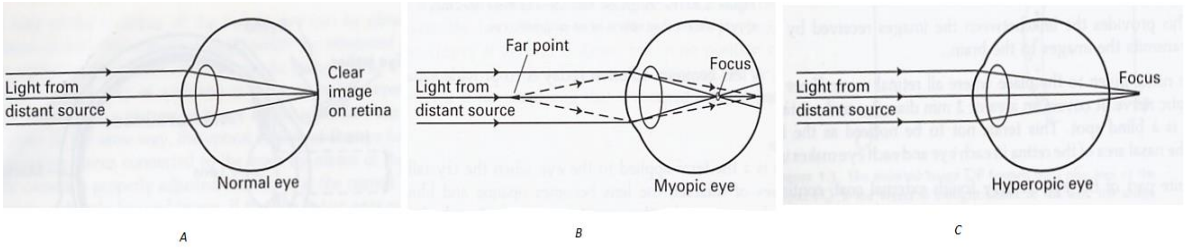
stromal deturgescence, and act as a barrier system which allows nutrients to passively diffuse across the endothelium from the aqueous humour into the stroma (Doshi, 2004).

In order to maintain corneal function, a stable endothelium must have an adequate cell density comprising cells of a uniform size and shape (Meek et al., 2003). Endothelial cells do not undergo mitosis (cell reproduction) after the age of 17 years and therefore naturally diminish through life (Efron, 2007; Larke, 1997b). Variations in endothelial cell size (polymegathism), and changes to the hexagonal cell shape (pleomorphism) are associated with long-term SCL wear (Carlson et al., 1988; Leem et al., 2011; Sanchis-Gimeno et al., 2003; Setälä et al., 1998b). Polymegathism and pleomorphism may indicate altered cell function and a reduction in corneal endothelial health (Lee et al., 2001a). It has been hypothesised that corneal hydration control is impaired in corneas with endothelial morphological changes (Nieuwendaal et al., 1994). There is a significant correlation between duration of SCL use and morphological changes in the endothelium (Lee et al., 2001a; Setälä et al., 1998a). Endothelial changes are thought to be related to an alteration in cell metabolism caused by hypoxia induced with SCL wear and appear to be irreversible (Sanchis-Gimeno et al., 2003). A healthy endothelium, prior to surgery, is important for corneal endothelial resiliency following CRS (Dawson et al., 2009; Edelhauser and Ubels, 2003). It has been shown that when endothelial cell density (ECD) reduces below 200 to 400 cells/mm^2, corneal hydration cannot be regulated sufficiently resulting in oedema and increased light scatter (Latour et al., 2010).

1.2 Refractive error

Emmetropia refers to the refractive state where an image is focused on the retina (Patel and Bourne, 2009). Ametropia exists when incoming light rays are not focused on the retina and can be classified according to where the focus lies in relation to the retina. If a point object comes to a point focus in front of the retina, the eye is myopic. Whereas, hyperopia occurs when the point focus lies behind the retina. Additionally, there is a situation, known as astigmatism, in which a point object forms two, mutually perpendicular, line foci. These may lie within the eye, behind the retina, or one on each side of the retina (Figure 1-3) (Ang et al., 2009).

Figure 1-3: Refractive errors of the human eye



Emmetropia (A), myopic (B) and hyperopic (C) refractive errors (Wakefield, 1994) .

1.2.1 Visual acuity

Visual acuity (VA) is a quantitative measurement of vision (Westheimer, 2002). Good VA is dependent on the cornea's performance as an optical element. If the eye is ametropic, the overall power of the eye can be corrected for by the use of spectacles, contact lenses (CLs) or CRS. The aim of CRS is to achieve unaided distance visual acuity (UDVA) which is similar to best corrected visual acuity (BCSVA) pre-operatively, thus ensuring patient satisfaction (Alió et al., 2008b; O' Connor et al., 2006; Taneri et al., 2004b).

1.2.2 Contrast sensitivity

Contrast sensitivity function (CSF) is a measure of functional vision and can be reduced even when high contrast VA remains good (Regan and Neima, 1983). CSF can be reduced with low DK/t hydrogel SCL wear, and following CRS (Grey, 1987; Holladay et al., 1999; Marcos, 2001; Yasoubi et al., 2008).

1.2.3 Contact lenses

A CL is a refractive or therapeutic lens, which is placed directly onto the anterior surface of the eye (Gordon, 1976).

1.2.4 CL materials

The most commonly worn CL materials are soft and include hydrogel and SiHy materials (Efron et al., 2014; Morgan et al., 2011; Schorner, 2010). Young's modulus describes the rigidity of the CL and the way the material can resist strain to keep its shape. SCLs with a higher modulus are more rigid (French, 2007). Hydrogel SCLs contain 2 main components: a stable cross-linked polymer matrix and a less stable aqueous (water content) component which can vary with environmental factors (Plotnik et al., 1991a). The DK/t value of a hydrogel SCL is dependent on the aqueous component (Plotnik et al., 1991a). SiHy SCLs are composed of a polymer of silicone and hydrogel. These materials have significantly increased DK/t compared with conventional hydrogel due to the incorporation of silicone (Jones et al., 2002), meaning these SCLs can be worn for EW (Schorner, 2010; Sweeney, 2003). SiHy SCLs are grouped into first (G1SiHy), second (G2SiHy) and third generation (G3SiHy) materials, the properties of these are summarised in Table 1-1.

Table 1-1: Properties of silicone hydrogel CL materials

Generation	SiHy properties
1	-High DK/t -High modulus -Low water content
2	-Mid range DK/t -Modulus comparable with hydrogel CL -Higher water content
3	-High DK/t -Low modulus -Higher water content

1.2.5 Corneal refractive surgery

CRS is a common elective medical procedure, which aims to correct refractive error and eliminate the need for spectacles and CLs (Sandoval et al., 2005). The most commonly performed CRS procedures are Photorefractive Keratectomy (PRK), Laser Assisted Sub-Epithelial Keratomileusis (LASEK) and Laser in Situ Keratomileusis (LASIK), a comparison of these procedures is provided in Table 1-2.

PRK involves complete removal of the corneal epithelium (Ang et al., 2009; Shah et al., 2001; Taneri et al., 2011). Ablation is then performed on the exposed stroma using an Excimer Laser. The Laser ablates the sub-basal nerves, Bowman's layer and a variable amount of stromal tissue depending on the change in prescription being attempted (Tervo and Moilanen, 2003). During LASEK, an alcohol solution is used to loosen the epithelial layer and remove it as a single flap of tissue (S et al., 2004; Taneri et al., 2004b). Following stromal ablation with the Excimer Laser, this flap is then replaced. The flap of tissue creates a mechanical buffer between the eyelids, tear film and stroma (Dupps and Wilson, 2006). This has a major effect in reducing both pain and haze compared with PRK (Taneri et al., 2011). There is a strong healing response invoked in the cornea through removal of the epithelium, which causes pain, swelling, light

sensitivity and blurred vision. To promote comfort and healing, a therapeutic SCL is inserted, following laser ablation, for 3-5 days until the new epithelial layer has regenerated. There can also be corneal haze formation following PRK (Tervo and Moilanen, 2003). This haze can be persistent up to 12 months post-operatively (Autrata and Rehurek, 2003). The large wound healing response generated as a result of PRK and LASEK accounts for a higher rate of refractive regression and haze compared with LASIK (Dupps and Wilson, 2006).

Table 1-2: Comparison of corneal refractive surgery procedures.

	PRK	**LASEK**	**LASIK**
Refraction correctable	Low to moderate myopia and astigmatism	Low to moderate myopia and astigmatism	Myopia to -10DS, Hyperopia to +4.50 DS, Astigmatism to -4.50 DC
Pain	24 - 48 hours	24 - 48 hours	Minimal
Post-operative medications	Topical 7- 8 weeks Oral 2 - 3 days	Topical 7- 8 weeks Oral 2 - 3 days	Topical 2-3 weeks
Functional visual recovery	3 days to 1 week	3 days to 1 week	< 12 hours
Refractive stability	Achieved at 3 weeks to several months	Achieved at 3 weeks to several months	Achieved at 1 to 6 weeks
Complications	Haze	Haze	Flap complications such as free caps, button hole flaps, incomplete flaps associated with micro-keratome. Flap wrinkles, flap melt, epithelial ingrowth, diffuse lamellar keratitis, interface debris
Risk of scarring	1-2%	< 1-2%	< 1%
Risk of dry eye	1-8 weeks	1-8 weeks	Possibly longer than 12 months
Thin corneas	Usually not contra-indicated	Usually not contra-indicated	Usually contra-indicated if less than 500μm

A summary of the indications and outcomes from commonly performed CRS procedures. The differences between these CRS procedures are highlighted (Taneri, 2004).

During LASIK, a corneal flap of predetermined thickness is resected using either a femtosecond LASER or a microkeratome blade (Ang et al., 2009). The Excimer Laser is then used to ablate the corneal stroma. Unlike PRK or LASEK, the epithelium and Bowman's layer remain relatively undisturbed. With LASIK, there is no major epithelial defect, thus no large healing response is invoked resulting in faster visual

recovery compared with PRK and LASEK (Rao and Padmanabhan, 2000). Long-term follow-up shows LASIK to be a relatively safe and effective procedure for the treatment of myopia (Alió et al., 2008b; Alió et al., 2008a; Condon et al., 2007; Taneri et al., 2011).

1.2.6 High order aberrations and wavefront technology

Low order aberrations (first and second order) relate to the sphero-cylindrical refractive errors and prismatic errors and can be corrected by spectacles (Yoon et al., 2004). High order aberrations can be analysed in terms of Zernike polynomials. Wavefront analysis technology can be used to correct high order aberrations during CRS. The wavefront analysis technology used to measure and correct high order aberrations described in this thesis are discussed in section 2.5. SCL wear for myopia can also induce high order aberrations (Roberts et al., 2006). The high order aberrations induced by SCL wear tend to vary according to the SCL material and design (Berntsen et al., 2009).

1.3 Corneal parameters

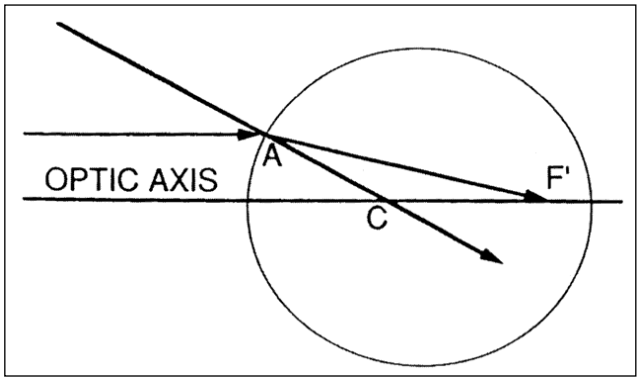
Prior to CRS, the cornea is evaluated using diagnostic techniques that measure shape (topography) and thickness (pachymetry). The instrumentation used in this research for these measurements are described in Chapter 2. However, the theory behind the techniques is described in the following section.

1.3.1 Corneal parameters: shape

The anterior cornea contributes approximately two thirds of the eye's total refractive power. Small changes in curvature can result in large changes to image focusing on the retina (Cairns and McGhee, 2005; Corbett et al., 1999; Klyce, 2000).

Corneal curvature can be expressed in millimetres (mm) or dioptres (D). A steep corneal surface has a small radius of curvature (mm) and high corneal power (D). As the cornea becomes flatter, the radius of curvature becomes larger and the corneal power smaller. The dioptric power value only has a relative relationship to the true corneal power. In the optical sense, if a peripheral light ray enters the eye, the light ray is refracted resulting in a difference between the optical axis of this ray and the true optical axis of the system (Figure 1-4). Clinically, when monitoring changes in corneal curvature due to SCL wear or disease, it is the changes in the relative values that are important rather than the absolute value of the radius or dioptric power of the cornea (Mandell, 1992).

Figure 1-4: Single refracting surface power



When using the formula P = (n-1)/r: the surface power at a peripheral point A is referred to the optical axis AC instead of the true optical axis of the system. Therefore, one would expect a defocus of an amount equivalent to the difference in dioptres at the central and peripheral points (Mandell, 1992).

The 'normal' cornea is an aspheric surface, which is prolate (has a central steep contour and flattens toward the limbus) (Dingeldein and Klyce, 1989a; Holladay and Janes, 2002). Following myopic CRS the corneal shape becomes more oblate (flatter centrally and getting progressively steeper toward the periphery) (Holladay and Janes, 2002).

1.3.1.1 Methods commonly used to describe curvature

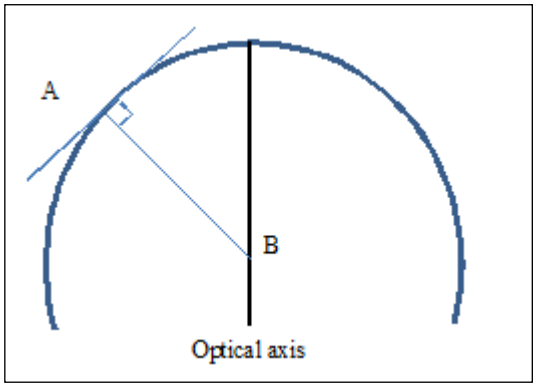
Keratometry and topography are techniques used to measure the curvature of the cornea, carried out using a keratometer or a videokeratoscope (Rabinowitz et al., 1993). Keratometry is based on the relationship between the size of an object and the size of its image reflected within a 3mm para-central annulus of the cornea. Keratometers do not measure the central zone (0 - 1.6mm in diameter) (Holladay, 2005). Simulated keratometry (SimK) readings are calculated by the Pentacam (Oculus, Germany) and provide values of the steep and flat meridians from the same para-central area of the cornea that a traditional keratometer measures. SimK values have been shown to correlate well with traditional keratometry values (Klyce, 2000).

A videokeratoscope, used to measure corneal shape, employs optical principles similar to those of the keratometer, but measures curvature at a greater number of locations over a larger surface area. Computer algorithms are used to analyse the data collected, presenting the results in a number of different ways, including measurements and graphical representations of corneal shape (Mandell, 1992; Rabinowitz, 2006; Rabinowitz et al., 1993).

Two methods of calculating corneal curvature are used: sagittal and tangential which are described in detail below. Sagittal and tangential curvature values are similar at the centre of the cornea, but they differ in the periphery with the tangential calculations resulting in flatter values than do the sagittal calculations for the same location (Corbett et al., 1999). Both sagittal and tangential topography ought to be used for corneal assessment as each method has its own characteristics and advantages (El Hage and Leach, 1999).

Sagittal or axial radius of curvature is the perpendicular distance from the tangent at a point to the optical axis (Tang et al., 2005). Similar to keratometry, this assumes the optical axis is at the centre of curvature and provides an average value of adjacent corneal curvature. This method assumes the centre of curvature for a specific surface point is located on the optical axis; however, this is true only for a sphere. As most corneas are nearly spherical at the apex, this assumption is acceptable for keratometry, which measures the para-central zone only. The sagittal radius gives a good indication of optical power for normal corneas. Following CRS or with disease processes such as keratoconus, the refractive indices used in calculations of sagittal topography may result in errors as these refractive indices assume a normal ratio of anterior to posterior corneal surface curvature (Cairns and McGhee, 2005). Sagittal curvature is generally recommended to be used for corneal power and intra-ocular lens calculations as well as screening for pathology prior to CRS (Friedman, 2009).

Figure 1-5: The sagittal radius of curvature

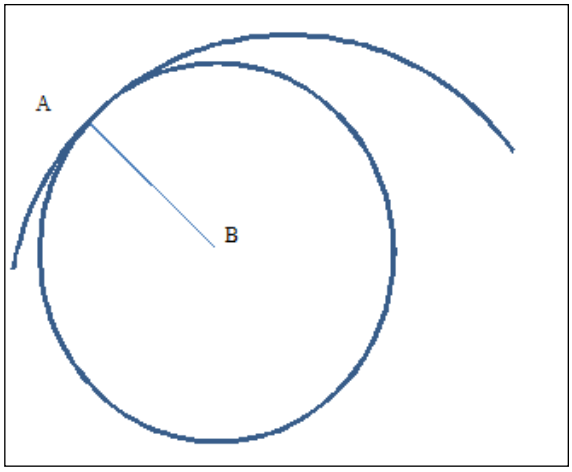


The sagittal or axial radius of curvature is the distance from point A (the point at which the perpendicular line from the tangential line running through the point A on the anterior or posterior corneal surface) and the central optic axis (point B) (Image adapted from Saitoh et al. 2004).

The tangential radius of curvature is the measure of the curvature at each point with respect to its neighbouring points, and uses a best-fit sphere (BFS). As its centre lies off

axis, it gives an indication of local power only. Tangential curvature measurements do not assume normal incident rays and, are more accurate toward the periphery, and are less affected by instrument misalignment. This method is more sensitive than sagittal curvature to subtle deviations from the normal corneal shape, such as those which occur in early keratoconus (Klein and Mandell, 1995a; Pascucci, 2007). Tangential topogrpahy maps are useful for detecting local irregularities in corneal shape, such as those induced by CRS, SCL wear or ectasia, and in the examination of the peripheral cornea (El Hage and Leach, 1999; Pascucci, 2007).

Figure 1-6: The tangential radius of curvature



The tangential radius of curvature is the radius of curvature of the arc (AB) at the single point A on the anterior or posterior corneal surface (Image adapted from Saitoh et al. 2004).

Corneal elevation

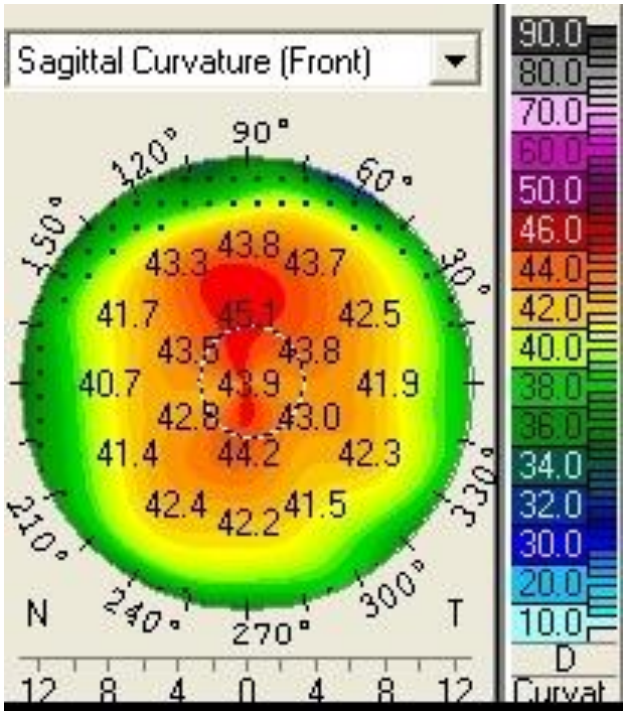
Although the cornea has a prolate shape, it is often compared with a reference spherical surface known as a best fit sphere (BFS) (Hashemi and Mehravaran, 2010). When corneal curvature is being measured the diameter and position of the BFS is altered to fit the corneal surface using a least squares methodology to determine the most appropriate reference sphere (Hashemi and Mehravaran, 2010). Elevation is a relative

measurement of the difference in height between a point on the cornea, relative to a reference surface such as a BFS (Naroo and Cerviño, 2004). The default floating BFS provides a useful means of analyzing the surface profile of the entire cornea (Cairns and McGhee, 2005). Elevations are plotted against the BFS where the algebraic sum of points above (elevations) and below (depressions) the sphere are equal (Lim and Fam, 2006). This method accurately represents true corneal shape, as it is independent of corneal axis or orientation (Mejía-Barbosa and Malacara-Hernández, 2001).

1.3.1.2 Method of displaying corneal shape

Most computerised corneal topography systems represent the corneal surface in terms of a topographical map, this is similar to an Ordnance Survey map where points of equal height are displayed with equal numbers.

Figure 1-7: Sagittal topography map



(Lloyd McKernan.2012)

Corneal quantitative indices

Corneal quantitative indices are single values, which summarise information derived from established measurements (including corneal thickness, central curvature, sagittal and tangential radius, height regularity indices: Fourier analysis and Zernike analysis). Indices assist in the identification, diagnosis and classification of corneal abnormalities such as keratoconus and the presence of previous CRS (Maeda et al., 1994; Rabinowitz and Rasheed, 1999; Wei et al., 2011). These indices are described in terms of various mathematical estimates of the visual disturbance that can be expected due to anterior corneal surface irregularities (Fedor and Kaufman, 2002). Corneal thickness, curvature and regularity indices measured with other topographers have been shown to be elevated with SCL wear (Alba-Bueno et al., 2009; Liu and Pflugfelder, 2000; Pflugfelder et al., 2002). The indices used in the Pentacam are outlined in

Table 1-3.

Table 1-3: Pentacam indices

Index		Abnormal	Pathological
Index of surface variance (ISV)	ISV- gives the deviation of individual corneal radii from the mean value. This value is elevated with corneal irregularity.	≥ 37	≥ 41
Index of vertical asymmetry (IVA)	IVA- gives the degree of symmetry of the corneal radii with respect to the horizontal meridian as axis of reflection, the symmetry of upper and lower area. This value is elevated in cases of oblique axes	≥ 0.28	≥ 0.32
Keratoconus index (KI)	KI - is elevated with keratoconus	> 1.07	> 1.07
Centre keratoconus-index (CKI)	CKI- is elevated with keratoconus	> 1.03	> 1.03
Radii minimum (Rmin)	Rmin- is the minimum sagittal curvature. This value is elevated with keratoconus	> 6.71	> 6.71
Index of height asymmetry (IHA)	IHA- gives the amount of decentration of height data between upper and lower areas in the 8 mm measurement zone. This value is steeper with keratoconus.	≥ 19	> 21
Index of height decentration (IHD)	IHD- is calculated from Fourier analysis of height and gives the degree of vertical decentration. It is steeper in keratoconus	≥ 0.014	≥ 0.016
Aberration coefficient (ABR)	ABR- is the value of the aberrations of the cornea calculated from Zernike analysis. If there are no corneal aberrations ABR = 0.0, ABR increases with increasing high order aberration (Iwanczuk, 2010).	≥ 1	≥ 1

Pentacam indices are derived from established measurements (central curvature, sagittal and tangential radius, height and corneal aberrations). The quantitative indices assist in the identification, diagnosis and classification of corneal abnormalities such as keratoconus and the presence of previous CRS, abnormal and pathological values are listed (Oculus, 2007).

1.3.2 Corneal parameters: thickness

Corneal pachymetry is the measurement of corneal thickness. Normal corneas are thinnest centrally and get progressively thicker toward the periphery (Doughty and Zaman, 2000). The average 'normal' human central corneal thickness (CCT) value is 534 microns (µm) (Doughty and Zaman 2000). CCT remains stable throughout life, however the peripheral cornea may thin with the ageing process (Doughty and Zaman, 2000). It is well accepted that there is a diurnal variation in corneal thickness. During sleep the human cornea swells by approximately 4%. Swelling rapidly subsides in the first hour after opening the eyes and remains at consistent levels through the day (Aakre et al., 2003; Du Toit et al., 2003; Efron, 2007; Giráldez-Fernández et al., 2008; Lattimore et al., 1999; Mandell, 1992). Diurnal changes in corneal thickness result from an osmotic response in the stroma to the change in tear pH levels, which occurs through evaporation from the POTF during opening the eyelid following sleep when the eyes are open (Liesegang, 2002a). Lattimore et al. (1999) found the maximum value for diurnal variation, at the corneal apex was 8µm. CRS corrects myopic refractive error by flattening the anterior corneal curvature with an associated reduction of corneal thickness using a laser (Ambrósio and Wilson, 2001; Arbelaez et al., 2009). It is important to obtain accurate corneal thickness measurements prior to CRS in order to ensure that an adequate residual bed thickness remains following CRS ablation. It is known that over wear of low-DK/t SCLs can results in oedema, giving rise to an artificial increase in corneal thickness. However, with long-term SCL wear of low DK/t SCLs, overall corneal thickness can be reduced (Holden et al., 1985). The influence of previous SCL wear on CCT following CRS has not been investigated previously.

1.3.3 The effect of disease processes on corneal structure

Primary corneal ectasia is a non-inflammatory disease in which the cornea protrudes forward due to abnormal stromal thinning. This results in exaggerated prolate corneal shape, irregular corneal astigmatism and myopic shift, all of which impairs visual quality (Dupps and Wilson, 2006). Corneal ectasia can occur naturally through disease processes such as keratoconus, keratoglobus, pellucid marginal degeneration and Terrien's disease, or can be induced following CRS (iatrogenic ectasia) (Hardten and Gosavi, 2009). SCL wear can induce corneal warpage that produces topography patterns that resemble those found in keratoconic ectasia (Wilson et al., 1990). These include steeper keratometry readings, increased variations in sagittal and tangential curvature, increased corneal toricity and larger and more variable shape factors (Lebow and Grohe, 1999). Corneal thickness varies from normal values with disease processes such as keratoconus (localised corneal thinning) and Fuchs' endothelial dystrophy (cornea becomes thicker) (Adamis et al., 1993).

The biomechanics of the cornea is altered in cases of ectasia. There is a reduction in keratocyte density, reduced collagen interweaving and increased hydrophilic proteoglycans (Dupps and Wilson, 2006). The presence of any corneal dystrophy is a contra-indication for CRS, as it may result in viscoelastic failure and abnormal repair. Therefore, topography and pachymetry are important screening tools to eliminate the presence of these diseases in CRS patients.

1.3.3.1 Forme fruste keratoconus

Forme fruste keratoconus (FFK) or sub-clinical- keratoconus is difficult to diagnose as there may be normal VA and no clinically visible signs of the disease (Wang et al., 2006). Topography is one of the most sensitive screening methods for FFK. The folloing topography findings are indicative of FFK (Belin et al., 2007b; Rao et al., 2002):

- An inferior area of steepening (I-S value) of the central vertical gradient in corneal power in the central 6mm of greater than 1.4 to 1.9D (Klyce, 2009) with an oblique cylinder
- Anterior steepness power of greater than 47D (equivalent to a corneal radius of curvature of 7.18mm)

Anterior and posterior corneal elevations are also higher in keratoconic patients (Rao et al., 2002). These presenting characteristics are similar to those seen with SCL-induced corneal warpage as discussed in section 4.1.1. It is important to be able to differentiate SCL-induced corneal warpage from FFK and also to detect early FFK prior to CRS in order to limit the risk of post-CRS ectasia (Pallikaris et al., 2001; Srivannaboon et al., 2012). This thesis explores the impact of SCL wear on the accuracy and stability of corneal measurements following cessation of SCL wear.

2 CHAPTER TWO: INSTRUMENTATION

This chapter will review the instrumentation used for the acquisition of corneal measurements prior to, during and following CRS.

2.1 The Pentacam

The Pentacam (Oculus, Wetzlar, Germany) is a non-contact ocular tomographer, and was used to obtain corneal curvature and thickness measurements in this research. Tomography provides a 3-D reconstruction of the entire cornea, so that the anterior and posterior surfaces can be measured (Ambrósio and Belin, 2012). Images are captured automatically on the Pentacam with a rotating Scheimpflug camera and comprehensive analysis of the anterior ocular segment is produced (Junk, 2003).

Figure 2-1: The Pentacam tomographer.

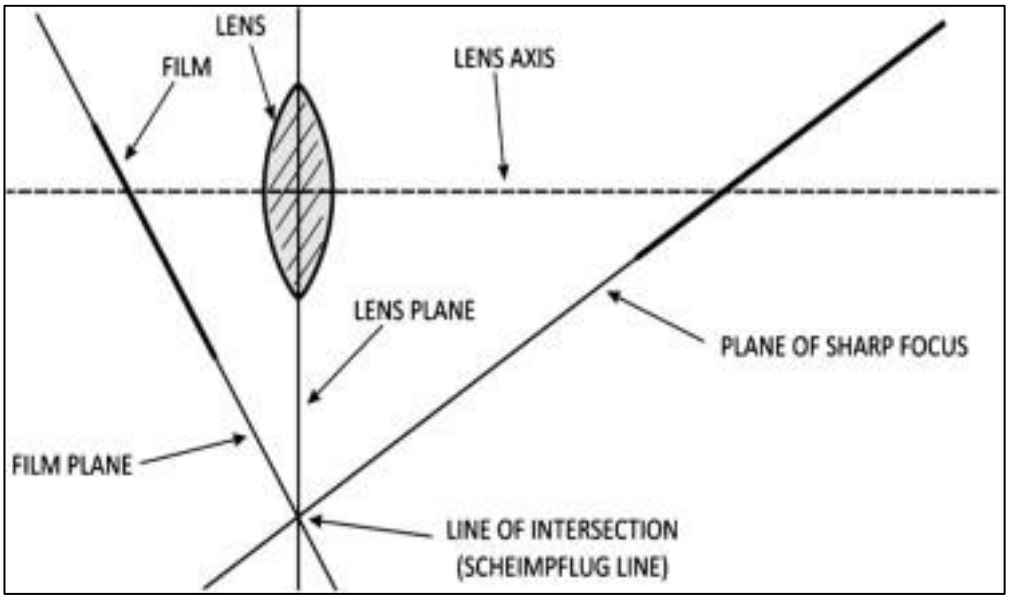
(Lloyd McKernan.2012)

2.1.1 Principles of Scheimpflug photography

The Scheimpflug camera operates according to the Hinge Rule, which states that three planes must converge along a common line (Figure 2-2) (Merklinger, 1996). The

Scheimpflug technique operates on this principle, where an image of an oblique object can be obtained with sufficient depth of field once the plane of the object, the plane of the camera objective and the image plane meet at one point (Hockwin et al., 1990).

Figure 2-2: The Scheimpflug principle describing three planes must converge along a single line. These three planes are the film plane, the subject plane and lens plane (Grewal and Grewal, 2012)

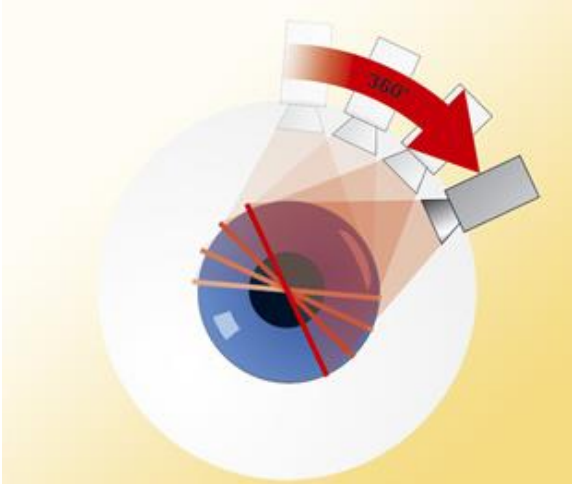


2.1.2 Pentacam instrument description

The Pentacam system uses a 14mm slit of blue light, at a wavelength of 475nm to illuminate the eye. A Scheimpflug camera and a monochromatic slit light source rotate together through 360° around the optic axis of the eye (Figure 2-3) (Choi et al., 2008). Accuracy is improved with a peripheral camera, which captures eye movements that occur during recording and makes appropriate corrections, enabling the instrument to re-register the central point for all meridians captured. A total of 25,000 elevation values are detected and processed (Choi et al., 2008). These values are mathematically transformed into a three-dimensional volume that can be visualized on any meridian (Masters, 1997). In study 5, the Pentacam HR was used. In this newer version, the

resolution of the images has improved as 138,000 points are processed (Hashemi and Mehravaran, 2010). The Pentacam topographers measure geometrical corneal slope values, which are then converted into sagittal and tangential curvature radius (mm) values. The Pentacam automatically converts these geometrical radius (mm) values to optical power values (D) using the formula: (1.3375 – 1) x (1000) / Rmm, where the refractive index of the cornea is taken as 1.3375 (Oculus, 2007).

Figure 2-3: Pentacam camera rotation (image from http://www.pentacam.com/sites/messprinzip.php)



The slit beam penetrates the anterior ocular segment and passes through zones of varying reflectance and light scatter. The transparent cells of the anterior and posterior corneal surfaces disperse light differently and therefore both surfaces can be detected (Choi et al., 2008). This allows the calculation of the corneal radii for each point on the topographic surface map. Reflection and light scatter result in contrast differences. Using a densitometer, the difference in contrast can be recorded as differences in density (Hockwin et al., 1990; Kirkwood et al., 2009; Takacs et al., 2011; Wegener and Laser-Junga, 2009). Corneal transparency can be examined using the densitometry function of the Scheimpflug camera in the Pentacam (Jinabhai et al., 2012b; O' Donnell

and Wolffsohn, 2004; Rashad, 2012). The Pentacam provides an objective measure using a scale from 0 (clear, no haze) to 100 (completely opaque) (Takacs et al., 2011).

Each Pentacam instrument is calibrated in the factory and self-calibrates each time the instrument is started. Following each scan acquisition, the Pentacam software provides the user a value for quality specification. Only scans of good quality ('OK' displayed on the overview screen) were used for analysis and the scan with the highest percentage values for these quality specification values was chosen for analysis in this research.

2.2 Ultrasound pachymetry

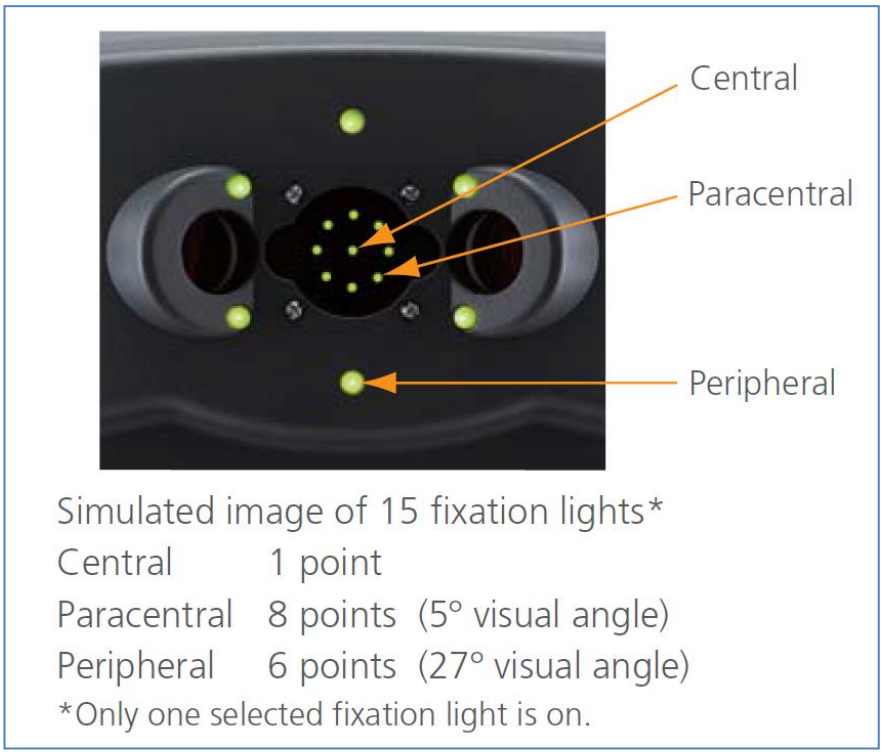
An MMD Palmscan AP 2000 (Micromedical Devices, Calabasas, USA) ultrasound (US) pachymeter was used in this study. Ultrasound (US) pachymetry is considered to be the gold-standard for corneal thickness measurements (Doors et al., 2010; Paul et al., 2008). US pachymetry works by taking the average scan of several rapidly repeated A-scans, which are one dimensional amplitude modulation scans. US is commonly used as it is relatively inexpensive, portable and easy to operate (Parafita et al., 2000). However, the accuracy of US pachymetry depends on the placement of the probe on the centre of and normal to the cornea, displacement of the tear layer and the use of anaesthetic drops (Paul et al., 2008).

2.3 Nidek CEM-530 specular microscope

The CEM-530 (Nidek, Aichi, Japan) specular microscope was used to analyze the corneal endothelium. The CEM-530 specular microscope projects light onto the optical interface between the corneal endothelium and the aqueous humour. The attached camera captures a digital image of the pattern of light reflected by the cellular structure of the endothelium, and the proprietary software then analyses this in terms of cell size,

shape and density. This instrument has the ability to capture para-central images (8 points at a 5º visual angle within a 0.25 x 0.55mm field) in addition to the conventional central and peripheral points (Nidek, 2012) (see Figure 2-4).

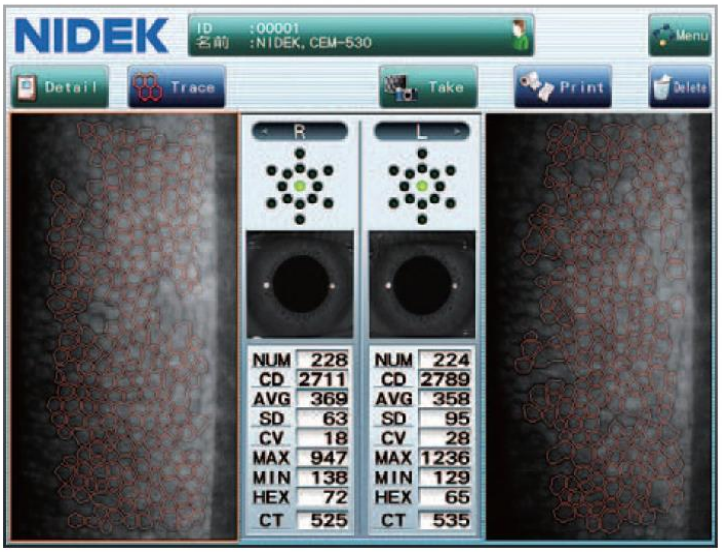
Figure 2-4: Corneal points captured by the CEM-530 specular microscope



(Nidek CEM 530 product manual, 2012).

Sixteen images of each point were captured and automatically sorted in terms of quality. The best quality image, as chosen by the instrument was analysed in this research. Endothelium cells were analysed in terms of endothelial cell density (ECD; cell/mm^2), mean cell area (MCA; µ^2), coefficient of variation of cell size (COV) and hexagonality (%).

Figure 2-5: Endothelium output analysis screen in the CEM-530 specular microscope

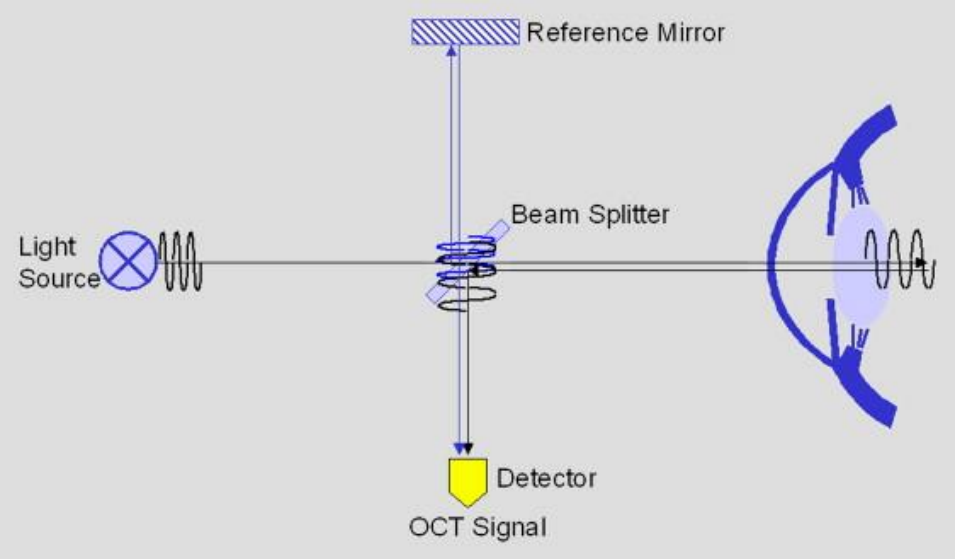


(Nidek CEM 530 product manual, 2012)

2.3.1 Optical coherence tomography

Optical coherence tomography (OCT) works by passing an infrared light beam through tissue and collecting the reflected signal (Stehouwer et al., 2010). Different tissue layers will produce a variety of backscatter and reflected light, allowing different structures and tissue layers to be differentiated (Chen and Lee, 2007; Gabriele et al., 2011). Inevitably, the clarity of the tissue in the optical pathway can affect the strength of the reflected beam (Mahon and McCrudden, 2011).

Figure 2-6: The basic principles of OCT



Light is directed into the eye from the light source and reflections emitted from the various layers in the eye are received by the detector and processed to form a 2D image (Doors et al., 2010).

Anterior segment OCT allows the visualisation of the cornea, anterior chamber angle and anterior surface of the crystalline lens (Chen and Lee, 2007). All corneal layers can be differentiated, thus pachymetry and the depth of corneal scarring and LASIK flaps can be evaluated (Mahon and McCrudden, 2011). OCT radial and raster scanning is used to measure corneal thickness for CRS and diagnosis of corneal conditions such as keratoconus (Li et al., 2008b; Tang et al., 2006).

2.3.2 Three dimensional OCT -2000

The 3D OCT-2000 (Topcon, Tokyo, Japan) was used in this research. The 3D OCT is based on spectral domain OCT. The technology captures scans on a charge-coupled device and uses Fourier transformation of the entire signal for image analysis. A default 6mm line scan was used for imaging the anterior segment. Due to spectral domain OCT speed and sensitivity, 3D tissue scans are possible (Chen and Lee, 2007; Gabriele et al.,

2011). Spectral domain OCT instruments which use shorter wavelengths (~830nm) can achieve higher resolution (~5µm). However, this may result in increased light scatter compared with those instruments of longer wavelength (~1340nm, e.g. Visante OCT). This may be of note with previous SCL wear, where light scatter in the cornea may be increased in cases of hypoxia and oedema. To date, the impact of SCL wear on the accuracy of OCT measurements has not been reported.

2.4 Instrumentation used during refractive surgery

Studies 2 and 5 involved analysis of CRS outcomes. During the course of this research, the CRS clinic where study 2 was carried out was taken over by different management and was finally forced to close due to the economic recession. Study 5 was carried out at a second CRS clinic where the Excimer and femtosecond Laser platforms were different. The new management of the CRS clinic during study 2 implemented a change in clinic policy regarding cessation of SCL wear prior to CRS (from 2 weeks to 24 hours), and also changed the Excmier Laser platform. It is recognised that the variance in CRS instrumentation in study 2 and 5, and ophthalmologists in study 5, is a flaw in the study design which must be considered. Statistical analysis was designed so that comparisons were carried out between SCL and NCL control groups who had the same procedures completed by the same practitioners using the same equipment in each of the studies. The flaws associated with this retrospective study design are discussed in greater detail in chapters 4, 5 and 8. Details of these Lasers and wavefront analysis systems used to ablate corneal tissue in LASIK, PRK and LASEK are outlined in Table 2-1.

Table 2-1: Instrumentation used during CRS

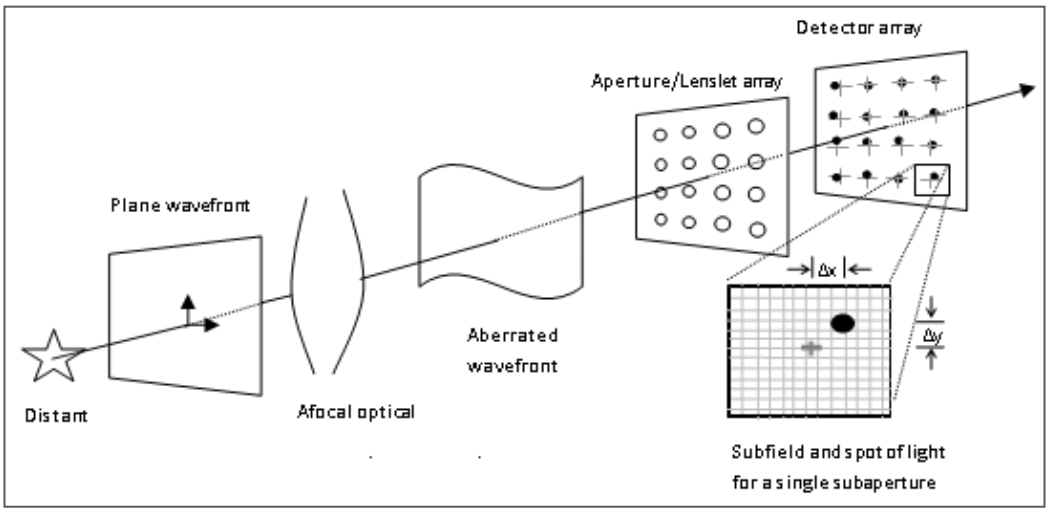
Study number, clinic	**Lasik flap creation**	**Excimer laser used**	**Wavefront anlysis**
1 & 2. Eye Laser Ireland (2 weeks SCL cessation policy)	Intralase ™ femtosecond laser (AMO, Irvine, CA, USA)	Visx Star S4 (AMO, USA)	CustomVue WaveScan WaveFront ® aberrometry system (Visx, Santa Clara, CA, USA)
2. Ultralase (24 hours SCL cessation policy)		Technolas 217z (Bauch and Lomb, Rochester NY, USA)	Zywave Zyoptix ® (Technolas, Basuch & Lomb, Germany)
5. Wellington Eye Clinic (2 weeks SCL cessation policy)	FS200 Wavelight femtosecond laser (Alcon Laboratories, Inc. USA)	WaveLight EX500 excimer laser (Alcon Laboratories, Inc. USA)	Allegretto Wavelight® Analyzer (Tscherning, Alcon Laboratories, Inc. USA)

2.5 Wavefront technology in corneal refractive surgery

Wavefront analysis technology in CRS is used to measure ocular aberrations (where light is deviated from the normal pathway, producing unwanted visual disturbances). Hartmann-Shack aberrometers are used in CRS to measure high and low order ocular aberrations, taking into account the patient's prescription, pupil diameter and corneal curvature. The Hartmann-Shack device is a sensor used to measure the aberrations of a wavefront which originate from a point of light on the retina, and is then refracted by the various surfaces it passes through on the way out of the eye (Liang et al., 1994). During wavefront analysis measurement, a plane wavefront of light is sent into the eye in a regular pattern (Figure 2-5). The wavefront passes through an objective set of lenses (lenslet array), where the wavefront is split into individual beams, producing multiple images of the same retinal point of light. A detector array then measures the

distortion of the aberrated wavefront. Wavefront analysis technology allows for the detection of high order aberrations and calculates how to correct them using the Excimer Laser. This results in improved visual outcomes and better CSF following CRS (Padmanabhan et al., 2008). Eye trackers engaged during wavefront guided treatments can measure and compensate for cyclotorison (rotation of the eyeball during CRS) and therefore enable greater precision and predictability for the Excimer Laser ablation process (Chang, 2008).

Figure 2-7: Hartmann-Shack wavefront analyser



Schematic diagram of Hartmann-Shack wavefront analyser. An incident wavefront moves through the Lenslet array to the detector array, where the difference between the plane and aberrated wavefront is measured (Spiricon, 2004).

The CustomVue WaveScan WaveFront ® system (Visx, Santa Clara, CA, USA), used in study 1, allowed 2 levels of treatment: with or without wavefront anlysis. Only those subjects for whom wavefront analysis treatment had been performed were included in the analysis.

The Zywave Zyoptix ® system (Technolas Perfect Vision, Munich, Germany) used in study 2 allowed 3 treatment options; plano-scan (no wavefront), zyoptix personalised or aspheric. The personalised wavefront-based treatment profile calculation was designed for each eye according to the Hartman-Shack Zywave and the Orbscan II tomographer (Technolas Perfect Vision, Munich, Germany). In addition to the Zywave- and Orbscan II- designed treatment profiles, the aspheric wavefront treatment profile incorporated an algorithm, which designed treatment profiles based on topography, asphericity, planned refractive correction and optical zone (Bausch&Lomb, 2007). In order to account for the impact of wavefront on the CRS outcomes, the groups were compared, statistically, according to the type of wavefront treatment applied. The Allegretto Wavelight® Analyzer used in study 5 offers 3 treatment types: wavefront-optimised, wavefront-guided and topography-guided. Wavefront-optimised CRS treats refractive error (sphere and cylinder) but has no planned effect on high order aberrations including spherical aberration. All subjects included for analysis in study 5 had wavefront-optimised treatment carried out.

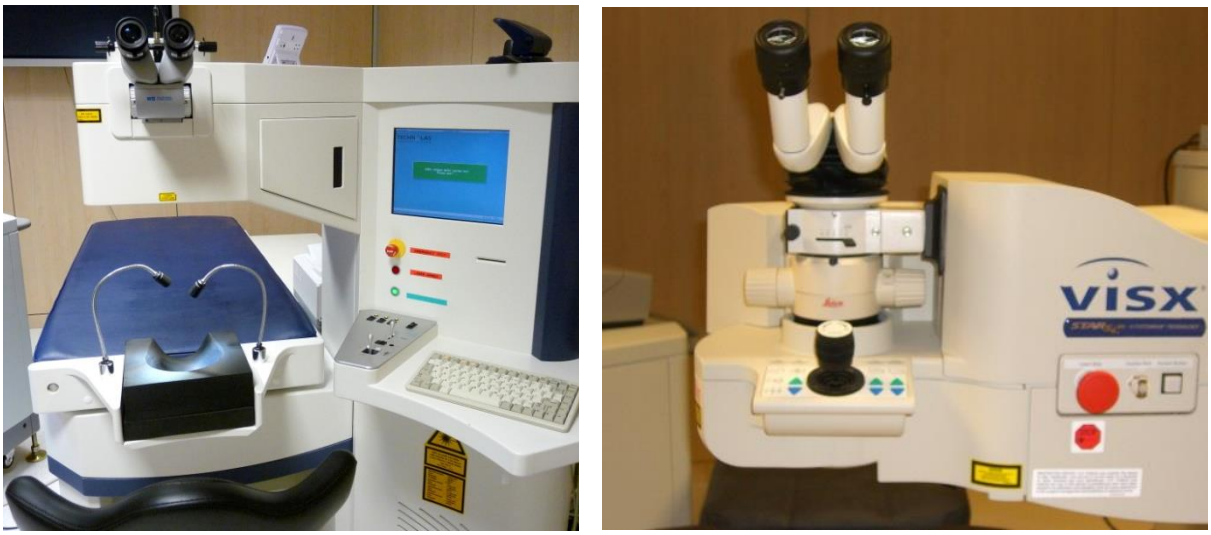
2.6 Lasers used during refractive surgery procedures

2.6.1 The Excimer Laser

An Excimer Laser is an argon-fluoride Laser which can be used for the removal of corneal tissue (keratectomy). The argon and fluorine gases are contained in a pressurised-cavity, and when high electrical-voltage is applied, the argon loses electrons. These electrons join with fluorine to form unstable compounds which rapidly dissociate, and in the process release ultraviolet (UV) light (Johnson, 2007). The UV light has a wavelength of 193nm and delivers 6.4 electron volts of photon energy

(Stevens, 2008). This cool UV light beam breaks the bonds that form the peptide backbone of the corneal collagen molecules, without harming adjacent tissues (Maurino and Nguyen, 2008). This results in molecular fragmentation, removing 0.21-0.27 microns of corneal tissue with each pulse (Johnson, 2007).

Figure 2-8: Technolas 217z (left) and Visx Star S4 (right) Excimer laser systems



(Lloyd McKernan, 2012)

2.7 The Femtosecond Laser

A femtosecond Laser was used to create corneal flaps during the LASIK procedures investigated in this research. Femtosecond lasers can be programmed to create flaps of 90-160µm thickness up to a diameter of 9.5mm. The femtosecond Laser delivers pulses of 1µm diameter at a predetermined depth in the cornea. The Laser pulse creates micro-photodisruption in the form of an expanding bubble (2-3µm) of carbon dioxide gas and water. These bubbles cleave the tissue and create a plane of separation. The bubbles can be created in a spiral or raster pattern (Kaiserman et al., 2008). In early LASIK procedures, a mechanical blade called a microkeratome was used to create corneal flaps. Since its introduction in 2002, the femtosecond Laser has become increasingly popular

for flap creation in LASIK refractive surgery. This due to the increased regularity and precision of flaps created by the femtosecond Laser (Kermani and Uwe, 2008; Neuhann et al., 2008; Von Jagow and Kohnen, 2009).

3 CHAPTER THREE: RESEARCH METHODOLOGY

The research was divided into 5 separate studies encompassing 2 retrospective and 3 prospective studies. These were all comparative studies in which normative data were obtained from a group of NCL patients who underwent the same procedures as the SCL wearing group. In order to ensure relevance, inclusion and exclusion criteria were strictly adhered to for all studies (section 3.1.1). In the retrospective studies (1 and 2), all the patient files of those who had received CRS were reviewed until a sufficient number of patients had been enlisted. In the prospective studies 3, 4 and 5, patients were recruited from those attending the National Optometry Centre at the Dublin Institute of Technology and the Wellington Eye Clinic, Dublin. Informed consent was obtained from all patients prior to enrolment in order to allow their data to be used anonymously for the purpose of research (Appendix A.2). This study was approved by the Ethics Committee Board of the Dublin Institute of Technology (Appendix A.3), and it adhered to the tenets of the Declaration of Helsinki (World Medical Association, 2008).

3.1.1 Inclusion criteria.

- Myopic prescriptions with low astigmatism (< -2.00DC).
- Free from systemic and ocular disease.
- For the SCL group:
    - Full-time SCL wear; determined as wearing SCLs at least 5 days per week for at least 1 year prior to enrolment.
- For the NCL control group: no history of CL wear.

The following exclusion criteria were applied:

- RGP CL wearers were excluded from the study. Different cessation times apply to RGP CL wearers prior to CRS, as there is a greater amount of corneal warpage in these patients FDA (2011).
- Patients who previously had CRS and attended to have retreatment due to refractive regression were excluded.
- Patients who had surface Laser procedures using Mitomycin-C (MMC) were excluded from the study. As MMC use can result in an abnormal healing response (De Benito-Llopis et al., 2009), there may be a hyperopic over-correction and a subsequent period of regression with these treatments (Teus et al., 2009).

3.1.2 Patient suitability for corneal refractive surgery

Patients were determined to be suitable for CRS if they achieved the suitability guidelines published by the United States FDA (2011) for CRS, as outlined in Appendix A.1. No LASIK procedures were performed if preoperative CCT values were less than 500µm; instead, these patients were treated using a PRK or LASEK surface Laser ablation. The minimum corneal thickness for surface PRK and LASEK was 450µm. The minimum residual bed allowance was 300µm. Corrections were therefore limited to a maximum of -12.00D.

3.1.3 Allocation of SCL groups

The SCL group was divided according to whether the subjects had been wearing hydrogel or SiHy lenses, and comprised disposable SCLs only (replaced on a daily/weekly/2-weekly or monthly basis). Full-time SCL wear has been defined as the

use of CLs between 4 (Efron et al., 2010) and 7 days per week (Ng et al., 2007). As corneal changes with SCL wear can increase with increasing years of SCL wear (Asbell and Wasserman, 1991), the SCL group was divided into short-term (less than 5 years), medium-term (between 5 and 10 years) long-term (greater than 10 years) wear in agreement with other authors (González-Pérez et al., 2003; Lee et al., 2001b; Patel et al., 2002).

3.1.4 Allocation of refractive error groups

The patients were divided into categorical groups based on the level of myopia (Table 3-1), as it has been reported that the efficacy and predictability of LASIK outcomes diminishes with high myopia (Kojima et al., 2008). This classification was carried out in accordance with the recommendations of the Royal College of Ophthalmologists (2011) and followed the standard set by previous studies (Halliday, 1995; Kawabata and Adachi-Usami, 1997; Kojima et al., 2008).

Table 3-1: Classification of myopic refraction

Low myopia	0.00 D to -3.00 D
Moderate myopia	> -3.00 D to -6.00 D
High myopia	> -6.00 D

3.1.5 Corneal refractive surgery groups

Photorefractive keratotomy (PRK) and Laser-Assisted Sub-Epithelial Keratectomy (LASEK) were analysed separately to Laser-Assisted in Situ Keratomileusis (LASIK) as it has been reported that there are variations between the outcomes of LASIK and LASEK/PRK procedures (Ambrósio and Wilson, 2003; Miyai et al., 2008; Reilly et al., 2010).

3.1.6 Pentacam Tomography

Two Pentacam instruments were used to acquire data for study 1. In accordance with recommendations of Bland and Altman (1986), intra-session reliability and internal consistency was examined between these two instruments using Cronbach's alpha and Intraclass Correlation Coefficient (ICC). Following intra-session reliability, the agreement between the two Pentacam instruments was then assessed in order to ensure data from each instrument could be interchanged freely (Bland and Altman, 1986). This inter-session repeatability was analysed using the Bland and Altman method of comparing the mean difference between the two methods of measurement (the bias). Comparison of the pairs of means is based on the 95% limits of agreement (LOA) for the difference in the means.

In the clinical setting where data were obtained, these two Pentacam instruments were used indiscriminately. Assessment of agreement between the instruments revealed high levels of agreement thus ensuring data from the two instruments could be used to assess changes in corneal parameters due to SCL wear and/or CRS. The statistical tests and results of this analysis are in section A.5.1

3.1.7 Statistical analysis

Data were recorded in an Excel spreadsheet and transferred to SPSS software (versions 19-21, SPSS Inc., Chicago, Illinois, USA) for statistical analysis by the author (ALM). Individual subjects were assigned an identification code, to ensure that data could be stored without any personal details. All data were safely stored in accordance with the Data Protection Act 1988 (Amendment Act 2003). The raw data collected in this study are in the attached data compact disc.

3.1.7.1 Normality

Normality for continuous data was assessed using Shapiro-Wilks method (normal distribution when $p > 0.05$) (Mendes and Pala, 2003). This test has been found to compute a more reliable measure of non-normality compared with other normality tests (Shapiro et al., 1968). This test assesses whether the distribution of the data, as a whole, deviates from a comparable normal distribution, which has the same mean and standard deviation (SD). Data that was found to have normal parametric distribution ($p > 0.05$), was analysed using parametric testing (Student's *t*-test, one-way ANOVA and two-way ANOVA). Data found to have non-parametric distribution ($p < 0.05$) was analysed using non-parametric tests (Mann-Whitney and Kruskal-Wallis tests) (Armstrong et al., 2000). As there is no non-parametric equivalent of a two-way ANOVA, non-parametric data was examined with this test (to limit family-wise error), in addition to a one-way non-parametric equivalent test. In these cases, both sets of statistical test results are reported.

Relationships or correlations between groups were assessed using Pearson's correlation coefficient for parametric data and Spearman's correlation coefficient for non-parametric data. An alpha value of $p < 0.05$ was considered significant. Levene's test of the assumption of equality of effort variances was tested for ($p > 0.05$).

3.1.8 Sample size

To ascertain that the sample size was sufficient to ensure statistical power, the statistical programme G*Power 3.1.2 was used (Erdfelder et al., 1996). In order to limit the chance of making Type I error (rejecting the null hypothesis when it is true), the alpha value was set at 0.05. To limit the possibility of making a Type II error (accepting the

null hypothesis when it is false), beta was set at 0.5. The effect size (d) is the smallest difference between the means of the 2 groups that is clinically significant.
It was calculated with the equation (Cohen, 1988):

$$\boxed{d = \mu_1 - \mu_2 / \sigma}$$

Where: μ_1 = Mean of population 1, μ_2 = Mean of population 2, σ = the standard deviation.

As this research focused on the impact of SCL wear on corneal curvature, corneal thickness and visual outcomes, the values examined in this study were VA, SimK, CCT and UDVA. It was possible that the SCL group could show an increase or decrease in curvature and thickness measurements compared with the NCL control group, therefore two-tailed *t*-tests were used for G*power analysis.

In order to determine which values to use for effect size, population means and standard deviations from previous studies with similar methods and outcomes were used. Ng et al. (2007) determined the criteria for assessing stability of measurements following cessation of SCL wear to be ≤ 0.50D change in curvature and ≤ 8µm change in thickness. Uçakhan et al. (2006) found a mean keratometry value of 43.2 ±1.4 D and a mean corneal thickness value of 557.6 ±6.5µm for normal corneas. Lackner et al. (2005) found a mean corneal thickness value of 542 ±29µm for normal corneas. Shankar et al. (2008) found the mean keratometry reading of the anterior corneal surface measured with the Pentacam to be 42.98 ±1.27D. The values assessed to compare the refractive outcomes for the groups were efficacy (UDVA) and predictability (residual refraction). The mean and SD values from study 1 were used to calculate subsequent sample sizes required. The mean difference between BCSVA pre-operatively and

UDVA at 1, 3 and 6 months was 2.5 letters and the SD was 4 letters. These values were input into the G*power program to calculate sample size. The results of the power analysis calculations are shown in Table 3-2. Based on this calculation of sample size, the total sample size of greater than 82 was taken to be sufficient to detect an effect size.

Table 3-2: G*power sample size analysis

	Simulated Keratometry	**Central corneal thickness**	**UDVA**
Alpha	0.05	0.05	0.05
Power (1-β)	0.95	0.95	0.95
Effect size d	0.37	0.45	0.51
Total sample size	**82**	**53**	**39**
Actual power	0.95	0.95	0.95
Critical value	1.99	2.01	2.03
Delta	3.66	3.68	3.70

*Results of G*power analysis to calculate the total sample size required to establish significant differences in the study.*

4 CHAPTER FOUR. STUDY ONE: THE INFLUENCE OF TWO WEEKS OF SOFT CL CESSATION ON CORNEAL CURVATURE AND THICKNESS

4.1 Introduction

Hydrogel SCLs create a barrier to the effective diffusion of oxygen, nutrients and products of metabolism to the cornea. Tissues must then perform anaerobic respiration, which results in excess lactic acid and acidosis (Jones and Jones, 2001; Liesegang, 2002; Schornack, 2003). Hypoxia and acidosis alter the corneal metabolism and result in transient and long lasting changes to corneal structure (Alba-Bueno et al., 2009). Corneal oedema is defined as the presence of excessive fluid in or around cells or tissues in the body (Millodot, 2004) and is an acute response to hypoxia. It results in loss of transparency and an increase in corneal thickness (Bergmanson and Chu, 1982). Over long periods of time, SCL wear can result in chronic changes to corneal metabolism such as endothelial polymegathism and corneal thinning (Böhnke and Masters, 1997; Wiffen et al., 2000). Hypoxia also leads to local changes in the epithelial refractive index due to oedema, resulting in increased light scatter, haze and halos around lights (McCally et al., 2007; Meek et al., 2003; Wang et al., 2004a) These effects are known as 'Sattler's Veil' (Liesegang, 2002).

Refraction, corneal curvature and thickness measurements are used together, to determine the most appropriate CRS treatment and to generate treatment plans. These measurements may be affected by SCL wear (Hardten and Gosavi, 2009; Pflugfelder et al., 2002; Ruben et al., 1976; Ryan and Jacob, 1996; Tseng et al., 2007). The time required for resolution of hypoxia and SCL-induced changes to corneal curvature and thickness can vary according to SCL type or material and with years of previous wear. If sufficient time, since stopping lens wear, is not allowed in order for the effects of

SCL wear to resolve, this could result in spurious readings, which might influence the outcome of the CRS procedure. In most cases, each clinic will adopt individual policies regarding when SCL wear must stop prior to CRS, and will assume stability following a standard time period with no SCL wear. This time can vary between practices from 24 hours to 2 weeks (Sharma et al., 2003).

4.1.1 Corneal shape and thickness in SCL wear

Corneal thickness changes have been found with all types of SCL wear (Wilson and Klyce, 1994) and vary according to SCL material and modality (Ruiz-Montenegro et al., 1993).

4.1.2 Corneal shape in hydrogel SCL wear

SCL wear has been found to result in significant changes to mean keratometry, corneal astigmatism and corneal eccentricity (Alba-Bueno et al., 2009). Typically, following initial flattening of keratometry values (Yeniad et al., 2003), anterior corneal topography and keratometry values steepen in all corneal meridians with hydrogel SCL wear (Collins and Bruce, 2004; Jalbert et al., 2004; Liu and Pflugfelder, 2000; Yeniad et al., 2003). In extreme cases, DW of hydrogel SCLs can even result in irregular corneal curvature (Alba-Bueno et al., 2009; Arranz et al., 2003) and corneal warpage manifesting as pseudo-keratoconic topography (Cheng et al., 2003; Wilson et al., 1990). In contrast to the softer, high water content materials common nowadays, in the past outdated low DK/t materials could induce the opposite problem, resulting in significant flattening of the posterior corneal curvature compared with high DK/t SCL wear (Martin et al., 2009a). These changes may be explained through hypoxia-associated corneal thinning in low-DK/t hydrogel wearers.

4.1.3 Corneal shape in SiHy SCL wear

High DK/t SiHy SCLs reduce the frequency of complications associated with hypoxia and have been found to maintain excellent long-term ocular tissue tolerance (Guillon and Maïssa, 2010). However, they can induce mechanically related changes in the cornea (Holden et al., 2001; Sweeney, 2003), and, due to the stiffer, relatively flat design of SCLs, can result in a flattening of keratometry values (Alba-Bueno et al., 2009; Bergenske et al., 2007; Dumbleton et al., 2006; González-Méijome et al., 2003b; Liesegang, 2002; Schorner, 2010). Surprisingly, resolution of these changes can take longer than 3 months (González-Méijome et al., 2003a; Liu and Pflugfelder, 2000). It is hypothesised that these pressure-related changes in corneal curvature result in slight myopic reduction with SiHy SCL wear (Jalbert et al., 2004).

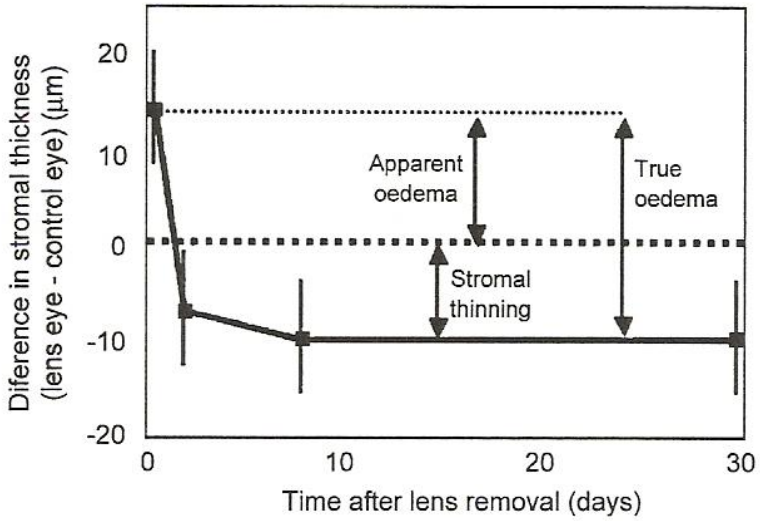
4.1.4 Corneal thickness in hydrogel SCL wear

The acute response to corneal hypoxia induced by low DK/t SCL wear, is an increase in corneal thickness due to oedema (Leem et al., 2011; Liesegang, 2002; Martin et al., 2011; Ruben et al., 1976; Yeniad et al., 2003). Oedema is especially evident with prolonged wearing times of low DK/t SCLs (Holden et al., 1985; Martin et al., 2009a; Moezzi et al., 2004). Fluctuations in CCT of 30-50µm have been reported following cessation of SCL wear (Liu and Pflugfelder, 2000).

While the acute response to hypoxia is an increase in CCT, the chronic response, which follows resolution of oedema, is actually a thinning of the cornea (see Figure 4-1) (Holden et al., 1985; Liesegang, 2002; Pflugfelder et al., 2002; Sanchis-Gimeno et al., 2007; Yeniad et al., 2003). CCT must be assessed following a sufficient period of lens

cessation to ensure there is no residual oedema masking the change in corneal thickness (Efron, 2007).

Figure 4-1: Oedema following SCL removal



The relationship between apparent and true oedema and stromal thinning is demonstrated in this image. Following 10 days SCL cessation there is resolution of oedema. Once the oedema is resolved, the stromal thinning can be seen (adapted from Holden et al. 1985).

4.1.5 Corneal thickness in SiHy SCL wear

High DK/t SiHy lenses induce less corneal oedema than low DK/t hydrogel lenses (Jalbert et al., 2004; Martin et al., 2009a). However, corneal thinning may be induced as a result of the mechanical pressure from the increased modulus associated with these materials (Doughty et al., 2005; González-Méijome et al., 2003a).

4.1.6 Contact lens-induced corneal warpage

The term CL-induced corneal warpage was coined by Harstein in 1965. It describes all modifications of the corneal surface, reversible or permanent, associated with CL wear, not including corneal oedema (Cigales et al., 2002; Wang et al., 2002b). CL-induced

warpage is more common with RGP CL wear, but approximately 30% of reported cases are associated with SCLs (Klyce, 1991; Michaud; Ryan and Jacob, 1996; Schornack, 2003; Tseng et al., 2007; Wilson et al., 1990). CL warpage results in irregular astigmatism, generally with inferior steepening, loss of radial symmetry, reversal of prolate shape and previous innate corneal astigmatism may increase or decrease (Hoyos and Cigales; Wilson et al., 1990). This can lead to a reduction of surface regularity (Liu and Pflugfelder, 2000), which can reduce the BCSVA (Baker-Schena, 2001). Presenting symptoms of CL-induced corneal warpage may vary. Some patients report poor and fluctuating vision and ocular discomfort with CLs, while others may be asymptomatic (Asbell and Wasserman, 1991; Weissman, 2007; Wilson et al., 1990). Refractive error changes can occur and manifest as fluctuations in myopia (Fonn et al., 2002; Hoyos and Cigales). Corneal topography is the most sensitive tool used in the analysis of CL-induced corneal warpage (Hoyos and Cigales). The following signs of topographical changes may be induced with CL-warpage. These can mimic FFK as outlined in section 1.3.3.1 (Asbell and Wasserman, 1991; Hardten and Gosavi, 2009; Hoyos and Cigales, 2002; Tseng et al., 2007):

- Irregular central astigmatic topography
- Loss of radial symmetry
- Loss of normal topographical peripheral flattening
- Subtle inferior steepening

It is important to be able to differentiate true FFK from CL-induced corneal warpage. True keratoconic eyes exhibit steeper K readings, greater variations in maximum sagittal and tangential curvature and higher corneal shape indices compared with CL-induced corneal warpage patients (Lebow and Grohe, 1999). If suspicious topography

is detected, it is recommended that stable serial topography and keratometry measurements, as well as manifest refractions, are taken to ensure correct diagnosis (Tseng et al., 2007). Large changes in CCT can accompany the CL-induced corneal warpage associated with conventional hydrogel SCL wear (Tseng et al., 2007). Resolution of these changes in CCT can take up to 8 weeks following cessation of SCL wear (Schornack, 2003). Such a change in CCT can have a huge influence on a candidate's suitability for CRS, as sufficient CCT must be preserved following Laser ablation if ectasia is to be prevented. It is possible that, following the resolution of SCL related oedema, patients may be left with lower than acceptable CCT.

In summary, previous SCL wear may adversely affect the accuracy of corneal curvature and thickness measurements for CRS patients. It is important to ensure there is no CL-induced corneal warpage or oedema present, in order to accurately evaluate and ensure patient's suitability for CRS. Sufficient periods of cessation of SCL are vital for this.

4.1.7 Aims and hypotheses

The aim of Study 1 was to answer 5 hypotheses:

1) Overall steepness and irregularity (as depicted by abnormal corneal topographical indices provided by the Pentacam) and a reduction in corneal thickness would be evident with SCL wear (Hardten and Gosavi, 2009; Pflugfelder et al., 2002; Ruben et al., 1976; Ryan and Jacob, 1996; Tseng et al., 2007).

2) Superior flattening and inferior steepening of corneal radii would be apparent in the SCL group compared with the NCL control group (Tabbara and Kotb 2006).

3) Resolution of SCL-induced corneal changes in the SCL group, manifesting as flattening of SimK and topography radii values, would be evident in the SCL group following cessation of SCL wear.

4) The hydrogel SCL wearing group would show a mean flattening of inferior radii following cessation of SCL wear, as corneal warpage was resolving. Furthermore, that the SiHy group would show a mean steepening as the effect of the stiff modulus of the lenses resolved.

5) Large fluctuations in corneal thickness would occur in the SCL group compared with the NCL group, following cessation of SCL wear, due to the resolution of oedema induced by SCL wear.

These hypotheses were explored through retrospective analysis of the changes in data obtained at baseline examination, versus the data obtained at a second consultation, from a group of full-time SCL wearers (hydrogel and SiHy SCL materials), following cessation of SCL for a 2 week period, and a NCL control group. The aim of this study is to validate current FDA guidelines relating to 2 weeks cessation of SCL wear, prior to taking measurements used for planning refractive CRS procedures.

4.2 Methods

4.2.1 Subject enrolment

A retrospective examination of CRS patient charts was carried out at a Dublin based CRS clinic (Eye Laser Ireland, Ultralase). Records for 316 patients were examined and those who fulfilled the inclusion criteria were included for analysis (n = 90) (section 3.1.1). Dominant eyes only were analysed retrospectively in order to account for the correlation, which exists between right and left eyes of a subject and to avoid overstatement of the validity of statistical analysis (Ederer, 1973; Glynn and Rosner, 1992; Katz et al., 1994). Although this resulted in a reduction of sample size, it was intended to improve the power of the study through appropriate statistical methodology (Glynn and Rosner, 1992).

4.2.2 Clinical procedure for data collection

The patients had attended an initial consultation (prior to cessation of SCL wear) in order to determine their suitability for CRS. SCL wearers were then asked to cease wear for a period of 2 weeks, and return for a second visit where clinical measurements used for calculation of the CRS procedure were obtained. Early post-operative visits (1 day to 1 week) were excluded from analysis as the spurious nature of these results. Corneal healing can vary greatly between patients in the week following CRS, this and the ensuing dry eye would limit the ability to confidently investigate the influence of SCL wear on these CRS outcomes. Refractive stability following CRS has been reported to occur between 1 and 6 weeks for LASIK and 3 weeks and 3 months for PRK/LASEK (Taneri et al., 2004b). Therefore, data obtained at the first and second pre-operative visits and post-operatively at 1, 3 and 6 months were included for

analysis. Data were also collected for the NCL control group for both pre-operative visits and all post-operative visits.

4.2.3 Corneal topography

Sagittal and tangential topography and SimK values from the Pentacam topometric display were analysed. Three points from the anterior surface and the same 3 points on the posterior surface were evaluated for sagittal and tangential curvature. These points were central (at the pupil centre), and a superior and inferior point 4.5mm from the central point. The data collected within the 5.00mm central corneal zone is considered to be the most important for CRS analysis as this is where ablation and flap creation takes place (Chen and Lam, 2009). Fluctuation in corneal curvature following cessation of SCL wear at these locations, may have an impact on the outcomes of CRS. As SCL wear can induce inferior steepening relative to central and superior points, superior and inferior topography was examined to investigate whether inferior points were steeper in SCL wearers.

4.2.3.1 Simulated Keratometry

The flattest and steepest SimK radii in the para-central 3mm zone were analysed. The influence of SCL wear on the resulting variations in curvature, and/or larger fluctuations in measurements, following cessation of SCL wear was explored and compared with the NCL control group.

4.2.3.2 Corneal topographical indices

Corneal topographical indices from visit 1, for both the SCL and NCL groups were compared in order to assess whether there was increased irregularity in the SCL group.

Following 2 weeks SCL cessation, analysis was carried out to assess whether any possible irregularity resolved.

4.2.3.3 Corneal thickness

CCT in Pentacam tomography is displayed at the pupil centre. It is recommended that this value be interpreted with caution as there may be small variations in size due to external lighting and hippus (McAlinden et al., 2011). Therefore, two central corneal thickness measurements were included- CCT measured at the pupil centre and the thinnest location (TL) in the central cornea which was automatically generated by the Pentacam). Additionally, 4 peripheral points at 2.25mm from centre- superiorly (SCT), temporally (TCT), inferiorly (ICT) and nasally (NCT) were analysed. Corneal thickness at these 6 points was compared between the SCL and NCL groups prior to and following SCL cessation.

4.3 Results

4.3.1 Demographics of the study population

Forty-five SCL wearers and 45 NCL control patients met the study inclusion criteria, all of whom were Caucasian. Patient demographics are outlined in table 4-1.

Table 4-1: Demographics of study 1

	SCL n = 45	**NCL n = 45**	**Statistical test (value)**	**Sig**
Sex n = (%)	Males: 23 (51) Females: 22 (49)	Males: 29 (64) Females: 16 (36)	Pearson Chi Square (1.64)	0.20
Age (years) Mean ±SD	32 ±7.5	37 ±10	Independent *t*-tests (2.47)	0.02

Table 4-2: Pre-operative refractive error and VA data for SCL and NCL control groups

	SCL n = 45	**NCL n = 45**	**Sig**
Sphere	-3.73 ±1.65	-2.56 ±1.48	0.01
Cylinder	-0.58 ±0.25	-0.63 ±0.34	0.94
MSE	-3.98 ±1.64	-2.85 ±1.49	0.01
BCSVA LogMAR (VAR)	-0.13 ±0.05 (106.58 ±2.49)	-0.11 ±0.06 (105.36 ±3.16)	0.50

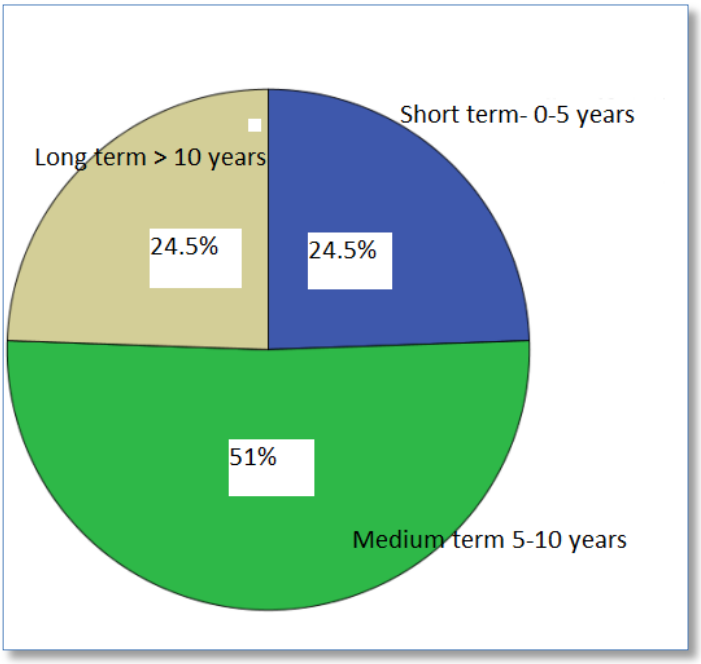
There was significantly higher myopia in the SCL group. BCSVA: best corrected spectacle visual acuity, MSE: mean spherical equivalent, VAR: visual acuity rating. Statistically significant differences are shown in shaded cells, ($p < 0.05$).

Two-way ANOVA was used to analyse differences in refractive error and BCSVA between the SCL and NCL control groups. Results are shown in Table 4-2. The mean spherical refractive error and the MSE were significantly higher in the SCL group.

4.3.2 CL wearing habits

At the time of consultation, SCLs had been worn for a mean of 9 ±4.5 years (range 1 to 22 years), for an average of 6.5 days per week (range 5 to 7 days) and 12 ±5 hours per day (range 4 to 24 hours) (Figure 4-2). The majority of the SCL group wore hydrogel lenses (n = 35, 75.6%), the remainder wore SiHy lenses (n = 6, 13.3%). Of these SiHy SCL wearers, 1 wore G1SiHy material and the remaining 5 wore G2SiHy material. As this was a retrospective study, it was not possible to determine the type of SCL some patients had worn since it had not been recorded at the initial pre-operative consultation.

Figure 4-2: The frequency of soft CL wear



Distribution of years of SCL wear prior to consultation. Just over half of the group (51%) wore lenses for a period of 5-10 years prior to surgery.

4.3.3 The influence of SCL wear on corneal topography

4.3.3.1 Corneal curvature at the first visit

A two-way ANOVA was carried out in order to investigate the influence of SCL wear on SimK values. As expected, the mean steep and flat SimK values were steeper in the SCL group. However, these results were not statistically significant (see Table 4-3).

Table 4-3: Keratometry at the first visit

	SCL group n = 45 (D)	**NCL group n = 45 (D)**	**Sig**
Flat K	42.98 ±1.25	42.56 ±1.31	0.12
Steep K	43.67 ±1.22	43.44 ±1.42	0.42

Statistical analysis of flat and steep curvature for SCL and NCL control groups at first visit. SimK readings are steeper in the SCL group. However, results of two-way ANOVA indicate no significant differences between the study groups (SCL vs NCL), ($p > 0.05$).

The influence of SCL material and years of SCL wear on SimK values at the first visit was also explored. Results of two-way ANOVA showed no significant differences in SimK values between the SCL material or years of wear groups and the NCL control group ($p > 0.05$). Full details of these results are in Appendix A.5.1.5.

4.3.3.2 Influence of pre-operative myopia on corneal curvature

As there was a significant difference in the pre-operative level of myopia and MSE between the SCL and NCL control groups, the influence of the level of myopia (low, medium or high) on corneal curvature at the first visit was explored. A two-way ANOVA revealed no significant differences between the 3 myopic groups and 2 SCL

groups or between the interaction of the myopic and SCL groups (all p- values > 0.05). Full statistical tables are in Appendix A.5.1.6.

4.3.3.3 Sagittal and tangential curvature at the first visit

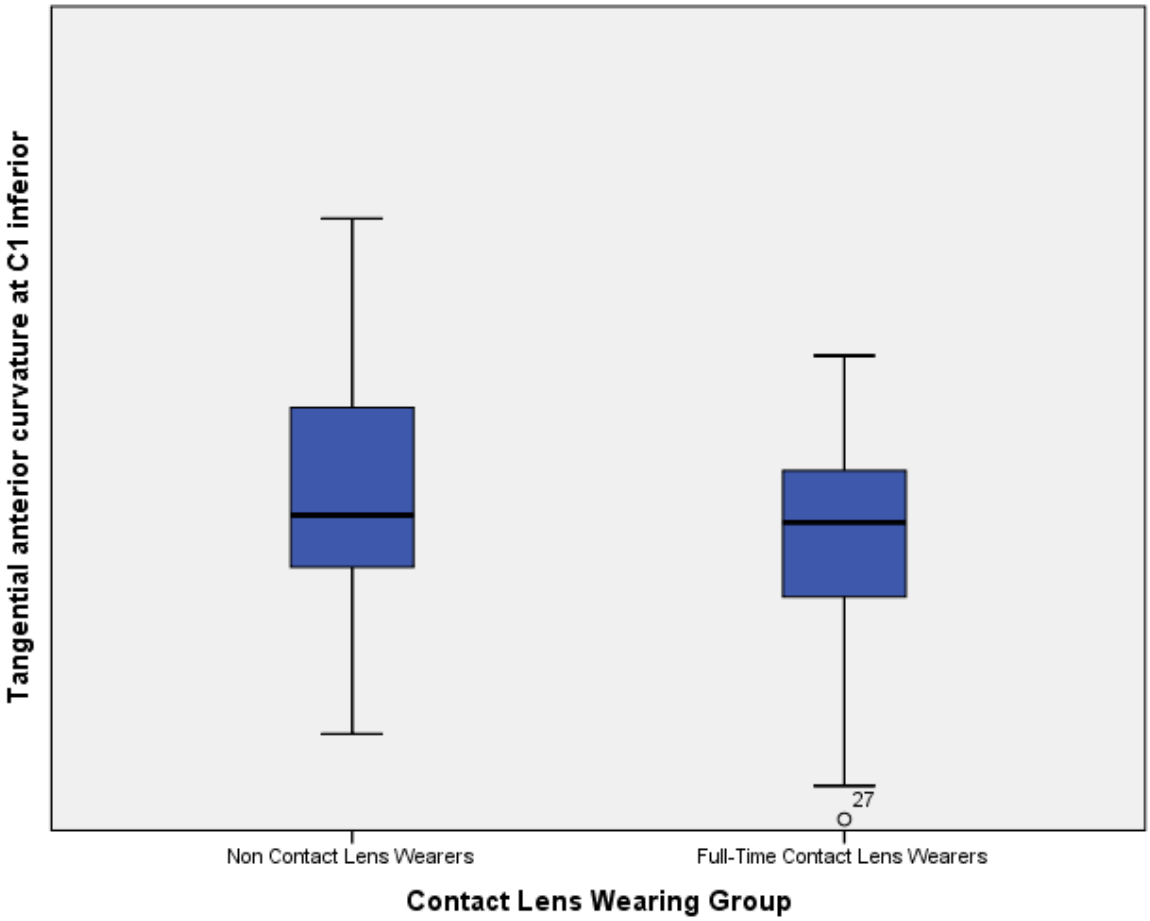
Two-way ANOVA was used to analyse the differences in radii measurements between the SCL and NCL groups. Sagittal radii were found to be steeper in the SCL group compared with NCL control group, however differences were found not to be statistically significant (Table 4-4). In contrast to this, anterior tangential radii showed signs of corneal warpage to be present. The inferior radii was significantly lower in the SCL group (average 7.77mm), indicating steepening, compared with the NCL control group (average 7.90mm, p = 0.04) (Figure 4-3). Superior tangential radii were increased in the SCL group, indicating flattening of the corneal curvature. Differences between groups at the central and superior corneal locations were not statistically significant.

Table 4-4: Topography: sagittal and tangential radii at first visit

	Sagittal radii (mm)			**Tangential radii (mm)**		
	SCL group Mean ±SD n = 45	**NCL group** Mean ±SD n = 45	**Sig**	**SCL group** Mean ±SD n = 45	**NCL group** Mean ±SD n = 45	**Sig**
Anterior radius (mm)						
Superior	7.78 ±0.26	7.80 ±0.27	0.63	7.83 ±0.32	7.81 ±0.34	0.81
Central	7.81 ±0.23	7.86 ±0.25	0.27	7.84 ±0.26	7.93 ±0.26	0.12
Inferior	7.72 ±0.21	7.79 ±0.29	0.20	7.77 ±0.30	7.90 ±0.30	0.04
Posterior radius (mm)						
Superior	6.21 ±0.32	6.23 ±0.31	0.80	6.36 ±0.50	6.40 ±0.62	0.70
Central	6.60 ±0.25	6.63 ±0.26	0.55	6.77 ±0.34	6.87 ±0.28	0.13
Inferior	6.34 ±0.26	6.36 ±0.25	0.65	6.25 ±0.33	6.34 ±0.32	0.19

Mean ±SD and two-way ANOVA statistics for sagittal and tangential radii measured at first visit in SCL and NCL control groups. Central (pupil centre) superior and inferior (4.5mm) values were measured on the anterior and posterior corneal surfaces. Statistically significant differences are shown in shaded cells ($p < 0.05$).

Figure 4-3: Boxplot portraying tangential curvature for the SCL and NCL group on at the inferior anterior corneal location.



The boxplot portrays the minimum and maximum values of tangential curvature for the NCL (left) and SCL (right) groups. The blue box represents where 50% of the data lies with the thick black line within the box representing the median. Outliers of individual cases are numbered.

These results confirmed the test hypothesis that SCL wear has an effect on corneal curvature as indicated by the steeper average radii of curvature in the SCL group. The presence of inferior corneal steepening in the SCL group was statistically significant for tangential curvature. Since sagittal and tangential radii values in the SCL group were found to be steeper, the possible influence of the type of SCL material and years of SCL wear on radii values at the first visit was explored. The test hypothesis that corneal warpage can vary according to lens material (hydrogel: inferior steepening; SiHy:

central flattening) was rejected as differences between the groups did not achieve statistical significance ($p > 0.05$), for results see Appendix A.5.1.5.

4.3.3.4 Corneal topographical indices at the first pre-operative visit

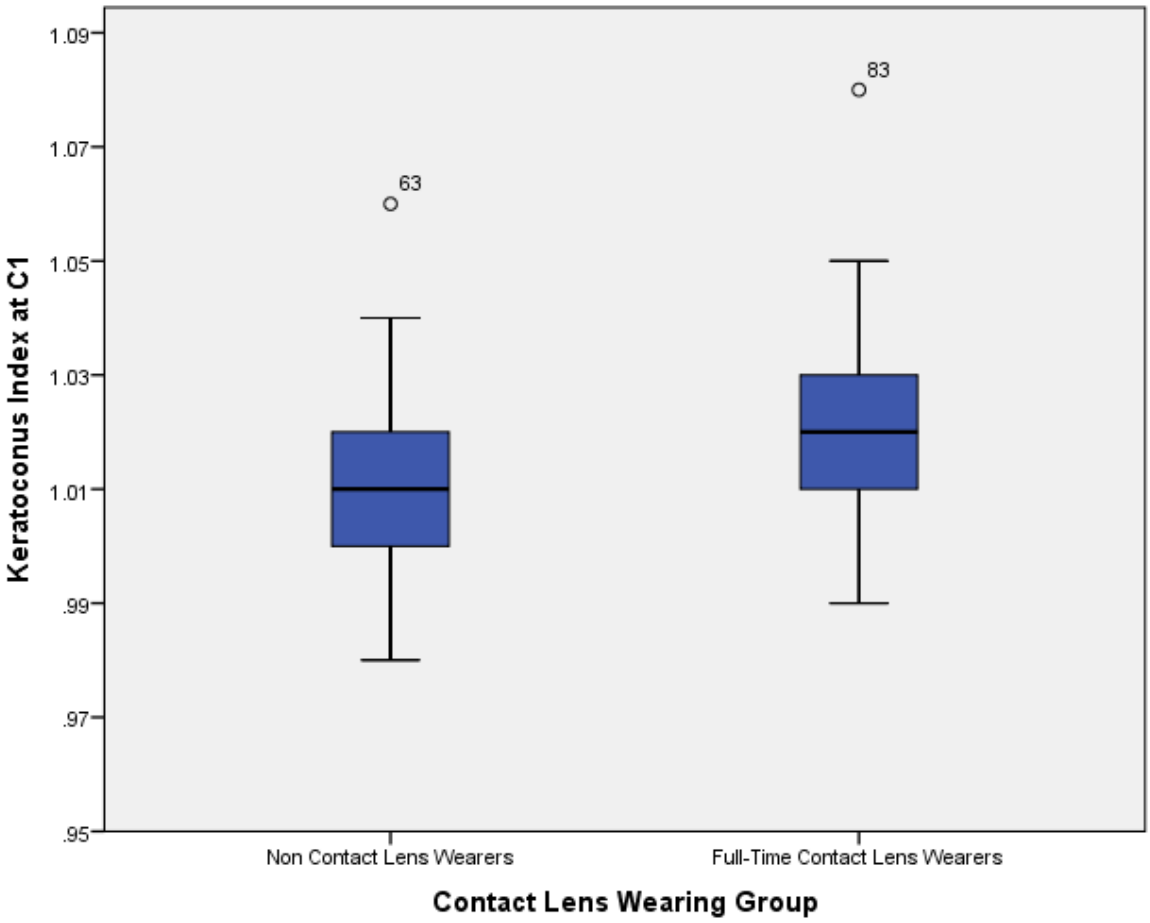
As indices data were found to show non-parametric distribution, Mann-Whitney testing was carried out. The influence of SCL wear on the changes to the corneal topographical indices was investigated. The mean ±SD data of corneal topographical indices measured at the first visit of the SCL and NCL control groups are in Table 4-5. Comparison of corneal topographical indices data showed the keratoconus index to be higher in the SCL group. This difference was, statistically, highly significant ($p = 0.00$) (Figure 4-4). However, the mean keratoconus index value for the SCL group (1.02 ±0.17) was lower than the accepted abnormal or pathological values (> 1.07), as published in the Pentacam instruction manual indicating the lack of clinical significance to this finding. This slight elevation in the index might due to changes in corneal shape induced by SCL wear, such as the inferior steepening, which was evident on tangential radii measured. Results of Kruskal-Wallis testing, comparing the SCL sub-groups, show no statistically significant effect of either material or years of wear on corneal topographical indices measured at the first visit ($p > 0.05$). Full statistical analysis are in Appendix A.5.1.7.

Table 4-5: Corneal topographical indices measured at the first pre-operative visit

	SCL group Mean ±SD n = 45	**NCL group Mean ±SD n = 45**	**Sig**
Surface variance	14.38 ±3.86	14.60 ±3.67	0.78
Vertical asymmetry	0.13 ±0.55	0.11 ±0.06	0.27
Keratoconus	1.02 ±0.17	1.01 ±0.17	0.00
Central keratoconus	1.00 ±0.01	1.00 ±0.01	0.58
Height asymmetry	2.95 ±1.90	4.05 ±3.81	0.09
Height decentration	0.01 ±0.00	0.01 ±0.00	0.68
Radii minimum	7.62 ±0.23	7.66 ±0.24	0.39
Aberration coefficient	0.96 ±0.67	0.98 ±0.64	0.89

Mean ±SD values of topographical indices obtained at the first visit are shown along with results of Mann-Whitney tests which were used to analyse the differences in indices between the SCL and NCL study groups. Statistically significant results are shown in shaded cells, $p < 0.05$.

Figure 4-4: Boxplot portraying Keratoconus index for the SCL and NCL group at the first pre-operative visit



The boxplot portrays the minimum and maximum values for keratoconic index for the NCL (left) and SCL (right) groups. The blue box represents where 50% of the data lies with the thick black line within the box representing the median. Outliers of individual cases are numbered.

4.3.3.5 Corneal curvature following 2 weeks cessation of CL wear

Mann-Whitney U testing showed that there were no statistically significant differences in the mean SimK measurements taken at the first and second visits between the study groups (SCL vs. NCL). This indicates a high degree of corneal curvature stability (Table 4-6). Further investigations into the influence of SCL material, and previous wearing times, on the stability of SimK values measured between the first and second

visits did not reveal statistically significant results either ($p > 0.05$). Detailed reports of these statistical findings are in Appendix A.5.1.8.

Table 4-6: Difference in keratometry measurements between the first and second visits

	SCL group Mean ±SD n = 38	**NCL group Mean ±SD n = 37**	**Sig**
Flattest K (D)	-0.09 ±0.32	0.06 ±0.52	0.62
Steepest K (D)	-0.03 ±0.25	0.10 ±0.59	0.56

Mean ±SD and statistical analysis of the differences in SimK values taken at the first and second visits. A negative value indicates steeper SimK, positive indicates flatter SimK at the second visit. Results of Mann-Whitney testing showed no statistically significant differences between SCL and NCL control groups, $p < 0.05$.

