SAFETY AND EFFICACY OF CORNEAL COLLAGEN CROSSLINKING WITH RIBOFLAVIN AND ULTRAVIOLET-A IN THE TREATMENT OF PROGRESSIVE KERATOCONUS

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CERTIFICATE

This is to certify that the thesis entitled **"SAFETY AND EFFICACY OF CORNEAL COLLAGEN CROSSLINKING WITH RIBOFLAVIN AND ULTRAVIOLET-A IN THE TREATMENT OF PROGRESSIVE KERATOCONUS"** is the original work of **Dr. Gitansha Sachdev** and was conducted under our direct supervision and guidance at Aravind Eye Hospitals and Postgraduate Institute of Ophthalmology, Madurai

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CONTENTS

SAFETY AND EFFICACY OF CORNEAL COLLAGEN CROSSLINKING WITH RIBOFLAVIN AND ULTRAVIOLET-A IN THE TREATMENT OF PROGRESSIVE KERATOCONUS

KEYWORDS

Keratoconus, collagen crosslinking, riboflavin, ultraviolet A, corneal ectasia

INTRODUCTION

Keratoconus is a non inflammatory progressive corneal thinning of unknown etiology in which the cornea assumes a conical shape, resulting in mild to marked impairment of visual acuity due to irregular astigmatism, progressive myopia and central corneal scarring. A reduced number of collagen cross-links and a pepsin digestion higher than normal induce an overall structural weakness of the corneal tissue, resulting in a stiffness that is only 60% of normal cornea. Changes in corneal collagen structure, organization and intercellular matrix as well as apoptosis and necrosis of keratinocytes, prevalently or exclusively involving the central anterior stroma and Bowman's lamina are documented in literature. Corneal collagen cross-linking (C3R) is a new approach to increase the mechanical and biochemical strength of corneal tissue.

BASIC PRINCIPLE-The aim of this treatment is to create additional chemical bonds inside the corneal stroma by means of highly localised photopolymerisation while minimising exposure to surrounding ocular structures.

Using UVA at 370nm and the photosensitizer riboflavin, the photosensitizer is excited into its triplet state generating the reactive oxygen species (ROS). These are mainly in the form of singlet oxygen and to a much less degree, they may be in the form of superoxide anion radicals. The ROS then reacts with various molecules, including chemical covalent bonds, bridging amino groups of collagen fibrils(type 2 photochemical reaction).The wavelength of 370nm was chosen because of an absorption peak of riboflavin at this wavelength.

AIMS AND OBJECTIVES

-To evaluate the safety of C3R as measured by intra operative and postoperative complications

-To measure the efficacy of C3R in bringing progressive keratoconus to a halt

MATERIALS AND METHODS

TYPE OF STUDY

Prospective interventional clinical trial

CASE COLLECTION PERIOD - 1 year

FOLLOW UP PERIOD - 1 year

SAMPLE SIZE - 50 patients

SELECTION CRITERIA

Inclusion criteria

Progressive keratoconus

Age between 12 to 30 years

Corneal pachymetry> 400 microns at thinnest point

Normal corneal endothelium

Maximum corneal curvature < 60 D

Willing for follow up

Exclusion criteria

Corneal thickness < 400 microns at thinnest point

H/O herpetic keratitis

Central or paracentral opacities

Prior corneal surgery

Severe dry eye and ocular surface disorders

Concurrent corneal infections

Concomitant autoimmune diseases

Pregnant/nursing women

Hormone therapy

EVALUATION PARAMETERS

- UDVA
- CDVA
- CLVA
- Refraction
- Slit lamp biomicroscopy
- Fundus evaluation
- Non contact tonometry
- Tear Film break up time
- OrbscanIIz (Bausch & Lomb)
- Specular microscopy (Topcon SP 3000 P)
- Clinical Photograph (Haag Streit)

SAFETY PARAMETERS

Post operative complications: -

- Non healing/Persistent Epithelial Defect

  (a) <2mm (b) 2-5 mm (c) >5 mm

- Permanent stromal Haze

  (a) mild (b) moderate (c) severe

- Corneal Scarring

  (a) nebular (b) macular (c) leucomatous

- Infective keratitis
- Corneal melting
- Corneal Infiltrate-

  1. Number (a) single (b) multiple
  2. Size (a) <2mm (b) 2-5 mm (c)>5 mm
  3. Type (a) bacterial (b) fungal (c) sterile

- Endothelial cell loss
- Cataract formation
- Retinal pathology
- Loss of 2 or more lines in BCVA

EFFICACY PARAMETERS

- Best corrected distance visual acuity-

1. Spectacle corrected
2. Contact lens corrected

- Refraction-

1. Spherical
2. Cylindrical with axis

3. Mean spherical equivalent

- ORBSCAN IIz

    1. Sim K
    2. K max
    3. Thinnest pachymetry
    4. Anterior float BFS difference
    5. Posterior float BFS difference
    6. 3mm zone irregularities
    7. 5mm zone irregularities

METHODOLOGY

-All patients with documented progression of keratoconus(more than 0.5 diopter increase in the past 1 year) were included.

-Preoperative measurements included uncorrected visual acuity,best corrected and contact lens visual acuity,refraction, intra ocular tension (Non contact tonometry), keratometry, specular microscopy and ORBSCAN IIzreadings.

-The eye with advanced keratoconus was treated with C3R while the other eye served as the control.

-The patients were called for follow-up at 1 week,1 month,3 months,6 months and 12 months postoperatively. All necessary investigations were done at each visit.

-The progression of keratoconus (if any) was documented and was compared with the fellow control eye.

-Intraoperative and postoperative complications (if any) were documented.

RESULTS

DEMOGRAPHICS

The mean age of presentation was 17.72 years (SD= 2.98) with a range of 12 to 26 years. A total of 50 patients were enrolled in the study, with 31 males (62%) and 19 females (38%)

VISUAL ACUITY

In our study,we found a significant improvement in uncorrected visual acuity (UDVA) at 12 months follow up visit by 0.11 log MAR units which was significant with respect to the controls where no significant change was observed.

In the corrected distance visual acuity, no significant improvement was observed at 6 months and 12 months in both the case and the control group.

REFRACTION

In our study, a mean decrease in refractive cylinder by 0.44D was observed at 6 months and 0.50D at 1 year, which however was not significant with respect to the control group. The spherical equivalent showed no significant change in the cases but a significant increase in the control group at 6 months and 12 months. There was no significant change in refractive sphere in either group

ORBSCAN IIz

There was a significant reduction in simulated keratometry, maximum keratometry, anterior float, posterior float, 3mm and 5 mm zone irregularities in the cases with respect to preoperative values and values at 6 months and 12 months. The thinnest pachymetry underwent significant reduction from one-month postoperative followup.

COMPLICATIONS

There was no significant change the intraocular pressure at follow up visits in either group. We also observed transient stromal haze in a majority of our patients, which persisted beyond 3 months in 30 patients (60%). Mild scarring was seen in 13(26%) of our patients. No cases of keratitis, infiltrate or corneal melting were seen.We observed no lens changes or induced retinal pathologies in our study.

CONCLUSION

Collagen crosslinking is a safe and effective procedure to halt the progression of disease in cases of mild to moderate keratoconus.

INTRODUCTION

Keratoconus is a bilateral non-inflammatory progressive corneal thinning and ectasia in which the cornea assumes a conical shape. It is associated with irregular astigmatism, central corneal scarring and progressive myopia resulting in impaired visual acuity. A reduction in the number of collagen crosslinks and an increase in pepsin digestion causes a structural weakness within the cornea, with a resultant stiffness that is about 60 % of normal tissue.[1]The disease process involves variations in structure of corneal collagen and it's organization, along with apoptosis of keratocytes in the anterior corneal stroma and Bowman's lamina.

Epidemiology- The reported incidence of keratoconus varies, with most estimates being approximately 1 per 2,000 in the general population.[2] The onset of keratoconus classically begins at puberty and progresses till the third to fourth decade, following which it usually arrests. It commonly occurs in isolation. The associations of keratoconus include Down's syndrome, Turner's syndrome, Marfan's syndrome, Lebers congenital amaurosis, Atopic keratoconjunctivitis, connective tissue disorders and disorders of collagen metabolism.[3] Keratoconus occurs in all age groups with no sex predominance, though few reports have reported a higher incidence among females.[4]

Signs of keratoconus

External signs of Keratoconus

- *Munson's sign*: V-shaped conformation of the lower lid produced by the ectatic cornea in down gaze in advanced keratoconus.[3]
- *Rizzuti phenomenon*: A beam of light focused near the nasal limbus is produced by lateral illumination of the cornea in patients with advanced keratoconus.[3]

Slit-lamp findings

- Stromal thinning
- Posterior stress lines (Vogt's striae) [5]
- Iron ring (Fleischer ring)
- Prominent corneal nerves
- Scarring - epithelial, subepithelial or anterior stromal [6]
- Subepithelial fibrillary lines [6]
- Epithelial nebulae
- Increased intensity of endothelial reflex [6]

Retroillumination signs

- Scissoring on retinoscopy [3]
- Oil droplet sign ("Charleaux") [3]

Early cases of keratoconus may be difficult to diagnose based on slit lamp examination. Topography holds the key to diagnosis of these cases and has today become essential in the diagnosis and assessment of keratoconus.

Table -1

External signs	-Munson's sign -Rizzuti phenomenon
Slit-lamp findings	-Stromal thinning -Posterior stress lines(Vogt's striae) -Iron ring(Fleischer ring) -Scarring:subepithelial or epithelial
Retroillumination signs	-Scissoring on retinoscopy -Oil droplet sign('Charleaux')
Photokeratoscopy signs	-Compression of mires infertemporally
Videokeratography signs	-Localized increased surface power -Inferior superior dioptric asymmetry -Relatively skewing of the steepest radial axes above and below the horizontal meridian

Management

The management options in keratoconus include optical correction, replacement technology, additive technology and strengthening technology.

1. **Optical correction-**The optical correction can be done with the help of spectacles and contact lenses.

Spectacles

They may be helpful in early stages by correcting the refractive error but do not alter the shape of the cornea.

Contact lenses

Contact lenses are optical aids used in 90% of the patients.[7] Early in the disease process soft lenses of toric design may suffice. However in more advanced disease, rigid gas permeable lenses, including multicurve spherical based lenses, aspheric lenses and bispheric lenses may be required. A hybrid lens that has a rigid central portion for obtaining best optics and a soft hydophilic peripheral skirt is also popular.[8]The complications associates with contact lenses include corneal abrasion, apical scarring, hypoxia [9], neovascularization [10] and lens discomfort.

2. **Replacement technology-** Replacement therapy involves corneal transplantation surgery in which the diseased layers of the cornea are replaced by healthy tissue. This includes penetrating keratoplasty and

lamellar keratoplasty depending upon the depth of involvement and presence or absence of scarring.