4.3.3.6 The effect of 2 weeks' cessation of SCL wear on stability of sagittal and tangential curvature values

A comparison of the differences between corneal radii (sagittal and tangential) taken prior to and following 2 weeks cessation of SCL wear was undertaken between the groups (SCL vs. NCL) using both two-way ANOVA and Kruskal-Wallis testing. The results showed a statistically significant difference for the tangential curvature on the anterior surface of the cornea measured inferiorly (two-way ANOVA $p = 0.02$, Kruskal-Wallis $p = 0.00$) (Figure 4-5), (Table 4-7). This measurement showed a mean flattening of inferior tangential radii in the SCL group (0.08 ±0.18mm) following cessation of SCL wear. This could indicate that there was a resolution of inferior steepening in the SCL group following cessation of lens wear, as the cornea returned to a prolate shape. Two-way ANOVA comparing the sagittal and tangential radii values measured at the

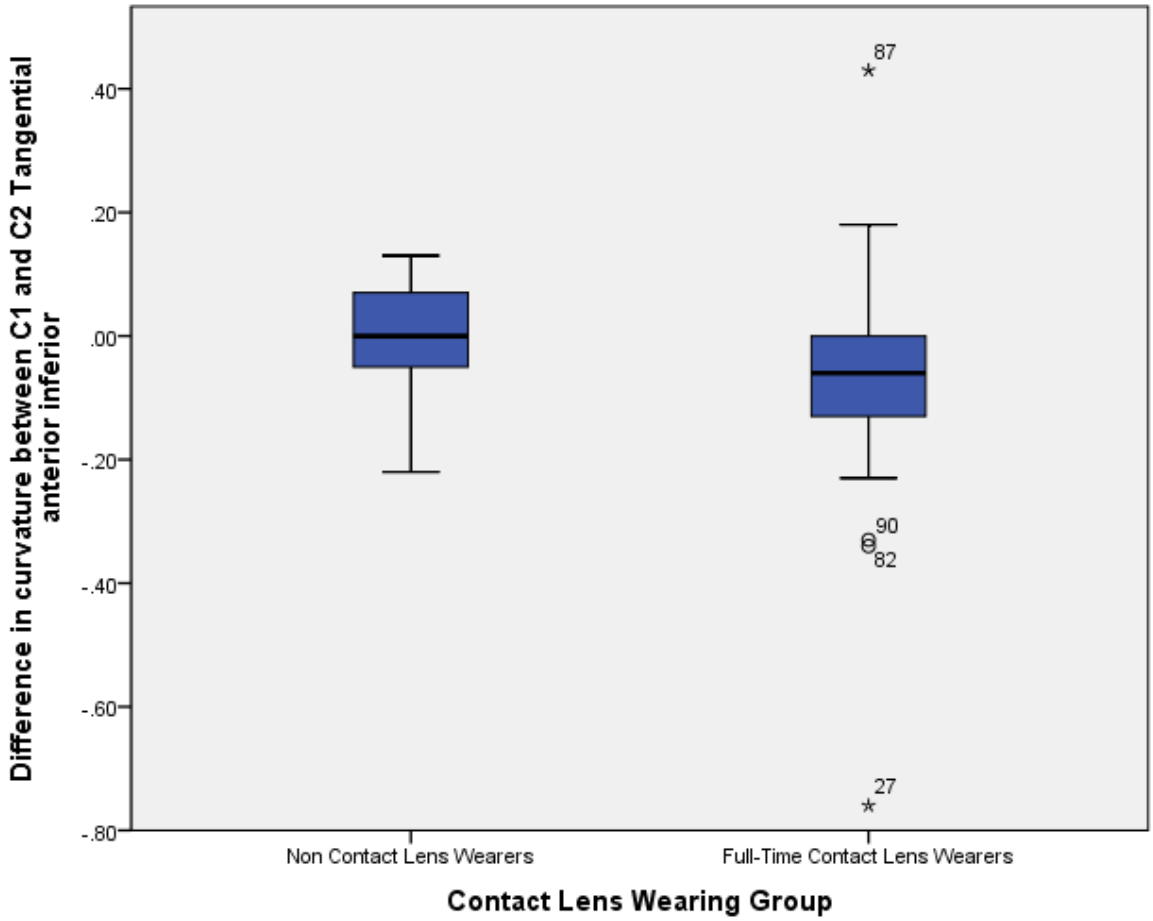
second visit showed no significant differences between the groups (SCL vs. NCL) (see Appendix A.5.1.8.1 for full statistical tables).

Table 4-7: Differences in corneal curvature at first and second visit

	Sagittal radius (mm)				**Tangential radius (mm)**			
	SCL group Mean ±SD n =38	**NCL control group Mean ±SD n = 37**	**Two-way ANOVA Sig**	**Kruskal-Wallis Sig**	**SCL group Mean ±SD n = 38**	**NCL control group Mean ±SD n = 37**	**Two-way ANOVA Sig**	**Kruskal-Wallis Sig**
Anterior corneal surface								
Superior	0.00 ±0.01	0.01 ±0.01	0.83	0.14	0.05 ±0.17	0.05 ±0.17	0.98	0.59
Central	0.00 ±0.01	0.02 ±0.12	0.12	0.17	-0.00 ±0.89	0.02 ±0.12	0.42	0.81
Inferior	-0.01 ±0.08	0.01 ±0.09	0.21	0.45	0.08 ±0.18	-0.01 ±0.08	0.02	0.00
Posterior corneal surface								
Superior	0.04 ±0.19	0.01 ±0.11	0.40	0.70	-0.11 ±0.330	-0.02 ±0.50	0.32	0.20
Central	0.01 ±0.12	-0.00 ±0.13	0.70	0.77	0.02 ±0.27	0.00 ±0.14	0.70	0.35
Inferior	-0.04 ±0.17	-0.01 ±0.08	0.36	0.14	0.01 ±0.24	-0.013 ±0.18	0.61	0.75

Mean ±SD and results of ANOVA and Kruskal Wallis testing of the differences in sagittal and tangential radii for SCL and NCL control groups between the first and second visit. A negative value (mm) indicates steepening, whereas a positive value (mm) indicates flattening at the second visit. Statistically significant differences between the groups are shown in shaded cells ($p < 0.05$).

Figure 4-5: Boxplot portraying the difference in tangential curvature between the first and second pre-operative visits between the SCL and NCL groups at the inferior location on the anterior cornea



The boxplot portrays the minimum and maximum values of the difference in tangential curvature for the NCL (left) and SCL (right) groups. The blue box represents where 50% of the data lies, with the thick black line within the box representing the median. Outliers of individual cases are numbered.

As there was a significant difference found in tangential radii between the study groups, the influence of SCL material and years of wear on the differences in radii between the first and second visits was explored. Results of two-way ANOVA indicate that the SCL material had a statistically significant effect on tangential radii, as superior and inferior radii on the anterior surface were flatter in the SiHy group. The largest change occurred at the inferior location (Hydrogel -0.05 ±0.14mm and SiHy -0.21 ±0.30mm, $p = 0.02$). Full statistical findings are in Appendix A.5.1.8.1.

4.3.3.7 The effect of 2 weeks' cessation of SCL wear on the stability of corneal topographical indices

Stability of corneal topographical indices following 2 weeks cessation of SCL wear was compared with the NCL control group.

Table 4-8: Difference in topographical indices following 2 weeks cessation of SCL wear

Index	**SCL group (n = 38)**	**NCL group (n = 37)**	**Sig**
Surface variance	-0.00 ±2.28	-0.03 ±2.67	0.41
Vertical asymmetry	0.00 ±0.03	0.00 ±0.04	0.81
Keratoconus	-0.00 ±0.01	0.00 ±0.01	0.33
Central keratoconus	0.00 ±0.01	0.00 ±0.08	0.75
Height asymmetry	0.09 ±2.77	-0.59 ±3.10	0.93
Height decentration	0.00 ±0.00	-0.00 ±0.00	0.76
Radii minimum	-0.01 ±0.05	0.01 ±0.07	0.14
Aberration coefficient	0.20 ±0.62	0.02 ±0.80	0.21

Mean ±SD and two-way ANOVA test results of differences in corneal topographical indices for SCL and NCL control groups between first and second visits. A positive value indicates an increase in the index and a negative value indicates a decrease in the index at the second visit. There were no statistically significant differences found between the groups ($p>0.05$).

Results of Mann-Whitney U testing showed that there was relative stability in corneal indices measured following 2 weeks cessation of SCL wear, with no statistically significant differences occurring between the groups (SCL vs. NCL) (Table 4-8). Thus indicating that analysis of stability of corneal topographical indices are not clinically relevant.

4.3.4 The influence of SCL wear on corneal thickness measurements

4.3.4.1 Time of measurement

Corneal thickness values can vary according to the time of day (Aakre et al., 2003; Du Toit et al., 2003). This diurnal variation is discussed in section 1.3.2. Pentacam measurements in this study were taken during normal clinic hours (8.30 to 19.00). In order to investigate possible diurnal variation on CCT, the groups (SCL vs. NCL) were divided into morning (measurements taken before 14.00 hours; SCL n = 30, NCL n = 31) and afternoon (measurements taken after 14.00 hours; SCL n = 15, NCL n = 14). This cut off time has been used previously (Módis Jr et al., 2011). The results of a two-way ANOVA showed that the time the measurements were taken did not have a significant effect on CCT measurements. The interaction of SCL group and time of measurement was also non-significant. Full statistical analysis is in Appendix A.5.1.11.1. As there were no significant differences in the time that CCT measurements were taken during the first, second or post-operative visits and because there was no significant influence of the time of measurements on the CCT, the groups were not divided according to when measurements were taken for corneal thickness analysis.

4.3.4.2 Corneal thickness at the first visit

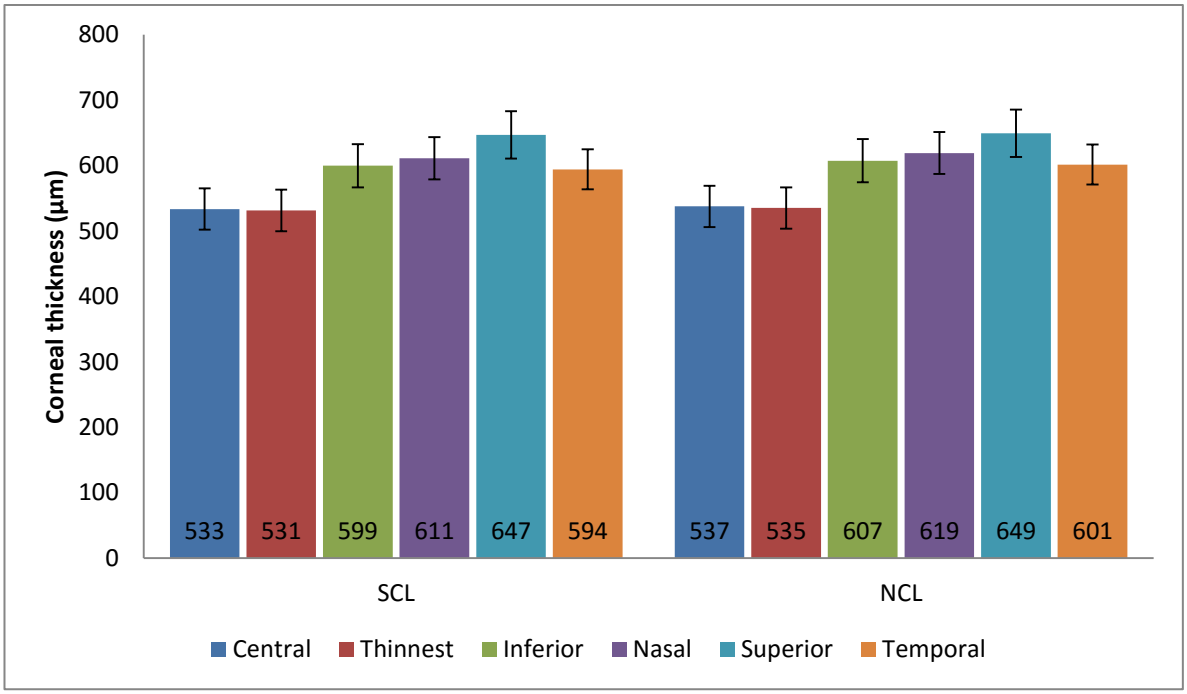
Corneal thickness was compared between the SCL and NCL groups at the first visit. A two-way ANOVA was used to assess differences between the groups (SCL vs. NCL). Mean ±SD data and ANOVA test results are shown in Table 4-9.

Table 4-9: Corneal thickness at the first visit

Location of corneal thickness	SCL group (n = 45) Mean ±SD (µm)	NCL group (n = 45) Mean ±SD (µm)	Sig
Central	533.40 ±31.72	537.40 ±29.40	0.54
Thinnest	531.24 ±31.61	535.04 ±29.60	0.56
Inferior	599.47 ±32.92	607.18 ±32.63	0.27
Nasal	610.98 ±32.18	619.02 ±32.12	0.24
Superior	646.76 ±36.19	649.02 ±35.84	0.77
Temporal	594.07 ±30.55	601.27 ±34.39	0.30

Mean ±SD for central and peripheral corneal thickness (µm) for SCL and NCL control groups at the first consultation. The results of two-way ANOVA show no significant differences between the groups (SCL vs. NCL), $p < 0.05$.

Figure 4-6: Graph depicting corneal thickness in the SCL and NCL group at the first pre-operative visit.



Corneal thickness was lower at all corneal locations in the SCL group compared with the NCL group (Figure 4-6). However, the results of the two-way ANOVA indicated that the differences in corneal thickness between the SCL and NCL control groups were not statistically significant. The influence of SCL material and years of SCL wear on

corneal thickness was explored. Results of two-way ANOVA indicate no significant effect of SCL material or previous wearing times on corneal thickness ($p > 0.05$). Full statistical analyses are in Appendix A.5.1.11.2.

4.3.4.3 The effect of 2 weeks cessation of SCL wear on stability of corneal thickness

Results of two-way ANOVA indicate that although corneal thickness remained thinner at all corneal locations in the SCL group compared with the NCL group following 2 weeks cessation of SCL wear, the differences between the groups were not statistically significant ($p > 0.05$). See Appendix A.5.1.12 for full statistical tables. Two-way ANOVA was then carried out on the stability of corneal thickness measurements between the first and second visits, results can be seen in Table 4-10.

Table 4-10: Stability of corneal thickness following 2 weeks SCL cessation

Location of corneal thickness	**SCL group (n = 38) Mean ±SD (µm)**	**NCL group (n = 37) Mean ±SD (µm)**	**Sig**
Central	0.66 ±8.79	-2.53 ±7.41	0.10
Thinnest value	0.55 ±9.25	-1.83 ±7.39	0.23
Inferior	2.71 ±12.10	-0.58 ±11.45	0.23
Nasal	3.26 ±12.56	-1.72 ±8.71	0.05
Superior	0.82 ±14.19	-2.50 ±10.87	0.27
Temporal	-0.47 ±10.28	-0.17 ±8.72	0.89

Mean ±SD of differences between corneal thickness between the first and second visits at measured locations for SCL and NCL groups. Negative values represent a decrease in corneal thickness, while a positive number represents an increase following 2 weeks cessation of SCL wear. No statistically significant differences were found, ($p < 0.05$).

There was relative stability of corneal thickness at all locations measured in both the SCL and the NCL control groups and results indicated no statistically significant differences between the groups ($p > 0.05$). There was a trend towards significance at

the nasal location ($p = 0.05$). Here, the SCL group showed an increase and the NCL control group showed a decrease in corneal thickness (SCL: 3.26 ±12.56µm vs. NCL: -1.72 ±8.71µm). This could indicate corneal moulding and thinning during SCL wear that has resolved once the SCLs were removed for 2 weeks. Stabilisation of corneal measurements can vary according to the SCL material worn, and the number of years SCLs were worn prior to lens cessation (see section 6.1). Results of two-way ANOVA showed no statistically significant effect for the differences in corneal thickness values measured at the first and second visits for any group (SCL material, years of SCL wear of the interaction between these groups). Full statistical findings are in Appendix A.5.1.12.

4.4 Discussion

The purpose of this research was to assess whether SCL wear had an influence on the accuracy or stability of corneal curvature and thickness measurements.

4.4.1 Retrospective study

This study was retrospective in nature, which could have resulted in some bias as it is difficult to limit unsystematic variations, also there can be no randomization in the allocation of patients into groups (Sackett, 1979). In order to limit this bias a NCL control group was used (Mantel and Haenszel, 1959). Furthermore, in order to limit the bias associated with subject selection in retrospective studies and improve the statistical accuracy of the results, all patient charts were reviewed and all subjects who fulfilled the inclusion criteria were included. Additionally, at the time clinical measurements were taken, the independent observer (the author, ALM) was unaware that the data would be used in a study thus limiting bias. Other authors have used similar methods for retrospective studies in the area of CL wear, corneal and CRS research (Naftali and Jabaly-Habib, 2013; Porazinski and Donshik, 1999; Vestergaard et al., 2013; Xie et al., 2009). The CRS environment in which my research was carried out demanded accurate, detailed and consistent measurements. Therefore, it was felt that the steps taken to account for bias imply that the data ought to be of a sufficiently high standard to be accepted for use in this thesis.

4.4.2 Sample size

G*power analysis was performed in order to calculate the sample size necessary to prove statistical significance in our research (Faul et al., 2007). Once the sample size was calculated, a sufficiently large sample size was initially included for analysis. While it was expected that the sample size was appropriate for analyzing the group as a

whole, the sample size diminished once further analysis of sub-groups took place. Notably, the small number of EW SCL modality, the lower number of LASEK/PRK patients and the drop-off of patients returning for post-operative visits following CRS meant that some of the significant results found ought to be interpreted with caution. Future larger studies comprising larger numbers of these distinctive groupings ought to be carried out.

4.4.3 The reliability and repeatability of the Pentacam instrumentation used

It was not possible to fully examine the repeatability of all of the equipment used in this research due to the inherent nature of retrospective studies. This lack of repeatability testing is a shortcoming of this research design. However, as previous studies have shown the repeatability of the Pentacam, Orbscan, US pachymeter, CEM-specular microscope and 3D OCT to be excellent, this limitation was not deemed to be critical (Cairns and McGhee, 2005; Chen and Lam, 2009; González-Pérez et al., 2011; Holladay, 2010; Lackner et al., 2005; Ortiz et al., 2013; Roberts, 1994; Uçakhan et al., 2006).

Two Pentacam instruments were used in study 1. These instruments were the same age and had the same software package installed, the corneal measurements from these were used interchangeably. As there was no comparison of the agreement between two individual Pentacam instruments, it was deemed necessary to examine their level of agreement (for full analysis see section A.5.1.3). Both Pentacam instruments were shown to have excellent intra-session reliability, with Cronbach's alpha and ICC values for pachymetry and SimK values being greater than 0.90, the ideal value that ought to be achieved for clinical applications (Bland and Altman, 1997). Cronbach's alpha and

ICC values of > 0.90 found were comparable to those reported in previous studies on neophyte and SCL wearing patients (Chen and Lam, 2009; Kawamorita et al., 2009a; Read and Collins, 2009), meaning that the data obtained with these two instruments could be used with confidence in this retrospective study.

In order to relate the Cronbach's alpha and ICC values to a clinical context, it is necessary to consider how narrow the limits of agreement (LOA) ought to be in order to conclude that the agreement of the two instruments is sufficient. Ng et al. (2007) defined repeated keratometry measurements as stable if values were within 0.50D (Ng et al., 2007). Hashemi and colleagues determined stability of CT measurements as being <10.5µm (Hashemi et al., 2008). The Pentacam inter-session curvature and thickness repeatability values from study one (see Appendix A.5.1.3) compare favourably with those of previous authors (see Table 4-11). The intra-session repeatability is less than those values outlined above, which indicates stability of measurements between sessions. Both Pentacam instruments showed good agreement for both corneal thickness and simulated keratometry measurements. Therefore, it was deemed suitable that the data from both instruments could be used interchangeably.

Table 4-11: A comparison of inter-session Pentacam repeatability findings for corneal curvature

Author, year **Variable (units)**	**Mean Difference**	**COR**	**95 % LOA**	**RR (%)**
Corneal curvature				
Study 1 Flat SimK (D)	0.00 ±0.18	±0.36	0.00 ±0.36	0.82%
Study 1 Steep SimK (D)	0.14 ±0.03	±0.61	0.14 ±0.61	1.37%
Study 1 Central Sagittal top (mm)	-0.03 ±0.16	±0.16	-0.03 ±0.16	2.11%
Kawamorita (2009) Flat SimK (D)			-0.03 ±0.27	
Kawamorita (2009) Steep SimK (D)			-0.10 ±-0.26	
Chen and Lam (2009) Flat SimK (D)		±0.19		0.46%
Chen and Lam (2009) Steep SimK (D)		±0.34		0.79%
Chen and Lam (2009) Sagittal top (mm)		±1.03		2.37%
Chen and Lam (2007) Posterior BFS (µm)			52.3 to -41.7 (in 5mm zone)	
Corneal thickness				
Study 1 CCT (µm)	5.8 ±10	±19.75	5.8 ±19.75	3.69 %
Study 1 CCT (µm)	5.8 ±9.5	±18.54	5.8 ±18.54	3.48 %
Hashemi & Mehravaran (2007) CCT (µm)			-31 to +19	
Lackner et al. (2008) CCT (µm)	1.0 ±6.1 (between visits) 0.1 ±3.0 (intra-observer)		-11 to +13 (between visits) -6.0 to +5.8 (intra-observer)	
O'Donnell & Maldonado-Codina (2005) CCT (µm)			-24.1 ±21.1	
Shankar (2008) CCT (µm)		±16.00		1.23%
(Belin and Khachikian, 2006b).	3µm			

Comparison of findings for corneal curvature show that the results of study 1 are similar to those previously reported in the literature. COR: coefficient of reliability, LAO: limits of agreement, RR: relative repeatability.

It has been recommended that an average of several readings be taken to improve accuracy of measurements taken with the Pentacam (Chen and Lam 2009, O'Donnell and Maldonado-Codina 2005). Unfortunately studies 1 and 2 involved retrospective analysis of data, thus there was no control on the number of measurements available for each patient. For this reason, this method of averaging of measures, could not be implemented and it was decided that the best available quality scan for each patient taken at that visit would be analysed. This method was continued through studies 3, 4 and 5 in all corneal measurements acquired.

Lackner et al. (2005) examined the influence of the number of measurements and observers on the repeatability of CCT measurements. The Pentacam showed the lowest inter-observer variability of the 3 instruments tested (Pentacam, Orbscan II and US). The 95% confidence intervals (CI) were less than 8.5μm for all modalities (this equates to an observer-related reproducibility of CCT within 1.6%). The accuracy of the Pentacam was proposed to be due to the beam rotation (as it is reported that each section runs through the corneal vertex (Oculus, 2007) and the higher intensity profiles due to the larger number of data points analysed (26,000 elevation points) of Pentacam images with less difference-to-noise ratios in the cornea.

Owing to the retrospective nature of study 1, it was not possible to restrict corneal measurements to those taken by only one observer. Therefore, it is not possible to exclude associated operator bias. However, as outlined above, previous studies have shown intra-observer repeatability of the instrumentation used to be high. In fact, in the case of the Pentacam the intra-observer repeatability was better than intra-session repeatability as depicted by lower mean difference and LOA values (see Table 4-11).

4.4.4 Population demographics

Our sample represents a cross section of SCL wearing patients presenting for CRS and NCL controls. The age of study population must be considered, as the average age of the NCL control group was significantly older (mean age 37 ±10 years; range 23 to 58 years) than the SCL group (mean age 32 ±7.5 years; range 21 to 49 years, $p = 0.02$). While no conclusive link has been established between age and corneal curvature or thickness measurements (Eysteinsson et al., 2002; Fledelius and Stubgaard, 1986; Khoramnia et al., 2007; Lee et al., 2011; Siu and Herse, 1993), VA can diminish with age and so this will be considered in study 2.

In these studies the level of myopic refractive error was higher in the SCL group compared with the NCL group, therefore the relationship between myopic refractive error and corneal curvature must be considered. Central corneal curvature is, generally, steeper with increasing myopia (Budak et al., 1999; Dubbelman et al., 2006), this may have contributed to the steeper average curvature in the SCL group. Lim and Fam (2006) found a significant correlation with mean keratometry and myopia. Corneal curvature and the effect of the severity of myopia (grouped according to low < -3.00D, moderate -3.00 to -6.00D, and high > -6.00D) were also assessed between the groups (SCL vs. NCL). No significant differences were found between the groups ($p > 0.05$), indicating that while there was significantly higher MSE in the SCL group compared with the NCL, this did not correlate with corneal curvature. Furthermore, the resolution of inferior corneal steepness, evident on in the tangential radii measurements taken at the first visit, resolved following 2 weeks' cessation of SCL wear. This indicats that it was the SCL wear and not the level of myopic refractive error in the SCL group that caused the steeper curvature evident at the first visit.

4.4.5 CL wear

In this study, SCLs were mainly worn following a DW modality. The majority of the SCL group wore hydrogel lenses (n = 35, 75.6%), 13.3% (n = 6) wore SiHy lenses and the type of SCLs worn was unknown in the remaining 4 patients. This sample represents a cross section of Irish SCL wearers, fewer of whom wear SiHy SCL compared with SCL wearers in the United Kingdom (UK). In the UK SiHy lenses accounted for 21% of the SCL market, while hydrogel lenses accounted for 71% (French and Jones, 2008). The difference may lie in the variation of SCL prescribing habits between Irish and UK optometrists (Efron et al., 2013; Efron et al., 2012). DW has increased in popularity in the UK as the most common modality of wear, with EW representing only 3% of newly fitted and 7% of refitted SCL patients (Guillon and Maïssa, 2010; Morgan et al., 2011). In line with recent research findings, the majority of SCL wearers included in this research wore SCL for DW rather than EW modalities.

4.4.5.1 Diurnal variation in corneal curvature

One must consider the implications of diurnal variation on corneal curvature. The anterior cornea is flattest and the posterior cornea steepest upon wakening (Giráldez-Fernández et al., 2008; Kiely et al., 1982; Read and Collins, 2009). These values are reported to resolve quickly (within 2 hours) and remain stable for the remainder of the day (Read and Collins, 2009). It is possible that diurnal variation may have had an implication on the difference in corneal curvature measured at the first and second visits if there was a significant time difference. However, the majority of diurnal variation happens within the first hour after awakening (Aakre et al., 2003). Therefore, when one allows for travel time to the CRS clinic for appointments, there is likely to have been sufficient time to allow for the resolution of diurnal variation of corneal curvature. The

link between diurnal variation in corneal curvature and the menstrual cycle must also be considered. While the impact of the menstrual cycle on corneal curvature has been reported as being minimal (Oliver et al., 1996), there may be increased diurnal variation in young women after menses (Handa et al., 2001). It was not possible to investigate the effect of diurnal variation which is a disadvantage of the retrospective nature of this study.

4.4.6 Corneal curvature with SCL wear

Corneal topography is necessary for pre-operative CRS screening in order to exclude ocular disease or SCL-induced corneal warpage. It is also important for the prediction of post-operative keratometry parameters. This information is vital in order to ensure the cornea will remain within the recommended curvature range, to assess corneal healing, to investigate poor outcomes and plan re-treatment.

While corneal topography is indispensable when assessing CRS patients, the accuracy of this tool may be hindered by poor quality scans caused by SCL wear. Poor topography or pachymetry measurements result in unsuitable patients being classified as suitable, or suitable patients being classified as unsuitable for CRS. For example, Ambrósio and Wilson (2003) found the highest proportion of candidates who were deemed unsuitable for CRS were SCL wearers (n = 8 SCL, n = 6 RGP, n = 6 NCL). These SCL wearers had ceased SCL wear 3 days prior to this examination, which may have been insufficient for resolution of SCL induced corneal distortion. In theory, there may have been some patients who demonstrated SCL-induced corneal warpage, the presentation of which was similar to FFK. The findings of study 1 in relation to tangential topography support this assumption.

Corneal topography and keratometry values, generally, become steeper in all corneal meridians with SCL wear (Collins and Bruce, 2004; Jalbert et al., 2004; Liu and Pflugfelder, 2000; Yeniad et al., 2003). The results in this study corroborated with the literature and showed that SimK and sagittal corneal curvature values were steeper with SCL wear. Although, the differences between the groups (NCL vs SCL) were not statistically significant. Tyagi et al. (2010) found large regional variations in corneal thickness (mean change of 20.1 ±9.1µm, $p < 0.001$) in DW of hydrogel SCLs (Tyagi et al., 2010). However, in the same subjects the mean change in sagittal curvature was very low (0.02 ±0.03mm, $p > 0.05$). These results are in agreement with those of this study and indicate that sagittal curvature may not be a sensitive measure to demonstrate corneal stability following cessation of SCL wear. Stability of the axes of the steep and flat SimK values, automatically generated by the Pentacam at each visit, were not analysed. It is possible that there were fluctuations in these axes which would indicate instability following cessation of SCL wear. This point could be addressed in future studies.

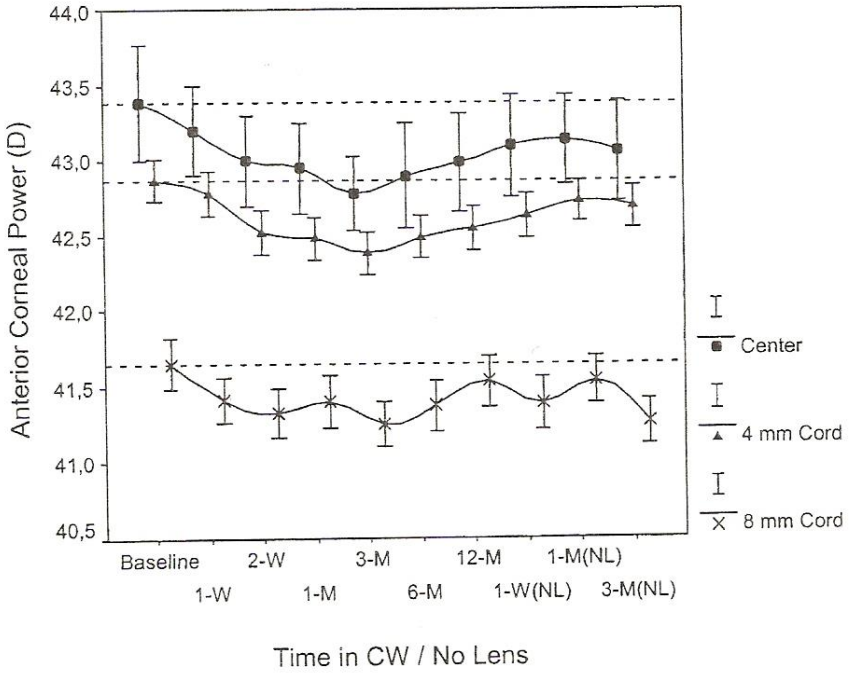
Instead, tangential curvature may be a more reliable tool for demonstration of stability. Prior to SCL cessation, there was some evidence of corneal warpage indicated by tangential radii analysis in this study. The mean anterior inferior tangential radius was significantly steeper for SCL group (7.77mm) compared with NCL control group (7.90mm, $p = 0.04$). These results indicate that caution ought to be exercised when assessing the suitability of patients for CRS procedures if they are SCL wearers. In some cases, suspicious topography may be missed if only sagittal radii are examined. Suspicious corneal inferior steepening may be more evident on tangential radii. While tangential topography is reportedly more accurate for examination of the peripheral

cornea (El Hage and Leach, 1999; Pascucci, 2007), one must also consider the accuracy of these measurements. Chen and Lam (2009) found Pentacam inter-session repeatability for both sagittal and tangential curvature to be poorer than ICC reliability values. This was especially evident at the superior region of the cornea (sagittal COR > ±1.03D; tangential COR > ±1.15D). The great variability in tangential peripheral curvature may be due to the greater rate of change in these peripheral measurements compared with the sagittal. It may also be linked to peripheral corneal distortion due to pressure or shadows induced by upper eyelids. However, in the current study the inferior location was influenced by SCL wear, so the effect of the upper lid would have been negligible.

The effects of SCL wear on corneal curvature vary according to the SCL material and wearing times (Alba-Bueno et al., 2009; Yeniad et al., 2003). Longer wearing times of low DK/t hydrogel lenses, result in significant flattening of the posterior corneal curvature compared with high DK/t SCL wear (Martin et al., 2009b). High DK/t SiHy SCLs reduce complications associated with hypoxia and have been found to maintain excellent long-term ocular tissue tolerance (Guillon and Maïssa 2010). There is disagreement in the literature as to the effect of short-term and DW of SiHy lenses. Del Águila-Carrasco (2015) reported a significant increase in CCT (8.9 ±2.8μm, $p < 0.01$) and a trends towards steepening of anterior sagittal curvature (-0.01 ±0.02mm, $p = 0.12$) following 8 hours of G2SiHy SCL wear compared with baseline and DW of other hydrogel daily disposable SCLs (n= 28 eyes). These effects may have been due to the effect of the stiffer modulus of these SCLs compared with NCL and hydrogel SCL wear. However, this finding was not discussed by these authors and although the subject population were not “regular” SCL wearers, it was unclear as to how long

previous SCL wear had been ceased prior to inclusion in the study (Del Águila-Carrasco et al., 2015). In opposition to this, Santodomingo-Rubido (2005) reported that when worn on a DW basis, SiHy lenses have been found to maintain baseline flat and steep keratometry values over 18 months of wear (Santodomingo-Rubido et al., 2005).

Figure 4-7: Corneal curvature with 12 months of silicone hydrogel lens wear



Graph showing the change in corneal curvature with SiHy CL wear. W: week, M: month, NL: no lens, CW: continuous/extended wear (González-Méijome et al. 2003).

Modality of SCL wear also must be considered, as with increased wear, the effect of the SCL material on corneal curvature can vary (Jalbert and Stapleton, 1999; Ruiz-Montenegro et al., 1993). Further analysis into the effect of SCL material on corneal curvature in study 1 revealed no significant differences between hydrogel and SiHy materials. Hydrogel SCLs were not worn on an EW basis prior to CRS procedures and modality of SCL wear was not explored in this study. Furthermore, SCL materials were not analysed according to the generation of SiHy material involved, and therefore the

modulus of the materials was not be taken into account. This may explain the differences between the findings of this study and others reported in the literature.

4.4.7 Corneal curvature following 2 weeks cessation of SCL wear

Results of the analysis of differences in curvature between the first and second visits indicated that SimK and sagittal curvature remained stable in SCL and NCL groups. However, the significant inferior tangential curvature steepening that was evident at the first visit for the SCL group, appeared to have resolved following 2 weeks cessation of lens wear. There was significant flattening at this location (SCL 0.08 ±0.18mm, NCL 0.01 ±0.08mm, $p = 0.02$). This could indicate that there was a resolution of inferior steepening in the SCL group following cessation of SCL wear as the cornea returned to a prolate shape. While these values were statistically significant, the small values involved lack clinical significance. In general, a vertical asymmetry of less than 1.5D would not be indicative of FFK or ectasia (Mertens et al., 2006).

An examination of the influence of SCL material on the stability of curvature between visits 1 and 2 was carried out. Flattening of all tangential radii was present in the hydrogel and SiHy groups following 2 weeks' cessation of SCL wear. These changes were greatest in superior and inferior locations and relatively small in the central location, indicating a return to a more prolate shape following cessation of SCL wear. The greatest flattening was seen in the SiHy group at the inferior corneal location, this result was statistically significant (0.21 ±0.30mm, $p = 0.02$). These results suggest that SCL modulus, and not DK/t, may have a greater effect on corneal curvature. Future studies with larger sample sizes in the 3 generations of SiHy SCL material groups ought to be carried out to investigate this hypothesis fully.

Ng et al. (2007) examined the time taken for resolution of CL related changes to corneal topography. The standard values given for stability of corneal curvature following cessation of SCL wear was a change of < 0.50D or 0.1mm since the previous visit. Using this criterion, only the inferior tangential radii measured in the SiHy SCL group showed instability in measurements following cessation of SCL wear. As previously discussed, over-wear of SCL wear can result in corneal warpage, the first signs of which can mimic FFK, see section 4.1.1. Inferior corneal steepening of > 1.4D relative to the superior value is indicative of FFK (Klyce 2000). The values measured in this study were less than this at the first (sagittal: 0.30 ±0.75D, tangential: 0.30 ±1.15D) and second visit (sagittal: 0.45 ±0.65D, tangential: 0.20 ±1.10D) in the SCL group.

These results emphasise the differences between sagittal and tangential topography values in the peripheral cornea. Furthermore, they reinforce previous research advising the use of tangential curvature to demonstrate stability and screen for local irregularities in corneal shape (such as those induced by refractive surgery, CL wear or ectasia) in the peripheral cornea (Klein and Mandell, 1995a).

4.4.8 Corneal thickness with SCL wear

4.4.8.1 Diurnal Variation and corneal thickness

This study was retrospective in nature and the time at which corneal thickness measurements were taken was not controlled. The mean time that measurements were taken was similar between the groups (SCL vs. NCL). Although there was a larger diurnal change in the SCL group (mean change of 4.90µm) this value was still less than those taken to demonstrate stability between corneal thickness measurements (8-10.5µm) (Hashemi et al., 2008; Ng et al., 2007). Furthermore, analysis of the data in

this study revealed no significant differences in corneal thickness between morning (before 14.00 hrs) and afternoon (after 14.00 hrs) time groups ($p = 0.285$). For this reason, corneal thickness for the SCL and NCL groups was analysed regardless of the time these measurements were taken. The cornea is thickest following eye opening after sleep, swelling by approximately 4%. The cornea rapidly thins in the first hour after opening the eyes, and remains at consistent levels through the day (Aakre et al., 2003; Du Toit et al., 2003; Efron, 2007; Giráldez-Fernández et al., 2008; Lattimore et al., 1999; Mandell, 1992). Therefore, diurnal variation in this study may have resolved within travel time to the clinic.

The results of this study are in agreement with those authors who report varying degrees of diurnal variation. Feng (2001) found there was no change between baseline measurements and those taken at 8.30am in a normal cornea (Feng et al., 2001). Aakre (2003) found that corneal thickness declines rapidly over the first hour after awakening and then remains essentially constant over a 16 hour period of measurement. Furthermore, it has been reported that there is inconsistency in diurnal variation between subjects due to individual corneal metabolic activity (Bonanno et al., 2003). This may account for the disagreement in the current literature with regards to diurnal variation in corneal thickness.

4.4.8.2 Corneal thickness prior to SCL cessation

Corneal thickness was found to be lower at all locations measured in the SCL group compared with the NCL control group (CCT SCL: 533.40 ±31.72µm vs. NCL: 537.40 ±29.40µm) in this study. However, these differences were not statistically significant ($p = 0.54$). A reduction in corneal thickness with SCL wear is the chronic response to corneal hypoxia resulting in decreased corneal thickness in long-term low DK/t SCL

(Holden et al., 1985; Liesegang, 2002; Pflugfelder et al., 2002; Yeniad et al., 2003). This reduced corneal thickness is thought to be related to keratocyte loss following short-term exposure to an anoxic environment. This can result in corneal oedema and a reduction in the number of keratocytes in the stroma (Kallinikos 2004). With keratocyte loss there is induced stromal thinning, as their function is to synthesise new stromal tissue (Efron 2007). Previously, in a retrospective study, CCT measured using US pachymetry was found to be significantly reduced, by an average of 22µm, in fulltime SCL wearers compared with a NCL control group, over a 2 year period ($p < 0.01$) (Braun and Anderson Penno, 2003). This reduced corneal thickness in SCL wear has been seen over long time periods. A mean reduction in corneal thickness of 14-30µm (Orbscan II) was found in a SCL wearing group ($n = 30$) compared with a NCL control group ($n = 35$) over 15 years (Sanchis-Gimeno et al., 2003).

Table 4-12: Corneal thickness of SCL and NCL wearers measured by the Orbscan topographer and results of study 1 measured by the Pentacam

	SCL group Mean ±SD n = 40 (mm)	**NCL control group Mean ±SD n = 64 (mm)**	**Sig**
Results of Liu et al. 2000			
Central	0.52 ±0.03	0.56 ±0.02	<0.01
Inferior	0.57 ±0.03	0.62 ±0.03	<0.01
Nasal	0.57 ±0.03	0.61 ±0.03	<0.01
Superior	0.61 ±0.03	0.64 ±0.03	<0.01
Temporal	0.55 ±0.03	0.58 ±0.03	<0.01
Results of study one	**SCL group n = 45 (µm)**	**NCL group n = 45 (µm)**	
Central	533.40 ±31.72	537.40 ±29.40	0.54
Thinnest	531.24 ±31.61	535.04 ±29.60	0.56
Inferior	599.47 ±32.92	607.18 ±32.63	0.27
Nasal	610.98 ±32.18	619.02 ±32.12	0.24
Superior	646.76 ±36.19	649.02 ±35.84	0.77
Temporal	594.07 ±30.55	601.27 ±34.39	0.30

Corneal thickness was significantly lower in SCL wearers compared with NCL wearers measured by the Orbscan topographer, significant differences shown in shaded cells ($p < 0.05$), adapted from Liu et al. 2000. Results of this study show no significant differences between groups (SCL vs. NCL).

The results of study 1 conflict with those previously published by Liu and Pflugfelder (2000), who found significantly reduced CCT and peripheral corneal thickness (3mm from centre) in a SCL group (n = 40 eyes) compared with a NCL control group (n = 64 eyes) over long-term SCL wear (> 5 years) (Liu and Pflugfelder, 2000). A mean reduction of 30 to 50 microns was found in the CL wearing group (see Table 4-12). Orbscan pachymetry was performed 2 weeks after removal of SCLs. The stability of corneal thickness was not examined, as no baseline or successive measurements were taken prior to cessation of SCL wear. Although the type of SCL material was not disclosed by the authors, as the study was published in the year 2000 it is unlikely that SiHy SCL materials were included. Furthermore, the modality of SCL wear was not

disclosed, therefore extended wear of hydrogel SCLs may account for the large fluctuations in CCT quoted by the authors.

The difference between these results of Liu et al. (2000) and this study may be related to the difference in instrumentation (Pentacam vs. Orbscan). As the Orbscan is an optical instrument, it is dependent on the clear transmission of light through the cornea. It requires distinct images of epithelial and endothelial surfaces and consistent configuration of optical media to obtain accurate measurements (Boscia et al., 2002). SCL wear may induce increased light scatter in cases of oedema and therefore affect the accuracy of the Orbscan in SCL wearers. The accuracy of Orbscan pachymetry diminishes in corneas with haze and the instrument has been found to underestimate corneal thickness when compared with the Pentacam and US (Kim et al., 2007). Although the Pentacam is also an optical device, these authors found it did not demonstrate the same under-estimation of CCT in corneas with haze (Kim et al., 2007; Matsuda et al., 2008). The difference may lie in the way the instrument acquires scan images, the Orbscan uses a horizontal scanning slit, whereas, the Pentacam uses a rotating system as discussed in section 4.4.3.

The results of this study also differed from those reported by Pflugfelder et al. (2002), where corneal thickness was examined in a NCL control group (n = 67) and CL wearers (n = 75) using the Orbscan. SCL wearers (n = 60) were instructed to remove their lenses 2 weeks before the study began. The CL group also included RGP wearers (n = 15) who were instructed to remove their SCL 4 weeks before the study began. The 2 groups of CL wearers were not analysed separately. Results showed corneal thickness to be significantly reduced in the CL wearers compared with the NCL wearing normal

group at all locations except nasally (see Table 4-13). Differences between the current study and these results may be due to the inclusion of RGP wearers and the aforementioned differences between Pentacam and Orbscan instruments.

Table 4-13: Corneal thickness measurements in normal and CL wearers

	CL group (n = 75) Mean ±SD (µm)	**NCL group (n = 67) Mean ±SD (µm)**	**Sig**
Centre	524.8 ±27.1	566.4 ±34.7	0.00
Inferior	578.11 ±29.5	625.6 ±34.1	0.00
Nasal	568.3 ±33.0	588.9 ±33.6	0.02
Superior	604.5 ±30.3	636.2 ±32.9	0.00
Temporal	552.5 ±29.5	615.0 ±34.0	0.00

Corneal thickness for CL and NCL wearers reported by Pflugfelder et al. (2002). Statistically significant differences are shown in shaded cells ($p < 0.05$)

The influence of SCL material on corneal thickness in this study showed the average corneal thickness was greater at all locations measured in the hydrogel SCL group compared with the SiHy group. However, differences were small and did not reach statistical significance ($p > 0.05$). Furthermore, there was no further reduction in corneal thickness evident with long-term SCL wear and the lowest corneal thickness values were found in the short-term SCL group.

These findings agree with other studies in which reduced CCT was found to vary according to the SCL material worn (Doughty et al., 2005; González-Méijome et al., 2003a). CCT (US pachymetry) was reduced, mid-peripheral corneal thickness showed a tendency to increase and peripheral corneal thickness remained stable when neophytes (n = 6) were fitted with G1SiHy SCL over 12 months of EW (González-Méijome et al.,

2003b). However, these results were not statistically significant ($p > 0.05$). The small sample size ($n = 6$) may have accounted for the lack of significance in the data. Central and mid-peripheral corneal thinning was attributed to the increased modulus of the SCL material, combined with compression effects experienced through EW. Errors may have been induced by variations in the US probe placement at the same corneal location for each measurement. These changes were still evident following 3 months cessation of lens wear. The authors suggested more time may be required for the cornea to return to baseline.

Table 4-14: Corneal thickness at baseline and following 12 months of soft CL wear

Corneal thickness n = 16	**Prior to SCL Mean ±SD (µm)**	**6 months of SCL wear Mean ±SD (µm)**	**Mean change (µm)**	**Sig**
Central	547 ±3	542 ±3	5	> 0.05
Superior	601 ±5	571 ±3	30	<0.01
Nasal	583 ±5	566 ±3	17	<0.01
Inferior	559 ±3	541 ±3	18	<0.01
Temporal	569 ±4	559 ±2	10	<0.01

Statistically significant differences are shown in shaded cells ($p < 0.05$), (Yeniad et al., 2003).

Yeniad et al. (2003) examined the influence of hydrogel SCL wear, of a variety of DK/t (20 to 32 x 10^{-11}), on corneal thickness (US pachymetry) in a group of neophytes ($n = 16$). Hydrogel SCL wear ($n = 12$) results in corneal thickening in the short term (1 month) and corneal thinning over longer time periods (12 months) (Yeniad et al., 2003). The results of Yeniad's study can be seen in Table 4-14. Corneal thickness was found to be statistically significantly less than baseline values at all peripheral corneal locations measured. The central value was also thinner but did not achieve statistical significance. The difference between the significantly thinner peripheral corneal thickness found by Yeniad et al. (2003) compared to the lack of difference in corneal

thickness found in study one may be due to reduced accuracy in peripheral corneal thickness measurements taken using the US pachymeter (Wheeler et al., 1992).

4.4.9 Stability of corneal thickness following 2 weeks cessation of SCL wear

A comparison of the differences in corneal thickness between the SCL and NCL groups was carried out following 2 weeks cessation of SCL wear in this study. The SCL group showed a minor increase in corneal thickness at all locations compared with the NCL group, with greater increases in corneal thickness evident in SiHy SCL wearers compared with hydrogel. This tendency for an increase in corneal thickness following cessation of SCL wear may be due to the stiffer modulus of the SiHy material causing some amount of corneal moulding prior to SCL cessation. Although the findings of study one did not achieve statistical significance, there was a trend towards statistical significance at the nasal location (SCL: increase -3.26 ±12.56, NCL: decrease 1.72 ±8.71, $p = 0.05$), with these values indicating a high degree of stability. Reduced corneal thickness and horizontal displacement of the thinnest pachymetry nasally has been suggested as a predicting factor for the development of post-CRS ectasia (Nilforoushan et al., 2008). The accuracy and reproducibility of these peripheral corneal thickness measurements must be considered, as it's reported that peripheral corneal measurements have reduced intra-observer reproducibility in the Pentacam (Miranda et al., 2009). Miranda et al. found good repeatability for CCT and mid-peripheral corneal thickness over time for healthy NCL wearing subjects ($n = 23$). However, confidence intervals increased towards the periphery, (see Table 4-15).

Table 4-15: Reproducibility of Pentacam peripheral corneal thickness measurements.

	Mean CCT ±SD (µm)	**Confidence interval (µm)**	**Mean corneal thickness at 4mm diameter ring (µm)**	**Confidence interval (µm)**
Baseline	546.23 ±5.24	-10.91 to 13.00	576.33 ±5.51	-11.73 to 13.73
After 1 hour	545.13 ±5.49	-13.43 to 11.23	5.75.64 ±5.64	-14.08 to 12.69
After 1 week	543.23 ±4.96	-11.99 to 10.02	575.95 ±4.90	-12.78 to 12.63

(Miranda et al. 2009)

Sanchis-Gimeno et al. (2007) found CCT was significantly reduced from baseline following 3 years of SCL wear (Sanchis-Gimeno et al., 2007). Baseline CCT was measured using the Orbscan in 15 myopic adolescent (aged 15 - 16 years) SCL wearers, 31 NCL adolescent controls (aged 15 - 16 years) and 34 myopic SCL wearers (aged 25 - 40 years). Both SCL wearing groups showed a significant reduction in CCT at 3 years (adolescent group baseline: 552 ±7.14µm; at 3 years: 545 ±8.35µm, $p = 0.012$), (older group: baseline: 550 ±9.40µm; at 3 years 539 ±8.81µm, $p < 0.01$). Recovery from corneal thinning following cessation of SCL wear was also measured; at 2 weeks' cessation time, the CCT was still significantly lower in the adolescent group (545 ±8.35µm, $p = 0.012$). This took a further 2 weeks to resolve (4 weeks: 549 ±7.32µm, $p = 0.201$). Although these values are statistically significant, the reduction in CCT may not be clinically significant as the overall mean reduction in the adolescent group was only 7µm. This value is less than the accepted value for stability in CCT used in other stability studies of 8µm (Ng et al., 2007). Differences between these findings and those of this study may be due to the age of the subjects included. All subjects in this study were adults aged older than 18 years, and had to exhibit a period of recent refractive stablility lasting greater than 2 years. This may explain the difference between Sanchis-

Gimeno et al.'s (2003) findings and those of this study, as the corneal becomes stiffer with age (Elsheikh et al., 2007), and it was only the adolescent group which took longer than 2 weeks for CT to resolve.

4.5 Conclusion

The key finding of this study was that inferior tangential curvature was significantly steeper in the SCL group compared with the NCL group at the first pre-operative visit. This SCL-induced inferior steepening appeared to have resolved following 2 weeks of cessation of SCL wear, thus indicating a return to the normal prolate shape. However, I maintain that best-practice would be to repeat topography scanning in cases of inferior corneal steepening in order to rule out subtle FFK. It has been reported in the literature that cases of unilateral corneal ectasia can occur following LASIK, where the only pre-operative sign was subclinical inferior corneal steepening (Kymionis et al., 2007). This finding stresses the importance of using all topographical maps when evaluating patients suitability for CRS.

No significant differences in corneal thickness were found between SCL and NCL groups at the first pre-operative visit, following 2 weeks cessation of SCL wear. Doughy and Zaman (2000) reported that pachymetry may not be a useful tool to objectively monitor corneal changes due to SCL wear, as the magnitude of the changes with SCLs are unlikely to exceed the normal diurnal rhythm. Our findings are in agreement with this.

Guidelines relating to cessation of SCL wear prior to CRS vary greatly from 24 hours (The Royal College of Ophthalmologists in the UK) to 2 weeks (FDA in the USA). The

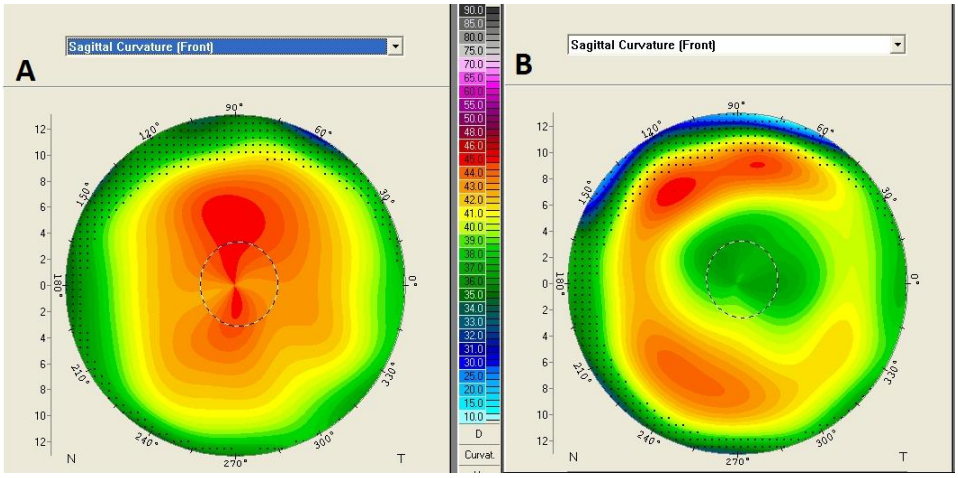
findings of study 1 showed that even myopic patients who were deemed suitable for CRS, had resolution of inferior corneal steepening within the 2 weeks following SCL cessation. The effect of previous SCL wear on the outcomes of CRS has not been explored in the literature. The next study in this thesis compared the outcomes of CRS between the SCL and NCL groups for two SCL cessation times (24 hours and 2 weeks).

5 CHAPTER FIVE. STUDY TWO: THE EFFECT OF SOFT CL WEAR ON CORNEAL REFRACTICE SURGERY OUTCOMES

5.1 Introduction

CRS is a common elective medical procedure, which aims to correct refractive error and eliminate the need for spectacles and CLs (McGhee et al., 1996; Sandoval et al., 2005; Tan and Tan, 1993; Whittaker, 1996). CRS involves ablation of stromal tissue to change corneal curvature and thickness, thereby correcting refractive error of the eye. This thesis focuses on the correction of myopia, where the Excimer Laser is used to flatten and thin the central optic zone (Figure 5-1).

Figure 5-1: Corneal topography before and following myopic ablation



Pre- and post-operative topography showing the results of myopic ablation. A. Pre-operative corneal topography showing central steepening. B. Post-operative topography showing central flattened optic zone. (Oculus, 2009).

CRS procedures achieve a high level of predictability (Alió et al., 2009; Ambrósio and Wilson, 2003; O' Brart, 2014). However, patient satisfaction with the post-operative outcomes is dependent on the ability of the procedure to achieve emmetropia and maintain levels of UDVA, which are similar to preoperative levels of BCSVA. The

outcome of CRS is dependent on the accuracy of the topographic measurements and the appropriateness of the procedure followed. These pre-operative measurements may be negatively affected by SCL wear. Hypoxia induced by over-wear of SCLs can result in reduced corneal metabolism and endothelial function (Liesegang, 2002; Nieuwendaal et al., 1994). Thus, resulting in increased light scatter, less light transmission and may affect corneal healing (McCally et al., 2007; Meek et al., 2003).

It has been reported in the literature that the time required for resolution of corneal changes can vary according to CL material, modality and length of previous CL wear and can be longer than 2 weeks (Hashemi et al., 2008; Nourouzi et al., 2006; Schornack, 2003). Despite these differences in effects relating to the properties of the SCL materials, prior to CRS, a standard SCL cessation time is advised for all patients. This cessation time varies according to governing bodies. While no specific guidelines are given in relation to SCL type, modality or wearing time, the United States Food and Drug Administration (FDA) guidelines recommend that SCLs be left out for at least 2 weeks prior to initial consultation (FDA, 2014). Whereas, the Royal College of Ophthalmologists in the United Kingdom recommend removing SCL for 1 day before consultation, and does not specify how long to cease SCL wear prior to the CRS procedure (Royal College of Ophthalmologists, 2011).

5.1.1 Complications and risks with CRS

There are many potential intra- and post-operative complications associated with CRS. The reported incidence of all CRS complications are 0.7% to 11.8% (Ambrósio and Wilson, 2001). A review of the literature shows that none of these have been be directly

attributable to pre-operative SCL wear. The most serious and prevalent of these complications are outlined in Table 5-1.

Corneal ectasia is considered the most serious post-operative complication. So far the current literature has focused on thin corneas and irregular topography as being risk factors for the development of ectasia following CRS. However, whether these risk factors are increased by long-term SCL wear remains unclear. A summary of the risk factors and the possible relation to SCL wear is outlined in Table 5-2.

Table 5-1: Corneal refractive surgery complications

Complication	**Causes/ associated finding**	**Incidence**
Potential Intra-operative Complications		0.7% to 2.2% (Ambrósio and Wilson, 2001)
Flap complications	Occur mainly with microkeratome	0.3% (Melki and Azar, 2001; Stevens, 2008)
Potential Post-Operative Complications		
Reduction in vision quality	Due to central islands or decentred flaps	5.8% to 11.7% (Alió et al., 2008a)
Over- and under-correction of refractive error	Possibly due to inaccurate refractive error (Melki and Azar, 2001)	4% (Rajan et al., 2004)
Refractive regression	Higher following hyperopic and high myopic correction	2.9 % -18% (Alió et al., 2008b; Taneri et al., 2004b).
Dry eye	Decreased corneal sensitivity due to damage to the corneal nerves in the ablation process	3% - 3.4% (Ambrósio and Wilson, 2001; Rajan et al., 2004)
Infection	The healing response involved by infection can lead to a higher rate of refractive regression in these patients and a loss of BCSVA	1 in 1102 patients (Solomon et al., 2011)
Epithlial ingrowth		1.7% (Ambrósio and Wilson, 2001)
Sterile inflammation Diffuse lamellar keratitis	Diffuse lamellar keratitis can stimulate an increased healing response which may in turn lead to a higher rate of refractive regression in these patients	0.02% and 3.2% (Ambrósio and Wilson, 2001; Melki and Azar, 2001)
Iatrogenic ectasia	Deep ablation depths and thinner residual stromal bed depths can cause a reduction of the biomechanically effective stress-bearing thickness of the cornea, resulting in ectasia	Ratio of occurrence LASIK (95.9%): PRK (4.1%), (Randleman et al., 2008).

A summary of the cause and incidence of the most common intra- and post-operative CRS complications (Ambrósio and Wilson, 2001; Bragheeth et al., 2008; Dupps and Wilson, 2006; Jacobs and Taravella, 2002; Linna and Tervo, 1997; McLeod, 2000; Melki and Azar, 2001; Solomon et al., 2011; Soong and Malta, 2009).

Table 5-2: Corneal ectasia and SCL wear

Risk factors for corneal ectasia	Relation to SCL wear
• Thin baseline cornea • Thick corneal flap • Excessive ablation • Irregular corneal thickness • Young patient • Low residual corneal bed (< 300µm)	• Accurate corneal pachymetry is essential in order to screen for suitability pre-operatively, and to determine the required flap thickness and post-operative residual bed depth. • Corneal screening for irregular thinning which might indicate corneal disease such as keratoconus is important. • SCL wear may induce corneal oedema or thinning which may result in inaccurate pre-operative pachymetry.
• Corneal topography irregularities	• SCL wear may induce corneal warpage, which may result in inaccurate pre-operative topography. • Irregular topography patterns (differences between inferior and superior corneal dioptric power : >1D and <1.4D inferior steepening: suspect > 1.4 dioptres: abnormal)

Risk factors in the development of post-CRS ectasia (Ambrósio, 2006a; Barraquer, 1981; McLeod, 2000; Naftali and Jabaly-Habib, 2013; Randleman, 2006; Tabbara and Kotb, 2006).

5.1.2 Aims and hypotheses

A review of the literature revealed no known links between previous SCL wear and complications or risks associated with CRS. However, no previous study had investigated the influence of SCL wear on outcomes of CRS procedures. The appropriate choice of CRS ablation profiles are based on precise pre-operative corneal topography measurements. If these measurements are inaccurate, due to prior SCL wear, the outcome may be negatively affected. To test this hypothesis, the influence of SCL wear on the outcomes of CRS was explored, when SCL wear was ceased for a period of 2 weeks in one group of patients and 24 hours in a second group of patients.

In both cases, CRS outcomes were compared to a NCL control group following surface laser epithelial keratomileusis (LASEK)/ photorefractive keratectomy (PRK) or laser in situ keratomileusis (LASIK) procedures.

5.2 Methods

5.2.1 Subject enrolment

A retrospective analysis of data previously collected by the author (ALM) was undertaken from the groups outlined in study 1 (SCL n = 45 and NCL n = 45). A further retrospective analysis was carried out for a second group of full-time SCL wearers (n = 48) who had ceased SCL wear for 24 hours prior to the data collection. The results were also compared with a NCL control group at this time (n = 48). This study focused on visual acuity (UDVA and BCSVA) and refractive error measurements taken pre-operatively and at 1, 3 and 6 months post-operatively. Quantitative comparison of the variations between the expected and actual changes in vision and refractive results was carried out between the two groups (SCL and NCL) for both SCL cessation time periods.

Data inclusion for the 2 week SCL cessation group has been discussed in section 4.2.1. For the 24 hour SCL cessation group, a retrospective review of CRS patients' files, was carried out, over a 12 month period (March 2011 to March 2012). Those who fulfilled the inclusion criteria (as outlined in section 3.1.1) were included for analysis (n = 96). These SCL wearers had been asked to cease SCL wear for a period of 24 hours prior to the data collection and scanning, used for CRS planning and calculations. Dominant eyes only were analysed retrospectively.

5.2.2 Clinical procedure for data collection

The clinical procedure for data collection of those who ceased SCL wear for 2 weeks is outlined in section 4.2.2. For the second group of SCL wearers, SCL wear was ceased for a period of 24 hours prior to their appointments. Once suitability for CRS was

determined, clinical measurements used for calculation of the CRS procedure were obtained for both SCL and NCL patients.

5.2.2.1 Subjective refraction prior to refractive surgery

Subjective refraction was determined following auto-refraction and subjective refraction using a phoropter for all patients. Stability of the patient's refractive status was assessed by comparing the manifest refraction at this visit to the patient's prescription from two years previously. Less than 0.50D change over the previous 2 years was termed stable (Allan, 2008; Dupps et al., 2011; Tantayakom et al., 2008).

5.2.2.2 Ocular dominancy

Ocular dominancy was tested using the Dolman method, asking the patient to look towards a distant target through a hole in a piece of card held by both hands at arm's length, the eyes were covered in turn to determine which eye could still see the target (Miles, 1929). This eye was recorded as the dominant eye and used for analysis in this thesis (Handa et al., 2004; Murakami and Manche, 2012).

5.2.2.3 Clinical measurements: visual acuity

VA (monocular and binocular) was measured in a room with no windows with the room lights on using a projected Snellen chart (Hamblin, London, U.K.). VA was recorded initially as a Snellen fraction with letters gained and missed accounted for (e.g. 6/6+2, 6/5-1). VA was then converted to the logarithm (base 10) of the minimum angle of resolution (LogMAR) and visual acuity rating (VAR) for analysis. This was done in order to account for the error which can be induced by recording the number of letters

seen and missed on a line of letters read from the Snellen chart (Frost et al., 2014). The VAR scale is a simple method of designating VA using a transformation of the LogMAR scale: VAR = 100 - 50(LogMAR) (Bailey and Lovie-Kitchin, 2013). On the VAR scale, 0.0 LogMAR (6/6 Snellen) corresponds to 100, 1.0 LogMAR (6/60 Snellen) corresponds to 50, each letter per line has a value of 1. For example, 6/6-1 = 99 (Bailey, 1988). The VAR value was then converted to the corresponding LogMAR value (Holladay, 1997). This method has been used in other studies examining VA following CRS (Ghadhfan et al., 2007; Wang et al., 2002b). It is recommended that for scientific studies LogMAR charts are more accurate (Lovie-Kitchin, 1998). However, in the refractive clinic where measurements were taken, there was no other chart available. Although, this Snellen chart used had a lower number of letters for the larger letters, from 6/24 to 6/5 sized lines, there were 5 letters on each line. All of the CRS outcomes analysed in this thesis were carried out on lines which contained 5 letters. This method of using a similar Snellen chart and conversion table from Snellen to LogMAR has been used in previous peer-reviewed studies (De Benito-Llopis et al., 2009; Ghadhfan et al., 2007).

5.2.2.4 Post-operative VA

Refractive outcome, was defined as the difference between the target spherical refraction (as the dominant eye was analysed, in all cases this equals zero), and the spherical equivalent of the residual refractive error. Examination of UDVA, achievement of target refraction, stability of vision and post-operative complications, following CRS between the groups was undertaken to investigate the possible influence of pre-operative SCL wear.

5.2.2.5 Analysis of refractive surgery outcomes

Due to the large variety of CRS procedures available, it is recommended that a set of standardised graphs and reporting terms are used for analysis of CRS outcomes (Dupps et al., 2011; Reinstein and Waring III, 2009). The standardised parameters used to examine the outcomes of CRS in study 2 were "efficacy" and "predictability".

- **Efficacy** was determined by assessing UDVA and manifest refraction values post-operatively. The efficacy index was calculated as the ratio of the post-operative UDVA to the pre-operative best corrected VA (Alió et al., 2008a; Alió et al., 2008b; Tantayakom et al., 2008).
- **Predictability** was depicted by the number of eyes within ±0.25D and ±0.50D of the desired refractive outcome at 1, 3 and 6 months (Dupps et al., 2011; Tantayakom et al., 2008).

It is recommended that the safety of CRS procedures should be reported in terms of the change in lines of BCSVA pre-operatively compared with post-operative BCSVA (Ang et al., 2009; Schor et al., 2003; Taneri et al., 2004b). A flaw due to the retrospective nature of study 2 meant that it was not standard clinic practice to record post-operative BCSVA at all post-operative visits. Therefore it was not possible to report safety using this method. Instead, a comparison of pre-operative BCSVA and post-operative UDVA is reported, as this method has been recommended by the European registry of quality outcomes for cataract and refractive surgery (Lundström et al., 2015). Safety can also be evaluated by looking at the number of intra- and post-operative complications associated with the CRS procedure (Ang et al., 2009). Safety is reported using this method was used in this used. In this study, there were no serious intra- or post-operative complications in

any group. There were two cases of grade 2 diffuse lamellar keratitis. Both occurred in the NCL group, which were treated successfully with topical steroids. As there is higher risk of regression and increasing myopia following diffuse lamellar keratitis (Alió et al., 2009; Condon et al., 2007), these cases were excluded from the post-operative analysis.

5.3 Results

5.3.1 Preoperative demographics, visual acuity and refraction parameters of the 2 weeks SCL cessation group

Demographics of the SCL and NCL groups for LASIK and PRK/LASEK are outlined in Table 5-3. A comparison of pre-operative BCSVA and refraction data (sphere, cylinder and MSE) was carried out between the SCL and NCL groups. Results of Mann-Whitney U testing indicate that there were significantly lower pre-operative sphere and MSE values found for the NCL group compared with the SCL group ($p < 0.05$) (see Table 5-3).

Table 5-3: Preoperative demographic, VA and refraction parameters

	LASIK			LASEK/ PRK		
	SCL (n = 23)	**NCL (n = 23)**	**Sig**	**SCL (n = 22)**	**NCL (n = 22)**	**Sig**
LogMAR VA	-0.13 ±0.06	-0.13 ±0.04	0.19	-0.13 ±0.05	-0.10 ±0.07	0.25
Sphere (D)	-3.72 ±1.84	-2.43 ±1.65	0.01	-3.75 ±1.50	-2.68 ±1.30	0.01
Cylinder (D)	-0.61 ±0.25	-0.66 ±0.36	0.80	-0.55 ±0.25	-0.60 ±0.32	0.68
MSE (D)	-3.97 ±1.84	-2.75 ±1.66	0.01	-3.98 ±1.43	-2.95 ±1.33	0.02
Age (years) (Range)	32.6 ±7.5 (21 to 49)	36 ±9.6 (23 to 57)	0.16	31.4 ±8 (21 to 49)	37.2 ±11 (23 to 58)	0.22
Sex Males: Females	48 : 52 (%)	52 : 48 (%)		54.5 : 45.5 (%)	77 : 23 %)	
SCL wear: years (Range)	9 ±5 (4-22)	0		9 ±4 (1-20)	0	
SCL wear: days/week (Range)	6.5 (5-7)	0		6 (5-7)	0	
SCL wear: hours/day (Range)	12.5 ±5 (5-24)	0		12 ±5 (4-24)	0	

Mean ±SD of preoperative demographic and refractive parameters. Mann-Whitney U-test, significant differences are shown in shaded cells ($p < 0.05$).

5.3.1.1 Post-operative visual acuity and refraction parameters of the 2 weeks SCL cessation group

Follow-up compliance (as a percentage of patients included in the group) was:
At the 1 month visit: 96% (n = 43) of LASIK and 100% (n = 45) LASEK/PRK,
At the 3 months visit, 93% (n = 42) of LASIK and 84% (n = 38) of LASEK/PRK,
At the 6 months visit, 78% (n = 35) of LASIK and 80% (n = 36) of LASEK/PRK.
In the course of the follow-up some patients did not attend the clinic, as they received follow-up care in clinics closer to their place of residence or work. In addition, some patients had emigrated.

5.3.1.2 One month post-operative results for the 2 weeks SCL cessation group

The 1 month efficacy and predictability outcomes of LASIK and LASEK/PRK procedures were compared between the SCL and NCL groups. The data were analysed using Kruskal-Wallis testing. The efficacy of both LASIK and LASEK/ PRK procedures showed superior levels of UDVA in the SCL group when compared with the NCL group (Table 5-4). Results showed there were no statistically significant differences in the mean efficacy or predictability values between the SCL and NCL control groups who had LASIK procedures. However, SCL patients who underwent LASEK/PRK showed significantly better UDVA (-0.05 ±0.09), compared with the NCL group (0.02 ±0.09; p = 0.04) (Table 5-4). These findings may be related to the significantly lower residual cylinder following CRS which was recorded at 1 month post-LASEK/PRK in the SCL group (-0.50 ±0.40) compared with the NCL group (-0.76 ±0.40; p = 0.02) (see Table 5-4).

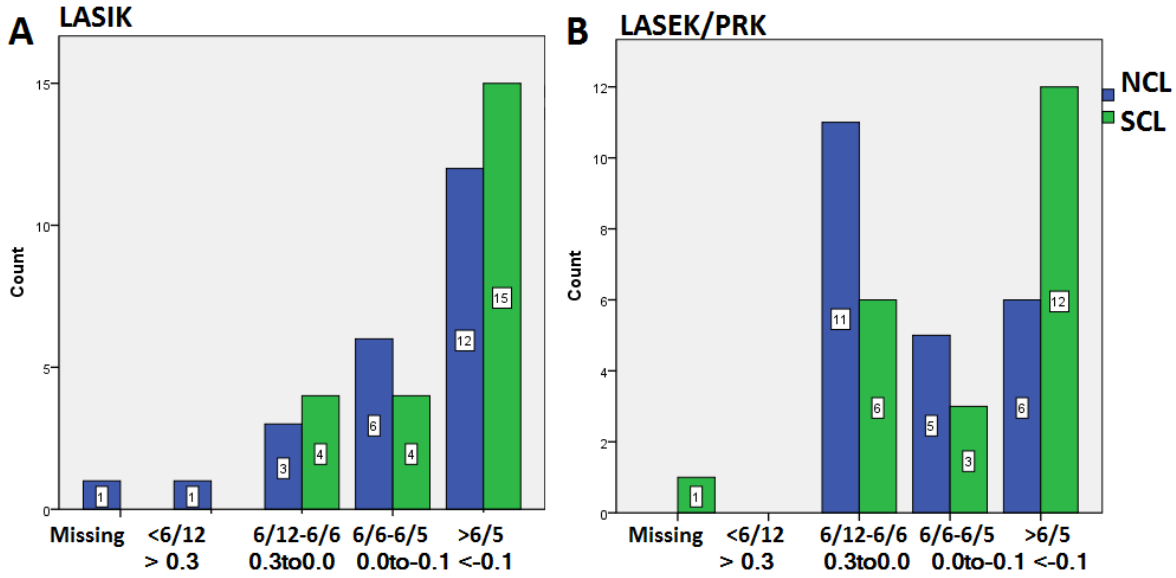
Table 5-4: Comparison of 1 month post-operative parameters.

	LASIK			**LASEK/PRK**		
	SCL (n = 23)	**NCL (n = 23)**	**Sig**	**SCL (n = 22)**	**NCL (n = 22)**	**Sig**
LogMAR UDVA	-0.04 ±0.13	-0.08 ±0.07	0.53	-0.05 ±0.09	0.02 ±0.09	0.04
Efficacy index LogMAR, Snellen	95%	92.5%		95%	94%	
>0.3, <6/12 n (%)	0	0	0.58	0	0	0.17
<0.3, >6/12 n (%)	23 (100)	21 (91)		21 (96)	22 (100)	
< 0.0, >6/6 n (%)	19 (83)	18 (78)		15 (68)	11 (50)	
<-0.1, >6/5 n (%)	15 (65)	12 (52)		12 (55)	6 (27)	
No show	0	1 (4)		1 (4.5)	0	
Predictability						
Sphere (D)	+0.24 ±0.38	-0.02 ±0.52	0.16	+0.11 ±0.46	+0.34 ±0.67	0.16
Cylinder (D)	-0.44 ±0.20	-0.42 ±0.34	0.31	-0.50 ±0.40	-0.76 ±0.40	0.02
MSE (D)	+0.06 ±0.35	-0.21 ±0.63	0.15	-0.10 ±0.50	-0.03 ±0.70	0.46
Within ±0.25D	15 (65%)	13 (57%)	0.94	12 (55%)	10 (46%)	0.66
Within ±0.50D	20 (87%)	15 (65%)		13 (59%)	12 (55%)	
> ±0.50D	3 (13%)	6 (26%)		7 (32%)	8 (36%)	

Comparison of the 1 month post-operative parameters. Significant differences found with Kruskal-Wallis testing are shown in shaded cells. "No show" refers to patients who did not attend their post-operative appointments.

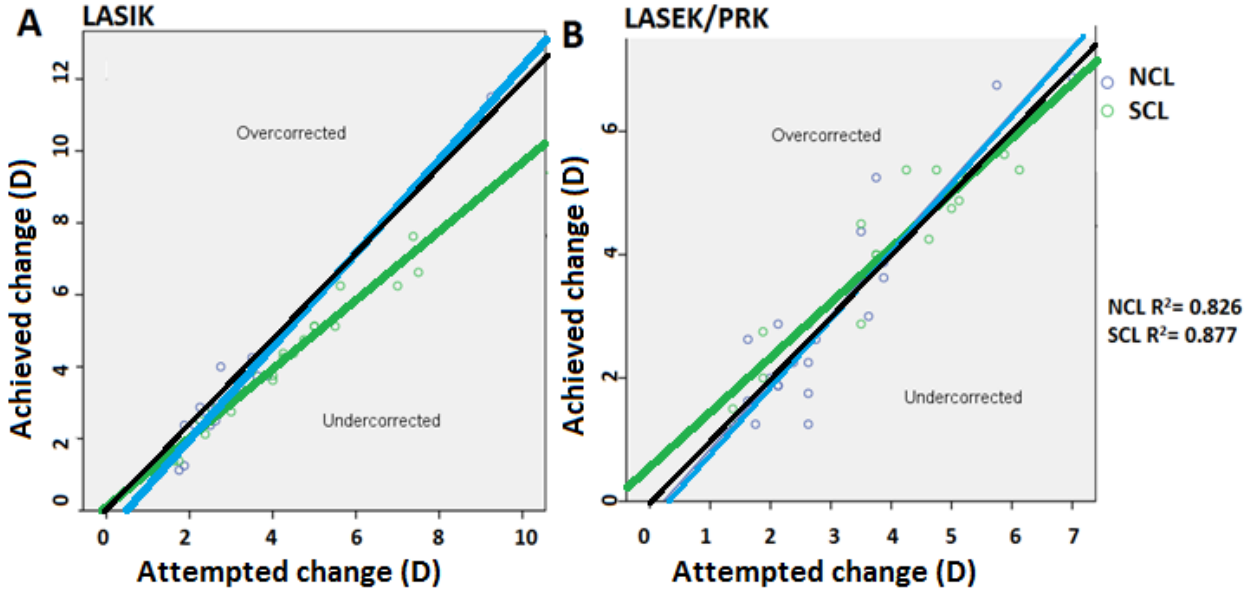
The efficacy and predictability of the CRS procedures, to achieve the desired correction, for the SCL and NCL groups is displayed in Figure 5-2, Figure 5-3 and Figure 5-4. The SCL group, who had LASIK, showed a tendency towards under-correction with higher myopic corrections compared with the NCL control group. A higher proportion of the SCL group had a MSE of within ±0.25D at 1 month compared with the NCL group.

Figure 5-2: Unaided distance visual acuity values at 1 month



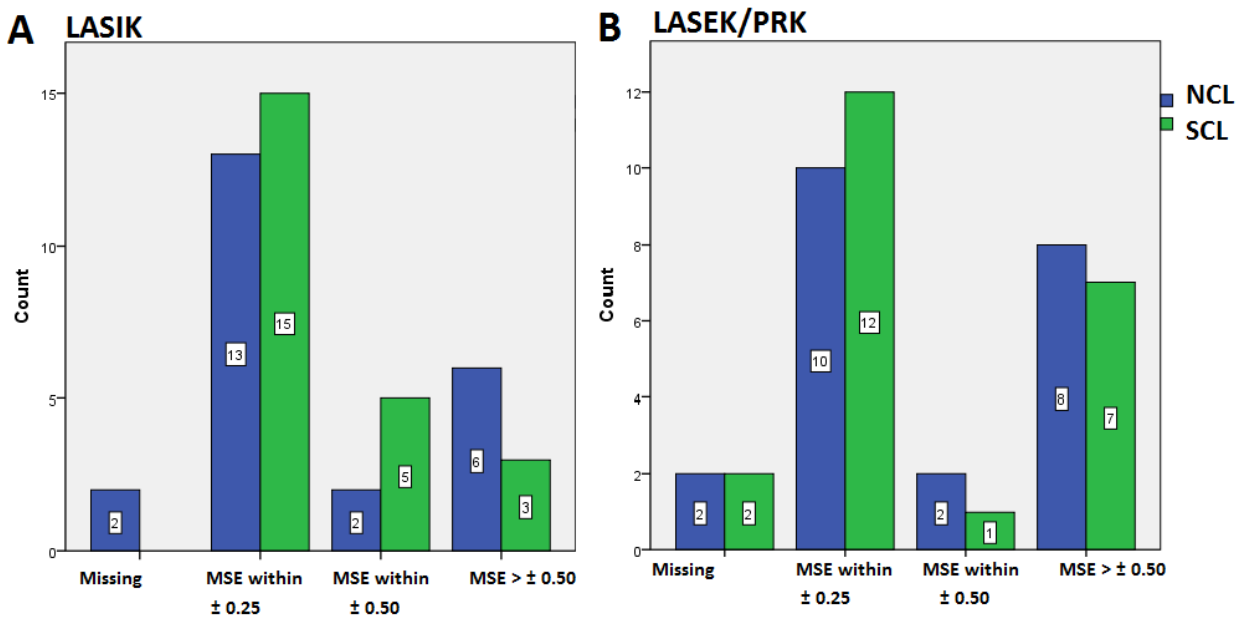
Snellen and LogMAR UDVA achieved at 1month. SCL wearers (green) had a greater tendency to achieve VA of -0.1 or better when compared with the NCL wearers (blue), for both LASIK (A) and LASEK/PRK (B) procedures. Missing data refers to patients who did not show for their1 month follow-up visit.

Figure 5-3: Predictability: attempted vs. achieved dioptric change in spherical equivalent (D) at 1 month



Scattergram showing the relationship between the attempted and achieved change at 1 month. SCL group is shown in green and the NCL group in blue. The black line indicates the desired correction of 0 dioptres has been achieved. The SCL group who had LASIK procedures (A) showed a tendency towards under-correction with higher myopic corrections compared with the NCL control groups.

Figure 5-4: Refractive accuracy of 1 month post-operative mean spherical equivalent refraction



Number of eyes achieving mean spherical acuity values within ±0.25 and 0.50 dioptres of the target change at 1 month, SCL group in green, NCL control group in blue. Missing data refers to patients who did not show for their1 month follow-up visit.

5.3.1.3 Three month post-operative results for the 2 weeks SCL cessation group

The efficacy and predictability of LASIK and LASEK/PRK outcomes for the SCL and NCL groups, measured 3 months after CRS, were compared, in order to explore the influence of pre-operative SCL wear. The results of LASIK and LASEK/PRK procedures were analysed using Kruskal-Wallis testing (Table 5-5).

Table 5-5: Three-month post-operative VA and refraction parameters

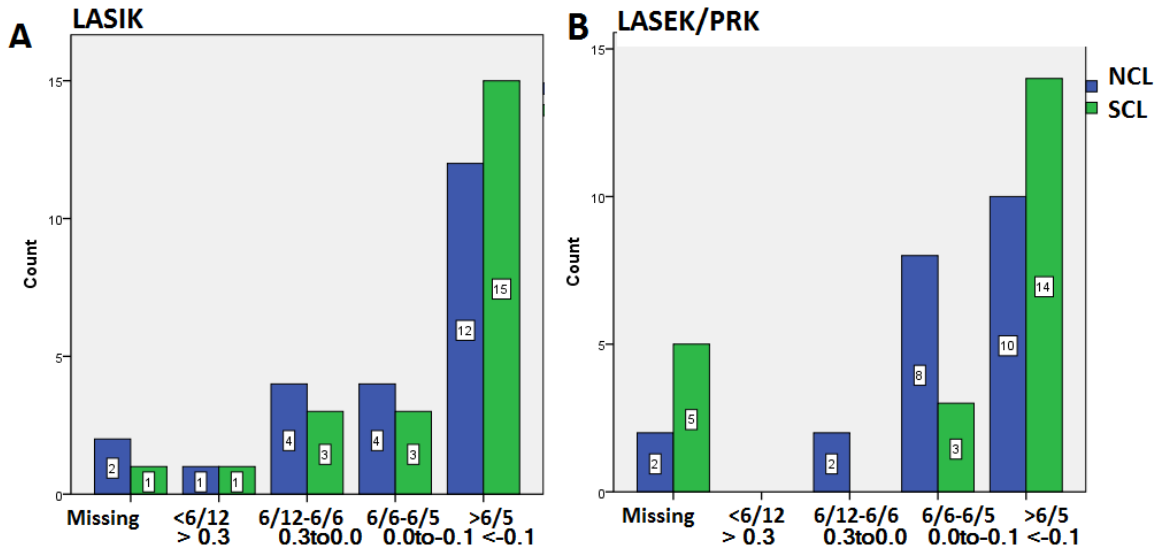
	LASIK			**PRK/LASEK**		
	SCL (n = 22)	**NCL (n = 21)**	**Sig**	**SCL (n = 17)**	**NCL (n = 20)**	**Sig**
Efficacy						
UDVA LogMAR VA	-0.06 ±0.13	-0.05 ±0.11	0.32	-0.10 ±0.04	-0.07 ±0.05	0.07
Efficacy index LogMAR, Snellen	96%	96%		98%	97%	
> 0.3, < 6/12 n (%)	22 (96)	21 (91)	0.92	0	0	0.52
< 0.3, > 6/12 n (%)	21 (91)	20 (87)		0	20 (91)	
< 0.0, > 6/6 n (%)	18 (78)	16 (70)		17 (77)	18 (82)	
< -0.1, > 6/5 n (%)	15 (65)	12 (52)		14 (64)	10 (45.5)	
No show	1 (4)	2 (9)		5 (23)	2 (9)	
Predictability						
Sphere (D)	+0.07 ±0.43	-0.01 ±0.47	0.58	+0.17 ±0.32	+0.22 ±0.56	0.78
Cylinder (D)	-0.38 ±0.18	-0.46 ±0.25	0.31	-0.40 ±0.19	-0.50 ±0.30	0.35
MSE (D)	-0.08 ±0.44	-0.22 ±0.50	0.30	-0.01 ±0.37	+0.01 ±0.65	0.82
Within ±0.25D	14 (61%)	10 (43.5%)	0.64	9 (41%)	8 (36%)	0.07
Within ±0.50D	18 (78%)	17 (74%)		13 (59%)	14 (64%)	
> ±0.50D	4 (17%)	4 (17%)		2 (9%)	2 (23%)	

Comparison of the 3-month post-operative outcomes. Kruskal-Wallis significant differences are shown in shaded cells. "No show" refers to patients who did not attend their post-operative appointments.

The efficacy of both LASIK and LASEK/ PRK procedures was higher in the SCL group, for achieving superior levels of VA, when compared with the NCL group 3-months following CRS (see Figure 5-5). The tendency towards overcorrection for high

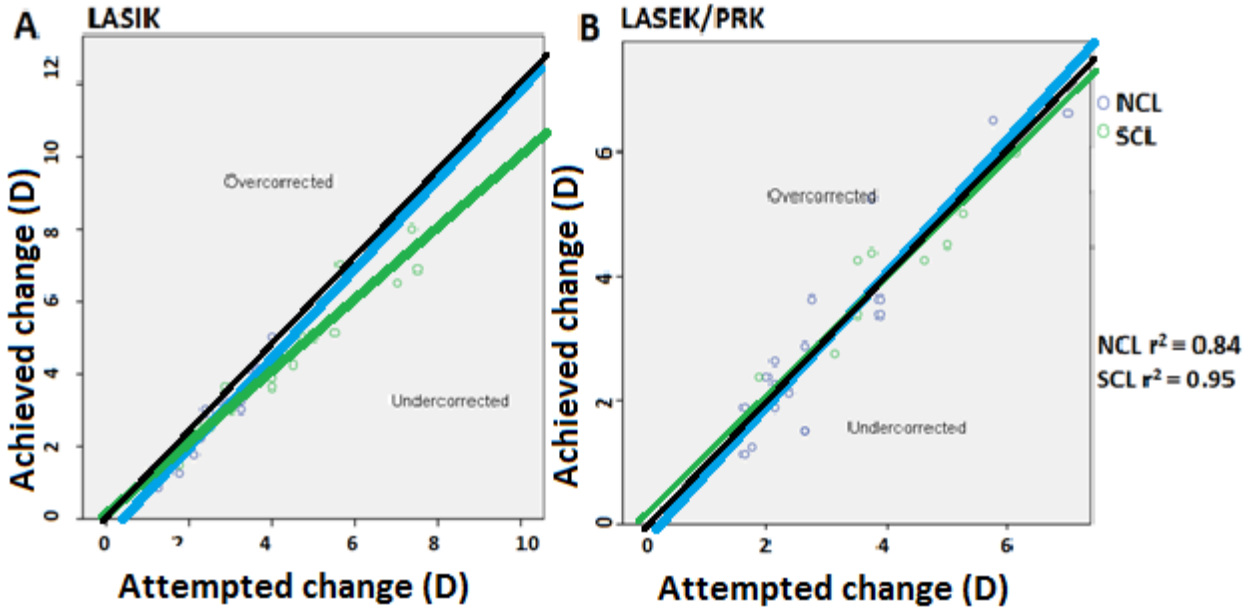
pre-operative myopic refractions, was still evident at 3-months in the SCL group who had LASIK procedures carried out (see Figure 5-6). However, these results were not statistically significant for any efficacy or predictability measures tested between the groups for LASIK or LASEK/PRK procedures.

Figure 5-5: Efficacy index at 3 months



Efficacy at 3-months, shows a tendency for achieving higher levels of UDVA in the SCL group(shown in green) compared with the NCL control group (shown in blue) for LASIK (A) and LASEK/PRK (B). Both Snellen and LogMAR VA values are displayed. Missing data refers to patients who did not show for their 3-month follow-up visit.

Figure 5-6: Predictability at 3 months



Scattergram showing the attempted change versus the achieved change at 3 months. SCL group in green, NCL control group in blue. Values falling on the black line indicate that the desired correction of 0 D was achieved. The SCL group who had LASIK procedures (A) showed a tendency towards under-correction with higher myopic corrections compared with the NCL control groups.

5.3.1.4 Six month post-operative data for the 2 weeks SCL cessation group

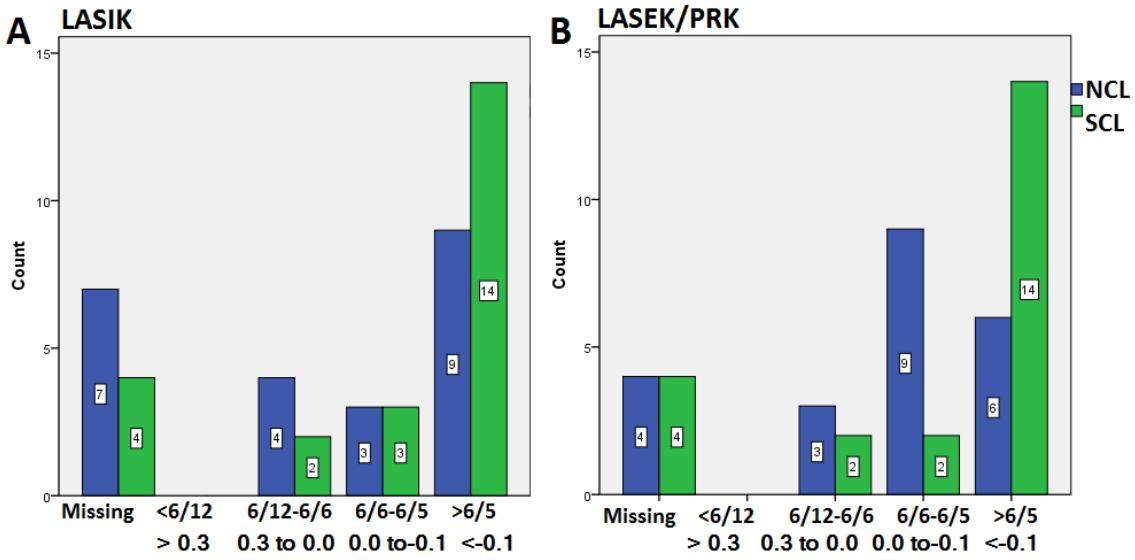
The efficacy and predictability of LASIK and LASEK/PRK outcomes 6 months after CRS, were compared between the SCL and NCL groups using the Kruskal-Wallis test (see Table 5-6). The outcomes found at 1- and 3-months post-operatively were maintained at 6 months. The SCL group achieved better VA than the NCL, following LASIK and LASEK/PRK procedures, as depicted graphically in Figure 5-7.

Table 5-6: Six month post-operative visual acuity and refraction parameters

	LASIK			**LASEK/PRK**		
	SCL (n = 19)	**NCL (n = 16)**	**Sig**	**SCL (n = 18)**	**NCL (n = 18)**	**Sig**
Efficacy						
UDVA LogMAR	-0.10 ±0.10	-0.06 ±0.07	0.03	-0.10 ±0.08	-0.04 ±0.08	0.03
Efficacy index	97%	98%		98%	97%	
> 0.3, < 6/12 n (%)	0	0	0.13	0	0	0.10
< 0.3, > 6/12 n (%)	19 (83)	16 (70)		18 (82)	18 (82)	
< 0.0, > 6/6 n (%)	17 (74)	12 (52)		16 (73)	15 (68)	
< -0.1, > 6/5 n (%)	14 (61)	9 (39)		14 (64)	6 (27)	
No show	4 (17)	7 (30)		4 (18)	4 (18)	
Predictability						
Sphere (D)	+0.08 ±0.31	-0.08 ±0.45	0.36	+0.06 ±0.55	+0.20 ±0.56	0.69
Cylinder (D)	-0.42 ±0.22	-0.44 ±0.19	0.81	-0.37 ±0.23	-0.28 ±0.13	0.29
MSE (D)	-0.08 ±0.31	-0.24 ±0.45	0.30	-0.08 ±0.60	+0.07 ±0.52	0.80
Within ±0.25D	14 (61%)	9 (39%)	0.92	8 (36%)	7 (32%)	0.71
Within ±0.50D	18 (78%)	13 (56.5%)		10 (45.5%)	11 (50%)	
Greater than ±0.50D	1 (4%)	3 (13%)		6 (27%)	4 (18%)	
Comparision of pre-operative BCSVA and post-operative UDVA						
Loss 1 line VA	4 (21%)	6 (37.5%)	0.11	3 (17%)	9 (50%)	0.25
Loss 2 or more lines VA	4 (21%)	6 (37.5%)		2 (11%)	0 (0%)	

Comparison of the 6 month post-operative parameters. Significant differences revealed by the Kruskal-Wallis test are shown in shaded cells. "No show" refers to patients who did not attend their post-operative appointments.

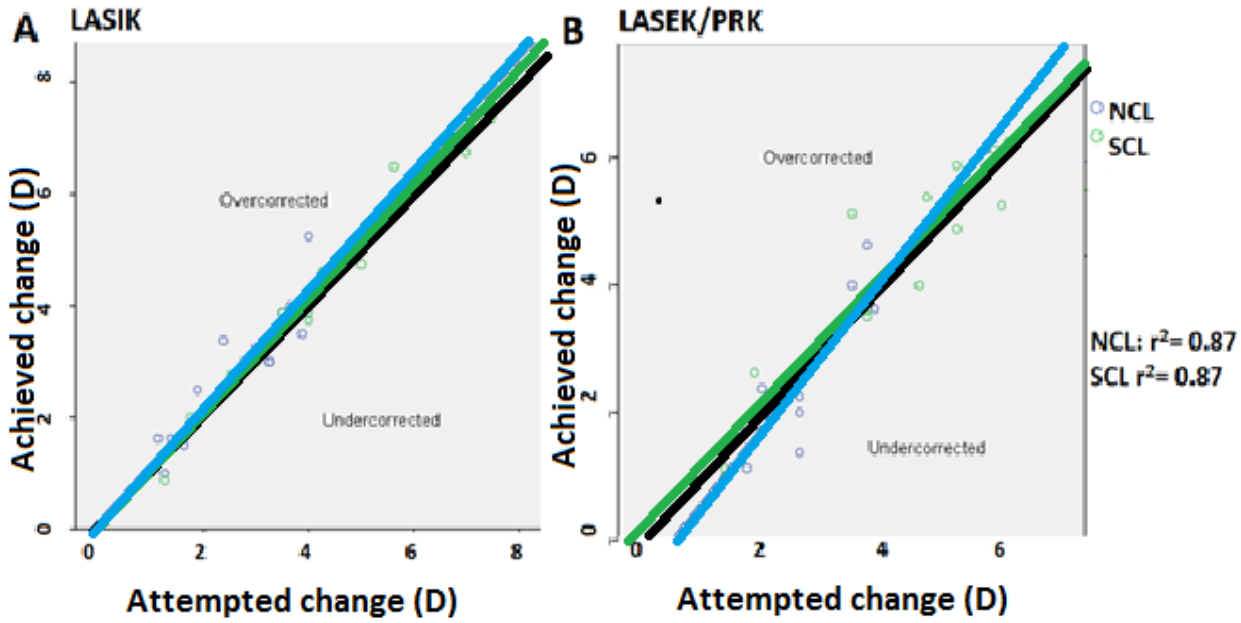
Figure 5-7: Efficacy index at 6 months



Results showed that the SCL group (in green) tended to achieve superior levels of UDVA compared with the NCL control group (in blue) for both LASIK (A) and LASEK/PRK (B) procedures. Both Snellen and LogMAR VA values are displayed. Missing data refers to patients who did not show for their 6 month follow-up visit.

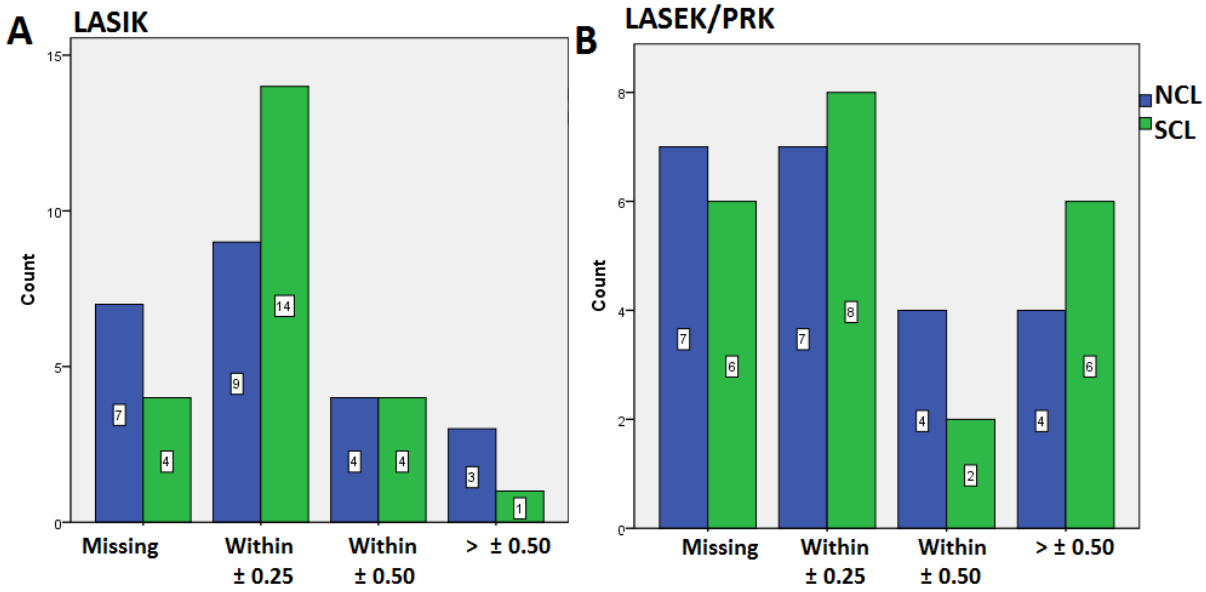
The predictability of LASIK, that is the attempted change (set at a target of 0 D) versus the achieved post-operative refractive error improved by 6 months (see Figure 5-8).