Lamellar keratoplasty- It is an extra ocular procedure in which only diseased anterior part of corneal tissue is removed, leaving the recipients normal anatomical structures intact.[11]

Epikeratoplasty- It is a type of onlay lamellar keratoplasty in which the partial thickness donor cornea is placed on de-epithelized recipient cornea. It may be preferred over penetrating keratoplasty in selected cases like Down's syndrome because of it's non invasive nature and decreased potential for graft rejection.[12]

Deep anterior lamellar keratoplasty (DALK)- It is a type of lamellar keratoplasty in which lamellar dissection is performed up to the descemet's membrane and then the donor corneal button is sutured in its place. It decreases the incidence of endothelial graft rejection.[13]

Automated lamellar therapeutic keratoplasty (ALTK)- In this procedure a microkeratome is used to excise the pathological part of a host cornea up to a particular depth and a healthy donor cornea, which is also cut using an automated microkeratome and an artificial chamber is sutured in its place.

Penetrating keratoplasty-It is the procedure of choice for management of cases of keratoconus not adequately rehabilitated by contact lenses. The success rate varies from 93%-96%.[14] The indications for penetrating keratoplasty include contact lens failures or intolerance, central scarring and poor visual acuity despite contact lenses. However a full thickness graft is associated with complications like graft rejection, post operative astigmatism and recurrence of keratoconus.[15]

3. Additive technology- The additive technology for the treatment of keratoconus consists of the use of intrastromal corneal ring segments (ICRS) which are manufactured under two names- Intacs prescription inserts and Ferrara intrastromal corneal ring segments.[16]

Intrastromal corneal ring segments- Two thin arcs made up of PMMA are slid between the layers of the corneal stroma through incisions made in the corneal periphery. The segments flatten the peak of the cone, thus reducing the amount of myopia and make patients more contact lens tolerant.[17,18] The potential complications include accidental penetration through the anterior chamber, infection, migration or extrusion of segments.

4.Strengthening technology

Corneal collagen cross-linking is a new approach to increase the mechanical and biochemical strength of the corneal tissue.

BASIC PRINCIPLE- Crosslinking is a widespread method in the polymer industry to harden material e.g. chemical crosslinking with glutaraldehyde is used in the preparation of prosthetic heart valves and physical cross linking by Ultraviolet-A (UVA) is used in dentistry to harden filling material. Cross linking of human collagen is a physiological process and stiffening of the connective tissue is well known in diabetes and ageing.[19]

This is related to the age related glycosylation of collagen molecules. The aim of this treatment is to create additional chemical bonds inside the corneal stroma by means of highly localised photopolymerisation while minimising exposure to surrounding ocular structures.

Using UVA at 370nm and the photosensitizer riboflavin, the photosensitizer is excited into it's triplet state generating the reactive oxygen species (ROS). These are mainly in the form of singlet oxygen and to a much less degree, they may be in the form of superoxide anion radicals. The ROS then reacts with various molecules, including chemical covalent bonds, bridging amino groups of collagen fibrils (type 2 photochemical reaction). The wavelength of 370nm is chosen because of an absorption peak of riboflavin at this wavelength.

Table -2

TREATMENT MODALITY	
Optical correction	Spectacles,Contact lenses
Replacement technology	Lamellar keratoplasty-DALK,ALTK, epikeratoplasty,Penetrating keratoplasty
Additive technology	Intrastromal corneal ring segments
Strengthening technology	Collagen cross linking

REVIEW OF LITERATURE

ANIMAL STUDIES

Wollensak et al[20] *in 2003* first introduced the procedure of collagen cross-linking (CXL). They evaluated the effect of treatment using riboflavin and ultraviolet A on human and porcine corneas. A total of 25 corneal strips were subjected to treatment, 5 of which were obtained from porcine eyes and the remaining from human cadavers. The corneas were treated with UV-A (370 nm, irradiance-3mW/cm^2) for half an hour following treatment with riboflavin. The treated corneas were subjected to a static stress test using a biomaterial tester. A significant increase in the rigidity was noted, indicated by a 71.9 % and 328.9 % increase in stress of porcine and human corneas respectively. The greater stiffening effect of the human corneas was due to the relatively thinner nature.

Wollensak et al [21] *in 2003* evaluated possible in vitro cytotoxic effects on corneal keratocytes following treatment with riboflavin and ultraviolet-A irradiation. They treated endothelial cell cultures of porcine corneas with varying levels of UV-A irradiances ranging from 0.4 to 1.0 mW/cm^2 , after treatment with riboflavin. They used Yopro fluorescence and tryphan blue staining to evaluate cell death in endothelial cultures, 24 hours following treatment. The effect of either treatment alone (UVA irradiation ranging from 0.4 to 9 mW/cm^2) was also tested. An abrupt cytotoxic irradiance level was found at 0.5 mW/cm^2 after UVA irradiation combined with photosensitizer riboflavin, which was 10 fold lower than the cytotoxic irradiance of 5mW/cm^2 after UV-A irradiation alone. Riboflavin alone was not cytotoxic. They noted a cytotoxic effect upto a corneal depth of 300um following combined treatment.

Spoerl et al[22] *in* 2004 evaluated the resistance of collagen cross-linking treated corneas to enzymatic degradation. The study group included 80 porcine corneas, 60 of which were treated with riboflavin and ultraviolet-A while the remaining served as controls. They exposed the trephined treated corneal buttons to collagenase, trypsin and pepsin enzymes. The buttons were then examined by light microscopy. The treated corneas underwent dissolution by pepsin enzyme by day 14 while the untreated cases underwent digestion by day 6. Corneal resistance to collagen digesting enzymes markedly increased following collagen cross-linking.

Wollensak et al[23] *in 2004* studied corneal keratocytes for the possible cytotoxic effect of riboflavin and UV-A treatment. They subjected corneas of thirty-four New Zealand white rabbits to cross linking treatment, following which they euthanized the rabbits four to twenty four hours postoperatively. Four eyes were treated with corneal debridement alone and served as the control group. Histopathological evaluation of the treated corneas was done. They detected keratocyte apoptosis using TUNEL technique and transmission electron microscopy. The apoptotic keratocytes were found within the anterior 50 microns of the control eyes. The depth of apoptotic cells in the treated eyes varied depending upon the strength of the irradiance applied. A strength of 0.5-0.7 $mw/cm^2$of UVA irradiance was found to be toxic. Dose dependent keratocyte damage up to a depth of 300um in human corneas can be expected following treatment with UVA dose of $5.4J/cm^2$.

Wollensak et al[24] *in 2004* studied changes in the diameter of collagen fiber following cross-linking of rabbit corneas. The right eyes of 10 New Zealand white rabbits underwent cross linking and the fellow eyes served as the control. They divided the control group into three groups- eyes left untreated (1-4), eyes de-epithelialized only (5-7) and de-epithelialized eyes treated with riboflavin alone (8-10). There was a significant increase in the diameter of collagen fiber by 12.2% and 4.6% in the anterior and posterior stroma respectively, compared to the left eyes. There was also a significant increase in the diameter of anterior corneal fibers compared to fibers in the posterior stroma of the same eye. There is a stronger effect of cross-linking in the anterior half of the stroma due to rapid decrease in irradiance across the cornea following absorption by riboflavin.

Kohlhaas et al[25] *in 2006* evaluated the depth of corneal tissue up to which stiffening effect of crosslinking was biomechanically detectable. They evaluated 40 enucleated porcine eyes, half of which underwent treatment with riboflavin and Ultraviolet-A while the remaining half served as control. Following treatment 2 flaps of 200 microns each were cut using a microkeratome. Corneal strips of 7mm length and 5mm width were prepared and were subjected to stress-strain behaviour with a material tester. There was a stronger stiffening effect in the anterior treated flaps as compared to the posterior treated flaps and the control group (p=0.001). There was a significant increase in stress of treated anterior corneal flaps compared to those of the control group. There was however no significant difference between the posterior treated flaps and the control group. The greater stiffening effect in the anterior stroma was attributed to the absorption of 65-70% of UV-A by the anterior 200 microns and the remaining 20% by the next 200 microns. Thus crosslinking has no effect on deeper structures and endothelium.

Wollensak et al[26] *in* 2009 studied the efficacy of cross-linking treatment without epithelial debridement in rabbit eyes. The cross-linked eyes were divided into three groups- standardized crosslinking following epithelial debridement (Group 1), using benzalkonium chloride-containing proxymetacaine eye drops without epithelial removal (Group 2),or using preservative-free oxybuprocaine eye drops without epithelial removal (Group 3). All three groups were treated with riboflavin solution and were irradiated with an ultraviolet-A double diode for 30 minutes(irradiance 3 mW/cm^2).The rabbits were euthanised 1 day following crosslinking. The corneas were subjected to biochemical and histological analyses. Group 1 (102.45%) and Group 2 (21.30%) showed a significant increase in Young's modulus. No significant changes were observed in Group 3. Histological evaluation revealed complete loss of keratocytes and endothelium in Group 1 and an inhomogeneous loss of keratocytes in Group 2. Group 3 showed no changes.Biochemical effect of crosslinking without epithelial debridement was reduced probably due to restricted and heterogenous stromal distribution of riboflavin. The cytotoxic effect was however restricted to 200 mm.

CLINICAL STUDIES

Wollensak et al [27] *in 2003* were the first to evaluate the clinical effect of corneal cross-linking using riboflavin and UV-A for halting the progression of keratoconus. The study included twenty-three eyes of twenty-two patients who presented with moderate or advanced progressive keratoconus. The procedure involved application of riboflavin drops and UVA irradiation (370 nm,3mW/cm^2) following corneal epithelial debridement. Post-operative evaluation included visual acuity, slit lamp evaluation, corneal topography, endothelial cell count and clinical picture. Patients were followed up from 3 months to 4 years.All eyes in the study failed to progress following treatment. 16 eyes (70%) showed a regression of keratoconus with a 2.01D reduction in maximum keratometric value and a 1.14 D reduction in refractive error. There was no effect on intraocular pressure, corneal transparency and endothelial density. A slight improvement in visual acuity was noted in 15 eyes (65%).

Wollensak et al[28] *in 2006* evaluated the effect of cross-linking on the progression of keratoconus in 60 eyes over a period of 3 to 5 years. They concluded a halt in the progression of the disease in all eyes. Moreover, there was a minimal reversal of the keratoconus in 31 eyes. An improvement of 1.4 lines was noted in the best-corrected visual acuity.

Caporossi et al[29] *in 2006* carried out a prospective non-randomized study to evaluate the efficacy of crosslinking in halting the progression of keratoconus. The study included 10 eyes of 10 patients with progressive disease, while the fellow eyes of 8 patients served as controls. Clinical evaluation included measurement of uncorrected and best-corrected visual acuity. Corneal topographic evaluations, linear scan optical tomography, endothelial cell density, ultrasound pachymetry, intraocular pressure measurement and HRT 2 system confocal was performed at 1,2,3 and 6 months. The study showed a significant improvement in uncorrected and best spectacle corrected visual acuity.Topographic analysis revealed a reduction of mean K by 2.1 +/- 0.13 dioptres (D) in the central 3 mm. There were no significant difference in the intraocular pressure and endothelial cell density within the cases. 37.5% of the eyes showed a progression of disease within the control group.

Seiler et al [30] *in 2006* performed cross-linking in 16 patients of keratoconus with a maximum keratometry of 60D and central corneal thickness of at least 400 microns. The corneal epithelium was mechanically removed with a diameter of 6 mm and riboflavin drops 0.1% instilled repeatedly for 20 minutes. UVA radiations were given at irradiance of $3mW/cm^2$ at a working distance 1 cm. Biomicroscopic and topographic evaluation of eyes was carried out preoperatively and at subsequent follow-ups. A thin demarcation line was seen at around 300 microns of corneal depth on slit lamp evaluation in 14 eyes.

Mazzotta et al [31] *in* 2007 evaluated changes in the corneal stroma of eyes with advanced keratoconus following treatment with collagen cross-linking.10 patients with progressive keratoconus were treated by collagen cross-linking and assessed by means of Heidelberg Retinal Tomography II Rodstock Corneal Module (HRT II-RCM) in vivo confocal microscopy. The eye that had progressed further in the disease process was treated while the fellow eye served as the control. Eyes were evaluated at 1, 3 and 6 months postoperative with HRT II-RCM confocal microscopy. Stromal edema with refraction of keratocytes in the anterior and intermediate stroma was noted postoperatively. Resolution of edema with associated keratocyte repopulation was observed 3 months postoperatively. Complete keratocyte repopulation with increased stromal density was noted at 6 months. There was no endothelial cell damage noted postoperatively.

Wittig-Silva et al[32] *in* 2008 randomized 66 eyes of 49 patients with documented progressive keratoconus into treatment and control groups. Collagen cross-linking was performed in all the eyes in accordance with previously published protocols.On every follow-up a complete ocular evaluation was conducted including confocal microscopy and endothelial cell count. Statistical analysis of treated eyes revealed a significant flattening of the simulated keratometry value (K max) at 3, 6 and 12 months postoperatively. The cases also showed an improvement in best-corrected visual acuity. On the other hand, a significant steeping of K max and associated reduction of best spectacle-corrected visual acuity was noted in the control eyes at 3, 6 and 12 months postoperatively. No statistically significant changes in spherical equivalent and endothelial cell density were observed. Postoperative confocal microscopy revealed some highly reflective stria in mid to posterior stroma between 1-3 months after treatment, which became less marked in subsequent visits. One patient with a highly atopic predisposition developed an inflammatory reaction in anterior chamber on post-operative day 2 and one patient developed a small sub-epithelial, paracentral infiltrate, after prematurely resuming wear of his rigid contact lens on day 3 with no persistent scarring.

Dhaliwal et al[33] *in* 2008 used confocal, electron and light microscopy to study changes in corneas treated with collagen cross-linking. The procedure involved removal of central epithelium followed by treatment with riboflavin 0.1 % and ultraviolet – A light. Preoperative evaluation revealed normal appearing corneas with reduced stromal detail on confocal microscopy. Postoperative evaluation revealed a superficial layer of hyper reflective structures upto a depth of 300 microns. Keratocyte apoptotic changes within the superficial layers of the cornea were seen on electron microscopy.

Kymionis et al[34] *in 2008* evaluated changes in corneal tissue following crosslinking in eyes with post laser in situ keratomileusis(LASIK) keratectasia and keratoconus. The study group included five patients with progressive keratoconus and five with post LASIK ectasia. The treated eyes were evaluated by corneal in vivo confocal microscopy. The control group included three healthy corneas and three post LASIK eyes with no evidence of ectasia. Corneal evaluation within the first three postoperative months revealed apoptosis of keratocyte nuclei and alterations in collagen structure.Over subsequent visits a gradual increase in keratocyte population was observed. The changes seen were similar in both keratoconic and post LASIK ectasia patients.

Mazzotta et al [35] *in 2008* used Heidelberg Retinal Tomography (HRT) II confocal microscopy to evaluate morphological changes in cross-linked corneas. The study included 44 eyes with progressive keratoconus that were treated based on the Siena protocol: Pilocarpine 1% drops 30 minutes before, topical anaesthesia with lidocaine 4% drops 15 minutes before irradiation, mechanical scraping of epithelium (9mm diameter area),pre irradiation soaking for 10 minutes in riboflavin solution 0.1% (Ricolin, Sooft, Italy) applied every 2.5 minutes for 30 minutes,30 minutes exposure to solid state UVA illuminator (Caporossi; Baiocchi; Mazzotta; X linker, CSO, Italy),8-mm diameter irradiated area, energy delivered 3 mW/cm^2. Confocal scans were taken preoperatively and at subsequent postoperative follow-ups at 1, 3, 6 months and 1, 2 and 3 years. Complete epithelial regrowth was noted within four days of removal of bandage contact lens removal. Sub-epithelial plexus was restored to original anatomical structure within first postoperative year. A late demarcation line was noted at a depth of 340 microns. 5 out of 44 eyes presented with transitory corneal opacity similar to corneal haze. Resolution of opacity was seen within a month following administration of topical steroid drops. An increased evidence of preoperative Vogt striae was noted in patients with postoperative corneal haze.

Raiskup-Wolf et al[36] *in 2008* conducted a long-term study on the dampening effect of collagen crosslinking on progressive keratoconus. The study included 488 eyes of 272 patients with a mean age of 30.04 +/- 10.46 years. Investigations done preoperatively and at all subsequent follow-ups included uncorrected and best-corrected visual acuity, corneal pachymetry, corneal topography and intraocular pressure evaluation. The period of follow-up ranged from 6 months to a maximum of 6 years. There was a significant decrease in the steepest keratometry reading at first, second and fourth postoperative year. There was a significant improvement in BCVA by at least one Snellen's line in 53% of 142 eyes in the first year,57% of 66 eyes in the second year, and 58% of 33 eyes in the first year or remained stable(no lines lost) in 20%,24% and 29% respectively. Keratoconus continued to progress in two patients at 18 and 24 months follow-up following acute exacerbation of neurodermatitis. The procedure was repeated in both eyes.

Koller et al [37] *in 2008* used Scheimpflug imaging to compare geometrical shape factors of post corneal crosslinking corneas with untreated fellow eyes. The study group included 21 patients with progressive disease, all of whom underwent Scheimpflug imaging (Pentacam) of the corneal surface. The eye of the patient more advanced in the disease process was treated, while the fellow eye served as the control. There was no significant topographic progression seen in the cases. On the other hand 8 out of 21 eyes showed progression in the control group. There was a significant decrease in the minimal curvature radius between the preoperative and one year postoperative readings in the cases, while a significant increase was noted in the control group. A significant reduction in the thinnest pachymetry was noted following treatment. No intraoperative or postoperative complications were seen.

Santonja et al [38] *in 2008* reported a case of a 29-year-old woman presenting with multiple corneal infiltrates in the upper quadrant of her right eye. She underwent uneventful corneal crosslinking in the same eye previously. Microbiological evaluation confirmed staphylococcus epidermis keratitis, following which treatment with fortified antibiotics was initiated. There was a significant increase in the best spectacle corrected visual acuity and decrease in spherical equivalent between preoperative and 5 months postoperative values. Mild residual haze following treatment was seen in the corneal stroma.

Rama et al [39] *in 2008* reported a case of corneal melt in 32-year-old male, five days following treatment with corneal crosslinking for keratoconus. Microbiological evaluation was positive for acanthamoeba keratitis. The patient gave history of washing his face repeatedly with tap water. Therapeutic keratoplasty was done following corneal perforation.

Sharma et al[40] *in 2009* reported a case of a 19-year-old woman presenting on fourth postoperative day with complaints of redness, pain and defective vision in her right eye. Clinical examination revealed corneal infiltration measuring 7mm x 8 mm. Microbiological evaluation of corneal and contact lens scraping confirmed Pseudomonas aeruginosa. Posterior segment analysis on ultrasound revealed no abnormalities. The infiltrate responded to treatment with antibiotics leaving behind a leucomatous corneal opacity.

Koppen et al[41] *in 2009* reported severe keratitis in four eyes from a total of 117 eyes treated with corneal crosslinking. Patients experienced delayed signs and symptoms of inflammation. Clinical features included circumciliary congestion, diffuse keratic precipitates on the corneal endothelium, anterior chamber reaction and multiple white infiltrates along the edge of the treated cornea. The symptoms improved following administration of topical or subconjunctival steroids. Two eyes showed a persistent decrease in visual acuity secondary to corneal scarring.

Koller et al[42] *in 2009* studied the rate of complications of crosslinking procedure. The study included 117 eyes of 99 patients presenting with primary corneal ectasia. Clinical evaluation at preoperative and postoperative visits at 6 and 12 months included uncorrected and best corrected visual acuity, slitlamp examination, intraocular pressure measurement and corneal topography (Pentacam).

Statistical analysis included analysis of variance and the Mann-Whitney U test to detect risk factors for complications. 2.9 % of the eyes two or more Snellen lines of visual acuity. 7.6 % of the eyes continued to progress in the disease process. The studies identified old age (of more than 35 years) and a preoperative corrected distance visual acuity better than 20/ 25 as significant risk factors for complications.7.6 % of the patients presented with sterile corneal infiltrates while 2.8 % showed stromal scarring. A resolution of stromal infiltrates was seen within one month following administration of topical steroids. There was no significant loss of final corrected visual acuity in any of the complications. Corneal scarring faded almost completely within first postoperative year.

Vinciguerra et al[43] *in 2009* evaluated refractive, topographic, tomographic and abberometric outcome 12 months after corneal cross-linking in 28 eyes with progressive advanced keratoconus. There was an improvement in mean UCVA and BSCVA between preoperative and 12 months postoperative values. A significant decrease was seen in the mean spherical equivalent. Mean baseline simulated keratometry (SIM K) flattest, steepest and SIM K average decreased from 46.10 D,50.37 D and 48.08 D to 40.22 D,44.21 D and 42.01 D respectively at 12 months, a difference that was significant for all three indices($P<0.005$).Mean average pupillary power (APP) changed significantly from 47.50 to

41.40D at 12 months(P<0.005) and apical keratometry(AK) from 58.94 to 55.18(P<0.05).The treated eyes showed no deterioration of the Klyce indices at 6 months postoperatively whereas the untreated contralateral eyes did show deterioration. For a 3mm pupil there was a significant reduction (P<0.05) in whole eye, corneal, higher order, and astigmatic wavefront aberrations. They observed a significant difference in the total coma and spherical aberration following the procedure. There was no significant decrease in the endothelial counts.