Figure 5-8: Predictability-attempted vs. achieved dioptric change in spherical equivalent (D) at 6 months



Scattergram showing the attempted change versus the achieved change at 6 months. SCL group in green, NCL control group in blue. Any point falling on the black line indicates that the desired correction was achieved. Results for LASIK (A) and LASEK/PRK (B).

Figure 5-9: MSE predictability at 6 months



Refractive accuracy of mean spherical equivalent at 6 months post-operative showed a greater tendency for the SCL group (shown in green) to be within 0.25D than the NCL control group (shown in blue), for both LASIK (A) and LASEK/PRK procedures (B). Missing data refers to patients who did not attend their 6 month follow-up visit.

5.3.1.5 Comparision of pre-operative BCSVA and 6 month post-operative UDVA

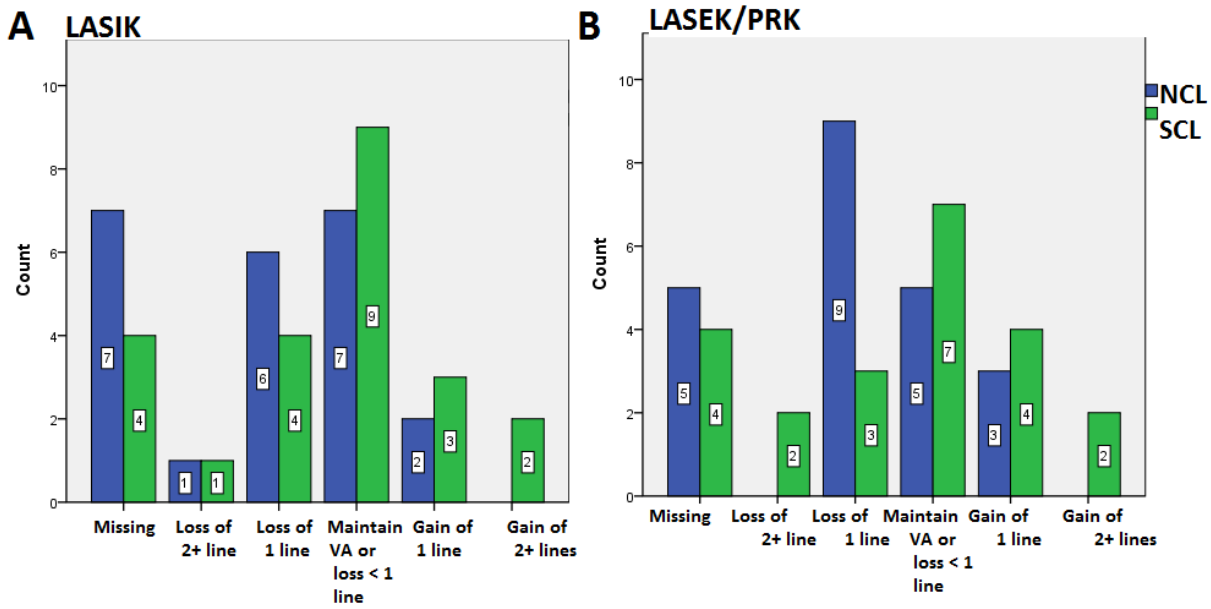
Results of a two-way ANOVA indicated that there was a tendency for less loss in lines of VA (pre-operative BCSVA vs. post-operative UDVA) in the SCL group (Figure 5-10); these results were not statistically significant (Table 5-7).

Table 5-7: Comparision of pre-operative BCSVA and 6 month post-operative UDVA

	LASIK			LASEK/PRK		
	SCL (n = 19)	**NCL (n = 16)**	**Sig**	**SCL (n = 18)**	**NCL (n = 18)**	**Sig**
Loss of 1 line VA	4 (21%)	6 (37.5%)	0.11	3 (17%)	9 (50%)	0.25
Loss of 2 or more lines VA	4 (21%)	6 (37.5%)		2 (11%)	0 (0%)	

There was a greater tendency to lose 1 or more lines of post-operatively UDVA compared with pre-operatively BCSVA in the NCL control group. However, these results were not statistically significant, (all p values > 0.05).

Figure 5-10: Graph showing the comparision of pre-operative BCSVA and 6 month post-operative UDVA



SCL group showed greater gain of VA compared with NCL control group for both LASIK (A) and LASEK/PRK (B). Missing data refers to patients who did not show for their 6 month follow-up visit.

Safety was evaluated by looking at the number of intra- and post-operative complications associated with the CRS procedure. In this study, there were no serious intra- or post-operative complications in any group. Serious complications were defined

as infection, greater than grade 2 corneal haze, serious dry eye or flap complications, as outlined by previous authors (Melki and Azar, 2001).

In summary, the results of this study, on the influence of 2 weeks of SCL cessation on the outcomes of CRS, indicated that previous SCL wear had no negative impact on efficacy or predictability of either LASIK or LASEK/PRK. Moreover, it was found that SCL wearers had significantly better visual outcomes following both LASIK and LASEK/PRK at the 6 month follow-up visit compared with the NCL group. While the differences in VA levels were found to be statistically significant, we cannot conclude they were clinically significant due to the small difference in letters seen between the groups. The test hypothesis, that SCL wear prior to CRS might be detrimental to the outcome, was rejected.

5.3.2 Demographics of the 24 hour SCL cessation group

A retrospective evaluation was carried out on the influence of 24 hours' SCL cessation on corneal measurements and on the outcomes of CRS, between a group of full-time SCL wearers and a NCL group. Ninety-eight patients (49 SCL and 49 NCL wearers) met the study's inclusion criteria as outlined in section 3.1.1. Patient ethnicity and sex are outlined in Table 5-8.

Table 5-8: Study 2 patient demographics

	SCL (n = 49) n (%)	**NCL (n = 49) n (%)**	**ANOVA (Chi Square) Sig**
Sex			
Male	17 (34.7)	30 (61.2)	(0.01)
Female	32 (65.3)	19 (38.8)	
Race			
Caucasian	44 (89.8)	46 (93.9)	(0.33)
Asian	4 (8.2)	1 (2.0)	
Black	1 (2.0)	2 (4.1)	
Age (mean ±SD) years	29.49 ±7.42	34.00 ±8.76	0.01
Visual acuity and Refractive error			
UDVA (mean ±SD) LogMAR	0.99 ±0.27	0.84 ±0.31	0.01
Sphere (mean ±SD) D	-3.48 ±1.52	-2.40 ±1.47	0.00
Cylinder (mean ±SD) D	-0.55 ±0.36	-0.63 ±0.36	0.27
MSE (mean ±SD) D	-3.76 ±1.55	-2.72 ±1.46	0.01
BCSVA (mean ±SD) LogMAR	-0.10 ±0.02	-0.10 ±0.03	0.26

Comparisons carried out between the groups showed the SCL group to have more females, be older, have higher refractive error and poorer UDVA compared with the NCL control group. Parametric data were tested using two-way ANOVA, non-parametric data were tested using Pearson Chi-Square testing (non-parametric results are shown in brackets). Statistically significant results are shown in shaded cells ($p < 0.05$).

In the SCL group, 46 patients (94%) wore SCLs over a daily wear modality and 3 patients (6%) wore lenses over an extended wear modality. Hydrogel SCLs were worn by 35 patients (71%) while the remaining 14 patients (29%) wore SiHy SCLs. Patients

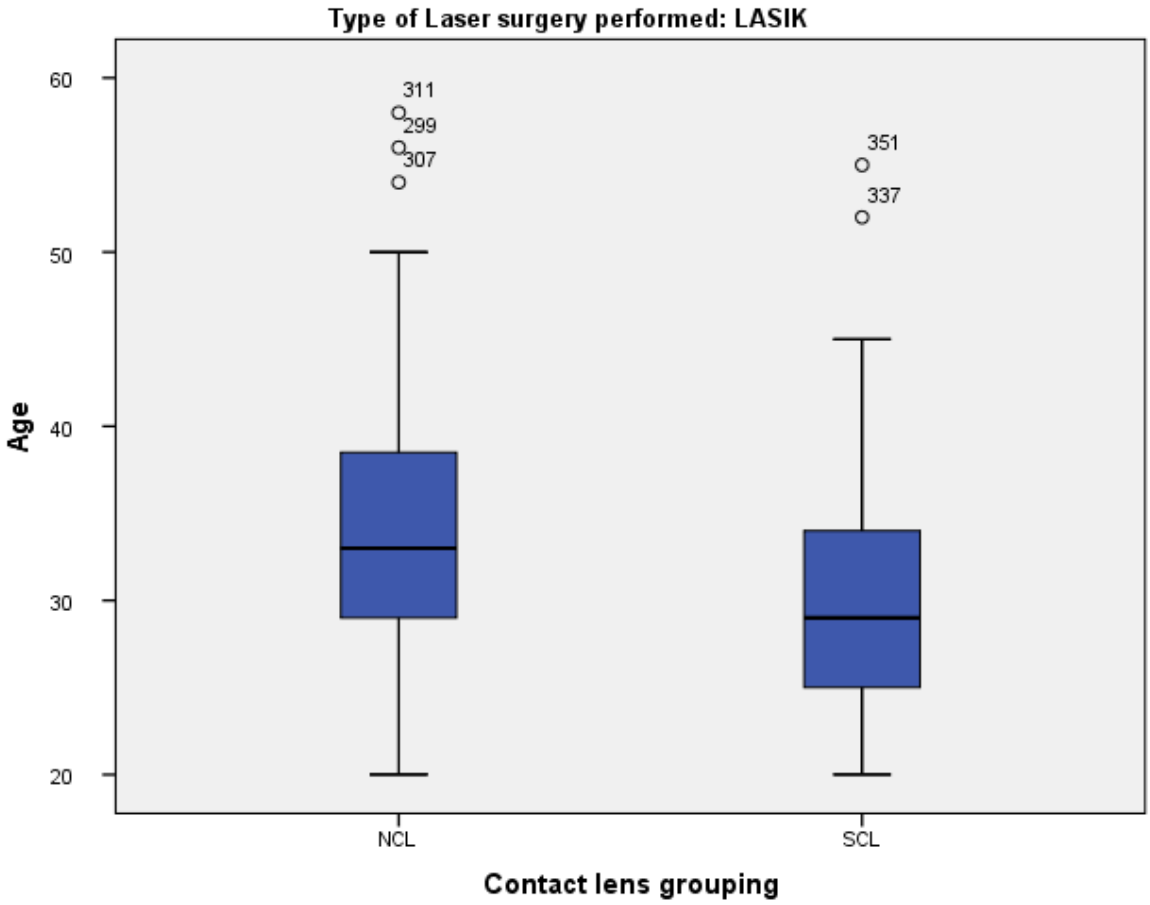
ceased SCL wear an average of 1.21 ±0.43 (range 0.5 to 2) days prior to consultation. Prior to this patients had worn SCLs an average of 6.33 ±0.92 (range 5-7) days per week. The details of the CRS procedures for both SCL and NCL group are outlined in Table 5-9.

Table 5-9: Patient demographics regarding CRS procedure following 24 hours of SCL cessation

	SCL (n = 49) n (%)	**NCL (n = 49) n (%)**	**Chi square Sig**
CRS procedure			
LASIK	33 (67.3)	39 (79.6)	0.17
LASEK/PRK	16 (32.7)	10 (20.4)	
Wavefront analysis			
Plano-scan	6 (12.2)	7 (14.3)	0.71
Personalised wavefront analysis	9 (18.4)	7 (14.2)	
Personalised aspheric wavefront analysis	34 (69.4)	35 (71.4)	

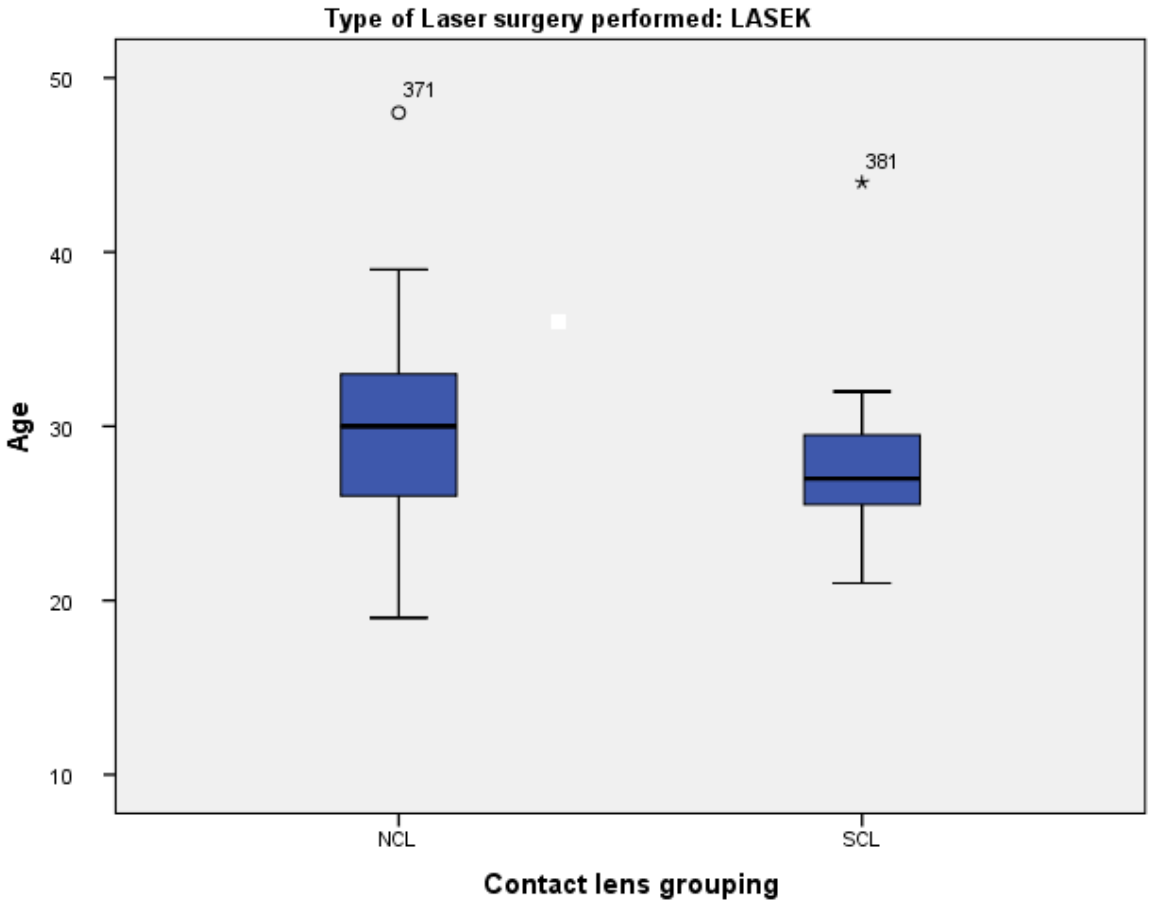
Although the NCL group was significantly older, when the entire group was compared (Table 5-8), the differences in age between the SCL and NCL control groups who underwent LASIK was not statistically significant (independent samples t-test, p = 0.05) (Figure 5-9). The differences in age between the SCL and NCL control groups who underwent LASEK/PRK were also not found to be statistically significant (independent samples t-test, p = 0.14) (Figure 5-12).

Figure 5-11: Boxplot depicting the age of the SCL and NCL patients who underwent LASIK.



Mean age ±SD: SCL = 30.2 ±8.25 years (range 20 to 55). NCL = 34.8 ±8.85 years (range 28 to 58). The boxplot portrays the minimum and maximum values of the age of LASIK patients for the NCL (left) and SCL (right) groups. The blue box represents where 50% of the data lies with the thick black line within the box representing the median. Outliers of individual cases are numbered.

Figure 5-12: Boxplot depicting the age of the SCL and NCL patients who underwent LASEK/PRK.



Mean age ±SD: SCL = 28.0 ±5.23 years (range 21 to 44). NCL = 30.9 ±8.08 years (range 19 to 48). The boxplot portrays the minimum and maximum values of the age of LASEK/PEK patients for the NCL (left) and SCL (right) groups. The blue box represents where 50% of the data lies with the thick black line within the box representing the median. Outliers of individual cases are numbered.

5.3.2.1 Pre-operative visual acuity and refraction parameters for the 24 hours SCL cessation group

Refractive error and VA data were compared between the SCL and NCL groups using two-way ANOVA and Kruskal-Wallis testing. Pre-operatively the NCL group had significantly better UDVA than the SCL group (Table 5-10). This was expected as the MSE was significantly lower in the NCL group compared with the SCL group (SCL -3.76 ±1.55D (range -1.13 to -7.38D), NCL -2.72 ±1.46D (range -0.88 to -6.38D), (p = 0.01) (Table 5-10).

Table 5-10: Pre-operative VA and refraction parameters

LogMAR (mean ±SD)	**LASIK (n = 72)**			**LASEK/PRK (n = 26)**		
	SCL group n = 33	**NCL group n = 39**	**Sig**	**SCL group n = 16**	**NCL group n = 10**	**Sig**
UDVA	1.01 ±0.27	0.81 ±0.32	0.01	0.96 ±0.26	0.92 ±0.26	0.73
BCSVA	-0.11 ±0.02	-0.10 ±0.03	0.14	-0.10 ±0.03	-0.10 ±0.01	0.74
Efficacy index	95%	92.5%	0.91	95%	94%	
> 0.3, < 6/12 n (%)	32 (97)	38 (97.4)		16 (100)	10 (100)	
< 0.3, > 6/12 n (%)	1 (3)	1 (2.6)		0	0	

Comparison of the pre-operative parameters. UDVA= unaided distance visual acuity, LASIK= Laser in situ Keratomileusis, LASEK= Laser epithelial Keratomileusis, PRK = Photo-Refractive Keratectomy BCSVA= best corrected spectacle visual acuity. Significant results of two-way ANOVA testing are shown in shaded cells (p < 0.05).

Follow-up compliance in this group was as follows:

At 1 month, 98.6% (n = 71) of LASIK and 100% (n = 26) LASEK/PRK patients.

At 3 months, 75% (n = 54) of LASIK and 73% (n = 19) of LASEK/PRK patients.

At 6 months, 51% (n = 37) of LASIK and 50% (n = 13) of LASEK/PRK patients.

In the course of the follow-up some patients did not attend the clinic as they had follow-up care done in clinics closer to their place of residence or place of work. Some patients also emigrated.

5.3.2.2 One month post-operative results for the 24 hours SCL cessation group

The 1 month efficacy and predictability outcomes of LASIK and LASEK/PRK procedures were compared between the SCL and NCL groups using two-way ANOVA and Kruskal-Wallis testing. The efficacy and predictability of both LASIK and LASEK & PRK procedures were similar for both groups and no statistically significant differences were found between SCL and NCL groups (Table 5-11). Graphs depicting these results are in Appendix A.5.2.

Table 5-11: One month post-operative VA and refraction parameters

	LASIK			**LASEK/PRK**		
	SCL (n = 33)	**NCL (n = 37)**	**Sig**	**SCL (n = 16)**	**NCL (n = 10)**	**Sig**
LogMAR (mean ±SD)						
UDVA	-0.05 ±0.10	-0.07 ±0.09	0.44	0.00 ±0.09	-0.01 ±0.07	0.77
BCSVA	-0.08 ±0.07	-0.10 ±0.04	0.17	-0.04 ±0.06	-0.05 ±0.06	0.51
Efficacy index LogMAR, Snellen	97%	99%		95%	96%	
> 0.3, < 6/12 n (%)	0	0 (0)	0.47	0	0	0.42
< 0.3, > 6/12 n (%)	33 (100)	37 (97.4)		16 (100)	10 (100)	
< 0.0, > 6/6 n (%)	25 (75.7)	33(84.6)		8 (50)	7(70)	
< -0.1, > 6/5 n (%)	21 (63.6)	26 (66.7)		4 (25)	2 (20)	
No show	0	1 (2.6)		0	0	
Predictability						
Sphere (D)	-0.07 ±0.38	0.07 ±0.36	0.13	0.22 ±0.48	0.33 ±0.39	0.56
Cylinder (D)	-0.29 ±0.39	-0.27 ±0.20	0.80	-0.50 ±0.38	-0.50 ±0.39	1.00
MSE (D)	-0.21 ±0.34	-0.07 ±0.38	0.10	-0.03 ±0.46	0.08 ±0.37	0.55
Within ±0.25D	22 (66.7)	24 (61.5)	0.59	9 (56.3)	6 (60)	0.59
Within ±0.50D	8 (24.2)	7 (17.9)		3 (18.8)	3 (30)	
Greater than ±0.50D	3 (9.1)	7 (17.9)		4 (25)	1 (10)	
Comparision of pre-operative BCSVA and post-operative UDVA						
Loss of 2 or more lines	7 (21.2)	3 (7.7)	0.16	1 (6.3)	1 (10)	0.64
Loss of 1 line	4 (12.1)	6 (15.4)		10 (62.5)	6 (60)	
Maintain VA or loss < 1 line	17 (51.5)	20 (51.3)		3 (18.8)	3 (30)	
Gain of 1 line	5 (15.2)	4 (10.3)		2 (12.5)	0	
Gain of 2 or more lines	0	5 (12.8)		0	0	
Missing data	0	1 (2.6)		0	0	

UDVA= unaided distance visual acuity, LASIK= Laser in situ Keratomileusis, LASEK= Laser epithelial Keratomileusis, PRK = Photo-Refractive Keratectomy BCSVA= best corrected spectacle visual acuity. Two-way ANOVA results showed no significant differences between the SCL and NCL groups for CRS, ($p < 0.05$).

5.3.2.3 Three month post-operative results for the 24 hours SCL cessation group

The 3 month efficacy and predictability outcomes of LASIK and LASEK/PRK procedures were compared between the SCL and NCL groups. Similar to the findings at the 1 month post-operative visit, two-way ANOVA and Kruskal-Wallis test results for the 3 month post-operative data indicate the efficacy and predictability of both LASIK and LASEK/ PRK procedures were similar for both SCL and NCL groups. No statistically significant differences were found between SCL and NCL groups (Table 5-12).

Table 5-12: Three-month post-operative VA and refraction parameters

	LASIK			**LASEK/PRK**		
	SCL (n = 28)	**NCL (n = 27)**	**Sig**	**SCL (n = 13)**	**NCL (n = 6)**	**Sig**
LogMAR (mean ±SD)						
UDVA	-0.04 ±0.11	-0.03 ±0.12	0.78	-0.06 ±0.07	0.00 ±0.10	0.17
BCSVA	-0.09 ±0.04	-0.09 ±0.04	0.98	-0.08 ±0.06	-0.05 ±0.07	0.30
Efficacy index LogMAR, Snellen	97%	97%		98%	95%	
> 0.3, < 6/12 n (%)	0 (0)	27 (69.2)	0.25	0 (0)	0 (0)	0.29
< 0.3, > 6/12 n (%)	28 (84.8)	25 (64.1)		13 (81.3)	6 (60)	
< 0.0, > 6/6 n (%)	23 (69.7)	18 (46.2)		11 (68.8)	3 (30)	
< -0.1, > 6/5 n (%)	17 (51.5)	14 (35.9)		8 (50)	2 (20)	
No show	5 (15.2)	12 (30.8)		3 (18.7)	4 (40)	
Predictability						
Sphere (D)	-0.20 ±0.41	-0.04 ±0.38	0.15	0.31 ±0.56	0.21 ±0.25	0.73
Cylinder (D)	-0.24 ±0.24	-0.29 ±0.26	0.49	-0.33 ±0.21	-0.29 ±0.19	0.72
MSE (D)	-0.32 ±0.39	-0.18 ±0.36	0.19	-0.09 ±0.06	0.06 ±0.23	0.30
Within ±0.25D	11 (33.3%)	17 (43.6%)	0.06	10 (62.5%)	5 (50%)	0.60
Within ±0.50D	13 (39.4%)	5 (12.8%)		2 (12.5%)	1 (10%)	
> ±0.50D	4 (12.1%)	5 (12.8%)		1 (6.3%)	0	
Comparision of pre-operative BCSVA and post-operative UDVA						
Loss of 2 or more lines	4 (12.1%)	4 (10.3%)	0.42	1 (6.3%)	1 (10%)	0.16
Loss of 1 line	6 (18.2%)	8 (20.5%)		3 (18.8%)	3 (30%)	
Maintain VA or loss < 1 line	17 (51.5%)	14 (35.9%)		9 (56.3%)	1 (10%)	
Gain of 1 line	0	1 (2.6%)		0	1 (10%)	
Gain of 2 or more lines	1 (3%)	0		0	0	
No show	5 (15.2%)	12 (30.8%)		3 (18.8%)	4 (40%)	

UDVA= unaided distance visual acuity, LASIK= Laser in situ Keratomileusis, LASEK= Laser epithelial Keratomileusis, PRK = Photo-Refractive Keratectomy BCSVA= best corrected spectacle visual acuity. Two-way ANOVA results showed no significant differences between the SCL and NCL groups for CRS, (p > 0.05).

5.3.2.4 Six month post-operative results for the 24 hours SCL cessation group

Six month efficacy and predictability outcomes of LASIK and LASEK/PRK procedures were compared between the SCL and NCL groups using two-way ANOVA and Kruskal-Wallis testing. The efficacy of LASIK procedures were similar for both SCL and NCL groups, with no statistically significant differences evident between these groups (Table 5-13). The difference in refractive predictability for the cylindrical component was significantly different between the SCL and NCL groups, with a higher residual cylinder present in the NCL patients following LASIK (SCL -0.18 ±0.12 DC, NCL -0.29 ±0.25DC, $p = 0.01$). However, the residual sphere was lower in the NCL group so there was no significant difference in the residual MSE between the SCL and NCL groups.

The predictability of LASEK/ PRK procedures were similar for both groups and no statistically significant differences were found between the SCL and NCL groups (see Table 5-13). However, the UDVA was significantly better in the SCL group compared with the NCL group (SCL -0.11 ±0.03D, NCL -0.04 ±0.07D, $p = 0.03$). This may be explained when the predictability results are taken into account, as the SCL group had lower residual hyperopic spherical refractive error. When combined with the negative residual cylindrical element this resulted in lower MSE at 6 month following surface CRS (SCL 0.05 ±0.31D, NCL -0.23 ±0.31D, $p = 0.13$) in the SCL group. It must be considered that there were far fewer surface LASEK/PRK patients compared with LASIK which may have impacted on the statistical validity of these results.

Table 5-13: Six month post-operative VA and refraction parameters

	LASIK			**LASEK/PRK**		
	SCL (n = 17)	**NCL (n = 20)**	**Sig**	**SCL (n = 7)**	**NCL (n = 6)**	**Sig**
LogMAR (mean ±SD)						
UDVA	-0.06 ±0.09	-0.04 ±0.10	0.53	-0.11 ±0.03	-0.04 ±0.07	0.03
BCSVA	-0.10 ±0.04	-0.09 ±0.04	0.35	-0.11 ±0.03	-0.08 ±0.04	0.18
Efficacy index	98%	97%		100%	97%	
> 0.3, < 6/12 n (%)	0	0	0.74	0	0	0.14
< 0.3, > 6/12 n (%)	17 (51.5)	20 (51.3)		0	6 (60)	
< 0.0, > 6/6 n (%)	14 (35.9)	16 (48.5)		0	4 (40)	
< -0.1, > 6/5 n (%)	12 (30.8)	11 (33.3)		7 (43.7)	3 (30)	
No show	16 (48.5)	19 (48.7)		9 (56.3)	4 (40)	
Predictability						
Sphere (D)	-0.13 ±0.37	0.01 ±0.31	0.20	0.18 ±0.31	-0.13 ±0.26	0.09
Cylinder (D)	-0.18 ±0.12	-0.29 ±0.25	0.01	-0.25 ±0.14	-0.21 ±0.19	0.66
MSE (D)	-0.22 ±0.37	-0.13 ±0.29	0.42	0.05 ±0.31	-0.23 ±0.31	0.13
Within ±0.25D	10 (30.3%)	17 (43.6%)	0.23	5 (31.3%)	3 (30%)	0.69
Within ±0.50D	2 (6.1%)	2 (5.1%)		1 (6.3%)	2 (20%)	
Greater than ±0.50D	5 (15.2%)	1 (2.6%)		1 (6.3%)	1 (10%)	
Comparision of pre-operative BCSVA and post-operative UDVA						
Loss of 2 or more lines	2 (6.1%)	2 (5.1%)	0.76	0	0	0.17
Loss of 1 line	4 (12.1%)	4 (10.3%)		0	3 (30%)	
Maintain VA or loss < 1 line	9 (27.3%)	10 (25.6%)		5 (31.3%)	3 (30%)	
Gain of 1 line	1 (3%)	4 (10.3%)		1 (6.3%)	0	
Gain of 2 or more lines	1 (3%)	0		1 (6.3%)	0	

UDVA= unaided distance visual acuity, LASIK= Laser in situ Keratomileusis, LASEK= Laser epithelial Keratomileusis, PRK = Photo-Refractive Keratectomy BCSVA= best corrected spectacle visual acuity. Two-way ANOVA results: significant differences between the SCL and NCL groups for CRS are shown in shaded cells, p < 0.05.

5.4 Discussion

The purpose of this study was to examine the impact of two different SCL cessation times on the outcomes of CRS. It was hypothesised that the outcomes of CRS might be poorer in the SCL group compared with the NCL group. As the accuracy of corneal and refractive measurements, acquired for the execution of CRS, is vital in ensuring successful outcomes, it was proposed that 24 hours SCL cessation would not be sufficient to ensure accuracy. Therefore, the outcomes of these patients would be worse than those found for SCL wearers who ceased SCL wear for a period of 2 weeks.

5.4.1 Demographics

The influence of demographics on VA and CRS outcomes must be considered. There were fewer males in the SCL group for those who ceased SCL wear for 24 hours prior to CRS ($p = 0.01$). While patient demographics such as sex and race are known to have an effect on the outcomes of intra-ocular and cataract surgery (Anderson et al., 2003; Oshika et al., 1998), their impact on the outcomes of LASIK and LASEK/PRK has not been fully explored in the literature.

The SCL group who ceased SCL wear for 24 hours prior to CRS were found to be younger (29.49 ±7.42 years) than their NCL control counterparts (34.00 ±8.76years, $p = 0.01$). The precision of corneal measurements used for planning CRS treatment profiles were not expected to have been affected by the difference in age between the groups as no link has been established between age and corneal curvature or thickness measurements (Eysteinsson et al., 2002; Fledelius and Stubgaard, 1986; Khoramnia et al., 2007; Siu and Herse, 1993). Post-operative CRS outcomes may be affected by age as corneal keratocyte and endothelial cell density reduces with advancing age (Niederer

et al., 2007). The quality of VA diminishes with age, due to general ageing of the visual system, in addition to increased light scatter caused by the onset of age-related crystalline lens opacities and brunescence (Artal et al., 1993; Roche et al., 2014; Ross et al., 1985). However, there is disagreement in the literature as to the effect of age on the outcomes of CRS. Younger patients have been reported to require greater number of retreatments following CRS. This is attributed to an increased corneal healing response (Loewenstein et al., 1997). However, younger patients have been reported to achieve better visual outcomes following CRS due to the increased levels of accommodation, which may provide the ability to accommodate over low levels of hyperopic residual refraction (Ghanem et al., 2007; Hersh et al., 1996). Perlman and Reinert (2004) looked retrospectively at retreatment rates following LASIK for myopic correction (total sample size n = 393 eyes; retreatment rate n = 58 eyes). Significantly higher retreatment rates were reported in males, in patients aged over 45 years, and in those with a recent history of RGP CL wear (Perlman and Reinert, 2004).

Advancing age has also been reported to result in a trend towards poorer efficacy outcomes following CRS. Ghanem et al. (2007) reported worse BCSVA, increased myopic residual refractions and higher retreatment rates following LASIK. However, these results were not statistically significant. The authors performed a retrospective chart analysis and did not report whether the refractive outcome was intended to be plano, or a slight myopic refraction which would benefit these presbyopic patients with near work. Greater risk of loss of lines of BCSVA after CRS was not reported with advancing age (Ghanem et al., 2007). The mean age of groups reported by Ghanem et al. (45, 53 and 63 years) was much older than those of this study (SCL 32 ±7.5 years, NCL 37 ±10 years). Furthermore, statistical analysis on the differences in age between

the SCL and NCL groups who underwent LASIK and LASEK/PRK in this study, indicated that there was no significant difference in age between the groups for both 2 week and 24 hours SCL cessation times when CRS procedure groups was taken into account. As comparison of outcomes between SCL and NCL groups was undertaken separately for LASIK and LASEK/PRK, it was felt that age should not have had an impact on the results reported.

5.4.2 Refractive error and visual acuity

Owing to the retrospective nature of this study, it was not possible for one observer to take all visual acuity and refraction measurements. Therefore, it was not possible to exclude the possibility of associated operator bias from the two observers who had recorded the measurements. Refractive error is not measured more precisely than ±0.25D for low refractive errors and ±0.50D for high refractive errors, due to uncertainty about final refraction, effect of vertex distance and uncertainties in trial lenses (Smith, 2006). Smith did not specify the classification values for low and high refractive error. Additionally, the reproducibility of spherical refractive error data was found to be within ±0.25D 90% of the time (n = 102 optometrists) (Shah et al., 2009).

The level of VA can depend on a number of factors including refractive error, pupil size and the health or clarity of the ocular media in the eye (Westheimer, 2002). Furthermore, the use of a Snellen acuity chart in this study may have induced error in the statistical analysis of VA data. Although Snellen VA is used in the standardised reporting of outcomes of CRS (efficacy, predictability and stability) (Koch et al., 1998). The Bailey-Lovie LogMAR chart has been proven to be a better chart design for research purposes (Lovie-Kitchin, 1988). This is due to the uniform progression of

letter size, equal number of letters per line with equal proportional spacing and the use of Sloan letters which are equally difficult to read (Lovie-Kitchin, 1988). It was not possible to use a LogMAR chart as this was a retrospective study. Standard uncertainty for VA is approximately 2 letters on the Snellen chart (0.04 LogMAR) due to variation in pupil size, accommodation and subjective response (Smith, 2006). For a 95% confidence level, this equates to 0.6D and 4 letters when using International Standards Organisation (ISO) guidelines (Smith, 2006). Each optometrist worked in equivalent testing conditions (same room size, same lighting conditions, same equipment which was installed and serviced at the same times). Furthermore, standard methods of forced choice were used for measurement of VA and refractive error, thus ensuring optimum accuracy of measurements (Kohnen, 2001). Due to the precise nature of pre-operative refractive error measurements, as is demanded in a CRS clinical setting, and the use of standardised measurement procedures, it was expected that the influence of operator bias on refractive error and VA measurements would be limited (Huang and Chen, 2008; Klein et al., 1983). It is recommended that more precise methods of reporting outcomes of CRS would include the use of LogMAR VA and CSF testing. These methods were adopted in studies 3 and 5.

5.4.3 SCL influence on refractive error and visual acuity- before CRS

The cornea is a living tissue and its biomechanical and physical properties are affected by SCL wear and CRS (Muñoz et al., 2011; Roberts, 2000). If CL-induced corneal warpage is present and sufficient time is not provided for the complete stabilisation of corneal changes, the biophysical response of the cornea will be compromised. The efficacy of CRS may be influenced and there may be refractive over-correction (Hoyos and Cigales, 2002). It has been reported that CL-induced corneal warpage can result in

a transient increase in myopia. This can lead to over-correction following CRS (Hoyos and Cigales, 2002).

Mean myopic refractive error can be influenced by SCL material worn (Bergenske et al., 2007; Blacker et al., 2009; Fonn et al., 2002). Fonn et al. (2002) found a significant increase in myopia with low DK/t SCL wear compared with high DK/t SCL wear- these differences between the groups were proposed to be due to hypoxia and mechanical moulding. The mechanism of the slowing of myopic progression was reportedly associated with the stiffer modulus of SiHy SCL materials (Bergenske et al., 2007; Blacker et al., 2009). As this study was retrospective in nature, and the generation of SiHy SCL material patients wore prior to CRS was not recorded at the time of data collection, it was not possible to explore the impact of SCL modulus on the outcomes of CRS.

5.4.3.1 Follow-up compliance

Diminished sample size post-operatively is a limitation of this study. Patients might have thought it unnecessary to return if they were happy with the level of UDVA, thereby affecting the overall results. Post-operative follow-up compliance is outlined in Table 5-14. This issue is commonly reported in the literature, Cheng et al. (2006) reported a follow-up compliance of 14% at 6 months following myopic LASIK (n = 237). Twa et al. (2005) found follow-up attrition rate at 6 months following CRS to be 46.08% (n = 2439) (Twa et al., 2005). Guillon and Maïssa (2012) reported that the follow-up compliance rate of 71% reported in long-term (2 year) follow-up studies to be excellent. As in a previous study by the same authors (n = 64), the follow-up was 54% over 2 years (Guillon and Maïssa, 2010). Van de Pol et al. (2001) found follow-up

compliance in their prospective study was 43% at 1 month, 82% at 3 months, 79% at 6 months, 59% at 9 months and 39% at 12 months (n = 44). The follow up compliance rate of study 2 compared favourably to these authors.

Table 5-14: Post-operative following up compliance

	1 month		**3 months**		**6 months**	
SCL cessation time	**LASIK**	**PRK**	**LASIK**	**PRK**	**LASIK**	**PRK**
2 weeks	96%	100%	93%	84%	76%	82%
24 hours	99%	100%	75%	73%	51%	50%

It is commonly accepted that refractive stability can vary between surface LASEK/PRK and LASIK techniques. For this reason the outcomes of these two types of CRS procedures were analysed separately (Ghadhfan et al., 2007; Miyai et al., 2008; O' Keefe and Kirwin, 2010). PRK and LASEK procedures were analysed in the same group, as it has been reported that both treatments are safe and reliable, with no statistically significant differences in the outcomes measured between the PRK and LASEK groups for myopic eyes (Lee et al., 2001b; Litwak et al., 2002; Reilly et al., 2010; Shahinian, 2002). In addition to these factors, the manner in which the corneal flap is created (microkeratome vs. femtosecond laser) may also have an influence on visual outcomes (Lim et al., 2006; Patel et al., 2007). As all LASIK procedures included for analysis in this thesis were made using the femtosecond laser, this factor is not within the parameters of this discussion.

The use of two excimer Lasers in this study may also have affected the outcomes of the CRS for the groups who ceased SCL wear for 2 weeks, compared with those who ceased wear for 24 hours. It is a flaw due to the retrospective nature of this study, and

the fact that the study was carried out within a working clinical practice. Although the Lasers did vary between these groups (24 hours vs. 2 weeks), each study had its own control group who had treatment using the same excimer Laser, and the results were only compared within that particular study. Furthermore, as it is recognised that there is a large variety of CRS procedures available, a standardised method of graphs and reporting methods for CRS outcomes was adopted to ensure comparison of results are acceptable (Dupps et al., 2011).

5.4.4 Post-operatively results

Results of this study for the 2 weeks' cessation group and their NCL controls indicated that the efficacy of both LASIK and LASEK/ PRK procedures were higher in the SCL group when compared with the NCL group 1 month following CRS. While these results were not statistically significant in the LASIK group, the SCL group who underwent LASEK/PRK had significantly better UDVA (-0.05 ±0.09) than the NCL group (0.02 ±0.09; $p = 0.04$). Furthermore, the residual cylinder in this cohort was significantly lower LASEK/PRK (-0.50 ±0.40) than the NCL group (-0.76 ±0.40; $p = 0.02$). These results were maintained at the 6 month follow-up visit, where significantly better UDVA was found for the SCL group compared with the NCL group for both LASIK (SCL -0.10 ±0.10, NCL -0.06 ±0.07, $p = 0.03$) and LASEK/PRK procedures (SCL -0.10 ±0.08, NCL -0.04 ±0.08, $p = 0.03$). The significantly higher residual cylindrical refractive error in the NCL group had resolved by the 6 month post-operative visit, so while the difference in UDVA between the SCL and NCL groups 1 month post-operatively may have been explained by this, at the 6 month post-operative visit, this was not the case.

Results of this study, for the 24 hours cessation group and their controls, found no significant differences in CRS outcomes between the SCL and NCL groups at 1 or 3 months following CRS. However, at the 6 month follow-up visit, there was significantly higher residual cylinder found in the NCL group following LASIK compared with the SCL group (SCL -0.18 ±0.12 DC, NCL -0.29 ±0.25, p = 0.01). As the residual spherical refractive error was lower in the NCL group, the MSE was similar between the SCL and NCL groups, so there was no significant difference found.

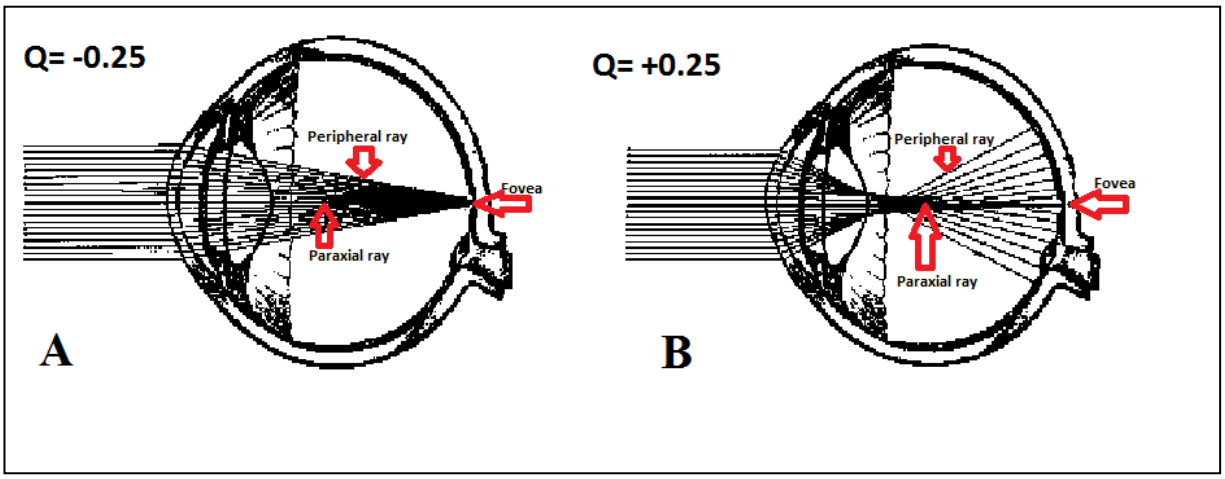
The UDVA was significantly better in the SCL group compared with the NCL group (SCL -0.11 ±0.03, NCL -0.04 ±0.07, p = 0.03) following LASEK/PRK at the 6 month visit. This may be explained by the predictability results. The SCL group had low residual hyperopic spherical refractive error, and when combined with the negative residual cylindrical element, this resulted in lower MSE at 6 month following surface CRS (SCL 0.05 ±0.31, NCL -0.23 ±0.31, p = 0.13) in the SCL group. These results vary from those reported for the 2 weeks SCL cessation group, which indicated significantly better outcomes for the SCL groups for both LASIK and LASEK/PRK procedures. The numbers of patients who ceased SCL wear for 24 hours and their controls, were lower for surface LASEK/PRK patients compared with LASIK. This may explain the difference in these statistical findings. While these results are statistically significant, one cannot conclude that they are clinically significant due to the small number of letters gained in the SCL group compared with the NCL (LASIK: SCL group had 2 more letters than the NCL; LASEK/PRK: SCL group had 3 more letters than the NCL), as standard uncertainty for VA is approximately 2 letters (4 letters for a 95% confidence interval) (Smith, 2006). The hypothesis, that previous SCL wear would negatively impact CRS outcomes, was rejected.

Definitive reporting on the impact of previous CL wear on the outcomes of CRS in the literature is lacking. Gimbel (1993) found there was no significant difference in refractive and epithelial healing between NCL, SCL and RGP patients following PRK (n = 130). Follow-up was carried out at 1 week, 2 weeks, 4 months and 6 months. This was before the advent of LASIK or SiHy lens materials. PRK was found to be effective in previous CL wearers with associated dry eye for high myopia, (mean -7.50 ±1.00D, range -6.00 to -10.00D) (Toda et al., 1996). Post-operative UDVA of greater than 6/12 was present in 80.0% of eyes at 6 months. 92.8% of eyes achieved refraction within ±1.00D of the intended correction at 6 months. LASEK has been found to be a safe and effective procedure for low to high myopia (-1.25 to -14.38D) with astigmatism (up to +4.50Dc) in previous SCL wearers (Shahinian, 2002). Subjects (n = 146 eyes) were prospectively followed for 12 months following CRS. Subjects had a mean age of 42 years (range 18 to 69 years), 41% of patients were male and 59% female. Daily SCL wearers ceased SCL wear 1 week and toric SCL wearers ceased lens wear for 3 weeks prior to examination. No eye lost more than 2 lines of BCSVA. At the 6 month post-operative visit, UDVA was 6/6 or better in 57% of eyes and 6/12 or better in 96% of eyes. Furthermore, no eye developed corneal haze which affected VA, and there were no sight-threatening complications reported. Hersh et al. (1996) reported a higher proportion of SCL wearers achieved UDVA of 6/12, or better, using bivariate analysis. However, no detailed examination of this association was outlined in the paper by Hersh et al. and the type of previous CL was not detailed. As higher myopic ablations led to greater chance of over- or under-correction, regression and higher post-operative optical ablations, this was linked to the lower efficacy with higher pre-operative myopia. Recent studies examining the effect of pre-operative SCL wear on CRS outcomes is lacking.

It is estimated that up to a third of SCL wearers required astigmatic correction of between -0.50 to -2.00Dc (Young et al., 2011). However, only 13% of patients worldwide wear toric CLs (Morgan et al., 2014) and in this study no toric SCL wearing patients were included. Patients with low levels of astigmatism are routinely fitted with spherical SCLs lenses (Morgan and Efron, 2009). These patients are likely to have previously adapted to under-correction of refractive cylinder, and be more tolerant of post-operative residual cylindrical refractive error.

Furthermore, SCL wear can result in increased corneal surface irregularities, which may negatively impact upon VA (Liu and Pflugfelder, 2000). SCL wear can reduce tear break up time, which can result in reduced image quality (Tutt et al., 2000). Following myopic CRS, the cornea becomes more oblate. This shape results in increased spherical aberrations with excessive refraction of light rays incident on the periphery of the cornea (Holladay and Janes, 2002) (see Figure 5-13). It is therefore possible that previous SCL wearers, with experience of increased corneal surface irregularities, adapted better to induced spherical aberration and possible residual refractive error following CRS. Thus, allowing them to maintain better levels of UDVA when compared with NCL wearers.

Figure 5-13: Asphericity of the cornea before and after refractive surgery



A: The normal human cornea is prolate (mean asphericity (Q value) of -0.25). This aids in the reduction of spherical aberration as peripheral light rays are not refracted as much as paraxial and all rays come to a single point focus.
B: Following myopic CRS, the cornea becomes more oblate. This shape results in increased spherical aberrations with excessive refraction light rays incident on the periphery of the cornea. Image adapted from (Holladay and Janes, 2002).

5.4.5 Post-operative efficacy results

The efficacy results of study 2 compare favourably with those reported by previous authors (Alió et al., 2008c; Alió et al., 2008d; Ghadhfan et al., 2007; O' Doherty et al., 2006; Shahinian, 2002; Taneri et al., 2004a; Yuen et al., 2010). The findings for the efficacy of LASIK following 2 weeks' SCL cessation in this study were 97% for SCL wearers and 98% for NCL wearers, and for LASEK/PRK procedures, were 98% for SCL wearers and 97% for the NCL wearers. The findings for the efficacy of LASIK following 24 hours' SCL cessation in this study were 98% for SCL wearers and 97% for NCL wearers, and for LASEK/PRK procedures, were 100% for SCL wearers and 97% for the NCL wearers. These findings are similar to those found by Alió et al. (2008) in a control-matched comparison of PRK (n = 34) and LASIK (n = 34) for moderate to high myopia (-6.00 to -10.00D). Here, the efficacy was 95% for LASIK and 90% for PRK. Visx Excimer Laser was used in both studies. However, in Alió's study LASIK

flaps were created using a microkeratome (Automated Corneal Shaper, Chiron, Irvine, CA). Alió et al. (2008) had advised no CL wear for 4 weeks before CRS. The National Institute for Health and Clinical Excellence (NICE) undertook a systematic review of safety and efficacy of LASIK between the years 2000 and 2006 (n = 293,278) (Murray et al., 2005). UDVA results greater than 6/6 were found to be 64% for LASIK, results of 6/12 or better were 94% for LASIK. The superior results found in study 2, compared with those reported by Murray et al. (2005) and Alió et al. (2008), may be due to the inclusion of low myopes and the use of the femtosecond laser in LASIK flap creation.

Figure 5-14: Efficacy results of myopic CRS

Author, year	N	Level of myopia correction	CRS procedure	% eye achieved ≥ 6/6	% eye achieved ≥ 6/12	Post-op efficacy
Study 2, 2 weeks' SCL cessation	19	-1.13 to -9.25D	LASIK	SCL 74 NCL 52	SCL 83 NCL 70	SCL 79 NCL 62.5
Study 2, 24 hours' SCL cessation	17	-0.88 to -7.38D	LASIK	SCL 82 NCL 80	SCL 100 NCL 100	SCL 100 NCL 100
Ghadhfan et al. 2007	464	0 to -6.00 D	LASIK	55.1	98.4%	96.6%
Ghadhfan et al. 2007	464	-6.00 to -11.25D	LASIK	28.4	85.1 %	80.1%
O'Doherty et al. 2006	49	-1.50 to -13.00D	LASIK	53	88%	93%
Yuen et al., 2010	37932	0 to >-10.00D	LASIK	72.8%		
Study 2, 2 weeks' SCL cessation	18	-1.38 to -6.13D	LASEK/ PRK	SCL 73% NCL 68%	SCL 82% NCL 82%	SCL 89 NCL 100
Study 2, 24hours' SCL cessation	7	-1.25 to -7.13 D	LASEK/ PRK	SCL 100 NCL 67	SCL 100 NCL 100	SCL 100 NCL 100
Alió et al. (2008)	34	-6.00 to -10.00	PRK			
Ghadhfan et al. (2007)	104	0 to -6.00	LASEK PRK	47.8% 73.5%		
Ghadhfan et al. (2007)	104	-6.00 to -11.25	LASEK PRK	29.7% 25.0%		
Shaninian (2002)	146	-1.25 to -14.38 (cyl to 4.50DC)	LASEK			
Taneri et al., 2004	171	-0.38 to -7.75D (cyl to 6.00DC)	LASEK		96%	
NICE Review Murray et al., 2005	15 785		LASEK PRK	64% 70%	92% 92%	

5.4.5.1 The influence of myopia on CRS outcomes

It is well agreed in the literature that the outcomes of CRS are dependent on the pre-operative level of myopia, with lower myopic corrections achieving better and more stable visual outcomes (Alio et al., 2008; Ang et al., 2009; Condon et al., 2007; Ghadhfan et al., 2007; Reilly et al., 2010; Serrao et al., 2009). It was not possible to analyse the impact of SCL wear in higher myopic groups in this study as the low sample size with these myopic sub-groups would have meant the statistical analysis lacked validity.

5.4.5.2 Safety of CRS procedures

In this study, there were no serious intra- or post-operative complications in any group. In study 2, 2 patients required an enhancement 6 months following CRS. Both were previous SCL wearers who had ceased SCL wear for 2 weeks prior to CRS. Neither had any post-operative complications such as diffuse lamellar keratitis. Pre-operative MSE refractive error was not high (-5.625D and -3.50D). Due to the low numbers of refractive enhancements required, it was not possible to conclude that the need for enhancement with these patients may have been due to SCL wear prior to the CRS procedure.

Table 5-15: Pre- and post-operative refractive data for the 2 patients with myopic regression who required CRS enhancement.

CRS performed	Preoperative refractive	1 month residual	3 months residual refractive error	6 months residual
LASIK	-5.25/-0.75 x 20	-0.25/-0.75 x 10	-1.00/-0.75 x 17	-0.50/-0.75 x 17
LASEK	-3.25/-0.50 x 160	-0.75/-0.50 x 180	-0.50/-0.50 x 160	-1.25/-0.75 x 170

5.5 Conclusion

Results of this study found that previous SCL wear did not negatively affect the outcomes of CRS, and that SCL cessation times of 2 weeks and 24 hours did not result in negative outcomes compared with a NCL control group. These results were surprising, and disproved the initial hypothesis, that outcomes of CRS would be poorer in the SCL group compared with the NCL control group. For the 2 weeks' SCL cessation group: at the six month post-operative visit the SCL wearers had statistically significantly better outcomes in terms of visual efficacy compared to the NCL control group. These six month results were repeated for the surface LASEK/PRK SCL group who ceased lens wear for 24 hours. The SCL wearers in this LASIK group also experienced higher UDVA compared to the NCL group, but the results were not statistically significant. However, while these results were statistically significant, there was a very small number of letters difference in the VA between the SCL and NCL groups. Therefore, one cannot conclude that these results are clinically significant when using the standard uncertainty value of two letters of Snellen VA (0.04 LogMAR), with a 95% confidence level of 4 letters as outlined in the International Standards Organisation guidelines (Smith 2006). It is likely that the SCL wearers may have adapted to some under-correction of astigmatism in their SCLs and to the increased surface irregularity with SCL as discussed in section 5.4.4.

Thus far, the effect of SCL wear on corneal curvature and thickness has been examined. The significant inferior steepening evident in the SCL group resolved over a 2 week period. The effect of previous SCL wear (when ceased for 2 weeks and 24 hours prior to CRS) on CRS outcomes was explored. In the next study, the stability of corneal curvature, thickness, VA and refractive error measurements, following cessation of SCL wear over a two week period, was examined to assess when stability of measurements occurs within this timeframe.

6 CHAPTER SIX. STUDY THREE: STABILITY OF CORNEAL, REFRACTIVE ERROR AND VIUSAL ACUITY MEASURMENTS FOLLOWING CESSATION OF SOFT CL WEAR

6.1 Introduction

The current literature indicates that the time taken, to achieve stability of corneal measurements, can vary following cessation of SCL wear. Stability is dependent on many factors including CL material, modality and previous years of SCL wear (Ng et al., 2007; Nourouzi et al., 2006; Schornack, 2003; Tsai et al., 2004; Wang et al., 2002b). The results of study 1 indicated that SCL wear had a significant effect on corneal thickness and curvature, and these effects appeared to have resolved following 2 weeks' cessation of SCL wear. There is some disagreement in the literature about the precise time required to achieve stability following SCL cessation. Hashemi et al. (2008) reported that corneal thickness and curvature measurements show stability following 2 weeks' cessation of SCL wear for most patients (Hashemi et al., 2008). Nourouzi et al. (2006) similarly reported resolution times of within 2 weeks, for corneal oedema, following cessation of hydrogel SCL wear prior to LASIK. However, in some cases, stability of corneal measurements can take weeks or months, following cessation of SCL wear (González-Méijome et al., 2003a; Ng et al., 2007; Schornack, 2003; Wang et al., 2002b; Wilson et al., 1990). Prolonged instability of corneal curvature is particularly evident in cases of CL-induced corneal warpage (Wang et al., 2002b). Wang et al. (2002b) reported resolution of the refractive and topographical effects of long-term SCL wear were longer with EW (average 11.6 weeks), compared with RGP wear (average 8.8 weeks). Ng et al. (2007) also found that the modality of wear influenced the time taken to achieve stable corneal measurements. EW of hydrogel SCLs required the longest times (35.6 ±23.6 days) to achieve stability following

cessation of SCL wear, while EW of SiHy SCLs (6.0 ±1.2 days) took the shortest times, followed by DW of hydrogel SCLs (9.9 ±7.0 days).

6.1.1 Aims and hypotheses

The review of the literature revealed discrepancies between the reported times required to achieve stability of corneal measurements prior to CRS (Ng et al., 2007; Nourouzi et al., 2006; Schornack, 2003; Tsai et al., 2004; Wang et al., 2002b). As CRS depends on manipulation of the corneal thickness and curvature in order to achieve a desired optical effect, the accuracy in measuring these properties is crucial. Corneal warpage results in inaccurate corneal curvature measurements and limits the ability to screen for disease processes. Furthermore, over-estimation of corneal thickness in cases of oedema, increases the risk of ectasia. The aim of this study was to determine the time required to achieve stability of corneal measurements, following 2 weeks' SCL cessation, as recommended by the FDA prior to CRS. Suspicion of the presence of corneal warpage would deem a candidate unsuitable for CRS. As our groups did not contain any EW hydrogel SCL wearers, this 2 week cessation period was therefore deemed sufficient for stability to be achieved (Taneri et al., 2013; Xu et al., 2011). It was hypothesised that SCL wear would alter corneal structure and affect the time taken for stability of corneal curvature and thickness, VA and refractive error. This hypothesis was explored by comparing the time taken for stability of corneal curvature, thickness measurements in a full time SCL group (of hydrogel and SiHy SCL materials) with a NCL control group.

6.2 Methods

6.2.1 Subject enrolment and data collection

A prospective analysis was undertaken on a full-time SCL group (n = 33 eyes) and a NCL control group (n = 28 eyes). Subjects were enrolled from the student body of the Dublin Institute of Technology between October 2012 and March 2013. Those who fulfilled the inclusion criteria (as outlined in section 3.1.1) were included for analysis.

Following enrolment, SCL wearers were asked to attend the initial consultation wearing their SCLs (baseline), and following 1, 2 7 & 14 days of SCL cessation. NCL control subjects were asked to attend the clinic at the same time intervals. Appointments were scheduled at the same time of day (within 2 hours, for each subject) to limit the possible influence of diurnal variation. The stability of vision, refractive error, corneal thickness and curvature was compared between the SCL and NCL control groups.

VA was recorded using a LogMAR Thomson Chart (Test Chart 2000 XPert, U.K.). In order to ensure the robust mathematical treatment and correct determination of geometrical means of the VA values, both LogMAR and raw MAR VA values were analysed (Holladay, 1997). For statistical analysis normality was tested and then the relevant parametric or non-parametric test was applied to determine and analyse the mean and SD of VA values.

Full refraction was carried out at the baseline visit, and the difference between this and subsequent refractions was recorded. Criteria for determining stability were used in accordance to previously published studies and are in Table 6-1.

Table 6-1: Criteria for assessing successful stability following cessation of SCL wear

Method of assessment	**Criteria for stabilisation (compared with measurement taken at previous visit)**
Manifest refraction	Spherical equivalent with -0.50 D change Cylindrical refraction with -0.50 D change MSE ≤ 0.25D change
Keratometry	-0.50 D/0.1mm change in both the horizontal or vertical axis
Corneal topography	-0.50 D/0.1mm change within the central 3mm cornea in both the steep and flat meridians
Pachymetry	8µm changed at the thinnest Point < 10.5µm changed at the thinnest Point

Criteria adopted from stability studies reported in the literature (De Benito-Llopis et al. 2009, Hashemi et al. 2008, Ng et al. 2007).

6.3 Results

6.3.1 Demographics of the study population

Seventeen myopic SCL wearers (4 males, 13 females; mean age 20.82 ±1.69 years, range 18 to 25 years) and 14 NCL control subjects (7 males, 7 females; mean age 21.14 ±2.85 years, range 18 to 27 years) participated in this study. The time taken for stability of measurements was analysed in both eyes. All subjects were Caucasian. Independent t-testing was used to compare the difference in age between the SCL and NCL control groups, no significant differences were found ($p = 0.58$). Pearson's chi-square test was used to compare the difference in sex between the SCL and NCL control groups, while no significant differences were found the result was close to statistical significance ($p = 0.06$).

Details of refractive error data are displayed in Table 6-2. As the NCL group was formed mainly of emmetropic subjects. There were significantly higher UDVA and lower MSE in this group compared with the SCL group. However, two-way ANOVA showed there was no significant difference in BCSVA between the SCL and NCL control groups.

Table 6-2: Baseline refractive error and visual acuity data for SCL and NCL groups.

	SCL (n = 33 eyes)	**NCL (n = 28 eyes)**	**ANOVA Sig**	**Mann-Whitney Sig**
Unaided distance LogMAR VA	1.03 ±0.68	0.02 ±0.22	0.00	
Unaided distance MAR VA	12.62 ±9.86	1.20 ±0.83	0.00	0.00
MSE (range)	-4.17 ±1.98 (-1.00 to -8.00)	-0.24 ±0.58 (-0.75 to -1.63)	0.00	
Best Corrected Spectacle LogMAR VA	-0.14 ±0.29	-0.13 ±0.07	0.85	
Best Corrected Spectacle MAR VA	0.82 ± 0.22	0.75 ±0.13	0.17	<0.00

Two-way ANOVA revealed a significant difference in unaided distance VA and MSE ($p < 0.05$).

6.3.2 CL wearing habits

Ten subjects from the SCL group wore hydrogel lenses (n = 19 eyes), and the remaining 7 wore SiHy lenses (G1SiHy n = 2 eyes, G2SiHy n = 4 eyes, G3SiHy n = 8 eyes). Due to the low numbers of the various generations of SiHy SCLs, the data were analysed using all SiHy SCL wearers in one group. All subjects wore their SCLs on a DW modality. A two-way ANOVA statistical analysis was applied to the data in order to investigate the SCL wearing habits between the SCL material groups. No statistically significant differences were found (Table 6-3).

Table 6-3: The average wearing schedule and previous years of SCL wear of each SCL participant.

Time Frame	**SCL (n = 33)**	**Hydrogel (n = 19)**	**SiHy (n = 14)**	**Sig**
Hours per day	12.24 ±2.60	12.11 ±3.21	12.43 ±1.50	0.12
Days per week	5.48 ±1.34	5.32 ±1.37	5.71 ±1.33	0.70
Years of SCL wear	4.15 ± 2.74	4.42 ±3.12	3.79 ±2.18	0.43

Two-way ANOVA revealed no significant differences in the SCL wearing habits of the various SCL material groups ($p < 0.05$).

6.3.3 Stability of refractive error following cessation of SCL wear

Following SCL cessation, one-way ANOVA and Mann-Whitney U tests were used to analyse the stability of refractive error between the SCL and NCL groups. Instability of refractive error results were found to be highly significant, for the SCL group following 1 day cessation of SCL wear, compared with the NCL group. The NCL group showed stability in refraction with fluctuations in refractive error showing a maximum mean change of -0.03D between baseline and 1 day following cessation of SCL wear. Whereas, the SCL group showed a maximum mean change of refractive error of -0.20D between baseline and 1 day ($p = 0.00$). Following this, both groups remained relatively stable with no significant differences between them (SCL vs. NCL) (Table 6-4). Despite the highly significant differences between the groups (SCL vs. NCL) between baseline and 1 day, at all time periods the difference in refraction remained lower than the criteria for stability of refractive error (< 0.25 to 0.50D) as adopted by previous authors (De Benito-Llopis et al., 2009; Ng et al., 2007).

Table 6-4: Stability of refractive error following cessation of SCL wear between baseline and days 1, 2, 7 and 14

Time Frame	**NCL (n = 28) SCL (n = 33)**	**Mean ±SD**	**Two-way ANOVA Sig**	**Mann-Whitney Sig**
Between baseline and day 1	NCL	-0.03 ±0.18	0.00	0.01
	SCL	-0.20 ±0.15		
Between day 1 and 2	NCL	-0.01 ±0.16	0.68	0.79
	SCL	-0.03 ±0.23		
Between day 2 and 7	NCL	-0.02 ±0.20	0.74	0.79
	SCL	-0.00 ±0.22		
Between day 7 and 14	NCL (n = 26)	0.00 ±0.10	1.00	0.79
	SCL (n = 25)	0.00 ±0.14		

Stability of refractive error data for SCL and NCL control groups following SCL cessation. Significant differences are shown in shaded cells, ($p < 0.05$).

The influence of SCL material on the stability of subjective refraction following cessation of SCL wear was explored. The results of two-way ANOVA showed that there were no significant differences in the stability of refraction following SCL cessation between the SCL material and NCL groups at any time period (see Table 6-5).

Table 6-5: Effect of SCL material on stability of refractive error following SCL cessation

SCL material groups **NCL (n = 28)** **SiHy (n = 14)** **Hydrogel (n = 19)**		**Mean**	**SD**	**Sig**	**Post hoc Scheffe**
Between baseline and day 1	NCL	-0.05	0.17	0.04	> 0.05* NCL and: Hydrogel 0.12 SiHy 0.10
	SiHy	-0.16	0.16		
	Hydrogel	-0.14	0.15		
Between day 1 and 2	NCL	-0.04	0.13	0.12	
	SiHy	-0.14	0.21		
	Hydrogel	-0.11	0.17		
Between day 2 and 7	NCL	-0.02	0.13	0.03	> 0.05* NCL and: Hydrogel 0.17 SiHy 0.05
	SiHy	-0.14	0.19		
	Hydrogel	-0.11	0.15		
Between day 7 and 14	NCL	-0.03	0.12	0.14	
	SiHy	-0.04	0.13		
	Hydrogel	-0.11	0.15		

*Mean ±SD and two-way ANOVA results for SCL material groups and the stability of refraction following SCL cessation between baseline and days 1, 2, 7 and 14. A negative value means the MSE was more myopic at the later visit. *Note that although the two-way ANOVA showed a statistically significant difference the Scheffe post-hoc testing did not. This indicated that the Scheffe test (which controls the Type I error rate) required a larger difference to declare significance compared to when no adjustment was used. Therefore, the significance of these findings is lacking statistical power.*

6.3.4 Stability of corneal curvature measurements

The stability of corneal curvature (SimK, sagittal and tangential topography) was compared between the groups (SCL vs. NCL) prior to, and following cessation of SCL wear. Two-way ANOVA and Mann-Whitney U testing were used to analyse differences in the corneal curvature measurements between the SCL and NCL groups. Prior to cessation of SCL wear, results showed that there were significantly steeper corneal curvature values at all corneal locations tested in the SCL group (see Table 6-6). This finding may be explained by the significantly higher myopic refractive error in the

SCL group compared with the NCL control group, as increased myopia has been found to be correlated with steeper corneas (Budak et al., 1999; Mehravaran et al., 2013; O' Donnell et al., 2011; Scholz et al., 2009). This finding was maintained at day 1, 2, 7 and 14 following cessation of SCL wear. Full details of corneal curvature on these days are in Appendix A.5.3.

The influence of cessation of SCL wear on the stability of corneal curvature measurements between the groups (SCL vs. NCL) was examined. Results of two-way ANOVA and Mann-Whitney U testing showed significant differences in stability of superior tangential curvature measured on day 1 and 2 between the groups. Interestingly, the largest difference was detected in the NCL group (n = 21), which showed a mean flattening of 0.46 ±1.02D, whereas the SCL group (n = 25) showed a mean steepening of -0.12 ±0.51D (F 6.19, p = 0.02). No significant differences were found between the groups for the other variables tested. Full details of all results can be seen in A.5.3.

Table 6-6: Corneal curvature prior to cessation of SCL wear (baseline)

Baseline	**CL group NCL (n = 28) SCL (n = 33)**	**Mean**	**SD**	**Two- way ANOVA Sig**	**Mann-Whitney Sig**
Flat SimK (mm)	NCL	8.00	0.25	0.00	0.01
	SCL	7.79	0.23		
Steep SimK (mm)	NCL	7.85	0.26	0.00	0.00
	SCL	7.59	0.25		
Sagittal curvature centrally (D)	NCL	42.75	1.46	0.00	0.01
	SCL	43.98	1.44		
Sagittal curvature superiorly (D)	NCL	42.80	1.50	0.00	0.00
	SCL	44.21	1.56		
Sagittal curvature inferiorly (D)	NCL	43.38	1.91	0.01	0.00
	SCL	44.63	1.49		
Tangential curvature superior (D)	NCL	42.37	1.61	0.02	0.02
	SCL	43.46	1.52		
Tangential curvature centrally (D)	NCL	42.45	1.61	0.00	0.02
	SCL	43.62	1.14		
Tangential curvature inferiorly (D)	NCL	42.15	1.43	0.00	0.00
	SCL	43.42	1.36		

Mean ±SD stability of corneal curvature for SCL and NCL groups prior to cessation of SCL wear (baseline). Two-way ANOVA show significant differences between the groups for all variables tested, $p < 0.05$.

6.3.4.1 The influence of SCL material on stability of corneal curvature measurements

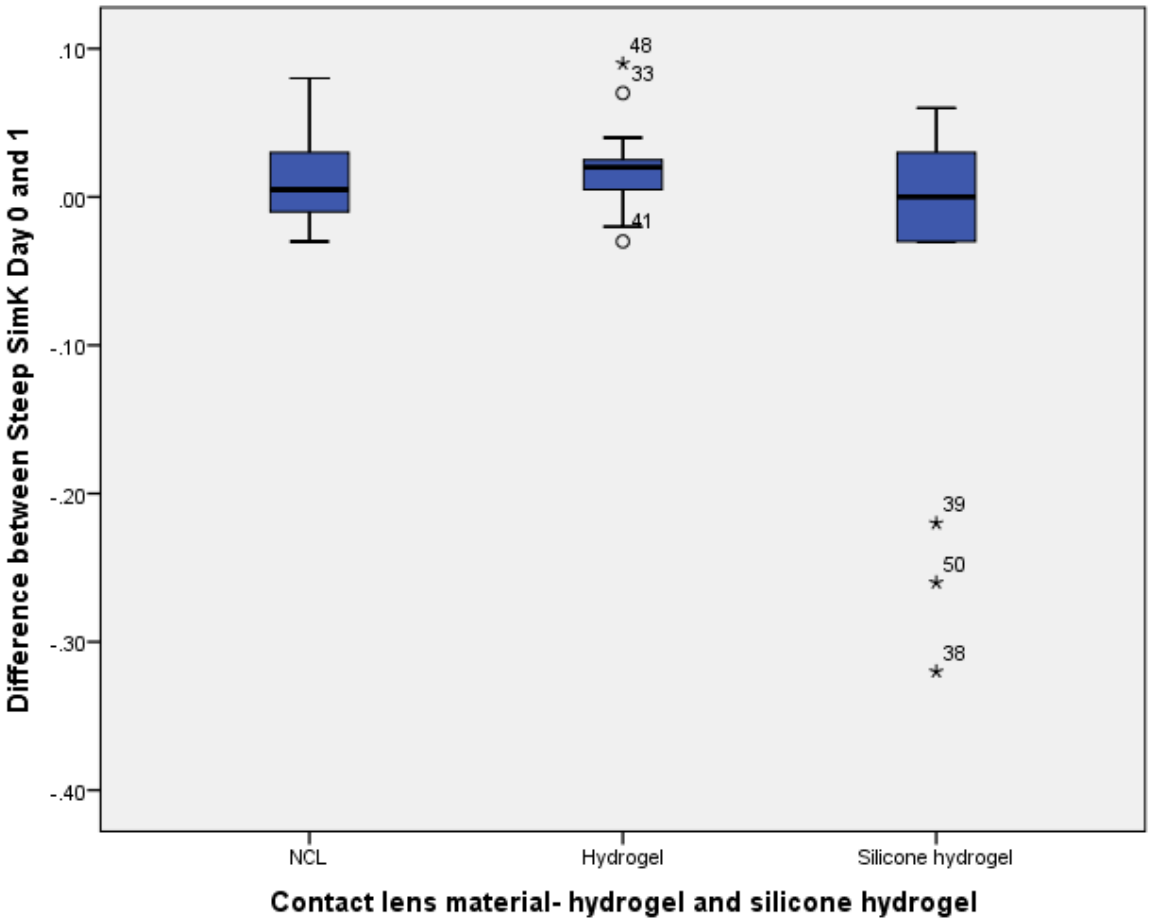
The influence of SCL material on the stability of corneal curvature measurements was explored using a two-way ANOVA. The results indicated that the type of SCL material worn had a significant impact on the stability of steep SimK following 1 day's SCL cessation (Table 6-7, Figure 6-1) No other significant differences were found between NCL, hydrogel and SiHy SCL groups at any time tested (all p values > 0.05). Full statistical analysis and results of the influence of SCL material on the stability of corneal curvature measurements following cessation of SCL wear at 1, 2, 7 and 14 days are in AppendixA.5.3.4.

Table 6-7: The influence of SCL material on the stability of corneal curvature measurements following SCL cessation between baseline and days1, 2, 7 and 14.

Curvature variable	**SCL material Group**	**Stability between**	**Mean difference ±SD**	**Direction of change**	**Sig**	**Post hoc Scheffe Sig**
Steep SimK (D)	NCL (n = 26) SiHy (n = 13) Hydrogel (n = 19)	Day 0 and 1	0.008 ±0.03 0.003 ±0.07 0.009 ±0.03	Flatter	0.01	NCL and SiHy 0.03

Summary of statistical results of two-way ANOVA examining the influence of SCL material on the stability of corneal curvature measurements following SCL cessation between baseline and days 1, 2, 7 and 14. Mean differences ±SD and results of Scheffe post-hoc testing are shown. Statistically significant differences are shown in shaded cells (p < 0.05).

Figure 6-1: Boxplot depicting the stability of the steepest K value following one day's SCL cessation



The boxplot portrays the minimum and maximum values of the stability of steepest K for the NCL (left) and SCL (right) groups. The blue box represents where 50% of the data lies with the thick black line within the box representing the median. Outliers of individual cases are numbered. While there are no outliers present in the NCL group there are in both SCL groups. The outliers in the SiHy group in particular indicate more instability of steep SimK in these three patients.

6.3.5 The influence of SCL wear on the stability of corneal thickness measurements following cessation of SCL wear.

A two-way ANOVA was used to analyse differences in the corneal thickness measurements between the SCL and NCL groups prior to and following cessation of SCL wear. The cornea was thinner at all locations tested at baseline, for the SCL group. However, there were no differences at later time points (Table 6-8). A full breakdown

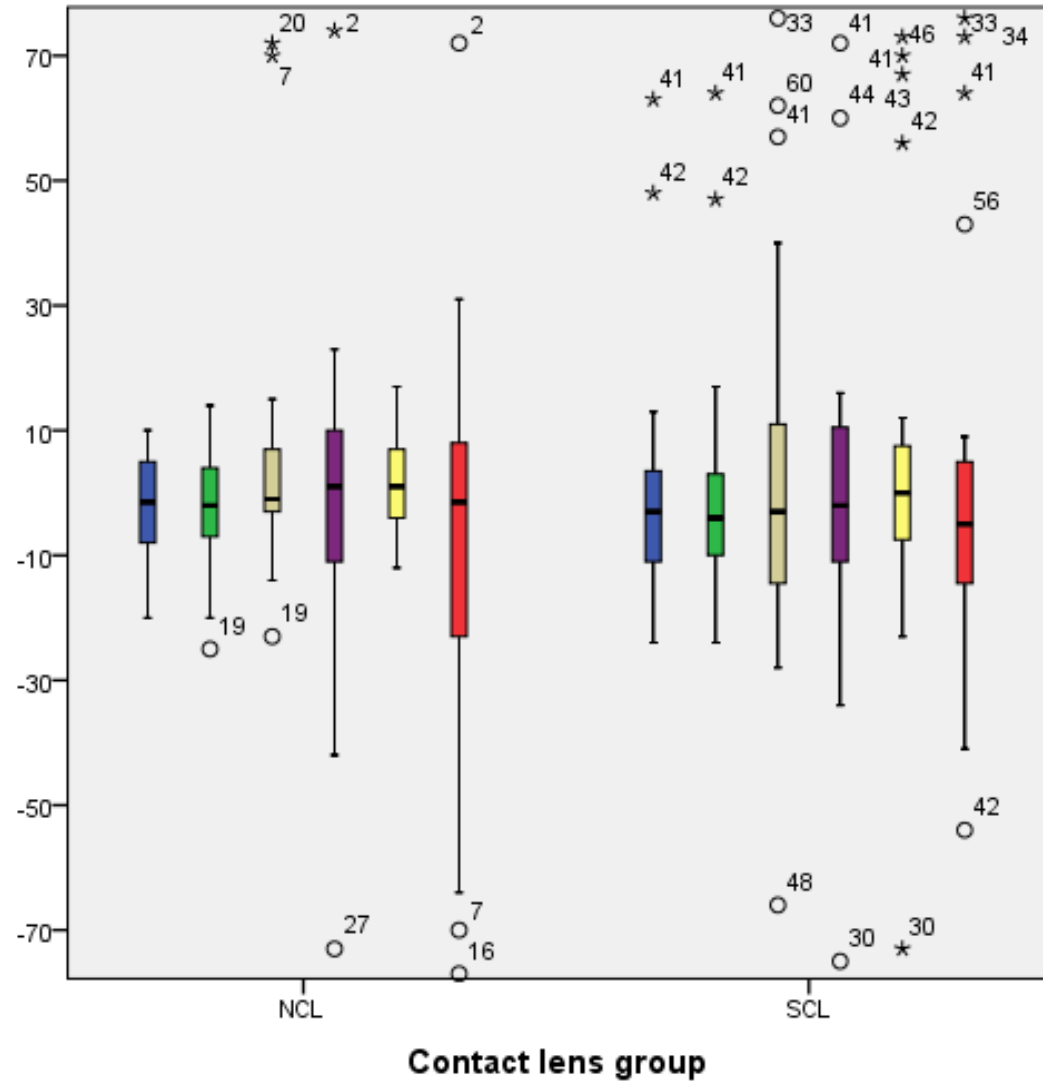
of statistical analysis and mean ±SD of corneal thickness on days 1, 2, 7 and 14 are in Appendix A.5.3.5.

Table 6-8: Corneal thickness data prior SCL cessation (baseline)

CL group **NCL (n = 28)** **SCL (n = 33)**		**Mean**	**SD**	**Sig**
Central	NCL	542.58	33.65	0.10
	SCL	527.94	33.23	
Thinnest location	NCL	539.88	32.74	0.09
	SCL	525.09	32.87	
Inferior	NCL	608.81	29.85	0.13
	SCL	596.03	32.76	
Nasal	NCL	623.31	36.92	0.06
	SCL	604.85	37.38	
Superior	NCL	650.85	33.94	0.19
	SCL	638.52	36.32	
Temporal	NCL	597.88	33.53	0.38
	SCL	589.55	38.04	

Mean ±SD of corneal thickness measurements prior to and following the cessation of SCL wear for NCL and SCL groups. Results of two-way ANOVA show no significant differences between the groups, all p-values > 0.05.

Figure 6-2: Boxplot depicting the difference in corneal thickness between baseline and following one day's SCL cessation



The boxplot portrays the minimum and maximum values of stability of corneal thickness for the NCL (left) and SCL (right) groups. Corneal thickness is depicted using the following colours: central in blue, thinnest location in green, inferior in brown, nasal in purple, superior in yellow and temporal in red. The coloured box represents where 50% of the data lies, with the thick black line within the box representing the median. Outliers of individual cases are numbered, there are more outliers present in the SCL group compared with the NCL.

The stability of corneal thickness measurements following cessation of SCL wear was analysed. Two-way ANOVA and Mann-Whitney U testing was carried out to assess the impact of previous SCL wear on the stability of corneal thickness. In all cases, corneal thickness increased following SCL cessation in the SCL group, and was significantly

thicker temporally between baseline and day 1, compared with the NCL group, which showed relative stability. (NCL -1.31 ±12.38µm, SCL 7.58 ±18.85µm, p = 0.04) (see Table 6-9).

Table 6-9: Stability of corneal thickness measurements following SCL cessation between baseline and day 1

CL group NCL (n = 33) SCL (n = 28)		**Mean ±SD (µm)**	**Two-way ANOVA Sig**	**Mann-Whitney Sig**
Central	NCL	0.58 ±9.71	0.11	0.16
	SCL	4.42 ±8.71		
Thinnest location	NCL	0.73 ±10.29	0.10	0.09
	SCL	4.88 ±8.61		
Inferior	NCL	0.58 ±10.76	0.34	0.36
	SCL	3.64 ±13.09		
Nasal	NCL	-0.69 ±17.16	0.14	0.13
	SCL	4.97 ±12.26		
Superior	NCL	3.50 ±9.82	0.24	0.17
	SCL	0.12 ±11.52		
Temporal	NCL	-1.31 ±12.38	0.04	0.06
	SCL	7.58 ±18.85		

Mean ±SD of stability of corneal thickness measurements between baseline and day 1 following the cessation of SCL wear for NCL and SCL groups. A negative value for mean difference indicates corneal thickness was less following lens cessation. Significant results of two-way ANOVA are shown in shaded cells, ($p < 0.05$).

Results of two-way ANOVA and Mann-Whitney U testing show this significant difference in TCT between the groups (SCL vs. NCL) remained between days 1 and 2 SCL cessation (see Table 6-10). However, the SCL group displayed a large fluctuation in TCT between days 1 and 2 SCL cessation, and on day 2 was found to be significantly thinner than on day 1 (NCL 4.08 ±17.19µm, SCL -8.94 ±21.12µm, p = 0.01). There were no further significant differences between the SCL and NCL at any time period tested (including the stability between baseline and day 14) indicating that there was

stability of measurements. A full breakdown of statistical analysis and mean ±SD of corneal thickness between days 2 and 7, 7 and 14 and between baseline and day 14 are in Appendix A.5.3.5.

Table 6-10: Stability of corneal thickness measurements following SCL cessation between days 1 and 2

CL group NCL (n = 26) SCL (n = 32)		**Mean ±SD (µm)**	**Two-way ANOVA Sig**	**Mann-Whitney Sig**
Central	NCL	0.81 ±8.93	0.72	0.69
	SCL	-0.00 ±8.32		
Thinnest location	NCL	0.81 ±9.91	0.65	0.55
	SCL	-0.28 ±8.47		
Inferior	NCL	3.85 ±12.37	0.23	0.32
	SCL	-0.00 ±11.85		
Nasal	NCL	1.73 ±14.01	0.55	0.27
	SCL	-0.44 ±13.10		
Superior	NCL	2.58 ±10.25	0.84	0.82
	SCL	3.13 ±10.47		
Temporal	NCL	4.08 ±17.19	0.01	0.02
	SCL	-8.94 ±21.12		

Mean ±SD of stability of corneal thickness measurements between day 1 and 2 following the cessation of SCL wear for NCL and SCL groups. A negative value for mean difference indicates corneal thickness was thinner following lens cessation. Significant results of two-way ANOVA are shown in shaded cells, $p < 0.05$.

6.3.5.1 The influence of SCL material on the stability of corneal thickness

The influence of SCL material on the stability of corneal thickness measurements following cessation of SCL wear was analysed. Two-way ANOVA results showed that there were no significant differences in corneal thickness for the groups between baseline and day 1, or between days 2 and 7, or between baseline and day 14. There was however, significantly lower TCT in the SCL groups (both hydrogel 7.21 ±24.87µm and SiHy 11.46 ±14.60µm) compared with the NCL group (-4.08 ±17.19µm,

p = 0.04) following 2 days SCL cessation. Full statistical results can be seen in Appendix A.5.3.6.

6.4 Discussion

Study 3 involved a prospective non-randomised control study to investigate the time taken to achieve stability of corneal curvature, thickness and refractive error measurements following SCL cessation. A review of the current literature indicated that the time required to achieve stability of corneal curvature measurements following cessation of SCL wear is variable and dependent on the SCL material and modality of wear (Hashemi et al., 2008; Nourouzi et al., 2006; Wang et al., 2002b). Advances in SCL materials and prescribing techniques have meant that low DK/t SCLs are now rarely worn over EW modalities and instead high DK/t SiHy SCLs are used (Morgan and Efron, 2006, Woods et al., 2007). Guidelines regarding SCL cessation, prior to CRS, do not differentiate according to SCL materials or modalities (FDA, 2014; Royal College of Ophthalmologists, 2011). Previous authors have investigated the time taken for stability of corneal and refractive error following SCL cessation, however, they have not examined the influence of different SCL materials or wearing modality (Hashemi et al., 2008; Ng et al., 2007).

The criteria used to assess the stability of measurements are of vital importance. In order to compare the findings of study 3 to those documented in the literature, the same criteria for documenting stabilisation were used. These values were summarised in Table 6-1.

6.4.1 The influence of SCL cessation on the stability of refractive error

Statistical analysis on the stability of refractive error indicated highly significant instability in the SCL group compared with the NCL group following 1 day's SCL cessation. The NCL group showed refractive stability, with fluctuations in refractive error showing a mean increase in myopic refraction of -0.03D between baseline and day 1. However, the SCL group showed a mean increase in myopic refraction of -0.20D following 1 day's SCL cessation ($p = 0.00$). This increase was evident in both the hydrogel and SiHy SCL material groups. Following this, both groups remained relatively stable with no significant differences between them (SCL vs. NCL) between days 2, 7 and 14. Despite the highly significant differences between the groups (SCL vs. NCL) between baseline and day 1, at all time periods the difference in refraction remained lower than the criteria for stability of refractive error (< 0.25 to 0.50D) as adopted by previous authors (De Benito-Llopis et al., 2009; Ng et al., 2007). Therefore, while the results were statistically significant, they were not deemed clinically significant.

Mean myopic refractive error can be influenced by SCL material worn (Bergenske et al., 2007; Blacker et al., 2009; Fonn et al., 2002). Fonn et al. (2002) found a significant increase in myopia (-0.50D) following low DK/t SCL wear, compared with the high DK/t G1SiHy SCL wear (-0.06D; $p < 0.01$) over 4 months of EW ($n = 24$). A significant difference in keratometry values was also recorded for the 2 SCL materials: 0.28D steeper in the low DK/t group compared with 0.05D steeper in the high DK/t group ($p < 0.01$). The differences between the groups were proposed to be due to hypoxia and mechanical moulding.

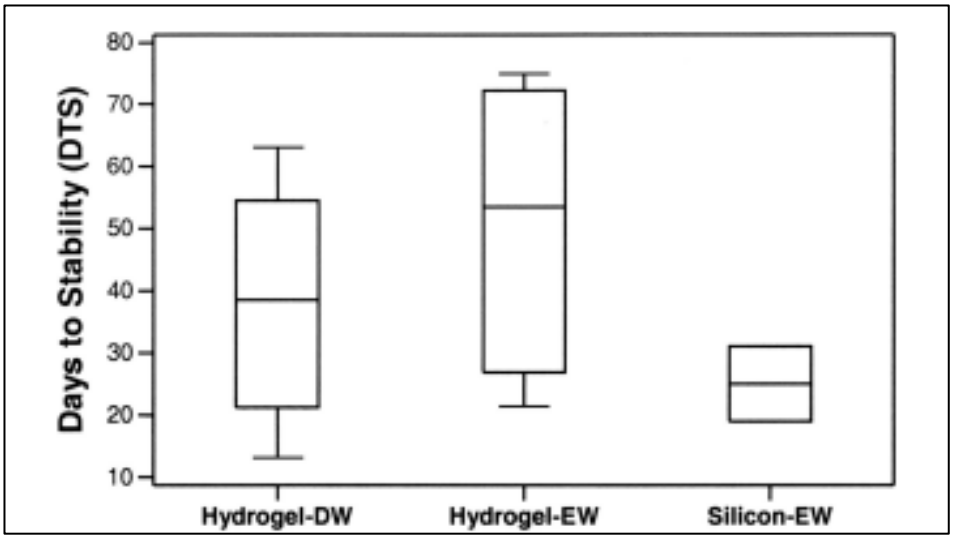
Further investigations into the mechanism of this increased myopia were subsequently carried out by Bergenske et al. (2007) who reported that DW of hydrogel SCLs (n = 81) resulted in significantly increased myopia (with a mean change of -0.40D) over a 3 year period. However, refractive error remained stable ($p < 0.01$) over the same period for EW of G1SiHy SCLs (n = 317). The authors concluded that while the mechanism for the change in refractive error is not completely understood (axial length measurements were not taken), it is thought that the change is related to the change in topography.

Blacker et al. (2009) also analysed the effect of SCL material on the progression of myopia. SCL wearers were fitted with hydrogel lenses on a DW basis (n = 54) or G1SiHy on an EW 30 night basis (n = 230) and followed the progression of myopia over 3 years. Multivariate analysis found that refractive error changes over the 3 years was significantly affected by lens material ($p < 0.001$) and subject age ($p < 0.001$). Subject age was analysed as a continuous variable and grouped according to decade of life, the age-adjusted changes in refractive error were +0.02D for SiHy and -0.41D for hydrogel lenses. This study is in agreement with that of Bergenske et al. (2007), in proposing the slowing of myopic progression with stiffer SiHy lens materials.

Ng et al. (2007) found the overall mean time for stability of manifest refraction measurements, that is < 0.50D change, was 10.7 ±10.4 days (n = 15 SCL wearers). Ng et al. (2007) confirmed the findings that EW hydrogel SCL wearers take the longest time to achieve refractive stability following cessation of SCL wear (12.9 ±7.4 days), while EW SiHy SCL wearers took the shortest time (6.0 ±1.2 days), followed by DW hydrogel SCL wearers (7.9 ±2.3 days). Although there were no DW SiHy SCL wearers included in Ng et al.'s sample, the trend indicated by these results imply that DW of

SiHy would have resulted in shorter time to stability, and similar to the finding of this study. The authors acknowledged that measurements from traditional methods of manifest refraction and keratometry, resolved in a shorter time period than topography and pachymetry. The overall mean time for stability of manifest refraction measurements for the SCL group was 10.7 ±10.4 days, for keratometry was 16.2 ±17.5 days, for axial topography was 28.1 ±17.7 days and for Orbscan pachymetry was 35.1 ±20.8 days (see Figure 6-1).

Figure 6-3: The time taken for stability of measurements following cessation of SCL wear



A boxplot of the time taken for stability of measurements following cessation of SCL wear for DW and EW of hydrogel and SiHy SCLs, adapted from Ng et al. 2002.

6.4.2 The influence of SCL cessation on stability of corneal curvature

As discussed in the previous section, the influence of SCL wear on refractive error has been linked to mechanical moulding and alterations to corneal curvature. Furthermore, that refraction and keratometry take shorter time periods to resolve compared with topography and pachymetry. In study 1, the significant inferior tangential topography

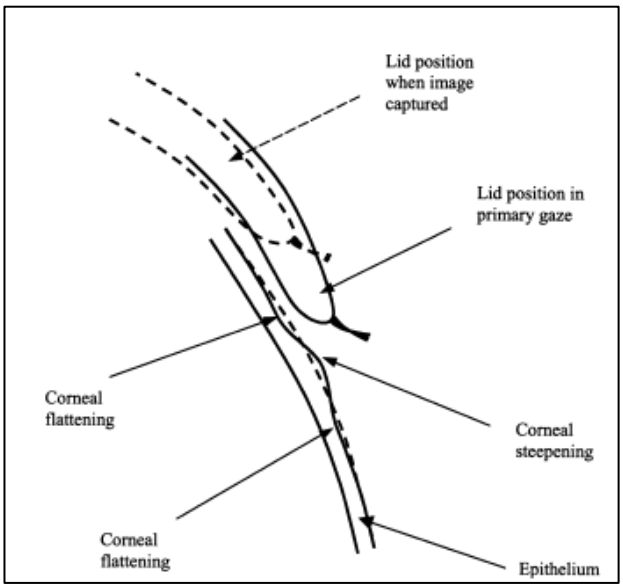
steepening which was evident in the SCL group had resolved following 2 weeks cessation of SCL wear. The aim of study 3 was to document the time taken for stability to occur, within this 2 week period, following SCL cessation. It has been reported that the time taken for resolution of corneal curvature changes induced by SCL wear can be greater in older patients (Nourouzi et al. 2006). This, perhaps, is an indication that the resolution of corneal changes can slow with age, or possibly that these patients may have worn SCLs for longer time periods. In order to control for this factor, the sample size for study 3 was a young university population (age range 18 to 28 years).

The results of this study showed that prior to cessation of SCL wear, there were significantly steeper corneal curvature measurements at all corneal locations tested in the SCL group. This finding demonstrates the difference of this control group (sourced from a NCL student population who were mostly emmetropic) compared with study 1 (sourced from NCL patients attending a CRS clinic for correction of their myopia). Results of statistical analysis on the stability of corneal curvature measurements following cessation of SCL wear showed significant differences in stability of superior tangential curvature measured on days 1 and 2 between the groups (SCL vs. NCL). Interestingly, the largest difference was detected in the NCL group who showed a mean flattening of 0.46 ±10.02mm. Whereas, the SCL group showed a mean steepening of -0.12 ±0.51mm ($p = 0.02$). No significant differences were found between the groups for the other variables tested. The difference in the SCL group was in the opposite direction to that found in study 1 (where a mean flattening and return to prolate shape had been found following cessation of SCL wear). Therefore, although a time period for stability of corneal curvature appeared to be isolated to between 1 and 2 days the accuracy of these peripheral measurements is questionable.

Kawamorita et al. (2009) reported that the Pentacam produced repeatable and reproducible corneal measurements centrally, but repeatability outcomes indicated that superior corneal measurements ought to be interpreted with caution. The significant findings of study 3 must be considered, especially at this superior location where shadows due to the brow bone or the influence of the top eyelid may result in reduced accuracy in the measurement of corneal curvature at this location (Buehren et al., 2001). Buehren et al. (2001) examined the stability of corneal topography in the post-blink interval and found tangential topography in particular to show larger variation in the superior periphery, with central standard variations being less than 0.50D and peripheral variations increasing to 1.00D. Buehren et al. concluded that this variability was due to the effects of eyelid pressure as depicted in Figure 6-4. Chen et al. (2009) also reported poor reliability and repeatability for the Pentacam at the superior corneal region (Cronbach's alpha = 0.891, ICC = 0.732). The authors also concluded the discrepancy at this location was due to the eyelids and shadows from the eyelashes (Chen and Lam, 2009).

Further analysis into the effect of SCL wear on the stability of corneal measurements following SCL cessation was carried out and the impact of SCL material was explored. Although statistically significant differences were found between the stability of steep SimK measured following 1 day's SiHy SCL cessation and the NCL group, all measurements were lower than the criteria for stability of < 0.50D and remained stable thereafter.

Figure 6-4: Changes to superior tangential topography due to the upper eyelid



(Buehren et al. 2001)

The results in study 3 did not show significant instability in inferior tangential curvature measurements, which were found in study 1. The discrepancies in these findings may relate to the differences in the study populations. The study population in study 1 was older, and wore SCLs for longer (mean previous SCL wearing time 9 ±4.5 years), compared to the younger subjects in study 3 (mean previous SCL wearing time 4 ±2.7 years).

The results of study 3 differ to those of Alba-Bueno (2009), who found that subjects wearing G1SiHy (Focus Night& Day) (n = 7 eyes) and G2SiHy (Acuvue Oasys) (n = 7 eyes) SCLs showed no significant changes in topography measurements, VA or over-refraction over 3 months of DW. The control group (n = 5 eyes) wore hydrogel SCLs with a 38% water content (Alba-Bueno et al., 2009) and showed statistically significant flattening of mean keratometry, corneal astigmatism and corneal eccentricity measurements. Limitations to the study lie in the short follow-up time (3 months),

small sample size and that previous CL wearers were included and asked to cease lens wear for a certain period prior to beginning the study (Soft: 10 days, RGP: 4 weeks). It is possible that the period of cessation of previous CL wear was not sufficient for the stabilisation of previous topographically-induced changes due to SCL and RGP wear.

Hashemi et al. (2008) studied corneal curvature stability following discontinuation of SCL wear in a prospective study (n = 42 eyes, 21 patients). Curvature was examined upon SCL removal and following this on days 3, 7 and weekly thereafter. Criteria for stability were also less than 0.50D (0.1mm) change in curvature between visits. There was no NCL control group. Thirty per cent (14 eyes) fulfilled the stability criteria after the first assessment, 15% (7 eyes) were grouped as unstable, and required at least 1 week to achieve stability. At this point only the right eyes were analysed to account for the effect of inter-eye correlation (Hashemi et al., 2008). There were no statistically significant differences in population demographics, years of SCL wear, refractive error, topography or pachymetry between the stable and unstable groups. Topography measurements were taken using an EyeSys Corneal analysis system (EyeSys Laboratories, Texas). It was concluded that the majority of patients reached corneal thickness and curvature stability following cessation of SCL wear for a 2 week period. However, it was noted that for some patients this may not be sufficient and a better approach would be to take repeated scans prior to CRS in order to document stability. Analysis into the predictability of stability time did not yield any firm associations between risk of instability with refractive data, topography or duration of CL wear. It is not possible to compare these results directly to this study as the influence of the type of SCL material worn was not explored.