Agrawal et al[44] *in 2009* studied the results of corneal collagen cross-linking with riboflavin using ultraviolet-A light in sixty-eight eyes of 41 patients with progressive keratoconus. The mean age was 16.9 +/- 3.5 years. Thirty-seven eyes with a follow up of atleast 12 months were analysed. BCVA improved at least one line in 54% (20/37) of eyes and remained stable in 28%(10/37) of eyes (P=0.006).Astigmatism decreased by a mean of 1.20D in 47%(17/37) of eyes and remained stable(within +/- 0.50D) in 42% (15/37) of eyes. The K value of the apex decreased by a mean of 2.73D in 66%(24/37) of eyes and remained stable(within +/- 0.50D) in 22% (8/37) of eyes. The maximum K value decreased by a mean of 2.47 D in 54% (20/37) eyes and remained stable (within +/- 0.50D) in 38%(14/37) eyes. Corneal wavefront analysis revealed that spherical and higher-order aberrations did not show significant variations in the follow-up period. The coma component showed a very significant reduction at six months after treatment and persisted throughout the follow up period(P=0.003).

Grewal et al[45] *in* 2009 studied the effects of CXL on the corneal elevation, curvature and thickness in 102 eyes with progressive keratoconus. Clinical evaluation included uncorrected and best-corrected visual acuity, Scheimpflug imaging and optical coherence tomography at preoperative and postoperative visits at 1,3,6 and 12 months. No significant difference in BCVA, spherical equivalent or cylindrical refraction was noted between preoperative and postoperative values. Similarly no significant changes were noted in corneal curvature and pachymetry between preoperative and postoperative values.

Goldich et al[46] *in 2009* evaluated biomechanical changes in the cornea after treatment with CXL. The study included 10 eyes of progressive keratoconus, with a mean age of 26.5 years. Investigations done on every visit included Ocular Response Analyzer (ORA) to measure corneal hysteresis(CH),corneal resistance factor (CRF) and intraocular pressure analysis using Goldmann applanation tonometry. There was no statistically significant increase in the CH and CRF between preoperative and postoperative values. There was a significant increase in the IOP at 1 and 3 months postoperative compared to preoperative values.

Caporossi et al[47] *in 2009* studied the effects of CXL on 44 eyes over a follow-up period of 48 months. Clinical investigations at each visit included uncorrected and best corrected spectacle visual acuity, endothelial cell count(I Konan, Non Con Robo; Konan Medical Inc.,Hyogo, Japan),optical (Visante OCT; Zeiss, Jena, Germany) and ultrasound (DGH; Pachette, Exton, Pennsylvania, USA) pachymetry, corneal topography and surface abberometry (CSO EyeTop, Florence, Italy),tomography (Orbscan IIz; Bausch & Lomb Inc., Rochester, New York, USA), posterior segment optical coherence tomography(Stratus OCT; Zeiss, Jena, Germany), and in vivo confocal microscopy(HRT II; Heidelberg Engineering, Rostock, Germany). There was a stabilization of keratoconus noted in 44 out of 48 eyes, while the fellow eyes showed a progression of the disease process. A significant decrease in mean k value and coma aberration was noted. There was a statistically significant improvement in mean UCVA and BCVA between preoperative and postoperative values. The study noted no side effects of the treatment, either intraoperative or postoperatively.

Hersh et al[48] *in 2011* evaluated 1-year treatment outcomes following corneal crosslinking in eyes with keratoconus and corneal ectasia. The treatment group received standard CXL treatment and the sham group received treatment with riboflavin alone. Parameters measured included uncorrected (UDVA) and corrected visual acuity

(CDVA), refraction and corneal topography. There was a significant improvement in the UDVA and CDVA within the treated eyes. Fifteen patients (21.1%) gained and 1 patient lost (1.4 %) 2 or more Snellen lines of CDVA. There was a significant decrease in K max in both keratoconic and corneal ectasia eyes. Both CDVA and K max value worsened between baseline and 1 month, followed by improvement between 1,3,and 6 months postoperatively and stabilization thereafter.

George D kymionis et al[49] in 2011 studied 14 eyes of 21 patients with corneal thickness less than 400 microns (following epithelial debridement). The patients underwent CXL procedure based on standardized treatment protocols. Preoperative and postoperative evaluation included uncorrected and best-corrected distance visual acuity and corneal topographic examination at 1,3,6 and 12 months postoperatively. Corneal endothelium was evaluated using Confocal scanning laser ophthalmoscope. No intraoperative and postoperative complications were noted. A significant decrease of endothelial cell density was observed.

LACUNAE IN KNOWLEDGE

There are limited prospective clinical trials available which evaluated efficacy and safety of collagen cross linking in keratoconus in South Indian population.

AIM OF STUDY

To conduct a clinical trial to evaluate the safety and efficacy of corneal collagen cross linking using riboflavin and UVA in progressive keratoconus.

MATERIALS AND METHODS

STUDY DESIGN – Prospective interventional clinical trial

PLACE OF STUDY – Aravind Eye Hospital And Postgraduate Institute, Madurai – a tertiary eye care hospital

CASE COLLECTION PERIOD – 1 Year

FOLLOW UP PERIOD – 1 Year

SAMPLE SIZE – 50 patients

Case – Eye subjected to CXL procedure

Control – Fellow eye

INCLUSION CRITERIA

- Progressive Keratoconus (1 dioptre or more within 1 year)
- Age 12 to 30 years
- Corneal pachymetry > 400 microns at thinnest point
- Normal corneal endothelium
- Maximum corneal curvature < 60 D
- Willing for follow up

EXCLUSION CRITERIA

- Corneal thickness < 400 microns at thinnest point
- H/O herpetic keratitis
- Central or paracentral opacities
- Prior corneal surgery
- Severe dry eye and ocular surface disorders
- Concurrent corneal infections
- Concomitant autoimmune diseases
- Pregnant/nursing women
- Hormone therapy

EVALUATION PARAMETERS

- UDVA
- CDVA
- CLVA
- Refraction
- Slit lamp biomicroscopy
- Fundus evaluation
- Non contact tonometry
- Tear Film break up time
- Orbscan IIz (Bausch & Lomb)

- Specular microscopy (Topcon SP 3000 P)
- Clinical Photograph (Haag Streit)

SAFETY PARAMETERS

Post operative complications: -

- Non healing/Persistent Epithelial Defect

  (a) <2mm (b) 2-5 mm (c) >5 mm

- Permanent stromal Haze

  (a) mild (b) moderate (c) severe

- Corneal Scarring

  (a) nebular (b) macular (c) leucomatous

- Infective keratitis
- Corneal melting
- Corneal Infiltrate-

  1. Number (a) single (b) multiple
  2. Size (a) <2mm (b) 2-5 mm (c) >5 mm
  3. Type (a) bacterial (b) fungal (c) sterile

- Endothelial cell loss
- Cataract formation
- Retinal pathology
- Loss of 2 or more lines in BCVA

EFFICACY PARAMETERS

- Best corrected distance visual acuity-

1. Spectacle corrected
2. Contact lens corrected

- Refraction-

1. Spherical
2. Cylindrical with axis
3. Mean spherical equivalent

- ORBSCAN IIz

1. Sim K
2. K max
3. Thinnest pachymetry
4. Anterior float BFS difference
5. Posterior float BFS difference
6. 3mm zone irregularities
7. 5mm zone irregularities

SURGICAL TECHNIQUE

Procedure was performed under all aseptic precautions. Patient's eye was cleaned and draped. Proparacaine 0.5 % was instilled thrice at 5 minute intervals, 15 minutes before the procedure. A 15mm blade was used to debride the corneal epithelium following marking of central 9 mm using a corneal trephine. One drop of Riboflavin 0.1 % in 20 % dextran (Isotonic, 3ml vial by Medio-Cross Italy) was instilled every 2 minutes for first 30 minutes and one drop every 2 minutes under UVA radiation for the next 30 minutes. UVA radiations 365 nm with desired irradiance of 3 mW/cm^2 was used at a distance of 5 cm (UV-X Zurich Switzerland). On completion of the procedure a bandage contact lens was applied, which was removed on the third postoperative day.

POSTOPERATIVE THERAPY

The postoperative therapy included-

Eye drops Vigamox 0.5% QID for 1 month

FOL**LOW UP**

The follow up schedule was as follows

1 week

1 month

3 months

6 months

12 months

Necessary investigations were repeated at all follow up visits.

ORBSCAN IIz (Bausch & Lomb)

It is based on the principle of placido disc and slit scanning system. Patient details are entered in the proprietary software information window and “acquisition” is selected. The patient is comfortably seated on the device with chin at chinrest and forehead placed against the forehead rest. He is directed to fix on the center of the target and to maintain a steady gaze. Following appropriate alignment of the instrument the acquisition sequence is triggered. The placido disc in the Orbscan is illuminated, causing mires to reflect from the anterior surface of the cornea. The machine stores the reflected mires. The machine projects 40 slits in total, 20 each from the right and left side onto the anterior corneal surface. Each slit measures 12.50 mm by 0.30 mm and is projected onto the cornea at an axis of 45 degrees from the instrument. The light from the slit on passing the cornea is scattered in various directions. A part of this light is back scattered towards the camera of the device and a two dimensional image is recorded. The assessment of the acquired images is the first step in processing. The acquired image is rejected when the patient moves his eyes excessively, and a new image is required. On the other hand, if the acquired image is satisfactory, a proprietary technique compensates for minute eye movements. The anterior edge of each slit is detected first by the machine, following which an anterior corneal surface topographic image is created. Subsequent software processing detects the edges of the reflected ring mires of the Placido disc, which allows curvature reconstruction of the anterior surface of the cornea. Further processing using the sampled data enables the Orbscan system to digitally recreate the internal surface of the eye i.e. posterior cornea. This procedure requires more sophisticated triangulation, integrating refractive variables and the use of two previously generated anterior topographic representations, elevation and curvature. The entire procedure typically takes 30 seconds or less, and a total of more than 30 anterior segment topographic maps can subsequently be created.

SPECULAR MICROSCOPY (Topcon SP 3000P)

Specular microscopy is based on the principle of specular reflection where the angle of incidence is equal to the angle of reflection. As the beam of light strikes the posterior corneal surface, almost all of it is transmitted into the aqueous humour. Because there is a change in the index of refraction at the endothelium aqueous humour interface, about 0.022 percent of total incident light is reflected, this reflected light is captured by the clinical specular microscope and forms the endothelial image.

UV-X^{TM} ILLUMINATION SYSTEM VERSION 1000 (IROC, SWITZERLAND)

It is a portable optoelectronic device in which light emitting diodes of the device create UV-A light at a wavelength of 365 nm. An internal microprocessor unit that controls the electric current to drive the unit controls the device.

Parts of the device

1. Mechanical stand- It is used to mount the UV-X light source on a stable table

2. Power supply – Low voltage is delivered to the light source with a DC cord

3. UV-X light source – the light source has a beam aperture of 25mm diameter. The treatment plane is about 50mm distance from the beam aperture. The aperture wheel determines the diameter of the treatment plane. Three sizes available are small (7.5mm), medium (9.5 mm) and large (11.5mm)

4. UV light meter – it is used to check the correct UV light irradiation. The meter is battery operated

5. Sensor probe adapter- The sensor probe attached to the UV light meter is mounted in the beam aperture. The device is switched on and the displayed value is checked.

The nominal value for correct irradiance is 3.0 +/- 0.3 mW/cm2

To use the device, it is first mounted on a table and the irradiation checked using the UV light meter. Then medium aperture (9.5mm) is selected and the device is switched on. The beam is adjusted on the patients cornea at a distance of 50 mm. UV radiations at the appropriate dosage is given for half an hour and the device gets switched off automatically after 30 minutes.

STATISTICAL ANALYSIS

Data was recorded on a predesigned proforma and managed on an excel spreadsheet. All the entries were checked for any possible keyboard error. All the quantitative variables were assessed for normal distributions. Variables following normal distribution were summarized by mean and standard deviation and other variables which were non-normative as median (minimum-maximum) values at each point for both case and control eyes. For all parameters following analysis were performed,

1. Before comparing the post interventional values, the baseline for variables following normal distribution were compared by student t test and baseline for non-normative variables were compared using Freidman test.

2. Repeated measure analysis of variance were used to compare the mean values at different time points within the groups

3. To compare two groups at different follow up times, percentage change at each time point from baseline were computed for every patient. Since the percentage change was non-normally distributed, median was used as summary measure and Wilcoxon rank sum test was used to compare the median percentage change from baseline between the two groups at different follow up time points.

CLINICAL PHOTOGRAPH

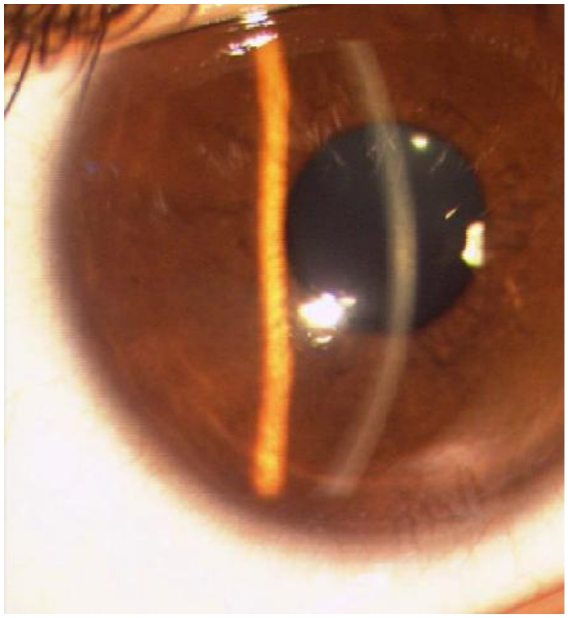


Figure 1 a -The preoperative clinical photograph showing clear stroma

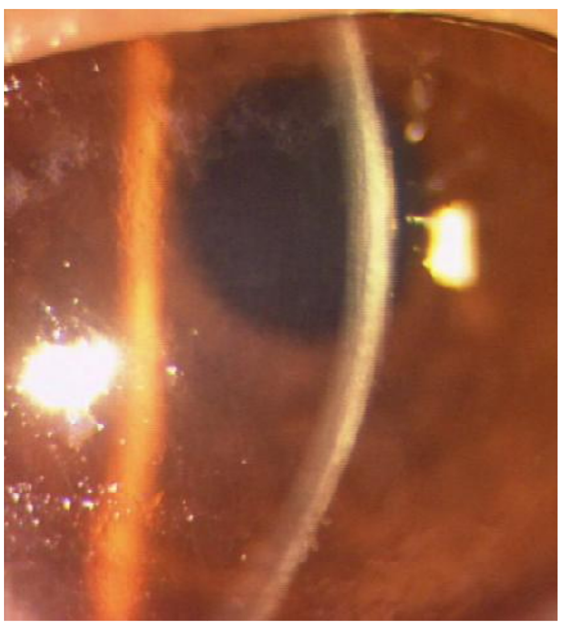


Figure 1 b -Three month postoperative photograph showing scarring

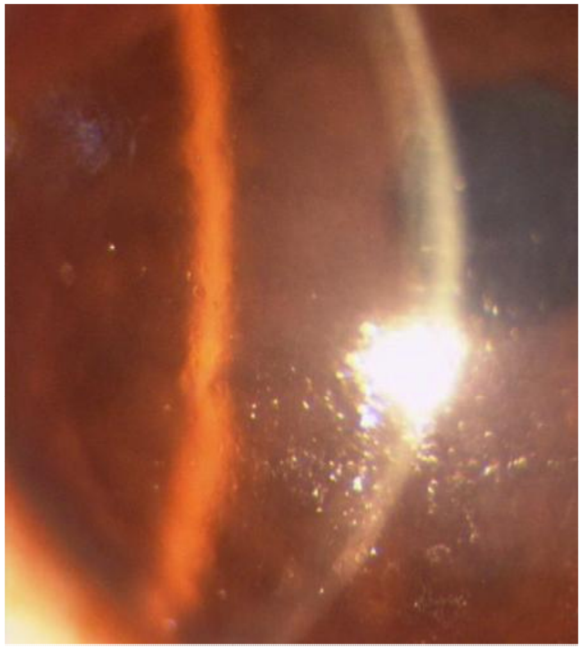


Figure 2 a -1 week postoperative photograph showing stromal haze due to oedema

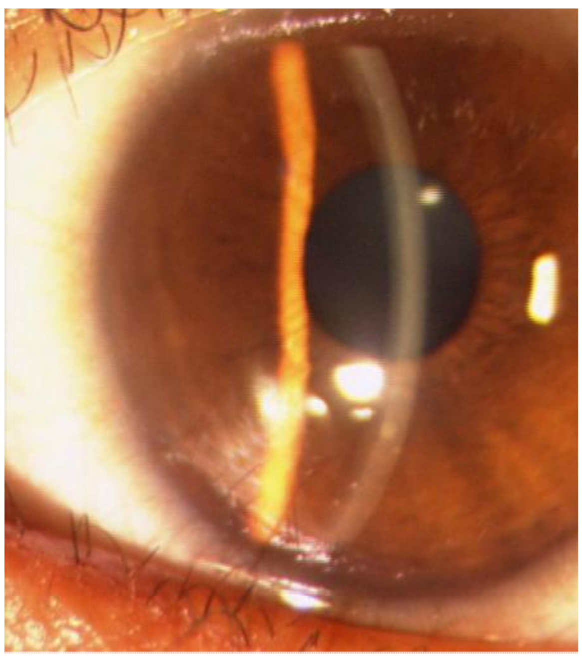
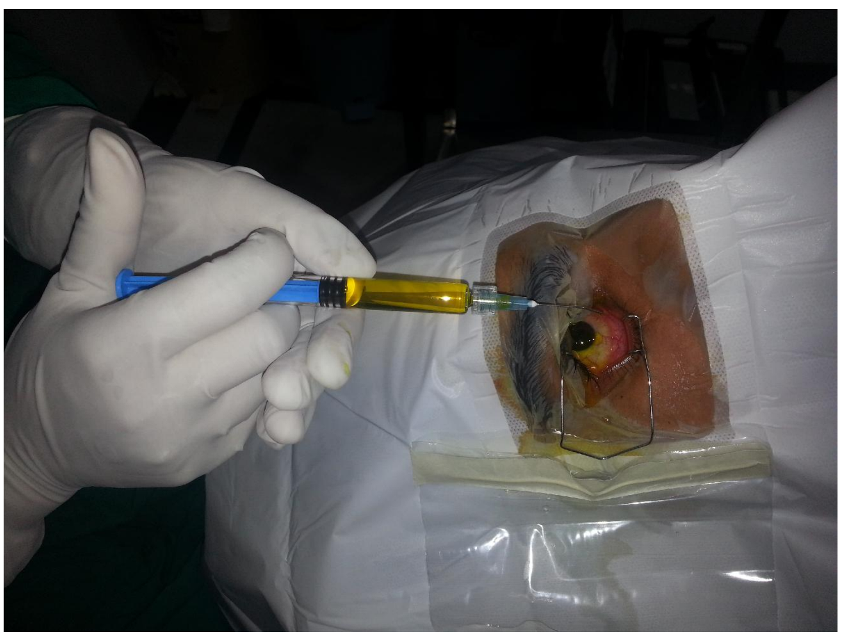


Figure 2 b - At three months there was no haze with clear stroma

RIBOFLAVIN (MEDIO-CROSS ITALY) – RIBOFLAVIN IS AVAILABLE AS 0.1 % PRE PREPARED ISOTONIC SOLUTION IN 20 % DEXTRAN AS A 3 ML VIAL



RIBOFLAVIN INSTILLED ON PATIENT'S CORNEA

UV LIGHT FOCUSSED ON PATIENTS CORNEA

UV LIGHT SOURCE WITH SENSOR PROBE AND UV LIGHT METER

ORBSCAN IIz

RESULTS

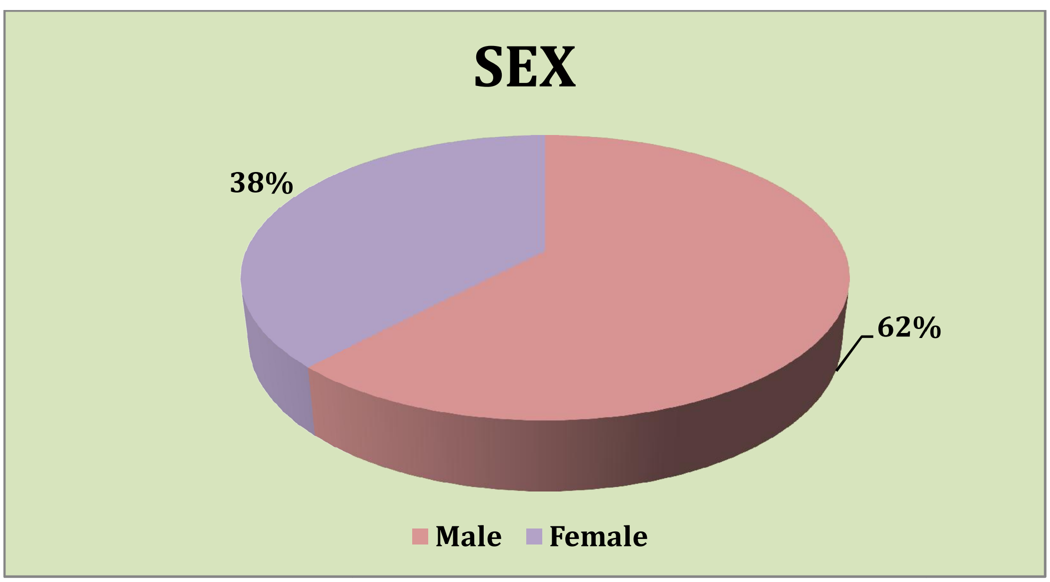
AGE

The mean age of presentation was 17.72 years (SD= 2.98) with a range of 12 to 26 years.