As previous discussed, Ng et al. (2007) reported longest stability times with sagittal topography values. Ng et al. confirmed the findings that EW of hydrogel lenses resulted in the longest time taken to achieve stability of topography (< 0.50D change); hydrogel EW 30.0 ±16.3 days, SiHy EW 23.3 ±13.7 days, hydrogel DW 29.6 ±19.5 days (n = 15 SCL wearers). The disparity between the findings of this study and those reported by Ng et al. may be related to the variation in the CL wearing subject population and lead one to question whether more specific guidelines are required for CRS patients – specifically for long term wearers (> 10 years) and in cases of EW.

6.4.3 The influence of SCL cessation on stability of corneal thickness

In study 3, lower corneal thickness was found at all corneal locations in the SCL group compared with the NCL control group prior to SCL cessation; however, results lacked statistical significance. These results were comparable to those reported in the literature (Holden et al., 1985; Liesegang, 2002; Pflugfelder et al., 2002; Yeniad et al., 2003) and those found in study 1. Following 1 day's SCL cessation, there was a significant increase in TCT in the SCL group (7.58 ±18.85µm) compared with the NCL who showed a decrease (-1.31 ±12.38µm, $F = 4.30$, $p = 0.04$). However, the SCL group displayed a large fluctuation in TCT between days 1 and 2, and on day 2, TCT was found to be significantly thinner than on day 1 (NCL 4.08 ±17.19µm, SCL -8.94 ±21.12µm, $p = 0.01$). This change could indicate an initial rebound effect following the initial cessation of SCL wear, with the increase in TCT on day 1 settling to the reduced level on day 2. However, it might also indicate reduced accuracy of repeated corneal thickness readings at this peripheral corneal location (Miranda et al., 2009). These results remained relatively stable until day 14. No significant influence of SCL material on the stability of corneal thickness measurements following the cessation of SCL wear

was found. The value taken in determining stability of corneal thickness measurements is crucial. If the value is too low (and beyond the repeatability capabilities of the pachymetry instrument) then it is impossible to determine whether fluctuation in CCT is due to instability following cessation of SCL wear or errors in repeatability of the CCT measurements. The accuracy of the Pentacam in measurement of corneal thickness has been reported as 3µm (Belin and Khachikian, 2006b). The mean diurnal variation in CCT has been reported as 7.9 ±1.1µm (Tyagi et al., 2010). Therefore, previous authors have advocated the use of 8µm as a suitable value to demonstrate stability of corneal thickness. Taking this 8µm stability criterion into account, it was only the SCL group who exhibited instability between days 1 and 2.

Ng et al. (2007) reported largest stability times of corneal thickness with EW hydrogel SCL wearers (49.9 ±23.5 days) followed by DW hydrogel SCL wearers (29.0 ±16.9 days), while EW SiHy wearers (25.0 ±14.5 days) took the shortest time to achieve stability. Results were not statistically significant ($p = 0.29$). Pachymetry was measured using the Orbscan. As previous discussed, the disparity in time taken for stability of corneal thickness following cessation of SCL wear between this study and those of Ng et al. (2007) may be explained by the lack of EW hydrogel or EW SiHy SCLs in this study. However, the accuracy of the Orbscan for pachymetry measurements must also be considered. Corneal thickness measured by the Orbscan has been reported as being inferior to that taken by the Pentacam or Ultrasound pachymeter (Boscia et al., 2002; Cairns and McGhee, 2005; González-Méijome et al., 2003b; Nilforoushan et al., 2008). The Orbscan consistently overestimates corneal thickness when compared with US pachymetry therefore, manufacturers recommend an acoustic correction factor of 0.92 to compensate for this overestimation (Swartz et al., 2007).

This use of a single correction factor across the entire cornea has been criticised, as a constant linear relationship may not be applicable for various populations and across the entire cornea (Chakrabarti et al., 2001, González-Méijome et al., 2003, Cho and Cheung, 2002, Guarnieri and Guarnieri, 2002). Furthermore, accuracy of Orbscan pachymetry is dependent on the transmission of a slit light beam through the cornea. The back scattered light is detected by a digital video camera in the instrument which processes the images into 2 dimensional maps (Cairns and McGhee, 2005). Therefore anything which effects back scatter of these slits, such as haze from CRS or sub-clinical haze possibly induced by SCL wear, may have an effect on the accuracy of the Orbscan (Kim et al., 2007).

When considering stability of CCT one must consider the influence of diurnal variation. In study 3, repeat appointments were scheduled at the same time of day (within 2 hours) to limit the possible influence of diurnal variation. Large variability in corneal thickness repeatability has been found when corneal thickness measurements are taken at various times throughout the day (Braun and Anderson Penno, 2003). Braun (2003) found a mean reduction in corneal thickness of 22µm in the SCL group compared with the control population. Whereas very small fluctuations in corneal thickness with short-term SCL wear have been found when diurnal variation has been controlled for. Tyagi et al. (2010) examined regional stability in corneal thickness following short-term (8 hours) SCL wear (n = 12) of a variety of SCL designs (toric stabilisation, using a single prism ballast design, vs. spherical) and materials (hydrogel vs. G2SiHy) (Tyagi et al., 2010). The hydrogel toric SCL caused the greatest increase in CCT (20.3 ±10.0µm) and peripheral corneal thickness (24.1 ±9.1µm; $p < 0.00$). The G2SiHy SCLs resulted in relative stability of corneal thickness. No changes in CCT were larger than those

normal diurnal variations experienced by the patients. The SCLs worn were empirically ordered and interestingly, the modulus of the hydrogel lens was greater than the G2SiHy (0.50 vs. 0.35 respectively). Also, the DK/t was low in the hydrogel group compared with the G2SiHy (8-10 vs. 53 respectively). It was not clear whether the small study population were all previous SCL wearers. These authors reported on patients who were not regular SCL users and 1 subject had not worn SCL for at least 1 month. In addition to this, some error may have been introduced by the short time given between the various SCLs worn – with only 2 days given between SCL wear of the various varieties.

Table 6-11: CCT prior to and following 3 years of SCL wear

Time period	**Before CL use**	**After 3 years of SCL wear, 2 weeks after CL removal**	**Sig**	**4 weeks after CL removal**	**Sig**
NCL	554 ±11.40	552 ±11.3	0.476		
CL adolescents	552 ±7.14	545 ±8.35	0.01	549 ±7.32	0.20
CL adults	550 ±9.40	539 ±8.81	<0.00		

(Sanchis-Gimeno et al., 2007)

One must also consider the change in corneal thickness at true baseline (prior to commencement of any SCL wear) and following SCL cessation. CCT thinning due to SCL wear can take up to 4 weeks to resolve to baseline pre-SCL wear levels (Sanchis-Gimeno et al., 2007). Sanchis-Gimeno et al. compared the CCT of 15 SCL wearing myopic adolescents (aged 15-16 years) to 31 NCL wearing myopic adolescents (aged 15-16 years) and 34 SCL wearing myopic adults (aged 24-40 years). The Orbscan II was used to measure CCT before SCL wear and after 3 years of SCL wear (using an acoustic factor of 0.92). The SCLs worn were conventional hydrogel lenses of 66%

water content. The SCL wearing adolescents and adults showed a significant decrease in CCT over the 3 years (Table 6-11).

However, following up to 4 weeks of SCL removal the CCT returned to baseline levels. Recovery values, for the return to baseline CCT, were not quoted for the adult group. It is possible that light scatter induced by SCL wear, may have affected the accuracy of the CCT measurements taken with the Orbscan at the 2 weeks of lens cessation time point (Kim et al., 2007). True corneal thickness stabilisation was not determined in this study, as there were no baseline corneal thickness measurements available for the SCL wearers prior to SCL wear, making it impossible to compare these results directly to those reported by Sanchis-Gimeno et al (2007). One must also consider the criteria for stability here. While there was a statistically significant mean difference in corneal thickness, between baseline and 2 weeks of SCL cessation, for the CL wearing adolescents of 7µm, it was less than the limits of stability (given as ±8µm for this study). No findings of CCT were reported earlier than 2 weeks following SCL cessation. It may be possible that corneal stability occurred earlier than the 2 week period quoted. This is comparable to the results of this study, where the hydrogel group showed a mean change in CCT of 6.42µm following 1day; this result remained stable until day 14.

Nourouzi et al. (2006) examined the time taken for corneal oedema to resolve in a group of SCL candidates (n = 100 eyes) who had been wearing DW hydrogel SCLs (38% water content) for at least 6 months prior to pre-operative assessment for LASIK. Mean CCT was measured using the US pachymeter (NIDEK UP1000, Japan) immediately after lens removal and then daily (between 12 noon and 2 pm). Following SCL

removal, CCT was 557 ±32μm and subsequent to the resolution of oedema was 522 ±24μm. These results were inconclusive and could not be linked to any causative factor. It is possible that the use of anaesthetic and the probe placement may have led to some variability in the CCT measurements (Paul et al., 2008). Stabilisation of corneal thickness took place in the first week for 74% of the patients, but required an additional week for the remaining 26%, with the second group being composed of mainly older patients. The lack of older patients with longer SCL wearing times in study 3, and the discrepancies between the instrumentation used (US vs. Pentacam), may account for the discrepancies between these results and those of Nourouzi et al. (2006).

6.5 Conclusion

True corneal stabilisation, in terms of a return to baseline measurements, cannot be determined from these results, as it was not possible to examine corneal measurements prior to SCL wear. Looking at consistency over a 2 week time period, stability of refractive error occurred following 1 day's SCL cessation. Despite the highly statistically significant differences in refractive error between the groups (SCL vs. NCL) between baseline and day 1, the difference in refraction remained lower than the criteria for stability of refractive error (< 0.25 to 0.50D) at all time points evaluated.

Stability of corneal thickness occurred following 2 days' SCL cessation, again despite significant differences in stability of TCT between the groups (SCL vs. NCL). At all times, the difference in corneal thickness remained lower than the criteria for stability value (< 8μm). Stability of corneal curvature occurred centrally after 1 day SCL cessation for all SCL wearers. The repeatability of peripheral corneal curvature measurements was questionable, especially at the superior corneal location examined;

this finding is in agreement with those reported by Kawamorita et al. (2009). For this reason, the criteria for stability recommended in the literature were adopted in this study, i.e. to examine stability within the central 3mm (Ng et al., 2007). Using this criteria, after 2 days' SCL cessation, there were no significant differences between the SCL and NCL groups. Given the results of this study, it was concluded that a standard SCL cessation time of 24 hours as suggested by the Royal College of Ophthalmologists (2011) is inadequate for corneal stabilisation to occur. At least 2 days' SCL cessation times ought to be adopted. However, extrapolated conclusions from these findings can only be applied to a DW modality in young myopic patients.

In order to ensure accuracy, stability of corneal tangential curvature and corneal thickness ought to be confirmed prior to CRS. Ideally, clinical measurements ought to be taken daily until stability is demonstrated. If shorter SCL cessation times are to be implemented prior to CRS, in order to ensure accuracy of corneal measurements, taking the average of 3 consecutive readings, at each session, would improve reproducibility and repeatability (Chen and Lam, 2009). Furthermore, taking at least 2 measurements during the SCL cessation time to ensure stability of corneal curvature would be desirable. Further investigation is required into the influence of SCLs for the correction of hyperopia, SCL designs such as toric SCLs and the influence of stiff modulus associated with G1SiHy SCL materials on stability times following SCL cessation. In the absence of these safeguards, a longer SCL cessation period of 2 weeks, as recommended by the FDA, ought to be applied.

Thus far, the influence of SCL wear on corneal parameters (shape and thickness) and vision has been investigated. In order to maintain good vision and normal corneal

curvature, thickness and fluid levels within the cornea must be maintained and regulated (Freegard, 1997;Kaufman, 2002). This regulation is controlled by the endothelium and may be affected by SCL wear (Edelhauser and Ubels, 2003). The influence of SCL wear on the corneal endothelium will be investigated in the following chapter.

7 CHAPTER SEVEN. STUDY FOUR: THE EFFECT OF SOFT CONTACT LENSES ON THE CORNEAL ENDOTHELIUM

7.1 Introduction

Over-wear of SCL's with low oxygen transmissibility (DK/t) can result in corneal hypoxia and chronic changes to corneal metabolism, including endothelial polymegathism and corneal thinning (Böhnke and Masters, 1997; Wiffen et al., 2000). High DK/t SiHy materials are reported to have negligible effects on the corneal endothelium (Covey et al., 2001; Doughty et al., 2005).

It is well agreed in the literature that refitting previous low DK/t CL wearers with higher DK/t CLs results in reversal of the hypoxia-induced endothelial changes (Doughty et al., 2005; Holden et al., 1985; Setälä et al., 1998b). The reversal of these endothelial changes has been proposed to be linked to both the resolution of hypoxia and also due to a mechanical reorganisation of the corneal endothelium following resolution of oedema-induced increased corneal thickness (Doughty et al., 2005).

7.1.1 Aims and hypotheses

Over-wear of low DK/t SCL's can result in changes to the corneal endothelium (Böhnke and Masters, 1997; Wiffen et al., 2000). It was hypothesised that endothelial changes would be present in full-time SCL wearers and would be more significant in previous low DK/t hydrogel SCL wearers. This hypothesis was explored by comparing endothelial measurements taken using a spectral microscope in a full-time SCL wearing group (of hydrogel and SiHy SCL materials) to a NCL control group. Central, para-central and peripheral areas of the endothelium were analysed as studies have shown

differences in morphology between the central and peripheral areas of the endothelium in CL wear (Doughty and Aakre, 2007; MacRae et al., 1989).

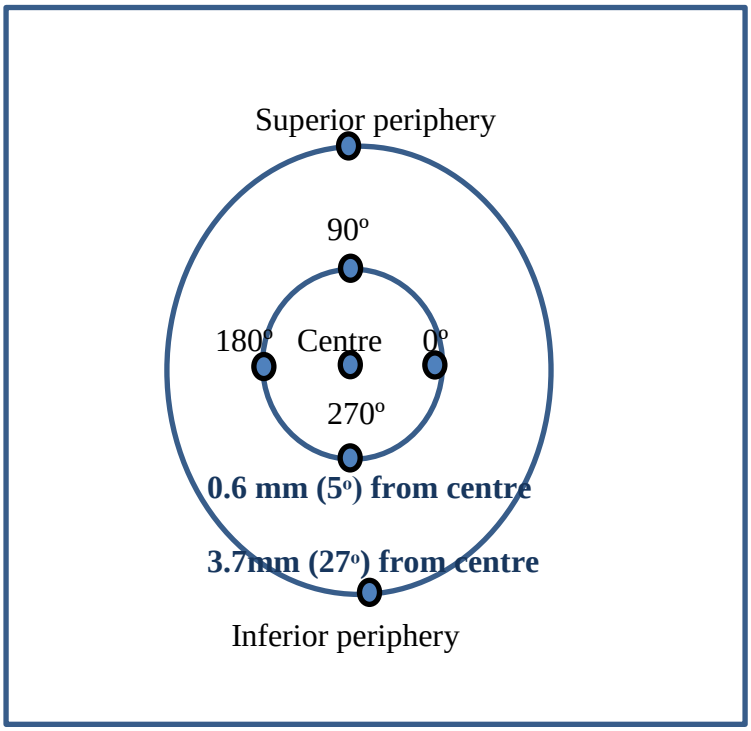
The stability of endothelial parameters in study 4 was examined over a 2 week period, following cessation of SCL wear. This time period was chosen as it was demonstrated in studies 1 and 3 that the resolution of corneal thickness occurs within this time, and as it is the time recommended by the FDA for SCL cessation prior to CRS (FDA, 2014). It was hypothesised that, if reversal of endothelial changes is linked to a change in corneal thickness following cessation of SCL wear, then this would be evident in the stability of endothelial parameters in the SCL group (particularly the low DK/t hydrogel group).

7.2 Methods

7.2.1 The effect of SCLs on the corneal endothelium.

A prospective analysis was undertaken on the full-time SCL group (n = 31 eyes) and NCL control group (n = 28 eyes) described in study 3. Analysis was carried out to assess the effect of SCLs on corneal endothelial cell density and regularity centrally, paracentrally (0.6mm from centre) and peripherally (3.7mm from centre). Results were compared with the NCL control group.

Figure 7-1: Endothelial measurements taken with CEM-530 specular microscope



(Adapted from Fujimoto et al., 2014)

7.2.2 Clinical procedure for data collection

Specular microscopy was performed on the corneal endothelium of each eye using the CEM-530 (Nidek, Japan) non-contact specular microscope at each visit. From the endothelial scan, 7 areas of the endothelium were analysed: centre, para-centrally (0.6mm from centre) at 0°, 90°, 180°, 270°, and in the superior and inferior periphery (3.7mm from centre) (Figure 7-1). Central, para-central and peripheral areas of the endothelium were analysed as studies have shown differences in morphology between the central and peripheral areas of the endothelium in SCL wear (Doughty and Aakre, 2007; MacRae et al., 1989). Parameters included in this analysis were endothelial cell density (cell/mm^2), mean cell area (μ^2), coefficient of variation of cell size (SD/area) and hexagonality (%), all of which are indicators of corneal stress (Miller and Colvard, 1999; Sheng and Bullimore, 2007). All subjects were of a similar age (SCL: 20.82

±1.69 years, range 18 to 25 years; NCL: 21.14 ±2.85 years, range 18 to 27 years), thus limiting the variability of morphology of the endothelium as a function of age (Laing et al., 1976; Laule et al., 1978; Suda, 1983; Yee et al., 1985). Endothelial measurements taken prior to SCL cessation (baseline) were compared with the NCL group to assess whether SCL wear had an effect on the endothelium. The differences in measurements taken between baseline and following 14 days cessation of SCL wear were calculated and analysed.

7.3 Results

7.3.1 Reliability of CEM specular microscope

Internal consistency of the CEM-530 endothelial measurements was explored using ICC (Bland 1996). Results for ICC of cell density were examined between baseline and day 1 for the NCL group (see Table 7-1). The CEM-530 showed excellent consistency centrally. All cell density values remained higher than 0.70 which is considered satisfactory, but values taken at 270º paracentrally and in the inferior periphery were lower than the recommended minimum value of > 0.90 for clinical applications (Bland and Altman, 1997).

Table 7-1: Intraclass Correlation Coefficient for cell density

Group	Central	0º	90º	180º	270º	Inferior periphery	Superior periphery
NCL n = 28	0.974	0.957	0.938	0.944	0.858	0.840	0.927

An ICC value of 1 indicates perfect agreement and 0 no agreement.

7.3.2 The influence of SCL wear on the corneal endothelium prior to SCL cessation

Results of two-way ANOVA showed that, prior to SCL cessation, significant differences between the SCL and NCL groups were found for 3 of the tested variables (see Table 7-2). Contrary to what was expected, endothelial cell density was significantly higher in the SCL compared with the NCL control group in the inferior periphery. The coefficient of variation of cell size was highly significantly higher in the SCL group compared with the NCL group in the superior periphery. No other significant differences in endothelial parameters were found between SCL and NCL groups (p > 0.0 5). Details of all endothelial parameters tested are in Appendix A.5.4.1.

Table 7-2: Endothelial parameters for the SCL and NCL groups prior to SCL cessation

SCL (n = 31) **NCL (n = 28)**		**Mean ±SD**	**Sig**
Inferior periphery			
Cell density (cells/mm^2)	NCL	2935.08 ±352.78	0.03
	SCL	3109.88 ±153.64	
Mean cell area (μ^2)	NCL	346.92 ±36.75	0.00
	SCL	322.25 ±15.79	
Superior periphery			
Coefficient of variation of cell size (SD/mean)	NCL	25.63 ±2.79	0.00
	SCL	29.13 ±5.03	

Mean ±SD and two-way ANOVA results for endothelial parameters compared between the SCL and NCL groups prior to SCL cessation. Statistically significant differences are displayed in shaded cells ($p < 0.05$).

7.3.2.1 The influence of SCL materials on the corneal endothelium

As significant differences in these endothelial parameters existed between SCL and NCL groups at baseline, comparisons were carried out to explore the influence of SCL material on the corneal endothelial parameters.

Results of the two-way ANOVA and post-hoc Scheffe testing found that there was a significantly higher mean coefficient of variation of cell size at 180º and in the superior periphery in hydrogel wearers compared to the NCL group. The endothelial cell density was significantly higher in the hydrogel group compared with the NCL group at the inferior peripheral location. The mean cell area in the inferior periphery was significantly higher in the NCL group compared with the hydrogel SCL group. The results of the two-way ANOVA, which showed significant differences between the groups, are displayed in Table 7-3. Details of the influence of SCL material on all endothelial parameters tested prior to cessation of SCL wear are in Appendix A.5.4.1.

Table 7-3: The influence of SCL material on endothelial parameters prior to SCL cessation

SCL Groups NCL (n = 24) Hydrogel (n = 12) SiHy (n = 12)		**Mean**	**ANOVA Sig**	**Scheffe Post hoc tests Sig**
Coefficient of variation of cell size at 180º (SD/mean)	NCL	25.79 ±3.46	0.03	Hydrogel and NCL, SiHy Sig = 0.05
	Hydrogel	29.83 ±6.51		
	SiHy	25.58 ±4.03		
Cell density at the inferior periphery (cell/mm^2)	NCL	2935.08 ±352.78	0.04	Hydrogel and NCL Sig = 0.04
	Hydrogel	3184.08 ±161.84		
	SiHy	3035.67 105.59		
Mean cell area at the inferior periphery (μ^2)	NCL	346.92 ±36.75	0.008	Hydrogel and NCL Sig = 0.009
	Hydrogel	314.92 ±16.57		
	SiHy	329.58 ±11.37		
Coefficient of variation of cell size at the superior periphery (SD/mean)	NCL	25.63 ±2.79	0.01	Hydrogel and NCL Sig = 0.02
	Hydrogel	29.92 ±6.22		
	SiHy	28.33 ±3.60		

Mean ±SD and two-way ANOVA results for the SCL material groups which showed significant differences in parameters tested prior to SCL cessation. Post-hoc Scheffe test results showing significance values between the groups. Statistically significant differences displayed in shaded cells ($p < 0.05$).

7.3.2.2 The influence of SCL wear on the stability of corneal endothelium measurements following 2 weeks cessation of SCL wear

In order to explore whether previous SCL wear had an effect on stability of endothelial measurements, the differences between endothelium measurements collected at baseline and following 14 days cessation of SCL wear was calculated. The influence of SCL

wear on these differences was explored using two-way ANOVA. No statistically significant differences in endothelial parameters were detected between NCL and SCL groups (all p values > 0.05). No statistically significant differences in endothelial parameters were detected between NCL SCL material groups (all p values > 0.05). Full results are in Appendix A.5.4.4.

7.4 Discussion

The corneal endothelial cell layer can be affected through disease process, CL wear and normal ageing (Leem et al., 2011; Sheng and Bullimore, 2007). Low DK/t SCL wear results in reduced endothelial cell density, increased polymegathism (clinically indicated by an increased coefficient of variation of cell size) and increased pleomorphism (indicated clinically by a decreased percentage of hexagonal cells) (Connor and Zagrod, 1986; Doughty et al., 2005; Liesegang, 2002). Examination of the endothelium is achieved using specular microscopy (contact and non-contact) and in vivo microscopy. Direct comparisons between these contact and non-contact methods cannot be undertaken as central and peripheral cell densities have been found to be approximately 6% higher using contact methods compared with non-contact with similarly aged patients due to variances in calibration between these methods (Amann et al., 2003).

7.4.1 CEM-530 Specular microscope

Endothelial analysis in this study was undertaken using the CEM-530 specular microscope (Nidek, Japan), which has been reported to show good repeatability and reproducibility (Kaiser et al., 2013). Mizuno (2013) compared the agreement of the CEM-530 with the Cellchek plus (Konan Medical Inc. Irvine CA, USA), in 74 eyes (including 24 non-pathologic young eyes, 25 non-pathologic adult eyes, and 25 pathologic adult eyes) (Mizuno, 2013). Both instruments were found to show excellent agreement, with differences in mean endothelial cell density of 3-5% reported. ICC values reported were high; the 95% LOA were the same for endothelial cell density, coefficient of variation of cell size and mean cell area. The 95% LOA were better in the CEM-530 for hexagonality. In this study, internal consistency of the CEM-530 showed

excellent consistency for the NCL groups, with values > 0.90 at all central locations. Although ICC values dropped off inferiorly, they still remained close to values expected for clinical applications (para-centrally at 270º: 0.86 and in the inferior periphery: 0.84). The lower ICC of peripheral endothelial measurements implies that the validity of the peripheral measurements cannot be confirmed. It is possible that error may have been induced in peripheral measurements due to subjects not looking in the correct position of gaze when specular microscopy was being performed. As the instrument took 16 images automatically at each measurement and selected the best based on image quality and on the ability of the image to be analysed, it was taken that the measurements were of a sufficient quality to be included for analysis. No study has investigated the consistency of endothelial measurements in a SCL group where light scatter may be induced by oedema with SCL wear. It is a flaw of this study design that this was not done prior to SCL cessation in the SCL group.

7.4.2 The influence of demographics on the endothelium

It is well reported that age has an effect on the corneal endothelium, with increased polymegathism evident with advancing age (Bourne et al., 1997; Carlson et al., 1988; Liesegang, 2002). In study 4, a young subject population was chosen to limit the variability of morphology of the endothelium as a function of age (Laing et al., 1976; Laule et al., 1978; Suda, 1983; Yee et al., 1985). The endothelium has been studied in a large population of older normal healthy Caucasian eyes (Zoega et al., 2013). The older population studied by Zoega et al. displayed lower cell density, higher coefficient of cell variation and a lower percentage of hexagonal cells compared with both NCL and SCL wearers of this study (Table 7-4). Previous CL wear was not reported by Zoega et al. (2013). In these older eyes, at a 7-year follow-up, endothelial cell density was

maintained, while there was a reduction of cell size variation and increase in the number of hexagonal cells. These results vary from previous reports of an annual decrease in cell density of 0.5-0.6%, and increased cell variation (polymegathism and pleomorphism) (Bourne et al., 1997; Niederer et al., 2007). Zoega et al. (2013) suggested their disparity in findings with those of Bourne et al. (1997) and Niederer et al. (2007) was due to the normal corneas examined, which maintained cell density (Zoega et al., 2013). Zoega et al. proposed that stressed or diseased corneas exhibited cell death and a loss of cell density while maintaining cell shape regularity and hexagonality, which may require less biological effort than maintaining the presence of heterogeneous cells. These studies looked at one image from the central endothelium only (central area: 0.24 to 0.4mm) (Zoega et al., 2013). The CEM-530 specular microscope used in this study had advantages over this, as the best image of 16 was analysed for each area. This may have also contributed to the differences between the results reported by these authors and those of this study.

In a similarly aged population to that of study 4, Delshad and Chun (2013) examined the influence of myopia on endothelial cell density and morphology. In Chinese eyes, decreased cell density and a reduction in the hexagonal appearance of cells was found with increased myopia (Delshad and Chun, 2013). Subjects were divided into a low myopia group (< -3.00 Ds) and moderate myopia (-3.00 to -6.00 Ds). Endothelial parameters are displayed in Table 7-4. No subject had worn contact lenses previously or had any history of ocular disease or ocular surgery. Despite the similar age and myopic range between this study and that of Delshad and Chun (2013), the Chinese eyes exhibited higher cell density and lower coefficient of variation and percentage of hexagonal cells. Furthermore, a significant difference in endothelial cell density was

found between the low and moderate myopic group, whereas no significant correlation was found between refractive error and endothelial cell density in study 4. The differences between these results and those of this study is likely to be due to the different ethnic populations studied, as normative data for the endothelium is dependent on ethnicity with variations in normative data found between Turkish, Japanese, Caucasian, Chinese, Filipino, Indian, Thai and Iranian eyes (Arıcı et al., 2014; Padilla et al., 2004; Sopapornamorn et al., 2008).

A review of the literature revealed few studies, which examined in-vivo para-central and peripheral endothelial cells. Although a relatively new instrument, the CEM-530 specular microscope has been used to study disease processes such as Fuch's endothelial dystrophy. In this condition, the central and para-central cornea showed greater damage compared with the periphery (Fujimoto et al., 2014).

Table 7-4: Normal endothelial parameters reported in the literature

Study Author (year)	**Instrument**	**Location**	**Age (yrs)**	**Myopia (n =)**	**Cell density (cell/mm^2)**	**Coefficient of variation (SD/mean)**	**Hexagonal appearance (%)**
Study 4 NCL	CEM 530 non-contact specular microscope	Central Average para-central Average peripheral	21.14 ±2.85	-0.24 ±0.58 (n = 28 eyes)	2751 ±284.16 2759.04 ±291.40 2831.65 ±328.11	25.79 ± 2 25.63 ±3.23 26.26 ±3.21	68.25 ±4.59 68.31 ±5.23 67.92 ±6.15
Study 4 SCL		Central Para-central (average 0, 90, 180, 270°) Peripheral	20.82 ±1.69	-4.17 ±1.98 (n = 33 eyes)	2822.67 ±183.68 2849.74 ±198.46 2931.21 ±175.06	26.79 ±4.39 27.33 ±4.85 28.44 ±5.54	67.13 ±4.42 67.41 ±4.32 66.07 ±5.29
Amann et al. (2003)	Non-contact specular microscopy (SP-9000, Noncon Robo, Japan)	Central Paracentral Peripheral	29.3 ±7.1, range 19 to 50	(n = 48) (n = 48) (n = 48)	2,730 ±244 2,887 ±213 2,993 ±229 (p < 0.05)	32 ±40 31 ±30 31 ±30	63 ±60 65 ±40 65 ±50
Delshad (2013)	Non-contact specular microscopy (Topcon SP3000P, Tokyo, Japan)	Central	21.22 ±1.51 21.82 ± 1.40	Low (n = 78) Moderate (n = 78)	3 063.0 ± 176.2 2961.6 ± 159.0 (p < 0.00)	33.4 ±4.0 33.9 ±3.60 (p = 0.55)	57.9 ±2.70 56.2 ±4.70 (p < 0.005)
Lee et al. (2001)	Non-contact specular microscopy (SP-9000)	(Central) < 6 years 6-10 years > 10 years	26.4 ±6.30 27.1 ±5.90 30.7 ±7.10	(n = 30) (n = 30) (n = 30)	2898.6 ±180.5 2769.7 ±197.6 2613.6 ±215.80	30 ±7 33 ±9 33 ±8	67.5 ±8.40 59.1 ±5.7 55.4 ±6.50
Leem et al. (2011)	Non-contact specular microscopy (Konan Robo 8000, Japan)	Central	28.00 ±5.56	-4.26 ±2.21 Ds (n = 60)	3368.15 ±287.07	32 ±5	64.55 ±9.02
Zoega et al. (2013)	Non-contact specular microscopy (SP-9000)	Central	range 50 to 84	(n = 282)	2495 ±29	36 ±0.60	58.4 ±0.70

Amann et al. (2003) reported that endothelial cell density increases towards the periphery, while the hexagonality and coefficient of variation is unaffected (Amann et al., 2003). These authors studied the central, para-central (2.4 -2.9mm) and peripheral (4.2 - 5.3mm) endothelium of 24 normal healthy patients (aged 29.3 ±7.1 years, range 19 to 50 years). Ten patients were previous CL wearers but no detail was reported of CL type, material, modality or when CL wear was terminated. Amann et al. found an increase of endotheial cell density between the centre and para-central cornea of 5.8%, and 9.6% between the centre and periphery. This was much higher than those found in study 4, where we found an increase between the centre and average para-central values of 0.27% in the NCL group and 0.96% in the SCL group; and an increase of 2.91% between the centre and periphery (average of inferior and superior) in the NCL group and 3.85% in the SCL group. Furthermore, coefficients of variation values reported by Amann et al. were higher than those of study 4. These differences are likely due to the different location of the of the para-central and peripheral measurements, which were more central in study 4 (paracentral: 0.6mm, peripheral: 3.7mm) and so results published by Amann et al. cannot be compared directly to those of this study.

7.4.3 The influence of SCL wear on the endothelium

It is well agreed in the literature that SCL wear can result in morphologic changes to the central corneal endothelium (Chang et al., 2001; Gong et al., 1994; Nieuwendaal et al., 1994; Setälä et al., 1998a; Sibug et al., 1991; Wiffen et al., 2000). These morphologic changes have been attributed to long-term exposure to hypoxia and hypercapnia relating to low DK/t hydrogel SCL wear. High DK/t SiHy SCLs have been found to have minimal effects on the corneal endothelium when viewed using a slit lamp biomicroscope (Covey et al., 2001; Lee et al., 2001a). Early studies conducted on the

effects of long-term (62 ±29 months) EW of soft hydrogel lenses (71% water content) established the induction of significant changes to all corneal layers (Holden et al. 1985). SCLs were worn in one eye with the second NCL eye acting as a control (Age: 29 ±8 years (range 15 – 53 years), n = 27). Following SCL cessation, subjects were monitored on days 1, 2, 7 and 33. Endothelial polymegathism increased by 22% relative to the control eye, and this did not resolve following 33 days' SCL cessation. Furthermore, the CL wearing eye experienced unstable stromal thickness. Following an initial period of oedema, there remained a constant reduction of stromal thickness, measured at 4.8%, following 33 days' SCL cessation. In study 4, there were no significant differences in any endothelial parameters or CCT measured centrally between the NCL and SCL groups. The difference between these results and those of Holden et al. is likely to be due to the lack of EW low DK/t SCL wearers in this study.

It has been reported that SCL wear results in a redistribution of endothelial cells from the centre of the corneal towards the periphery (Wiffen et al., 2000). While the results of this study are in agreement with this finding, they are not directly comparable, due to variances between contact and non-contact microscopy methods. Wiffen et al. examined cell density centrally and in the temporal periphery, in 43 long-term SCL wearers and 84 age- and sex-matched control patients using a contact specular microscope. The peripheral cell density was significantly lower for the NCL group (2646 ±394 cells/mm^2) compared with central cell density (2723 ±366 cells/mm^2, p = 0.01), while there was no difference between central (2855 ±428 cells/mm^2) and peripheral measurements for the SCL group (2844 ±494 cells/mm^2, p = 0.84). This 3% reduction in normal cell density from the central to peripheral endothelium in NCL patients suggests that SCL wear causes a redistribution of cells towards the periphery.

The results found by Wiffen et al. were found supported by those of study 4, where a decrease in cell density between the centre and periphery (average of superior and inferior) of 2.91% in the NCL group and 3.85% in the SCL group was found. The reverse relationship was, however, found for the inferior central periphery (SCL: 3109.88 ±153.64 cells/mm^2, NCL: 2935.08 ±352.78 cells/mm^2, p = 0.03). Furthermore, in agreement with the findings reported by Wiffen et al., there were no significant differences in central cell density between SCL (2751 ±284 cells/mm^2) and NCL wearers (2822 ±183 cells/mm^2, p = 0.31).

Patel et al. (2002) also reported no significant difference in central cell density between a DW SCL group and an age-matched NCL group (p = 0.41) (Patel et al., 2002). The cell densities reported by these authors were lower than those of study 4. This difference is likely to be due to the older subject population (mean age of 36.9 years, range 26 – 50 years), as the SCL wearers examined by Patel et al. wore their SCLs for much longer (mean 14.1 ±3.7 years) than the younger patients in this study. Patel et al. also found no significant differences between the groups (SCL vs. NCL) for mean cell area, skewness of cell area and percentage of hexagonal cells. However, a significantly higher coefficient of variation of cell size was found in the SCL group compared with the NCL, these results are outlined in Table 7-5.

In agreement to the findings reported by Wiffen et al. (2000), a significantly higher coefficient of variation of cell size was found in the SCL wearers compared with the NCL group at the superior periphery. Further analysis into the influence of the SCL material on the corneal endothelium revealed that the hydrogel group had a significantly higher coefficient of variation of cell size (at 180º and at the superior periphery)

compared to both the SiHy and NCL groups (Table 7-3). The hydrogel group also had significantly lower cell density and mean cell area compared with the NCL group. These morphologic endothelium changes have been attributed to hypoxia with low DK/t SCL wear (Chang et al., 2001; Gong et al., 1994; Nieuwendaal et al., 1994; Setälä et al., 1998b; Sibug et al., 1991; Wiffen et al., 2000). There were no significant differences between the SiHy and NCL groups, indicating that the lower DK/t of the hydrogel SCL material impacts upon these endothelial parameters. Covey et al. (2001) examined the effect of hyper DK/t SiHy SCL (24% water content, 175 x $^{10\text{-}9}$ cm.mlO_2/s.ml.mm Hg DK/t) on the corneal endothelium, and also found no significant difference in endothelium polymegathism between a SCL (n = 16) and NCL (n = 16) group (SCL 2.10 ±0.60, NCL 1.90 ±0.50, p = 0.321). However, the endothelium was only examined for signs of polymegathism using a slit lamp biomicroscope (with x 35 to x 40 magnification) and the CCLRU grading scale. It was also not reported whether the SCL wearers (who were fitted with new SiHy SCL and followed for a period of 9 months) had been previous CL wearers (Covey et al., 2001).

Table 7-5: Central corneal endothelial cell parameters in SCL and NCL wear

	SCL group (n = 11)	**NCL group (n = 20)**	**Sig**
Endothelial cell density (cells/mm^2)	2726 ±513	2735 ±236	0.41
Mean cell area (µm^2)	384 ±96	368 ±32	0.41
Coefficient of variation of cell area	0.37 ±0.10	0.30 ±0.04	0.01
Skewness of cell area	0.86 ±0.50	0.62 ±0.22	0.06
Hexagonal cells (%)	53.6 ±11.9	57.3 ±7.6	0.24

(Patel et al. 2002.)

Patel et al. (2002) reported a higher central mean cell area in the SCL group (384 ±96µm^2) compared with the NCL (368 ±32µm^2, p = 0.41), although results were not significant, therefore indicating similarity centrally between SCL and NCL groups. In study 4, the mean cell area in the inferior periphery was significantly higher in the NCL group (346.92) compared with the hydrogel SCL group (314.92, p = 0.03).

Reduced endothelial cell density and increased coefficient of variation of cell size are more prevalent with longer wearing times of low DK/t SCLs (Lee et al., 2001a; Setälä et al., 1998b; Stocker and Schoessler, 1985). Only one subjects included in study 4 wore SCLs over 10 years, therefore the effect of various years of previous SCL wear on endothelial parameters could not explored in this study, and ought to be examined in future studies.

7.4.4 Stability of corneal endothelium measurements following 2 weeks cessation of SCL wear

The permanency of the effects of SCL wear on the corneal endothelium has not been fully evaluated. Doughty et al. (2005) explored the reversibility of SCL induced endothelial changes by using a non-contact specular miscroscope to analyse the effects of increasing the amount of oxygen to the cornea. Previous hydrogel SCL wearers were refitted into SiHy materials. During a 6 month period, a decrease in polymegathism (30.2 to 29.1%), pleomorphism (58.3 to 60.1%) and improvement in endothelial cell density (2774 to 2821cells/mm^2) was found. While these changes were not statistically significant, they did show a significant relationship to the change in CCT- as the CCT decreased, the endothelial cell density decreased ($r = 0.747$, $p < 0.001$). Doughty et al. (2005) concluded that it must be established whether the resolution of endothelial changes, following refitting low DK/t SCL wearers with high DK/t lenses, are linked to increased oxygen, or a mechanical redistribution of corneal endothelial cells.

In study 3, the stability of CCT following 2 weeks cessation of SCL wear was evaluated. While increased CCT was found in the SCL group, following 2 weeks' SCL cessation, the differences were not statistically significant (SCL 4.19 ±10.03, NCL: 0.62 ±9.92, $p = 0.22$), regardless of previous SCL material worn. The stability of endothelial parameters was examined in the same group of subjects in study 4. Results of this study indicated relative stability of endothelial measurements following 2 weeks cessation of SCL wear. No statistically significant differences in endothelial parameters were detected between NCL and SCL or SCL material groups (all p values were > 0.05). Following on from the trend reported by Doughty et al. (2005), one would have expected that, as the CCT increased following cessation of SCL wear, the endothelial

cell density should have increased. However, the results found in study 4 indicate the opposite: centrally, the endothelial cell density increased more in the NCL group (15.32 ±79.84) compared with the SCL (-0.76 ±98.96) following 2 weeks of SCL cessation; and results were non-significant ($p = 0.61$). Future studies, over longer time periods, ought to be carried out to examine the stability of endothelial parameters, centrally and in the periphery, for a variety of SCL materials. In so doing, the hypothesis put forward by Doughty et al. (2005), linking resolution of endothelial changes with mechanical redistribution of endothelial cells following SCL cessation, could be fully investigated.

7.5 Conclusion

These results of study 4 suggest that SCL wear has an effect on peripheral corneal endothelial measurements in SCL wearers compared with NCL wearers, with the largest significant differences seen between NCL and hydrogel SCL groups. These results are in agreement with those of Amann et al. (2003) who found increased peripheral cell density in SCL wearers compared with NCL wearers. However, Amann et al. proposed that this increased peripheral cell density was due to redistribution of cells towards the periphery, whereas, in study 4, it was accounted for by the reduced cell area found in SCL wearers. The consequences of these SCL induced endothelial changes are unclear and have been reported to be benign (Liesegang, 2002). However, polymegathism has been linked to corneal hydration control (Nieuwendaal et al., 1994).

Following 2 weeks SCL cessation, there was relative stability of all endothelial measurements, regardless of which SCL material was worn prior to SCL cessation. The lack of any baseline measurements for the SCL group from before they began SCL wear limits the ability to judge whether 2 weeks SCL cessation was sufficient for endothelial

measurements to return to baseline levels. However, in most cases 2 weeks cessation of SCL wear did not affect stability of central and para-central endothelial measurements. CRS appears to have little effect on the corneal endothelium (Baldwin and Marshall, 2002), and resolution of endothelial changes induced by pre-operative SCL wear occurs following LASIK (Muñoz et al., 2011). Patients who wore SCLs pre-operatively showed between 1.5 and 5.5% resolution of endothelial changes (cell density and percentage of hexagonal cells) 12 months following LASIK (Muñoz et al., 2011). These results indicate that in order to monitor changes in the endothelium in study 4, a much longer follow-up time following SCL cessation would have been required.

SCL wear can deplete the pre-ocular tear film which nourishes the corneal epithelium and protects against infection (Kaufman and Alm, 2002). SCL wear can result in corneal epithelium damage and changes in VA and contrast sensitivity function (CSF) (Alonso-Caneiro et al., 2009;Guillon and Maïssa, 2005;Nichols and Sinnott, 2006;Ruben et al., 1976). The effect of SCL wear on the corneal epithelium and CSF will be investigated in the final study.

8 CHAPTER EIGHT. STUDY FIVE: THE EFFECT OF SOFT CONTACT LENSES ON THE CORNEAL EPITHELIUM

8.1 Introduction

SCL wear effects corneal epithelial function (reduced metabolism) and structure (oedema and reduced epithelial thickness) (Liesegang, 2002). Epithelial thickness has been reported to be reduced following long-term SCL wear, due to a loss of superficial cells and a flattening of deeper cells (González-Pérez et al., 2003; Holden et al., 1985; Sweeney, 2003). Recovery of epithelial thickness can take up to 1 month to resolve (Holden et al., 1985). This reduction in thickness was found to be inversely related to DK/t of the SCL material, and may be due to altered epithelial cell activity in chronic hypoxia (González-Pérez et al., 2003; Holden et al., 1985; Sweeney, 2003). Epithelial cells, from the peripheral cornea, must regenerate in order to heal the epithelial defect created during LASEK/PRK procedures. Epithelial healing and post-operative results are linked to the DK/t of the bandage SCL inserted (Edwards et al., 2008; Engle et al., 2005; Plotnik et al., 1991b).

Corneal epithelial thickness measurements in this study were taken using the 3D OCT (Topcon). The OCT depends on the transmission of light through the cornea. Inaccuracy can be caused by reduced corneal transparency which can occur through SCL wear, disease processes and following CRS (Van De Pol et al., 2001). There is a lack of published results on the accuracy of post-operative corneal and epithelial thickness measurements taken using the OCT. However, the literature is in agreement that the accuracy of optical instruments (including the Pentacam and Orbscan) is reduced in cases of light scatter and haze following CRS (Chakrabarti et al., 2001; Hashemi and Mehravaran, 2007; Prisant et al., 2003).

Corneal transparency or clarity is an important indicator of corneal health (O' Donnell and Wolffsohn, 2004). Transparency may be affected by CL wear and CRS. Corneal oedema, induced by low DK/t SCL wear, results in loss of corneal transparency. CSF is reduced with faster break-up of the POTF in SCL wearers (Thai et al., 2002). The reduced visual performance, with SCLs, may be due to light scatter produced by changes in hydration levels of the SCL or POTF (Lohmann and Guell, 1998). A review of the literature revealed several methods of assessing corneal transparency, however, no gold-standard method has been agreed (O' Donnell and Wolffsohn, 2004). Assessment of corneal clarity with the slit lamp is not easily determined as the technique lacks sensitivity to detect mild amounts of haze and there are no definite areas of clear cornea to compare with (O' Donnell and Wolffsohn, 2004). Furthermore, the subjective scoring method can have poor intra-observer reliability, reproducibility and sensitivity (Van De Pol et al., 2001). The Schiempflug camera has been used to provide densitometric analysis for grading lens opacity and corneal haze (Kaji et al., 2001; Kirkwood et al., 2009; Takacs et al., 2011). It quantitatively measures the intensity of light scatter in the corneal Scheimpflug images. SCL wear results in reduced POTF stability (Thai et al., 2002) and increased corneal dryness (reduced quality of the POTF and epithelial staining), which in turn, results in reduced OCT signal strength (Stein et al., 2006).

The impact of SCL wear on light scatter was explored in 2 ways:

- Firstly, by examining the influence of SCL wear on corneal transparency (using the Pentacam corneal densitometry function) and on OCT scan quality (signal strength).

- Secondly, examining the influence of light scatter on vision (VA and CSF), as increased intraocular light scatter due to corneal disease significantly affects CSF (Jinabhai et al., 2012b).

8.1.1 Aims and hypotheses

As the epithelium has a function in light scatter and may be affected by SCL wear (Corbett et al., 1996; Wang et al., 2004b), it was hypothesised that light scatter would be increased in SCL wearers compared to the NCL control group and that this may have an effect on VA and CSF. To explore this hypothesis VA and CSF was compared between a SCL and NCL group prior to, and following CRS. SCL wear can cause a reduction in epithelial thickness (González-Pérez et al., 2003; Holden et al., 1985; Sweeney, 2003). Therefore, it was hypothesised that epithelial thickness would be reduced in a group of previous full time SCL wearers when compared to a NCL control group. The effect of previous SCL material on epithelial thickness prior to, and following, CRS has not been reported in the literature. It was hypothesised that epithelial thickness would be reduced in the SCL group compared with the NCL group, and that the reduction in epithelial thickness would be dependent on the SCL material, being lower with low DK/t hydrogel lens materials compared with SiHy materials. The epithelial barrier function reduces with extended wear of SCLs (Lin et al., 2003). It was hypothesised that an alteration to epithelial function in SCL wear may have an influence on healing following LASEK/PRK procedures. To investigate this hypothesis epithelial thickness was examined in a full-time SCL wearing group and results were compared to a NCL control group following surface LASEK/PRK procedures and LASIK.

8.2 Methods

Subjects were prospectively recruited from patients who attended a Dublin based CRS clinic (The Wellington Eye Clinic). Twenty-seven SCL wearing subjects (n = 54 eyes) and 14 NCL control subjects (n = 26 eyes) met the inclusion criteria (outlined in section 3.1.1) and were enrolled over a 6 month period (February 2013 to June 2013). The effect of previous SCL wear on light scatter in the corneal was assessed by examining the impact of SCL wear on Pentacam densitometry, OCT signal strength and vision (VA and CSF). The impact of previous SCL wear on epithelial thickness prior to and following CRS and compared with the NCL control group.

8.2.1 Clinical procedure for data collection

Patients attended the CRS clinic in order to determine their suitability for CRS. Prior to this visit, they were asked to cease SCL wear for a period of 2 weeks, in accordance with normal clinic routine. Once suitability for CRS was determined, clinical measurements used for calculation of the CRS procedure were obtained for both SCL and NCL patients. This included corneal measurements using the Pentacam and 3D-OCT (Topcon, Japan) in anterior segment mode. US pachymetry was carried out pre-operatively in theatre, it was not carried out post-operatively due to the risk of corneal abrasion and possible infection (Doors et al., 2010). Post-operative visits were scheduled at day 1, day 4 (for bandage CL removal with LASEK/PRK), and 4-6 weeks following CRS. Data collected pre-operatively, at the early post-operative (LASIK: 1 day, LASEK/PRK: 6 days) and late post-operative (LASIK: 6 weeks, LASEK/PRK: 4 weeks) visits was included for analysis. VA (LogMAR) and CSF measurements were recorded at each visit except day 1 post-operatively and immediately following bandage

CL removal (LASEK/PRK patients), due to the poor and variable VA which is present at this time (Gortzak, 2010; Naroo, 2009)

8.2.2 Clinical measurements: Visual acuity

VA was recorded using a high contrast Bailey Lovie LogMAR chart. CSF was measured using the Pelli-Robson chart (Sussex Vision International Ltd, West Sussex, UK, chart dimensions: 97 x 82cm). Both VA and CSF measurements were taken in the same room. Chart luminance was measured with a Minolta luminance meter (LS-110, Minolta, Japan). The Bailey-Lovie chart luminance was 42.58 cd/m^2 and the Pelli-Robson chart luminance was 71.04 cd/m^2 - these lie within a satisfactory range as CSF shows no significant variations for luminance ranging from 7 to 514 cd/m^2 (Zhang, 1989). Ideal luminance for the Pelli-Robson chart is 85 cd/m^2 , the accepted range is 60 to 120 cd/m^2 (Mäntyjärvi and Laitinen, 2001). Patients were seated 3m from the charts and were asked to read to the lowest line (grouped in sets of three letters) they could see. In order to reduce variability which can occur due to psychophysical procedure and variation in criteria (Brown and Lovie-Kitchin, 1993), all patients were asked to make a response on letters until a standard number of letters (LogMAR: 3 out of 5, CSF 2 out of 3) were read incorrectly. This threshold value was recorded for VA and CSF (Carkeet, 2001). Measurements were taken monocularly.

8.2.2.1 Corneal transparency

Corneal transparency was examined using the densitometry function of the Scheimpflug camera in the Pentacam. The densitometry figure chosen for analysis was located at the 0-180º meridian, as calculated automatically on the Pentacam over-view screen. This meridian was chosen as some patients have narrow palpebral apertures and this may

influence oxygen transmission to the superior and inferior cornea, which may in turn affect corneal transparency in cases of SCL wear (Wang et al., 2004a). Therefore, the 0-108º meridian of the cornea ought to be exposed naturally in all patients and is not dependent on palpebral aperture height.

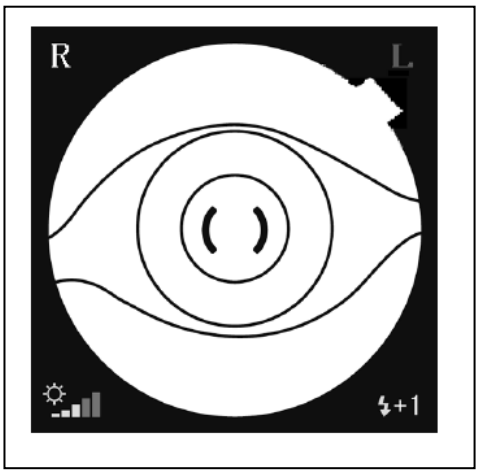
8.2.3 US pachymetry

The MMD Palmscan AP 2000 (Micromedical devices) US pachymeter was used to measure CCT. 1 drop of Proxymetacaine Hydrochloride 0.5% w/v was instilled into each eye. The probe was cleaned using a disposable alcohol wipe and allowed to air dry. The patient was instructed to look straight ahead at the letter chart. The probe was touched against the central cornea 3 times for each eye by the same observer. The average of these 3 measurements was taken as the CCT.

8.2.4 OCT pachymetry

The patient was instructed to fixate on the external target while the operator aligned the instrument with the control lever, until the tomogram of the anterior segment was displayed and aligned on the OCT (3D OCT, Topcon) live image area of the monitor (see Figure 8-1).

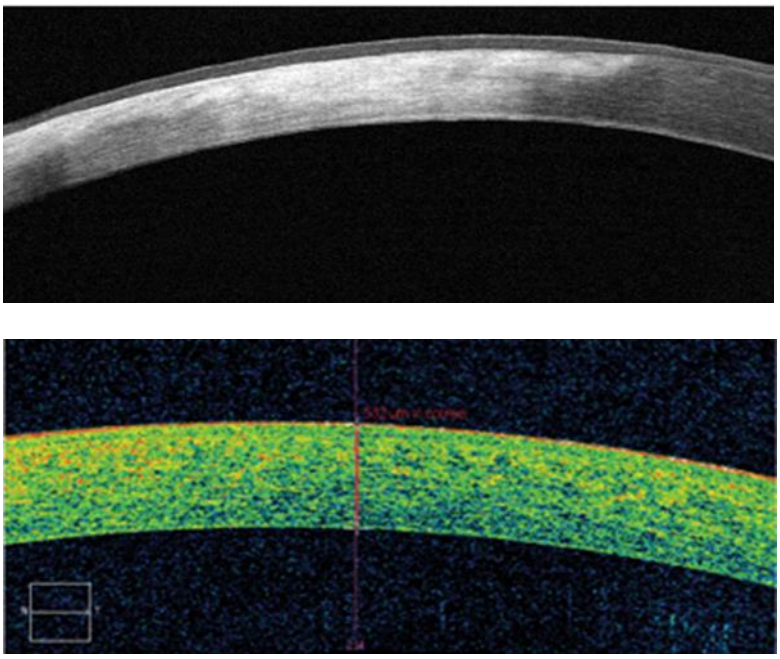
Figure 8-1: Alignment for anterior segment tomograph on 3D-OCT



(Image adapted from Topcon 3D-OCT instrument manual)

The corneal epithelium was examined using a 6.00mm radial anterior segment scan in fine analysis mode (512 x 128 image scanning). The scan chosen for analysis was also the 0-180º scan. Display volume scale of 1:4, B-scan mode of 1:2 and reference plane height settings of 120µm were used. Images were displayed in greyscale and false colour (Figure 8-2). The bright colours (white to red) correspond to areas of high optical reflectivity and dim colours (blue to black) to low reflectivity (Ustundag et al., 2000). Only scans of sufficient quality were used for analysis (as determined automatically by the instrument and indicated by a green quality indicator mark).

Figure 8-2: Anterior segment OCT displayed in greyscale and false colour (Sowka, 2010)



During scan analysis, automatic settings for detection of corneal layers were used. The instrument automatically delineated the borders between the tear film, epithelium and Bowman's membrane. The measurement calliper tool was then used to measure the epithelial thickness (from outer to inner depth) centrally, at 1mm and 2mm nasal and temporal to the central point. In an effort to limit error, the image was magnified to its maximum level for all measurements and a clear acetate sheet, with markings corresponding to where the measurements were to be taken, was placed over the screen. All epithelial measurements were taken by one observer (ALM). At the time of measurement, details of the surgery type and CL group was unknown to the observer, although in early post-operative images from the OCT, sub-conjunctival haemorrhages and the presence of bandage CL may have been visible on the OCT camera images.

8.3 Results

8.3.1 Demographics of the study population

Forty-one patients, comprised of 24 SCL wearers (48 eyes) and 14 NCL wearers (26 eyes) were enrolled. Patient demographics were similar between the groups, although the SCL group was significantly younger than the NCL group. Results are outlined in Table 8-1 .

Table 8-1: Patient demographics.

	SCL **n = 54** **n = eyes**	**NCL** **n = 26** **n = eyes**	**ANOVA** **(Chi square)** **Sig**
Right eyes	24	14	(0.75)
Left eyes	24	12	
Sex			
Male	22	10	(0.54)
Female	26	16	
Race			
Caucasian	46	26	(0.29)
Asian	2	0	
Age (mean ±SD) years	28.77 ±7.65	36.85 ±11.46	0.00
CRS procedure			
LASIK	36	21	(0.57)
LASEK/PRK	12	5	

Comparisons carried out between the groups showed the SCL group to be significantly younger compared with the NCL control group. ANOVA significant differences are shown with shaded cells, $p < 0.05$.

All patients had wavefront analysis CRS treatments, full details of SCLs worn and CRS are outlined in Table 8-2.

Table 8-2: Details of SCL wearers and CRS details

Days of SCL cessation prior to enrolment Mean ±SD (range)	**Modality n = eyes**	**Material n = eyes**	**Previous Mean ±SD (range)**
LASIK			
13.1 ±3.76 days (7 to 20 days)	SCL (n = 36) NCL (n = 21) DW 30 EW 6	Hydrogel 26 SiHy 10 (G1SiHy 2, G2SiHy 6, G3 SiHy 2)	6.64 days per week (5 to 7 days) 15.11 ±4.45 hours per day (8 to 24 hours) 8.5 ±5.51 years (2 to 30 years)
LASEK/PRK			
12.5 ±2.68 days (7 to 14 days)	SCL (n = 12) NCL (n = 5) DW 10 EW 2	Hydrogel 8 SiHy 4 (G1SiHy 2, G2SiHy 2)	6.67 days per week (5 to 7 days) 14.41 ±4.99 hours per day (8 to 24 hours) 12.5 ±3.55 years (6 to 15 years)

8.3.1.1 Post-operative visits

Following LASIK, early post-operative visits were scheduled for 1 day (all patients presented at 1 day), the late post-operative visits were scheduled at 6 weeks (SCL mean time 40.27 ±8.73 days, NCL mean time 38.56 ±15.82 days). Following LASEK/PRK, early post-operative visits were scheduled for 1 week (SCL mean time 4.50 ±1.98 days, NCL mean time 6.00 ±0 days). The late post-operative visits were scheduled at 1 month (SCL mean time 26.27 ±9.98 days, NCL mean time 44.00 ±0 days). Follow-up compliance was as follows: at the early post-operative visit, 95% (n = 55, SCL = 6, NCL = 19) of LASIK and 100% (n = 16, SCL = 12, NCL = 4) LASEK/PRK patients attended. At the late post-operative visit, 85% (n = 49, SCL = 32, NCL = 17) of LASIK and 100% (n = 16, SCL = 12, NCL = 4) of LASEK/PRK patients attended.

8.3.2 The influence of SCL wear on corneal light scatter

The influence of SCL wear on corneal transparency was assessed using the Pentacam corneal densitometry function and, on the OCT, scan quality was assessed by examining signal strength values. Measurements were taken prior to and following CRS at the early and late post-operative visits. Results of two-way ANOVA and Mann-Whitney testing showed that there were no statistically significant effects of SCL wear on corneal densitometry or OCT scan quality prior to CRS. For full results see Appendix A.5.5.1.

8.3.3 The influence of SCL wear on vision and contrast sensitivity function

The influence of SCL wear on CSF and VA was compared for the SCL and NCL groups. Two-way ANOVA testing showed there were no significant differences in CSF and BCSVA. UDVA was lower in the SCL group due to the significantly higher myopic refractive error in this group (see Table 8-3).

Table 8-3: Visual acuity and contrast sensitivity function pre-operatively for SCL and NCL groups

	SCL n = 46 mean ±SD	**NCL n = 26 mean ±SD**	**Sig**
CSF	1.54 ±0.14	1.52 ±0.16	0.64
UDVA LogMAR	1.17 ±0.15	1.00 ±0.24	0.00
BCSVA LogMAR	-0.09 ±0.04	-0.10 ±0.01	0.47
UDVA MAR	15.49 ±4.89	11.34 ±4.75	0.00
BCSVA MAR	0.82 ±0.74	0.79 ±0.01	0.12
Sphere (D)	-4.32 ±1.97	-2.42 ±1.30	0.00
Cylinder (D)	-0.74 ±0.55	-0.88 ±0.52	0.35
MSE (D)	-4.65 ±2.07	-2.83 ±1.33	0.00

Mean ±SD and two-way ANOVA results for VS and CSF pre-operatively for SCL and NCL groups. Two-way ANOVA significant differences are shown with shaded cells, ($p < 0.05$).

As there was significantly higher myopia in the SCL group, the influence of myopic group on pre-operative CSF and VA was explored between the groups (SCL vs. NCL) using a two-way ANOVA. Results showed no significant differences between the myopic and SCL groups for CSF or BCSVA pre-operatively. For full statistical results, see Appendix A.5.5.2.

8.3.3.1 The influence of SCL material on pre-operative VA and CSF

The role of the SCL material on VA and CSF prior to CRS was explored using a two-way ANOVA, in order to investigate whether DK/t had any effect. Results are expressed in Table 8-4. There was significantly better UDVA in the NCL group compared with the SiHy group prior to CRS.

Table 8-4: The influence of SCL material on pre-operative visual acuity, contrast sensitivity function and refractive error

Type of SCL material NCL (n = 26), SiHy (n = 12) Hydrogel (n = 34)		**Mean ±SD**	**Sig**	**Post hoc Scheffe Sig**
UDVA LogMAR	NCL	1.00 ±0.24	0.002	NCL and: SiHy (0.02) Hydrogel (0.01)
	SiHy	1.19 ±0.19		
	Hydrogel	1.16 ±0.13		
UDVA MAR	NCL	11.35 ±4.75	0.002	NCL and: SiHy (0.02) Hydrogel (0.01)
	SiHy	16.96 ±7.07		
	Hydrogel	14.98 ±3.86		
CSF	NCL	1.52 ±0.16	0.58	
	SiHy	1.50 ±0.13		
	Hydrogel	1.55 ±0.15		
Spherical refractive error (D)	NCL	-2.42 ±1.30	0.00	NCL and: SiHy (0.02) Hydrogel (0.00)
	SiHy	-4.09 ±2.33±		
	Hydrogel	-4.42 ±1.83		
Cylindrical refractive error (D)	NCL	-0.88 ±0.52	0.19	
	SiHy	-0.52 ±0.31		
	Hydrogel	-0.82 ±0.60		
MSE (D)	NCL	-2.83 ±1.33	0.00	NCL and: SiHy (0.06) Hydrogel (0.01)
	SiHy	-4.29 ±2.39		
	Hydrogel	-4.81 ±1.95		
BCSVA LogMAR	NCL	-0.10 ±0.01	0.11	
	SiHy	-0.10 ±0.03		
	Hydrogel	-0.08 ±0.04		
BCSVA MAR	NCL	0.79 ±0.13	0.10	
	SiHy	0.80 ±0.07		
	Hydrogel	0.82 ±0.08		

Mean ±SD and two-way ANOVA statistics on visual acuity, CSF (contrast sensitivity function) and refractive error pre-operatively for SCL material and NCL groups. Significant differences are shown with shaded cells ($p < 0.05$).

8.3.3.2 The influence of SCL on CRS outcomes

The role of SCL wear on the outcomes of LASIK (VA and CSF) was explored. Early post-operative results for LASIK are expressed in Table 8-5.

Table 8-5: The influence of SCL wear on LASIK outcomes at the early post-operative visit

SCL group **NCL (n = 15)** **SCL (n = 34)**		**Mean ±SD**	**Sig**
UDVA LogMAR	NCL SCL	-0.17 ±0.15 -0.18 ±0.09	0.83
UDVA MAR	NCL SCL	0.69 ±0.61 0.64 ±0.18	0.46
UDVA VAR	NCL SCL	93.75 ±7.91 101.12 ±5.84	0.02
CSF	NCL SCL	1.38 ±0.08 1.55 ±0.19	0.03
Spherical refractive error (D)	NCL SCL	0.03 ±0.36 0.07 ±0.35	0.78
Cylindrical refractive error (D)	NCL SCL	-0.47 ±0.21 -0.44 ±0.30	0.82
Mean spherical equivalent (D)	NCL SCL	-0.20 ±0.41 -0.15 ±0.41	0.75
BCSVA	NCL SCL	100.50 ±4.84 104.12 ±3.14	0.03
Loss of BCSVA between pre- and early postoperative visit (letters lost)	NCL SCL	4.50 ±4.87 0.00 ±3.46	0.01
UDVA measured at 1 week post-op	NCL SCL	-0.17 ±0.15 -0.18 ±0.09	0.83

Mean ±SD and two-way ANOVA statistics exploring the influence of SCL wear on VA, CSF and refractive error following LASIK in the early post-operative time period (1 week). Statistically significant results are displayed in shaded cells ($p < 0.05$).

Results indicate there were significantly higher UDVA (Snellen Acuity) and CSF in the SCL group, compared with the NCL group. While there were no significant differences between groups in LogMAR UDVA or post-operative refractive error, there was a significant difference in BCSVA with the NCL group showing a significant loss compared with the SCL.

No refraction was carried out at the early post-operative visit for the LASEK/PRK patients. UDVA and CSF measurements were taken prior to bandage SCL removal.

Results showed no significant effect of SCL wear on UDVA or CSF at the early post-operative visit (Table 8-6).

Table 8-6: The influence of SCL material on LASEK/PRK outcomes at the early post-operative visit

SCL group NCL (n = 4) SCL (n = 10)		**Mean ±SD**	**Sig**
UDVA LogMAR	NCL	0.06 ±0.06	0.27
	SCL	-0.04 ±0.11	
UDVA MAR	NCL	1.19 ±0.30	0.13
	SCL	0.95 ±0.23	
CSF	NCL	1.33 ±0.04	0.19
	SCL	1.41 ±0.08	

Mean ±SD and two-way ANOVA statistics exploring the influence of SCL wear on VA and CSF following LASEK/PRK in the early post-operative time. No statistically significant results were found (all p-values > 0.05).

The NCL group showed more myopic refractive error than the SCL at the late post-operative visit following LASIK (see Table 8-7). There was also significantly higher UDVA [MAR (LogMAR chart) and VAR (Snellen chart)] in the SCL group compared with the NCL group. No other significant differences were found between the SCL and NCL groups (all other p-values > 0.05).

Comparisons between LASEK/PRK outcomes at the late post-operative are not reported as due to the low sample size these findings lack statistical validity.

Table 8-7: The influence of SCL wear on LASIK outcomes at the late post-operative visit

SCL group **NCL (n = 15 eyes)** **SCL (n = 28eyes)**		**Mean ±SD**	**Sig**
UDVA LogMAR	NCL SCL	-0.21 ±0.16 -0.31 ±0.11	0.08
UDVA MAR	NCL SCL	0.65 ±0.24 0.52 ±0.16	0.04
UDVA VAR	NCL SCL	94.57 ±10.69 104.00 ±3.42	0.00
CSF	NCL SCL	1.49 ±0.20 1.61 ±0.12	0.10
Spherical refractive error	NCL SCL	-0.25 ±0.58 0.13 ±0.29	0.03
Cylindrical refractive error	NCL SCL	-0.39 ±0.20 -0.28 ±0.22	0.23
Mean spherical equivalent	NCL SCL	-0.45 ±0.60 -0.01 ±0.30	0.02
BSCVA VAR	NCL SCL	104.14 ±1.86 104.79 ±2.42	0.53
Loss of BCSVA between pre- and late post-op visit	NCL SCL	-0.86 ±1.95 -0.26 ±1.69	0.45

Mean ±SD and two-way ANOVA statistics exploring the influence of SCL wear on VA, CSF and refractive error following LASIK in the late post-operative time period (1 week). Statistically significant results are displayed in shaded cells ($p < 0.05$).

8.3.3.3 The influence of SCL material on visual outcomes following CRS

The role of the SCL material on VA and CSF following CRS was explored. Outcomes were analysed at the early and late post-operative visits. Early post-operative results for both LASIK and LASEK/PRK indicate there was no significant effect of SCL material for the LASIK group. Late post-operative results for LASIK indicate that there was no significant effect of SCL material on CRS outcomes. The results for LASEK procedures

are not reported as the low sample size means these results lack statistical validity. Full results can be seen in Appendix A.5.5.4

8.3.4 The influence of SCL wear on central corneal thickness

SCL wear may have different effects on the accuracy of corneal thickness measurements in these instruments (Pentacam vs. OCT) (see section 8.2). CCT was compared between the Pentacam, OCT and the US pachymeter.

Table 8-8: The influence of SCL wear on corneal thickness measured with the Ultrasound, Pentacam and OCT instruments

Pre-operative Central corneal thickness (µm)	**SCL Mean ±SD n = 52**	**NCL Mean ±SD n = 26**	**Sig**
US	562.53 ±36.16	570.10 ±27.69	0.55
Pentacam	557.72 ±29.70	568.40 ±25.50	0.31
OCT	523.88 ±42.06	526.80 ±48.67	0.85
Difference Pentacam and Ultrasound	4.81 ±14.99	1.70 ±9.18	0.20
Difference OCT and Ultrasound	38.66 ±41.32	43.30 ±44.67	0.00

Mean ±SD and two-way ANOVA statistics for pre-operative CCT. Statistically significant differences are shown in shaded cells ($p < 0.05$).

Two-way ANOVA showed that although mean corneal thickness was lower in the SCL group, there were no significant differences between the SCL and NCL control groups for any of the instruments tested. However, while the Pentacam and US showed no significant differences in CCT, the OCT measured CCT significantly lower than the US in both the SCL and NCL control groups ($p = 0.00$). This indicates a highly significant difference in CCT between the instruments for both groups (Table 8-8).

8.3.5 The influence of SCL wear on corneal epithelial thickness

Epithelial thickness data were explored using two-way ANOVA and Kruskal-Wallis analysis, to investigate the influence of previous SCL wear and the various SCL materials (hydrogel vs. SiHy). Results showed that there were no significant differences between the SCL and NCL groups (see Table 8-9), or the SCL material groups and NCL control group (Table 8-10) prior to CRS.

Table 8-9: The influence of SCL wear on pre-operative epithelial thickness

Pre-operative OCT epithelial thickness (µm)	**SCL Mean ±SD (n = 34)**	**NCL Mean ±SD (n = 12)**	**Sig ANOVA (Kruskal-Wallis)**
Temporal periphery	58.94 ±5.89	57.75 ±5.40	0.54
Temporal para-central	58.62 ±4.72	60.92 ±3.87	0.14 (0.17)
Central	58.76 ±7.09	58.67 ±5.18	0.97
Nasal para-central	59.82 ±6.24	60.33 ±5.69	0.80
Nasal periphery	59.74 ±5.92	58.67 ±6.76	0.61
Average	59.18 ±4.01	59.27 ±3.74	0.95

Mean ±SD and two-way ANOVA statistics for pre-operative epithelial thickness in the SCL and NCL groups. There were no statistically significant differences between the groups (all p values >0.05).

Table 8-10: The influence of SCL material on pre-operative epithelial thickness

Type of CL material NCL (n = 26) SiHy (n = 14) Hydrogel (n = 34)		**Mean ±SD Epithelial thickness (µm)**	**Sig**
Temporal periphery	NCL	±59.12 ±6.44	0.58
	SiHy	±58.43 ±6.05	
	Hydrogel	±57.50 ±5.60	
Temporal para-central	NCL	58.85 ±13.0	1.00
	SiHy	58.79 ±4.85	
	Hydrogel	58.85 ±5.14	
Central	NCL	60.44 ±4.97	0.36
	SiHy	58.00 ±7.61	
	Hydrogel	58.50 ±5.98	
Nasal para-central	NCL	60.28 ±5.49	0.27
	SiHy	57.86 ±4.90	
	Hydrogel	60.79 ±6.22	
Nasal periphery	NCL	58.60 ±5.46	0.53
	SiHy	59.86 ±4.88	
	Hydrogel	60.29 ±6.26	

Mean ±SD and two-way ANOVA results for central epithelial thickness between the SCL material and NCL groups, ($p < 0.05$).

8.3.5.1 The influence of SCL wear on post-operative epithelial thickness

Following LASIK, at the late post-operative visit, results of two-way ANOVA indicated that central epithelial thickness was significantly thicker in the SCL group compared with the NCL group. Whereas the epithelial thickness in the nasal periphery was significantly thinner in the SCL group compared with the NCL group (see Table 8-11). There were no other significant differences found following CRS between the groups at the either post-operative time (see Appendix A.5.5.7). Further analysis was carried out into the recovery of epithelial thickness following CRS by comparing the difference in epithelial thickness recorded at the post-operative visit with the pre-operative value measured for LASIK and LASEK/PRK procedures. Two-way ANOVA showed no significant differences in the pre-operative and post-operative epithelial thickness

measured except for the nasal periphery at the late post-operative visit for those patients who had LASIK. The NCL group were found to have significantly thicker post-operative epithelial thickness (9.78 ±11.91µm) compared with the SCL group, who showed relative stability (0.15 ±8.36µm, p = 0.01) between pre- and late post-operative visits. Full details of these findings are in Appendix A.5.5.7.

Table 8-11: The influence of SCL wear on epithelial thickness following LASIK at the late post-operative visit

SCL group NCL (n =12) SCL (n = 23)		**Mean ±SD Epithelial thickness (µm)**	**Sig**
Temporal peripheral	NCL SCL	59.00 ±6.08 59.09 ±4.81	0.96
Temporal para-central	NCL SCL	58.00 ±5.39 61.26 ±6.45	0.14
Central	NCL SCL	54.42 ±8.12 59.65 ±6.20	0.04
Nasal para-central	NCL SCL	58.25 ±5.48 60.61 ±6.90	0.31
Nasal peripheral	NCL SCL	65.83 ±9.16 59.52 ±7.01	0.03

Two-way ANOVA results indicate significant differences in epithelial thickness between SCL and NCL groups. Significant results shown in shaded cells, (p < 0.05).

8.3.5.2 The influence of SCL material on post-operative epithelial thickness

The results of two-way ANOVA indicated no significant effect of SCL material following CRS, at either the early or late post-operative visit. For results see Appendix A.5.5.8.

8.4 Discussion

SCL wear results in a loss of superficial cells and a flattening of deeper cells which manifests as a reduction in overall epithelial thickness (González-Pérez et al., 2003; Holden et al., 1985; Sweeney, 2003). However, the results of study 5 indicated no significant differences between epithelial thickness in a SCL group and NCL group. The difference between this finding and those reported in the literature is likely due to the two weeks SCL cessation time prior to epithelial thickness measurements in study 5.

8.4.1 Anterior segment OCT analysis

The OCT has a high axial resolution, thus allowing corneal layers to be clearly defined and free of stromal reflection interference (Li et al., 2006). Anterior segment OCT analysis using the Topcon 3D-OCT 1000 (Topcon, Tokyo, Japan) has been found to be highly repeatable with inter-observer ICC values of 0.99, COR of 15.22µm and coefficient of variation of cell size of 0.01% reported (Northey et al., 2012). Vidal et al. (2013) evaluated CCT (central 2mm) and para-central (2-4mm) corneal thickness in 30 eyes of 30 healthy subjects; intra-observer agreement was found to be excellent for CCT (ICC 0.99, 95% CI 0.987 to 0.997). Intra-observer repeatability was also found to be very good for CCT (ICC 0.99). Precision values of 1 - 5µm have been reported for differentiation of corneal layers (epithelium, corneal flap, and CCT) (Muscat et al., 2002; Wang et al., 2002a). However, the OCT is unable to differentiate the POTF from the epithelium, therefore epithelial thickness measurements reported in the literature and in this study include the thickness of the POTF (Wolffsohn et al., 2013). The POTF is about 3µm thick, so should have minimal effect on these measurements (King-Smith et al., 2000).

In study 5, statistical analysis showed that, while the Pentacam and US showed no significant differences in CCT, the OCT measured CCT significantly lower than the US in both the SCL and NCL control groups ($p = 0.00$). These findings corroborated with those in the literature, reporting good agreement between the Pentacam and US for corneal thickness measurements, as previously discussed in section 4.4.3. There is little agreement on the accuracy of CCT measurements using the OCT in the literature. Some studies report the AS-OCT to underestimate CCT compared with the US pachymeter (Kim et al., 2008; Leung et al., 2006; Li et al., 2007; Northey et al., 2012), while others report strong agreement (Dada et al., 2007; Kim et al., 2008; Li et al., 2007; Li et al., 2008a), and another author reports the OCT to over-estimate CCT (Leung et al., 2006). These findings must be considered as they may have an implication on the accuracy of the OCT epithelial thickness measurements. There is a lack of published studies on the agreement of epithelial thickness measurement with the OCT and other instruments. Althoug, intra-observer reliability and reproducibility for central epithelial thickness by Fourier domain OCT ($n = 210$ eyes) was reported to be good (Prakash et al., 2012). The Prakash study found ICC values of 0.87 to 0.99 using the same calliper tool software as used in this study.

Previous CRS may affect the accuracy of OCT pachymetry. The OCT (Visante, Carl Zeiss, Meditech) has been found to provide similar measurements of CCT to the US in a small group ($n = 5$) who presented between 1 and 6 months following LASIK (Avila et al., 2006). Despite the presence of post-operative complications such as keratectasia, haze, regression or flap-interface problems, the OCT showed good agreement with the US pachymeter. Mean differences in CCT between these instruments were reported as $6.4 \pm 11.7\mu m$, $p < 0.03$.

8.4.2 The influence of SCL wear on corneal transparency

No significant differences in either Pentacam densitometry or OCT signal strength measurements, were found between SCL and NCL groups prior to or following CRS in study 5. Stein et al. (2006) reported reduced OCT signal strength with corneal dryness, it is likely that any dryness related to SCL wear had resolved in the two weeks SCL cessation period prior to examination in study 5. There is disagreement in the literature as to the impact of SCL on light scatter. Lohmann and Guell (1998) reported that corneal light scatter was increased and visual performance diminished in low DK/t SCL wear (n = 35). Lohmann and Guell (1998) found CSF was superior and light scatter was less pronounced in those who wore spectacles and RGPs, and in subjects who had PRK > 1 year previously, compared with low DK/t SCL wearers. However, Patel et al. (2002) found no significant differences between corneal light back scatter (measured using confocal microscopy) in a DW SCL group and an age-matched NCL control group.

The impact of SCL wear on the outcomes of CRS was examined in study 2 and significantly better UDVA was found, following CRS, in the SCL group compared with the NCL group. However, as study 2 was retrospective in nature, it was not possible to assess the role CSF may have played in these findings. Better UDVA following CRS was also found in study 5, where the impact of CRS and SCL wear on CSF was examined. Prior to CRS, there were no significant differences in CSF between the SCL (1.54 ±0.14) and the NCL group (1.52 ±0.16, $p = 0.55$), which is in agreement with the findings of Patel et al. (2002). Furthermore, pre-operatively, there was no significant difference in LogMAR and MAR BCSVA between the SCL and NCL groups ($p > 0.05$). Analysis into the influence of SCL material on pre-operative CSF and BCSVA

also found no significant differences between any SCL material and NCL groups ($p > 0.05$). The CSF values found in study 5 were lower than reported normal values for a similar age group of Finnish eyes (mean at 3m: RE 1.81 ±0.12, LE: 1.76 ±0.14). Differences may lie between the chart luminance which in study 5 was 71.04 cd/m^2, the ideal value being 85 cd/m^2, although the accepted range is 60 to 120 cd/m^2 (Mäntyjärvi and Laitinen, 2001).

It is important to consider the difference in age between the SCL and NCL groups in study 5, as the SCL group was significantly younger than the NCL. This may have implications on the amount of light scatter within the eye, as corneal transparency can diminish with increasing age (Daxer et al., 1998). However, CSF was similar between the groups prior to CRS ($p > 0.05$). Furthermore, no correlation has been found between the amount of light scattered from the central human cornea (detected using the Scheimpflug camera) and age of the patients (Smith et al., 1998).

8.4.3 Corneal transparency following CRS

In study 5, significant differences were found between the SCL groups for UDVA, CSF and BCSVA, 1 day following LASIK. Results indicate there was significantly higher CSF in the SCL group (1.55 ±0.03) compared with the NCL group (1.38 ±0.08, $p = 0.02$). As there was no significant difference in residual refractive error between the groups, one can conclude that it was the difference in CSF which resulted in the significantly lower UDVA (Snellen) and BCSVA in the NCL group. It is interesting that there was no significant difference between MAR and LogMAR UDVA between the groups (SCL vs. NCL) (see Table 8-12). The difference in these results may be related to the differences in Snellen vs. LogMAR VA as already discussed (section

5.2.2.3). Furthermore the Snellen chart was projected while the LogMAR chart was a cardboard chart which may also have impacted on these results. The lack of significantly different findings between the SCL and NCL group for Pentacam densitometry indicates that either there was no significant difference in light scatter between the groups, or light scatter was sub-clinical and so the Pentacam was unable to detect it.

Table 8-12: The influence of SCL wear on visual acuity LASIK outcomes at the early post-operative visit

SCL group **NCL (n = 8)** **SCL (n = 17)**		**Mean ±SD**	**Sig**
UDVA LogMAR	NCL SCL	-0.17 ±0.15 -0.18 ±0.09	0.83
UDVA MAR	NCL SCL	0.69 ±0.61 0.64 ±0.18	0.46
UDVA VAR (Snellen)	NCL SCL	93.75 ±7.91 101.12 ±5.84	0.02
BCSVA VAR (Snellen)	NCL SCL	100.50 ±4.84 104.12 ±3.14	0.03

Mean ±SD and two-way ANOVA statistics exploring the influence of SCL wear on VA following LASIK at the early post-operative visit (1 week). Statistically significant results are displayed in shaded cells ($p < 0.05$).

Pentacam densitometry has been successful in objectively measuring mild corneal haze, prior to (n = 76 eyes) and following CRS (n = 91 eyes) (Takacs et al., 2011). Following PRK, haze was first determined using the slit-lamp and patients were allocated into a post-operative haze or no haze group. Results showed that the Pentacam densitometry function detected and objectively measured pre-operative (25.1 ±2.4) and post-operative mild corneal haze (with haze: 46.2 ±16.2, no haze: 29.9 ±8.7). Takacs et al. (2011) also reported a positive correlation between increasing haze and increasing age, following the PRK procedures. Takacs et al. proposed that this finding was related to the

increased presence of arcus senilis with age, the presence of arcus senilis in each patient in study 5 was not recorded so it was not possible to confirm this proposition in this study population.

The significant differences in CSF and BCSVA, found 1 day following LASIK in study 5, had resolved by the late post-operative visit (6 weeks), when CSF was similar for SCL and NCL groups. UDVA (Snellen) remained significantly lower in the NCL group (visual acuity rating (VAR) 94.57 ±10.69) compared with the SCL (VAR 104.00 ±3.42, $p = 0.00$). However, this could be attributed to the higher residual myopic refractive error in the NCL group (-0.39 ±0.20 DS) compared with the SCL group (-0.28 ±0.22, $p = 0.02$). As visual outcomes are, generally, worse due to increased ablations with increasing myopia (Kojima et al., 2008).

8.4.4 The effect of SCLs on corneal epithelium thickness prior to CRS

In Study 5, pre-operatively, the level of myopic refractive error was higher in the SCL group compared with the NCL resulting in significantly better UDVA in the NCL group compared with the SCL. There was no significant difference in CSF pre-operatively between the groups, indicating 2 weeks' cessation of SCL wear was sufficient for the resolution of previous SCL-related effects on CSF, or diminished visual quality due to increased light scatter (Liesegang, 2002).

One must consider the age of the study cohort. The SCL (28.69 ±7.57 years) group was significantly younger than the NCL group (36.85 ±11.46 years) ($p = 0.00$). While no significant difference in epithelial thickness has been found with age (Reinstein et al.,

2008), older CL wearers show reduced response of the corneal epithelium to changes in cornea curvature to orthokeratology (Jayakumar and Swarbrick, 2005). This finding may have influenced our findings of significantly better VA in the SCL group following CRS. The epithelial barrier function reduces with age (Chang and Hu, 1993). This may result in diminished ability of the epithelium to heal following trauma (Faragher et al., 1997).

Disease processes and dry eye can also impact upon epithelial thickness. Cui et al. (2014) examined epithelial thickness in symptomatic dry eye patients (n = 100) compared with normal controls (n = 35) using the OCT. Increased dry eye resulted in significantly thinner superior (p = 0.037) epithelial thickness compared with normal eyes (Table 8-13). The influence of dry eye on epithelial thickness was not explored in study 5, considering that dry eye is more prevalent with SCL wear (Nichols et al., 2002). This area ought to be examined in future studies.

Table 8-13: Epithelial thickness in dry eye patients

Epithelial thickness (µm)	**Central Mean ±SD**	**Superior Mean ±SD**	**Inferior Mean ±SD**
Normal (n = 35)	52.00 ±3.39	53.03 ±3.67	52.71 ±2.83
Dry eye (n = 100)	52.71 ±2.83	50.58 ±3.44	52.53 ±3.63

(Cui et al., 2014)

Li et al. (2012) measured epithelial thickness using the OCT in normal and keratoconic eyes (n = 145: n = 76 normal, 35 keratoconic eyes). Results showed epithelial thickness

was significantly lower in keratoconic compared with normal eyes ($p < 0.0001$) (see Table 8-15).

Table 8-14: Epithelial thickness in keratoconic patients

Epithelial thickness (µm)	**Central Mean ±SD**	**Superior Mean ±SD**	**Inferior Mean ±SD**
Normal (n = 76)	52.3 ±3.6	49.6 ±3.5	51.2 ±3.4
Keratoconic (n = 35)	51.9 ±5.3	51.2 ±4.2	49.1 ±4.3

(Li et al., 2012)

Li et al. included CL wearers in their study, although no details were given as to the type of CL and cessation times prior to enrolment. In study 5, central epithelial thickness was found to be higher than the normal values reported by Li el al. in both NCL and SCL groups (Table 8-14).

Table 8-15: Epithelial thickness in study 5

Epithelial thickness (µm)	**Central Mean ±SD**	**Average Mean ±SD**	**Sig**
SCL (n = 35)	58.76 ±7.09	59.27 ±3.74	0.97
NCL (n = 100)	58.67 ±5.18	59.18 ±4.01	0.95

While both Li et al. and this study included the thickness of the POTF in these measurements, there may be differences in the thickness of the POTF between the groups. The ethnicity of the subjects was not reported by these authors, which may have accounted for the differences. There is no known effect of ethnicity on epithelial thickness, and CCT is similar between Caucasian, Chinese, Hispanic, and Filipino eyes

(Aghaian et al., 2004). However sub-groups of Asian eyes may differ with CCT being thinner in Japanese eyes compared with Chinese or Filipino (Aghaian et al., 2004). Furthermore, epithelial permeability induced by SCL wear is significantly greater in Asian eyes compared with Caucasian (Lin et al., 2003). Asian eyes have smaller palpebral apertures and tighter eyelids (Li et al., 2013) which may impact on epithelial thickness and ought to be borne in mind when comparing epithelial thickness within the literature.

8.4.4.1 Epithelial pachymetry methods

In order to accurately compare and evaluate epithelial thickness values reported in the literature the method of epithelial pachymetry must be considered. Epithelial thickness is lower when measured using a contact method as opposed to a non-contact methods (see Table 8-16).

Table 8-16: Central epithelial thickness values reported in the literature

Author, Year	SCL details if given (n = eyes)	Central epithelial thickness Mean ±SD (µm)	Method
Study 5	SCL (n = 34) NCL (n = 12)	58.76 ±7.09 58.67 ±5.18	OCT
Hong et al. (2014)	SCL (n = 40) NCL (n = 40)	49.2 ±1.9 54.4 ±1.1	OCT
Feng and Simpson (2005)	(n = 20)	58.4 ±2.5	OCT
Wang et al. (2004)	(n = 28)	59.9 ±5.9	OCT
Wirbelauer et al. (2004)	(n = 25)	57.7 ±0.7	OCT
Haque et al. (2004)	(n = 66)	52.0 ±2.6	OCT
Li et al. (1997)	(n = 14)	50.6 ±3.9	Confocal microscope
Patel et al. (2002)	(n = 19)	49.0 ±5.5	Confocal microscope
Møller-Pederson et al. (1997)	(n = 34)	51.0 ±4.0	Confocal microscope
Reinstein et al. (1993)	(n = 20)	50.7 ±3.7	Rectilinear scanning Digital US
Reinstein et al. (2008)	(n = 110)	53.1 ±4.5	Arc scanning VHF Digital US
Pérez et al. (2003)	(n = 36)	48.0 ±5.0	Optical pachymeter

8.4.4.2 Effect of SCL wear on the epithelial thickness

SCL wear results in reduced epithelial thickness which is inversely related to the SCL oxygen transmissibility (DK/t) (Gonzalez-Perez et al., 2003; B Holden et al., 1985; Sweeney, 2003). Long-term (62 ±29 months) EW of hydrogel SCLs (71% water content) results in reduced epithelial thickness and oxygen uptake in the short term following SCL cessation (Holden et al. 1985). However, these factors appeared to have returned to the same level as the control eye on day 33. There were no significant differences between epithelial thickness in the SCL and NCL groups in study 5 prior to CRS (SCL: 59.18 ±4.01, NCL: 59.27 ±3.74µm). These findings differ from those

reported by Lei et al. (2015) and Hong et al. (2014), who found significantly reduced epithelial thickness in SCL wearers. The difference in results is likely to be due to the lack of EW hydrogel SCL wearers in the data set and also the effect of the 2 weeks cessation of SCL period which may have allowed any epithelial thinning in the SCL group to resolve. Recently, the OCT has been used to map epithelial thickness in long-term (> 2 years) SCL wearers (Lei et al., 2015). Lei et al. (2015) reported reduced epithelial thickness in a long-term SCL wearing group immediately following SCL cessation (n = 56) and following 2 weeks SCL cessation (n = 56) compared with the NCL control group (n = 94). Hong et al. (2014) also compared epithelial thickness in 40 long-term disposable hydrogel SCL wearing eyes and 40 NCL control eyes. Results showed significantly thinner epithelial thickness in at all locations in the SCL group compared with the NCL ($p < 0.05$). Both SCL and NCL wearers had lower epithelial thickness than those of study 5 (Table 8-14). The differences between the results of Hong et al. (Table 8-17) and study 5 is likely due to the SCL cessation time which was < 1 day compared with 2 weeks.

Table 8-17: Epithelial thickness in SCL wear

Epithelial thickness (µm)	**Central (2 mm) Mean ±SD**	**Para-central (2 to 5mm) Mean ±SD**	**Mid-peripheral (5-6 mm) Mean ±SD**	**Sig**
SCL (n = 40)	49.20 ±1.90	48.80 ±2.20	48.70 ±2.80	< 0.00
NCL (n = 40)	54.40 ±1.10	53.20 ±2.20	52.30 ±2.00	< 0.00

Significantly thinner epithelial thickness was found in the SCL group compared with the NCL (Hong et al., 2014).

Confocal microscopy has been used to compare epithelial thickness between DW of SCL and age-matched NCL control group (Patel et al., 2002). While there were no significant differences in central epithelial thickness between the groups (SCL 47.0

±4.0µm, NCL 49.03 ±5.5µm, p = 0.20), temporal epithelial thickness was significantly lower in the SCL group (46.3 ±4.7µm) compared with the control group (50.9 ±4.7µm) (p = 0.02). The SCL group was comprised of patients who had worn SCL for > 10 years duration. The type of SCL material and breakdown of wearing modality was not provided. Measurements were taken 12-24 hours after SCL removal. This, and the use of a confocal microscope accounts for the lower epithelial thickness, compared with that of this study. No significant differences in epithelial thickness were found between central and peripheral measurements from the same group (SCL and NCL). These results conflict with those published by Reinstein et al. (1994) who stated that peripheral epithelial thickness was reduced compared with central in SCL wearers (Reinstein et al., 1994). This difference may be as a result of the different instrumentation used in these studies (confocal microscope vs. US).

Ladage et al. (2001) examined the influence of DW SCL and RGPs on central epithelial thickness as determined by confocal microscopy. Myopic subjects were fitted with hydrogel SCL G1SiHy SCLs or RGP CLs. Measurements were taken at baseline, 2 and 4 weeks later (Ladage et al., 2001). Results showed no significant change in central epithelial thickness after 4 weeks wear in the SCL groups, however, the RGP group did show a significant decrease of 9.8% in epithelial thickness (p < 0.001) (Table 8-18). The epithelial thickness reported by Ladage et al. was thinner than those of this study due to the use of the confocal microscope.

Table 8-18: Findings of central corneal epithelial thickness

CL material	Baseline Mean ±SD (µm)	2 weeks DW Mean ±SD (mm)	4 weeks DW Mean ±SD (mm)
Hydrogel (n = 36)	48.55 ±3.20	48.07 ±3.04	47.9 ±3.20
G1SiHy (n = 135)	49.26 ±3.44	48.77 ±3.48	48.86 ±3.30
RGP (n = 75)	49.79 ±3.25	(no data reported)	44.92 ±4.30

Hydrogel SCL: Acuvue Etafilcon A, 58% water content, DK/t 32.5. G1SiHy: Purevision, Balaficon A, 35% water content, DK/t 110 (Ladage et al. 2001.)

While these findings did not show any significant differences between SCL groups, they also suggest that rigidity of the CL has a larger effect on epithelial thickness than DK/t. Ladage et al. (2001) included in the study previous CL wearers who had ceased lens wear for at least 1 month prior to enrolment. It is possible the effects of previous SCL wear on the epithelium had not resolved in the case of previous high modulus lens materials. The difference may also be accounted for by the differences between the OCT and the confocal microscope, including the ability of the confocal microscope to detect the junction between the POTF and epithelium (Chiou et al., 2006). The thinning of central epithelial thickness with RGP CL wear was proposed to be linked to a loss of surface epithelial cells, a significant decrease in epithelial basal cell growth or movement upwards, or by the compression or possible redistribution of corneal epithelial cells (Ladage et al., 2001; Swarbrick et al., 1998).

8.4.5 Corneal epithelium and SCL wear following CRS

SCL wear can result in a significant increase in the density of Langerhans cells in the central and peripheral epithelium in response to the chronic mechanical friction (Zhivov et al., 2007). The function of Langerhans cells is to control the proliferation and

differentiation of epithelial cells and epithelial immune response (Hendricks et al., 1992; Stingl et al., 1980). An increased volume of Langerhans cells with SCL wear may affect epithelial healing following CRS. Specifically, as Langerhans cells deteriorate with age (Choi and Sauder, 1987), there may be implications on epithelial healing in the NCL group who were older than the SCL group.

In study 5 the early post-operative LASEK/PRK visit included was at 1 week following CRS. It was felt that this visit would be sufficient to allow for corneal re-epithelialisation which has been reported to occur between 3 and 4 days for both LASEK and PRK (Lee et al., 2001b; Litwak et al., 2002; Pang et al., 2011). Furthermore, confocal microscopy reveals that these newly formed epithelial cells show only minor abnormalities at post-operative day 7 (Linna and Tervo, 1997).

Study 5 compared the influence of previous SCL wear on epithelial thickness following LASEK/PRK. Previous SCL wear had no significant effect on epithelial thickness at either post-operative visit. These results are in agreement with those previously published who found epithelial thickness values were similar pre- and post-PRK (Lee et al., 2001c; Møller-Pedersen et al., 2000). The results of study 5 differ from those reported by Ma et al. (2014), who found that long-term SCL wear did not affect epithelial flap formation following LASEK compared with a NCL group, but did result in epithelial oedema at 1 day and 1 week post-operatively (Ma et al., 2014). The percentage oedema was positively correlated with increasing years of SCL wear. Ma et al. included hydrogel SCL wearers who ceased SCL wear at least 1 week before enrolment (n = 219 eyes) and a NCL control group (n =370 eyes). It was not possible to compare the oedema reported by Ma et al. directly to the results of this study, as

epithelial oedema was quoted in terms of the percentage amount of haze noted in the epithelium and corneal using the slit lamp. Furthermore, all patients examined by Ma et al. were treated with MMC, which may have impacted upon the healing and results (De Benito-Llopis et al., 2009; Teus et al., 2009).