SEX DISTRIBUTION

Table -3

Sex	n	%
Male	31	62
Female	19	38
Total	50	100



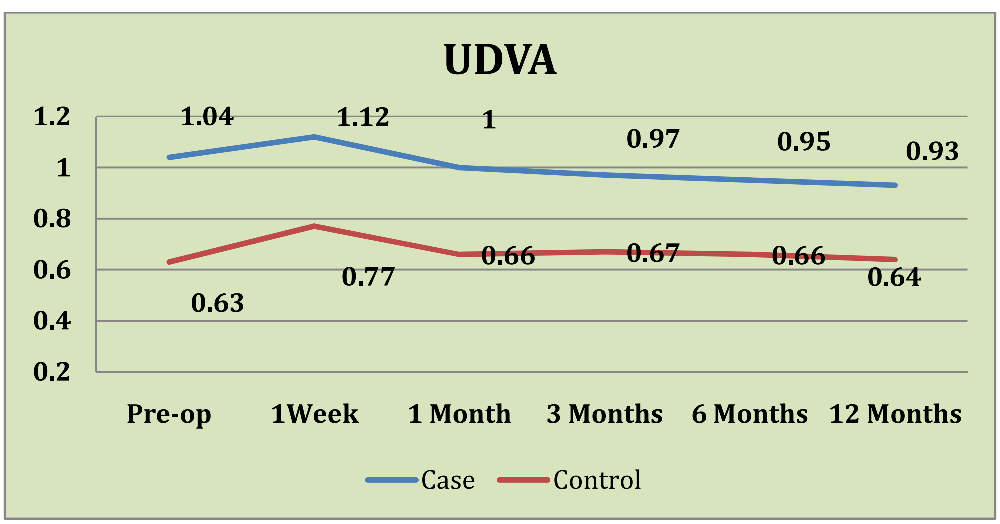
A total of 50 patients were enrolled in the study, with 31 males (62%) and 19 females (38%)

UNCORRECTED DISTANCE VISUAL ACUITY

Table – 4 UDVA in LogMAR

UDVA	Case			Control			P-value (between groups)*	P-value Case (within group)*	P-value Control (within group)*
	n	Mean(SD)	Min-max	n	Mean(SD)	Min-max			
Pre-op	49	1.04(0.28)	0.48-1.78	50	0.63(0.46)	0-1.78	<0.001	-	-
1 week	35	1.12(0.35)	0.3-1.78	32	0.77(0.44)	0-1.78	0.0001	0.224	0.026
1 month	50	1.00(0.29)	0.3-1.78	48	0.66(0.44)	0-1.48	<0.001	0.160	0.100
3 month	50	0.97(0.32)	0.3-1.78	49	0.67(0.47)	0-1.78	<0.001	0.007	0.030
6 month	46	0.95(0.31)	0.3-1.78	47	0.66(0.47)	0-1.78	<0.001	0.004	0.092
12 months	48	0.93(0.30)	0-1.3	48	0.64(0.45)	0-1.78	<0.001	0.009	0.163

*Wilcoxon signed-rank test



The mean (SD) uncorrected visual acuity in eyes that underwent CXL was 1.04 (0.28) log MAR preoperatively, 0.97 (0.32) at 3 months, 0.95 (0.031) at 6 months and 0.93 (0.30) at 1 year. There was a significant improvement in UCVA among the cases with respect to preoperative vision and vision and 3 months (p value = 0.007), 6 months (p value = 0.004) and 12 months (p value = 0.09).

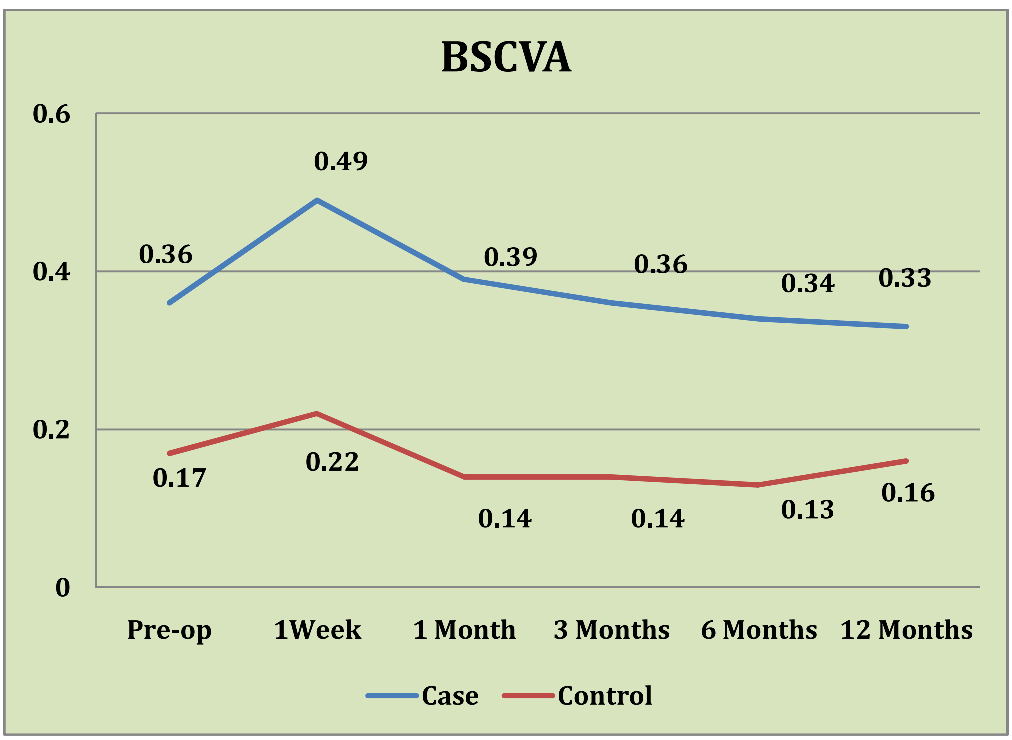
The mean (SD) uncorrected visual acuity in control eyes was 0.63 (0.46) log MAR preoperatively, 0.67 (0.47) at 3 months, 0.66 (0.47) at 6 months and 0.64 (0.45) at 12 months. There was no statistically significant change with respect to preoperative vision and final vision at 6 months and 12 months.

BEST SPECTACLE CORRECTED VISUAL ACUITY

Table – 5 BSCVA in logMAR

BSCVA	Case			Control			P-vale (between groups)*	P-value Case (within group)*	P-value Control (within group)*
	n	Mean(SD)	Min-max	N	Mean(SD)	Min-max			
Pre-op	50	0.36(0.26)	0-1	50	0.17(0.22)	0-1	<0.001	-	-
1week	31	0.49(0.30)	0.18-1.48	32	0.22(0.25)	0-1	0.001	0.005	0.989
1 month	49	0.39(0.26)	0-1.48	48	0.14(0.17)	0-0.6	<0.001	0.272	0.104
3 months	50	0.36(0.23)	0-1	50	0.14(0.20)	0-1	<0.001	0.831	0.078
6 months	49	0.34(0.20)	0-1	48	0.13(0.15)	0-0.48	<0.001	0.324	0.188
12 months	49	0.33(0.22)	0-1	49	0.16(0.20)	0-1	0.0001	0.361	0.807

* Wilcoxon signed-rank test



The mean (SD) best spectacle corrected visual acuity in eyes that underwent CXL was 0.36 (0.26)log MAR preoperatively, 0.36 (0.23) at 3 months, 0.34 (0.020) at 6 months and 0.33 (0.22) at 1 year. There was no statistically significant improvement in the BSCVA with respect to preoperative vision and vision at subsequent follow-ups.

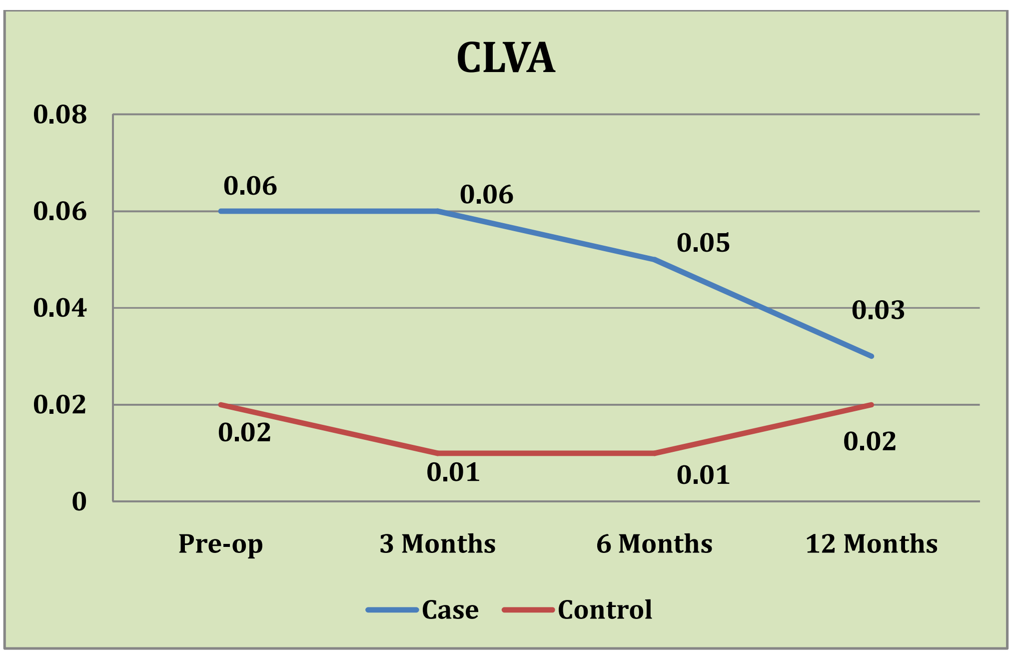
The mean (SD) best spectacle corrected visual acuity in control eyes was 0.17(0.22) logMAR preoperatively, 0.14 (0.20) at 3 months, 0.13 (0.15) at 6 months and 0.16 (0.20) at 1 year. There was no significant decrease in BSCVA in the control group.

CONTACT LENS VISUAL ACUITY

Table -6 CLVA in logMAR

CLVA	**Case**			**Control**			**P-vale (between groups)**	**P-value Case (within group)**	**P-value Control (within group)**
	n	Mean(SD)	Min-max	N	Mean(SD)	Min-max			
Pre-op	49	0.06(0.10)	0-0.3	49	0.02(0.06)	0-0.3	0.014	-	-
3 months	48	0.06(0.11)	0-0.48	46	0.01(0.05)	0-0.3	0.003	0.769	0.317
6 months	49	0.05(0.09)	0-0.3	47	0.01(0.05)	0-0.3	0.030	0.438	0.317
12 months	48	0.03(0.07)	0-0.3	49	0.02(0.06)	0-0.3	0.115	0.122	>0.99

- Wilcoxon signed-rank test



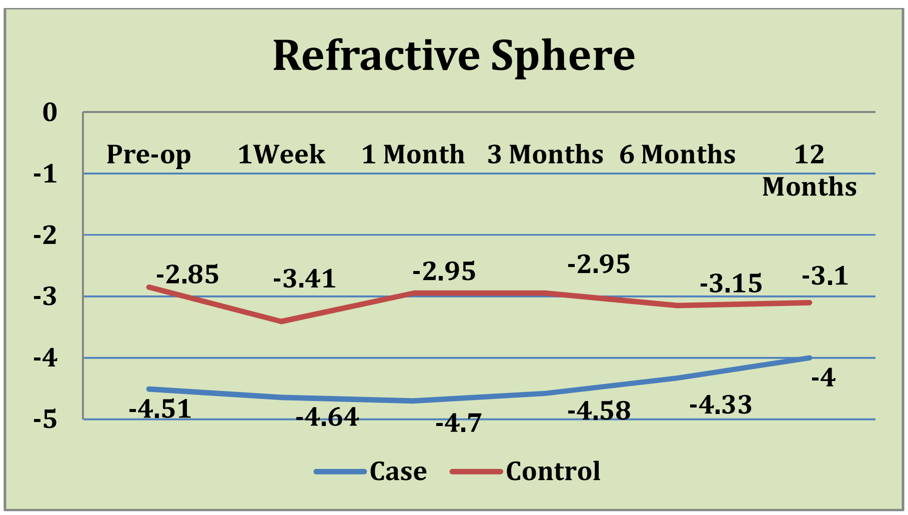
The mean (SD) contact lens corrected visual acuity in eyes that underwent CXL was 0.06 (0.10)logMAR preoperatively, 0.06 (0.11) at 3 months, 0.05(0.09) at 6 months and 0.03 (0.07) at 1 year. There was no significant improvement in the CLVA in the cases.

The mean (SD) contact lens visual acuity in control eyes was 0.02 (0.06) log MAR preoperatively, 0.01 (0.05) at 3 months, 0.01 (0.05) at 6 months and 0.02 (0.06) at 1 year. There was no significant change in CLVA in the control group.

REFRACTIVE SPHERE

Table-7 Refractive sphere in Dioptre

Sphere	Case			Control			P-vale (between groups) *	P-value Case (within group)*	P-value Control (within group)*
	n	Mean(SD)	Min-max	n	Mean(SD)	Min-max			
Pre-op	37	-4.51(3.39)	-14 to -0.5	31	-2.85(2.64)	-9 to 0.75	0.031	-	-
1week	23	-4.64(2.99)	-13 to -0.5	25	-3.41(2.68)	-9 to -0.5	0.008	0.276	0.026
1month	38	-4.70(3.46)	-15 to -0.75	32	-2.95(2.43)	-9 to -0.5	0.002	0.021	0.069
3month	38	-4.58(3.14)	-15 to -0.75	31	-2.95(2.29)	-9 to -0.5	0.0004	0.345	0.314
6month	35	-4.33(3.16)	-14 to -0.75	30	-3.15(2.55)	-9 to -0.5	0.003	0.762	0.135
12mnth	36	-4.00(2.76)	-14 to -0.5	29	-3.10(2.47)	-9 to -0.5	0.021	0.921	0.013



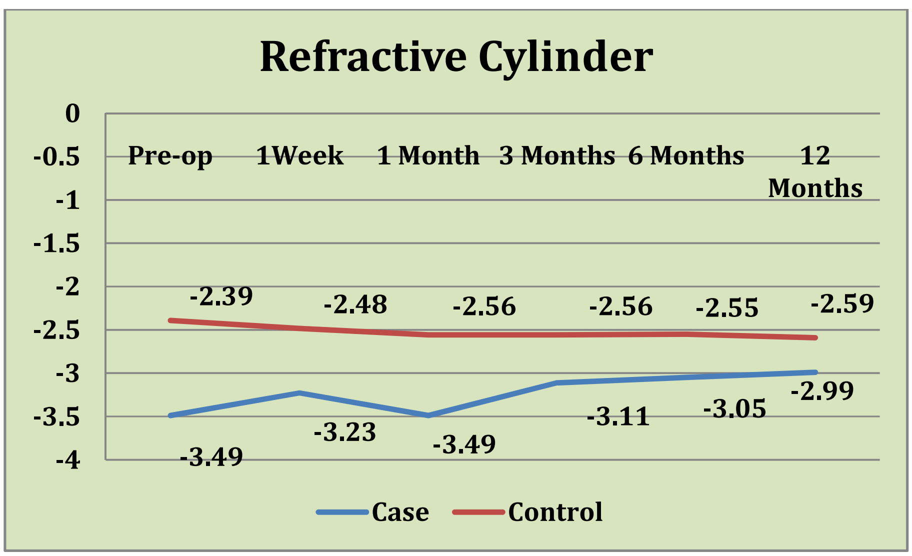
The mean (SD) spherical value in eyes that underwent CXL was -4.51D (3.39) preoperatively, -4.58D (3.14) at 3 months, -4.33D (3.16) at 6 months and -4.00D (2.76) at 12 months. There was no significant decrease in the spherical value of the cases.

The mean (SD) spherical value in the control eyes was -2.85D (2.64) preoperatively, -2.95D (2.29) at 3 months, -3.15D (2.55) at 6 months and -3.10 (2.47) at 12 months. There was a significant increase in the spherical value of the control group at 1 year as compared to preoperative values.

REFRACTIVE CYLINDER

Table- 8 Refractive cylinder in Dioptre

Cylinder	**Case**			**Control**			**P-value (between groups) ***	**P-value Case (within group)***	**P-value Control (within group)***
	n	Mean(SD)	Min-max	n	Mean(SD)	Min-max			
Pre-op	46	-3.49(1.39)	-6 to -1	36	-2.39(1.58)	-6 to -0.5	0.0004	-	-
1 week	24	-3.23(1.42)	-6 to -1	25	-2.48(1.62)	-6 to -0.5	0.0066	0.322	0.415
1 months	46	-3.49(1.40)	-6 to -0.75	36	-2.56(1.64)	-6 to -0.5	0.0033	0.785	0.682
3 months	48	-3.11(1.31)	-6 to -0.75	35	-2.56(1.62)	-6 to -0.5	0.071	0.066	0.449
6 months	44	-3.05(1.28)	-6 to -0.75	33	-2.55(1.55)	-6 to -0.5	0.032	0.114	0.212
12 months	46	-2.99(1.26)	-6 to -0.75	33	-2.59(1.40)	-6 to -0.75	0.080	0.133	0.212



The mean (SD) cylindrical value in eyes that underwent CXL was -3.49D (1.39) preoperatively, -3.11D (1.31) at 3 months, --3.05D (1.28) at 6 months and -2.99D (1.26) at 12 months. There was no significant decrease in the cylindrical value of the cases.

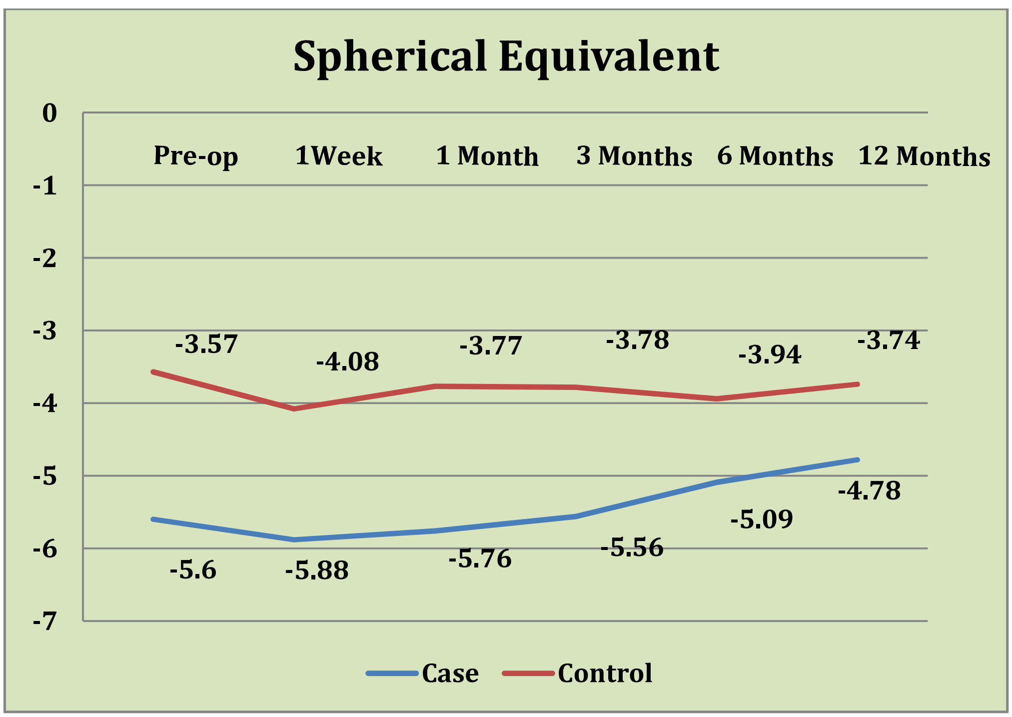
The mean (SD) cylindrical value in control was -2.39D (1.58) preoperatively, -2.56D (1.62) at 3 months, -2.55D (1.55) at 6 months and -2.59D (1.40) at 12 months. There was no significant increase in the cylindrical value of the control group.

SPHERICAL EQUIVALENT

Table- 9 Spherical equivalent in Dioptre

SPH EQ	Case			Control			P-value (between groups) *	P-value Case (within group)*	P-value Control (within group)*
	n	Mean(SD)	Min-max	n	Mean(SD)	Min-max			
Pre-op	47	-5.60(3.28)	-15.25 to -1.00	39	-3.57(2.92)	-11.5 to -0.5	0.0002	-	-
1 week	26	-5.88(3.16)	-14.75 to -1.25	29	-4.08(3.33)	-11.5 to -0.5	0.0005	0.807	0.271
1 month	46	-5.76(3.47)	-16.25 to -0.75	39	-3.77(2.88)	-11.5 to -0.5	<0.001	0.244	0.101
3 months	49	-5.56(3.46)	-16.25 to -0.75	38	-3.78(2.75)	-11.5 to -0.5	0.0007	0.497	0.099
6 months	43	-5.09(3.05)	-15.25 to -0.75	37	-3.94(2.96)	-11 to -0.5	0.0004	0.078	0.032
12 months	45	-4.78(2.94)	-15.25 to -0.75	38	-3.74(2.73)	-10.88 to -0.68	0.017	0.074	0.008

*Wilcoxon signed-rank test



The mean (SD) spherical equivalent in eyes that underwent CXL was -5.60 (3.28) preoperatively, -5.56 (3.46) at 3 months, -5.09(3.05) at 6 months and -4.78 (2.94) at 1 year. There was a no significant reduction in the spherical equivalent in the cases.