Møller-Pedersen et al. (2000) reported that the epithelium returns to pre-operative thickness levels following PRK, although the time taken for this was greater than in study 5. The confocal microscope was used to measure epithelial thickness prior to and following PRK (n = 17 eyes). Pre-operative epithelial thickness was 51 ±4µm, and post-operatively measured 45 ±10µm at 1 month, 50 ±8µm at 3 months, and 52 ±6µm at 12 months. Møller-Pedersen et al. reported a constant increase in epithelial thickness post-operatively. While this increase in epitheial thickness was also seen in the LASEK/PRK patients in study 5, there were no significant differnce found between SCL and NCL groups. The small sample size and difference between the instrumentation may account for the difference between the two sets of results.

In study 5, central epithelial thickness was significantly greater in the SCL group compared with the NCL at the late post-operative visit following LASIK, and the nasal epithelial thickness was significantly thinner in the SCL group compared with the NCL group in the periphery (Table 8-20).

Table 8-19: Epithelial thickness following LASIK at the late post-operative visit in study 5

Epithelial thickness (µm)	**Central Mean ±SD**	**Nasal Mean ±SD**	**Sig**
SCL	59.65 ±6.20	59.52 ±7.01	0.04
NCL	54.42 ±8.12	65.82 ±9.16	0.03

In general, epithelial thickness is found to be greatest in the nasal corneal of normal eyes (Hall et al., 2011; Reinstein et al., 2008), indicating the NCL group was following the normal trend. The reliability of epithelial pachymetry following CRS may also account for the higher epithelial thickness found in study 5. A comparison of pre- and post-LASIK corneal thickness found that the OCT tended to underestimate CCT pre-operatively (n = 42 eyes) (546.9 ±29.4µm) compared with the US pachymeter (553.3 ±33.0µm) (Li et al., 2006). Whereas by the third post-operative month (n = 26 eyes), the OCT tended to overestimate CCT (513.7 ±44.5µm) compared with the US (498 ±46.6µm). The pre-operative 95% LOA were -23.2µm to 10.4µm and were greater following LASIK (-1.6µm to 33µm).

Wirbelauer and Pham (2004) reported an increase in CCT in the immediate post-operative period (CCT: 555 ±47µm, flap: 211 ±28µm, residual stroma: 344 ±48µm), which resolved by 1 day post-operatively (CCT: 448 ±39µm, flap: 164 ±21µm, residual stroma: 284 ±32µm) and remained stable at 8, 35 and 160 days post-operatively. Epithelial, flap and stromal thickness were monitored post-myopic LASIK in 25 eyes using the OCT (Wirbelauer and Pham, 2004). The epithelial thickness did not show similar changes to other parameters tested. It remained similar to pre-operative levels immediately post-operatively (59 ±7.3µm) and at 1 day (55 ±6.3µm) and 8 days post-operatively (59 ±7.9µm) (p = 0.27), but showed an increase at 35 days post-operatively (61 ±8.1µm) and 160 days post-operatively (61±7.5µm). Wang et al. (2004) also found an increase in epithelial thickness in the month following LASIK. Epithelial thickness was measured using the OCT. One day following LASIK, epithelial thickness was similar to baseline measurements (59.9 ±5.9µm, p = 0.26). Following this, epithelial thickness continued to increase at week 1 (60.8 ±5.8µm, p = 0.04) to the value found at

the 1 month visit (64.6 ±6.1µm). These results were similar to those of the SCL wearers in study 5, where there was an increase in central epithelial thickness between the 1 day (NCL: 57.43 ±5.93µm, SCL: 57.93 ±6.92µm) and 6 week visit (NCL: 54.42 ±8.12µm, SCL: 59.65 ±6.2µm, p = 0.04). Wang et al. did not report the CL wearing history of these subjects, so the impact of SCL wear in these results cannot be considered.

Epithelial thickness in the nasal periphery was significantly thicker in the NCL group post-operatively (9.78 ±11.91µm) compared with pre-operative values. The SCL group showed relative stability at this location (0.15 ±8.36µm, p = 0.01). It is possible that these results may be influenced by the older age of the NCL group and also may indicate reduced accuracy of epithelial thickness measurements in the peripheral cornea. Especially considering the possibility of increased light scatter due to the inflammatory response induced by the femtosecond laser at the edge of the LASIK flap. Following LASIK, epithelial cells fill the wound cleft formed at the edge of the flap. This may have impacted peripheral epithelial thickness (Linna et al., 2000; Tervo and Moilanen, 2003; Vesaluoma et al., 2000). The epithelium and corneal flap may undergo re-thickening following LASIK (Lohmann and Guell, 1998; Spadea et al., 2000). At 1 month post-LASIK the epithelium was found to have increased in thickness by 22% using the confocal microscope (Erie et al., 2002). This increase in thickness was still evident at 12 months following surgery, while the stromal bed and flap remained unchanged (Erie et al., 2002). The NCL group in study 5 showed significantly increased nasal epithelial thickness at the late post-operative visit following LASIK, which followed the normal trend (Reinstein et al., 2008). Centrally, the NCL group had significantly lower epithelial thickness compared with the NCL group (NCL: 54.42 ±8.12µm, SCL: 59.65 ±6.2µm, p = 0.04). Mechanical friction due to previous SCL

wear, resulting in an increased density of Langerhans cells, may have impacted on the ability of the epithelium to heal following CRS (Zhivov et al., 2007).

8.5 Conclusion

No significant differences were found in corneal transparency or CSF between SCL and NCL groups prior to CRS. Post-operatively, the significantly lower CSF and reduced BCSVA found in the NCL group 1 day following LASIK, had resolved by the 6 week post-operative visit. CSF remained stable at all times for the SCL group and did not show the same fluctuations as the NCL group. It is possible that these previous SCL wearers had adapted to sub-clinical changes in light-scatter due to SCL wear and were able to compensate for these without impacting on CSF.

Results of this study showed that although CCT was lower in the SCL group, there were no significant differences between SCL group and NCL control group for any of the instruments tested. However, while the Pentacam and US showed no significant differences, the OCT measured CCT significantly lower than the US in both the SCL and NCL control groups both prior to and following CRS. This implies that the CCT measurements may not be accurate using the OCT. Consequently, the accuracy of epithelial thickness measurements may also be questionable. Unfortunately, there is no gold-standard method to measure epithelial thickness, and the clinic where this study was carried out was not equipped with another instrument capable of taking epithelial thickness measurements, so direct epithelial thickness comparisons could not be made. Ideally, a full Bland-Altman analysis should have been carried out on epithelial thickness repeatability and reliability to assess the instrument's accuracy.

In this study, no significant differences in epithelial thickness were found pre-operatively between SCL and NCL groups. Furthermore, preoperatively, the influence of SCL material did not have a significant effect on epithelial thickness. This may have

been due to resolution of any effects of SCL on epithelial thickness during the 2 weeks' SCL cessation period. However, it may also be due to the scan location (along the 180º meridian) of the epithelial thickness measurements. In order to maintain a smooth optical surface, the epithelium can alter its thickness in areas where the underlying stromal thickness has been affected through disease or injury (Reinstein et al., 2009). Reinstein et al. propose that the profile of epithelial thickness is similar to a form of "stromal surface topography" (Reinstein et al., 2010). If this is the case, analysis of a vertical slit through the 90º meridian may show irregularities in epithelial thickness due to SCL wear. As significantly steeper inferior corneal topography was evident in SCL wearers in study 1, future studies ought to examine epithelial thickness along the vertical meridian to explore whether compensation of epithelial thickness has occurred due to SCL wear.

Interestingly at the late post-operative visit following LASIK, the SCL group had significantly thicker central epithelial thickness and significantly thinner epithelial thickness in the nasal periphery. The statistical validity of these differences in epithelial thickness between the SCL and NCL groups, six weeks following LASIK, may be reduced due to the lower sample size as the attrition rate deteriorated at this visit. However, it is possible that there may be lasting effect from the mechanical friction induced by SCL wear on the epithelium, resulting in an increased density of Langerhans cells, which may have impacted on the ability of the epithelium to heal following CRS (Zhivov et al., 2007). However, in light of these findings further studies examining the impact of previous SCL wear on epithelial thickness and CRS with larger sample sizes ought to be considered.

Despite the significant differences found between the SCL and NCL groups for CSF and epithelial thickness, following 2 weeks SCL cessation for CRS, there were no negative visual outcomes that could be attributed to previous SCL wear. In fact, visual outcomes were superior in SCL wearers compared with NCL. Therefore, one can conclude that 2 weeks SCL cessation is sufficient prior to CRS in order to achieve satisfactory outcomes following CRS.

9 CHAPTER NINE: SUMMARY AND FUTURE STUDIES

The key finding from study 1 was that although keratometry and sagittal curvature showed no statistically significant differences between the groups (SCL vs. NCL), the inferior tangential curvature was significantly steeper in the SCL group. This finding is concerning, as inferior steepness is a sign of SCL-induced corneal warpage and forme fruste keratoconus. It is important to note that this finding relates to patients who were deemed suitable for, and went on to have CRS. This inferior steepness was not noted in their pre-operative screening as, at the time of screening, it was clinical practice to focus on sagittal curvature and elevation maps (which are automatically displayed on the refractive setting of the Pentcam display unit). This finding stresses the importance of using all topographical maps when evaluating a patient's suitability for CRS. For example, following two weeks of SCL cessation, there was significant flattening of the inferior tangential steepness, thus indicating a return to the normal prolate shape. This significant finding is useful when considering what ought to be adopted as "best-practice" when screening patients prior to CRS.

The importance of accurate refractive error measurements, prior to CRS, are understandably vital, thus it is common practice to ask patients to present a spectacle prescription which is 1-2 years old, in order to document refractive stability. It would also be good practice to seek baseline keratometry readings as recorded prior to SCL fitting, in case there has been corneal warpage. In so doing, the stability of corneal curvature measurements can be thoroughly examined and understood. It is important that sagittal topography continues to be screened pre-operatively for all patients, as this method gives more accurate measurements of central corneal curvature and power,

where the majority of ablation occurs for CRS. The importance of elevation, particularly posterior elevation, is well documented as this can show the first signs of FFK (Ambrósio, 2006a; Belin 2006a; Holladay, 2008a). However, the importance of careful examination of peripheral curvature using tangential topography maps has been demonstrated in this thesis. It is important that this be implemented in pre-operative screening for CRS, especially whenever contact lenses have been used for a significant number of years. This is especially important with toric SCL designs as the effect of the prism ballast may greatly impact on corneal stability. The lower DK/t of the thicker prism ballast, and possible influence of pressure due to the lower eyelids, at this inferior location results in increased corneal distortion compared to spherical SCLs (Tyagi et al., 2010).

The results of study 2 were surprising, and contradicted the hypothesis that prior SCL wear would have a negative impact on CRS outcomes. Following 2 weeks of SCL cessation, at the six month post-operative visit, the SCL wearers had statistically significantly better outcomes in terms of visual efficacy compared to the NCL control group. Patients who ceased SCL wear 24 hours prior to LASEK/PRK also had significantly better visual efficacy compared with the NCL group. While those patients who ceased SCL wear 24 hours prior to LASIK also experienced, on average, better UDVA compared to the NCL group, but the results were not statistically significant. The visual efficacy in the 2 weeks' SCL cessation group and 24 hours' SCL cessation group, prior to LASEK/PRK, were superior in terms of statistical significance. However, we can't conclude they are clinically significant due to the small number of letters difference between the groups.

In study 3, stability of all refractive and corneal measurements analysed, occured 2 days following SCL cessation. Peripheral tangential topography, took the longest time to stabilise, confirming the findings of study 1 in relation to tangential topography.
The effect that SCLs have on the endothelium was examined in study 4 using the Nidek CEM 530 spectral microscope which has the capability of examining the para-central and peripheral endothelium. Results indicated that centrally there was no significant difference between the SCL and NCL groups. However, compared with the NCL group, the SCL group showed significant differences in the periphery for endothelial cell density, coefficient of variation of cell size and mean cell area. The most significant differences were found between the NCL and Hydrogel groups, indicating these differences were linked to hypoxic factors.

In study 5, the impact of previous SCL wear on vision and CSF, prior to and following CRS, was explored. Pre-operatively no significant effect of SCL wear was found, however post-operatively, following both LASIK and LASEK/PRK, superior visual outcomes in terms of UDVA were found in the SCL group compared to the NCL group. Interestingly, at the 1 day post-op visit, CSF for the LASIK patients was similar to pre-operative levels, but had dropped in the NCL group. This finding may explain the better visual efficacy outcomes in the SCL group compared to the NCL group, who had significantly reduced CSF which would have impacted on VA. Pre-operatively, following two weeks' cessation of SCL wear, there was no significant differences in epithelial thickness between the SCL and NCL groups.

It is important to place these findings into context, with regards to the current literature and clinical practice relating to SCL wear and CRS. It is well agreed in the literature

that SCL wear impacts on all corneal layers, resulting in changes to corneal shape and thickness. This is particularly evident with hypoxia, often related to over-wear of low DK/t SCLs (Bergmanson and Chu, 1982; Doughty et al., 2005; González-Méijome et al., 2003a; González-Pérez et al., 2003; Holden et al., 1985; Kallinikos and Efron, 2004). The study population analysed in this work was comprised of normal, myopic patients, the majority of whom wore SCLs following a daily wear modality. They had been previously deemed suitable for CRS and so did not demonstrate significant signs of hypoxia or corneal warpage. This, in addition to modern SCL prescribing techniques (the lack of hydrogel SCLs for extended wear and use of SiHy for daily wear) indicates that these corneas were healthy and not compromised by SCL wear. It is concerning that even with these normal myopic eyes, significant alterations to the cornea was evident with SCL wear- including the significant inferior steepening evident on tangential topography maps (study 1), the significant variations in peripheral endothelial cell density, coefficient of variation of cell size and mean cell area (study 4).

In light of these findings it is essential that we consider recent studies by Moezzi et al (2014) and Lira et al (2015) who investigate the impact of various myopic and hyperopic prescriptions on manufacturers' published DK/t figures. Both sets of authors agree that even the highest DK/t SiH lenses, when used for EW, fail to meet the oxygen transmissibility criteria in moderate and high hyperopia as published by either Holden and Mertz (1985), Harvitt and Bonanno (1999) or by Fonn & Bruce (2004). More worryingly still, hydrogel lenses (> +3.00D) do not, even, achieve the oxygen transmissibility criteria required for daily wear. In light of these reports, it is likely that problems with hypoxia are still evident in hyperopic patients and these must be thoroughly screened and stability must be documented carefully prior to CRS. This is

especially important in these hyperopic patients, where the central cornea is made steeper during hyperopic ablation during LASIK CRS. Therefore, there is a much greater risk of inducing ectasia if FFK is mis-diagnosed as SCL-induced corneal warpage.

It was the aim of this work to investigate the impact of prior SCL wear on the outcomes of CRS. Results of study 2 and study 5 indicated that there was no negative impact of previous SCL wear on CRS outcomes and that the SCL wearers achieved better CRS outcomes, in terms of visual efficacy, compared to the NCL control group. In study 5, it was found that following 2 weeks' cessation of SCL wear, there were no significant differences in CSF between the SCL and NCL groups. Surprisingly, following LASIK at the early post-operative visit, CSF was maintained in the SCL group but was significantly reduced in the NCL group. This finding may account for the superior visual outcomes in the SCL wearers. These patients may have adapted to the diminished image quality which occurs due to light scatter, corneal surface alterations and reduced CSF following hypoxia and oedema with overwear of low DK/t SCLs. It is also likely that as this SCL wearing population did not include any toric SCL wearers, they may have adapted to small amounts of cylindrical refractive error which was not corrected in their SCLs.

As with any research project, the presented work suffers from some limitations that could be addressed in future studies. These findings indicate that the SCL modulus in SiHy SCL wear may have a significant effect on corneal stability and epithelial thickness. Unfortunately, the sample size in the G1SiHy group was insufficient to ensure statistical power. Research ought to be carried out on the impact of a variety of

SCL materials on corneal stability and on CRS outcomes. Furthermore, it has been reported that the time taken for resolution of corneal changes induced by SCL wear can be greater in older patients (Nourouzi et al. 2006). This perhaps is an indication that the resolution of corneal changes can slow with age, or that these patients may have worn SCLs for longer time periods. In G1SiHy wear, EW or in older patients who have worn SCLs over a long number of years further studies ought to be carried out to determine more appropriate SCL cessation times prior to CRS. Consideration should also be given to hyperopic and toric SCL corrections. Toric SCLs are reported to result in significantly increased corneal curvature changes compared with spherical SCLs, therefore longer SCL cessation times have been advised prior to CRS for toric SCLs (Shahinian, 2002).

The physical fit of previous SCLs worn ought to be considered in future studies. It is well understood that fitting flat or reverse geometry RGP lenses in orthokeratology results in corneal flattening which helps to control myopia progression (Cho et al., 2005). The changes in corneal parameters following cessation of CL wear (RGP) have been reported to be dependent on the previous CL fit (Jinabhai et al., 2012a). Changes to epithelial thickness can be affected by the SCL edge position and design (Wolffsohn et al., 2013). SCL replacement should also be considered and the effect of daily disposable SCLs ought to be compared against planned frequent replacement lenses, where multipurpose cleaning solutions are used. Gorbet et al. (2013) reported increased epithelial cell shedding with some SiHy SCL materials and SCL cleaning solutions combinations (Gorbet et al., 2013).

Consideration must be given to the accuracy of specular microscopy in the para-central and peripheral endothelium. As discussed in study 4, magnification differences appear with various corneal thickness' prior to CRS, and with the reduction in corneal thickness and corneal power following CRS (Isager et al., 1999). This reduction in magnification gives the impression of increased cell density. Using the correction values proposed by Isager et al., we found no significant differences between SCL and NCL groups prior to or following 2 weeks SCL cessation in this study. However, this magnification factor uses the CCT value and in study 4, para-central and peripheral endothelial cell density was found to be significantly different between the SCL and NCL groups. The effect of corneal thickness at these locations ought to be measured and the appropriate correction factor determined in order to assess whether thicker peripheral corneal thickness affects the accuracy of these endothelial measurements. Further studies, over longer time periods to examine the stability of endothelial parameters centrally, para-centrally and in the periphery for a variety of SCL materials, are required to fully investigate Doughty et al.'s (2005) hypothesis, linking resolution of endothelial changes with mechanical redistribution of endothelial cells following SCL cessation.

It was not possible to analyse the reliability of OCT epithelial thickness as part of this research. A study of this nature ought to be carried out, in order to investigate the influence of SCL wear on the accuracy of repeated epithelial thickness measurements prior to and following CRS. No significant differences were found in epithelial thickness between the SCL and NCL groups, thus it is possible that any differences that had been present may have resolved in the 2 weeks' cessation of SCL wear prior to enrolment in the study. Further studies would be beneficial to examine light scatter,

densitometry and CSF measurements immediately following SCL removal and repeated until stability can be demonstrated. Furthermore, the direction of the OCT scanning slit ought to be considered in future. Changes to epithelial thickness may be one of the first indicators of FFK, therefore analysis of a vertical slit, through the 90º meridian, may show more irregularities in epithelial thickness due to SCL wear (Reinstein et al., 2009).

Significantly increased epithelial thickness was found in the NCL group following LASIK. A similar increase was not seen in the SCL group. Mechanical friction due to previous SCL wear may have resulted in an increased density of Langerhans cells which impacted on the ability of the epithelium to heal following CRS (Zhivov et al., 2007). As significantly thinner average and central epithelial thickness were found post-operatively in the G1SiHy group, this theory was supported. Future studies using a larger sample of G1SiHy wearers ought to be carried out to investigate this hypothesis.

The full effects of SCL wear on the cornea cannot be understood, until further investigations into the influence of hyperopic, toric and stiff modulus SiHy SCLs on stability following SCL cessation are carried out. In order to ensure patient safety and achieve desirable CRS outcomes, it is recommended that a longer SCL cessation period of 2 weeks, as recommended by the FDA, ought to be applied to all previous SCL wearers prior to CRS.

Appendix A

A.1 Suitability criteria for corneal refractive surgery procedures

Table A-1: Suitability criteria for CRS procedures (FDA, 2014).

Age: 21 or older
Best corrected vision in both eyes of 6/9 or better
Stable refraction (documented evidence of a change of less than 0.50D in the year prior to consultation)
Not pregnant or lactating Able to tolerate local anaesthetic
Able to lie flat without difficulty
Able to fixate steadily and accurately for the duration of the Laser procedure
Able to give informed consent
No tear film abnormalities, significant dry eye which was unresponsive to treatment
No corneal dystrophies, keratoconus, or evidence of corneal distortion from CL wear or forme fruste keratoconus.
No lenticular opacities
No systemic diseases such as uncontrolled diabetes, collagen vascular diseases, auto-immune or immunodeficiency diseases
No history of *Herpes simplex* or *Herpes zoster keratitis*
Not taking the following medications: Isotretinoin (Accutane ®, Hoffmann-La Roche Inc.), Amiodarone hydrochloride (Cordarone ®, Sanofi-Synthelabo, Inc)

A.2 Patient consent forms

EYE LASER IRELAND, DUNDRUM EYE CLINIC

EXCIMER LASER CONSENT FORM

<u>LASIK</u>

I _____ of_____

_____

_____hereby consent to undergo

Excimer Laser Surgery the nature and effect of which has been explained to me by

Dr/Mr/Prof. _____

In addition, I consent that I have read all the educational literature presented to me and that I understand that the Laser's long term effectiveness is unpredictable.

Date: _____ Signature: _____

I confirm that I have explained the nature and effect of the operation/ treatment to the person who signed the above form of consent in my presence.

Date: _____ Signature: _____

Consultant Ophthalmic Surgeon.

EXCIMER LASER PHOTOREFRACTIVE KERATECTOMY (PRK / LASEK)

CONSENT FORM

I_____ of_____

_____ Hereby consent to undergo Excimer Laser Surgery the nature and effect of which has been explained to me by Mr /Prof _____

In addition, I consent that I have read all the educational literature presented to me and that I understand that the Laser's long term effectiveness is unpredictable.

Date: _____ Signature:_____

I confirm that I have explained the nature and effect of the operation / treatment to the person who signed the above form of consent in my presence.

Date: _____ Signature:_____

Consultant Ophthalmic Surgeon

This copy is for information only.
Please read but do not complete, as this will be carried out on the day of treatment.

ultralase

MEDICAL CONSENT FOR PERFORMING LASER EYE TREATMENT FOR SHORT-SIGHT, LONG-SIGHT AND/OR ASTIGMATISM

This form contains important information about all Ultralase laser eye procedures and their associated risks. PLEASE READ IT CAREFULLY.

This form is provided in addition to the information you have already received prior to your treatment day. This includes the information pack, the patient information form completed at your consultation and our 'Correcting Sight' booklet. This has been designed so that you can make a decision whether or not to give informed consent to allow laser eye treatment to be performed on your eye(s). Consenting to your treatment is therefore a process which involves reading and understanding this form, all the documents mentioned in this paragraph and the information provided to you throughout your patient journey, including your appointment(s).

This consent form is used for all laser eye treatments; however, where the information is specific to any one particular treatment we have indicated accordingly.

Your laser eye treatment will be performed in an attempt to correct or reduce your short sight *(myopia)*, long sight *(hyperopia)* and/or astigmatism. One alternative to Ultralase laser eye treatment is to wear corrective lenses, such as glasses or contact lenses. Other alternatives are intra-ocular lenses (IOLs) and other refractive surgery techniques.

Should you have any questions regarding laser eye treatment or its alternatives, your Ultralase ophthalmologist (medical eye specialist) will be pleased to answer them, and you can arrange to see your surgeon in advance of your treatment day if you wish. Your surgeon may also ask to see you in advance to discuss aspects of your treatment.

The purpose of this form is to document the information provided to you, before you decide whether or not to proceed with laser eye treatment. It also documents your decision whether to proceed with the treatment in the light of the information provided. It has been compiled with reference to the current Royal College of Ophthalmologists guidelines (2009). **Only sign the form if you are completely happy to proceed with laser eye treatment. You have the right to change your mind at any time, including after you have signed this form.**

Do not sign this form until you speak to your ophthalmologist on the day of treatment.

The notes below set out the risks and potential side-effects of laser eye treatment. Your laser eye treatment will always be carried out with all due skill and care.

INFORMATION

1. This is an elective surgical procedure, and there is no medical reason that requires the patient to proceed with treatment.

2. Patients may experience discomfort (or even pain in rare cases) and poor vision for the first few days after treatment, particularly following LASEK-based procedures. Around 80% of our patients describe their Intralase procedure as causing either no or mild discomfort only. Less than 1% of patients describe their Intralase procedure as very painful. Some discomfort, light sensitivity or (rarely) pain may occur, particularly in the early postoperative period. The final outcome of any laser eye treatment is very dependent on the individual healing process of each patient and this may result in an under- or over-response leading to a residual amount of short-sight or long-sight and/or astigmatism. If this occurs, further treatment may remove the residual prescription although **there remains a risk that, to remove blurring, corrective appliances (e.g. glasses or contact lenses) may need to be worn for near and/or middle and/or distance vision.** Although final visual outcome can be suggested from studies of treated patients (and therefore the visual results can be considered reasonably predictable), **the final amount of correction cannot be guaranteed due to variations in healing responses by each individual.** For severe degrees of short-sight, long-sight and/or astigmatism, the primary aim of laser eye treatment is to reduce the patient's dependency on glasses or contact lenses.

3. There may be short-term and long-term side effects of the laser eye procedure, and whilst short-term side effects tend to cause no long-term visual problems, long-term problems include (but are not limited to): mild scarring or haziness of the cornea; glare; haloes or 'starburst' effects around bright lights; light sensitivity; dry eyes; and discomfort, which may not be correctable with glasses or contact lenses. Such effects are occasionally possible, even with wavefront-guided treatment. Some of these effects and those listed in paragraph 13 may produce a permanent reduction in the patient's best corrected vision (with glasses or contact lenses), but these complications are rare and usually only associated with higher levels of short-sight, long-sight and/or astigmatism. **The patient may experience several months of increased dryness of the eyes after treatment**, and the patient may require frequent lubricant eye drops to alleviate the condition. **This dryness could persist into the long term.** You are more likely to experience dryness symptoms if you experienced dry eyes in advance of treatment.

4. As referred to in paragraph 2, **it is possible that the patient's desired result from this procedure may not be obtained and the patient may still require glasses, contact lenses or (at the Ultralase surgeon's discretion) undergo further laser treatment in order to obtain the best vision possible.** This further treatment would be offered free of charge. **In a very small percentage of patients, further treatment of the lasered eye may not be medically advisable, for example if there is marked haze or scarring, or insufficient remaining corneal thickness, and retreatment is not possible in such patients.**

5. As with all forms of eye surgery, there is a risk of infection. Serious infection is very rare, but if it occurs it could lead to severely impaired vision in the infected eye(s) or could be potentially sight-threatening. The current rate of serious infection among treated patients is 1 in 10,000.

6. If you are between the ages of 18 and 21 you should note that the clinical work to ensure efficacy of the Technolas laser were carried out only on individuals over the age of 21 years. It is especially important in this age group that your prescription is relatively stable prior to treatment, and that you understand that there may be further changes in your prescription.

7. (This paragraph refers ONLY to LASIK-based procedures.) *Your surgeon will use a device known as an Intralase® laser to create a flap in the cornea prior to using an excimer laser to reshape the eye in order to correct your prescription. There is a risk that the visual outcome after surgery could be affected by side effects relating to the formation of the flap and subsequent healing response of the corneal tissue. These include (but are not limited to): inflammation of the cornea (either in the immediate, medium or (rarely) longer term); wrinkling, displacement or distortion of the flap; incomplete formation of the flap; ingrowth of epithelial cells; epithelial abrasions (patients with a history of epithelial erosion or clinical dry eye are at greater risk of abrasion) and inability to complete the treatment due to creation of an imperfect flap. Side effects will be managed, and the visual effects are generally short-term, although they can persist (rarely) into the long term. Whilst these complications are still possible with the Intralase® laser, most risks are reduced compared to a mechanical device to create the flap.*

8. It may be necessary for the surgeon to convert a treatment from that originally selected to one of the other Ultralase laser eye treatments - i.e from Ultra Plus to Ultra or from a LASIK-based procedure to a LASEK-based one. ***(In certain cases, it may be necessary to perform a wavefront-guided treatment without the use of the iris recognition system.)***

9. On very rare occasions, due to the failure of any one part of the equipment to pass its specific safety checks prior to treatment, the treatment may be postponed at very short notice. This decision will always be taken in the patient's best interests, and may result in a delay in carrying out the treatment.

10. On very rare occasions, due to circumstances that are not foreseeable before the treatment has commenced, the treatment may be abandoned before it is completed. The decision to abandon will always be taken by the surgeon in the patient's best interests, and the patient will be entitled, at their discretion, to a refund or to re-scheduled surgery. Should the treatment be abandoned in mid-process, it may be several months before the eye can be treated again.

11. Very rarely, the patient's vision could be made worse by laser eye treatment, for the reasons given in paragraphs 3, 4, 5 and 13. This is because although certain risks and side effects will resolve with time or with further treatment, some may not do so and there is a risk, therefore, of permanent damage to sight of unknown severity or type.

12. As they reach their mid-40s, most normally-sighted individuals start to require reading and/or intermediate glasses, and those with long-sight are likely already to have them. Some short-sighted people can read well at this age without reading glasses. **Whatever their pre-treatment prescription, if the patient has their distance vision corrected by laser eye treatment, they will require reading and/or intermediate glasses as they enter their mid-40s, which they may not otherwise have needed for some time. It is therefore likely that a reading prescription will be needed immediately after treatment, even if it was not required beforehand. The patient's intermediate vision may also be affected, which may result in their needing a specific prescription for middle distances, e.g. computer work.**

13. Further possible side effects from laser eye treatment have been reported, although rarely, after either one or both eyes have been treated: differences in spectacle requirement between both eyes, making comfortable spectacle correction for both eyes difficult *(anisometropia)*; difference in image size between the two eyes *(anisekonia)*; double vision *(diplopia)*; fluctuating vision and decreased visual acuity; possible inability to wear contact lenses; a progressive thinning of the cornea *(ectasia)*; or incomplete treatment due to laser malfunction. However, it is impossible to state every possible complication that may occur following surgery and therefore those complications stated in this consent form do not represent an exhaustive list.

14. To obtain the best result, the patient must comply with the use of prescribed medicine and handwashing as described in our literature and must attend follow-up appointments as advised by the clinical staff.

15. If the patient chooses to have simultaneous bilateral treatment (both eyes treated on the same occasion), some of the consequences listed above could occur in both eyes and therefore there is a theoretical additional risk involved. The current Royal College of Ophthalmologists' standards (2009) on refractive surgery highlight the

potential additional risks of bilateral treatment over having the two eyes treated on separate occasions. However, bilateral treatment is widely practised, both in the UK and worldwide and most patients choose bilateral treatment. This is due to the inconvenience and problems arising from severe imbalance that patients can suffer when waiting to have the second eye treated. **Any patient may choose to have one eye treated at a time if they so wish.**

16. After the age of 60, cataracts become more common. Cataracts describe the condition where the lens inside the eye becomes cloudy and this can affect your vision. Although they typically appear after the age of 60, they can appear sooner or later depending on individual variations. An operation to remove cataracts is typically carried out in one's late 60s or early 70s, although again there are individual variations. Laser eye treatment is not known to cause cataracts, increase existing cataracts or predispose individuals to cataracts, but if cataracts appear or worsen either immediately, or some time after, your procedure, they may affect your vision. You should understand these implications before deciding to go ahead with laser eye treatment. Where cataracts do occur, having had laser eye treatment would not usually affect your ability to have the cataracts removed.

17. Retinal detachment and the appearance of floaters (vitreous opacities) are conditions which occur more frequently in short-sighted individuals than in long-sighted or normal sighted individuals. This increased predisposition carries on throughout a short-sighted person's life and these conditions can develop at any time, regardless of whether the person undergoes laser vision correction or not. It is important that everyone who undergoes successful laser vision correction should continue to have regular check ups with their optician.

18. Whilst Ultralase may from time to time offer promotional incentives for specific treatment dates, this should not be taken into account in your decision whether to proceed with treatment.

19. 'SupraCor' treatments only – SupraCor treatments are designed for people who have presbyopia (normally those over 45) to improve reading vision at the same time as distance correction is performed, by carefully modifying the laser treatment given. Immediately after SupraCor treatment, patients are often temporarily short-sighted, and some notice a reduction in their distance vision, which may mean that they require glasses for driving or other activities during this period. This effect normally lasts 1-2 weeks, but can be longer in rare cases. Successful SupraCor treatment depends on the ability of the eyes and brain to adapt to this effect, and the change in the way the eyes work together, and we will carefully assess this ability during your suitability assessment. Clinical studies have shown that 90% of patients are satisfied with the results of their treatment. At the discretion of your surgeon, SupraCor treatments can normally be reversed if necessary.

Please note that, although the complications described above are rare, if they do occur you are likely to need additional appointments, and your recovery time after treatment until the final result is achieved may be longer than anticipated.

MONOVISION

Please read this section if you are having a monovision correction.

Laser vision-correcting surgery can precisely and accurately correct **fixed** prescriptions of the eye such as short-sightedness, long-sightedness and astigmatism. These optical conditions are fundamentally different from **presbyopia**, the loss of adjustability of focus for near tasks such as reading. Presbyopia is the reason that reading glasses become necessary, typically in the mid-40s, even for people who have excellent unaided distance vision. For those who require glasses or contact lenses to see clearly at distance, bifocals or separate reading glasses become necessary at that age to see clearly at close range.

There are several options available to those who are presbyopic, besides wearing bifocals or separate distance and reading glasses. For some individuals, wearing a contact lens in one eye for distance vision, and a contact in the other eye for reading, affords a reasonable solution. This is called **monovision**.

The same option can be created on a more permanent basis with laser vision-correcting surgery. If you are contemplating such correction for yourself, it is important to understand the advantages and drawbacks. **This is particularly important to consider if your profession or hobbies require precise near vision.**

Reduced depth perception: For most people, depth perception is best when viewing with both eyes optimally corrected for distance. Eye care professionals refer to this as binocular vision. Monovision can impair depth perception to some extent, because the eyes are not focused together at the same distance. Because monovision can reduce optimum depth perception, it is typically recommended that this option be demonstrated prior to surgical correction. Even after this demonstration, it is possible that you may not adapt to monovision after treatment. This may in turn affect your distance, reading or intermediate vision (including computer use), causing difficulties for visual tasks. In some rare cases the effect may be debilitating, and require further treatment or optical corrections such as glasses or contact lenses.

Ocular dominance,and choosing the 'distance' eye: Ocular dominance is similar to right- or left-handedness. For most individuals, one eye is the dominant or preferred eye for viewing. Several tests can be performed to determine which eye, right or left, is dominant in a particular person. Conventional monovision refers to the dominant eye being corrected for distance, and the non-dominant eye corrected for near. While this is a good guideline, it is not an absolute rule. A small percentage of people are co-dominant (similar to being ambidextrous), and sometimes a person may actually prefer using the dominant eye for near viewing. The methods for testing and determining ocular dominance are not always 100% accurate; there is some subjective component in the measurement process; and different clinicians may use slightly different methods of testing. It is possible that monovision may lead to visual discomfort due to the variability of response to the situation that cannot always be predicted in advance.

I have read the above and desire **MONOVISION** surgical correction.

Distance eye..... Near eye ..... Patient's signature ..... Date .....

Surgeon's signature ..... Date .....

OTHER MATTERS DISCUSSED

Surgeon's signature ..... Patient's signature ..... Date .....

PATIENT'S STATEMENT

Before signing this form, I will advise my ophthalmologist if I have a history of anxiety or depression and whether I am currently on, or have ever taken, any medication for these conditions.

Initial .....

My decision to undergo this procedure has been taken on my own and has been made without duress of any kind. I have been given full opportunity to discuss the operation, and I have had opportunity to ask questions relating to this treatment.

Initial .....

Data Protection

The data recorded on your medical file will be processed by Ultralase or such third parties as Ultralase deems appropriate. Such third parties will be placed under a contractual obligation only to process your data in accordance with our written instructions. Your data will be used for diagnosis, treatment and administration purposes. In addition, it may also be used for the purpose of clinical audit or research. Your details will be treated as confidential at all times. You have a right to access your personal record by writing to Ultralase Head Office, 3 The Embankment, Sovereign Street, Leeds LS1 4BJ, enclosing a cheque or postal order for £10.00 made payable to Ultralase Limited.

In signing below, I give my agreement to proceed with laser eye treatment and confirm I have received this consent form in advance of treatment day and with sufficient time to understand its contents.

Patient's Name .....

Date of Birth..... Postcode .....

Patient's Signature..... Date .....

SURGEON'S STATEMENT

I confirm that I have given the patient the opportunity to discuss the treatment and the information on this form and have answered any questions they have raised.

Surgeon's Name.....

Surgeon's Signature..... Date .....

Wellington Eye Clinic
Established 1980

Jan 2013

CONSENT TO LASIK SURGERY

Read through and initial each paragraph, making sure that you understand the content:

1. **READING GLASSES (after age 42 yrs.):** I understand that if both eyes are corrected to **zero** (= the perfect refraction for distance vision), then I will need reading glasses from around the age of 42 to 45 years. If I am older than this, I will need reading glasses for all close work with immediate effect. If I am younger than this, I will not need reading glasses immediately, but I will need them when I approach the age of 42 to 45 years.

Signed: _____

Monovision: if I decide to have monovision performed, I expect the following effects:
Zero / -1.00: reading glasses postponed to around 50 years of age
Zero / -2.00: reading glasses postponed indefinitely
I expect that distance and near vision is going to be compromised by this choice but that the overall vision is satisfactory for approximately 80% of people.
I know that there is increased glare as a result of monovision and that I may need to wear glasses for driving at night to reduce this glare.
I may have to wear reading glasses when reading for prolonged periods.

Signed: _____

In light of the above, I am opting for:
1. Zero / Zero
2. Zero / -1.00
3. Zero / -2.00
4. Isovison

Signed: _____

2. **ENHANCEMENT / RETREATMENT:** I understand that the procedure is not 100% predictable and that my healing response is going to influence the final result. Because of this, there is a chance that I may need an additional procedure at a later stage to enhance or adjust the outcome. This is usually less than 10% for myopia and around 20% for hyperopia. Rarely, a 3rd procedure may be necessary to achieve the required result, especially with hyperopia

Due to the nature of Lasik enhancement (i.e. lifting the original flap) during the healing process there is a possibility of epithelial cells migrating under the flap edge. If this happens it may require more frequent visits post-op to observe these cells die out naturally. Infrequently the flap may need to be lifted to remove the cells, or may require Yag laser treatment directly to the invading cells.

If your vision falls below driving standard, there will be no charge for laser enhancement.

Signed: _____

Ophthalmologists: Mr. Arthur Cummings, M.B. Ch.B, MMed(Ophth), (Pret), F.C.S.(SA), F.R.C.S.Ed,
Mr. Richard Corkin, MBChB (Cape Town) FCS (Ophth) SA, MRCOphth,
Dr. Paul Kenna, M.B.,D.O, F.R.C.S.I.
Optometrists: Ms. Ann-Marie Masterson, Ms. Avril Barnes, Ms Clare Maguire

Level 2, Suite 36, Beacon Hall, Beacon Court, Sandyford, Dublin 18.
Tel: +353 1 293 0470 Fax: +353 1 293 5978 e-mail: info@wellingtoneyeclinic.com website: www.wellingtoneyeclinic.com

3. **GLARE AT NIGHT:** I expect to have some glare at night and in dimly illuminated situations for a while after the procedure. It tends to take longer for the night vision to recover when the refraction is higher and a guideline is the caveat of "One month per diopter" for the glare to diminish to normal.

Signed: _____

4. **COMPLICATIONS:** Although the procedure is very safe and predictable, I understand that it is not entirely risk-free. I may develop any of the following complications as well as other complications not mentioned here but encountered very infrequently:

a) Infection (has not occurred in the clinic to date)
b) Inflammation (no serious case has occurred in the clinic)
c) Dry eyes (This occurs in most cases as a result of suddenly not having the protective effect of glasses or contact lenses anymore and the fact that the cornea has reduced sensitivity for some weeks to months after the procedure. It usually clears up well with the use of artificial tears and at the 6 week visit post-operatively, the great majority of people would no longer need to use artificial tears). Dry eyes tend to affect women around the menopause age more readily.
d) Aborting the procedure: There is a very small chance (±0.1%) that the procedure is aborted due to a complication with the making of the flap. The procedure will then be terminated and can be continued 6 weeks later once the flap has healed.
e) Displacement of the flap: The flap may displace during the first few hours after the procedure. It is simply repositioned if this occurs. The flap may also displace at any time after the procedure if the eye is subjected to severe trauma.
f) Corneal Ectasia may occur very rarely. This is a bulging of the cornea that can lead to distortion of vision and may require further intervention in the form of corneal cross-linking (CXL).

Signed: _____

5. I _____ consent to have the procedure of Right / Left / Bilateral Simultaneous LASIK performed by Dr. A.B. Cummings / Dr. R.H. Corkin

I have seen the video and have read and fully understand the literature provided.

I undertake to use the medications as prescribed and to attend all post-operative visits at the clinic. These are usually on the next day, at 6 weeks and 6 months.

I hereby consent to have my data used anonymously for the purpose of clinical audits, data analysis and for publications / presentations.

Signed: _____ Date: _____

Witness: _____ Date: _____

Surgeon: _____ Date: _____

Wellington Eye Clinic
Established 1980

Jan 13

CONSENT FOR ADVANCED SURFACE ABLATION

Read through and initial each paragraph, making sure that you understand the content:

1. **READING GLASSES (after age 42 yrs.):** I understand that if both eyes are corrected to **zero** (= the perfect refraction for distance vision), then I will need reading glasses from around the age of 42 to 45 years. If I am older than this, I will need reading glasses for all close work with immediate effect. If I am younger than this, I will not need reading glasses immediately, but I will need them when I approach the age of 42 to 45 years.

Signed: _____

Monovision: if I decide to have monovision performed, I expect the following effects:
Zero / -1.00: reading glasses postponed to around 50 years of age
Zero / -2.00: reading glasses postponed indefinitely
I expect that distance and near vision is going to be compromised by this choice but that the overall vision is satisfactory for approximately 80% of people.
I know that there is increased glare as a result of monovision and that I may need to wear glasses for driving at night to reduce this glare.
I may have to wear reading glasses when reading for prolonged periods.

Signed: _____

In light of the above, I am opting for:
1. Zero / Zero
2. Zero / -1.00
3. Zero / -2.00
4. Isovision

Signed: _____

2. **ENHANCEMENT / RETREATMENT:** I understand that the procedure is not 100% predictable and that my healing response is going to influence the final result. Because of this, there is a chance that I may need an additional procedure at a later stage to enhance or adjust the outcome. This is usually less than 10% for myopia and around 20% for hyperopia. Very seldom, a 3rd procedure may be necessary to achieve the required result, especially with hyperopia.

If your vision falls below driving standard, there will be no charge for laser enhancement.

Signed: _____

Ophthalmologists: Mr. Arthur Cummings, M.B. Ch.B, MMed(Ophth), (Pret), F.C.S.(SA), F.R.C.S.Ed,
Mr. Richard Corkin, MBChB (Cape Town) FCS (Ophth) SA, MRCOphth,
Dr. Paul Kenna, M.B.,D.O, F.R.C.S.I.
Optometrists: Ms. Ann-Marie Masterson, Ms. Avril Barnes, Ms Clare Maguire

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Tel: +353 1 293 0470 Fax: +353 1 293 5978 e-mail: info@wellingtoneyeclinic.com website: www.wellingtoneyeclinic.com

3. **GLARE AT NIGHT:** I expect to have some glare at night and in dimly illuminated situations for a while after the procedure. It tends to take longer for the night vision to recover when the refraction is higher and a guideline is the caveat of "One month per diopter" for the glare to diminish to normal.

Signed: _____

4. **COMPLICATIONS:** I understand that there are very few complications with LASEK.
The epithelial flap may be unsuitable to place back into position and it will then be discarded (This is now a PRK procedure)
Infection may occur that may result in a delay in the healing process or a loss of the quality of vision. This has not occurred in the clinic to date.
Haze can occur that would also delay the visual recovery. It is very uncommon not to clear. It is also uncommon for haze to have a lasting clinically significant effect.

Signed: _____

5. I _____ consent to have the procedure of Right / Left / Bilateral Simultaneous LASEK performed by Dr. A.B. Cummings / Dr. R.H. Corkin.

I have seen the video and have read and fully understand the literature provided.

I understand that the recovery period is longer than with LASIK and that I will be wearing a bandage contact lens for the next 4 to 5 days.

I understand that the vision is going to take longer to recover and that the vision will still be quite blurred when the contact lens is removed.

I undertake to use my post-operative medication and to attend the post-operative visits at the clinic on Day 1, Day 5, Month 1, Month 3 and Month 6.

I understand and accept the risks inherent to refractive surgery and LASEK in particular.

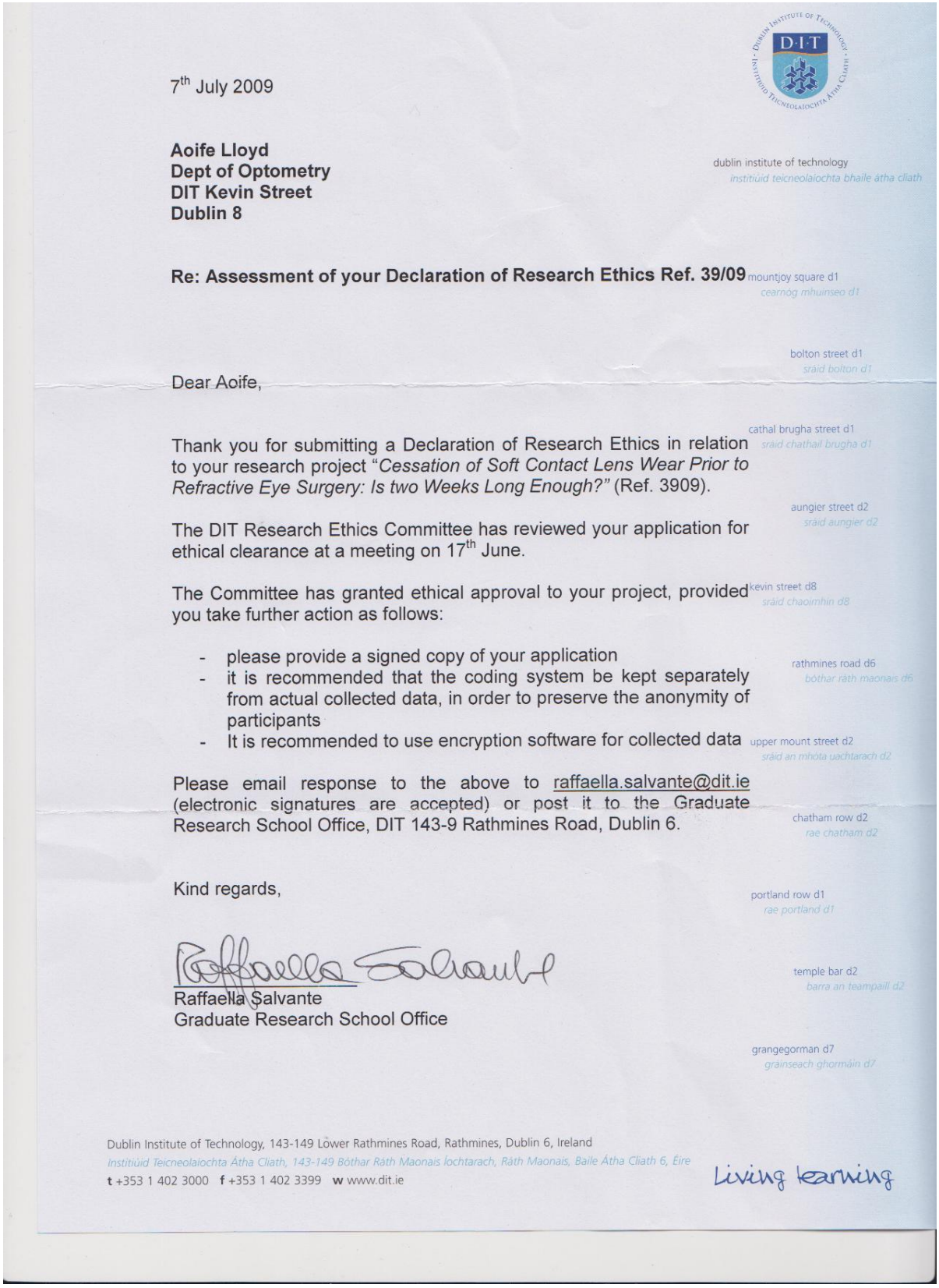
I hereby consent to have my data used anonymously for the purpose of clinical audits, data analysis and for publications / presentations.

Signed: _____ Date: _____

Witness: _____ Date: _____

Surgeon: _____ Date: _____

A.3 DIT Ethics approval letter



7th July 2009

Aoife Lloyd
Dept of Optometry
DIT Kevin Street
Dublin 8

dublin institute of technology
institiúid teicneolaíochta bhaile átha cliath

Re: Assessment of your Declaration of Research Ethics Ref. 39/09

mountjoy square d1
cearnóg mhuirseo d1

bolton street d1
sráid bolton d1

Dear Aoife,

cathal brugha street d1
sráid chathail brugha d1

Thank you for submitting a Declaration of Research Ethics in relation to your research project "*Cessation of Soft Contact Lens Wear Prior to Refractive Eye Surgery: Is two Weeks Long Enough?*" (Ref. 3909).

aungier street d2
sráid aungier d2

The DIT Research Ethics Committee has reviewed your application for ethical clearance at a meeting on 17th June.

kevin street d8
sráid chaoimhín d8

The Committee has granted ethical approval to your project, provided you take further action as follows:

- please provide a signed copy of your application
- it is recommended that the coding system be kept separately from actual collected data, in order to preserve the anonymity of participants
- It is recommended to use encryption software for collected data

rathmines road d6
bóthar ráth maonais d6

upper mount street d2
sráid an mhóta uachtarach d2

Please email response to the above to raffaella.salvante@dit.ie (electronic signatures are accepted) or post it to the Graduate Research School Office, DIT 143-9 Rathmines Road, Dublin 6.

chatham row d2
rae chatham d2

Kind regards,

portland row d1
rae portland d1

Raffaella Salvante
Graduate Research School Office

temple bar d2
barra an teampaill d2

grangegorman d7
gráinseach ghormáin d7

Dublin Institute of Technology, 143-149 Lower Rathmines Road, Rathmines, Dublin 6, Ireland
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Living learning

A.4 List of publications

Peer- reviewed publications

Lloyd McKernan, A, O'Dwyer, V, Simo Mannion, L., The influence of soft CL wear and two weeks lens cessation on corneal curvature. CL Anterior Eye. Feb 2014, 37 (1) : 31-37.

Publications

Lloyd, A, Simo Mannion, L, O'Dwyer, V. Moore, L., Soft Contact Lens-Induced Corneal Warpage. Radharc, Journal of Association of Optometrists Ireland. 2011, 4 (1):24-31.

Peer-reviewed papers and posters presented

Lloyd, A, Simo Mannion, L, O'Dwyer, V. , The influence of soft CL materials on the central, para-central and peripheral corneal endothelium. Poster presentation, British CL Association Conference. Liverpool, May 2015.

Lloyd, A, Simo Mannion, L, O'Dwyer, V. , The effect of two weeks and twenty four hours soft CL cessation times on corneal refractive surgery outcomes. Poster presentation, European Academy of Optometrists. Budapest, May 2015.

Lloyd McKernan, A, Cummings, A, Masterson AM., The impact of modern soft CL wear on the corneal epithelium as determined by OCT. Electronic poster presentation, American Academy of Ophthalmologists. Chicago, October 2014.

Lloyd, A, Simo Mannion, L, O'Dwyer, V. Moore, L., The impact of soft CL wear on corneal curvature and thickness and on the outcomes of refractive LASER surgery. Paper presentation, European Academy of Optometrists. Dublin, April 2012.

Lloyd, A, Simo Mannion, L, O'Dwyer, V. Moore, L., Cessation of soft CL wear prior to refractive laser surgery- is two weeks long enough? Poster presentation, American Academy of Optometrists. Boston, USA, October 2011.

Full copies of these publications can be found in the accompanying CD.

A.5 Additional statistical testing

Appendix 10.4 containing additional statistical testing and raw data lists can be found in the accompanying CD.

A.5 ADDITIONAL STATISTICAL TESTING

A.5.1 Study 1: the influence of 2 weeks of SCL cessation on corneal curvature and thickness

A.5.1.1 Analysis of agreement between 2 Pentacam tomographers

An analysis of the reliability and agreement between measurements taken using 2 Pentacam instruments was carried out to ensure the use of these measurements for statistical analysis was valid. For clarity, the instruments will be referred to as Pentacam 1 and Pentacam 2 in the following section.

A.5.1.2 Intra-session reliability

Bland and Altman (1986) advise that intra-session reliability is important in a study of agreement between instruments. If one instrument has poor reliability, then its agreement with a second instrument will be poor also. The reliability of each Pentacam instrument was assessed by comparing 3 measurements taken with each Pentacam on the same subject on the same day. Measurements from ten patients (5 SCL and 5 NCL wearers) on Pentacam 1 and 10 patients (5 SCL and 5 NCL wearers) on Pentacam 2 were analysed. Measurements chosen for this analysis were thinnest pachymetry (μm) and steep SimK (D) values.

The statistical method for assessing internal consistency of these measurements was Cronbach's alpha and Intraclass Correlation Coefficient (ICC). Cronbach's alpha is based on the principle that "the variance of the sum of a group of independent variables is the sum of their variances" (Bland and Altman, 1997). The coefficient tests the expected correlation between 2 sets of measurements. ICC is also used to measure the

reliability or consistency of 2 sets of measurements from the same class. It is calculated by measuring the average correlation among all possible ordering of the pairs of measurements (Bland 1996). The ICC value of 1 indicates perfect agreement and 0 no agreement. For clinical applications, it is recommended that the ICC is > 0.90. Results of Cronbach's alpha and ICC are shown in Table A-2. Patients included 13 males and 7 females, the mean age ±SD was 36 ±10 years (range 21 to 56 years), MSE -3.50 ±1.50D (range -1.25 to -7.00D). The Pentacam instruments were shown to be highly reliable for both pachymetry and simulated keratometry analysed using Cronbach's alpha and ICC testing, meaning the instruments agreement with each other can be assessed with confidence.

Table A-2: Pentacam: Analysis of reliability

Parameters	**Cronbach's alpha Pentacam 1 n = 10**	**Cronbach's alpha Pentacam 2 n = 10**	**ICC Pentacam 1 n = 10**	**ICC Pentacam 2 n = 10**
Thinnest pachymetry(µm)	0.993	0.980	0.979	0.943
Steep K (D)	0.998	0.997	0.995	0.990

Pentacam: Analysis of reliability of 2 Pentacam instruments used in the study. Cronbach's alpha and Intraclass Correlation Coefficient (ICC) results of reliability analysis applied to pachymetry and central steep keratometry data obtained. All values are greater than 0.9, recommended in clinical applications (Bland and Altman, 1997).

A.5.1.3 Agreement between Pentacam instruments

Following intra-session reliability, the agreement between the 2 Pentacam instruments was assessed, using Bland & Altman's method of comparing the mean difference between the 2 methods of measurement (the bias) (Bland and Altman, 1986). The nature of this study did not allow for comparison of measurements taken on the 2 Pentacam instruments on the same day, as the retrospective study started after refurbishment of the clinic took place and 1 of the instruments was removed. Therefore,

a modified version of Bland and Altman's method of comparison was used. Measurements taken from ten NCL patients using different Pentacam instruments at the first and second visits were compared. Only patients in the NCL wearers were chosen in order to eliminate any differences in measurements created by cessation of SCL wear. Measurements chosen for this analysis were central and thinnest pachymetry (μm) and flat and steep simulated keratometry (D) values.

In accordance with Bland and Altman's (1986) recommendations for assessing agreement between 2 methods of clinical measurements (inter-session repeatability), the data were first plotted against a line of equality, where all points would lie if there was complete agreement between the 2 instruments. This helps to gauge the degree of agreement between the 2 Pentacam instruments. The differences in these measurements taken on both instruments were then analysed. Bland and Altman (1986) recommend that the differences between the measurements are then plotted against their mean and the coefficients of agreement are calculated. If the differences are normally distributed, 95% of differences will lie between these limits (Limits of agreement (LOA): mean difference ±1.96 standard deviations). The coefficient of repeatability (COR; ±1.96 x SD of the differences) was calculated to provide an interval within which 95% of the differences lie. Relative repeatability (RR) was calculated as a percentage of the ratio of the COR to the mean value of the measurements. Results showed normal distribution of data in all cases (Shapiro-Wilks $p > 0.05$).

The mean difference between the two sets of measurements and the LOA were small. Paired sample t-tests showed that there were no statistically significant differences between the means of the two sets of measurements for any values analysed (Table A-3). In the clinical setting where data were obtained from, the two instruments were

used indiscriminately. Assessment of agreement between the instruments revealed high levels of agreement thus ensuring data from the two instruments could be used to assess changes in corneal parameters.

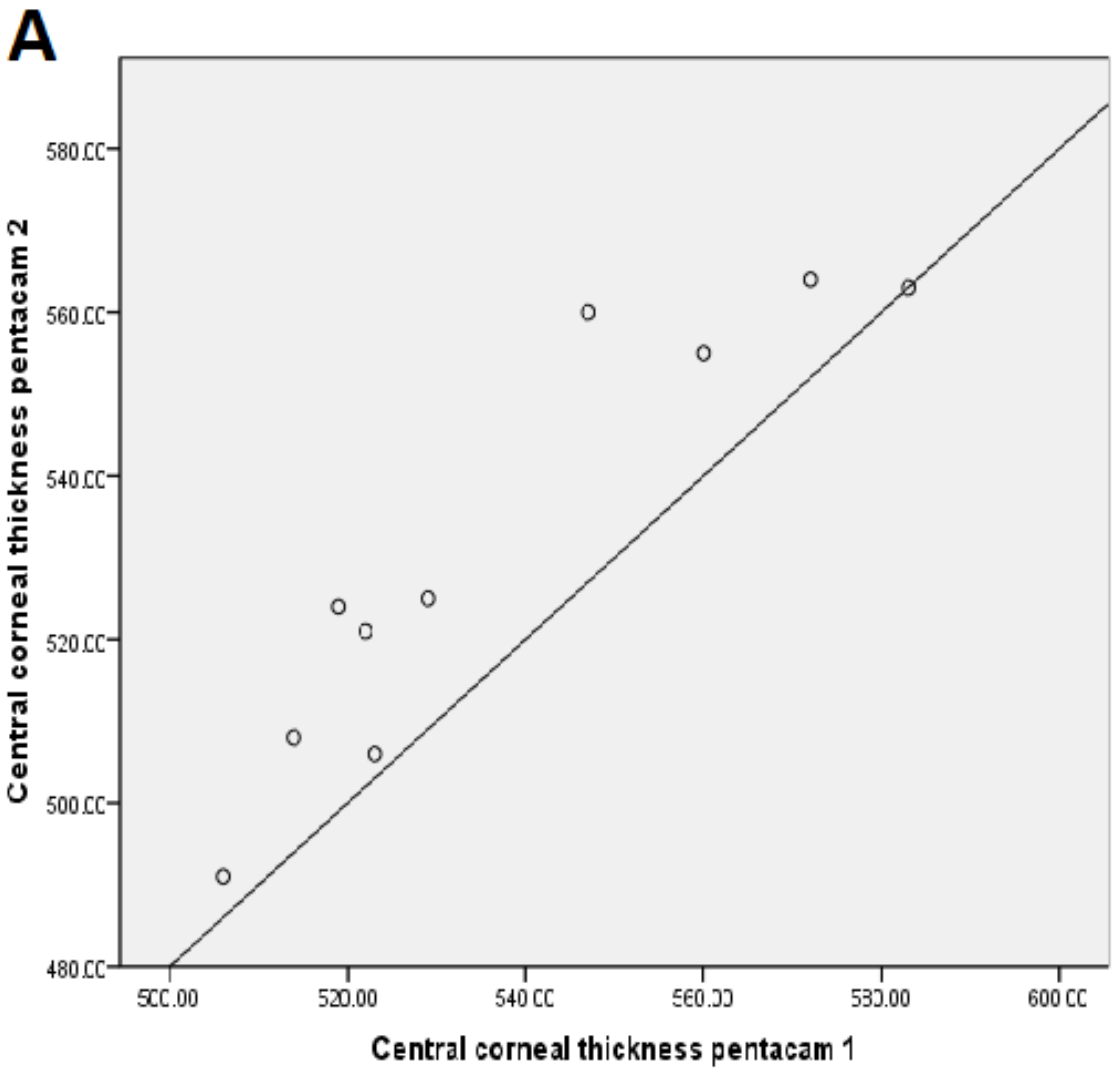
Table A-3: Repeatability of two Pentacam instruments

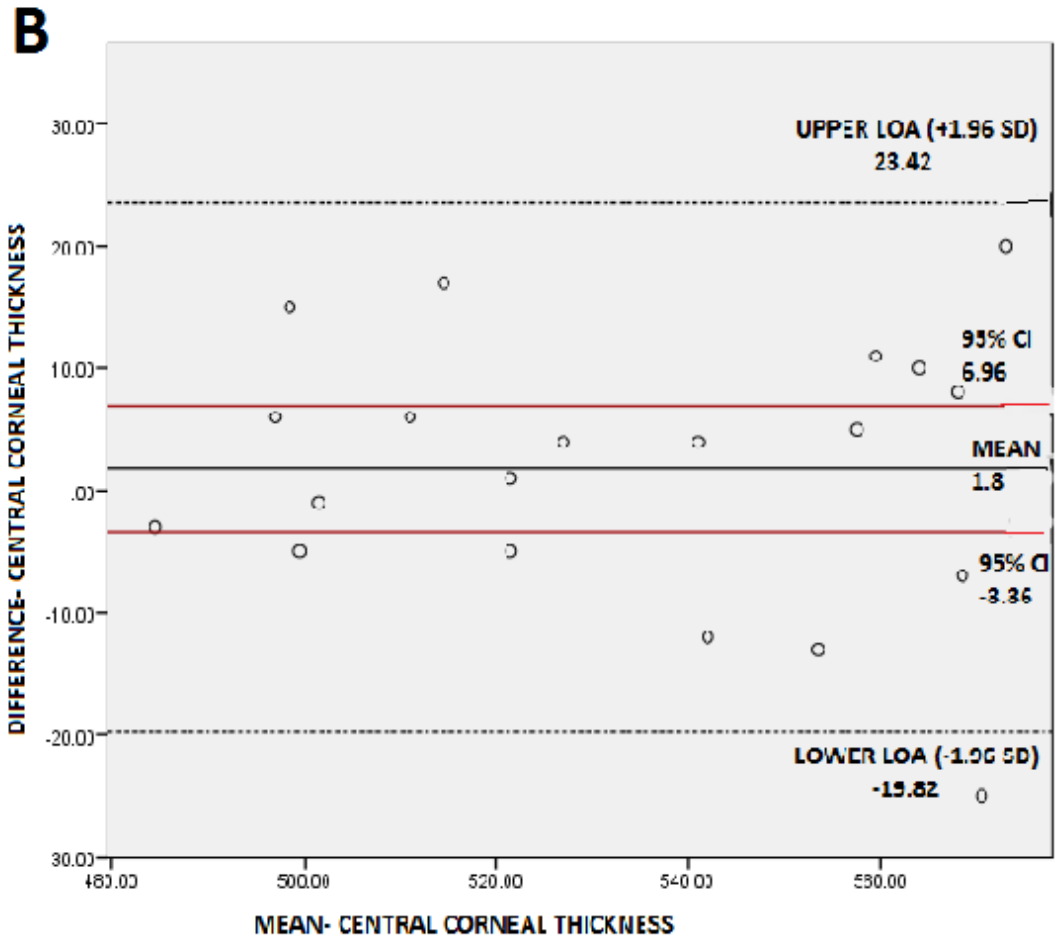
Parameters	**Mean ±SD**	**Mean difference ±SD**	**COR**	**LOA**	**RR (%)**	**Mean PC 1**	**Mean PC 2**	***t*-test Sig**
Central pachymetry (µm)	535 ±26	5.8 ±10	±19.75	5.8 ±19.75	3.69	537 ±26	532 ±27	0.10
Thinnest Pachymetry (µm)	532 ±26	5.8 ±9.5	±18.54	5.8 ±18.54	3.48	535 ±26	529 ±27	0.08
Flat SimK (D)	43.6 ±1.2	0.00 ±0.18	±0.36	0.00 ±0.36	0.82	43.6 ±1.2	43.6 ±1.2	1.00
Steep SimK (D)	44.4 ±1.1	0.14 ±0.3	±0.61	0.14 ±0.61	1.37	44.5 ±1.2	44.4 ±1.0	0.19

Summary of agreement between the 2 Pentacam instruments for pachymetry and curvature measurements. COR: coefficient of repeatability, LOA: limits of agreement, RR: relative repeatability. The mean differences between the 2 sets of measurements and the COR, LOA and RR are small indicating good repeatability. Paired sample t-tests show there is no statistically significant differences between the measurements taken with 2 Pentacam instruments.

Scatter plots and differences vs. means plots were used to visually inspect the data (see Figure A-1, Figure A-2, Figure A-3, Figure A-4). The Bland-Altman plots demonstrate that he limits of agreement were similar for both instruments, all corneal thickness parameters tested lie within the limits of agreement, while only 1 subject (5%) lies above the upper limit of agreement for flat and steep simulated keratometry.

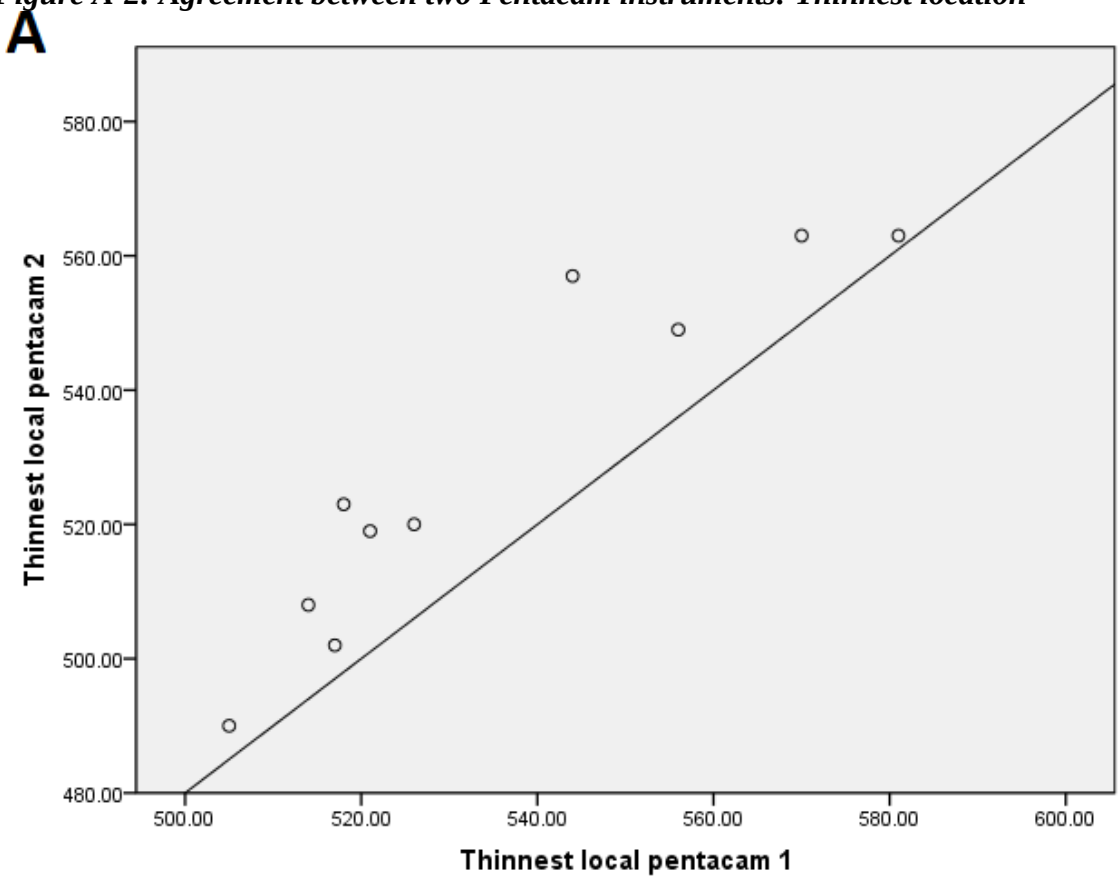
Figure A-1: Agreement between 2 Pentacam instruments: Central corneal thickness

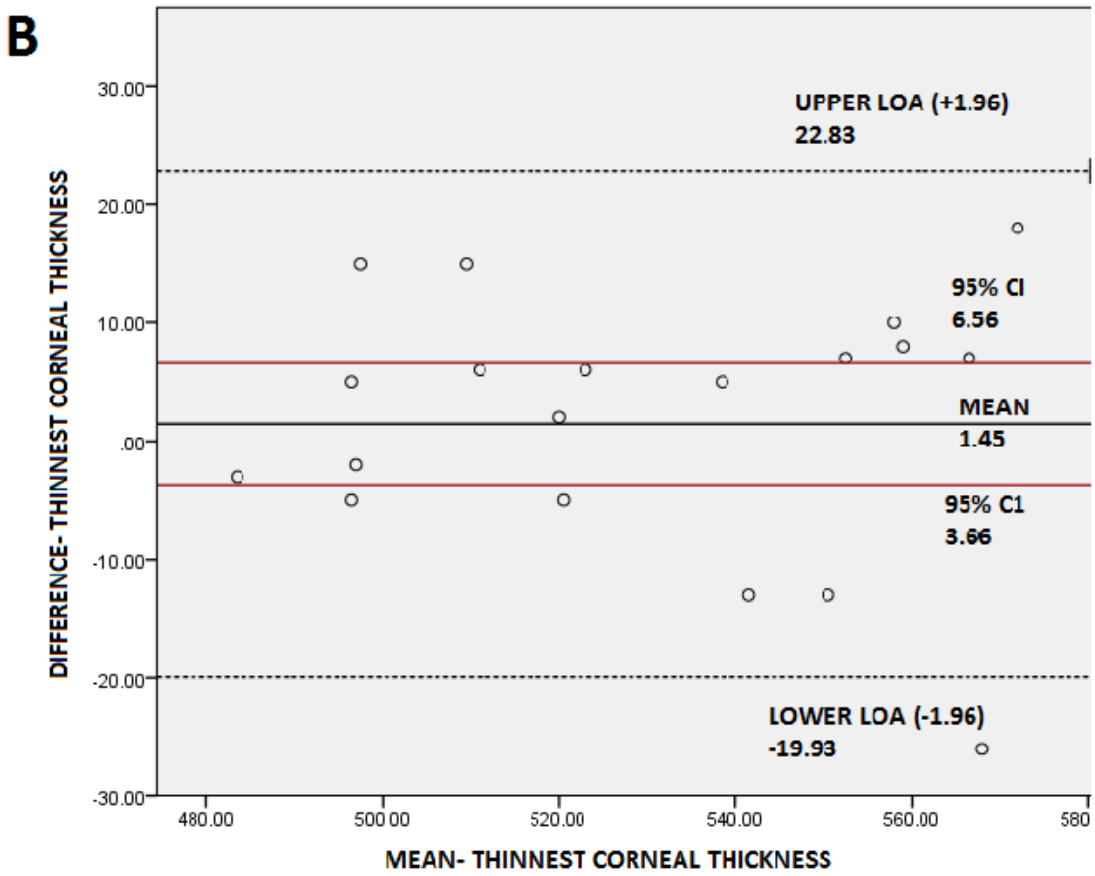




A. Measurements of central corneal thickness readings obtained with 2 Pentacams. Line represents x=y line of equality. B. Differences vs. means plot. Dashed black lines correspond to limits of agreement. 8 subjects (40%) lie within 95% confidence intervals for the bias (red lines) showing good agreement.

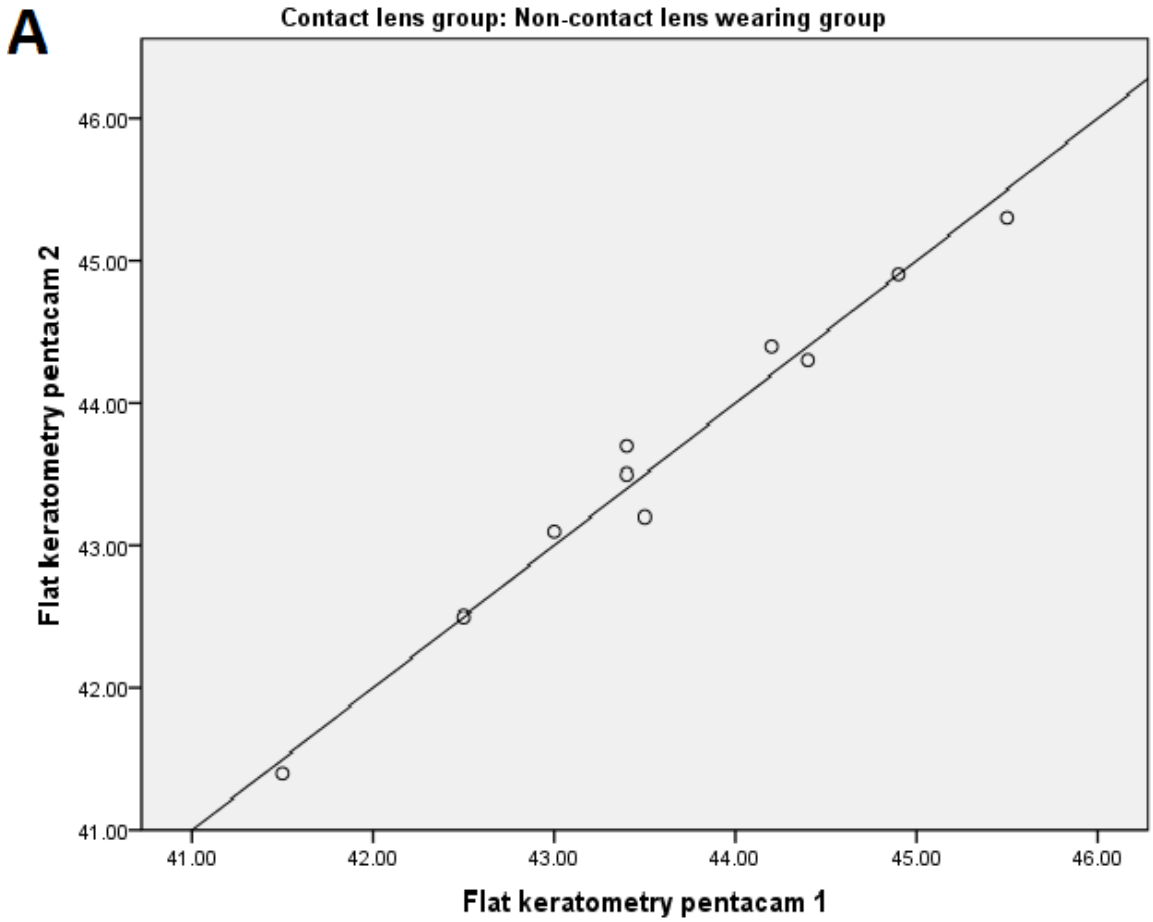
Figure A-2: Agreement between two Pentacam instruments: Thinnest location

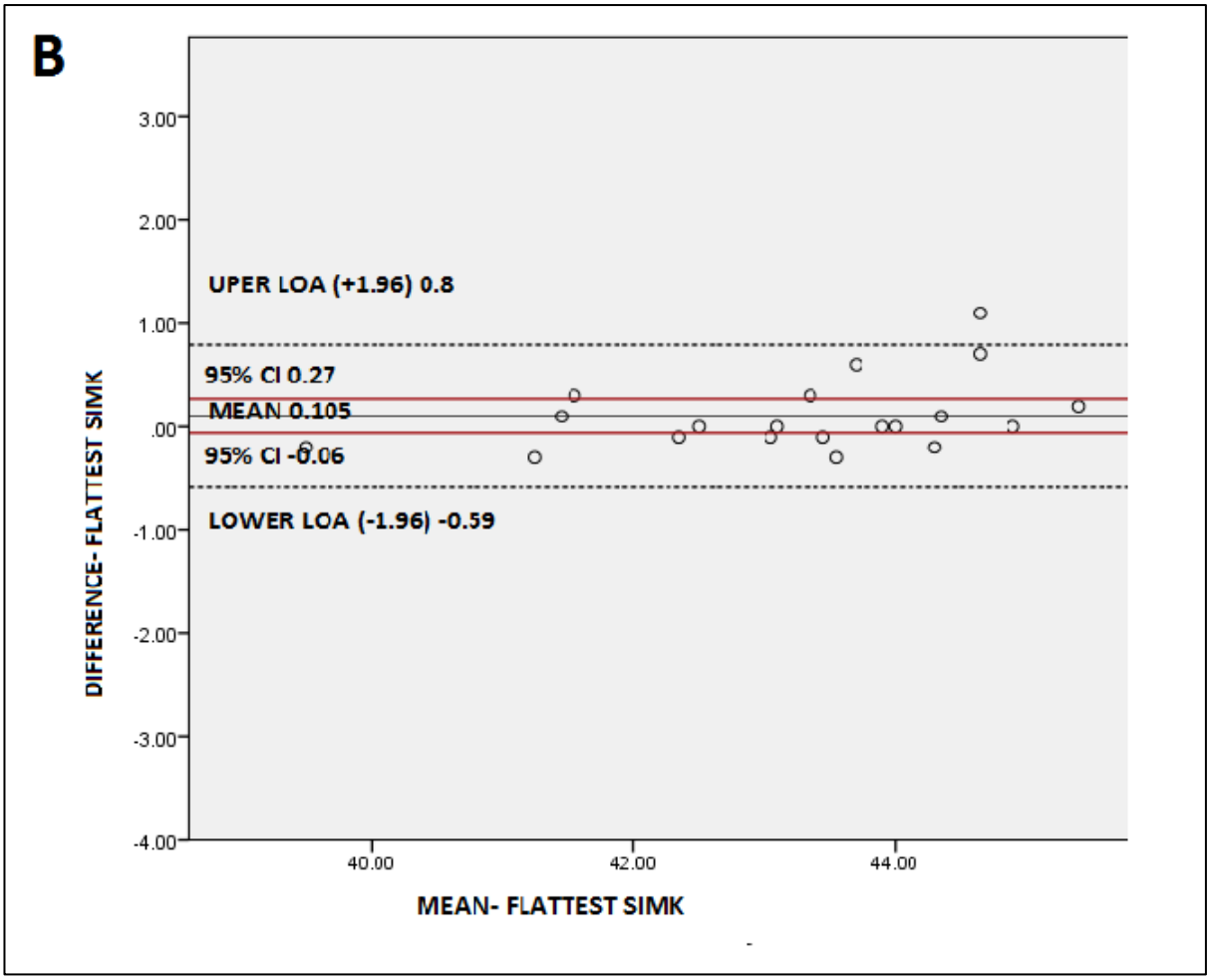




Measurements of thinnest corneal thickness readings obtained with 2 Pentacams. Line represents x=y line of equality. B. Differences vs. means plot. Dashed black lines correspond to limits of agreement, 9 subjects (45%) lie within 95% confidence intervals for the bias (red lines) showing good agreement.

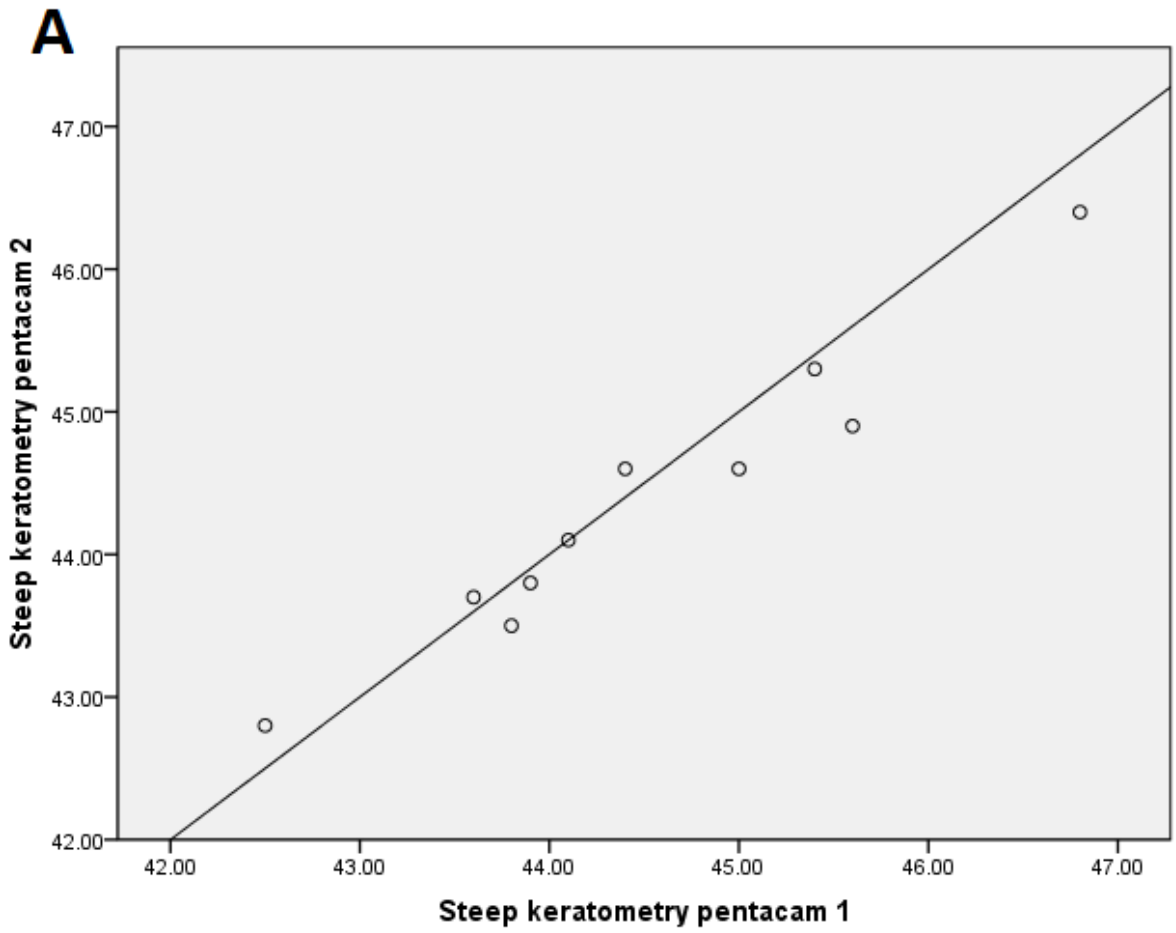
Figure A-3: Agreement between 2 Pentacam instruments: Flat keratometry

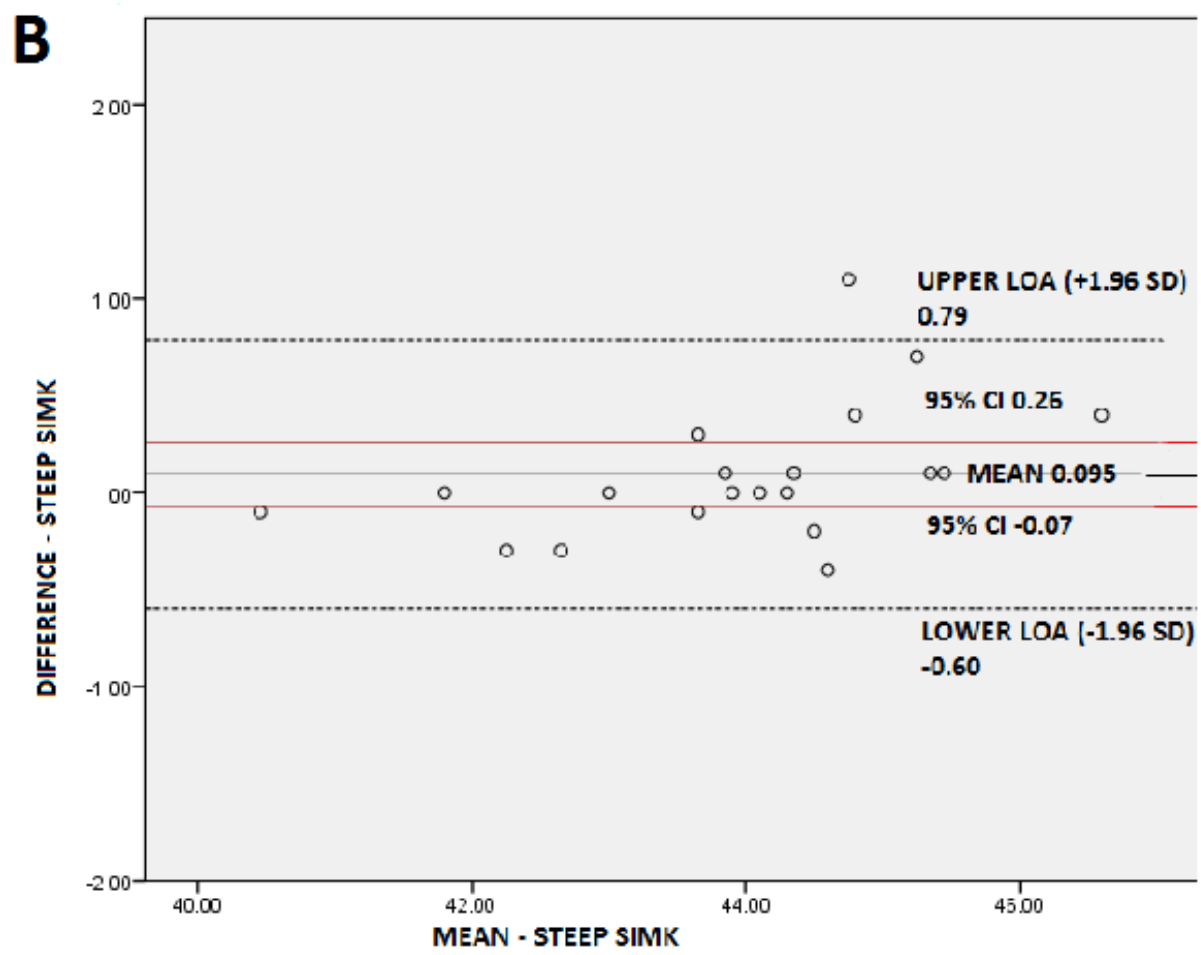




A. Measurements of flattest SimK readings obtained with 2 Pentacams. Line represents x=y line of equality. B. Differences vs. means plot. Dashed black lines correspond to limits of agreement, 10 subjects (50%) lie within 95% confidence intervals for the bias (red lines) showing good agreement.

Figure A-4: Agreement between two Pentacam instruments: Mean steep keratometry





A. Measurements of steepest SimK readings obtained with 2 Pentacams. Line represents x=y line of equality. B. Differences vs. means plot. Dashed black lines correspond to limits of agreement, 9 subjects (45%) lie within 95% confidence intervals for the bias (red lines) showing good agreement.

A.5.1.4 Quality of corneal scans obtained with the Pentacam

To investigate the influence of SCL on the quality of Pentacam scans, analysis of QS values was undertaken. Mann-Whitney U-testing was used to analyse differences in QS values between the SCL and NCL group. Results showed no statistically significant differences in the QS values between the SCL and NCL groups (Table A-4). Thus, it was presumed that the quality of scans obtained using the acquisition of corneal scans with the Pentacam instrument was not affected by the use of SCL wear in this thesis.

Table A-4: Pentacam scan quality at the first visit

	SCL group Mean ±SD n = 45 (%)	**NCL group Mean ±SD n = 45 (%)**	**Mann-Whitney Sig.**
QS at first visit	98.17 ±1.75	98.44 ±2.12	0.25
QS at the second visit	98.19 ±1.21	98.53 ±1.25	0.25

Mean ±SD scan quality specification expressed as a percentage of accurate usable data from of Pentacam measurements taken at the first and second visits. Results of Mann-Whitney testing indicate there were no significant differences in quality between the SCL and NCL groups ($p < 0.05$).

A.5.1.5 The influence of SCL material and previous wearing times on corneal curvature at the first visit

The effect of SCL material and previous wearing times on SimK values at the first visit between the SCL and NCL control groups was analysed with a two-way ANOVA . Results showed no statistically significant effect of SCL material or years of wear on SimK values between the groups (see Table A-5).

Table A-5: The influence of SCL material and years of wear on SimK values at the first visit

	Flat SimK Mean ±SD (D)	**Sig**	**Steep SimK Mean ±SD (D)**	**Sig**
Hydrogel (n = 35)	42.77 ±1.16	0.90	43.44 ±1.12	0.60
SiHy (n = 6)	43.13 ±1.5		44.08 ±1.37	
Short-term (n = 11)	43.39 ±1.01	0.25	43.98 ±0.93	0.56
Medium-term (n = 23)	42.59 ±1.31		43.35 ±1.21	
Long-term (n = 8)	42.64 ±1.10		43.34 ±1.35	
NCL (n = 45)	42.55 ±1.32		43.43 ±1.43	

Mean ±SD of flat and steep SimK values taken at the first visit. Results of Two-way ANOVA indicate no significant differences in quality between the SCL material or years of previous SCL wear and NCL groups (all p-values > 0.05). Short-term: < 5 years, medium-term: 5- 10 years, long-term: > 10 years.

A two-way ANOVA was conducted to analyse the effect of SCL material and previous wearing times on sagittal and tangential radii values at the first visit between the SCL and NCL control groups. There was no statistically significant effect of SCL material or years of wear on sagittal or tangential radii values between the groups (see Table A-6).

Table A-6: The influence of SCL material and years of wear on sagittal and tangential radii at the first visit

	Anterior			**Posterior**		
	Superior Mean±SD (mm)	**Central Mean±SD (mm)**	**Inferior Mean±SD (mm)**	**Superior Mean±SD (mm)**	**Central Mean±SD (mm)**	**Inferior Mean±SD (mm)**
Sagittal						
Hydrogel	7.84 ±0.24	7.84 ±0.22	7.75 ±0.20	6.26 ±0.31	6.63 ±0.21	6.36 ±0.26
SiHy	7.61 ±0.30	7.78 ±0.27	7.68 ±0.23	6.10 ±0.39	6.58 ±0.42	6.26 ±0.26
Sig	0.15	0.93	0.73	0.48	0.93	0.54
Short-term	7.73 ±0.26	7.73 ±0.17	7.66 ±0.16	6.16 ±0.24	6.55 ±0.29	6.26 ±0.20
Medium-term	7.84 ±0.26	7.87 ±0.25	7.77 ±0.22	6.30 ±0.27	6.66 ±0.24	6.39 ±0.27
Long-term	7.83 ±0.26	7.87 ±0.23	7.78 ±0.23	6.17 ±0.53	6.62 ±0.22	6.39 ±0.32
NCL	7.81 ±0.26	7.86 ±0.25	7.79 ±0.29	6.23 ±0.31	6.63 ±0.26	6.36 ±0.25
Sig	0.61	0.40	0.57	0.38	0.56	0.46
Tangential						
Hydrogel	7.87 ±0.31	7.88 ±0.24	7.85 ±0.25	6.35 ±0.49	6.80 ±0.33	6.29 ±0.31
SiHy	7.64 ±0.40	7.81 ±0.35	7.54 ±0.38	6.5 ±0.72	6.77 ±0.46	6.02 ±0.42
Sig	0.32	0.97	0.08	0.97	0.95	0.21
Short-term	7.70 ±0.30	7.72 ±0.23	7.74 ±0.36	6.14 ±0.50	6.72 ±0.29	6.13 ±0.31
Medium-term	7.90 ±0.35	7.92 ±0.26	7.79 ±0.29	6.47 ±0.53	6.87 ±0.33	6.30 ±0.33
Long-term	7.89 ±0.28	7.93 ±0.21	7.91 ±0.19	6.44 ±0.50	6.68 ±0.45	6.27 ±0.40
NCL	7.81 ±0.34	7.93 ±0.26	7.90 ±0.30	6.4 ±0.62	6.87 ±0.28	6.34 ±0.32
Sig	0.42	0.10	0.86	0.44	0.35	0.38

Mean ±SD of sagittal and tangential radii values taken at the first visit. Results of Two-way ANOVA indicate no significant differences in quality between the SCL material or years of previous SCL wear and NCL groups (all p-values > 0.05). Short-term: < 5 years, medium-term: 5- 10 years, long-term: > 10 years.

A.5.1.6 The influence of myopic group on corneal curvature at the first visit

The influence of the level of myopia on corneal curvature at the first visit was explored. It was hypothesised that the higher the pre-operative refractive error, the steeper the corneal curvature. Results of two-way ANOVA indicate no significant differences between the myopic or CL or interaction between the myopic and CL groups (Table A-7).

Table A-7: The influence of myopic group on corneal curvature at the first visit

		Low Myopes	**Medium Myopes**	**High Myopes**	**Sig**	
Curvature measurement at the first visit	**CL group**	**Mean ±SD (n = 31) SCL (n = 13)**	**Mean ±SD (n = 12) SCL (n = 28)**	**Mean ±SD NCL (n = 2) SCL (n =4)**	**CL group**	**Myopic group**
Sagittal: anterior-superior	NCL	7.84 ±0.27	7.73 ±0.28	7.77 ±0.13	0.93	0.69
	SCL	7.78 ±0.22	7.78 ±0.28	7.75 ±0.36		
Sagittal: anterior- central	NCL	7.90 ±0.24	7.80 ±0.29	7.73 ±0.03	0.89	0.67
	SCL	7.79 ±0.20	7.82 ±0.25	7.78 ±0.30		
Sagittal: anterior-inferior	NCL	7.85 ±0.28	7.66 ±0.28	7.64 ±0.17	0.99	0.38
	SCL	7.70 ±0.25	7.73 ±0.22	0.72 ±0.25		
Sagittal: posterior - superior	NCL	6.24 ±0.30	6.20 ±0.36	6.28 ±0.20	0.66	0.92
	SCL	6.24 ±0.26	0.21 ±0.35	6.13 ±0.34		
Sagittal: posterior - central	NCL	6.63 ±0.26	6.63 ±0.31	6.65 ±0.11	0.70	0.87
	SCL	6.64 ±0.20	3.58 ±0.28	6.59 ±0.24		
Sagittal: posterior - inferior	NCL	6.40 ±0.24	6.27 ±0.30	6.41 ±0.07	0.67	0.67
	SCL	6.33 ±0.26	6.35 ±0.26	6.29 ±0.29		
Tangential: anterior - superior	NCL	7.83 ±0.36	7.74 ±0.32	7.85 ±0.04	0.87	0.91
	SCL	7.79 ±0.29	7.84 ±0.34	7.84 ±0.33		
Tangential: anterior - central	NCL	7.96 ±0.26	7.89 ±0.27	7.67 ±0.06	0.99	0.52
	SCL	7.83 ±0.24	7.85 ±0.27	7.84 ±0.24		
Tangential: anterior - inferior	NCL	7.96 ±0.30	7.81 ±0.29	7.62 ±0.09	0.87	0.61
	SCL	7.73 ±0.34	7.79 ±0.30	7.82 ±0.26		
Tangential: posterior - superior	NCL	6.39 ±0.52	6.50 ±0.87	6.05 ±0.37	0.89	0.55
	SCL	6.28 ±0.48	6.40 ±0.52	6.34 ±0.53		
Tangential: posterior - central	NCL	6.87 ±0.30	6.90 ±0.24	6.61 ±0.24	0.67	0.47
	SCL	6.75 ±0.40	6.79 ±0.34	6.71 ±0.24		
Tangential: posterior - inferior	NCL	6.40 ±0.28	6.21 ±0.40	6.26 ±0.31	0.41	0.50
	SCL	6.22 ±0.30	6.29 ±0.35	6.10 ±0.27		
Flat K	NCL	42.40 ±1.27	42.78 ±1.45	43.65 ±0.07	0.85	0.57
	SCL	42.99 ±1.16	42.95 ±1.33	43.13 ±1.36		
Steep K	NCL	43.22 ±1.34	43.95 ±1.63	43.65 ±0.21	0.82	0.55
	SCL	43.72 ±0.99	43.63 ±1.26	43.80 ±1.88		

Mean ±SD of corneal curvature values taken at the first visit. Results of Two-way ANOVA indicate no significant differences between SCL and NCL and myopic groups (all p-values > 0.05).

A.5.1.7 The influence of SCL wear on corneal topographical indices at the first visit

The effect of SCL material and previous years of SCL wear on topographical indices at the first visit were compared between the SCL and NCL control groups. A two-way ANOVA and Kruskal-Wallis comparison was carried out (see Table A-8). The keratoconus index was higher in the hydrogel group compared with the SiHy and NCL control groups. There was a tendency for the corneal indices to increase with increasing years of SCL wear. However, there was no statistically significant effect of SCL material, or years of SCL wear or the interaction between SCL material and years of wear on topographical indices tested (Table A-8).

Table A-8: Corneal indices in SCL material and years of SCL wear groups

	Surface variance Mean ±SD	**Vertical asymmetry Mean ±SD**	**Keratoconus Mean ±SD**	**Central keratoconus Mean ±SD**
Hydrogel (n = 35)	14.09 ±3.69	0.13 ±0.06	1.02 ±0.02	1.00 ±0.01
SiHy (n = 6)	14.67 ±3.88	0.12 ±0.05	1.02 ±0.02	1.00 ±0.01
SCL material Sig ANOVA (Kruskal-Wallis)	0.64 (0.80)	0.54 (0.94)	0.92 (0.37)	0.90 (0.92)
Short-term (n = 11)	12.64 ±3.80	0.11 ±0.04	1.02 ±0.01	1.00 ±0.01
Medium-term (n = 21)	14.52 ±3.56	0.13 ±0.06	1.03 ±0.02	1.00 ±0.01
Long-term (n = 8)	15.25 ±3.85	0.14 ±0.06	1.02 ±0.02	1.00 ±0.01
NCL (n = 45)	14.59 ±3.71	0.12 ±0.06	1.01 ±0.02	1.00 ±0.01
Years of wear Sig Two-way ANOVA (Kruskal-Wallis)	0.50 (0.73)	0.53 (0.31)	0.79 (0.39)	0.96 (0.30)
	Height asymmetry Mean ±SD	**Height decentration Mean ±SD**	**Radii minimum Mean ±SD**	**Aberration coefficient Mean ±SD**
Hydrogel (n = 35)	2.86 ±1.68	0.01 ±0.00	7.66 ±0.21	0.95 ±0.60
SiHy (n = 6)	3.57 ±1.66	0.01 ±0.00	7.55 ±0.29	1.32 ±0.83
SCL material Sig ANOVA (Kruskal-Wallis)	0.74 (0.15)	0.52 (0.06)	0.66 (0.08)	0.80 (0.42)
Short-term (n = 11)	2.65 ±1.73	0.01 ±0.00	7.55 ±0.20	1.37 ±0.61
Medium-term (n = 21)	2.91 ±1.65	0.01 ±0.00	7.68 ±0.23	0.92 ±0.62
Long-term (n = 8)	3.51 ±1.86	0.01 ±0.00	7.68 ±0.25	0.74 ±0.62
NCL (n = 45)	4.05 ±3.81	0.01 ±0.00	7.66 ±0.24	0.98 ±0.64
Years of wear Sig ANOVA (Kruskal-Wallis)	0.89 (0.73)	0.67 (0.06)	0.38 (0.58)	0.43 (0.21)

Mean ±SD of corneal indices at the first visit. Results of Two- way ANOVA and Kruskal-Wallis testing found no significant differences between SCL material or SCL years of previous wear and NCL groups (all p-values > 0.05).

A.5.1.8 The effect of 2 weeks cessation of SCL wear on corneal curvature measurements

Two-way ANOVA was used to compare the means of flat and steep SimK values measured following 2 weeks cessation of SCL wear, between the SCL and NCL groups. Results showed an increase of SimK values, indicating steepening of corneal curvature, in the SCL group. However, differences in curvature between the SCL group and the NCL control group were not statistically significant (Table A-9).

Table A-9: The influence of SCL wear on SimK values following 2 weeks cessation of SCL wear

	SCL group Mean ±SD n = 38 (D)	**NCL group Mean ±SD n = 37 (D)**	**Sig**
Flat K	43.03 ±1.27	42.52 ±1.49	0.12
Steep K	43.66 ±1.20	43.39 ±1.54	0.42

Mean ±SD flat and steep SimK data at the second visit. Results of two-way ANOVA showed no statistically significant differences between the SCL and NCL control group, ($p < 0.05$).

The effect of SCL material and years of previous SCL wear was explored. Results of two-way ANOVA and Kruskall Wallis testing showed no statistically significant effects of either SCL material or previous years of SCL wear compared with the NCL control group (Table A-10).

Table A-10: SimK values between first and second visits for SCL material groups.

Difference in SimK first and second visit	**NCL n = 36**	**Hydrogel n = 30**	**SiHy n = 6**	**Sig Two-way ANOVA (Kruskal-Wallis)**
Flattest (D)	-0.06 ±0.53	0.02 ±0.26	0.18 ±0.31	0.50 (0.37)
Steepest (D)	-0.10 ±0.60	-0.01 ±0.19	0.03 ±0.12	0.82 (0.86)
	Short term n = 9	**Medium term n = 19**	**Long term n = 7**	**Sig Two-way ANOVA (Kruskal-Wallis)**
Flattest (D)	-0.02 ±0.34	0.06 ±0.20	0.10 ±0.37	0.87 (0.54)
Steepest (D)	-0.04 ±0.30	-0.01 ±0.13	0.04 ±0.08	0.93 (0.56)

Mean ±SD of the stability of flat and steep SimK data between the first and second visits. A positive value indicates steeper SimK at the second visit. Results of two-way ANOVA and Kruskal-Wallis testing showed no statistically significant differences between the SCL and NCL control group, (all p values > 0.05).

A.5.1.8.1 The influence of 2 weeks cessation of SCL wear on corneal topography

A two-way ANOVA compared the sagittal and tangential radii taken at the second visit, between the SCL and NCL control groups. Results showed that, while the mean sagittal radii measured at all locations were reduced (indicating steepening) in the SCL compared with the NCL group, differences between the groups (SCL vs. NCL) were not statistically significant. While the inferior tangential radii on the anterior surface remained steeper in the SCL group compared with the NCL group, results of two-way ANOVA also showed no statistically significant differences between the 2 groups (SCL vs. NCL) at any location measured (Table A-11).

Table A-11: Topography measurements following 2 weeks cessation of SCL wear

	Sagittal radius (mm)			**Tangential radius (mm)**		
	SCL group Mean ±SD n = 38	**NCL group Mean ±SD n = 37**	**Sig**	**SCL group Mean ±SD n = 38**	**NCL group Mean ±SD n = 37**	**Sig**
Superior	7.79 ±0.25	7.80 ±0.28	0.89	7.86 ±0.30	7.85 ±0.33	0.91
Central	7.80 ±0.23	7.88 ±0.28	0.19	7.85 ±0.25	7.95 ±0.29	0.12
Inferior	7.71 ±0.21	7.80 ±0.30	0.14	7.82 ±0.26	7.89 ±0.32	0.30
Superior	6.26 ±0.28	6.24 ±0.36	0.79	6.25 ±0.37	6.43 ±0.71	0.16
Central	6.62 ±0.25	6.60 ±0.26	0.81	6.79 ±0.33	6.86 ±0.26	0.34
Inferior	6.32 ±0.24	6.32 ±0.26	0.89	6.27 ±0.31	6.33 ±0.35	0.39

Mean ±SD sagittal and tangential radii and statistical results of two-way ANOVA at the second visit found no statistically significant differences between the SCL and NCL groups ($p < 0.05$).

The influence of SCL material and previous years of SCL wear on the differences in radii between first and second visits was explored. The results of the two- way ANOVA exploring the effect of SCL material on tangential radii, showed the tangential radii measured inferiorly on the anterior corneal was significantly flatter in the SiHy group (Table 10-12). All other results indicated there were no statistically significant effects of either SCL material, or years of previous SCL wear or the interaction effect of the 2 groups on the differences in sagittal and tangential radii values between first and second visits.

Table A-12: The differences between sagittal and tangential radii values measured at first and second visits for SCL material and years of SCL wear groups.

	Sagittal: Anterior Superior Mean±SD (mm)	**Sagittal: Anterior central Mean±SD (mm)**	**Sagittal: Anterior inferior Mean±SD (mm)**	**Sagittal: Posterior Superior Mean±SD (mm)**	**Sagittal: posterior central Mean±SD (mm)**	**Sagittal: posterior inferior Mean±SD (mm)**
Hydrogel (n = 30)	-0.01 ±0.05	0.02 ±0.05	0.01 ±0.09	-0.03 ±0.21	-0.01 ±0.11	0.05 ±0.14
SiHy (n = 6)	-0.05 ±0.08	0.02 ±0.05	0.02 ±0.06	-0.07 ±0.13	-0.02 ±0.14	-0.08 ±0.29
Sig	0.38	0.65	0.78	0.61	0.86	0.28
Short (n = 9)	0.00 ±0.08	-0.03 ±0.12	-0.01 ±0.07	-0.01 ±0.14	-0.04 ±0.09	0.01 ±0.09
Medium (n = 19)	-0.02 ±0.05	0.02 ±0.06	0.01 ±0.09	-0.04 ±0.17	0.00 ±0.12	0.02 ±0.21
Long (n = 7)	-0.04 ±0.05	0.05 ±0.05	0.04 ±0.09	-0.06 ±0.33	0.00 ±0.13	0.08 ±0.18
NCL (n = 37)	-0.01 ±0.1	-0.02 ±0.12	-0.01 ±0.09	-0.01 ±0.11	0.00 ±0.13	0.01 ±0.08
Sig	0.67	0.46	0.67	0.84	0.77	0.51
	Tangential: Anterior Superior Mean±SD (mm)	**Tangential: Anterior central Mean±SD (mm)**	**Tangential: Anterior inferior Mean±SD (mm)**	**Tangential: Posterior Superior Mean±SD (mm)**	**Tangential: posterior central Mean±SD (mm)**	**Tangential: posterior inferior Mean±SD (mm)**
Hydrogel (n = 30)	-0.05 ±0.18	-0.01 ±0.08	-0.05 ±0.14	0.07 ±0.3	-0.03 ±0.3	0.02 ±0.21
SiHy (n = 6)	-0.05 ±0.13	-0.02 ±0.06	-0.21 ±0.3	0.34 ±0.44	-0.01 ±0.18	-0.15 ±0.35
Sig	0.92	0.80	0.02	0.30	0.90	0.24
Short (n = 9)	-0.1 ±0.09	-0.07 ±0.07	-0.04 ±0.2	0.09 ±0.33	-0.01 ±0.42	-0.06 ±0.26
Medium (n = 19)	-0.05 ±0.22	0.00 ±0.06	-0.11 ±0.19	0.09 ±0.29	0.00 ±0.13	0.01 ±0.28
Long (n = 7)	0.01 ±0.08	0.04 ±0.09	-0.06 ±0.11	0.25 ±0.47	-0.14 ±0.38	-0.01 ±0.14
NCL (n = 37)	-0.05 ±0.17	-0.02 ±0.12	0.01 ±0.08	0.02 ±0.5	0.00 ±0.14	0.01 ±0.18
Sig	0.63	0.15	0.36	0.65	0.39	0.92

Mean ±SD of the stability of sagittal and tangential radii and statistical results of two-way ANOVA on the effect of SCL material and years of previous SCL wear. A negative value indicates steeper SimK and positive indicates flatter SimK at the second visit. Statistically significant differences are shown in shaded cells ($p < 0.05$).

A.5.1.9 Corneal topographical indices following 2 weeks cessation of SCL wear

The influence of SCL wear on corneal topographical indices following 2 weeks cessation were compared between the SCL and NCL control groups. Results of Mann-Whitney U testing found that although the vertical asymmetry, keratoconus, height asymmetry and aberration coefficient indices were higher in the SCL group, there were no statistically significant differences in corneal topographical indices between study groups at the second visit (SCL vs. NCL) (Table A-13).

Table A-13: Topographical Indices at the second visit

	CL group Mean ±SD (n = 38)	**NCL group Mean ±SD (n = 37)**	**Sig.**
Surface variance	13.89 ±3.15	14.49 ±3.49	0.54
Vertical asymmetry	0.13 ±0.54	0.12 ±0.63	0.28
Keratoconus	1.02 ±0.19	1.01 ±0.16	0.10
Central keratoconus	1.00 ±0.01	1.00 ±0.01	0.55
Height asymmetry	3.09 ±2.65	3.54 ±2.20	0.15
Height decentration	0.007 ±0.00	0.006 ±0.00	0.46
Radii minimum	7.61 ±0.23	7.67 ±0.25	0.45
Aberration coefficient	1.20 ±0.59	1.01 ±0.63	0.25

Mean ±SD of topographical indices data prior to and following 2 weeks cessation of SCL wear. Results of Mann-Whitney U tests show the indices to be similar between the SCL and NCL control group. There were no statistically significant differences between the groups ($p>0.05$).

The effect of SCL material and previous years of SCL wear on the stability of topographical indices following 2 weeks cessation of SCL wear was compared between the SCL and NCL groups. Two-way ANOVA and Kruskal-Wallis testing were carried out. The mean index of vertical asymmetry (IVA) in the hydrogel group increased at

the second visit (IVA: mean ±SD: -0.01 ±0.03), whereas, the IVA index in the SiHy group reduced at the second visit (IVA: mean ±SD 0.03 ±0.03), as the resolution of central flattening occurred following cessation of SCL wear (Table A-14). Results of two-way ANOVA indicate that SCL material had a significant effect on the index of vertical asymmetry (IVA $p = 0.02$), however results of Kruskal-Wallis testing were not statistically significant ($p = 0.08$). The topographical indices were not different between the first and second visits in the NCL group, there was no significant influence of years of SCL wear or the interaction effect of SCL material and years of lens wear on corneal indices between groups.

Table A-14: Topographical indices, wearing time and CL material

	Surface variance Mean ±SD	**Vertical asymmetry Mean ±SD**	**Keratoconus Mean ±SD**	**Central keratoconus Mean ±SD**
Hydrogel n = 30	0.25 ±2.05	0.01 ±0.03	-0.00 ±0.01	-0.00 ±0.01
SiHy n = 6	-2.00 ±2.76	-0.03 ±0.03	-0.01 ±0.01	-0.00 ±0.00
Sig Two-way ANOVA (Kruskal – Wallis)	0.05 (0.19)	0.02 (0.08)	0.60 (0.30)	0.81 (0.96)
Short-term n = 9	-0.11 ±3.59	0.01 ±0.05	0.00 ±0.01	0.00 ±0.01
Medium-term n = 19	0.12 ±1.65	0.01 ±0.02	0.00 ±0.01	0.00 ±0.01
Long-term n = 7	-0.71 ±2.06	-0.02 ±0.02	0.00 ±0.01	0.00 ±0.00
NCL n = 37	-0.03 ±2.67	-0.00 ±0.04	0.00 ±0.01	0.00 ±0.01
Sig Two-way ANOVA (Kruskal – Wallis)	0.38 (0.77)	0.08 (0.07)	0.80 (0.13)	0.94 (0.65)
	Height asymmetry Mean ±SD	**Height decentration Mean ±SD**	**Radii minimum Mean ±SD**	**Aberration coefficient Mean ±SD**
Hydrogel n = 30	0.03 ±2.50	0.00 ±0.00	-0.02 ±0.05	-0.14 ±0.64
SiHy n = 6	-0.43 ±3.84	0.00 ±0.00	0.03 ±0.05	0.23 ±0.71
Sig Two-way ANOVA (Kruskal – Wallis)	0.93 (0.87)	0.16 (0.47)	0.47 (0.38)	0.37 (0.82)
Short-term n = 9	0.18 ±3.02	0.00 ±0.00	0.01 ±0.06	0.21 ±0.72
Medium-term n = 19	0.01 ±2.71	0.00 ±0.00	-0.01 ±0.04	--0.22 ±0.55
Long-term n = 7	-0.37 ±2.91	0.00 ±0.00	-0.03 ±0.05	0.1 ±0.72
NCL n = 37	-0.59 ±3.10	0.00 ±0.00	0.01 ±0.07	0.02 ±0.8
Sig Two-way ANOVA (Kruskal – Wallis)	0.86 (0.98)	0.52 (0.76)	0.87 (0.18)	0.47 (0.66)

Mean ±SD of difference in corneal indices between the first and second visits in SCL material and years of SCL wear groups. A negative value indicates a decrease in index and positive indicates increase in index at the second visit. Statistically significant differences are shown in shaded cells ($p < 0.05$).

A.5.1.10 The influence of SCL wear on corneal posterior elevation

The influence of SCL wear on posterior corneal elevation at the first and second visits and the stability of these measurements was explored using independent *t*-testing and Mann-Whitney U testing. Results showed a mean forward protrusion present in both the SCL and NCL control groups, with the SCL group showing greater forward protrusion compared with the NCL control group. However, there were no statistically significant differences between the groups at any time measured (see Table A-15).

Table A-15: Corneal posterior elevation

First visit	**SCL group (n = 45) Mean ±SD**	**NCL group (n = 45) Mean ±SD**	**Independent *t* test Sig**	**Mann Whitney U test Sig**
Posterior elevation at first visit (mm)	1.69 ±2.95	1.33 ±2.80	0.56	0.42
Second visit	**(n = 38)**	**(n = 37)**		
Posterior elevation at second visit (mm)	1.18 ±3.38	1.38 ±3.21	0.79	0.92
Difference in posterior elevation following 2 weeks cessation of SCL wear (mm)	0.67 ±2.34	0.20 ±2.21	0.33	0.44

Mean ±SD and results of t-tests and Mann-Whitney U-tests of posterior elevation measurements taken at the first and second visits in the SCL and NCL control groups. A positive number represents measurement above the reference body or forward protrusion of the cornea relative to the best-fit sphere (similar to ectatic changes). The mean ±SD of the difference between the first and second visits was also analysed, a positive number represents less forward protrusion, the mean difference was positive in both groups (SCL and NCL), differences did not reach statistical significance (all p-values > 0.05).

Hydrogel and SiHy SCL materials can result in contrasting changes to corneal curvature as discussed in section 4.1.1. The influence of SCL material and previous SCL wearing time on posterior elevation was explored. It was hypothesised that hydrogel SCL

wearers would have increased posterior elevation compared with the SiHy and NCL control groups, due to the low DK/t of these lens materials. It was also hypothesised that this effect would be greater with increasing years of SCL wear. A two-way ANOVA statistical analysis showed a tendency for increased forward protrusion in the hydrogel group at the first visit. At the second visit there was increased forward protrusion in the SiHy group. No tendency for increasing forward protrusion was seen with increasing years of SCL wear. No statistically significant differences in posterior elevation either at the first or second visits or in the difference in measurements between the first and second visits were found between the groups (SCL material and years of SCL wear, or the interaction between these groups) (Table A-16).

Table A-16: The effect of CL material and wearing time on corneal elevation

Posterior elevation	**Hydrogel**	**SiHy**	**Sig**	**Short-term**	**Medium-term**	**Long-term**	**NCL**	**Sig**
First visit	n = 34	n = 6	0.75	n = 12	n = 21	n = 8	n = 45	0.26
	1.56 ±2.66	1.20 ±4.44		-0.20 ±2.59	2.21 ±2.94	1.00 ±3.56	1.63 ±3.39	
Second visit	n = 29	n = 6	0.97	n = 9	n = 19	n = 7	n = 37	0.28
	1.11 ±2.63	1.40 ±5.41		-0.20 ±3.11	2.14 ±3.3	-0.50 ±2.65	2.37 ±3.73	
Stability between first and second visits	0.94 ±2.04	2.4 ±3.29	0.56	0.20 ±1.79	1.93 ±2.56	0.25 ±1.71	1.37 ±2.99	0.57

A positive number represents measurement above the reference body or forward protrusion of the cornea relative to the best-fit sphere (similar to ectatic changes) at First and second visits. The difference between First and second visits was also analysed, a positive number represents less forward protrusion, the mean difference was positive in both groups.

A.5.1.11 The influence of SCL wear on corneal thickness

A.5.1.11.1 Time of measurement

Mann-Whitney U testing explored the differences in the mean time of Pentacam measurement taken at first and second visits and post-operatively between the groups (SCL vs. NCL) (Table A-17). Results showed that there were no statistically significant differences between the time of Pentacam measurements between the SCL and NCL control groups at first, second or post-operative visits.

Table A-17: Time of Pentacam measurements

Time of measurement	**SCL group (n = 45)**	**NCL group (n = 45)**	**Sig.**
First visit (hours)	12.66 ±2.55	12.44 ±2.91	0.46
Second visit (hours)	13.56 ±2.70	13.59 ±2.90	0.93
Post-operatively (hours)	12.48 ±2.58	12.06 ±2.77	0.47

Mean ±SD and results of Mann-Whitney U testing for the time of Pentacam measurements taken at first visit, second visit and post-operatively, ($p < 0.05$).

To investigate possible diurnal variation on CCT, the groups (SCL vs. NCL) were divided into morning (measurements taken before 14.00 hours) and afternoon (measurements taken after 14.00 hours). CCT was the value measured at the pupil centre as determined by Pentacam software. The mean CCT were compared using a two-way ANOVA for the SCL and NCL control groups. Results showed that the time the measurements were taken or previous SCL wear did not have a significant effect on CCT measurements (Table A-18).

Table A-18: Corneal thickness and time of measurement for SCL and NCL control group at the first and second visits.

	SCL group (µm)	**NCL control group (µm)**	**Time Sig**	**SCL wear Sig**	**Interaction Sig**
First visit					
Morning (8.30-14.00 hours)	535.10 ±32.02 (n = 30)	540.45 ±25.11 (n = 31)	0.29	0.67	0.74
Afternoon (14.00- 19.00 hours)	530.00 ±31.93 (n = 15)	530.64 ±37.41 (n = 14)			
Second visit					
Morning (8.30-14.00 hours)	528.13 ±30.45 (n = 22)	540.58 ±26.24 (n = 19)	0.62	0.38	0.38
Afternoon (14.00-19.00hours)	530.88 ±33.94 (n = 16)	530.88 ±30.31 (n = 17)			

Mean ±SD and results of two-way ANOVA for the time of Pentacam measurements taken for the morning and afternoon groups of SCL and NCL wearers at the first and second visit ($p < 0.05$).

A.5.1.11.2 The influence of SCL material and previous wearing times on corneal thickness

The influence of SCL material and years of SCL wear on corneal thickness was explored using two-way ANOVA testing. There was a trend towards reduced corneal thickness in both lens materials groups compared with the NCL control group, with lowest corneal thickness values was found in the SiHy group. However no statistically significant differences were found between corneal thickness measured in the SCL material or years of previous wear groups (Table A-19).

Table A-19: Corneal thickness for SCL material and years of wear groups at first visit.

Corneal thickness	Central (µm)	Thinnest (µm)	Inferior (µm)	Nasal (µm)	Superior (µm)	Temporal (µm)
Hydrogel (n = 35)	533.09 ±30.92	530.94 ±30.65	599.71 ±29.91	609.71 ±30.12	646.29 ±36.02	592.71 ±29.97
SiHy (n = 6)	523.17 ±27.27	521.17 ±27.3	593.5 ±29.62	600 ±20.36	636.83 ±33.77	591.17 ±25.71
Sig: SCL material	0.55	0.58	0.74	0.45	0.52	0.61
Short-term (n = 11)	515.45 ±27.13	513.36 ±26.9	585.82 ±26.89	596.36 ±25.01	632.45 ±32.16	574.91 ±27.51
Medium-term (n = 21)	539.67 ±30.54	537.29 ±30.37	603.9 ±31.4	615 ±32.09	652.48 ±37.92	601 ±28.79
Long-term (n = 21)	535.88 ±28.61	534.25 ±28.29	605.25 ±26.91	610.25 ±21.97	646.5 ±31.69	596.88 ±24.52
Sig: years previous wear	0.52	0.52	0.71	0.76	0.80	0.47
NCL (n = 45)	537.4 ±29.4	535.04 ±29.6	607.18 ±32.63	619.02 ±32.12	649.02 ±35.84	601.27 ±34.39

Mean ±SD of corneal thickness for SCL material and years of wear groups at first visit. Results of two-way ANOVA indicate there are no significant effects of either SCL material, years of SCL wear or the interaction effect of the 2 groups on corneal thickness at first visit, ($p < 0.05$).

A.5.1.12 The effect of 2 weeks SCL cessation on corneal thickness

A comparison of the differences in corneal thickness between the SCL and NCL groups was carried out following 2 weeks cessation of SCL wear. While corneal thickness remained thinner in the SCL group compared with the NCL group, results of two-way ANOVA showed that there were no statistically significant differences between the groups (Table A-20).

Table A-20: Corneal thickness at the second visit

Location of corneal thickness	SCL group (n = 38) Mean ±SD (µm)	NCL group (n = 37) Mean ±SD (µm)	Sig
Central	529.26 ±31.51	536.00 ±28.25	0.33
Thinnest value	527.00 ±31.81	534.22 ±29.57	0.31
Inferior	596.23 ±31.19	607.83 ±32.26	0.12
Nasal	607.56 ±28.96	618.61 ±31.44	0.12
Superior	643.13 ±36.57	648.64 ±38.65	0.53
Temporal	589.46 ±33.22	599.94 ±29.56	0.15

Mean ±SD of corneal thickness data measured at the second visit and two-way ANOVA statistics comparing SCL and NCL control groups. There were no significant differences between the groups ($p < 0.05$).

A.5.1.12.1 The influence of SCL material and previous SCL wear on corneal thickness stability following 2 weeks cessation of SCL wear

Stabilisation of corneal thickness can vary according to the lens material worn, and the amount of years SCL were worn prior to lens cessation (see section 6.1). Results of two-way ANOVA showed no statistically significant effect of SCL material of years of previous SCL wear on the stability of corneal thickness measured at first visit and following 2 weeks cessation of SCL wear (Table A-21).

Table A-21: Stability of corneal thickness between the first and second visits for the SCL material and years of SCL wear groups.

Corneal thickness	Central (µm)	Thinnest (µm)	Inferior (µm)	Nasal (µm)	Superior (µm)	Temporal (µm)
Hydrogel (n = 30)	1.00 ±7.79	0.97 ±8.26	3.43 ±11.56	2.57 ±11.66	2.87 ±13.07	0.97 ±9.06
SiHy (n =6)	3.67 ±8.73	3.50 ±9.09	3.17 ±9.60	11.00 ±10.95	-0.33 ±13.85	0.17 ±11.58
Sig: SCL material	0.55	0.58	0.95	0.14	0.80	0.84
Short-term (n = 9)	-0.11 ±5.71	-0.56 ±6.39	0.67 ±8.23	3.11 ±12.69	2.33 ±13.96	-4.67 ±8.11
Medium-term (n = 19)	1.32 ±9.72	1.32 ±10.02	2.89 ±12.32	3.79 ±13.79	1.05 ±15.01	1.84 ±10.44
Long-term (n = 7)	4.00 ±4.90	4.43 ±5.56	9.00 ±11.11	6.00 ±4.76	6.29 ±5.77	4.71 ±5.19
Sig: years previous wear	0.60	0.49	0.47	0.73	0.88	0.11
NCL (n = 36)	-2.53 ±7.41	-1.83 ±7.39	-0.58 ±11.45	-1.72 ±8.71	-2.50 ±10.87	-0.17 ±8.72

Mean ±SD of the differences in corneal thickness between first and second visits for SCL material and years of wear groups. Positive values represent an increase in corneal thickness; while a negative number represents a decrease at the second visit. Results of two-way ANOVA indicate no significant effects of either SCL material, years of SCL wear or the interaction effect of the 2 groups on the differences in corneal thickness between the first and second visits, ($p < 0.05$).

A.5.1.12.2 The influence of SCL material and previous SCL wear on the accuracy of ablation depth following CRS

The influence of SCL material, years of SCL wear and the refractive procedure carried out on the difference between expected and actual ablation depth following CRS was examined. Results of two-way ANOVA showed a trend towards less than expected change post-operatively in the hydrogel group and greater than expected change in the SiHy group. There was less than expected change with increasing years of SCL wear, with the long-term SCL group showing an ablation depth of -18.8 ±20.34µm less than

expected. There were no SiHy lens wearers in this long-term wear group. Therefore, this could be due to thinning of the cornea with hydrogel SCL wear, which had begun to resolve post-operatively. However, two-way ANOVA yielded no statistically significant effect for the influence of SCL wear, the effect of the Laser procedure performed or for the interaction effect of the CL and Laser procedure groups (Table A-22).

Table A-22: The effect of SCL material, years of SCL wear and refractive procedure on the difference between expected and actual ablation depth.

	LASIK Mean ±SD (µm)	**LASEK Mean ±SD (µm)**		Sig
Hydrogel	-5.06 ±18.44 n = 12	-8.07 ±13.97 n = 6	**SCL material**	0.57
SiHy	5.7 ±5.46 n = 3	3.6 ±4.67 n = 2	**Years of SCL wear**	0.27
Short-term	3.15 ±0.83 n = 4	10.2 ±4.67 n = 6	**Refractive procedure**	0.65
Medium-term	0.03 ±18.03 n = 8	-11.56 ±11.2 n = 5	**Interaction: SCL material * Years of SCL wear * Procedure**	0.71
Long-term	-18.8 ±20.34 n = 3	n = 0		
NCL	0.51 ±12.19 n = 14	1.78 ±10.02 n = 13		

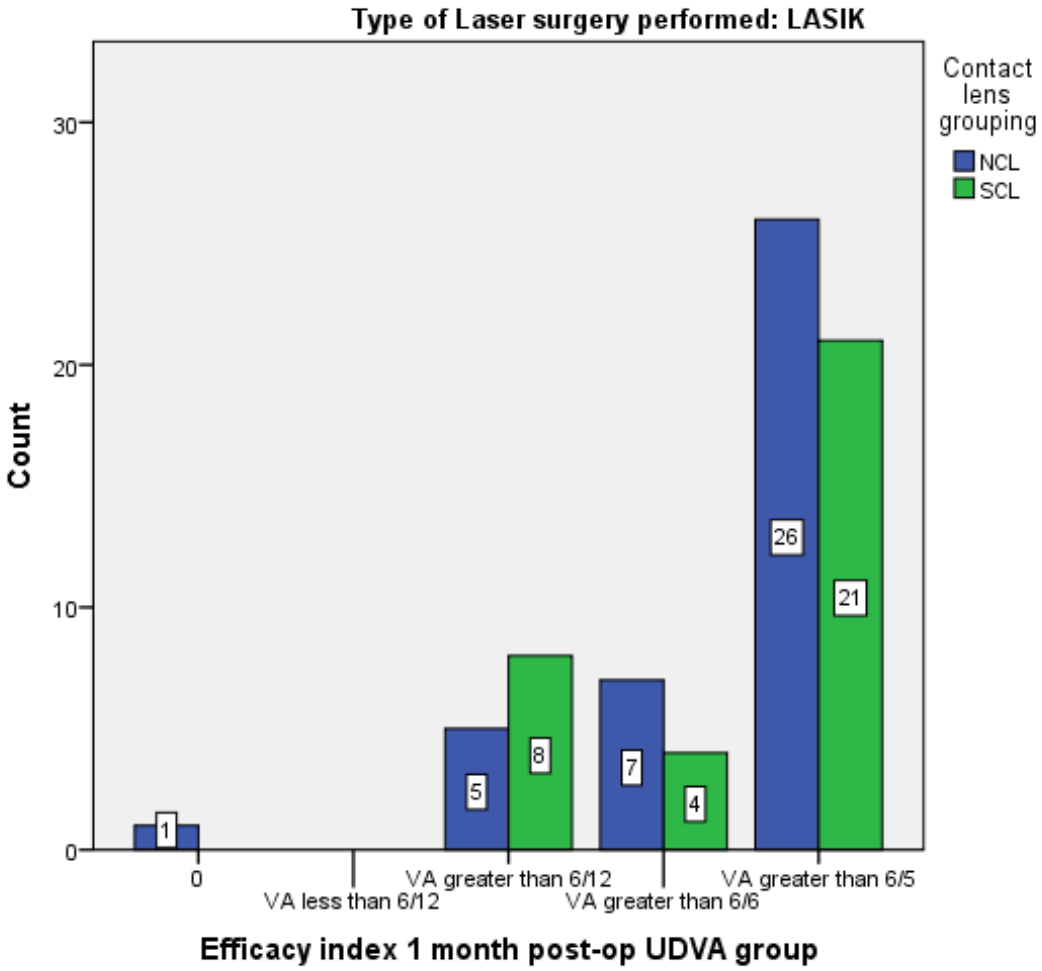
A negative value for the difference between expected and actual change in corneal thickness indicates there has been less than the expected change post operatively. Mean ±SD and results of two-way ANOVA on the effect of SCL material, years of SCL wear and refractive laser procedure performed on the difference between expected and actual ablation depth. There were no statistically significant differences between the groups ($P < 0.05$).

A.5.2 Study 2: The effect of 24 hours SCL cessation on pre-operative corneal measurements and on CRS outcomes.

A.5.2.1 Study 2: 1 month post-operative results

Graphs depicting the visual outcomes of CRS procedures performed in terms of efficacy and predictability at 1 month following surface LASEK/PRK or LASIK are displayed below.

Figure A-5: Efficacy index at the 1 month post-operative visit.



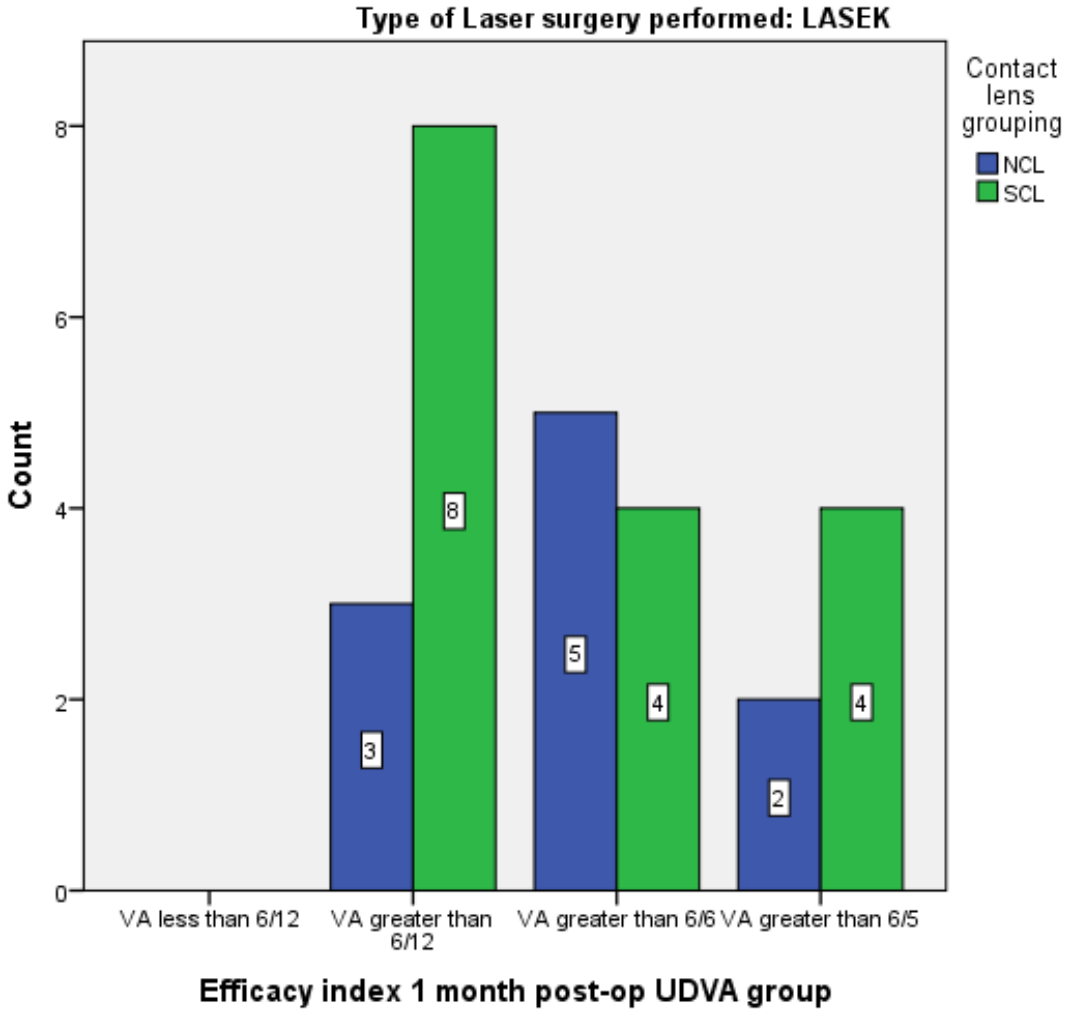
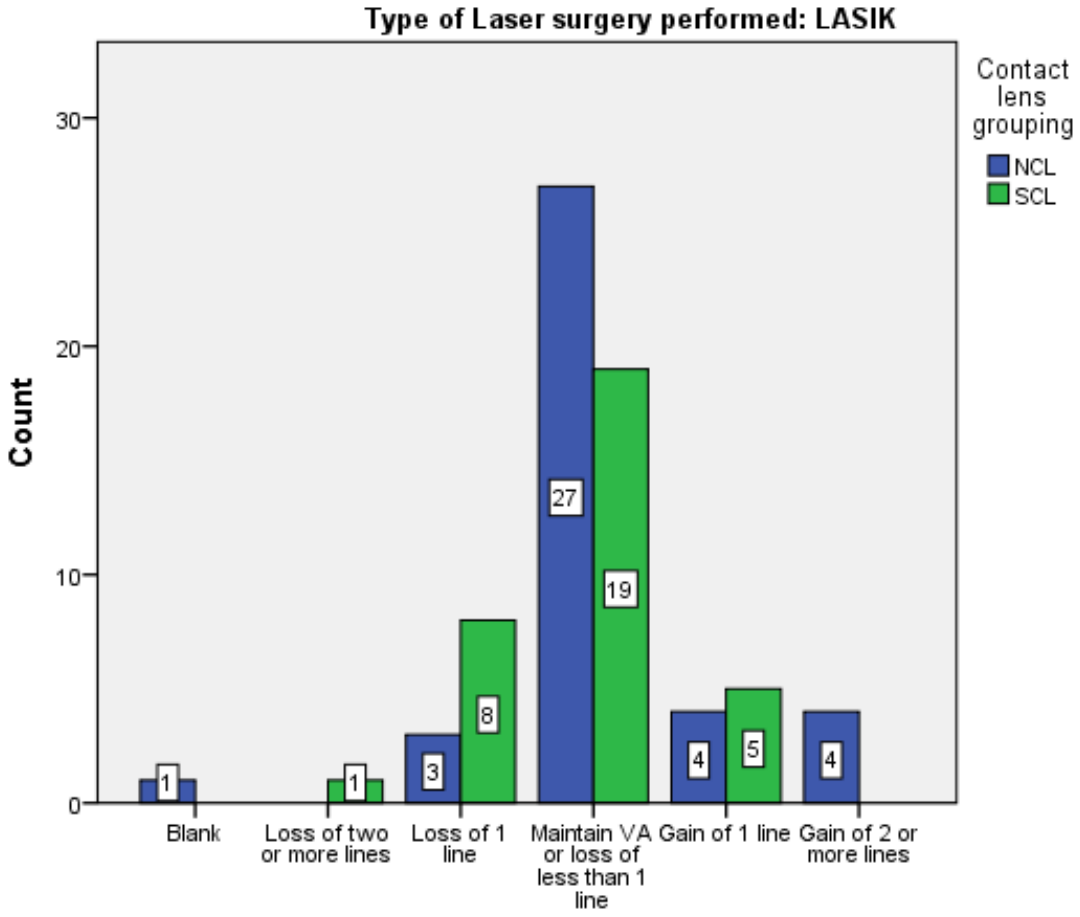

Type of Laser surgery performed: LASEK
Contact lens grouping
NCL
SCL
Count
0
2
4
6
8
3
8
5
4
2
4
VA less than 6/12
VA greater than 6/12
VA greater than 6/6
VA greater than 6/5
Efficacy index 1 month post-op UDVA group

Figure A-6: Comparision of pre-operative BCSVA and 1 month post-operative UDVA



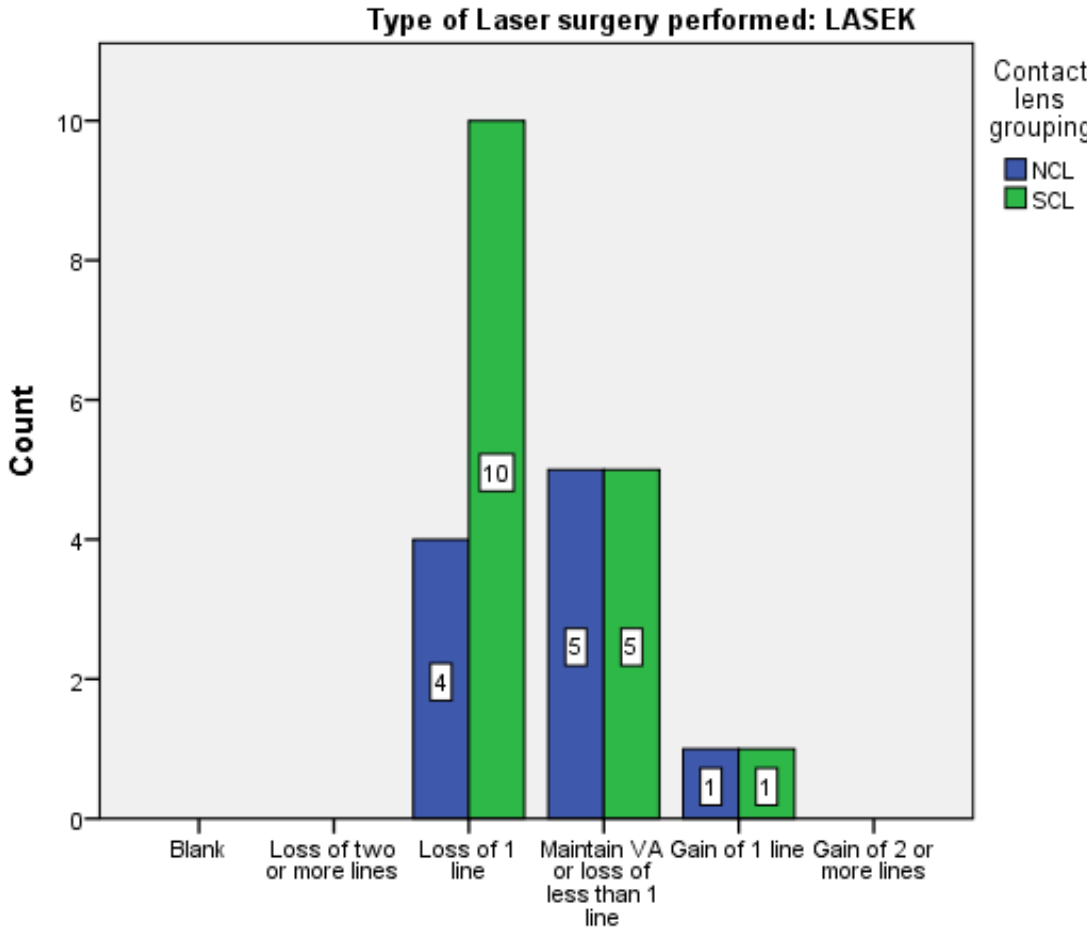
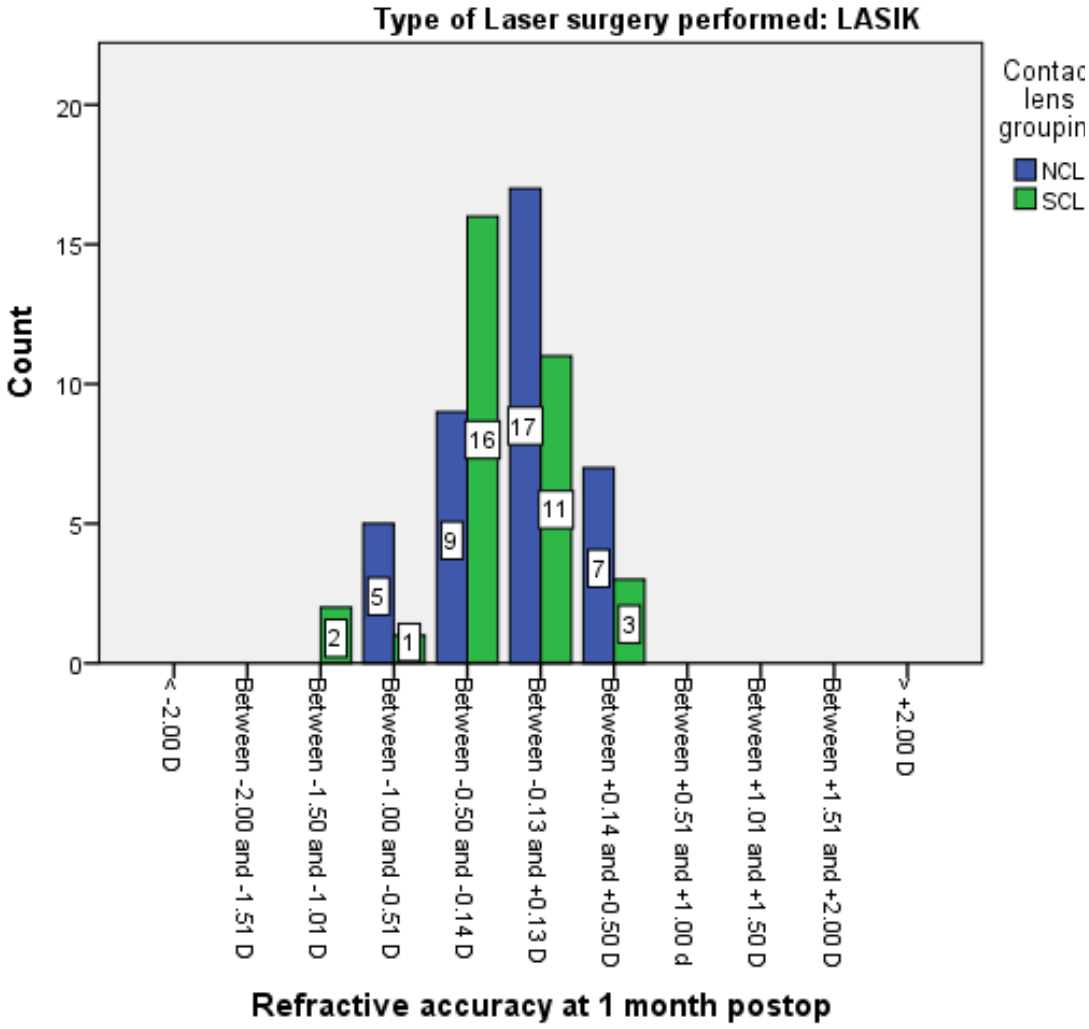

Type of Laser surgery performed: LASEK
Count
10
8
6
4
2
0
4
10
5
5
1
1
Blank
Loss of two or more lines
Loss of 1 line
Maintain VA or loss of less than 1 line
Gain of 1 line
Gain of 2 or more lines
Contact lens grouping
NCL
SCL

Figure A-7: Refractive accuracy for the 1 month post-operative visit.



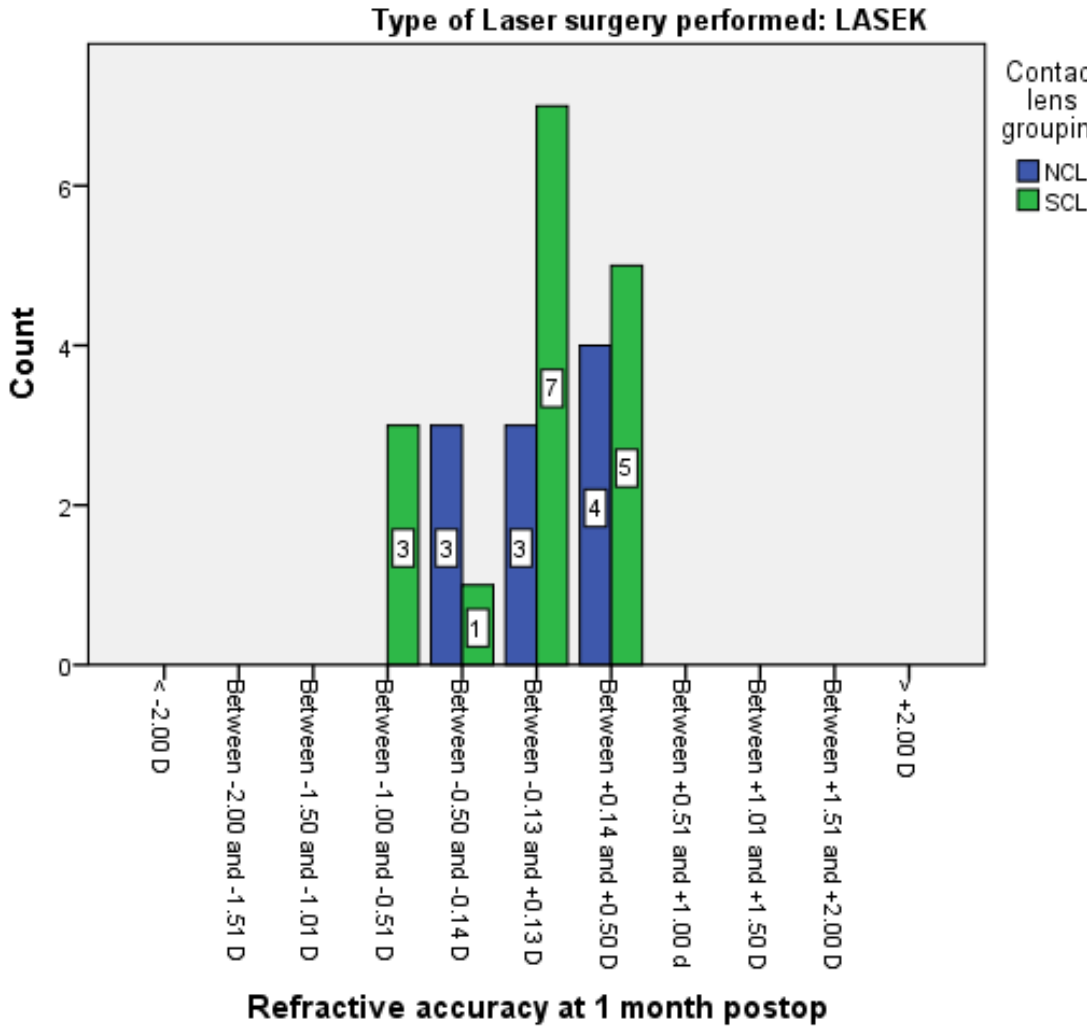
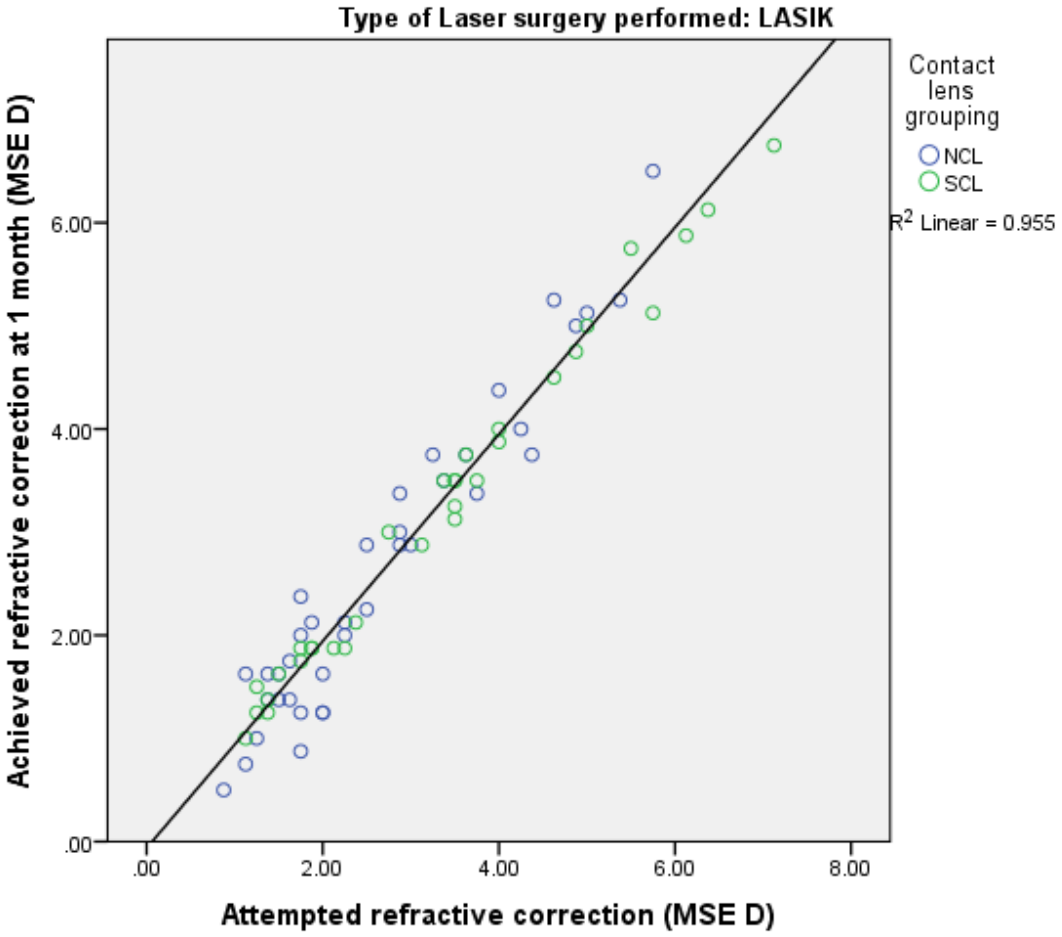

Type of Laser surgery performed: LASEK
Contac
lens
groupin
NCL
SCL
Count
0
2
4
6
3
3
1
3
7
4
5
< -2.00 D
Between -2.00 and -1.51 D
Between -1.50 and -1.01 D
Between -1.00 and -0.51 D
Between -0.50 and -0.14 D
Between -0.13 and +0.13 D
Between +0.14 and +0.50 D
Between +0.51 and +1.00 d
Between +1.01 and +1.50 D
Between +1.51 and +2.00 D
> +2.00 D
Refractive accuracy at 1 month postop

Figure A-8: Refractive accuracy at the 1 month post-operative visit.



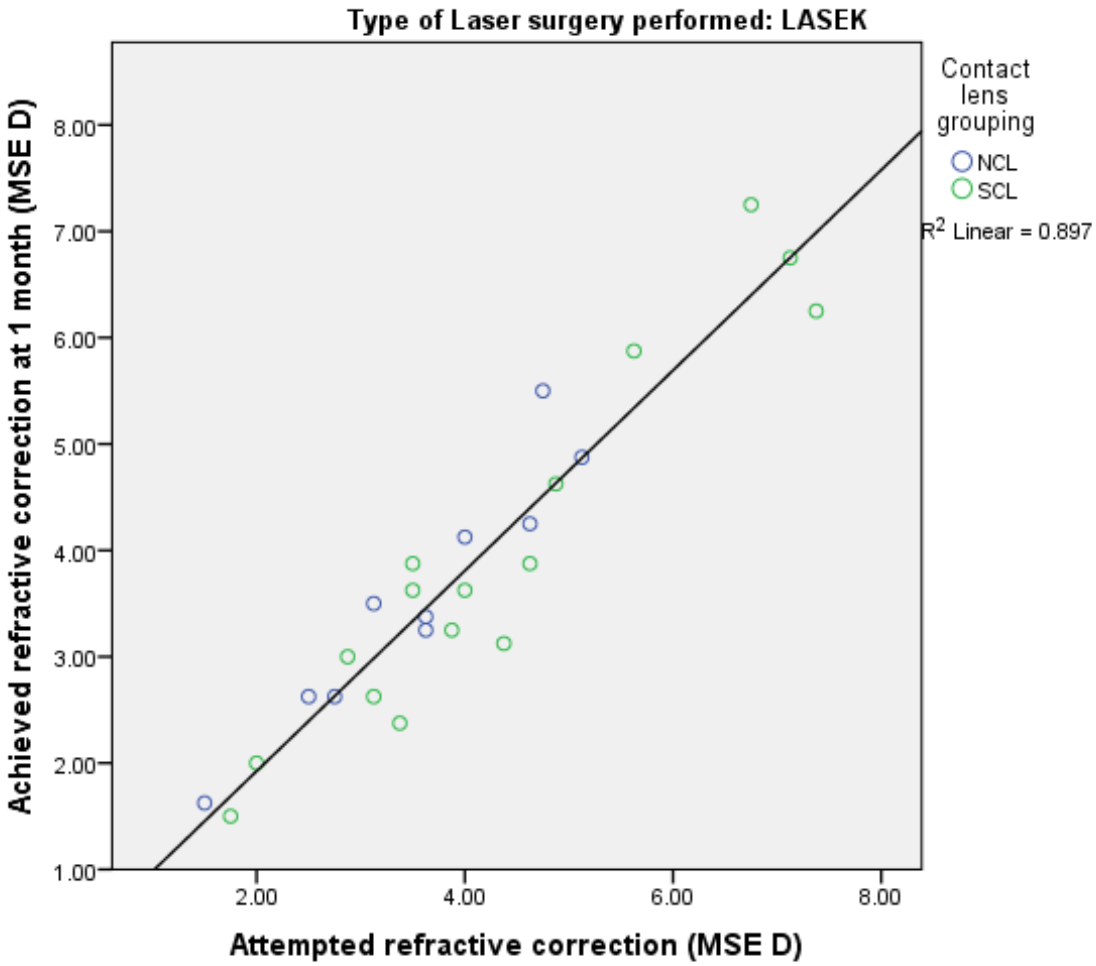
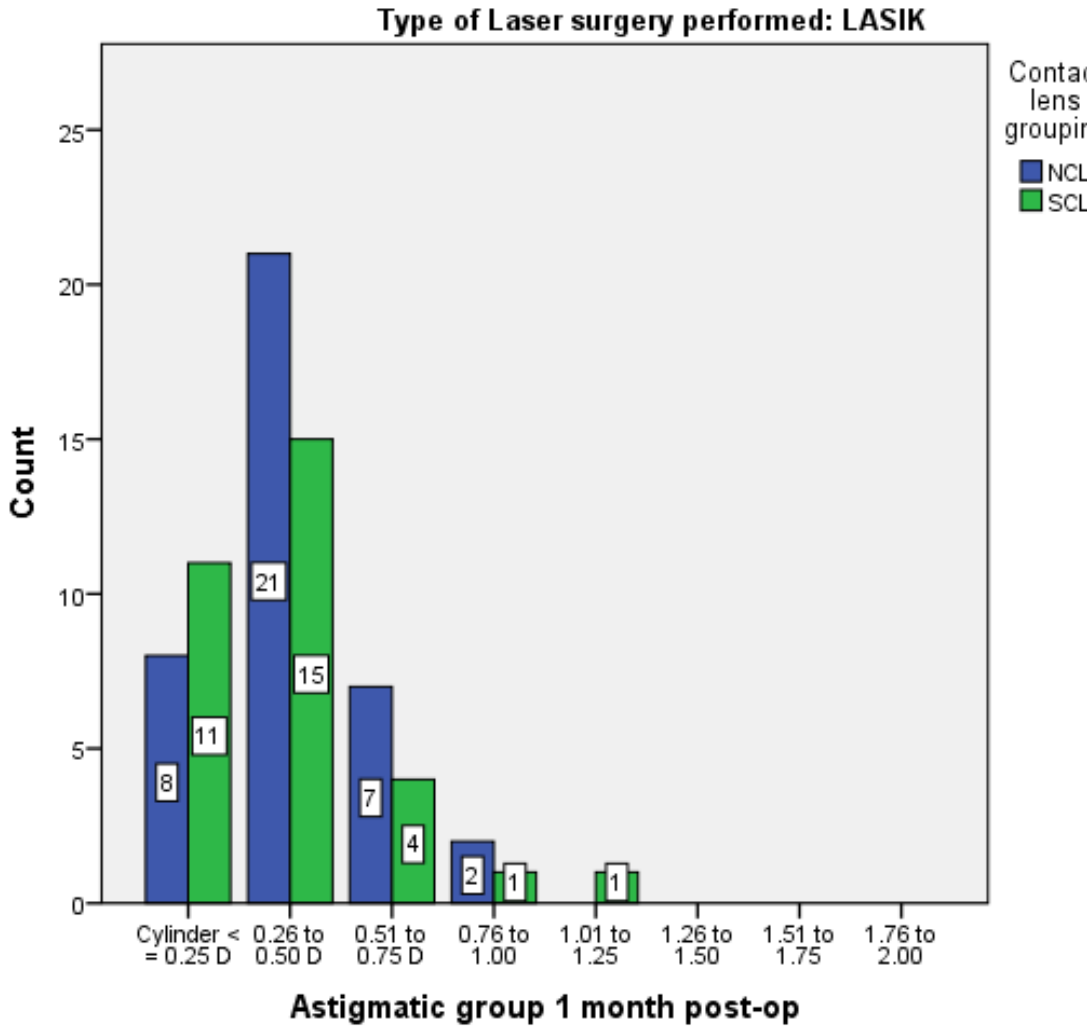
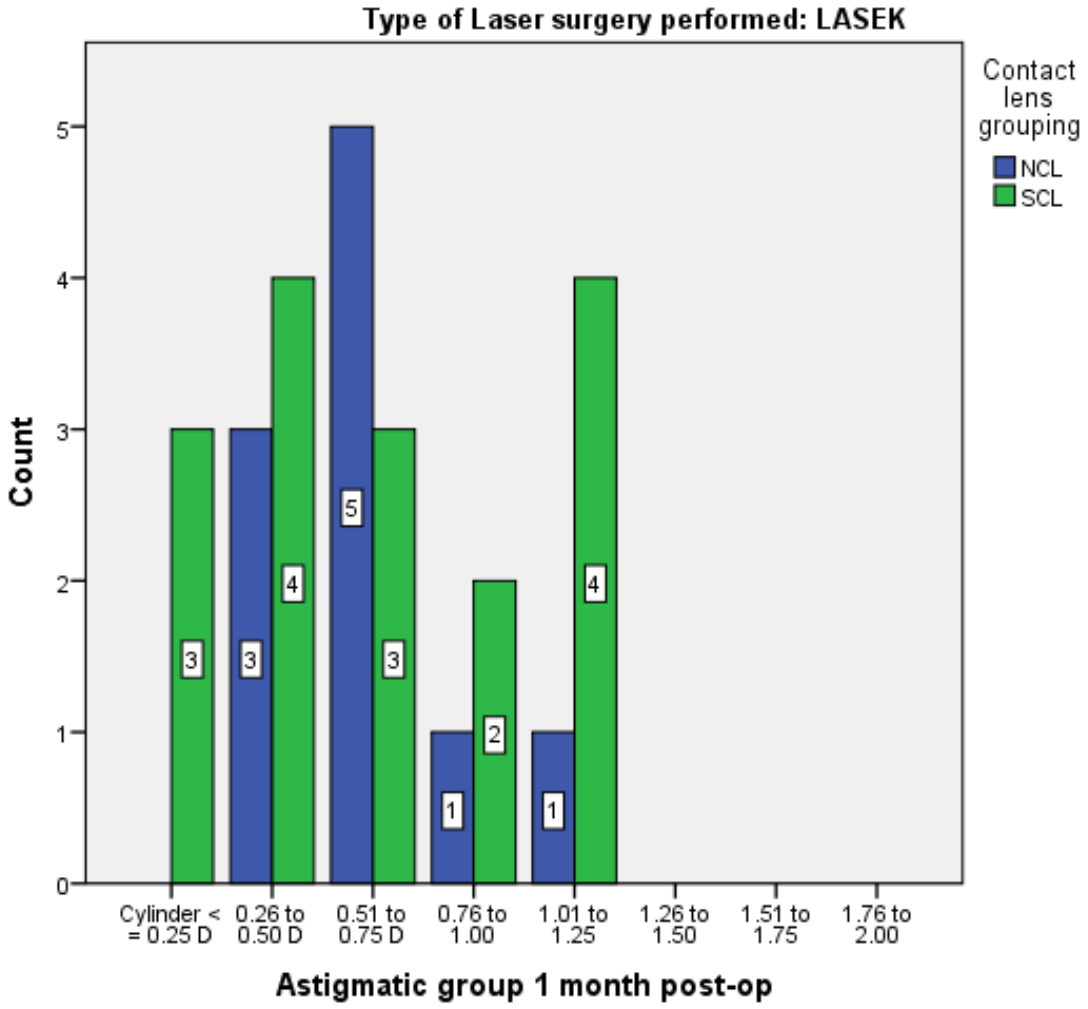

Type of Laser surgery performed: LASEK
Achieved refractive correction at 1 month (MSE D)
Attempted refractive correction (MSE D)
Contact lens grouping
NCL
SCL
R2 Linear = 0.897
1.00
2.00
3.00
4.00
5.00
6.00
7.00
8.00

Figure A-9: Refractive accuracy for astigmatism at the 1 month post-operative visit.




Type of Laser surgery performed: LASEK
Contact lens grouping
NCL
SCL
Count
0
1
2
3
4
5
3
3
4
5
3
1
2
1
4
Cylinder < = 0.25 D
0.26 to 0.50 D
0.51 to 0.75 D
0.76 to 1.00
1.01 to 1.25
1.26 to 1.50
1.51 to 1.75
1.76 to 2.00
Astigmatic group 1 month post-op

A.5.2.2 Study 2: the influence of myopic group on 1 month postoperative results for 2 weeks SCL cessation

The influence of the level of myopia on the outcomes of CRS at 1 months was explored using a two-way ANOVA (Table A-23). Analysis of the efficacy showed a significant effect of myopic group on efficacy for LASIK procedures; post hoc comparisons using the Bonferroni and Scheffe testing indicated that the mean UDVA measured one-month post operatively was significantly lower in the high myopic compared with the low myopic group (mean difference ±SD: -18.78 ±3.12) and the medium myopic group (mean difference ±SD: -18.19 ±3.14). Post hoc comparisons indicated that the mean residual cylindrical component of the refraction one-month post operatively was significantly higher in the high myopic group compared with the low myopic group (mean difference ±SD: 0.39 ±0.14). The MSE in the NCL control group was also significantly higher in the high myopic group compared with the low myopic group (mean difference ±SD: -0.17 ±0.24). There was only 1 patient in the highly myopic group who had LASIK carried out. As this was the only result which was statistically significant in this group, it is not possible to draw any conclusions from this finding. There were no statistically significant differences found between the groups for LASEK/PRK procedures.

Table A-23: Predictability and efficacy at 1 month for CL and myopic groups

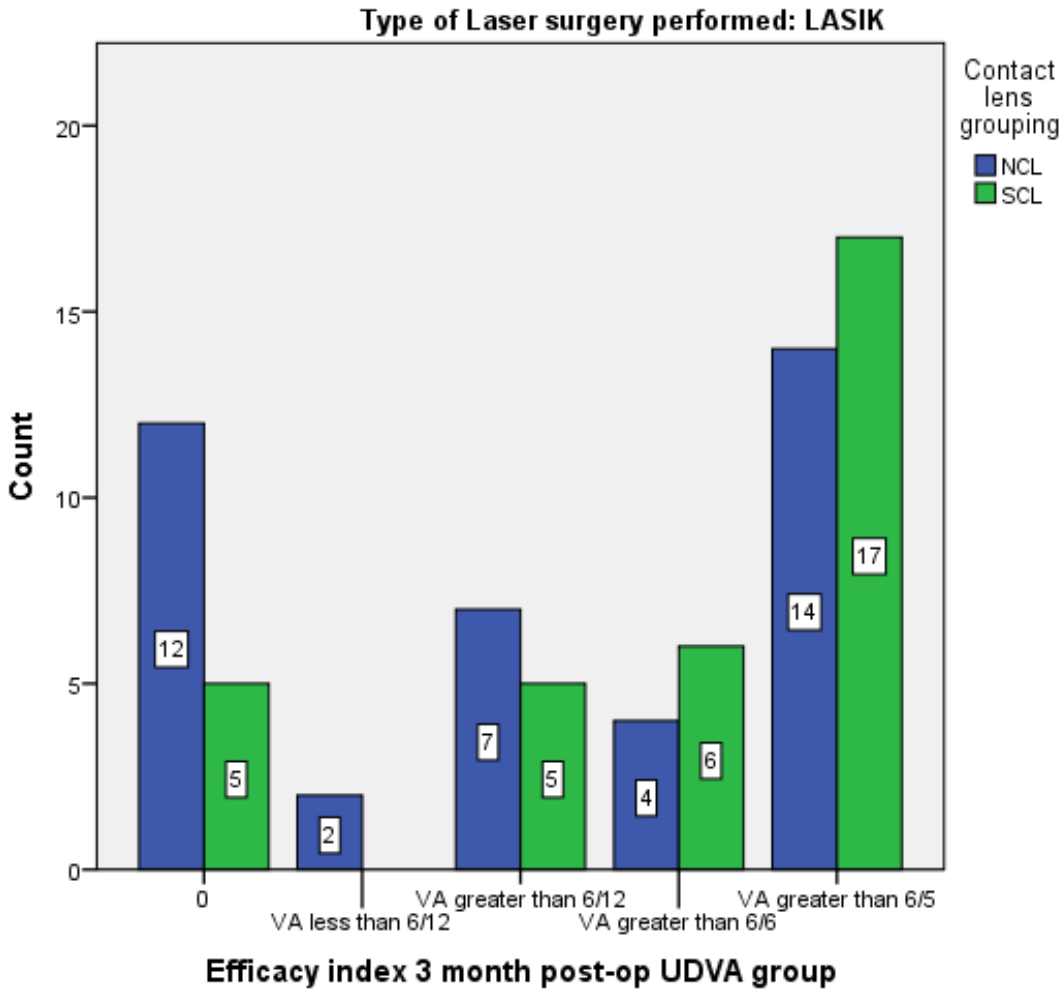
	LASIK			PRK/LASEK		
	SCL group Mean LogMAR ±SD	**NCL group Mean LogMAR ±SD**	**Sig**	**SCL group Mean LogMAR ±SD**	**NCL group Mean LogMAR ±SD**	**Sig**
Efficacy						
Low Myopes	-0.05 ±0.14 (n = 6)	-0.10 ±0.05 (n = 13)	0.00	-0.11 ±0.01 (n = 4)	0.02 ±0.10 (n = 12)	0.07
Medium Myopes	-0.06 ±0.09 (n = 10)	-0.04 ±0.09 (n = 5)		-0.05 ±0.09 (n = 12)	0.00 ±0.08 (n =6)	
High Myopes	0.07 ±0.21 (n = 3)	0.70 ±0 (n =1)		0.10 ±0 (n =1)	0.12 ±0 (n =1)	
Predictability						
Sphere (D)						
Low Myopes	0.30 ±0.27	0.08 ±0.47	0.22	-0.06 ±0.47	0.52 ±0.68	0.26
Medium Myopes	0.20 ±0.33	0.05 ±0.21		0.08 ±0.47	0.00 ±0.69	
High Myopes	1.00 ±0.00	-1.50 ±0.00		1.00 ±0.00	0.50 ±0.00	
Cylinder (D)						
Low Myopes	-0.45 ±0.21	-0.33 ±0.12	0.00	-0.38 ±0.25	-0.73 ±0.45	0.70
Medium Myopes	-0.45 ±0.22	-0.45 ±0.41		-0.54 ±0.45	-0.83 ±0.38	
MSE (D)						
High Myopes	-0.38 ±0.18	-1.50 ±0.00		-0.50 ±0.00	-0.75 ±0.00	
Low Myopes	0.08 ±0.31	-0.09 ±0.50	0.04	-0.25 ±0.43	0.16 ±0.64	0.23
Medium Myopes	-0.02 ±0.31	-0.18 ±0.34		-0.19 ±0.52	-0.42 ±0.83	
High Myopes	0.81 ±0.09	-2.25 ±0.34		0.75 ±0.00	0.13 ±0.00	

Mean ±SD and two-way ANOVA results for efficacy and predictability at one-month post-operative for SCL and myopic groups, low myopia (0 to -3.00D), medium myopia (-3.25 to -6.00D) and high myopia (>-6.00D). Statistically significant results are shown in shaded cells, ($p < 0.05$).

A.5.2.3 Study 2: 3 months post-operative results

Graphs depicting the visual outcomes of CRS procedures performed in terms of efficacy and predictability at 3 months following surface LASEK/PRK or LASIK are displayed below.

Figure A-10: Efficacy index at the 3 month post-operative visit.



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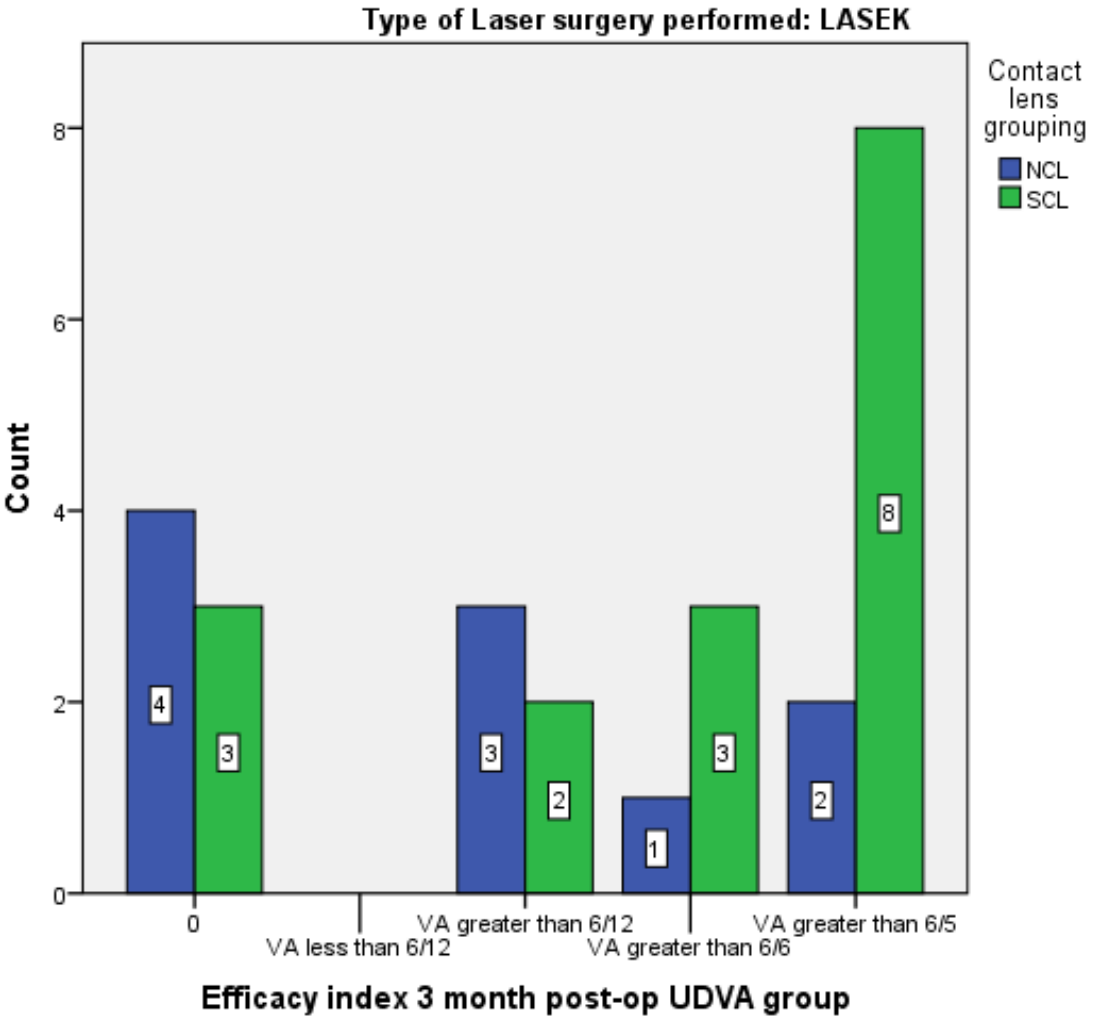
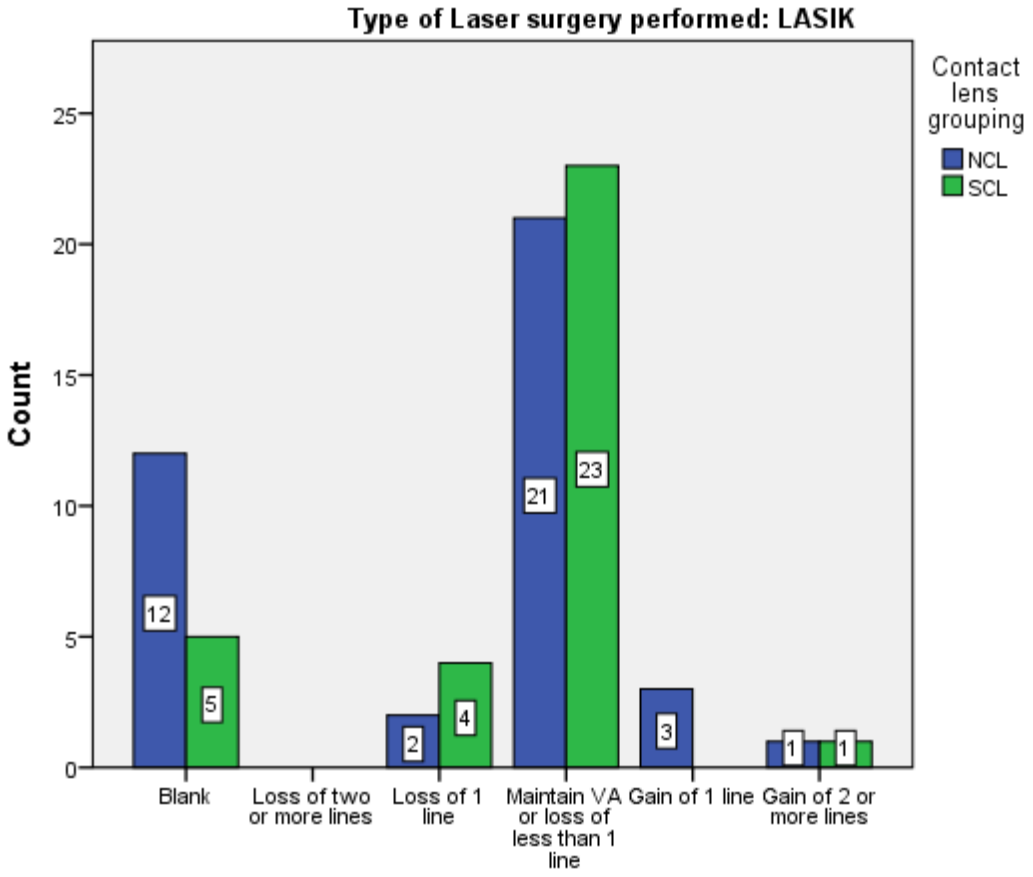
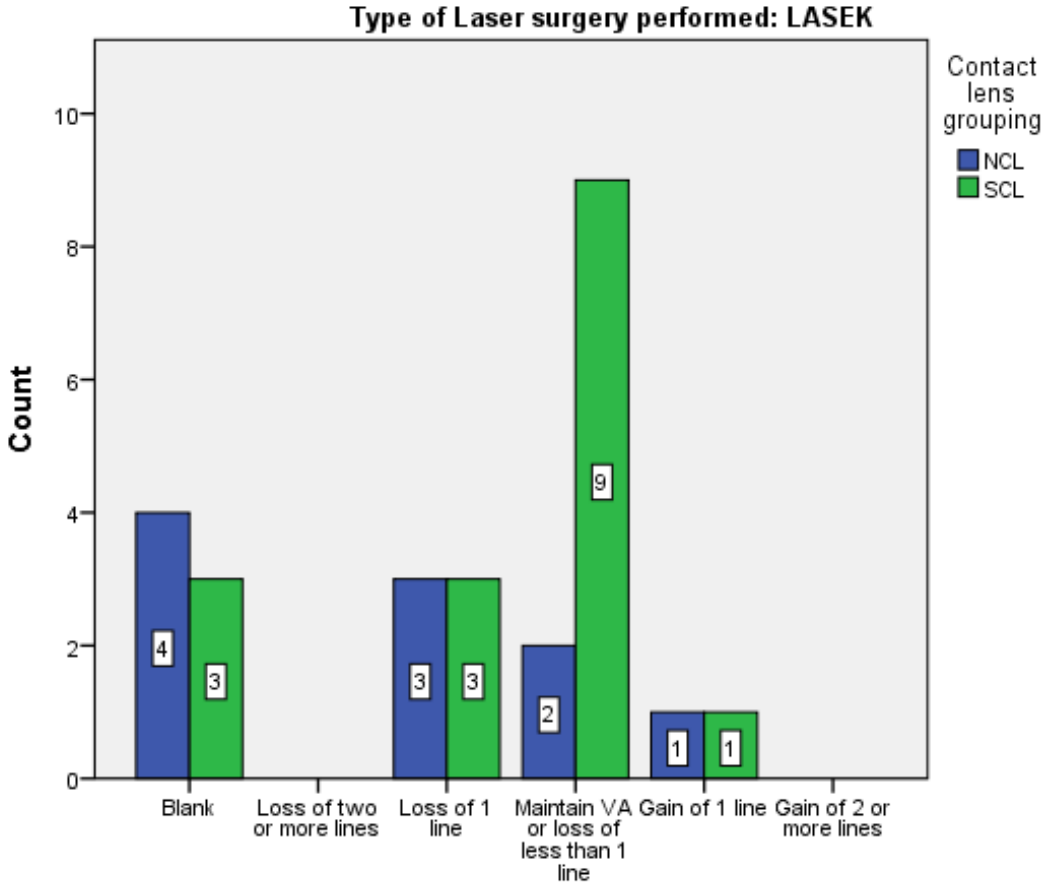
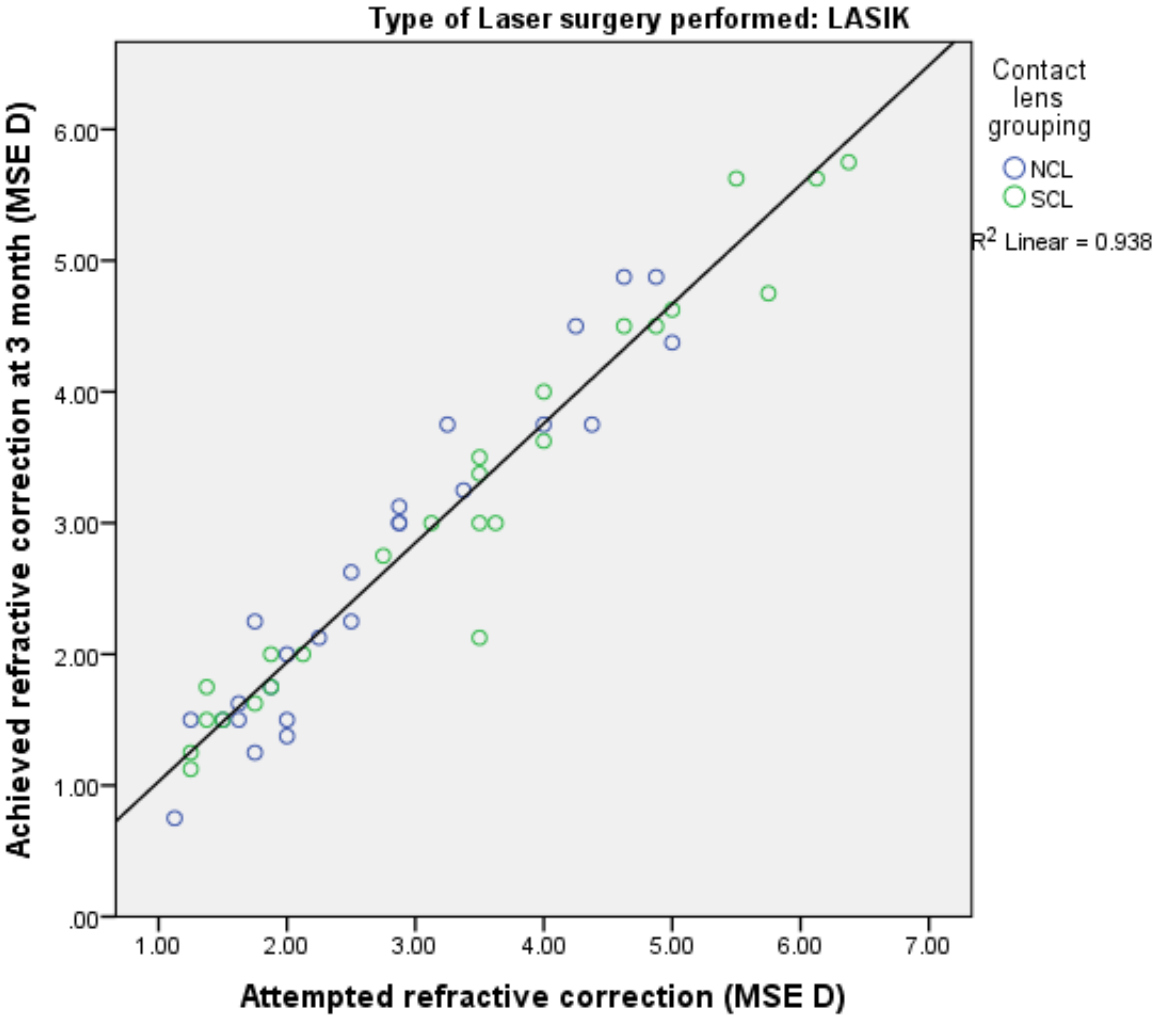

Type of Laser surgery performed: LASEK
Contact lens grouping
NCL
SCL
Count
0
2
4
6
8
4
3
3
2
1
3
2
8
0
VA less than 6/12
VA greater than 6/12
VA greater than 6/6
VA greater than 6/5
Efficacy index 3 month post-op UDVA group

Figure A-11: Comparision of pre-operative BCSVA and 3 month post-operative UDVA




Type of Laser surgery performed: LASEK
Count
10
8
6
4
2
0
4
3
3
3
2
9
1
1
Blank
Loss of two or more lines
Loss of 1 line
Maintain VA or loss of less than 1 line
Gain of 1 line
Gain of 2 or more lines
Contact lens grouping
NCL
SCL


Type of Laser surgery performed: LASIK
Achieved refractive correction at 3 month (MSE D)
6.00
5.00
4.00
3.00
2.00
1.00
.00
1.00
2.00
3.00
4.00
5.00
6.00
7.00
Attempted refractive correction (MSE D)
Contact lens grouping
NCL
SCL
R2 Linear = 0.938

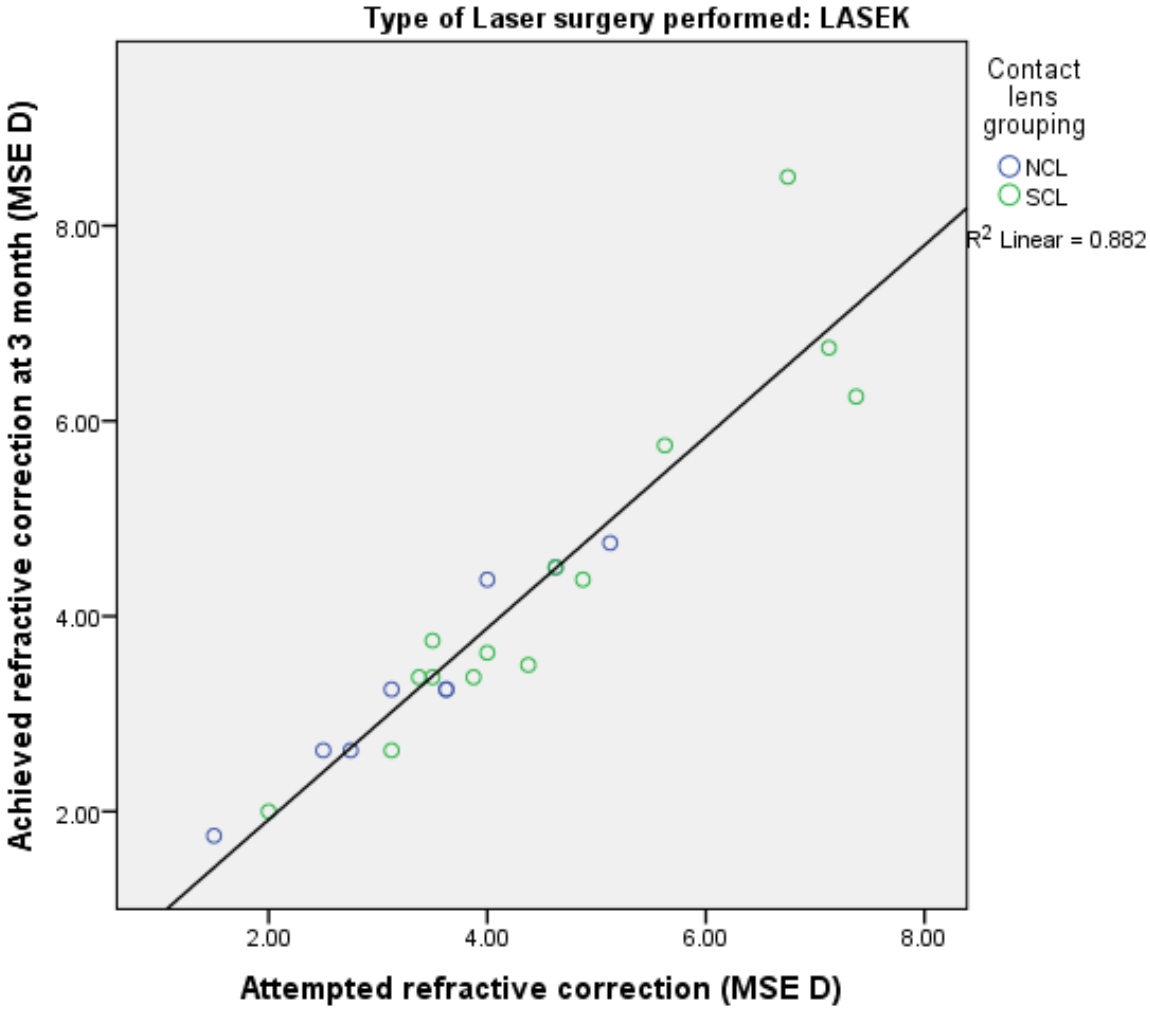
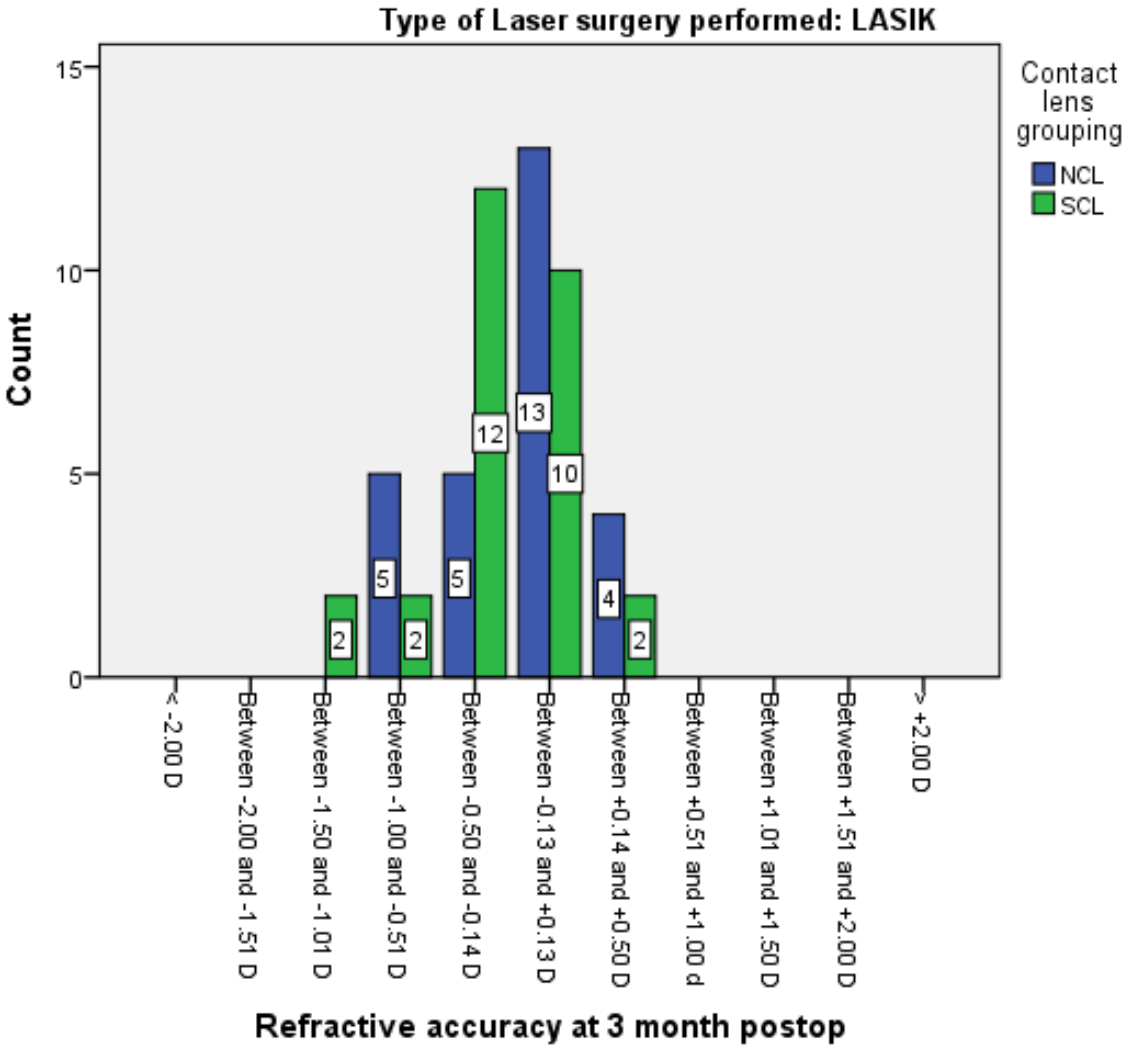

Type of Laser surgery performed: LASEK
Achieved refractive correction at 3 month (MSE D)
Attempted refractive correction (MSE D)
2.00
4.00
6.00
8.00
Contact lens grouping
NCL
SCL
R2 Linear = 0.882

Figure A-12: Refractive accuracy at the 3 month post-operative visit.



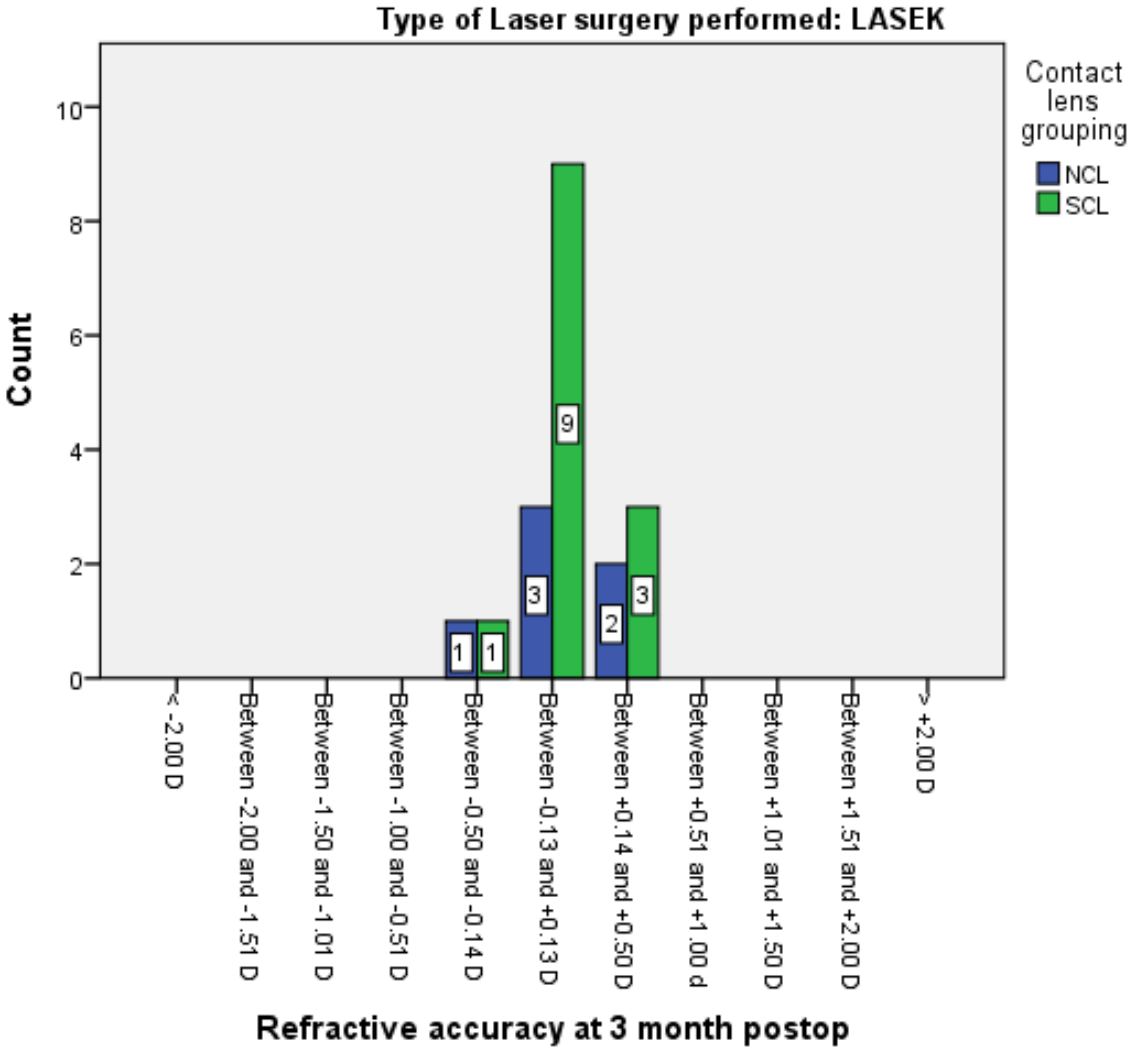
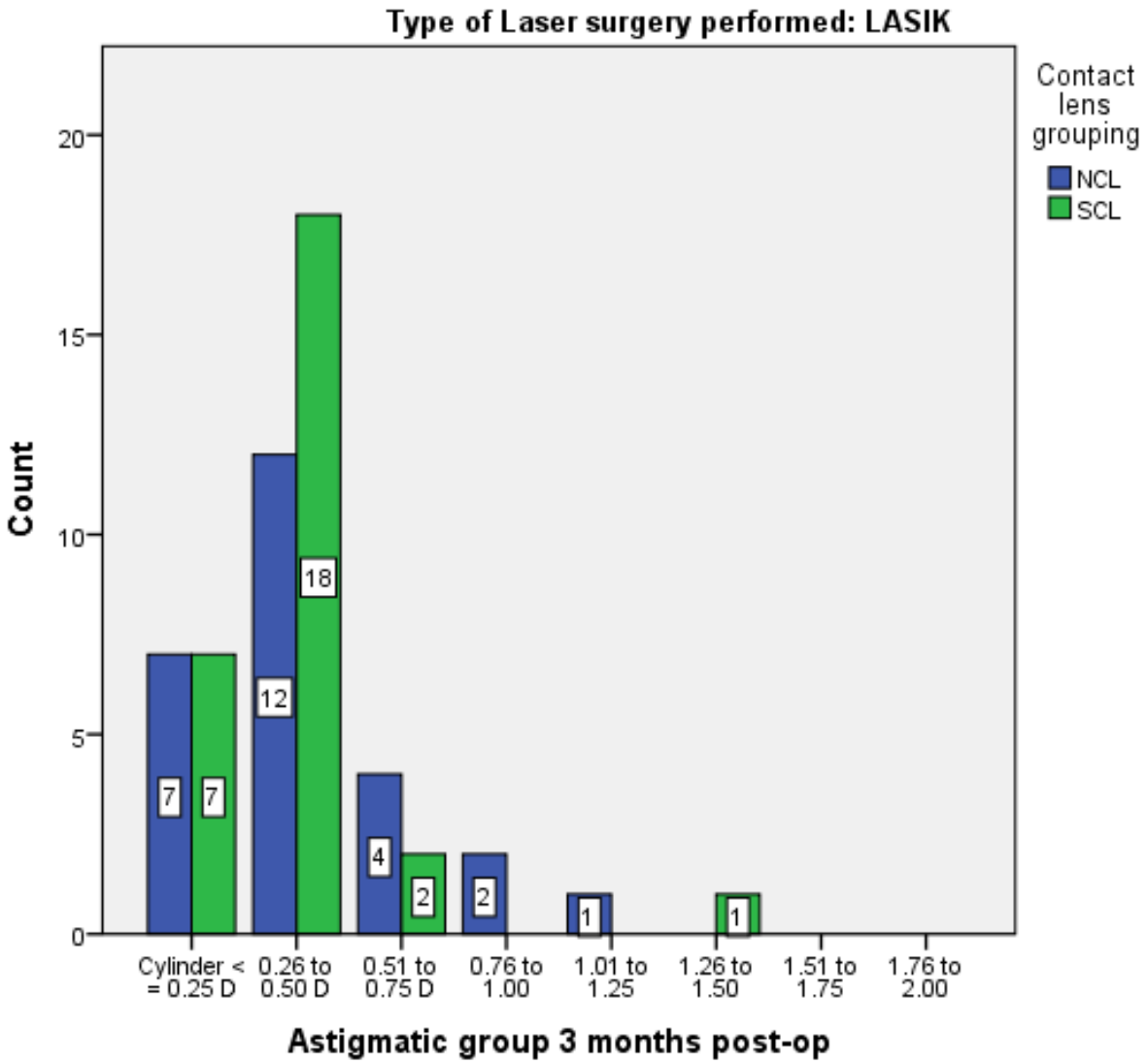
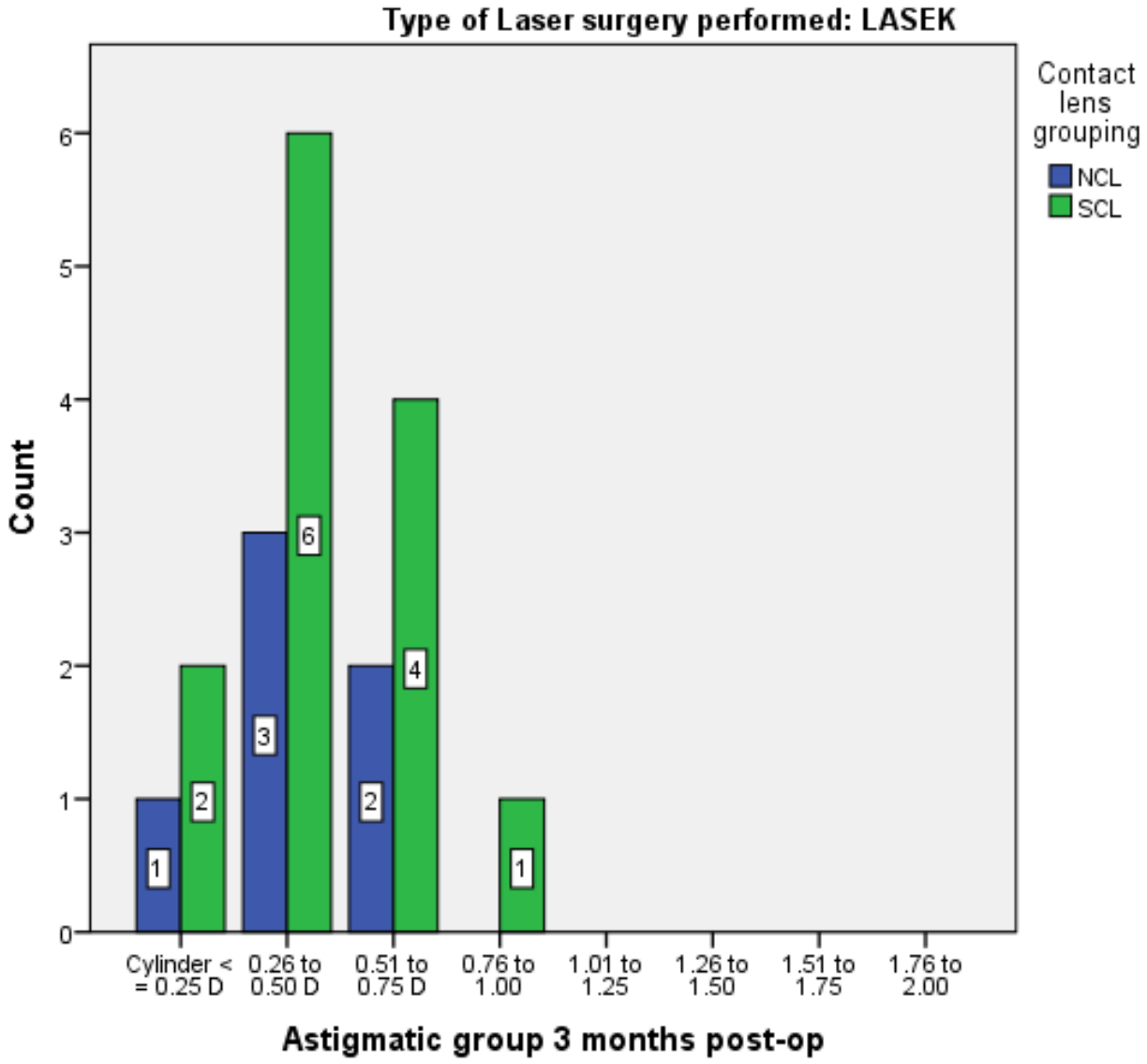

Type of Laser surgery performed: LASEK
Contact lens grouping
NCL
SCL
Count
0
2
4
6
8
10
1
1
3
9
2
3
< -2.00 D
Between -2.00 and -1.51 D
Between -1.50 and -1.01 D
Between -1.00 and -0.51 D
Between -0.50 and -0.14 D
Between -0.13 and +0.13 D
Between +0.14 and +0.50 D
Between +0.51 and +1.00 d
Between +1.01 and +1.50 D
Between +1.51 and +2.00 D
> +2.00 D
Refractive accuracy at 3 month postop

Figure A-13: Refractive accuracy for astigmatism at the 3 month post-operative visit.




Type of Laser surgery performed: LASEK
Contact lens grouping
NCL
SCL
Count
0
1
2
3
4
5
6
1
2
3
6
2
4
1
Cylinder < = 0.25 D
0.26 to 0.50 D
0.51 to 0.75 D
0.76 to 1.00
1.01 to 1.25
1.26 to 1.50
1.51 to 1.75
1.76 to 2.00
Astigmatic group 3 months post-op

A.5.2.4 Study 2: the influence of myopic group on 3 month postoperative results for 2 weeks SCL cessation

The influence of the level of myopia corrected on efficacy and predictability at 3 months was explored. Following on from the results at 1 month post-op, the significant effect of pre-operative myopic grouping on the efficacy of LASIK procedures was maintained (Table A-24). Post hoc comparisons using Bonferroni and Scheffe testing indicated that the mean UDVA measured 3 months post operatively was significantly lower in the high myopic compared with the low myopic group (mean difference ±SD: 10.76 ±3.28) and compared with the medium myopic group (mean difference ±SD: 9.57 ±3.34) for LASIK procedures. For the LASEK/PRK procedures post hoc comparisons using Bonferroni and Scheffe testing indicated that the mean UDVA measured 3 months post operatively was significantly lower in the high myopic compared with the low myopic group (mean difference ±SD: 1.12 ±1.78) and the medium myopic group (mean difference ±SD: 2.95 ±1.82). There were no significant differences between the groups for any of the predictability values measured.

Table A-24: Predictability and efficacy at 3 months for CL and myopic groups

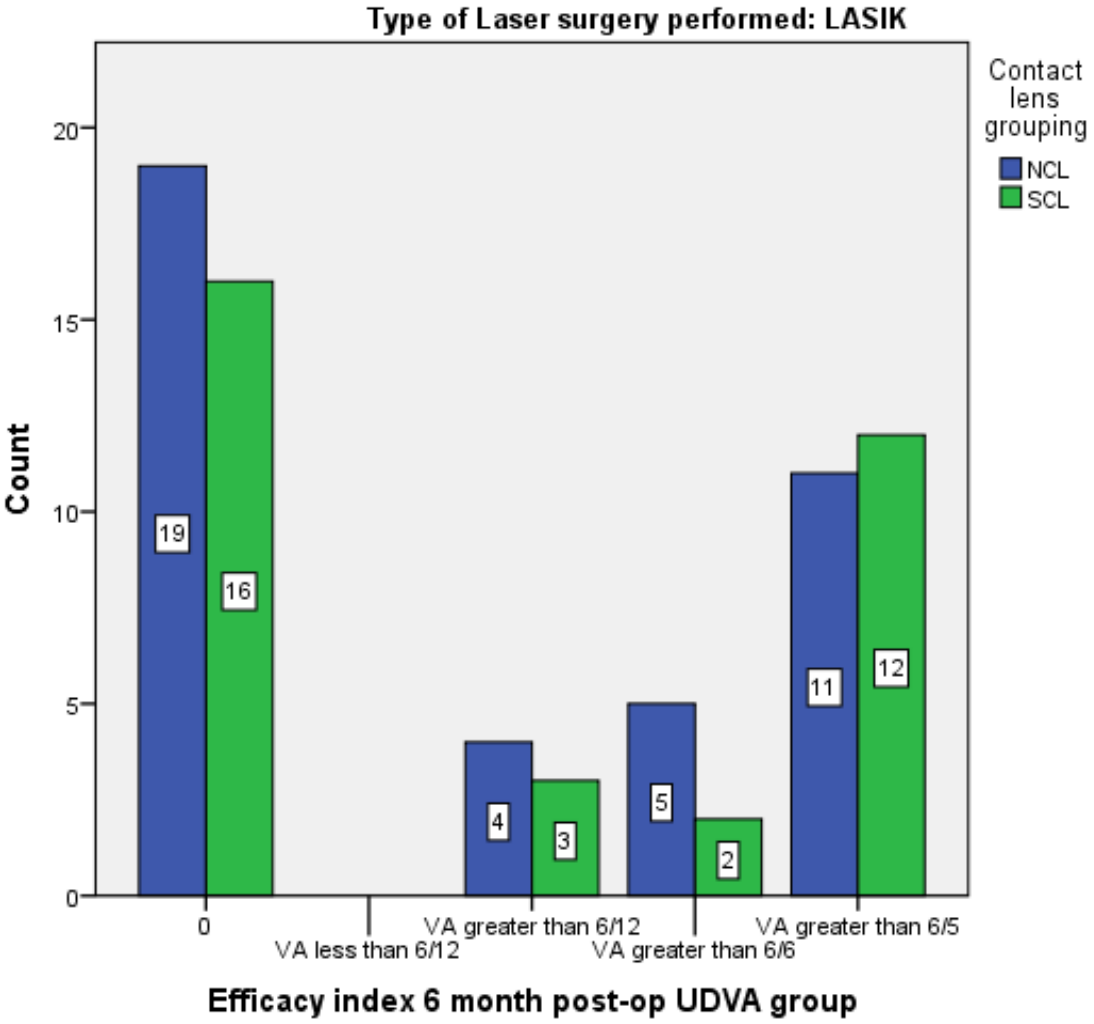
	LASIK			**LASEK/PRK**		
	SCL group Mean LogMAR ±SD	**NCL group Mean LogMAR ±SD**	**Sig**	**SCL group Mean LogMAR ±SD**	**NCL group Mean LogMAR ±SD**	**Sig**
Low Myopes	-0.09 ±0.09 (n = 4)	n = 13 -0.07 ±0.08	0.00	-0.15 ±0.05 (n = 12)	-0.08 ±0.05 (n = 4)	0.01
Medium Myopes	-0.07 ±0.14 (n = 10)	-0.03 ±0.16 (n = 4)		-0.09 ±0.03 (n = 3)	-0.02 ±0.04 (n = 8)	
High Myopes	0.05 ±0.16 (n = 3)	0.06 ±0.16 (n = 1)		-0.10 ±0 (n = 1)	-0.12 ±0 (n = 1)	
Sphere (D)			0.19			0.47
Low Myopes	-0.06 ±0.31	0.1 ±0.39		0.13 ±0.25	0.29 ±0.54	
Medium Myopes	0.08 ±0.49	0.06 ±0.31		0.19 ±0.42	-0.25 ±0.9	
High Myopes	0.33 ±0.72	-1.25 ±0.00		0.25 ±0.00	0.5 ±0.00	
Cylinder (D)			0.47			0.31
Low Myopes	-0.38 ±0.14	-0.4 ±0.19		-0.38 ±0.14	-0.48 ±0.31	
Medium Myopes	-0.4 ±0.21	-0.56 ±0.43		-0.44 ±0.22	-0.67 ±0.29	
High Myopes	-0.33 ±0.14	-0.75 ±0.00		-0.25 ±0.00	-0.25 ±0.00	
MSE (D)			0.14			0.36
Low Myopes	-0.25 ±0.34	-0.11 ±0.35		-0.06 ±0.3	0.05 ±0.61	
Medium Myopes	-0.13 ±0.51	-0.22 ±0.41		-0.03 ±0.47	-0.58 ±1.01	
High Myopes	0.17 ±0.69	-1.63 ±0.00		0.13 ±0.00	0.38 ±0.00	

Mean ±SD of efficacy and predictability at 3 months post-operatively for SCL and myopic groups, low myopia (0 to -3.00D), medium myopia (-3.25 to -6.00D) and high myopia (>-6.00D). The results of two-way ANOVA are shown with statistically significant results shown in shaded cells, ($p < 0.05$).

A.5.2.5 Study 2: 6 months post-operative results

Graphs depicting the visual outcomes of CRS procedures performed in terms of efficacy and predictability at 6 months following surface LASEK/PRK or LASIK are displayed below.

Figure A-14: Efficacy index at the 6 month post-operative visit.



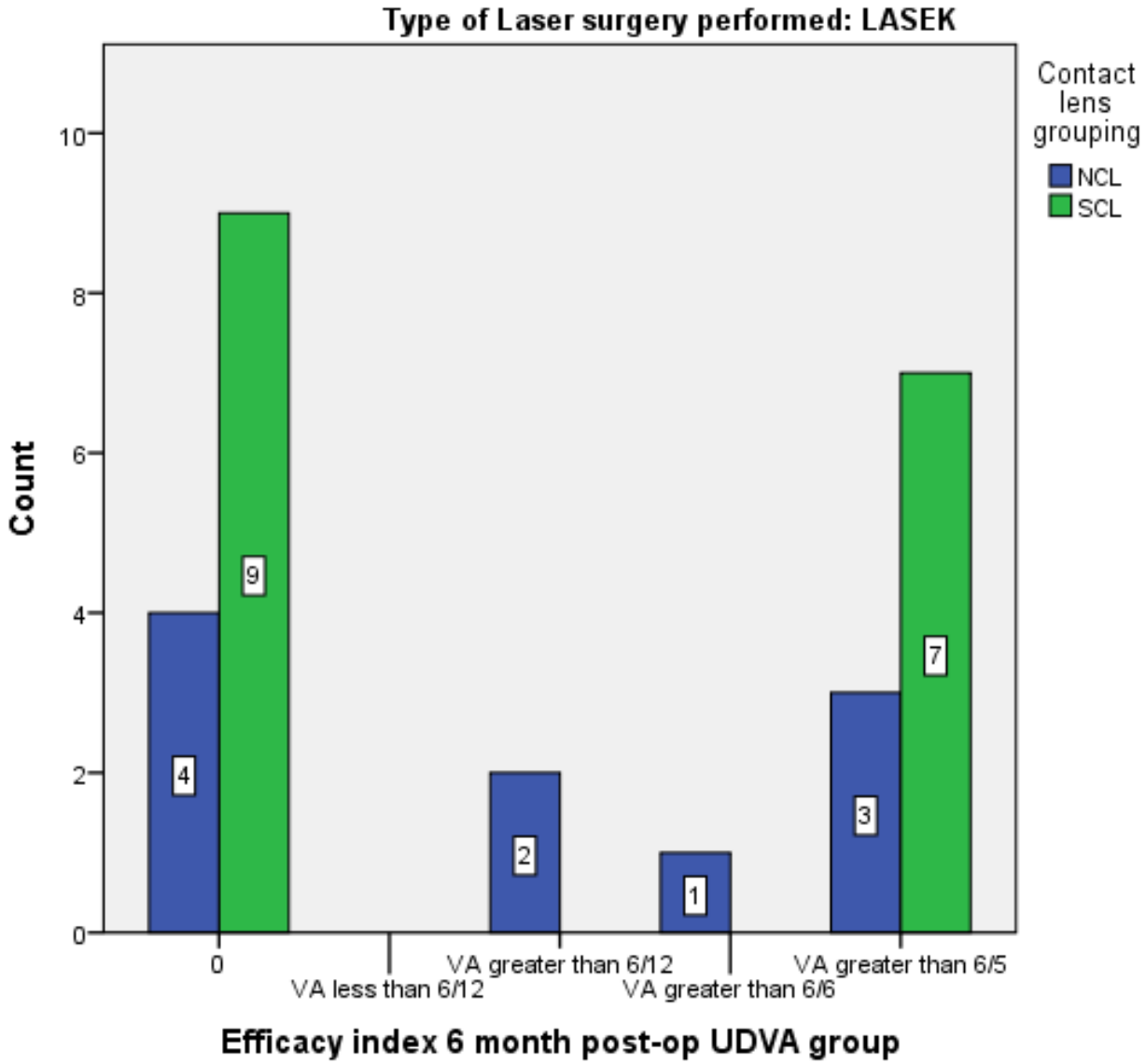
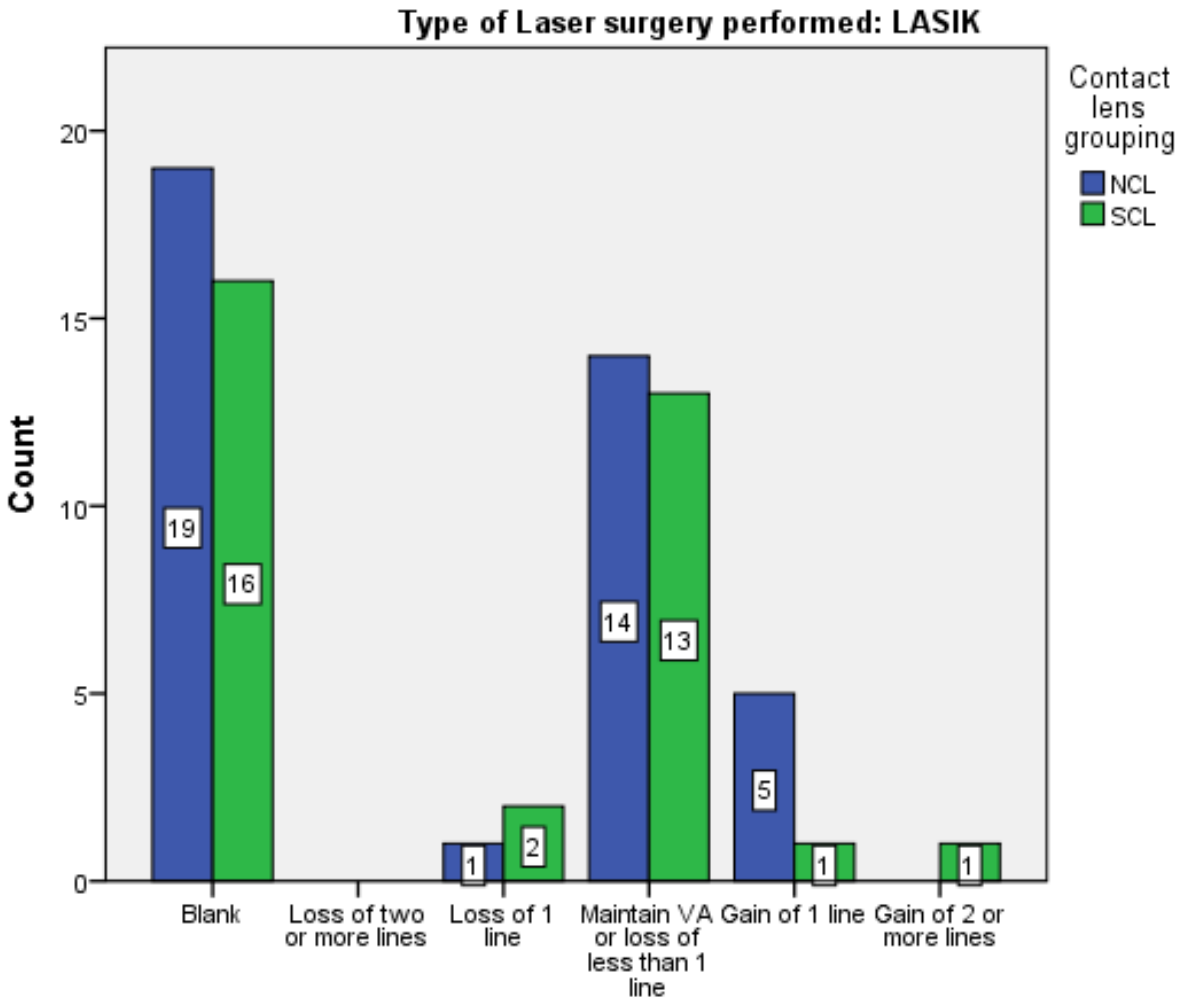

Type of Laser surgery performed: LASEK
Contact lens grouping
NCL
SCL
Count
10
8
6
4
2
0
4
9
2
1
3
7
0
VA less than 6/12
VA greater than 6/12
VA greater than 6/6
VA greater than 6/5
Efficacy index 6 month post-op UDVA group

Figure A-15: Comparision of pre-operative BCSVA and 6 month post-operative UDVA



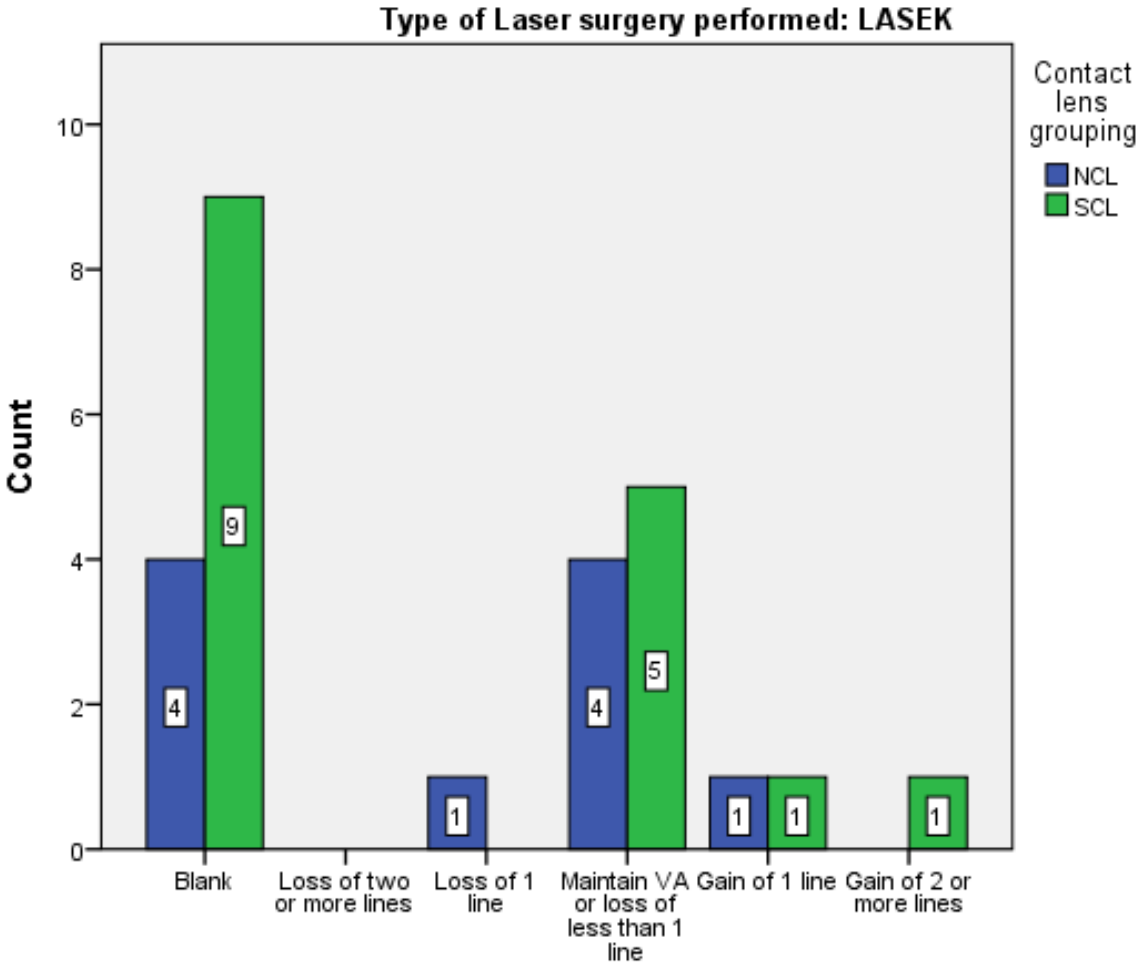
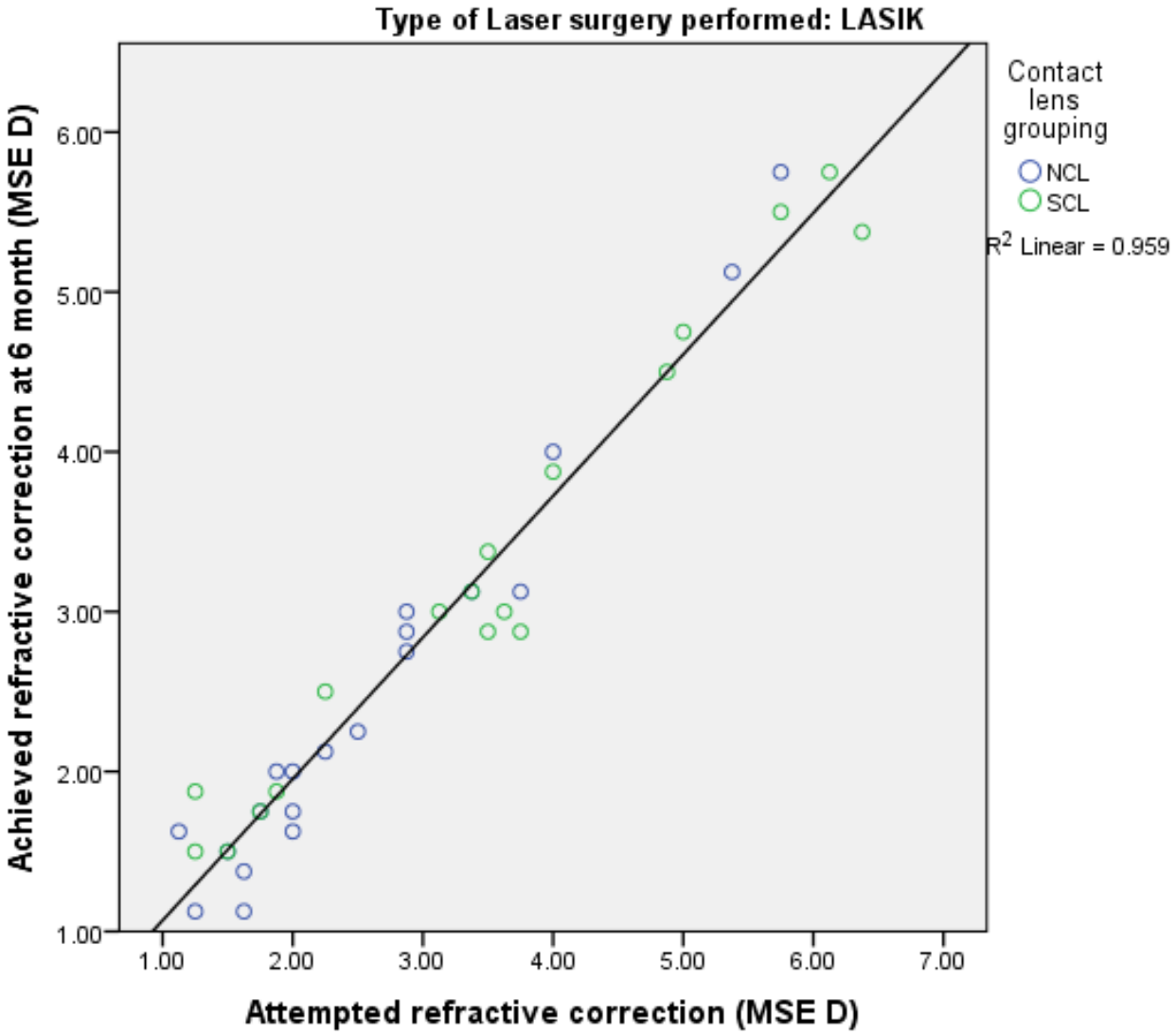

Type of Laser surgery performed: LASEK
Count
10
8
6
4
2
0
Contact lens grouping
NCL
SCL
4
9
1
4
5
1
1
1
Blank
Loss of two or more lines
Loss of 1 line
Maintain VA or loss of less than 1 line
Gain of 1 line
Gain of 2 or more lines

Figure A-16: Refractive accuracy at the 6 month post-operative visit.



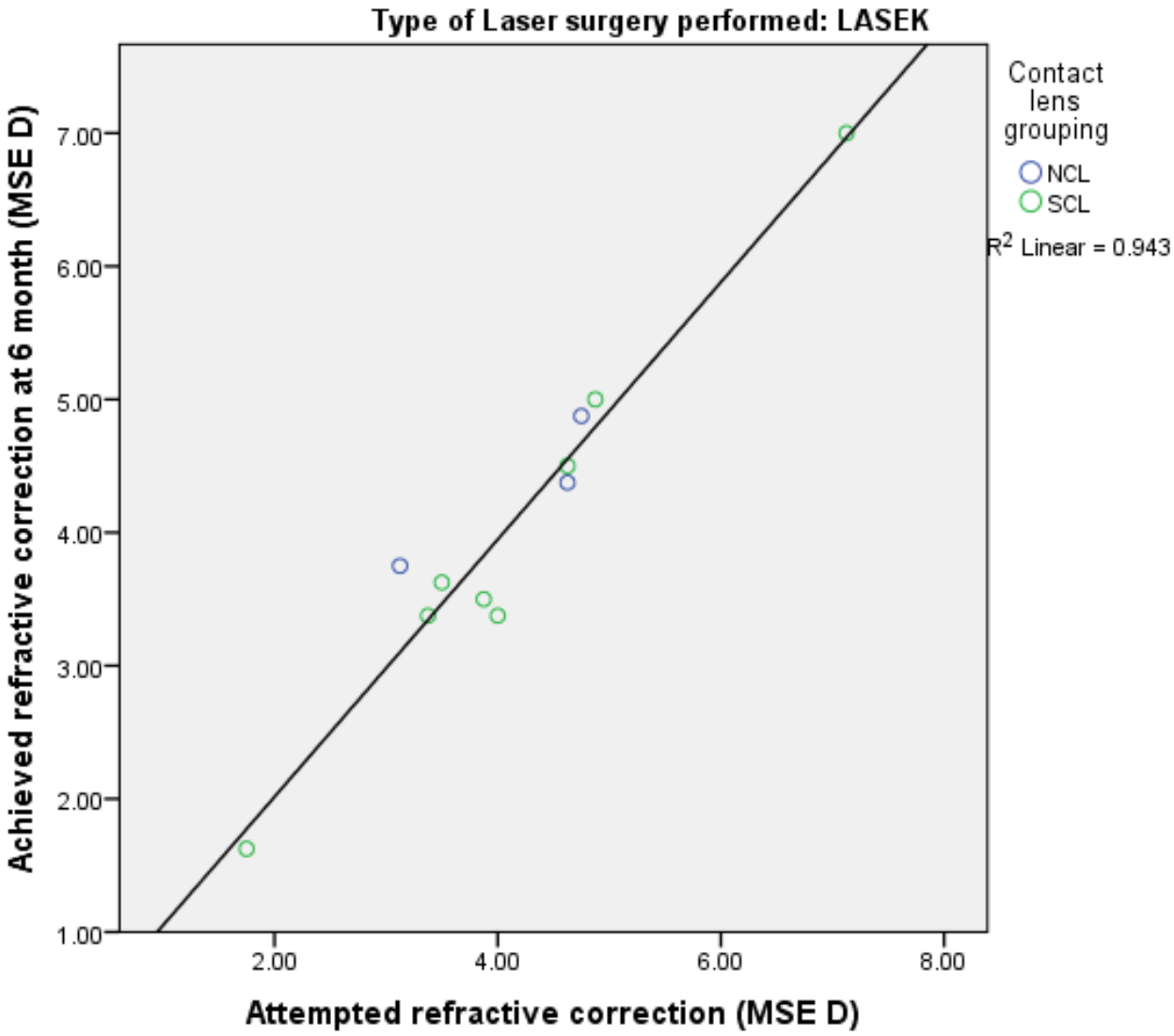
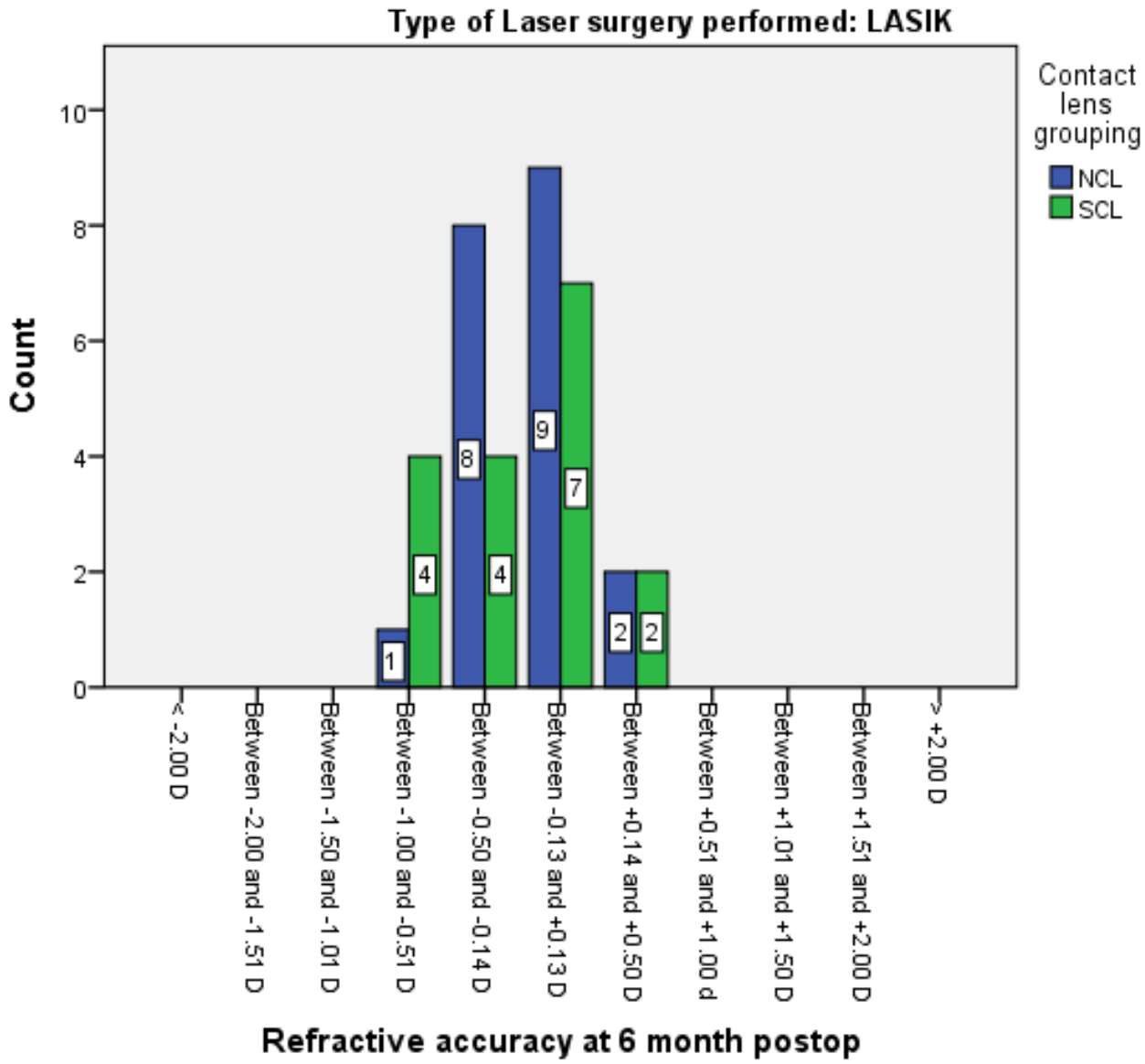

Type of Laser surgery performed: LASEK
Achieved refractive correction at 6 month (MSE D)
7.00
6.00
5.00
4.00
3.00
2.00
1.00
2.00
4.00
6.00
8.00
Attempted refractive correction (MSE D)
Contact lens grouping
NCL
SCL
R2 Linear = 0.943

Figure A-17: Refractive accuracy at the 6 month post-operative visit.



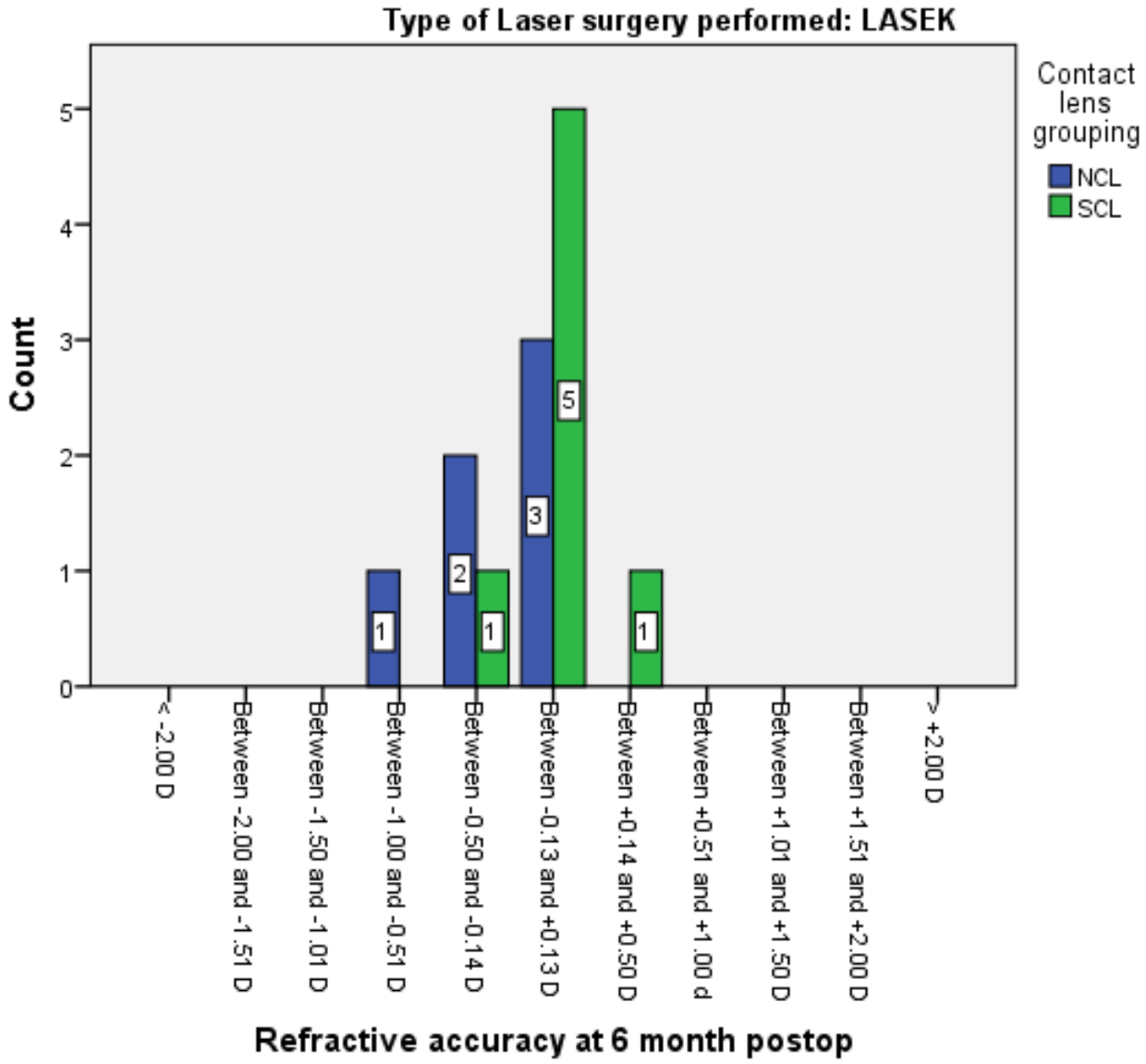
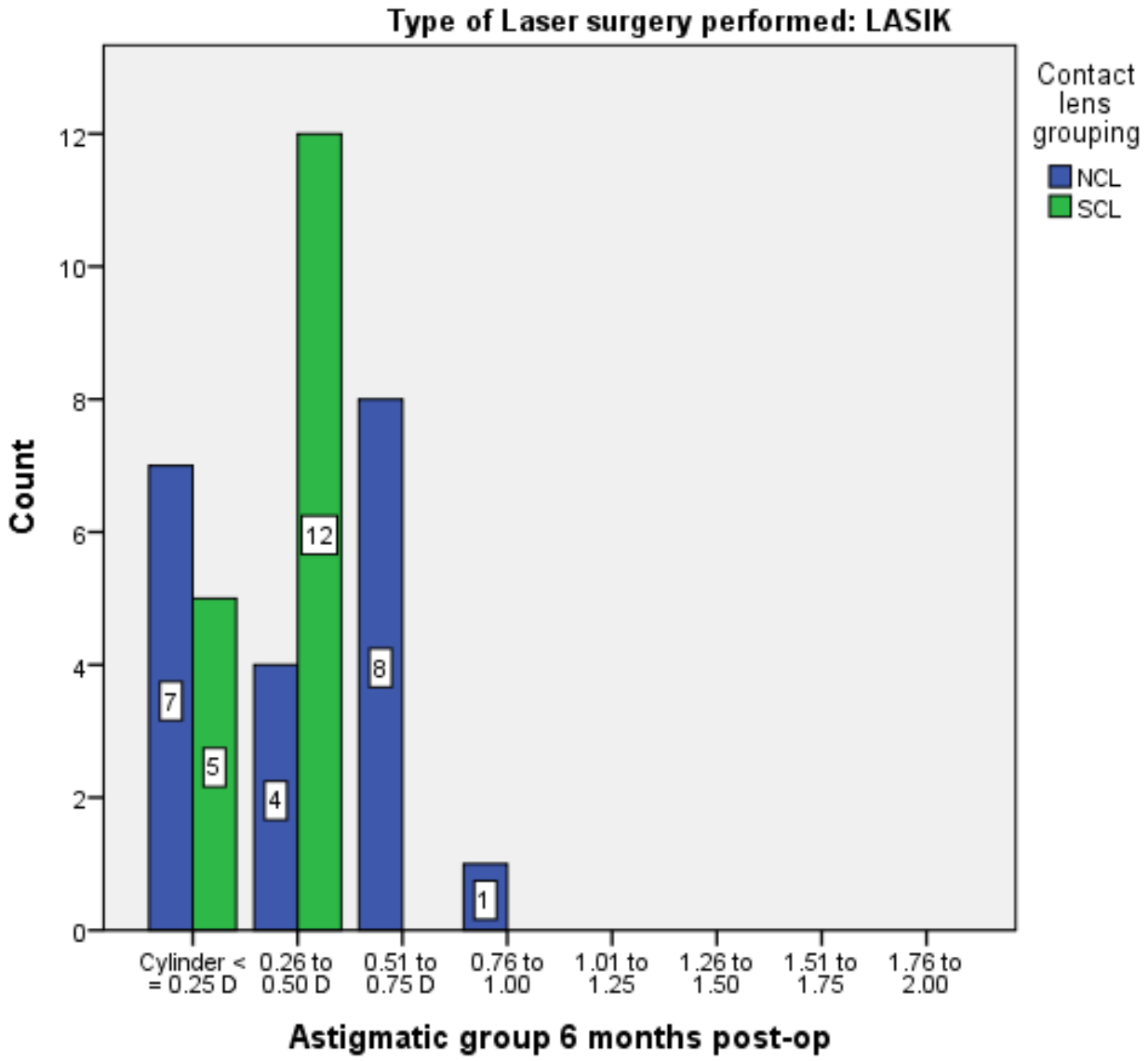
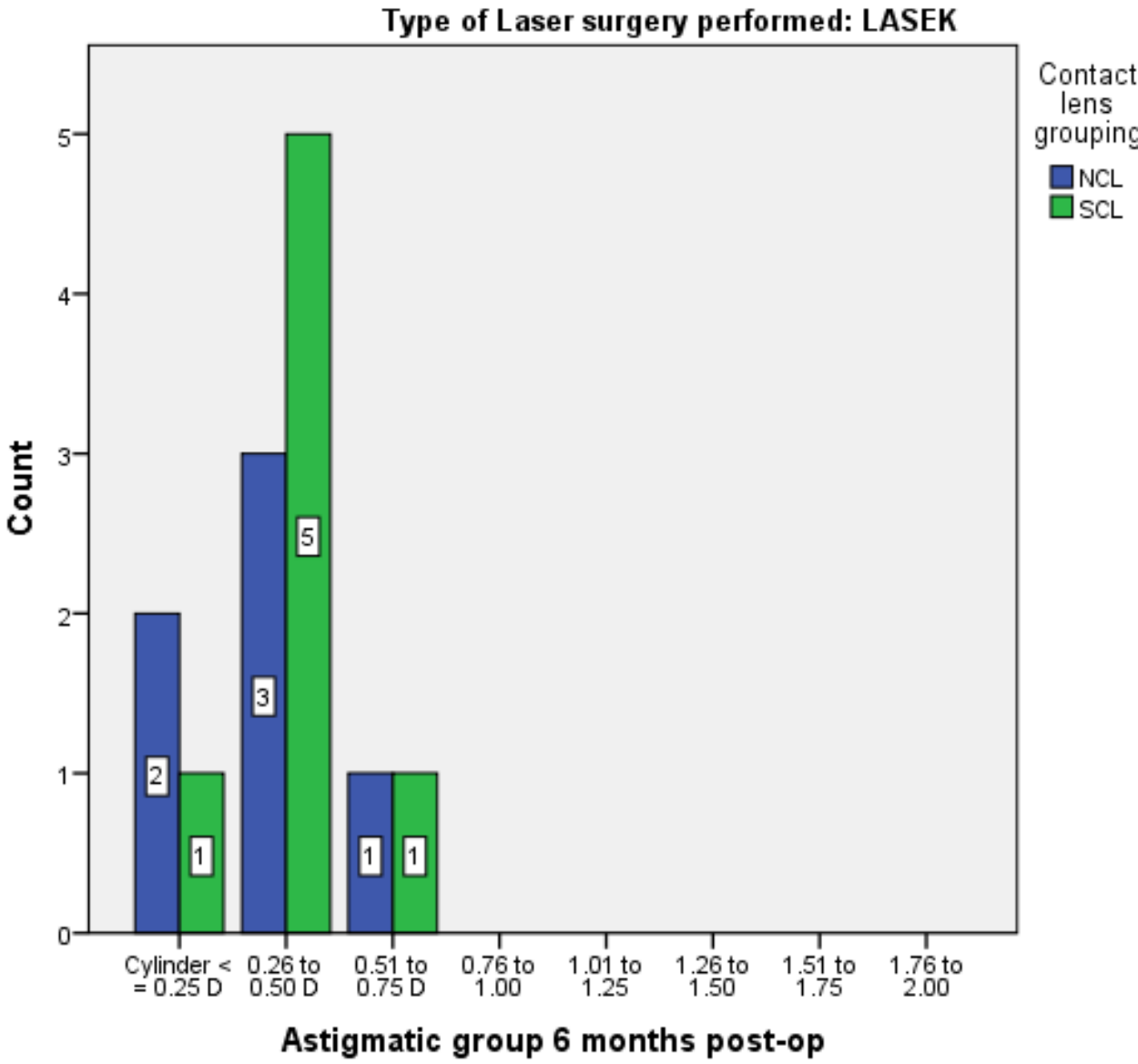

Type of Laser surgery performed: LASEK
Contact lens grouping
NCL
SCL
Count
0
1
2
3
4
5
1
2
1
3
5
1
< -2.00 D
Between -2.00 and -1.51 D
Between -1.50 and -1.01 D
Between -1.00 and -0.51 D
Between -0.50 and -0.14 D
Between -0.13 and +0.13 D
Between +0.14 and +0.50 D
Between +0.51 and +1.00 d
Between +1.01 and +1.50 D
Between +1.51 and +2.00 D
> +2.00 D
Refractive accuracy at 6 month postop

Figure A-18: Refractive accuracy for astigmatism at the 6 month post-operative visit.




Type of Laser surgery performed: LASEK
Contact lens grouping
NCL
SCL
Count
0
1
2
3
4
5
2
1
3
5
1
1
Cylinder < = 0.25 D
0.26 to 0.50 D
0.51 to 0.75 D
0.76 to 1.00
1.01 to 1.25
1.26 to 1.50
1.51 to 1.75
1.76 to 2.00
Astigmatic group 6 months post-op

A.5.2.6 Study 2: the influence of myopic group on 6 month postoperative results for 2 weeks SCL cessation

The influence of the level of myopia corrected on efficacy and predictability at 6 months was explored. Results of a two-way ANOVA indicate no significant effect of myopic group on UDVA or on spherical or MSE refractive predictability for either LASIK or LASEK/PRK procedures (see Table A-25).

Table A-25: Predictability and efficacy at 6 months for CL and myopic groups

Myopic group	**LASIK**			**LASEK/PRK**		
	SCL group Mean LogMAR ±SD	**NCL group Mean LogMAR ±SD**	**Sig**	**SCL group Mean LogMAR ±SD**	**NCL group Mean LogMAR ±SD**	**Sig**
Low	-0.15 ±0.06 (n = 4)	-0.06 ±0.07 (n = 10)	0.74	-0.10 ±0.10 (n = 3)	-0.05 ±0.08 (n = 10)	0.66
Medium	-0.09 ±0.12 (n = 9)	-0.08 ±0.05 (n = 5)		-0.11 ±0.08 (n = 9)	-0.01 ±0.08 (n = 4)	
High	-0.07 ±0.06 (n = 2)	n = 0		-0.10 ±0.00 n = 1	n = 0	
Sphere (D)			0.09			0.24
Low	0.06 ±0.31	-0.16 ±0.33		0.13 ±0.88	0.43 ±0.50	
Medium	0.06 ±0.30	0.25 ±0.29		-0.03 ±0.63	-0.38 ±0.32	
High	0.50 ±0.00			0.00 ±0.00		
Cylinder (D)			0.03			0.04
Low	-0.25 ±0.20	-0.38 ±0.13		-0.63 ±0.18	-0.33 ±0.12	
Medium	-0.44 ±0.21	-0.56 ±0.24		-0.33 ±0.22	-0.19 ±0.13	
High	-0.63 ±0.18			-0.25 ±0.00		
MSE (D)			0.44			0.40
Low	-0.06 ±0.3	-0.34 ±0.35		-0.19 ±0.8	0.26 ±0.48	
Medium	-0.17 ±0.34	-0.03 ±0.4		-0.19 ±0.68	-0.47 ±0.31	
High	0.19 ±0.09			-0.13 ±0		

Mean and SD of efficacy and predictability at 6 months post-operative for SCL and myopic groups, low myopia (0 to -3.00D), medium myopia (-3.25 to -6.00D) and high myopia (>-6.00D). The results of two-way ANOVA are also shown with statistically significant results shown in shaded cells, ($p < 0.05$).

There was a significant effect of myopic group for the predictability of the cylinder correction for the LASIK and LASEK/PRK groups. However, these effects varied for

the CRS procedure performed. The SCL group who had LASIK performed showed lower predictability for cylindrical correction with increasing pre-operative myopia corrected ($p = 0.03$). While the SCL group who had LASEK/PRK performed showed higher predictability for increasing pre-operative myopic group ($p = 0.04$). All results were not statistically significant.

A.5.3 Study 3: the influence of SCL wear on the stability of corneal curvature measurements

A.5.3.1 The influence of SCL wear on refractive error following cessation of SCL wear.

The influence of SCL material on the stability of subjective refraction following cessation of SCL wear was explored. The results of two-way ANOVA showed that there were no significant differences in the stability of refraction following SCL cessation between the SCL material and NCL groups at any time period (see Table A-26).

Table A-26: Effect of SCL material on stability of refractive error following SCL cessation

SCL material groups **NCL (n = 28)** **G1SiHy (n = 2)** **G2SiHy (n = 4)** **G3SiHy (n = 8)** **Hydrogel (n = 19)**		**Mean**	**SD**	**Sig**
Between baseline and day 1	NCL	-0.05	0.17	0.18
	G1SiHy	-0.25	0.00	
	G2SiHy	-0.13	0.14	
	G3SiHy	-0.11	0.13	
	Hydrogel	-0.14	0.15	
Between day 1 and 2	NCL	-0.01	0.16	0.66
	G1SiHy	0.13	0.18	
	G2SiHy	-0.13	0.25	
	G3SiHy	0.00	0.30	
	Hydrogel	-0.04	0.21	
Between day 2 and 7	NCL	-0.02	0.20	0.08
	G1SiHy	-0.38	0.18	
	G2SiHy	0.00	0.20	
	G3SiHy	0.09	0.13	
	Hydrogel	0.00	0.22	
Between day 7 and 14 NCL (n = 26) G1SiHy (n = 2) G2SiHy (n = 6) G3SiHy (n = 6) Hydrogel (n = 15)	NCL	0.00	0.10	0.59
	G1SiHy	-0.13	0.18	
	G2SiHy	0.00	0.00	
	G3SiHy	0.42	0.10	
	Hydrogel	0.03	0.14	

Mean ±SD and two-way ANOVA results for SCL material groups and the stability of refraction following SCL cessation between baseline and days 1, 2, 7 and 14.A negative value indicates more myopia at the second visit.

A.5.3.2 The influence of SCL wear on corneal curvature prior to and following cessation of SCL wear.

A comparison of corneal curvature (SimK, sagittal and tangential topography) was carried out between the groups (SCL vs. NCL) following cessation of SCL wear on days 1, 2, 7 and 14. Two-way ANOVA and Mann-Whitney U testing were used to analyse differences in the corneal curvature measurements. Results showed that there were significantly steeper corneal curvature at all corneal locations tested between the

groups (SCL vs. NCL) likely due to the higher myopia in the SCL group which is correlated with steeper corneas (Budak et al., 1999; Mehravaran et al., 2013; O' Donnell et al., 2011; Scholz et al., 2009). This finding was found following cessation of SCL wear on day 1 (Table A-27), day 2 (Table A-28), day 7 (Table A-29) and day 14 (Table A-30) following cessation of SCL wear.

Table A-27: Corneal curvature following 1 day's SCL cessation

CL group NCL (n = 27) SCL (n = 32)		**Mean ±SD**	**ANOVA Sig**	**Mann-Whitney Sig**
Flat SimK	NCL	7.99 ±0.25	0.00	0.01
	SCL	7.78 ±0.24		
Steep SimK	NCL	7.84 ±0.26	0.00	0.00
	SCL	7.59 ±0.26		
Sagittal curvature centrally	NCL	42.77 ±1.45	0.00	0.01
	SCL	44.03 ±1.48		
Sagittal curvature superiorly	NCL	42.88 ±1.46	0.00	0.00
	SCL	44.24 ±1.6		
Sagittal curvature inferiorly	NCL	43.11 ±1.42	0.00	0.00
	SCL	44.47 ±1.45		
Tangential curvature superior	NCL	42.1 ±1.8	0.01	0.00
	SCL	43.41 ±1.53		
Tangential curvature centrally	NCL	42.38 ±1.53	0.00	0.01
	SCL	43.58 ±1.17		
Tangential curvature inferiorly	NCL	42.07 ±1.2	0.00	0.00
	SCL	43.37 ±1.38		

Mean ±SD stability of corneal curvature for SCL and NCL groups following SCL cessation on day 1. Two-way ANOVA show significant differences between the groups for all variables tested, ($p < 0.05$).

Table A-28: Corneal curvature following 2 days of SCL cessation

CL group NCL (n = 24) SCL (n = 31)		**Mean ±SD**	**ANOVA Sig**	**Mann Whitney Sig**
Flat SimK	NCL	7.99 ±0.24	0.00	0.01
	SCL	7.8 ±0.23		
Steep SimK	NCL	7.85 ±0.26	0.00	0.00
	SCL	7.6 ±0.25		
Sagittal curvature centrally	NCL	42.79 ±1.42	0.00	0.01
	SCL	43.94 ±1.42		
Sagittal curvature superiorly	NCL	42.77 ±1.47	0.00	0.00
	SCL	44.29 ±1.57		
Sagittal curvature inferiorly	NCL	43.2 ±1.4	0.00	0.00
	SCL	44.49 ±1.56		
Tangential curvature superior	NCL	42.53 ±1.93	0.10	0.10
	SCL	43.37 ±1.64		
Tangential curvature centrally	NCL	42.49 ±1.48	0.00	0.01
	SCL	43.63 ±1.13		
Tangential curvature inferiorly	NCL	42.13 ±1.33	0.00	0.00
	SCL	43.52 ±1.36		

Mean ±SD stability of corneal curvature for SCL and NCL groups following SCL cessation on day 2. Two-way ANOVA show significant differences between the groups for all variables tested, ($p < 0.05$).

Table A-29: Corneal curvature following 7 days of SCL cessation

CL group (NCL = 28) SCL (n = 32)		**Mean ±SD**	**ANOVA Sig**	**Mann-Whitney Sig**
Flat SimK	NCL	8.00 ±0.24	0.00	0.00
	SCL	7.80 ±0.23		
Steep SimK	NCL	7.85 ±0.26	0.00	0.00
	SCL	7.60 ±0.26		
Sagittal curvature centrally	NCL	42.70 ±1.38	0.00	0.00
	SCL	43.97 ±1.46		
Sagittal curvature superiorly	NCL	42.85 ±1.52	0.00	0.00
	SCL	44.28 ±1.67		
Sagittal curvature inferiorly	NCL	43.10 ±1.34	0.00	0.00
	SCL	44.39 ±1.51		
Tangential curvature superior	NCL	42.21 ±1.62	0.02	0.03
	SCL	43.27 ±1.56		
Tangential curvature centrally	NCL	42.42 ±1.54	0.00	0.01
	SCL	43.62 ±1.11		
Tangential curvature inferiorly	NCL	42.21 ±1.48	0.01	0.00
	SCL	43.35 ±1.38		

Mean ±SD stability of corneal curvature for SCL and NCL groups following SCL cessation on day 7. Two-way ANOVA show significant differences between the groups for all variables tested, ($p < 0.05$).

Table A-30: Corneal curvature following 14 days of SCL cessation

CL group NCL (n = 26) SCL (n = 25)		**Mean ±SD**	**ANOVA Sig**	**Mann-Whitney Sig**
Flat SimK	NCL	8.00 ±0.24	0.00	0.01
	SCL	7.79 ±0.23		
Steep SimK	NCL	7.84 ±0.26	0.00	0.00
	SCL	7.60 ±0.26		
Sagittal curvature centrally	NCL	42.74 ±1.44	0.00	0.01
	SCL	44.00 ±1.46		
Sagittal curvature superiorly	NCL	42.83 ±1.49	0.00	0.01
	SCL	44.18 ±1.55		
Sagittal curvature inferiorly	NCL	43.12 ±1.34	0.00	0.00
	SCL	44.73 ±1.79		
Tangential curvature superior	NCL	42.32 ±1.58	0.02	0.03
	SCL	43.36 ±1.6		
Tangential curvature centrally	NCL	40.69 ±8.25	0.05	0.00
	SCL	43.7 ±1.11		
Tangential curvature inferiorly	NCL	42.33 ±1.47	0.01	0.01
	SCL	43.38 ±1.33		

Mean ±SD stability of corneal curvature for SCL and NCL groups following SCL cessation on day 14. Two-way ANOVA show significant differences between the groups for all variables tested, ($p < 0.05$).

A.5.3.3 The influence of SCL wear on the stability of corneal curvature measurements following cessation of SCL wear.

The influence of 2 weeks cessation of SCL wear on the stability of corneal curvature measurements between the groups (SCL vs. NCL) was examined. Results of two-way ANOVA and Mann-Whitney testing showed significant differences in stability of superior tangential curvature measured on days 1 and 2 following SCL cessation between the groups. Interestingly, the largest difference was detected in the NCL group who showed a mean flattening of 0.46 ±10.02mm, whereas the SCL group showed a mean steepening of -0.12 ±0.51mm (F 6.19, p = 0.02). No other significant differences were found between the groups for the variables tested at all other times (see Table A-31, Table A-32, Table A-33 and Table A-34).

Table A-31: Stability of corneal curvature for SCL and NCL groups between baseline and 1 day following cessation of SCL wear.

CL group NCL (n = 26) SCL (n = 33)		**Mean ±SD**	**Two-way ANOVA Sig**	**Mann-Whitney Sig**
Difference between flat SimK (D)	NCL	-0.01 ±0.04	0.83	0.73
	SCL	-0.01 ±0.05		
Difference between steep SimK (D)	NCL	-0.01 ±0.03	0.26	0.85
	SCL	0.01 ±0.09		
Difference between sagittal curvature centrally (mm)	NCL	0.02 ±0.22	0.68	0.44
	SCL	0.05 ±0.30		
Difference between sagittal curvature superiorly (mm)	NCL	0.09 ±0.30	0.47	0.68
	SCL	0.02 ±0.42		
Difference between sagittal curvature inferiorly (mm)	NCL	-0.27 ±1.18	0.53	0.98
	SCL	-0.13 ±0.51		
Difference in tangential curvature superior (mm)	NCL	-0.25 ±0.56	0.20	
	SCL	-0.02 ±0.64		
Difference in tangential curvature centrally (mm)	NCL	-0.07 ±0.28	0.46	
	SCL	0.00 ±0.32		
Difference in tangential curvature inferiorly (mm)	NCL n = 21	-0.10 ±0.58	0.82	
	SCL n = 25	-0.06 ±0.60		

Mean ±SD and two-way ANOVA results on stability of corneal curvature between baseline and following 1 days cessation of SCL wear. A negative difference value for SimK (D) and positive value for sagittal and tangential curvature indicates flattening following SCL cessation. Two-way ANOVA show no significant differences between the groups for all variables tested ($p < 0.05$).

Table A-32: Stability of corneal curvature for SCL and NCL groups following cessation of SCL wear between days 1 and 2.

CL group NCL (n = 21) SCL (n = 25)		**Mean ±SD**	**Two-way ANOVA Sig**	**Mann-Whitney Sig**
Difference between flat SimK (D)	NCL	-0.00 ±0.03	0.32	0.34
	SCL	0.01 ±0.04		
Difference between steep SimK (D)	NCL	0.01 ±0.04	0.81	
	SCL	0.01 ±0.04		
Difference between sagittal curvature centrally (mm)	NCL	0.01 ±0.31	0.15	0.41
	SCL	-0.12 ±0.31		
Difference between sagittal curvature superiorly (mm)	NCL	-0.17 ±0.38	0.08	
	SCL	0.03 ±0.36		
Difference between sagittal curvature inferiorly (mm)	NCL	0.13 ±0.31	0.20	0.47
	SCL	0.01 ±0.32		
Difference in tangential curvature superior (mm)	NCL	0.46 ±1.02	0.02	
	SCL	-0.12 ±0.51		
Difference in tangential curvature centrally (mm)	NCL	0.11 ±0.3	0.18	
	SCL	-0.02 ±0.38		
Difference in tangential curvature inferiorly (mm)	NCL	0.06 ±0.54	0.60	0.69
	SCL	0.14 ±0.48		

Mean ±SD and two-way ANOVA results for the stability of corneal curvature for SCL and NCL groups following cessation of SCL wear between days 1 and 2. A negative difference value for SimK (D) and positive value for sagittal and tangential curvature indicates flattening following SCL cessation. Significant differences are shown in shaded cells ($p < 0.05$).

Table A-33: Stability of corneal curvature for SCL and NCL groups following cessation of SCL wear between days 2 and 7.

CL group NCL (n = 21) SCL (n = 25)		**Mean ±SD**	**Two-way ANOVA Sig**	**Mann-Whitney Sig**
Difference between flat SimK (D)	NCL	0.00 ±0.02	0.99	
	SCL	0.00 ±0.03		
Difference between steep SimK (D)	NCL	0.00 ±0.03	0.29	0.26
	SCL	-0.01 ±0.04		
Difference between sagittal curvature centrally (mm)	NCL	-0.02 ±0.28	0.45	0.22
	SCL	0.06 ±0.37		
Difference between sagittal curvature superiorly (mm)	NCL	0.16 ±0.40	0.17	
	SCL	0.02 ±0.29		
Difference between sagittal curvature inferiorly (mm)	NCL	-0.11 ±0.32	0.62	
	SCL	-0.07 ±0.25		
Difference in tangential curvature superior (mm)	NCL	-0.34 ±0.88	0.16	
	SCL	-0.06 ±0.46		
Difference in tangential curvature centrally (mm)	NCL	-0.06 ±0.24	0.50	
	SCL	0.00 ±0.32		
Difference in tangential curvature inferiorly (mm)	NCL	0.06 ±0.41	0.43	
	SCL	-0.05 ±0.47		0.68

Mean ±SD and two-way ANOVA results on stability of corneal curvature between days 2 and 7 following cessation of SCL wear. A negative difference value for SimK (D) and positive value for sagittal and tangential curvature indicates flattening following SCL cessation. Two-way ANOVA show no significant differences between the groups for all variables tested ($p < 0.05$).

Table A-34: Stability of corneal curvature for SCL and NCL groups following cessation of SCL wear between days 7 and 14.

SCL group NCL (n = 21) SCL (n = 25)		**Mean ±SD**	**Two-way ANOVA Sig**	**Mann-Whitney Sig**
Difference between flat SimK (D)	NCL	0.01 ±0.03	0.07	
	SCL	-0.00 ±0.03		
Difference between steep SimK (D)	NCL	-0.00 ±0.03	0.83	
	SCL	-0.00 ±0.03		
Difference between sagittal curvature centrally (mm)	NCL	-0.04 ±0.22	0.40	
	SCL	0.03 ±0.34		
Difference between sagittal curvature superiorly (mm)	NCL	-0.09 ±0.44	0.92	0.72
	SCL	-0.1 ±0.29		
Difference between sagittal curvature inferiorly (mm)	NCL	-0.00 ±0.27	0.22	0.60
	SCL	0.34 ±1.23		
Difference in tangential curvature superior (mm)	NCL	0.12 ±0.62	0.97	
	SCL	0.11 ±0.78		
Difference in tangential curvature centrally (mm)	NCL	0.05 ±0.33	0.77	
	SCL	0.08 ±0.33		
Difference in tangential curvature inferiorly (mm)	NCL	0.1 ±0.73	0.21	0.23
	SCL	-0.14 ±0.52		

Mean ±SD and two-way ANOVA results on stability of corneal curvature between days 7 and 14 following cessation of SCL wear. A negative difference value for SimK (D) and positive value for sagittal and tangential curvature indicates flattening following SCL cessation. Two-way ANOVA show no significant differences between the groups for all variables tested ($p < 0.05$).

A.5.3.4 The influence of SCL material on the stability of corneal curvature

The influence of SCL material on the stability of corneal curvature was explored using two-way ANOVA. The groups were first analysed using the entire group of SiHy SCL wearers and results of corneal curvature stability can be seen in Tables 10-35, 10-36, 10-37 and 10-38.

Table A-35: Stability of corneal curvature between baseline and following 1days SCL cessation.

NCL (n = 26) Hydrogel (n = 19) SiHy (n = 13)		Mean ±SD (mm)	Sig
Flat SimK (D)	NCL	-0.01 ±0.04	0.89
	Hydrogel	-0.00 ±0.03	
	SiHy	-0.01 ±0.07	
Steep SimK (D)	NCL	-0.01 ±0.03	0.01
	Hydrogel	-0.02 ±0.03	
	SiHy	0.05 ±0.13	
Sagittal curvature centrally (mm)	NCL	0.02 ±0.22	0.81
	Hydrogel	0.06 ±0.23	
	SiHy	0.01 ±0.39	
Sagittal curvature superiorly (mm)	NCL	0.09 ±0.30	0.13
	Hydrogel	0.12 ±0.28	
	SiHy	-0.13 ±0.55	
Sagittal curvature inferiorly (mm)	NCL	-0.27 ±1.18	0.25
	Hydrogel	0.06 ±0.29	
	SiHy	-0.43 ±0.65	
Tangential curvature centrally (mm)	NCL	-0.27 ±0.55	0.29
	Hydrogel	0.06 ±0.71	
	SiHy	-0.07 ±0.75	
Tangential curvature superiorly (mm)	NCL	-0.07 ±0.28	0.43
	Hydrogel	-0.08 ±0.32	
	SiHy	0.04 ±0.29	
Tangential curvature inferiorly (mm)	NCL	-0.13 ±0.59	0.86
	Hydrogel	-0.08 ±0.64	
	SiHy	-0.02 ±0.63	

Mean ±SD and two-way ANOVA results on stability of corneal curvature following 1 day's cessation of SCL wear. A negative difference value for SimK (D) and positive value for sagittal and tangential curvature indicates flattening following SCL cessation. Two-way ANOVA show no significant differences between the groups for all variables tested ($p < 0.05$).

Table A-36: Stability of corneal curvature between 1 and 2 days SCL cessation

NCL (n = 26) Hydrogel (n = 19) SiHy (n = 13)		Mean ±SD	Sig
Flat SimK (D)	NCL	-0.00 ±0.03	0.51
	Hydrogel	0.01 ±0.04	
	SiHy	-0.01 ±0.06	
Steep SimK (D)	NCL	0.01 ±0.03	0.49
	Hydrogel	-0.00 ±0.04	
	SiHy	-0.01 ±0.09	
Sagittal curvature centrally (mm)	NCL	0.02 ±0.29	0.77
	Hydrogel	-0.05 ±0.42	
	SiHy	-0.02 ±0.25	
Sagittal curvature superiorly (mm)	NCL	-0.12 ±0.37	0.33
	Hydrogel	0.01 ±0.30	
	SiHy	0.08 ±0.59	
Sagittal curvature inferiorly (mm)	NCL	0.10 ±0.31	0.16
Tangential curvature centrally (mm)	Hydrogel	-0.04 ±0.31	
	SiHy	0.21 ±0.49	
	NCL	0.42 ±0.98	0.10
	Hydrogel	-0.07 ±0.62	
	SiHy	-0.02 ±0.54	
Tangential curvature superiorly (mm)	NCL	0.10 ±0.29	0.72
	Hydrogel	0.07 ±0.28	
	SiHy	-0.01 ±0.49	
Tangential curvature inferiorly (mm)	NCL	0.11 ±0.56	0.50
	Hydrogel	-0.24 ±0.60	
	SiHy	0.01 ±0.54	

Mean ±SD and two-way ANOVA results on stability of corneal curvature between 1 and 2 day's cessation of SCL wear. A negative difference value for SimK (D) and positive value for sagittal and tangential curvature indicates flattening following SCL cessation. Two-way ANOVA show no significant differences between the groups for all variables tested ($p < 0.05$).

Table A-37: Stability of corneal curvature between 2 and 7 days SCL cessation

NCL (n = 26) Hydrogel (n = 19) SiHy (n = 13)		Mean ±SD (mm)	Sig
Flat SimK (D)	NCL	0.01 ±0.02	0.34
	Hydrogel	-0.00 ±0.03	
	SiHy	-0.00 ±0.02	
Steep SimK (D)	NCL	0.01 ±0.04	0.05
	Hydrogel	0.01 ±0.04	
	SiHy	-0.02 ±0.03	
Sagittal curvature centrally (mm)	NCL	-0.10 ±0.31	0.48
	Hydrogel	-0.00 ±0.44	
	SiHy	0.04 ±0.32	
Sagittal curvature superiorly (mm)	NCL	0.09 ±0.40	0.37
	Hydrogel	-0.06 ±0.29	
	SiHy	0.08 ±0.37	
Sagittal curvature inferiorly (mm)	NCL	-0.10 ±0.30	0.97
	Hydrogel	-0.08 ± 0.26	
	SiHy	-0.10 ±0.30	
Tangential curvature centrally (mm)	NCL	-0.32 ±0.86	0.47
	Hydrogel	-0.08 ±0.41	
	SiHy	-0.10 ±0.63	
Tangential curvature superiorly (mm)	NCL	-0.06 ±0.23	0.64
	Hydrogel	0.02 ±0.39	
	SiHy	-0.04 ±0.28	
Tangential curvature inferiorly (mm)	NCL	0.09 ±0.42	0.23
	Hydrogel	-0.12 ±0.60	
	SiHy	-0.22 ±0.63	

Mean ±SD and two-way ANOVA results on stability of corneal curvature between 2 and 7 day's cessation of SCL wear. A negative difference value for SimK (D) and positive value for sagittal and tangential curvature indicates flattening following SCL cessation. Two-way ANOVA show no significant differences between the groups for all variables tested ($p < 0.05$).

Table A-38: Stability of corneal curvature between 7 and 14 days SCL cessation

NCL (n = 21) Hydrogel (n = 15) SiHy (n = 10)		Mean ±SD (mm)	Sig
Flat SimK (D)	NCL	0.01 ±0.03	0.19
	Hydrogel	-0.00 ±0.03	
	SiHy	-0.01 ±0.03	
Steep SimK (D)	NCL	-0.00 ±0.03	0.80
	Hydrogel	-0.00 ±0.03	
	SiHy	0.00 ±0.03	
Sagittal curvature centrally (mm)	NCL	-0.04 ±0.22	0.54
	Hydrogel	0.07 ±0.27	
	SiHy	-0.02 ±0.44	
Sagittal curvature superiorly (mm)	NCL	-0.09 ±0.37	0.77
	Hydrogel	-0.05 ±0.30	
	SiHy	-0.16 ±0.31	
Sagittal curvature inferiorly (mm)	NCL	-0.01 ±0.27	0.22
	Hydrogel	0.53 ±1.55	
	SiHy	0.05 ±0.38	
Tangential curvature centrally (mm)	NCL	0.12 ±0.62	0.10
	Hydrogel	0.11 ±0.58	
	SiHy	0.12 ±1.05	
Tangential curvature superiorly (mm)	NCL	0.05 ±0.33	0.94
	Hydrogel	0.07 ±0.32	
	SiHy	0.09 ±0.36	
Tangential curvature inferiorly (mm)	NCL	0.10 ±0.73	0.46
	Hydrogel	-0.13 ±0.47	
	SiHy	-0.14 ±0.61	

Mean ±SD and two-way ANOVA results on stability of corneal curvature between 7 and 14 day's cessation of SCL wear. A negative difference value for SimK (D) and positive value for sagittal and tangential curvature indicates flattening following SCL cessation. Two-way ANOVA show no significant differences between the groups for all variables tested ($p < 0.05$).

The influence of SCL material (including the various generations of SiHy SCL material) on the stability of corneal curvature was explored using two-way ANOVA. Results showed significant differences in stability of steep SimK between baseline and day 1 for SCL material and NCL groups (Table A-39). Post-hoc Scheffe testing revealed significant differences between the NCL and G3SiHy groups (NCL -0.01 ±0.03, G3SiHy 0.09 ±0.15, p = 0.01). A trend towards significance was found in the

tangential curvature centrally between days 1 and 2 between the groups (SCL material and NCL) (Table A-39). The significant difference was found between the NCL and G3SiHy groups (NCL 0.11 ±0.30, G3SiHy 0.30 ±0.60, p = 0.05). A trend towards significance was found in the tangential curvature inferiorly between days 2 and 7 between the groups (SCL material and NCL) (Table A-41). The significant difference was found between the G2SiHy and G3SiHy groups (G2SiHy 0.55 ±0.21, G3SiHy -0.37 ±0.58, p = 0.05). A significant difference was found in the tangential curvature superiorly between days 7 and 14 between the groups (SCL material and NCL) (Table A-42). The significant difference was found between the G1SiHy and G2SiHy groups (G1SiHy 1.15 ±1.91, G2SiHy -1.00 ±0.28, p = 0.04). A significant difference was found in the steep SimK between baseline and day 14 between the groups (SCL material and NCL) (Table A-43). The significant difference was found between the NCL and G3SiHy groups (NCL 0.00 ±0.04, G3SiHy 0.09 ±0.15, p = 0.02).

Table A-39: The influence of SCL material on the stability of corneal curvature following 1 day's SCL cessation.

NCL (n = 21), G1SiHy (n = 2), G2SiHy (n = 2), G3SiHy (n = 2), G3SiHy (n = 6), Hydrogel (n = 15)		**Mean ±SD**	**Sig**			**Mean ±SD**	**Sig**
Flat SimK (D)	NCL	-0.01 ±0.04	0.91	Steep SimK (D)	NCL	-0.01 ±0.03	0.01
	G1SiHy	-0.02 ±0.04			G1SiHy	-0.02 ±0.03	
	G2SiHy	-0.01 ±0.01			G2SiHy	0.02 ±0.02	
	G3SiHy	-0.03 ±0.11			G3SiHy	0.09 ±0.15	
	Hydrogel	-0.00 ±0.03			Hydrogel	-0.02 ±0.03	
Sagittal curvature centrally (mm)	NCL	0.03 ±0.21	0.91	Tangential curvature superior (mm)	NCL	-0.25 ±0.56	0.06
	G1SiHy	0.15 ±0.21			G1SiHy	-0.35 ±0.07	
	G2SiHy	0.00 ±0.00			G2SiHy	-0.95 ±0.78	
	G3SiHy	-0.02 ±0.56			G3SiHy	-0.10 ±0.70	
	Hydrogel	0.09 ±0.25			Hydrogel	0.18 ±0.55	
Sagittal curvature superiorly (mm)	NCL	0.09 ±0.33	0.35	Tangential curvature centrally (mm)	NCL	-0.07 ±0.28	0.11
	G1SiHy	0.00 ±0.00			G1SiHy	0.05 ±0.07	
	G2SiHy	-0.25 ±0.35			G2SiHy	-0.15 ±0.21	
	G3SiHy	-0.22 ±0.77			G3SiHy	0.18 ±0.36	
	Hydrogel	0.11 ±0.29			Hydrogel	-0.07 ±0.32	
Sagittal curvature inferiorly (mm)	NCL	-0.37 ±1.29	0.55	Tangential curvature inferiorly (mm)	NCL	-0.10 ±0.58	0.90
	G1SiHy	-0.05 ±0.21			G1SiHy	-0.10 ±0.42	
	G2SiHy	-0.05 ±0.21			G2SiHy	-0.30 ±0.00	
	G3SiHy	-0.70 ±0.74			G3SiHy	0.13 ±0.55	
	Hydrogel	0.02 ±0.25			Hydrogel	-0.09 ±0.69	

Mean ±SD of the stability of corneal curvature measurements following the cessation of SCL wear for NCL and SCL material groups. A negative difference value for SimK (D) and positive value for sagittal and tangential curvature indicates flattening following SCL cessation. Results of two-way ANOVA are shown with significant results displayed in shaded cells, ($p < 0.05$).

Table A-40: The influence of SCL material on the stability of corneal curvature between 1 and 2 days' SCL cessation.

SCL material groups NCL (n = 21), G1SiHy (n = 2), G2SiHy (n = 2), G3SiHy (n = 2), Hydrogel (n = 15)		**Mean ±SD**	**Sig**			**Mean ±SD**	**Sig**
Flat SimK (D)	NCL	0.00 ±0.03	0.28	Steep SimK (D)	NCL	0.01 ±0.04	0.42
	G1SiHy	-0.03 ±0.02			G1SiHy	0.03 ±0.01	
	G2SiHy	0.01 ±0.01			G2SiHy	-0.04 ±0.04	
	G3SiHy	0.03 ±0.01			G3SiHy	0.02 ±0.02	
	Hydrogel	0.01 ±0.04			Hydrogel	0.01 ±0.04	
Sagittal curvature centrally (mm)	NCL	0.01 ±0.31	0.48	Tangential curvature superior (mm)	NCL	0.46 ±1.02	0.15
	G1SiHy	-0.05 ±0.07			G1SiHy	0.25 ±0.21	
	G2SiHy	0.05 ±0.21			G2SiHy	0.10 ±0.57	
	G3SiHy	-0.23 ±0.10			G3SiHy	0.02 ±0.59	
	Hydrogel	-0.11 ±0.39			Hydrogel	-0.25 ±0.49	
Sagittal curvature superiorly (mm)	NCL	-0.17 ±0.38	0.30	Tangential curvature centrally (mm)	NCL	0.11 ±0.3	0.05
	G1SiHy	0.1 ±0.00			G1SiHy	0.40 ±0.00	
	G2SiHy	0.25 ±0.07			G2SiHy	0.05 ±0.07	
	G3SiHy	0.13 ±0.6			G3SiHy	-0.30 ±0.60	
	Hydrogel	-0.05 ±0.28			Hydrogel	0.02 ±0.23	
Sagittal curvature inferiorly (mm)	NCL	0.13 ±0.31	0.35	Tangential curvature inferiorly (mm)	NCL	0.06 ±0.54	0.99
	G1SiHy	-0.25 ±0.07			G1SiHy	0.15 ±0.78	
	G2SiHy	0.25 ±0.07			G2SiHy	0.15 ±0.07	
	G3SiHy	0.08 ±0.42			G3SiHy	0.17 ±0.55	
	Hydrogel	-0.01 ±0.31			Hydrogel	0.13 ±0.49	

Mean ±SD of the stability of corneal curvature measurements following the cessation of SCL wear for NCL and SCL material groups. A negative difference value for SimK (D) and positive value for sagittal and tangential curvature indicates flattening following SCL cessation Results of two-way ANOVA are shown with significant results displayed in shaded cells, ($p < 0.05$).

Table A-41: The influence of SCL material on the stability of corneal curvature between 2 and 7 days' SCL cessation.

SCL material groups NCL (n = 21), G1SiHy (n = 2), G2SiHy (n = 2), G3SiHy (n = 2), Hydrogel (n = 15)		**Mean ±SD**	**Sig**			**Mean ±SD**	**Sig**
Flat SimK (D)	NCL	-0.00 ±0.02	0.96	Steep SimK(D)	NCL	-0.00 ±0.03	0.37
	G1SiHy	0.01 ±0.01			G1SiHy	-0.04 ±0.04	
	G2SiHy	0.01 ±0.01			G2SiHy	0.01 ±0.03	
	G3SiHy	-0.00 ±0.03			G3SiHy	-0.02 ±0.04	
	Hydrogel	-0.00 ±0.03			Hydrogel	-0.00 ±0.04	
Sagittal curvature centrally (mm)	NCL	-0.02 ±0.28	0.61	Tangential curvature superior (mm)	NCL	-0.34 ±0.88	0.41
	G1SiHy	0.20 ±0.28			G1SiHy	-0.25 ±0.07	
	G2SiHy	-0.25 ±0.21			G2SiHy	0.50 ±0.57	
	G3SiHy	0.05 ±0.36			G3SiHy	-0.27 ±0.50	
	Hydrogel	0.08 ±0.40			Hydrogel	-0.02 ±0.42	
Sagittal curvature superiorly (mm)	NCL	0.16 ±0.40	0.68	Tangential curvature centrally (mm)	NCL	-0.06 ±0.24	0.84
	G1SiHy	0.15 ±0.07			G1SiHy	-0.15 ±0.07	
	G2SiHy	0.1 ±0.00			G2SiHy	-0.1 ±0.00	
	G3SiHy	-0.03 ±0.43			G3SiHy	0.00 ±0.39	
	Hydrogel	0.01 ±0.28			Hydrogel	0.03 ±0.33	
Sagittal curvature inferiorly (mm)	NCL	-0.11 ±0.32	0.55	Tangential curvature inferiorly (mm)	NCL	0.06 ±0.41	0.05
	G1SiHy	0.15 ±0.21			G1SiHy	-0.35 ±0.21	
	G2SiHy	0.05 ±0.21			G2SiHy	0.55 ±0.21	
	G3SiHy	-0.20 ±0.36			G3SiHy	-0.37 ±0.58	
	Hydrogel	-0.06 ±0.20			Hydrogel	0.04 ±0.36	

Mean ±SD of the stability of corneal curvature measurements following the cessation of SCL wear for NCL and SCL material groups. A negative difference value for SimK (D) and positive value for sagittal and tangential curvature indicates flattening following SCL cessation. Results of two-way ANOVA are shown with significant results displayed in shaded cells, ($p < 0.05$).

Table A-42: The influence of SCL material on the stability of corneal curvature between 7 and 14 days' SCL cessation.

SCL material groups NCL (n = 21), G1SiHy (n = 2), G2SiHy (n = 2), G3SiHy (n = 2), Hydrogel (n = 15)		**Mean ±SD**	**Sig**			**Mean ±SD**	**Sig**
Flat SimK (D)	NCL	0.01 ±0.03	0.45	Steep SimK (D)	NCL	0.00 ±0.03	0.93
	G1SiHy	0.01 ±0.01			G1SiHy	0.02 ±0.01	
	G2SiHy	-0.01 ±0.01			G2SiHy	0.00 ±0.00	
	G3SiHy	-0.01 ±0.04			G3SiHy	0.01 ±0.05	
	Hydrogel	0.00 ±0.03			Hydrogel	0.00 ±0.03	
Sagittal curvature centrally (mm)	NCL	-0.04 ±0.22	0.19	Tangential curvature superior (mm)	NCL	0.12 ±0.62	0.04
	G1SiHy	-0.35 ±0.35			G1SiHy	1.15 ±1.91	
	G2SiHy	0.30 ±0.14			G2SiHy	-1.00 ±0.28	
	G3SiHy	-0.02 ±0.49			G3SiHy	0.15 ±0.55	
	Hydrogel	0.07 ±0.27			Hydrogel	0.11 ±0.58	
Sagittal curvature superiorly (mm)	NCL	-0.09 ±0.44	0.56	Tangential curvature centrally (mm)	NCL	0.05 ±0.33	0.62
	G1SiHy	-0.30 ±0.14			G1SiHy	-0.20 ±0.14	
	G2SiHy	-0.45 ±0.21			G2SiHy	0.00 ±0.00	
	G3SiHy	-0.02 ±0.30			G3SiHy	0.22 ±0.42	
	Hydrogel	-0.05 ±0.29			Hydrogel	0.07 ±0.32	
Sagittal curvature inferiorly	NCL	0.00 ±0.27	0.49	Tangential curvature inferiorly (mm)	NCL	0.10 ±0.73	0.22
	G1SiHy	0.30 ±0.28			G1SiHy	0.00 ±0.42	
	G2SiHy	-0.30 ±0.42			G2SiHy	-0.95 ±0.07	
	G3SiHy	0.08 ±0.37			G3SiHy	0.08 ±0.55	
	Hydrogel	0.53 ±1.55			Hydrogel	-0.13 ±0.47	

Mean ±SD of the stability of corneal curvature measurements following the cessation of SCL wear for NCL and SCL material groups. A negative difference value for SimK (D) and positive value for sagittal and tangential curvature indicates flattening following SCL cessation. Results of two-way ANOVA are shown with significant results displayed in shaded cells, ($p < 0.05$).

Table A-43: The influence of SCL material on the stability of corneal curvature between baseline and 14 days' SCL cessation.

SCL material groups NCL (n = 21), G1SiHy (n = 2), G2SiHy (n = 2), G3SiHy (n = 2), Hydrogel (n = 15)		**Mean ±SD**	**Sig**			**Mean ±SD**	**Sig**
Flat SimK (D)	NCL	0.01 ±0.03	0.90	Steep SimK (D)	NCL	0.00 ±0.04	0.02
	G1SiHy	-0.03 ±0.03			G1SiHy	-0.01 ±0.00	
	G2SiHy	-0.01 ±0.01			G2SiHy	-0.01 ±0.03	
	G3SiHy	0.00 ±0.12			G3SiHy	0.09 ±0.15	
	Hydrogel	0.00 ±0.03			Hydrogel	-0.01 ±0.03	
Sagittal curvature centrally (mm)	NCL	-0.02 ±0.28	0.28	Tangential curvature superior (mm)	NCL	-0.02 ±0.64	0.08
	G1SiHy	-0.05 ±0.21			G1SiHy	0.80 ±1.70	
	G2SiHy	0.1 ±0.14			G2SiHy	-1.35 ±1.06	
	G3SiHy	-0.22 ±0.65			G3SiHy	-0.20 ±0.81	
	Hydrogel	0.12 ±0.17			Hydrogel	0.01 ±0.74	
Sagittal curvature superiorly (mm)	NCL	0.00 ±0.3	0.44	Tangential curvature centrally (mm)	NCL	0.03 ±0.33	0.79
	G1SiHy	-0.05 ±0.21			G1SiHy	0.10 ±0.00	
	G2SiHy	-0.35 ±0.49			G2SiHy	-0.20 ±0.14	
	G3SiHy	-0.13 ±0.39			G3SiHy	0.10 ±0.27	
	Hydrogel	0.01 ±0.18			Hydrogel	0.05 ±0.27	
Sagittal curvature inferiorly (mm)	NCL	-0.35 ±1.25	0.31	Tangential curvature inferiorly (mm)	NCL	0.12 ±0.66	0.57
	G1SiHy	0.15 ±0.21			G1SiHy	-0.30 ±0.28	
	G2SiHy	-0.05 ±0.49			G2SiHy	-0.55 ±0.21	
	G3SiHy	-0.73 ±0.92			G3SiHy	0.02 ±0.35	
	Hydrogel	0.47 ±1.62			Hydrogel	-0.06 ±0.69	

Mean ±SD of the stability of corneal curvature measurements following the cessation of SCL wear for NCL and SCL material groups. A negative difference value for SimK (D) and positive value for sagittal and tangential curvature indicates flattening following SCL cessation. Results of two-way ANOVA are shown with significant results displayed in shaded cells, ($p < 0.05$).

A.5.3.5 The influence of SCL wear on the stability of corneal thickness measurements following cessation of SCL wear.

A comparison of corneal thickness (at the pupil centre, the thinnest location, superiorly, inferiorly, nasally and temporally) was carried out between the groups (SCL vs. NCL) prior to and following cessation of SCL wear. Two-way ANOVA results showed, that although the SCL had lower corneal thickness at all locations tested, there were no significant differences in corneal thickness between the groups at any time tested except at the temporal location on day 7, when the mean temporal corneal thickness was significantly lower than the NCL group (Table 10-45).

Table A-44: Corneal thickness data prior to SCL cessation.

CL group NCL (n = 28) SCL (n = 33)		**Mean ±SD (µm)**	**Sig**
Baseline			
Central	NCL	542.58 ±33.65	0.10
	SCL	527.94 ±33.23	
Thinnest location	NCL	539.88 ±32.74	0.09
	SCL	525.09 ±32.87	
Inferior	NCL	608.81 ±29.85	0.13
	SCL	596.03 ±32.76	
Nasal	NCL	623.31 ±36.92	0.06
	SCL	604.85 ±37.38	
Superior	NCL	650.85 ±33.94	0.19
	SCL	638.52 ±36.32	
Temporal	NCL	597.88 ±33.53	0.38
	SCL	589.55 ±38.04	

Mean ±SD of corneal thickness measurements prior to and following the cessation of SCL wear for NCL and SCL groups. Results of two-way ANOVA show no significant differences between the groups, ($p < 0.05$).

Table A-45: Corneal thickness data following SCL cessation

CL group NCL (n = 28) SCL (n = 33)		**Mean ±SD (µm)**	**Sig**	**Mean ±SD (µm)**	**Sig**
Day 1				Day 7	
Central	NCL	543.15 ±33.65	0.20	544.23 ±31.06	0.11
	SCL	532.36 ±33.23		530.58 ±33.55	
Thinnest location	NCL	540.62 ±32.74	0.20	541.69 ±30.43	0.11
	SCL	529.97 ±32.87		527.88 ±33.31	
Inferior	NCL	609.38 ±29.85	0.24	611.65 ±30.74	0.17
	SCL	599.67 ±32.76		599.7 ±33.9	
Nasal	NCL	622.62 ±36.92	0.19	625.88 ±35.41	0.12
	SCL	609.82 ±37.38		609.94 ±40.97	
Superior	NCL	654.35 ±33.94	0.12	653 ±38.69	0.20
	SCL	638.64 ±36.32		638.85 ±43.58	
Temporal	NCL	596.58 ±33.53	0.95	598.92 ±26.92	0.02
	SCL	597.12 ±38.04		589.91 ±41	
Day 2				Day 14 NCL (n = 26), SCL (n = 25)	
Central	NCL	543.96 ±35.45	0.17	543 ±37.35	0.50
	SCL	532.12 ±30.08		536.78 ±28.55	
Thinnest location	NCL	541.42 ±34.77	0.16	540.5 ±36.8	0.49
	SCL	529.42 ±29.9		534.19 ±28.65	
Inferior	NCL	613.23 ±32.13	0.10	610.77 ±32.52	0.42
	SCL	599.12 ±31.76		603.74 ±30.33	
Nasal	NCL	624.35 ±40.45	0.13	625.96 ±41.33	0.34
	SCL	608.73 ±37.97		615.81 ±35.5	
Superior	NCL	656.92 ±37.56	0.12	653.27 ±37.7	0.52
	SCL	641.27 ±38.9		646.59 ±36.79	
Temporal	NCL	600.65 ±36.67	0.20	596.58 ±32.78	0.80
	SCL	588.73 ±34.3		594.19 ±34.34	

Mean ±SD of corneal thickness measurements prior to and following the cessation of SCL wear for NCL and SCL groups. Results of two-way ANOVA show no significant differences between the groups, ($p < 0.05$).

Analysis of the stability of corneal thickness using two-way ANOVA and Mann-Whitney U testing show a significant difference in temporal corneal thickness between days 1 and 2 (see Table A-46). There were no further significant differences between the SCL and NCL at any time period tested and all differences in corneal thickness measured were very small, see Table A-47, Table A-48 and Table A-49.

Table A-46: Stability of corneal thickness between 1 and 2 days' SCL cessation

CL group NCL (n = 28) SCL (n = 33)		**Mean ±SD (µm)**	**ANOVA Sig**	**Mann-Whitney Sig**
Central	NCL	0.81 ±8.93	0.72	0.69
	SCL	0.00 ±8.32		
Thinnest location	NCL	0.81 ±9.91	0.65	0.55
	SCL	-0.28 ±8.47		
Inferior	NCL	3.85 ±12.37	0.23	0.32
	SCL	0.00 ±11.85		
Nasal	NCL	1.73 ±14.01	0.55	0.27
	SCL	-0.44 ±13.1		
Superior	NCL	2.58 ±10.25	0.84	0.82
	SCL	3.13 ±10.47		
Temporal	NCL	4.08 ±17.19	0.01	0.02
	SCL	-8.94 ±21.12		

Mean ±SD of stability of corneal thickness measurements between day 1 and 2 following the cessation of SCL wear for NCL and SCL groups. A negative value for mean difference indicates corneal thickness was lower following lens cessation. Significant results of two-way ANOVA and Mann-Whitney testing are shown in shaded cells, ($p < 0.05$).

Table A-47: Stability of corneal thickness following SCL cessation between days 2 and 7

CL group NCL (n = 28) SCL (n = 33)		**Mean ±SD (µm)**	**ANOVA Sig**	**Mann-Whitney Sig**
Central	NCL	0.27 ±10.58	0.52	0.44
	SCL	-1.55 ±10.83		
Thinnest location	NCL	0.27 ±10.43	0.52	0.44
	SCL	-1.55 ±10.92		
Inferior	NCL	-1.58 ±8.6	0.58	0.30
	SCL	0.58 ±18.02		
Nasal	NCL	1.54 ±13.2	0.93	0.91
	SCL	1.21 ±15.83		
Superior	NCL	-3.92 ±13.38	0.73	0.51
	SCL	-2.42 ±18.2		
Temporal	NCL	-1.73 ±17.2	0.50	0.43
	SCL	1.18 ±15.71		

Mean ±SD of stability of corneal thickness measurements between day 2 and 7 following the cessation of SCL wear for NCL and SCL groups. A negative value for mean difference indicates corneal thickness was lower following lens cessation. Significant results of two-way ANOVA and Mann-Whitney testing are shown in shaded cells, ($p < 0.05$).

Table A-48: Stability of corneal thickness following cessation of SCL wear between days 7 and 14

CL group NCL (n = 28) SCL (n = 33)		**Mean ±SD (µm)**	**ANOVA Sig**	**Mann-Whitney Sig**
Central	NCL	-1.23 ±11.36	0.76	0.61
	SCL	-0.31 ±10.14		
Thinnest location	NCL	-1.19 ±11.73	0.71	0.48
	SCL	-0.04 ±10.58		
Inferior	NCL	-0.88 ±11.22	0.65	0.73
	SCL	-2.35 ±12		
Nasal	NCL	0.08 ±12.57	0.50	0.57
	SCL	-1.96 ±8.68		
Superior	NCL	0.27 ±14.76	0.97	0.72
	SCL	0.38 ±9.36		
Temporal	NCL	-2.35 ±13.34	0.71	0.60
	SCL	-3.65 ±11.65		

Mean ±SD of stability of corneal thickness measurements between day 2 and 7 following the cessation of SCL wear for NCL and SCL groups. A negative value for mean difference indicates corneal thickness was lower following lens cessation. Significant results of two-way ANOVA and Mann-Whitney testing are shown in shaded cells, ($p < 0.05$).

Table A-49: Stability of corneal thickness following cessation of SCL wear between baseline and day 14.

CL group NCL (n = 26) SCL (n = 27)		**Mean ±SD (µm)**	**ANOVA Sig**	**Mann-Whitney Sig**
Central	NCL	0.42 ±9.65	0.22	0.28
	SCL	3.74 ±10		
Thinnest location	NCL	0.62 ±9.93	0.20	0.21
	SCL	4.19 ±10.03		
Inferior	NCL	1.96 ±11.88	0.65	0.48
	SCL	3.52 ±12.94		
Nasal	NCL	2.65 ±15.81	0.52	0.66
	SCL	5.11 ±11.26		
Superior	NCL	2.42 ±12.14	0.99	0.53
	SCL	2.44 ±11.67		
Temporal	NCL	-1.31 ±13.29	0.85	0.52
	SCL	-0.56 ±15.33		

Mean ±SD of stability of corneal thickness measurements between baseline and day 14 following the cessation of SCL wear for NCL and SCL groups. A negative value for mean difference indicates corneal thickness was lower following lens cessation. Two-way ANOVA testing revealed no significant differences between the groups, ($p < 0.05$).

A.5.3.6 The influence of SCL material on the stability of corneal thickness

The influence of SCL material on the stability of corneal thickness measurements following cessation of SCL wear was analysed. Two-way ANOVA results showed that there were no significant difference in corneal thickness for the groups between baseline and day 1, or between days 2 and 7, or between baseline and day 14 (see Tables 10-49 – 10-52). There was however, significantly lower TCT in the SCL groups (both hydrogel -7.21 ±24.87µm and SiHy -11.46 ±14.60µm) compared with the NCL group (4.08 ±17.19µm, p = 0.04) following 2 days SCL cessation (see Table 10-51).

Table A-50: The influence of SCL material on the stability of corneal thickness measurements following SCL cessation between baseline and day 1

NCL (n = 26) Hydrogel (n = 19) SiHy (n = 14)		Mean	SD	Sig
Central	NCL Hydrogel SiHy	0.58 5.58 2.86	9.71 7.83 9.88	0.21
Thinnest corneal location	NCL Hydrogel SiHy	0.73 6.42 2.79	10.29 7.71 9.59	0.14
Inferior	NCL Hydrogel SiHy	0.58 5.37 1.29	10.76 9.40 17.01	0.41
Nasal	NCL Hydrogel SiHy	-0.69 6.16 3.36	17.16 10.60 14.47	0.30
Superior	NCL Hydrogel SiHy	3.50 0.47 -0.36	9.82 10.34 13.35	0.49
Temporal	NCL Hydrogel SiHy	-1.31 9.21 5.36	12.38 22.34 13.19	0.10

Mean ±SD of stability of corneal thickness measurements between baseline and day 1 following the cessation of SCL wear for NCL and SCL material groups. A negative value for mean difference indicates corneal thickness was lower following lens cessation. Two- way ANOVA test results indicate no significant differences between the groups, ($p < 0.05$).

Table A-51: The influence of SCL material on the stability of corneal thickness measurements following SCL cessation following 2 day's SCL cessation

NCL (n = 26) Hydrogel (n = 19) SiHy (n = 13)		Mean	SD	Sig
Central	NCL Hydrogel SiHy	0.81 0.37 -0.54	8.93 7.49 9.69	0.90
Thinnest corneal location	NCL Hydrogel SiHy	0.81 -0.37 -0.15	9.91 7.77 9.75	0.90
Inferior	NCL Hydrogel SiHy	3.85 0.58 -0.85	12.37 12.34 11.54	0.47
Nasal	NCL Hydrogel SiHy	1.73 -1.42 1.00	14.01 9.29 17.62	0.74
Superior	NCL Hydrogel SiHy	2.58 5.16 0.15	10.25 10.38 10.27	0.40
Temporal	NCL Hydrogel SiHy	4.08 -7.21 -11.46	17.19 24.87 14.60	0.04

Mean ±SD of stability of corneal thickness measurements following 2 days cessation of SCL wear for NCL and SCL material groups. A negative value for mean difference indicates corneal thickness was lower following lens cessation. Signifcant difference found by two- way ANOVA testing ($p < 0.05$) are shown in shaded cells.

Table A-52: The influence of SCL material on the stability of corneal thickness measurements following SCL cessation following 7 day's SCL cessation

NCL (n = 26) Hydrogel (n = 19) SiHy (n = 14)		Mean	SD	Sig
Central	NCL Hydrogel SiHy	0.27 -4.32 2.21	10.58 10.51 10.46	0.18
Thinnest corneal location	NCL Hydrogel SiHy	0.27 -4.21 2.07	10.43 10.54 10.73	0.20
Inferior	NCL Hydrogel SiHy	-1.58 -2.32 4.50	8.60 20.00 14.73	0.36
Nasal	NCL Hydrogel SiHy	1.54 -3.21 7.21	13.20 16.13 13.76	0.13
Superior	NCL Hydrogel SiHy	-3.92 -8.05 5.21	13.38 20.80 10.32	0.06
Temporal	NCL Hydrogel SiHy	-1.73 -2.32 5.93	17.20 17.98 10.82	0.29

Mean ±SD of stability of corneal thickness measurements following 7 days cessation of SCL wear for NCL and SCL material groups. A negative value for mean difference indicates corneal thickness was lower following lens cessation. Two- way ANOVA test results indicate no significant differences between the groups, ($p < 0.05$).

Table A-53: The influence of SCL material on the stability of corneal thickness measurements following SCL cessation following 14 day's SCL cessation

NCL (n = 26) Hydrogel (n = 16) SiHy (n = 10)		Mean	SD	Sig
Central	NCL Hydrogel SiHy	-1.23 3.63 -6.60	11.36 8.25 10.04	0.05
Thinnest corneal location	NCL Hydrogel SiHy	-1.19 4.13 -6.70	11.73 8.97 9.82	0.05
Inferior	NCL Hydrogel SiHy	-0.88 -1.44 -3.80	11.22 9.40 15.78	0.80
Nasal	NCL Hydrogel SiHy	0.08 -0.81 -3.80	12.57 6.65 11.38	0.63
Superior	NCL Hydrogel SiHy	0.27 3.00 -3.80	14.76 6.80 11.61	0.39
Temporal	NCL Hydrogel SiHy	-2.35 0.19 -9.80	13.34 9.51 12.59	0.13

Mean ±SD of stability of corneal thickness measurements following 14 days cessation of SCL wear for NCL and SCL material groups. A negative value for mean difference indicates corneal thickness was lower following lens cessation. Two- way ANOVA test results indicate no significant differences between the groups, ($p < 0.05$).

The influence of SCL material on the stability of corneal thickness measurements following cessation of SCL wear was analysed. Two-way ANOVA results showed that there were no significant difference in corneal thickness for the groups between baseline and day 1, or between days 1 and 2, days 2 and 7, or between baseline and day 14 (see Table A-54, Table A-55, Table 10-56, Table A-57 and Table A-58.). There was however, a significant difference between the G1SiH and hydrogel central corneal measurements between days 7 and 14. The G1SiH wearers showed significantly reduced corneal thickness between days 7 and 14 compared with the hydrogel goup (Central: G1SiH n = 2, -19.00 ±9.90µm, Hydrogel n = 16, 3.63 ±8.25µm, p= 0.03; Thinnest location: G1SiH -17.50 ±10.61µm, Hydrogel 4.13 ±8.97µm, p= 0.05). This reduction in CCT and TL corneal thickness between 7 and 14 days' SCL cessation is interesting, as it is the opposite to what would have been expected following cessation of stiff modulus SCLs. Corneal thickness at all other locations tested showed no significant differences at this time period (all p values >0.05). The low number of subjects in the G1SiH group means it is not possible to draw any conclusions from these results.

Table A-54: The influence of SCL material on the stability of corneal thickness measurements following SCL cessation between baseline and day 1

SCL material groups NCL (n= 26), G1SiHy (n = 2), G2SiHy (n = 2), G3SiHy (n = 6), hydrogel (n = 16)		**Mean ±SD (µm)**	**Sig**
Central	NCL	0.58 ±9.71	0.12
	G1SiHy	12.50 ±7.78	
	G2SiHy	-3.50 ±1.29	
	GG3SiHy	3.63 ±11.02	
	Hydrogel	5.58 ±7.83	
Thinnest location	NCL	0.73 ±10.29	0.13
	G1SiHy	11.5 ±7.78	
	G2SiHy	-2.75 ±2.63	
	GG3SiHy	3.38 ±10.94	
	Hydrogel	6.42 ±7.71	
Inferior	NCL	0.58 ±10.76	0.24
	G1SiHy	11.5 ±10.61	
	G2SiHy	-7.50 ±13.58	
	GG3SiHy	3.13 ±19.09	
	Hydrogel	5.37 ±9.40	
Nasal	NCL	-0.69 ±17.16	0.55
	G1SiHy	6.00 ±1.41	
	G2SiHy	-1.75 ±12.82	
	GG3SiHy	5.25 ±17.24	
	Hydrogel	6.16 ±10.6	
Superior	NCL	3.50 ±9.82	0.43
	G1SiHy	10.50 ±13.44	
	G2SiHy	-3.75 ±6.34	
	GG3SiHy	-1.38 ±15.69	
	Hydrogel	0.47 ±10.34	
Temporal	NCL	-1.31 ±12.38	0.13
	G1SiHy	-2.50 ±2.12	
	G2SiHy	-3.00 ±6.98	
	GG3SiHy	11.50 ±14.18	
	Hydrogel	9.21 ±22.34	

Mean ±SD of stability of corneal thickness measurements between baseline and day 1 following the cessation of SCL wear for NCL and SCL material groups. A negative value for mean difference indicates corneal thickness was lower following lens cessation. Two- way ANOVA test results indicate no significant differences between the groups, (p <0.05).

Table A-55: The influence of SCL material on the stability of corneal thickness measurements following SCL cessation between days 1 and 2

SCL material groups NCL (n= 26), G1SiHy (n = 2), G2SiHy (n = 2), G3SiHy (n = 6), hydrogel (n = 16)		**Mean ±SD (µm)**	**Sig**
Central	NCL	0.81 ±8.93	0.76
	G1SiHy	6.00	
	G2SiHy	2.50 ±14.73	
	G3SiHy	-2.88 ±7.10	
	Hydrogel	0.37 ±7.49	
Thinnest location	NCL	0.81 ±9.91	0.62
	G1SiHy	9.00	
	G2SiHy	3.50 ±14.15	
	G3SiHy	-3.13 ±6.88	
	Hydrogel	-0.37 ±7.77	
Inferior	NCL	3.85 ±12.37	0.30
	G1SiHy	20.00	
	G2SiHy	-0.25 ±7.72	
	G3SiHy	-3.75 ±11.44	
	Hydrogel	0.58 ±12.34	
Nasal	NCL	1.73 ±14.01	0.20
	G1SiHy	23.00	
	G2SiHy	7.75 ±20.76	
	G3SiHy	-5.13 ±14.48	
	Hydrogel	-1.42 ±9.29	
Superior	NCL	-2.58 ±10.25	0.48
	G1SiHy	-13.00	
	G2SiHy	-1.00 ±6.63	
	GG3SiHy	-0.88 ±11.68	
	Hydrogel	5.16 ±10.38	
Temporal	NCL	4.08 ±17.19	0.14
	G1SiHy	5.00	
	G2SiHy	-13.75 ±25.82	
	G3SiHy	-12.38 ±6.09	
	Hydrogel	-7.21 ±24.87	

Mean ±SD of stability of corneal thickness measurements between days 1 and 2 following the cessation of SCL wear for NCL and SCL material groups. A negative value for mean difference indicates corneal thickness was lower following lens cessation. Two- way ANOVA test results indicate no significant differences between the groups, ($p < 0.05$).

Table A-56: The influence of SCL material on the stability of corneal thickness measurements following SCL cessation between days 2 and 7

SCL material groups NCL (n= 26), G1SiHy (n = 2), G2SiHy (n = 2), G3SiHy (n = 6), hydrogel (n = 16)		**Mean ±SD (µm)**	**Sig**
Central	NCL	0.27 ±10.58	0.30
	G1SiHy	6.00 ±11.31	
	G2SiHy	-3.25 ±18.14	
	G3SiHy	4.00 ±4.38	
	Hydrogel	-4.32 ±10.51	
Thinnest location	NCL	0.27 ±10.43	0.30
	G1SiHy	6.00 ±9.90	
	G2SiHy	-3.75 ±18.71	
	G3SiHy	4.00 ±4.66	
	Hydrogel	-4.21 ±10.54	
Inferior	NCL	-1.58 ±8.60	0.71
	G1SiHy	4.50 ±10.61	
	G2SiHy	2.25 ±20.27	
	G3SiHy	5.63 ±14.36	
	Hydrogel	-2.32 ±20.00	
Nasal	NCL	1.54 ±13.20	0.18
	G1SiHy	0.50 ±12.02	
	G2SiHy	0.75 ±16.03	
	G3SiHy	12.13 ±12.51	
	Hydrogel	-3.21 ±16.13	
Superior	NCL	-3.92 ±13.38	0.22
	G1SiHy	6.50 ±17.68	
	G2SiHy	2.50 ±14.55	
	G3SiHy	6.25 ±7.52	
	Hydrogel	-8.05 ±20.80	
Temporal	NCL	-1.73 ±17.20	0.51
	G1SiHy	10.50 ±23.33	
	G2SiHy	-0.25 ±11.76	
	G3SiHy	7.88 ±6.96	
	Hydrogel	-2.32 ±17.98	

Mean ±SD of stability of corneal thickness measurements between days 2 and 7 following the cessation of SCL wear for NCL and SCL material groups. A negative value for mean difference indicates corneal thickness was lower following lens cessation. Two- way ANOVA test results indicate no significant differences between the groups, ($p < 0.05$).

Table A-57: The influence of SCL material on the stability of corneal thickness measurements following SCL cessation between days 7 and 14

SCL material groups NCL (n= 26), G1SiHy (n = 2), G2SiHy (n = 2), G3SiHy (n = 6), hydrogel (n = 16)		**Mean ±SD (µm)**	**Sig**	**Post hoc Scheffe (Bonferoni)**
Central	NCL	-1.23 ±11.36	0.03	Gen 1 SiHy and hydrogel Sig 0.07 0.04
	G1SiHy	-19.00 ±9.90		
	G2SiHy	2.50 ±4.95		
	G3SiHy	-5.50 ±7.79		
	Hydrogel	3.63 ±8.25		
Thinnest location	NCL	-1.19 ±11.73	0.05	Gen 1 SiHy and hydrogel Sig 0.13 (0.08)
	G1SiHy	-17.5 ±10.61		
	G2SiHy	2.00 ±5.66		
	G3SiHy	-6.00 ±8.20		
	Hydrogel	4.13 ±8.97		
Superior	NCL	-0.88 ±11.22	0.86	
	G1SiHy	-10.00 ±9.90		
	G2SiHy	0.50 ±0.71		
	G3SiHy	-3.17 ±20.13		
	Hydrogel	-1.44 ±9.40		
Nasal	NCL	0.08 ±12.57	0.80	
	G1SiHy	-8.50 ±9.19		
	G2SiHy	1.00 ±11.31		
	G3SiHy	-3.83 ±13.14		
	Hydrogel	-0.81 ±6.65		
Superior	NCL	0.27 ±14.76	0.56	
	G1SiHy	-9.50 ±6.36		
	G2SiHy	3.50 ±14.85		
	G3SiHy	-4.33 ±12.48		
	Hydrogel	3.00 ±6.80		
Temporal	NCL	-2.35 ±13.34	0.11	
	G1SiHy	-24.00 ±19.8		
	G2SiHy	-6.50 ±14.85		
	G3SiHy	-6.17 ±7.86		
	Hydrogel	0.19 ±9.51		

Mean ±SD of stability of corneal thickness measurements between days 7 and 14 following the cessation of SCL wear for NCL and SCL material groups. A negative value for mean difference indicates corneal thickness was lower following lens cessation. Two- way ANOVA test result: significant differences shown in shaded cells, ($p < 0.05$).

Table A-58: The influence of SCL material on the stability of corneal thickness measurements following SCL cessation between baseline and day 14

SCL material groups NCL (n= 26), G1SiHy (n = 2), G2SiHy (n = 2), G3SiHy (n = 6), hydrogel (n = 16)		**Mean ±SD (µm)**	**Sig**
Central	NCL	0.42 ±9.65	0.29
	G1SiHy	-1.50 ±7.78	
	G2SiHy	-1.50 ±0.71	
	G3SiHy	-0.50 ±9.59	
	Hydrogel	6.47 ±10.42	
Thinnest location	NCL	0.62 ±9.93	0.20
	G1SiHy	-0.00 ±8.49	
	G2SiHy	-0.50 ±2.12	
	G3SiHy	-1.50 ±9.33	
	Hydrogel	7.24 ±10.22	
Superior	NCL	1.96 ±11.88	0.62
	G1SiHy	7.00 ±8.49	
	G2SiHy	-9.50 ±6.36	
	G3SiHy	5.33 ±13.41	
	Hydrogel	4.00 ±13.59	
Nasal	NCL	2.65 ±15.81	0.23
	G1SiHy	-1.50 ±2.12	
	G2SiHy	23.00 ±16.97	
	G3SiHy	9.33 ±8.16	
	Hydrogel	2.29 ±10.32	
Superior	NCL	2.42 ±12.14	0.97
	G1SiHy	7.50 ±2.12	
	G2SiHy	1.50 ±4.95	
	G3SiHy	3.50 ±5.21	
	Hydrogel	1.59 ±14.37	
Temporal	NCL	-1.31 ±13.29	0.06
	G1SiHy	-9.00 ±0.00	
	G2SiHy	-27.00 ±42.43	
	G3SiHy	5.00 ±7.90	
	Hydrogel	1.59 ±11.70	

Mean ±SD of stability of corneal thickness measurements between baseline and day 14 following the cessation of SCL wear for NCL and SCL material groups. A negative value for mean difference indicates corneal thickness was lower following lens cessation. Two- way ANOVA test results indicate no significant differences between the groups, ($p < 0.05$).

A.5.4 Study 4: The influence of SCL on the corneal endothelium

A.5.4.1 The influence of SCL wear on the corneal endothelium prior to SCL cessation

Results of two-way ANOVA showed that, prior to SCL cessation, significant differences between the SCL and NCL groups were present for three of the tested variables, all other variables showed non-significant differences between groups (SCL vs. NCL) (Table A-59). Contrary to what was expected, cell density was higher in the SCL compared with the NCL control group in the inferior periphery at 270° (SCL=3109.88 ±153.64, NCL= 2935.08 ±352.78, p= 0.03). Mean cell area was lower in the SCL group compared with the NCL control group in the inferior periphery (SCL = 322.25 ±15.79, NCL = 346.92 ±36.75, p = 0.00). The coefficient of variation of cell size was higher in the SCL group compared with the NCL control group in the superior periphery (SCL = 29.13 ±5.03, NCL = 25.63 ±2.79, p = 0.00).

Table A-59: Endothelial parameters prior to SCL cessation

SCL n = 31 NCL n = 28		**Mean ±SD**	**Sig**	**Mean ±SD**	**Sig**
Centre				270°	
Cell D (cell/mm^2)	NCL	2751.54 ±284.16	0.31	2804.33 ±281.84	0.12
	SCL	2822.67 ±183.68		2915.38 ±193.4	
COV (SD/mean)	NCL	25.79 ±2.00	0.32	24.92 ±3.05	0.06
	SCL	26.79 ±4.39		26.88 ±3.86	
Hexagonal (%)	NCL	68.25 ±4.59	0.39	68.21 ±5.75	0.41
	SCL	67.13 ±4.42		67.04 ±3.82	
Average (μ^2)	NCL	351.38 ±73.62	0.78	360.13 ±37.46	0.09
	SCL	355.79 ±22.91		344.5 ±22.97	
0°				Inferior periphery	
Cell D (cell/mm^2)	NCL	2759.04 ±315.43	0.16	2935.08 ±352.78	0.03
	SCL	2867.29 ±200.38		3109.88 ±153.64	
COV (SD/mean)	NCL	25.42 ±3.28	0.15	26.88 ±3.62	0.55
	SCL	27.13 ±4.62		27.75 ±6.04	
Hexagonal (%)	NCL	68.75 ±5.15	0.18	67.13 ±5.70	0.30
	SCL	66.83 ±4.61		65.42 ±5.58	
Average (μ^2)	NCL	367.08 ±42.98	0.10	346.92 ±36.75	0.00
	SCL	350.04 ±24.68		322.25 ±15.79	
90°				Superior periphery	
Cell D (cell/mm^2)	NCL	2719.08 ±279.26	0.39	2728.21 ±303.44	0.74
	SCL	2779.83 ±200.76		2752.54 ±196.48	
COV (SD/mean)	NCL	26.38 ±3.13	0.33	25.63 ±2.79	0.00
	SCL	27.58 ±5.19		29.13 ±5.03	
Hexagonal (%)	NCL	68.25 ±4.2	0.86	68.71 ±6.59	0.24
	SCL	68.04 ±3.78		66.71 ±4.99	
Average (μ^2)	NCL	371.63 ±38.62	0.30	371 ±41.49	0.57
	SCL	361.58 ±26.11		365.25 ±25.89	
180°					
Cell D (cell/mm^2)	NCL	2753.71 ±289.08	0.25		
	SCL	2836.46 ±199.29			
COV (SD/mean)	NCL	25.79 ±3.46	0.17		
	SCL	27.71 ±5.72			
Hexagonal (%)	NCL	68.04 ±5.81	0.83		
	SCL	67.71 ±5.05			
Average (μ^2)	NCL	367.17 ±39.73	0.19		
	SCL	354.29 ±25.45			

Mean ±SD and two-way ANOVA results for endothelial parameters compared between the SCL and NCL groups prior to SCL cessation, statistically significant differences are displayed in shaded cells ($p < 0.05$).

Table A-60: Endothelial cell density prior to SCL cessation taking the magnification factor of CCT into account

Cell density (cells/mm^2)	**CL group**	**Mean ±SD**	**Sig**
Centrally	NCL SCL	2775.19 ±288.19 2741.54 ±561.22	0.78
0^o	NCL SCL	2787.11 ±320.83 2870.49 ±202.83	0.25
90^o	NCL SCL	2726.88 ±288.29 2795.84 ±218.17	0.32
180^o	NCL SCL	2754.51 ±282.28 2850.26 ±206.34	0.15
270^o	NCL SCL	2670.83 ±618.76 2615.85 ±923.14	0.80
Inferior periphery	NCL SCL	2605.75 ±1017.6 2968.12 ±604.39	0.11
Superior periphery	NCL SCL	2733.51 ±304.92 2675.83 ±554.65	0.64

Results of two-way ANOVA revealed no significant differences in endothelial cell density between SCL and NCL groups at baseline, ($p < 0.05$).

Table A-61: Endothelial cell density following 2 weeks SCL cessation taking the magnification factor of CCT into account

Cell density (cells/mm^2)	**CL group**	**Mean ±SD**	**Sig**
Centrally	NCL SCL	2816.17 ±233.65 2862.47 ±199.02	0.46
0^o	NCL SCL	2807.57 ±257.11 2901.46 ±199.21	0.16
90^o	NCL SCL	2764.86 ±260.20 2844.52 ±181.83	0.23
180^o	NCL SCL	2850.30 ±287.28 2880.95 ±177.24	0.66
270^o	NCL SCL	2877.19 ±264.47 2816.27 ±634.38	0.67
Inferior periphery	NCL SCL	3009.57 ±309.91 2955.22 ±231.50	0.49
Superior periphery	NCL SCL	2735.06 ±289.91 2785.70 ±239.27	0.51

Results of two-way ANOVA revealed no significant differences in endothelial cell density between SCL and NCL groups after 2 weeks cessation of SCL wear, ($p < 0.05$).

Table A-62: Stability of corneal endothelial cell density following 2 weeks SCL cessation taking the magnification factor of CCT into account

Cell density (cells/mm^2)	**CL group**	**Mean ±SD**	**Sig**
Centrally	NCL SCL	-3.87 ±87.60 -346.55 ±924.26	0.08
0^o	NCL SCL	26.91 ±113.35 -224.72 ±842.63	0.15
90^o	NCL SCL	-0.39 ±91.78 -236.77 ±790.51	0.15
180^o	NCL SCL	-54.89 ±218.95 -245.86 ±807.32	0.27
270^o	NCL SCL	-177.83 ±665.51 -472.2 ±1387.13	0.35
Inferior periphery	NCL SCL	-391.48 ±1099.96 -123.86 ±894.16	0.36
Superior periphery	NCL SCL	31.59 ±176.17 -187.22 ±799.53	0.20

Results of two-way ANOVA revealed no significant differences in the stability of endothelial cell density between SCL and NCL groups after 2 weeks cessation of SCL wear, ($p < 0.05$).

A.5.4.2 The impact of previous SCL material on the corneal endothelium

Results of two-way ANOVA showed that prior to SCL cessation, significant differences were present between the SCL material groups for 4 variables tested, all other variables showed non-significant differences between groups (SCL vs. NCL) (Table 10-62). The coefficient of variation was significantly higher in the hydrogel group at 180^o, cell density was significantly higher and mean cell area was significantly lower in the hydrogel group compared with the NCL group at the inferior periphery. The coefficient of variation was significantly higher in the hydrogel group compared with the NCL group in the superior periphery.

Table A-63: The influence of SCL material on endothelial parameters at baseline

NCL (n = 24) Hydrogel (n = 12) SiHy (n = 12)		Central	0º	90º	180º	270º	Inferior periphery	Superior periphery
Cell density	NCL	2751.54 ±284.16	2759.04 ±315.43	2719.08 ±279.26	2753.71 ±289.08	2804.33 ±281.84	2935.08 ±352.78	2728.21 ±303.44
	Hydrogel	2869.75 ±200.84	2937.08 ±209.26	2827.08 ±200.79	2847.58 ±235.34	3000.25 ±214.37	3184.08 ±161.84	2820.92 ±192.36
	SiHy	2775.58 ±159.29	2797.50 ±171.87	2732.58 ±197.69	2825.33 ±165.50	2830.50 ±128.59	3035.67 105.59	2684.17 ±183.07
	Sig (Post hoc Scheffe)	0.38	0.17	0.44	0.51	0.07	0.04 (0.04 NCL and hydrogel)	0.40
Coefficient of variation of cell size	NCL	25.79 ±2.00	25.42 ±3.28	26.38 ±3.13	25.79 ±3.46	24.92 ±3.05	26.88 ±3.62	25.63 ±2.79
	Hydrogel	27.50 ±4.87	27.50 ±5.25	28.67 ±6.34	29.83 ±6.51	27.42 ±4.62	28.00 ±6.05	29.92 ±6.22
	SiHy	26.08 ±3.94	26.75 ±4.09	26.50 ±3.68	25.58 ±4.03	26.33 ±3.03	27.50 ±6.29	28.33 ±3.60
	Sig (Post hoc Scheffe)	0.36	0.32	0.29	0.03 (0.05 NCL,SiHy and hydrogel)	0.13	0.81	0.01 (0.02 NCL and hydrogel)
Hexagonality	NCL	68.25 ±4.59	68.75 ±5.15	68.25 ±4.20	68.04 ±5.81	68.21 ±5.75	67.13 ±5.70	68.71 ±6.59
	Hydrogel	66.00 ±3.95	65.42 ±4.29	66.92 ±4.06	65.33 ±4.16	65.58 ±4.14	62.92 ±5.92	65.25 ±5.19
	SiHy	68.25 ±4.73	68.25 ±4.65	69.17 ±3.27	70.08 ±4.87	68.50 ±2.94	67.92 ±4.06	68.17 ±4.53
	Sig	0.33	0.15	0.38	0.09	0.25	0.05	0.24
Mean cell area	NCL	351.38 ±73.62	367.08 ±42.98	371.63 ±38.62	367.17 ±39.73	360.13 ±37.46	346.92 ±36.75	371.00 ±41.49
	Hydrogel	350.00 ±25.08	341.33 ±24.75	355.42 ±26.02	353.50 ±30.45	335.08 ±25.59	314.92 ±16.57	356.25 ±23.29
	SiHy	361.58 ±19.88	358.75 ±22.28	367.75 ±25.81	355.08 ±20.65	353.92 ±15.98	329.58 ±11.37	374.25 ±26.13
	Sig (Post hoc Scheffe)	0.84	0.12	0.39	0.42	0.08	0.008 (0.009 NCL and hydrogel)	0.38

Mean ±SD and two-way ANOVA statistics for the differences in the endothelial parameters measured between the various SCL materials (hydrogel, and SiHy) and the NCL control group. Statistically significant results are shown in shaded cells, ($p < 0.05$).

A.5.4.3 The influence of SCL wear on the stability of corneal endothelium following 2 weeks cessation of SCL wear

The differences between endothelium measurements collected at baseline and following 2 weeks SCL cessation were calculated to explore the stability of endothelial measurements. Results of two-way ANOVA indicate no statistically significant differences in endothelial parameters between the SCL and NCL group (Table A-64).

Table A-64: Stability of endothelium data after 2 weeks SCL cessation

SCL n = 17 NCL n = 22		**Mean ±SD**	**Sig**	**Mean ±SD**	**Sig**
Central				270°	
Cell density (cells/mm^2)	NCL	-15.32 ±79.84	0.61	3.55 ±12.42	0.92
	SCL	-0.76 ±98.96		4.06 ±20.96	
COV (SD/mean)	NCL	-0.05 ±2.06	0.22	-11.14 ±93.99	0.32
	SCL	-0.94 ±2.44		20.29 ±99.44	
Hexagonality (%)	NCL	0.73 ±4.60	0.67	0.14 ±3.21	0.51
	SCL	0.06 ±5.14		-0.47 ±2.27	
Average (μ^2)	NCL	2.64 ±10.05	0.39	0.68 ±4.26	0.32
	SCL	15.76 ±69.44		-0.35 ±3.69	
0°				Inferior periphery	
Cell density (cells/mm^2)	NCL	15.5 ±122.88	0.80	0.00 ±11.28	0.60
	SCL	5.18 ±124.6		-2.47 ±12.06	
Coefficient of variation (SD/mean)	NCL	-0.18 ±3.45	0.45	18.09 ±285.90	0.91
	SCL	0.59 ±2.62		96.35 ±158.27	
Hexagonality (%)	NCL	1.32 ±9.09	0.43	-1.18 ±3.70	0.16
	SCL	-0.59 ±4.56		-0.53 ±4.00	
Average (μ^2)	NCL	-1.45 ±14.55	0.97	1.23 ±6.1	0.28
	SCL	-1.29 ±14.76		1.00 ±5.55	
90°				Superior periphery	
Cell density (cells/mm^2)	NCL	49.36 ±215.72	0.16	0.36 ±27.8	0.50
	SCL	-35.29 ±133.91		-10.59 ±17.17	
COV (SD/mean)	NCL	-0.77 ±2.27	0.75	10.91 ±178.79	0.50
	SCL	-1.18 ±5.38		75.71 ±187.88	
Hexagonality (%)	NCL	0.68 ±3.96	0.25	-1.23 ±3.80	0.45
	SCL	2.53 ±5.86		-0.18 ±5.90	
Average (μ^2)	NCL	-0.55 ±10.76	0.68	1.41 ±6.37	0.27
	SCL	1.06 ±13.05		-0.18 ±6.60	
180°					
Cell density (cells/mm^2)	NCL	-18.91 ±99.61	0.71		
	SCL	-36.06 ±183.20			
Coefficient of variation (SD/mean)	NCL	-0.36 ±3.09	0.38		
	SCL	0.59 ±3.64			
Hexagonality (%)	NCL	2.50 ±13.82	0.98		
	SCL	2.59 ±5.03			

Mean ±SD of differences in endothelial parameters tested for the SCL and NCL control groups between baseline and following 2 weeks SCL cessation. Two- way ANOVA test statistics showed no significant differences in the endothelial parameters measured ($p < 0.05$).

A.5.4.4 The influence of SCL material on the stability of corneal endothelium following 2 weeks cessation of SCL wear

The influence of SCL material on the stability of endothelial parameters following 2 weeks cessation of SCL wear was compared between the groups. Two-way ANOVA tests showed no significant differences between the various SCL materials tested and the NCL control group (Table A-66, 10-65).

Table A-65: The influence of SLC material on the stability of endothelium measurement data following 2 weeks cessation of SCL wear

NCL (n = 22) Hydrogel (n = 11) SiHy (n = 6)		Central Mean ±SD	0º Mean ±SD	90.00	180.00	270.00	Inferior periphery	Superior periphery
Cell density	NCL	-15.32 ±79.84	15.50 ±122.88	49.36 ±215.72	-18.91 ±99.61	-11.14 ±93.99	18.09 ±285.90	10.91 ±178.79
	Hydrogel	-13.09 ±110.61	17.73 ±136.11	-66.09 ±128.47	-85.36 ±210.45	32.73 ±117.07	89.91 ±145.39	83.82 ±205.53
	SiHy	21.83 ±76.65	-17.83 ±107.90	21.17 ±135.85	54.33 ±60.55	-2.50 ±57.21	108.17 ±193.98	60.83 ±167.51
	Sig	0.66	0.83	0.25	0.14	0.48	0.60	0.55
Coefficient of variation of cell size	NCL	-0.05 ±2.06	-0.18 ±4.45	-0.77 ±2.27	-0.36 ±0.36	0.14 ±3.21	-1.18 ±3.70	-1.23 ±3.80
	Hydrogel	-0.36 ±1.69	0.64 ±2.94	-1.09 ±6.33	0.91 ±3.62	-0.55 ±2.73	-0.18 ±3.66	-0.64 ±7.10
	SiHy	-2.00 ±3.35	0.50 ±2.17	-1.33 ±3.50	0.00 ±3.95	-0.33 ±1.21	-1.17 ±4.88	0.67 ±3.01
	Sig	0.17	0.75	0.95	0.60	0.80	0.77	0.70
Hexagonality	NCL	0.73 ±4.60	1.32 ± 9.09	0.68 ±3.96	2.50 ±13.82	0.68 ±4.26	1.23 ±6.10	1.41 ±6.37
	Hydrogel	-0.73 ±3.32	-0.36 ±5.01	2.36 ±6.34	1.82 ±5.55	-0.82 ±4.12	2.18 ±4.73	-0.73 ±7.35
	SiHy	1.50 ±7.66	-1.00 ±4.00	2.83 ±5.42	4.00 ±3.95	0.50 ±2.88	-1.17 ±6.71	0.83 ±5.42
	Sig	0.61	0.73	0.51	0.93	0.60	0.53	0.68
Mean cell area	NCL	2.64 ±10.05	-1.45 ±14.55	-0.55 ±10.76	3.55 ±12.42	0.00 ±11.28	0.36 ±27.80	-1.59 ±23.83
	Hydrogel	25.45 ±85.90	-2.91 ±15.96	2.64 ±11.32	9.64 ±24.11	-4.00 ±14.25	-9.55 ±15.19	-11.73 ±27.99
	SiHy	-2.00 ±9.40	1.67 ±13.08	-1.83 ±16.52	-6.17 ±7.03	0.33 ±6.68	-12.50 ±21.80	-8.17 ±21.76
	Sig	0.35	0.83	0.70	0.17	0.62	0.37	0.53

Mean, standard deviation (SD) and two- way ANOVA test statistics for the differences in the endothelial parameters measured between the various SCL materials and the NCL control group, no statistically significant differences were found between the groups ($p < 0.05$).

Table A-66: The influence of SLC material on the stability of endothelium measurement data following 2 weeks cessation of SCL wear (central, 0º, 90º, 180º)

SCL material groups **NCL (n = 22)** **G2SiHy (n = 2)** **G3SiHy (n = 4)** **Hydrogel (n = 11)**		**Mean ±SD**	**Sig**	**Mean ±SD**	**Sig**
Central				90º	
Cell density (cells/mm^2)	NCL	-15.32 ±79.84	0.69	49.36 ±215.72	0.44
	G2SiHy	-19.50 ±106.77		19.50 ±136.47	
	G3SiHy	42.50 ±66.03		22.00 ±156.68	
	Hydrogel	-13.09 ±110.61		-66.09 ±128.47	
Coefficient of variation (SD/mean)	NCL	-0.05 ±2.06	0.18	-0.77 ±2.27	0.95
	G2SiHy	-0.50 ±3.54		-2.50 ±3.54	
	G3SiHy	-2.75 ±3.50		-0.75 ±3.86	
	Hydrogel	-0.36 ±1.69		-1.09 ±6.33	
Hexagonality (%)	NCL	0.73 ±4.60	0.74	0.68 ±3.96	0.32
	G2SiHy	3.00 ±9.90		7.00 ±1.41	
	G3SiHy	0.75 ±7.93		0.75 ±5.56	
	Hydrogel	-0.73 ±3.32		2.36 ±6.34	
Average (μ^2)	NCL	2.64 ±10.05	0.55	-0.55 ±10.76	0.87
	G2SiHy	2.50 ±13.44		-2.00 ±16.97	
	G3SiHy	-4.25 ±8.18		-1.75 ±18.95	
	Hydrogel	25.45 ±85.90		2.64 ±11.32	
0º				180º	
Cell density (cells/mm^2)	NCL	15.50 ±122.88	0.70	-18.91 ±99.61	0.27
	G2SiHy	-91.00 ±90.51		45.00 ±57.98	
	G3SiHy	18.75 ±106.4		59.00 ±70.01	
	Hydrogel	17.73 ±136.11		-85.36 ±210.45	
Coefficient of variation (SD/mean)	NCL	-0.18 ±3.45	0.62	-0.36 ±3.09	0.73
	G2SiHy	2.50 ±0.71		1.00 ±8.49	
	G3SiHy	-0.50 ±1.91		-0.50 ±1.00	
	Hydrogel	0.64 ±2.94		0.91 ±3.62	
Hexagonality (%)	NCL	1.32 ±9.09	0.84	2.50 ±13.82	0.96
	G2SiHy	-3.00 ±1.41		1.50 ±3.54	
	G3SiHy	0.00 ±4.69		5.25 ±3.95	
	Hydrogel	-0.36 ±5.01		1.82 ±5.55	
Average (μ^2)	NCL	-1.45 ±14.55	0.67	3.55 ±12.42	0.32
	G2SiHy	11.00 ±11.31		-5.50 ±7.78	
	G3SiHy	-3.00 ±12.46		-6.50 ±7.85	
	Hydrogel	-2.91 ±15.96		9.64 ±24.11	

Mean, standard deviation (SD) and two- way ANOVA test statistics for the differences in the endothelial parameters measured between the various SCL materials and the NCL control group, no statistically significant differences were found between the groups ($p < 0.05$)

Table A-67: The influence of SLC material on the stability of endothelium measurement data following 2 weeks cessation of SCL wear (270º,superior and inferior periphery)

SCL material groups **NCL (n = 22)** **G2SiHy (n = 2)** **G3SiHy (n = 4)** **Hydrogel (n = 11)**		**Mean ±SD**	**Sig**	**Mean ±SD**	**Sig**
270º				Superior periphery	
Cell density (cells/mm^2)	NCL	-11.14 ±93.99	0.69	10.91 ±178.79	0.85
	G2SiHy	-10.50 ±43.13		-71.5 ±194.45	
	G3SiHy	1.50 ±69.08		127 ±129.02	
	Hydrogel	32.73 ±117.07		83.82 ±205.53	
Coefficient of variation (SD/mean)	NCL	0.14 ±3.21	0.78	-1.23 ±3.8	0.83
	G2SiHy	1.00 ±0.00		-0.5 ±2.12	
	G3SiHy	-1.00 ±0.82		1.25 ±3.5	
	Hydrogel	-0.55 ±2.73		-0.64 ±7.1	
Hexagonality (%)	NCL	0.68 ±4.26	0.63	1.41 ±6.37	0.85
	G2SiHy	-1.50 ±0.71		1.5 ±10.61	
	G3SiHy	1.50 ±3.11		0.5 ±3.32	
	Hydrogel	-0.82 ±4.12		-0.73 ±7.35	
Average (μ^2)	NCL	0.00 ±11.28	0.81	-1.59 ±23.83	0.44
	G2SiHy	1.00 ±5.66		9 ±24.04	
	G3SiHy	0.00 ±7.96		-16.75 ±17.37	
	Hydrogel	-4.00 ±14.25		-11.73 ±27.99	
Inferior periphery					
Cell density (cells/mm^2)	NCL	18.09 ±285.9	0.80		
	G2SiHy	122.50 ±408			
	G3SiHy	101 ±83.77			
	Hydrogel	89.91 ±145.39			
Coefficient of variation (SD/mean)	NCL	-1.18 ±3.7	0.88		
	G2SiHy	-2 ±9.9			
	G3SiHy	-0.75 ±2.5			
	Hydrogel	-0.18 ±3.66			
Hexagonality (%)	NCL	1.23 ±6.1	0.43		
	G2SiHy	3 ±7.07			
	G3SiHy	-3.25 ±6.4			
	Hydrogel	2.18 ±4.73			
Average (μ^2)	NCL	0.36 ±27.8	0.83		
	G2SiHy	-14.5 ±45.96			
	G3SiHy	-11.5 ±9.15			
	Hydrogel	-9.55 ±15.19			

Mean, standard deviation (SD) and two- way ANOVA test statistics for the differences in the endothelial parameters measured between the various SCL materials and the NCL control group, no statistically significant differences were found between the groups ($p < 0.05$)

A.5.5 Study 5: the impact of SCL wear on the epithelium

A.5.5.1 The influence of SCL wear on Pentacam and OCT scan quality

The influence of SCL wear on densitometry and signal strength measurements was analysed prior to and following CRS. Results of two-way ANOVA and Mann-Whitney testing showed that there was no statistically significant effect of SCL wear on corneal densitometry or OCT scan quality prior to CRS (Table A-68).

Table A-68: Pentacam densitometry and OCT scan signal quality

	SCL n = 48	**NCL n = 26**	**Sig ANOVA (Mann-Whitney)**
Pre-operative			
Pentacam densitometry	28.63 ±2.68	28.97 ±3.97	0.70 (0.98)
OCT signal strength	62.76 ±10.62	61.00 ±10.66	0.23
LASIK	**SCL n = 25**	**NCL n = 9**	**Sig**
Early post-operative visit			
Pentacam densitometry	30.63 ±2.43	30.53 ±2.58	0.92
OCT signal strength	63.84 ±11.02	56.22 ±15.67	0.12
Late post-operative visit			
Pentacam densitometry	32.66 ±12.37	28.58 ±1.30	0.34
OCT signal strength	61.80 ±14.81	51.33 ±10.20	0.06
LASEK/PRK	**SCL n = 10**	**NCL n = 2**	**Sig**
Early post-operative visit			
Pentacam densitometry	25.32 ±2.28	28.35 ±0.49	0.10
OCT signal strength	60.20 ±13.69	64.00 ±2.83	0.71
Late post-operative visit			
Pentacam densitometry	31.28 ±10.81	26.00 ±4.81	0.53
OCT signal strength	52.20 ±15.48	74.00 ±15.56	0.10

Mean ±standard deviations and two-way ANOVA statistics for Pentacam densitometry and OCT scan signal quality. Comparisons carried out between the groups showed no significant differences in corneal densitometry and scan quality of OCT scans between the SCL and NCL control groups pre-operatively or following LASIK and PRK/LASEK CRS , ($p < 0.05$).

A.5.5.2 The influence of myopic group on pre-operative VA and CSF

The influence of myopic group on pre-operative CSF and VA was explored between the groups (SCL vs. NCL). Two-way ANOVA results showed no significant differences between the myopic and SCL groups for CSF or BCSVA pre-operatively (Table A-69).

Table A-69: Visual acuity and contrast sensitivity function pre- and post-operatively for myopic and SCL and NCL groups

Low (0 to -2.75D): NCL n = 18, SCL n = 18. Medium (-3.00 to -5.75D): NCL n = 7, SCL, n = 22. High (> -6.00D): NCL n = 1, SCL n = 11			**Mean ±SD**	**Sig, CL group**	**Sig, Myopic group**
CSF pre-operatively	NCL	Low	1.49 ±0.15	0.27	0.51
		Medium	1.56 ±0.16		
		High	1.75		
	SCL	Low	1.61 ±0.11		
		Medium	1.51 ±0.15		
		High	1.50 ±0.13		
LogMAR VA with habitual spectacles pre-operatively	NCL	Low	-0.23 ±0.12	0.19	0.16
		Medium	-0.19 ±0.15		
		High	-0.18		
	SCL	Low	-0.19 ±0.17		
		Medium	-0.09 ±0.12		
		High	-0.10 ±0.11		
BCSVA(VAR) pre-operatively	NCL	Low	104.89 ±0.32	0.26	0.17
		Medium	105.14 ±0.38		
		High	105		
	SCL	Low	105.67 ±1.61		
		Medium	104.86 ±1.49		
		High	102.55 ±2.46		

A.5.5.3 The influence of SCL modality of the pre-operative VA and CSF

Two-way ANOVA results for preoperative VA, CSF, and refractive error for NCL and SCL modality groups are expressed in (Table 10-68) . Significant differences were found between the groups. UDVA and VA with habitual spectacles were better in the NCL group compared with the EW. The higher refractive error in the DW and EW group compared with the NCL accounted for this difference in UDVA between the SCL modality and NCL groups.

Table A-70: The influence of SCL modality on VA, CSF and refractive error prior to CRS.

CL modality NCL (n = 24) DW (n = 41) EW (n = 4)		**Mean**	**Sig ANOVA (KW)**	**Post hoc tests**
UDVA LogMAR	NCL	1.02 ±0.24	0.02	NCL and EW 0.04
	DW	1.14 ±0.14		
	EW	1.20 ±0.23		
LogMAR visual acuity with habitual spectacles	NCL	-0.21 ±0.13	0.03 (KW)	NCL and EW 0.03
	DW	-0.14 ±0.14		
	EW	-0.06 ±0.06		
CSF	NCL	1.51 ±0.15	0.60	
	DW	1.54 ±0.14		
	EW	1.51 ±0.03		
Spherical refractive error (D)	NCL	-2.42 ±1.35	0.00	NCL and DW 0.00
	DW	-4.26 ±2.08		
	EW	-4.38 ±1.60		
Cylindrical refractive error (D)	NCL	-0.88 ±0.52	0.30	
	DW	-0.76 ±0.57		
	EW	-0.44 ±0.13		
Mean spherical equivalent (D)	NCL	-2.85 ±1.38	0.00	NCL and DW 0.00
	DW	-4.64 ±2.20		
	EW	-4.59 ±1.57		
BCSVA LogMAR	NCL	-0.10 ±0.01	0.04	DW and EW 0.08
	DW	-0.09 ±0.04		
	EW	-0.13 ±0.03		

Mean ±SD and two-way ANOVA statistics exploring the influence of SCL modulus on VA, CSF and refractive error prior to CRS. Statistically significant results are displayed in shaded cells ($p < 0.05$).

A.5.5.4 The influence of SCL material on visual outcomes following CRS

The influence of SCL material on VA and CSF following CRS was explored.

Outcomes were analysed at early and late post-operative visits.

Table A-71: The influence of SCL material on LASIK outcomes at early post-operative visit

Type of CL material **NCL (n = 15)** **G2SiHy (n = 10)** **Hydrogel (n = 24)**		**Mean ±SD**	**Sig**
UDVA LogMAR	NCL	-0.18 ±0.14	0.24
	SiHy	-0.16 ±0.12	
	Hydrogel	-0.23 ±0.12	
UDVA MAR	NCL	0.69 ±0.24	0.24
	SiHy	0.72 ±0.21	
	Hydrogel	0.61 ±0.17	
CSF	NCL	1.44 ±0.13	0.05
	SiHy	±1.43 ±0.15	
	Hydrogel	1.55 ±0.17±	
UDVA VAR	NCL	98.47 ±7.65	0.14
	SiHy	103.5 ±3.25	
	Hydrogel	101.6 ±6.10	
Spherical refractive error (D)	NCL	0.00 ±0.40	0.87
	SiHy	0.00 ±0.31	
	Hydrogel	0.05 ±0.35	
Cylindrical refractive error (D)	NCL	-0.47 ±0.21	0.11
	SiHy	-0.19 ±0.13	
	Hydrogel	-0.48 ±0.28	
MSE (D)	NCL	-0.11 ±0.42	0.85
	SiHy	-0.04 ±0.27	
	Hydrogel	-0.12 ±0.41	
BCSVA	NCL	102.5 ±4.69	0.39
	SiHy	103.9 ±3.28	
	Hydrogel	104.2 ±3.31	

Mean ±SD and two-way ANOVA statistics exploring the influence of SCL material on VA, CSF and refractive error following LASIK in the early post-operative time period (1 week). Statistically significant results are displayed in shaded cells ($p < 0.05$).

Early post-operative results indicated no significant effect of SCL material for the LASIK group) (Table A-71). Results showed no significant effect of SCL material on UDVA or CSF at this early post-operative visit (Table A-72).

Table A-72: The influence of SCL material on LASEK/PRK outcomes at early post-operative visit

Type of CL material NCL (n = 4), SiHy (n = 2), Hydrogel (n = 8)		**Mean ±SD**	**Sig**
UDVA LogMAR	NCL	0.06 ±0.11	0.14
	SiHy	0.06 ±0.06	
	Hydrogel	-0.06 ±0.11	
UDVA MAR	NCL	1.19 ±0.30	0.14
	SiHy	1.15 ±0.15	
	Hydrogel	0.89 ±0.22	
CSF	NCL	1.33 ±0.04	0.22
	SiHy	1.35 ±0.00	
	Hydrogel	1.42 ±0.08	

Mean ±SD and two-way ANOVA statistics exploring the influence of SCL material on VA, CSF and refractive error following LASEK/PRK in the early post-operative time period (1 week). Statistically significant results are displayed in shaded cells ($p < 0.05$).

Late post-operative results for LASIK indicated there was a significant loss of letters seen in the NCL group ±compared with the SiHy group and there was significantly higher BCSVA in the SiHy group compared with the hydrogel group (Table A-73).

Table A-73: The influence of SCL material on LASIK outcomes at late post-operative visit

Type of CL material NCL (n = 15) SiHy (n = 10) Hydrogel (n = 18)		**Mean ±SD**	**Sig**	**Post hoc Scheffe**
Loss of BCSVA between pre- and late postoperative visit	NCL	-6.27 ±10.22	0.01	NCL and SiHy 0.02
	SiHy	1.10 ±2.64		
	Hydrogel	-1.00 ±2.86		
UDVA LogMAR	NCL	-0.21 ±0.15	0.11	
	G2SiHy	-0.30 ±0.08		
	Hydrogel	-0.30 ±0.13		
UDVA MAR	NCL	0.65 ±0.24	0.12	
	SiHy	0.51 ±0.09		
	Hydrogel	0.53 ±0.18		
CSF	NCL	1.52 ±0.17	0.20	
	SiHy	1.64 ±0.10		
	Hydrogel	1.56 ±0.16		
Spherical refractive error (D)	NCL	-0.12 ±0.45	0.11	
	SiHy	0.07 ±0.21		
	Hydrogel	0.13 ±0.34		
Cylindrical refractive error (D)	NCL	-0.43 ±0.25	0.08	
	SiHy	-0.17 ±0.13		
	Hydrogel	-0.35 ±0.23		
MSE (D)	NCL	-0.26 ±0.46	0.05	
	SiHy	0.03 ±0.22		
	Hydrogel	0.01 ±0.32		
BCSVA VAR	NCL	105.00 ±2.40	0.04	Hydrogel and SiHy 0.04
	SiHy	106.50 ±2.42		
	Hydrogel	103.86 ±2.85		

Mean ±SD and two-way ANOVA statistics exploring the influence of SCL material on VA, CSF and refractive error following LASIK in the late post-operative time period. Statistically significant results are displayed in shaded cells ($p < 0.05$).

Table A-74: The influence of SCL wear on LASEK/PRK outcomes at late post-operative visit

SCL group **NCL (n= 1)** **SCL (n = 7)**		**Mean ±SD**	**Sig**
Day of late post-op visit	NCL SCL	44.00 27.71 ±10.19	0.19
Loss of BCSVA between pre- and late postoperative visit	NCL SCL	-10.00 -7.43±5.09	0.65
UDVA LogMAR	NCL SCL	0.00 -0.15 ±0.04	0.02
CSF	NCL SCL	1.30 1.51 ±0.12	0.15
Spherical refractive error (D)	NCL SCL	-0.50 0.43 ±0.45	0.10
Cylindrical refractive error (D)	NCL SCL	-0.25 -0.50 ±0.25	0.39
MSE (D)	NCL SCL	-0.63 0.18 ±0.38	0.10
Loss of BCSVA between pre- and late post-op visit	NCL SCL	-5.00 -2.29 ±2.93	0.42

Mean ±SD and two-way ANOVA statistics exploring the influence of SCL wear on VA, CSF and refractive error following LASEK/PRK in the late post-operative time period. Statistically significant results are displayed in shaded cells ($p < 0.05$).

A comparison of outcomes of LASEK/PRK at the late post-operative visit indicated significant better UDVA (LogMAR) in the entire SCL group (-0.15 ±0.04) compared with the NCL group UDVA ($p = 0.02$). As there was only one patient in the NCL group, these findings lack statistical validity. No other significant differences were found between the SCL and NCL groups (all other p-values > 0.05).

Two-way ANOVA was carried out to explore the influence of pre-operative SCL material on the outcomes of LASEK/PRK at the late-post operative visit. Results for the LASEK/PRK patients indicated significantly higher residual spherical refractive error and MSE in the SiHy group compared with the NCL group) at the late post-operatively visit (Table A-75).

Table A-75: The influence of SCL material on LASEK/PRK outcomes at late post-operative visit

Type of CL material NCL (n = 3), SiHy (n = 4), Hydrogel (n = 8)		**Mean ±SD**	**Sig**	**Post hoc Scheffe**
Loss of BCSVA between pre- and late postoperative visit	NCL	-5.00 ±5.57	0.75	
	SiHy	-8.50 ±5.20		
	Hydrogel	-8.37 ±7.80		
UDVA LogMAR	NCL	-0.11 ±0.28	0.85	
	SiHy	-0.15 ±0.04		
	Hydrogel	-0.16 ±0.04		
UDVA MAR	NCL	0.88 ±0.45	0.46	
	SiHy	0.71 ±0.07		
	Hydrogel	0.70 ±0.06		
CSF	NCL	1.43 ±0.23	0.31	
	SiHy	1.65 ±0.00		
	Hydrogel	1.51 ±0.12		
Spherical refractive error (D)	NCL	0.00 ±0.50	0.02	NCL and SiHy 0.02
	SiHy	0.94 ±0.13		
	Hydrogel	0.41 ±0.37		
Cylindrical refractive error (D)	NCL	-0.40 ±0.22	0.31	
	SiHy	-0.62 ±0.14		
	Hydrogel	-0.40 ±0.22		
MSE (D)	NCL	-0.18 ±0.41	0.04	NCL and SiHy 0.04
	SiHy	0.63 ±0.10		
	Hydrogel	0.28±0.46		
BCSVA VAR	NCL	101.33 ±3.21	0.0.05	
	SiHy	99.75 ±0.50		
	Hydrogel	103.63 ±2.56		

Mean ±SD and two-way ANOVA statistics exploring the influence of SCL material on VA, CSF and refractive error following LASEK/PRK in the late post-operative time period. Statistically significant results are displayed in shaded cells ($p < 0.05$).

A.5.5.5 The influence of SCL modality of the outcomes of CRS

The role of SCL modality on visual outcomes and residual refractive error following LASIK was explored. At the early post-operatively visit, the NCL group had a significantly lower BCSVA compared with pre-operative measurements (4.50 ±4.87 letters) while the DW SCL group had significantly better BCSVA (-0.07 ±3.69, p = 0.04) (Table 10-74). This was interesting as there were no significant differences in CSF or residual refractive error between the groups.

Table A-76: The influence of SCL modality on visual outcomes and residual refractive error following LASIK at the early post-operative visit

CL modality **NCL (n = 8)** **DW (n = 15)** **EW (n = 4)**		**Mean ±SD**	**Sig ANOVA (KW)**	**Post hoc Scheffe**
UDVA LogMAR	NCL	-0.17 ±0.15	0.90	
	DW	-0.17 ±0.09		
	EW	-0.14 ±0.12		
CSF	NCL	1.38 ±0.08	0.13	
	DW	1.54 ±0.20		
	EW	1.50 ±0.17		
Spherical refractive error (D)	NCL	0.03 ±0.36	0.54	
	DW	0.05 ±0.36		
	EW	0.25 ±0.20		
Cylindrical refractive error (D)	NCL	-0.47 ±0.21	0.13	
	DW	-0.48 ±0.29		
	EW	-0.19 ±0.13		
Mean spherical equivalent (D)	NCL	-0.20 ±0.41	0.26	
	DW	-0.19 ±0.41		
	EW	0.16 ±0.16		
BCSVA	NCL	-0.01 ±0.10	0.05	
	DW	-0.08 ±0.06		
	EW	-0.12 ±0.01		
Loss of letters of BCSVA between pre- and early postoperative visit	NCL	4.50 ±4.87	0.04	NCL and DW 0.04
	DW	-0.07 ±3.69		
	EW	0.25 ±0.50		
UDVA measured at 1 week post-op	NCL	-0.17 ±0.15	0.90	(KW)
	DW	-0.17 ±0.09		
	EW	-0.14 ±0.12		

Mean ±SD and two-way ANOVA statistics exploring the influence of SCL modulus on VA, CSF and refractive error at the early post-operatively visit following LASIK. Statistically significant results are displayed in shaded cells ($p < 0.05$).

This loss of BCSVA following LASIK in the NCL group was maintained at the late post-operative visit and there was significantly poorer BCSVA in this group compared with both the DW and EW SCL groups (Table 10-75). Results of two-way ANOVA were highly significant ($p = 0.00$). Again, there was no significant difference in the CSF between the groups.

Table A-77: SCL modality and visual outcomes and residual refractive error following LASIK at the late post-operative visit

CL modality **NCL (n = 8)** **DW (n = 15)** **EW (n = 5)**		**Mean ±SD**	**Sig**	**Post hoc**
Loss of BCSVA between pre- and late postoperative visit	NCL	-10.38 ±10.27	0.00	NCL and DW 0.01 NCL and EW 0.02
	DW	-1.40 ±3.11		
	EW	0.20 ±2.49		
UDVA LogMAR	NCL	-0.21 ±0.15	0.08	
	DW	-0.32 ±0.11		
	EW	-0.26 ±0.07		
CSF	NCL	1.51 ±0.19	0.29	
	DW	1.62 ±0.13		
	EW	1.59 ±0.12		
Spherical refractive error (D)	NCL	-0.19 ±0.56	0.14	
	DW	0.17 ±0.32		
	EW	0.10 ±0.22		
Cylindrical refractive error (D)	NCL	-0.47 ±0.28	0.07	
	DW	-0.33 ±0.22		
	EW	-0.15 ±0.14		
Mean spherical equivalent (D)	NCL	-0.42 ±0.56	0.05	
	DW	0.00 ±0.31		
	EW	0.03 ±0.27		
Late post-operative BCSVA VAR	NCL	-0.08 ±0.04	0.32	
	DW	-0.08 ±0.04		
	EW	-0.12 ±0.04		
Loss of BCSVA between pre- and late post-operatively visit	NCL	-0.75 ±1.83	0.63	
	DW	-0.40 ±1.35		
	EW	0.20 ±2.49		

Mean ±SD and two-way ANOVA statistics exploring the influence of SCL modulus on VA, CSF and refractive error at the late post-operatively visit following LASIK. Statistically significant results are displayed in shaded cells ($p < 0.05$).

A.5.5.6 The influence of myopic group on the outcomes of CRS

There was significantly higher myopia in the SCL group pre-operatively. As the efficacy and predictability of LASIK outcomes diminishes with increasing myopia (Kojima et al., 2008), the influence of pre-operative myopic group on CRS outcomes was explored. Results of two-way ANOVA showed significant differences between the groups for the influence of both previous SCL wear and myopic group. In the NCL

group, late post-operative LASIK outcomes (CSF and UDVA) were progressively worse with increasing myopia. In the SCL group however, while the differences between the low and medium myopic groups showed a similar trend to poorer results with increased myopia, the high myopic group had similar results to the low myopic group. The low sample size in the high myopic group means these results may not be statistically viable. The results of LASEK/PRK procedures showed a similar trend to the LASIK outcomes. However, the low sample size in the LASEK/PRK group means these results may not be statistically viable. Results of LASIK procedures are displayed in Table 10-76 and LASEK/PRK in Table 10-77.

Table A-78: Outcomes of LASIK at the late post-operative visit for myopic groups

Low (0 to -2.75D): Medium (-3.00 to -5.75D): High (> -6.00D):			**Mean ±SD**	**n**	**Sig, CL group**	**Sig, Myopic group**	**Sig Interaction effect of CL and myopic group**
UDVA (VAR) late post-operatively	NCL	Low	103.14 ±6.09	7	0.00	0.01	0.00
		Medium	93.80 ±11.17	5			
		High	80.00	1			
	SCL	Low	105.85 ±2.41	13			
		Medium	103.17 ±3.83	12			
		High	105.00 ±0.00	3			
UDVA (LogMAR) late post-operatively	NCL	Low	-0.32 ±0.09	7	0.01	0.00	0.21
		Medium	-0.10 ±0.16	5			
		High	-0.14	1			
	SCL	Low	-0.34 ±0.07	13			
		Medium	-0.23 ±0.12	12			
		High	-0.35 ±0.10	3			
CSF late post-operatively	NCL	Low	1.64 ±0.07	7	0.00	0.01	0.04
		Medium	1.36 ±0.17	5			
		High	1.35	1			
	SCL	Low	1.60 ±0.10	13			
		Medium	1.55 ±0.16	12			
		High	1.65 ±0.25	3			

Mean ±SD and two-way ANOVA statistics exploring the influence of SCL wear and pre-operative myopia on VA and CSF at the late post-operative visit following LASIK. Statistically significant results are displayed in shaded cells ($p < 0.05$).

Table A-79: Outcomes of LASEK/PRK at the late post-operative visit for myopic groups

Low (0 to -2.75D): Medium (-3.00 to -5.75D): High (> -6.00D):			**Mean ±SD**	**n**	**Sig, CL group**	**Sig, Myopic group**	**Sig Interaction effect of CL and myopic group**
UDVA (VAR) late post-operatively	NCL	Low	100.0 ±7.07	2	0.88	0.39	0.88
		Medium	99.00	1			
	SCL	Low	100.00 ±7.07	2			
		Medium	97.33 ±5.01	6			
		High	90.00 ±14.14	2			
UDVA (LogMAR) late post-operatively	NCL	Low	0.05 ±0.07	2	0.29	0.00	0.00
		Medium	-0.04	1			
	SCL	Low	-0.15 ±0.07	2			
		Medium	-0.15 ±0.03	6			
		High	-0.18 ±0.00	2			
CSF late post-operatively	NCL	Low	1.30 ±0.00	2	0.85	0.04	0.16
		Medium	1.70	1			
	SCL	Low	1.45 ±0.01	2			
		Medium	1.58 ±0.13	6			
		High	1.50 ±0.00	2			

Mean ±SD and two-way ANOVA statistics exploring the influence of SCL wear and pre-operative myopia on VA and CSF at the late post-operative visit following LASEK/PRK. Statistically significant results are displayed in shaded cells ($p < 0.05$).

A.5.5.7 The influence of previous SCL wear on post-operative epithelial thickness

The influence of previous SCL wear on post-operative epithelial thickness was examined. Following LASIK at the late post-operative visit, two-way ANOVA showed that central epithelial thickness was significantly thicker in the SCL group compared with the NCL: the epithelial thickness in the nasal periphery was significantly thinner in the SCL group compared with the NCL group (Table A-82). There were no other significant differences between the groups at the either post-operative time for LASIK or LASEK/PRK (Table A-80, Table A-81 and Table A-83).

Table A-80: Epithelial thickness following LASIK at the early post-operative visit

SCL group NCL (n = 14) SCL (n = 34)		**Mean ±SD (µm)**	**Sig**
Temporal peripheral	NCL SCL	57.07 ±3.58 57.27 ±6.61	0.91
Temporal para-central	NCL SCL	58.93 ±6.11 59.29 ±5.57	0.84
Central	NCL SCL	57.43 ±5.93 57.93 ±6.92	0.81
Nasal para-central	NCL SCL	59.64 ±3.82 59.92 ±5.85	0.87
Nasal peripheral	NCL SCL	55.5 ±7.60 58.99 ±5.89	0.09

Mean ±SD and two-way ANOVA statistics exploring the influence of SCL wear epithelial thickness following LASIK at the early post-operative visit, ($p < 0.05$).

Table A-81: Epithelial thickness following LASEK/PEK at the early post-operative visit

SCL group **NCL (n = 3)** **SCL (n = 10)**		**Mean ±SD (µm)**	**Sig**
Temporal peripheral	NCL SCL	47.33 ±6.03 53.00 ±4.69	0.11
Temporal para-central	NCL SCL	52.67 ±5.51 58.60 ±4.86	0.10
Central	NCL SCL	55.33 ±12.66 52.90 ±5.51	0.62
Nasal para-central	NCL SCL	54.33 ±6.43 53.60 ±3.10	0.78
Nasal peripheral	NCL SCL	51.00 ±1.73 52.60 ±5.38	0.63

Mean ±SD and two-way ANOVA statistics exploring the influence of SCL wear epithelial thickness following LASEK/PRK at the early post-operative visit, ($p < 0.05$).

Table A-82: Epithelial thickness following LASIK at the late post-operative visit

SCL group **NCL (n = 12)** **SCL (n = 23)**		**Mean ±SD (µm)**	**Sig**
Temporal peripheral	NCL SCL	59 ±6.08 59.09 ±4.81	0.96
Temporal para-central	NCL SCL	58 ±5.39 61.26 ±6.45	0.14
Central	NCL SCL	54.42 ±8.12 59.65 ±6.2	0.04
Nasal para-central	NCL SCL	58.25 ±5.48 60.61 ±6.9	0.31
Nasal peripheral	NCL SCL	65.83 ±9.16 59.52 ±7.01	0.03

Two-way ANOVA results indicate significant differences in epithelial thickness between SCL and NCL groups, significant results shown in shaded cells, (p < 0.05).

Table A-83: Epithelial thickness following LASEK/PEK at the late post-operative visit

SCL group NCL (n = 3) SCL (n = 10)		**Mean ±SD (µm)**	**Sig**
Temporal peripheral	NCL SCL	56.33 ±14.22 56.60 ±6.87	0.96
Temporal para-central	NCL SCL	55.00 ±8.00 55.90 ±4.56	0.80
Central	NCL SCL	49.67 ±5.86 53.60 ±4.20	0.22
Nasal para-central	NCL SCL	59.67 ±3.06 56.80 ±5.09	0.38
Nasal peripheral	NCL SCL	59.00 ±4.58 56.40 ±6.06	0.51

Mean ±SD and two-way ANOVA statistics exploring the influence of SCL wear epithelial thickness following LASEK/PRK at the late post-operative visit, ($p < 0.05$).

Further analysis was carried out on the recovery of epithelial thickness following CRS by comparing the difference in epithelial thickness recorded at the post-operative visit with the pre-operative value measured for LASIK and LASEK/PRK procedures. Two-way ANOVA indicate no significant differences in the pre-operative and post-operative epithelial thickness measured except for the nasal periphery at the late post-operative visit for those patients who had LASIK surgery. The NCL group showed significantly thicker post-operative epithelial thickness (9.78 ±11.91µm) compared with the SCL group who showed relative stability (0.15 ±8.36µm, $p = 0.01$) (Table A-84). No significant differences were found between the groups (NCL vs. SCL) following LASEK/PRK (Table A-85).

Table A-84: Recovery of epithelial thickness following LASIK

SCL group NCL (n = 9), SCL (n = 23)		**Mean ±SD (µm)**	**Sig**
Difference between pre- and early post-op epithelial thickness			
Temporal peripheral	NCL SCL	-0.78 ±6.04 -2.69 ±7.17	0.49
Temporal para-central	NCL SCL	-3.22 ±5.43 1.44 ±6.22	0.06
Central	NCL SCL	0.56 ±6.91 -0.41 ±9.10	0.78
Nasal para-central	NCL SCL	0.11 ±8.37 0.49 ±7.32	0.90
Nasal peripheral	NCL SCL	-3.78 ±6.55 0.48 ±8.25	0.18
Difference between pre- and late post-op epithelial thickness			
Temporal peripheral	NCL SCL	0.00 ±5.55 -1.18 ±6.46	0.63
Temporal para-central	NCL SCL	-2.33 ±6.00 3.00 ±8.01	0.08
Central	NCL SCL	-3.56 ±10.36 1.47 ±8.98	0.18
Nasal para-central	NCL SCL	0.44 ±7.42 1.56 ±8.16	0.72
Nasal peripheral	NCL SCL	9.78 ±11.91 0.15 ±8.36	0.01

Two-way ANOVA results for the recovery of epithelial thickness following LASIK for SCL and NCL groups. A positive number indicates thicker epithelial thickness post-operatively. Significant differences are shown in shaded cells, ($p < 0.05$).

Table A-85: Recovery of epithelial thickness following LASEK/PRK at the late post-operative visit.

SCL group **NCL (n = 3)** **SCL (n = 10)**		**Mean ±SD (µm)**	**Sig**
Difference between pre- and early post-op epithelial thickness			
Temporal peripheral	NCL SCL	-8.00 ±5.29 -2.10 ±6.85	0.20
Temporal para-central	NCL SCL	-11.33 ±1.53 -0.70 ±8.93	0.07
Central	NCL SCL	-4.33 ±11.06 -7.10 ±10.14	0.69
Nasal para-central	NCL SCL	-9.67 ±6.03 -7.10 ±9.16	0.66
Nasal peripheral	NCL SCL	-14.33 ±6.66 -8.00 ±7.83	0.23
Difference between pre- and late post-op epithelial thickness			
Temporal peripheral	NCL SCL	1.00 ±11.53 1.50 ±9.47	0.94
Temporal para-central	NCL SCL	-9.00 ±3.61 -3.40 ±7.12	0.23
Central	NCL SCL	-10.00 ±6.56 -6.40 ±9.07	0.54
Nasal para-central	NCL SCL	-4.33 ±1.53 -3.90 ±9.49	0.94
Nasal peripheral	NCL SCL	-6.33 ±3.51 -4.20 ±7.73	0.66

Two-way ANOVA results for the recovery of epithelial thickness following LASEK/PRK for SCL and NCL groups. A positive number indicates thicker epithelial thickness post-operatively. Significant differences are shown in shaded cells, ($p < 0.05$).

A.5.5.8 The influence of SCL material on post-operative epithelial thickness

The influence of previous SCL material on epithelial thickness following CRS was examined. Two-way ANOVA testing found no significant effect of SCL material following CRS at either the early or late post-operative visit.

Table A-86: The influence of SCL material on epithelial thickness following LASIK at the early post-operative visit

Type of CL material NCL (n = 14) SiHy (n = 10) Hydrogel (n = 24)		**Epithelial thickness Mean ±SD (µm)**	**Sig**
Temporal periphery	NCL	57.07 ±3.58	0.61
	SiHy	55.70 ±6.02	
	Hydrogel	57.93 ±6.85	
Temporal para-central	NCL	58.13 ±6.64	0.72
	SiHy	60.10 ±6.49	
	Hydrogel	58.96 ±5.26	
Central	NCL	58.00 ±6.13	0.86
	SiHy	58.90 ±10.34	
	Hydrogel	57.53 ±5.13	
Nasal para-central	NCL	59.47 ±3.74	0.96
	SiHy	60.10 ±6.84	
	Hydrogel	59.85 ±5.55	
Nasal peripheral	NCL	55.50 ±7.60	0.22
	SiHy	59.90 ±7.14	
	Hydrogel	58.61 ±5.42	

Mean ±SD and two-way ANOVA results for epithelial thickness between the SCL material and NCL control groups following LASIK at the early post-operative visit ($p < 0.05$).

Table A-87: The influence of SCL material on epithelial thickness following LASEK/PRK at the early post-operative visit

Type of CL material NCL (n = 3) SiHy (n = 2) Hydrogel (n = 8)		**Epithelial thickness Mean ±SD (µm)**	**Sig**
Temporal periphery	NCL	47.33 ±6.02	0.27
	SiHy	51.50 ±6.36	
	Hydrogel	53.37 ±4.66	
Temporal para-central	NCL	52.67 ±5.51	0.09
	SiHy	54.00 ±4.24	
	Hydrogel	59.70 ±4.49	
Central	NCL	55.33 ±12.66	0.88
	SiHy	52.00 ±1.41	
	Hydrogel	53.13 ±6.20	
Nasal para-central	NCL	54.33 ±6.43	0.79
	SiHy	52.00 ±1.41	
	Hydrogel	54.00 ±3.33	
Nasal peripheral	NCL	51.00 ±1.74	0.12
	SiHy	58.50 ±2.12	
	Hydrogel	51.13 ±4.91	

Mean ±SD and two-way ANOVA results for epithelial thickness between the SCL material and NCL control groups following LASEK/PRK at the early post-operative visit ($p < 0.05$).

Table A-88: The influence of SCL material on epithelial thickness following LASIK at the late post-operative visit

Type of CL material NCL (n = 12) SiHy (n = 10) Hydrogel (n = 15)		**Epithelial thickness Mean ±SD (µm)**	**Sig**
Temporal periphery	NCL	59.00 ±6.08	0.32
	SiHy	61.30 ±5.71	
	Hydrogel	58.13 ±3.70	
Temporal para-central	NCL	58.00 ±5.39	0.22
	SiHy	63.00 ±7.21	
	Hydrogel	59.07 ±7.07	
Central	NCL	54.42 ±8.12	0.12
	SiHy	60.11 ±5.60	
	Hydrogel	59.36 ±1.80	
Nasal para-central	NCL	58.25 ±5.48	0.51
	SiHy	61.44 ±5.36	
	Hydrogel	60.47 ±7.74	
Nasal peripheral	NCL	65.83 ±9.16	0.09
	SiHy	59.50 ±5.81	
	Hydrogel	59.67 ±7.57	

Mean ±SD and two-way ANOVA results for epithelial thickness between the SCL material and NCL control groups following LASIK at the late post-operative visit ($p < 0.05$).

Table A-89: The influence of SCL material on epithelial thickness following LASEK/PRK at the late post-operative visit

Type of CL material NCL (n = 3) SiHy (n = 2) Hydrogel (n = 8)		**Epithelial thickness Mean ±SD (µm)**	**Sig**
Temporal periphery	NCL	56.33 ±14.22	0.52
	SiHy	63.00 ±4.24	
	Hydrogel	55.00 ±6.59	
Temporal para-central	NCL	55.00 ±8.00	0.34
	SiHy	51.00 ±2.83	
	Hydrogel	57.13 ±4.13	
Central	NCL	49.67 ±5.86	0.38
	SiHy	51.50 ±2.12	
	Hydrogel	54.13 ±4.52	
Nasal para-central	NCL	59.67 ±6.06	0.15
	SiHy	62.00 ±1.41	
	Hydrogel	55.50 ±4.84	
Nasal peripheral	NCL	59.00 ±4.58	0.45
	SiHy	60.50 ±3.53	
	Hydrogel	55.37 ±6.28	

Mean ±SD and two-way ANOVA results for epithelial thickness between the SCL material and NCL control groups following LASIK at the early post-operative visit ($p < 0.05$).

The influence of previous generation of SiHy SCL material on epithelial thickness following CRS was examined. Following LASIK at the early post-operative visit; average and central epithelial thickness were significantly lower in the G1SiHy group compared with the G2SiHy, these results were highly significant. Peripheral nasal epithelial thickness was lower in the NCL group compared with the G2SiHy group, this result was also highly significant (Table A-90). There were no significant differences in epithelial thickness at any location for SCL material and NCL groups following LASEK/PRK (Table A-91).

Table A-90: The influence of SCL material on epithelial thickness following LASIK at the early post-operative visit

SCL material groups **NCL (n = 10)** **G1SiHy (n = 2)** **G2SiHy (n = 6)** **G3SiHy (n = 2)** **Hydrogel (n = 15)**		**Mean ±SD Epithelial thickness (µm)**	**Sig**	**Post hoc Scheffe**
Average	NCL	56.98 ±3.33	0.00	Gen 1 & 2 SiHy 0.01
	G1SiHy	51.60 ±2.83		
	G2SiHy	62.23 ±4.69		
	G3SiHy	56.40 ±1.98		
	Hydrogel	59.13 ±2.95		
Temporal peripheral	NCL	57.30 ±3.40	0.23	
	G1SiHy	50.00 ±4.24		
	G2SiHy	58.33 ±5.79		
	G3SiHy	53.50 ±4.95		
	Hydrogel	59.09 ±6.66		
Temporal para-central	NCL	56.70 ±5.62	0.28	
	G1SiHy	55.00 ±5.66		
	G2SiHy	62.50 ±6.98		
	G3SiHy	58.00 ±2.83		
	Hydrogel	59.40 ±4.98		
Central	NCL	58.00 ±5.73	0.04	Gen 1 & 2 SiHy 0.06,0.04
	G1SiHy	47.00 ±8.49		
	G2SiHy	64.00 ±9.12		
	G3SiHy	55.50 ±3.54		
	Hydrogel	57.51 ±5.81		
Nasal para-central	NCL	59.60 ±4.27	0.53	
	G1SiHy	55.00 ±11.31		
	G2SiHy	62.33 ±6.41		
	G3SiHy	58.50 ±0.71		
	Hydrogel	59.62 ±4.80		
Nasal peripheral	NCL	53.30 ±6.20	0.00	NCL & Gen 2 SiHy 0.01
	G1SiHy	51.00 ±1.41		
	G2SiHy	64.00 ±5.48		
	G3SiHy	56.50 ±4.95		
	Hydrogel	60.04 ±4.51		

Mean ±SD and two-way ANOVA results for epithelial thickness between the SCL material and NCL control groups following LASIK at the early post-operative visit. Statistically significant results are shown in shaded cells ($p < 0.05$).

Table A-91: The influence of SCL material on epithelial thickness following LASEK/PRK at the early post-operative visit

SCL material groups **NCL (n = 3)** **G1SiHy (n = 2)** **Hydrogel (n = 8)**		**Mean ±SD (µm)**	**Sig**
Average epithelial thickness	NCL	52.13 ±2.72	0.52
	G1SiHy	53.60 ±0.00	
	Hydrogel	54.28 ±2.86	
OCT temporal peripheral epithelial thickness	NCL	47.33 ±6.03	0.27
	G1SiHy	51.50 ±6.36	
	Hydrogel	53.38 ±4.66	
OCT temporal para-central epithelial thickness	NCL	52.67 ±5.51	0.09
	G1SiHy	54.00 ±4.24	
	Hydrogel	59.75 ±4.50	
OCT central epithelial thickness	NCL	55.33 ±12.66	0.88
	G1SiHy	52.00 ±1.41	
	Hydrogel	53.13 ±6.20	
OCT nasal para-central epithelial thickness	NCL	54.33 ±6.43	0.79
	G1SiHy	52.00 ±1.41	
	Hydrogel	54.00 ±3.34	
OCT nasal peripheral epithelial thickness	NCL	51.00 ±1.73	0.12
	G1SiHy	58.50 ±2.12	
	Hydrogel	51.13 ±4.91	

Mean ±SD and two-way ANOVA results for epithelial thickness between the SCL material and NCL control groups following LASEK/PRK at the early post-operative visit. There were no statistically significant differences between the groups (all p-values > 0.05).

Following LASIK at the late post-operative visit, results of two-way ANOVA showed the significantly thinner central and average epithelial thickness in the G1SiHy group and the peripheral nasal epithelial thickness in the NCL group had resolved and there were now no significant differences in epithelial thickness between the SCL material and NCL groups (Table A-92). Again, there were no significant differences found in epithelial thickness between the groups following LASEK/PRK at this late post-operative visit (Table A-93).

Table A-92: The influence of SCL material on epithelial thickness following LASIK at the late post-operative visit

SCL material groups **NCL (n = 12)** **G1SiHy (n = 2)** **G2SiHy (n = 5)** **G3SiHy (n = 2)** **Hydrogel (n = 14)**		**Mean ±SD (µm)**	**Sig**
Average	NCL	59.10 ±4.00	0.43
	G1SiHy	57.20 ±1.13	
	G2SiHy	62.80 ±3.00	
	G3SiHy	59.80 ±5.66	
	Hydrogel	59.47 ±4.44	
Temporal periphery	NCL	59.00 ±6.08	0.08
	G1SiHy	60.00 ±0.00	
	G2SiHy	64.20 ±2.68	
	G3SiHy	53.50 ±9.19	
	Hydrogel	57.93 ±3.75	
Temporal para-central	NCL	5.00 ±5.39	0.23
	G1SiHy	58.00 ±15.56	
	G2SiHy	63.20 ±4.44	
	G3SiHy	67.50 ±2.12	
	Hydrogel	60.14 ±5.92	
Central	NCL	54.42 ±8.12	0.17
	G1SiHy	53.50 ±4.95	
	G2SiHy	61.60 ±4.83	
	G3SiHy	63.00 ±4.24	
	Hydrogel	59.36 ±6.74	
Nasal para-central	NCL	58.25 ±5.48	0.84
	G1SiHy	59.50 ±6.36	
	G2SiHy	62.20 ±5.45	
	G3SiHy	61.50 ±7.78	
	Hydrogel	60.07 ±7.88	
Nasal periphery	NCL	65.83 ±9.16	0.12
	G1SiHy	55.00 ±1.41	
	G2SiHy	62.80 ±4.76	
	G3SiHy	53.50 ±4.95	
	Hydrogel	59.86 ±7.82	

Mean ±SD and two-way ANOVA results for epithelial thickness between the SCL material and NCL control groups following LASIK at the late post-operative visit. There were no statistically significant differences between the groups (all p-values > 0.05).

Table A-93: The influence of SCL material on epithelial thickness following LASEK/PRK at the late post-operative visit

SCL material groups NCL (n = 3) G1SiHy (n = 2) Hydrogel (n = 8)		**Mean ±SD (µm)**	**Sig**
Average	NCL	55.93 ±2.12	0.39
	G1SiHy	57.60 ±0.85	
	Hydrogel	55.43 ±1.96	
Temporal periphery	NCL	56.33 ±14.22	0.52
	G1SiHy	63.00 ±4.24	
	Hydrogel	55.00 ±6.59	
Temporal para-central	NCL	55.00 ±8.00	0.34
	G1SiHy	51.00 ±2.83	
	Hydrogel	57.13 ±4.12	
Central	NCL	49.67 ±5.86	0.38
	G1SiHy	51.50 ±2.12	
	Hydrogel	54.13 ±4.52	
Nasal para-central	NCL	59.67 ±3.06	0.15
	G1SiHy	62.00 ±1.41	
	Hydrogel	55.50 ±4.84	
Nasal periphery	NCL	59.00 ±4.58	0.45
	G1SiHy	60.50 ±3.54	
	Hydrogel	55.38 ±6.28	

Mean ±SD and two-way ANOVA results for epithelial thickness between the SCL material and NCL control groups following LASIK at the late post-operative visit. There were no statistically significant differences between the groups (all p-values > 0.05).

A.5.5.9 The influence of years of previous SCL wear on epithelial thickness

The impact of previous years of SCL wear on epithelial thickness was analysed. Two-way ANOVA results showed no significant influence of previous wearing times on epithelial thickness (Table A-94).

Table A-94: The influence of years of SCL wear on epithelial thickness

Years of SCL wear **NCL (n = 23)** **Short (0 - 5 years) (n = 10)** **Medium (> 5 -10 years) (n = 29)** **Long (> 10 years) (n = 17)**		**Mean ±SD (µm)**	**Sig**
Average	NCL	59.77 ±3.49	0.85
	Short-term	60.46 ±3.05	
	Medium-term	59.28 ±4.34	
	Long-term	59.70 ±3.14	
Temporal periphery	NCL	58.61 ±6.13	0.78
	Short-term	60.10 ±4.89	
	Medium-term	58.24 ±7.04	
	Long-term	57.65 ±4.33	
Temporal para-central	NCL	60.65 ±4.84	0.66
	Short-term	60.50 ±6.52	
	Medium-term	59.31 ±5.06	
	Long-term	59.00 ±3.98	
Central	NCL	60.65 ±4.90	0.69
	Short-term	60.40 ±7.38	
	Medium-term	58.62 ±7.62	
	Long-term	60.00 ±5.11	
Nasal para-central	NCL	60.65 ±5.50	0.69
	Short-term	61.70 ±4.45	
	Medium-term	59.55 ±6.68	
	Long-term	61.29 ±5.95	
Nasal peripheral	NCL	58.30 ±5.60	0.45
	Short-term	59.60 ±3.72	
	Medium-term	60.66 ±6.69	
	Long-term	60.59 ±4.29	

Mean ±SD and two-way ANOVA results for epithelial thickness between the years of SCL wear and NCL control groups. No significant differences were found between the variables for the groups tested (all p values >0.05).

A.5.5.10 The influence of SCL modality on epithelial thickness

Investigations into the impact of SCL modality on epithelial thickness were carried out in order to assess the impact of extended wearing times. Pre-operative epithelial thickness data were explored using two-way ANOVA and Kruskal-Wallis testing. No significant differences were found between the groups (Table A-95).

Table A-95: The influence of SCL modality on epithelial thickness pre-operatively

CL modality **NCL (n = 25)** **DW (n = 45)** **EW (n = 8)**		**Mean ±SD (µm)**	**Sig ANOVA (Kruskal-Wallis)**
Temporal periphery	NCL	58.56 ±5.90	0.96 (0.90)
	DW	58.31 ±6.15	
	EW	57.88 ±5.22	
Temporal para-central	NCL	61.20 ±5.02	0.09
	DW	59.51 ±4.91	
	EW	56.88 ±4.12	
Central	NCL	60.44 ±4.97	0.05 (0.09)
	DW	60.24 ±6.65	
	EW	54.63 ±7.09	
Nasal para-central	NCL	60.28 ±5.49	0.15 (0.14)
	DW	61.13 ±5.97	
	EW	56.75 ±5.55	
Nasal periphery	NCL	58.60 ±5.46	0.36
	DW	60.60 ±5.81	
	EW	59.38 ±5.01	

Mean ±SD and two-way ANOVA and Kruskal-Wallis test statistics for pre-operative epithelial thickness in SCL modality groups, ($p < 0.05$).

A.5.5.11 The effect of myopic prescription on epithelial thickness

As there was significantly higher myopia in the SCL group pre-operatively, the impact of pre-operative myopic group and SCL wear on epithelial thickness was explored in order to assess the effect of myopic prescription and the associated thicker SCL edge on peripheral epithelial thickness. Epithelial thickness data were explored using two-way ANOVA. Results revealed no significant differences between the SCL groups, myopic groups or the interaction between these ($p > 0.05$) (Table A-96).

Table A-96: The influence of myopic group on epithelial thickness

Myopic group Low (0 to -2.75D) Medium (-3.00 to -5.75 D) High (> -6.00D)		**n =**	**SCL Mean ±SD (µm)**	**n =**	**NCL Mean ±SD (µm)**	**CL group Sig**	**Myopic group Sig**	**Inter action Sig**
Average	Low	20	61.04 ±4.09	18	59.49 ±3.65	0.76	0.26	0.10
	Medium	22	58.79 ±3.81	6	61.47 ±1.85			
	High	12	58.65 ±2.70	1	55.80 ±0.00			
Temporal periphery	Low	20	59.90 ±7.03	18	57.67 ±6.42	0.96	0.24	0.20
	Medium	22	58.27 ±5.09	6	62.00 ±2.45			
	High	12	56.17 ±5.59	1	54.00 ±0.00			
Temporal para-central	Low	20	60.90 ±4.67	18	61.33 ±5.81	0.39	0.40	0.57
	Medium	22	57.64 ±4.82	6	61.00 ±2.45			
	High	12	58.92 ±4.42	1	60.00 ±0.00			
Central	Low	20	61.15 ±9.03	18	59.89 ±5.66	0.68	0.89	0.33
	Medium	22	58.14 ±5.41	6	62.33 ±1.97			
	High	12	58.83 ±4.78	1	59.00 ±0.00			
Nasal para-central	Low	20	61.90 ±6.09	18	60.39 ±6.27	0.55	0.55	0.63
	Medium	22	59.45 ±6.92	6	60.67 ±2.66			
	High	12	60.67 ±4.40	1	56.00 ±0.00			
Nasal periphery	Low	20	61.35 ±4.63	18	58.17 ±5.06	0.10	0.12	0.23
	Medium	22	60.45 ±7.18	6	61.33 ±5.65			
	High	12	58.67±3.45	1	50.00 ±0.00			

Mean ±SD of epithelial thickness for SCL and NCL and pre-operative myopic refractive error groupings. Two-way ANOVA indicate no statistically significant effect of myopic group on epithelial thickness, (all p values > 0.05).

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