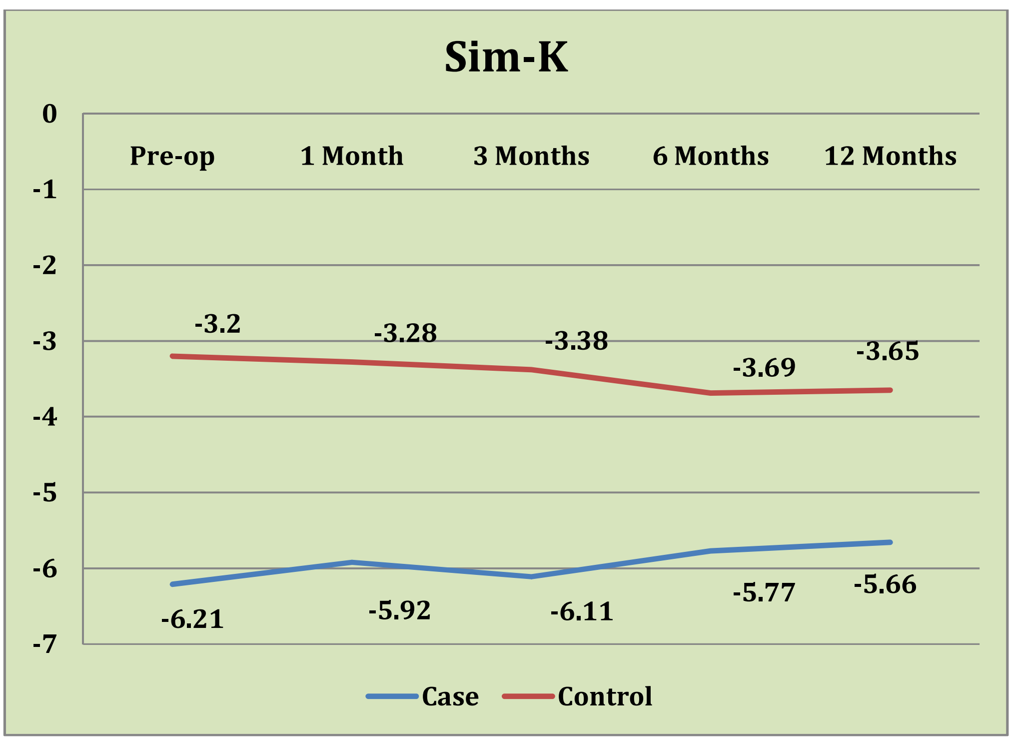
The mean (SD) spherical equivalent in control eyes was -3.57 (2.92) preoperatively, -3.78 (2.75) at 3 months, -3.94 (2.96) at 6 months and -3.74 (2.73) at 1 year. The increase in spherical equivalent was statistically significant at 6 months (p value = 0.032) and 12 months (p value = 0.008).

SIMULATED KERATOMETRY(ORBSCAN)

Table –10 Simulated keratometry (Orbscan) in Dioptre

Sim-k	Case			Control			P-value (between groups) *	P-value Case (within group)*	P-value Control (within group)*
	n	Mean(SD)	Min-max	n	Mean(SD)	Min-max			
Pre-op	48	-6.21(2.94)	-13.4 to -0.7	47	-3.20(2.13)	-8.2 to -0.5	<0.001	-	-
1 month	37	-5.92(3.67)	-13.8 to 7.8	44	-3.28(2.21)	-8.3 to -0.6	<0.001	0.240	0.0002
3 months	48	-6.11(2.93)	-14 to -1.00	46	-3.38(2.17)	-8.5 to -0.3	<0.001	0.216	0.013
6 months	46	-5.77(2.80)	-13.1 to -1	43	-3.69(2.32)	-9.4 to -0.5	0.0001	0.007	0.0007
12 months	46	-5.66(2.76)	-12.6 to -1	48	-3.65(2.33)	-9 to -0.4	0.0002	0.010	0.0001

*Wilcoxon signed rank test



The mean (SD) Sim K in eyes that underwent CXL was -6.21 (2.94) preoperatively, -6.11 (2.93) at 3 months, -5.77(2.80) at 6 months and -5.66 (2.76) at 1 year. There was a statistically significant reduction in the Sim K with respect to preoperative values and values at 6 months ($p = 0.007$) and 12 months ($p = 0.010$).

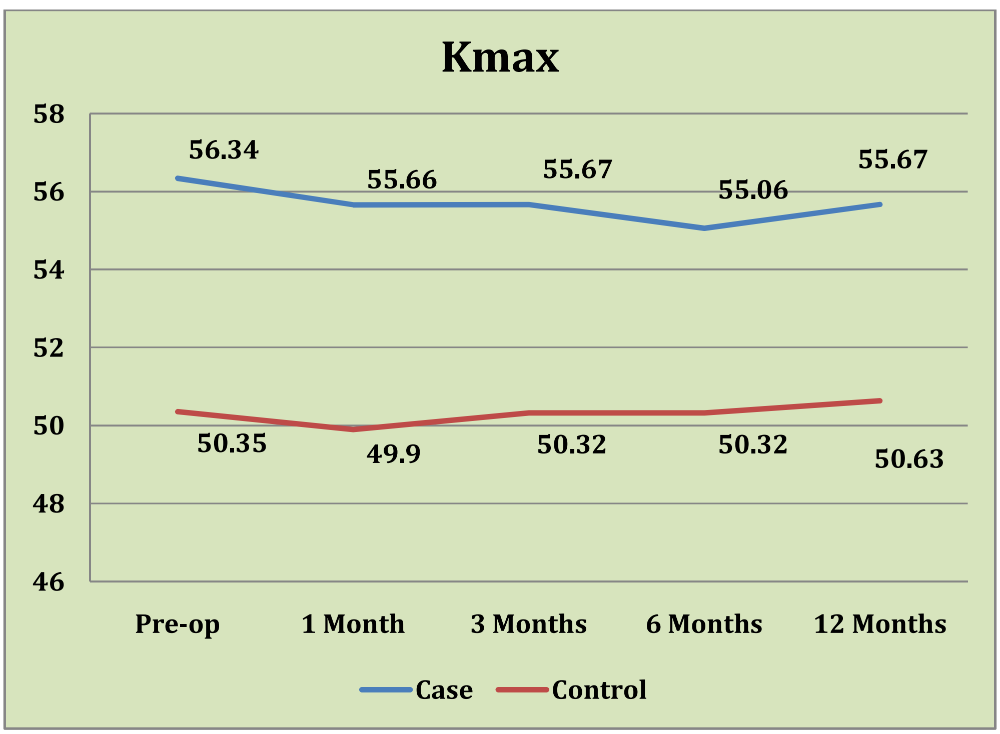
The mean (SD) Sim K in control eyes was -3.20 (2.13) preoperatively, -3.38 (2.17) at 3 months, -3.69 (2.32) at 6 months and -3.65 (2.33) at 1 year. There was a significant increase in Sim K values in the control group with respect to preoperative vision and vision at 6 months ($p = 0.0007$) and 12 months ($p = 0.0001$)

MAXIMUM KERATOMETRY (ORBSCAN)

Table- 11 Maximum Keratometry (Orbscan) in Dioptre

K max	Case			Control			P-value (between groups) *	P-value Case (within group)*	P-value Control (within group)*
	n	Mean(SD)	Min-max	n	Mean(SD)	Min-max			
Pre-op	47	56.34(5.13)	49.1-69.5	49	50.35(4.96)	43.9-64.8	<0.001	-	-
1 month	42	55.66(4.72)	49.2-69.0	40	49.90(4.46)	45.3-63.8	<0.001	0.436*	0.031
3 months	48	55.67(5.31)	48.6-68.4	47	50.32(5.05)	43.9-66.2	<0.001	0.0004	0.238
6 months	43	55.06(5.04)	48.2-68.4	46	50.32(4.69)	43.5-63.2	<0.001	0.0008	0.138
12 months	46	55.67(5.24)	47.7-68.3	46	50.63(4.64)	43.2-62.0	<0.001	0.103	0.115

*t-test



The mean (SD) K max in eyes that underwent CXL was 56.34 (5.13) D preoperatively, 55.67(5.31) at 3 months, 55.06(5.04) at 6 months and 55.67 (5.24) at 1 year. There was a significant decrease in the K max of the cases at 3 months (p value = 0.0004) and 6 months (p= 0.0008).

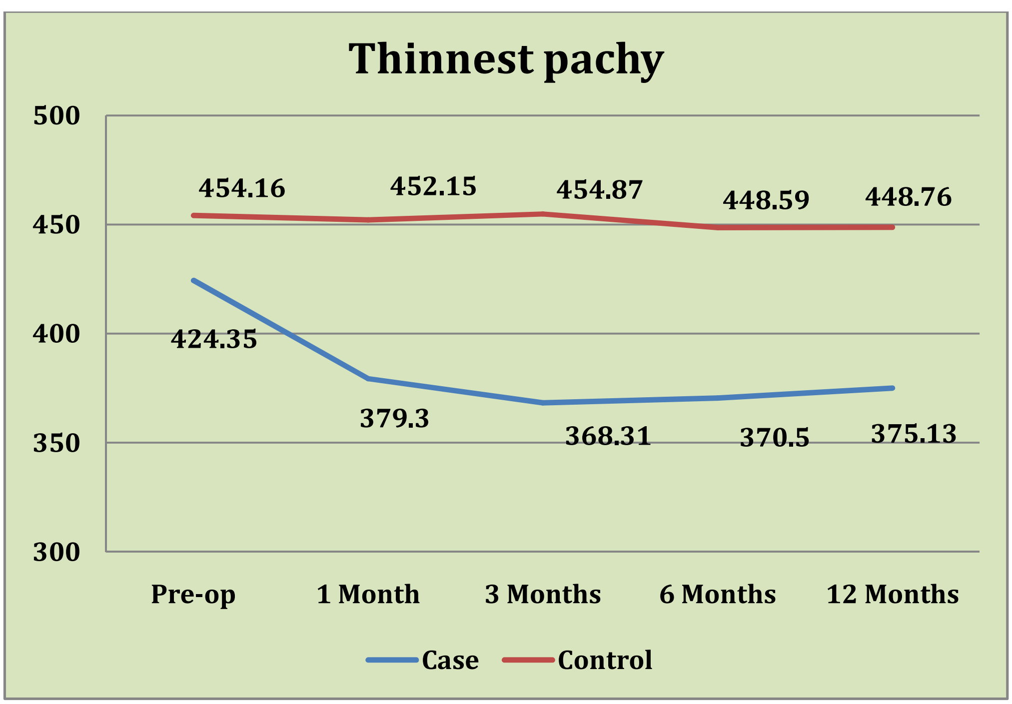
The mean (SD) K max in control eyes was 50.35(4.96) D preoperatively, 50.32 (5.05) at 3 months, 50.32 (4.69) at 6 months and 50.63 (4.64) at 1 year. There was no significant change in the K max within the control group.

THINNEST PACHYMETRY

Table-12 Thinnest pachymetry in microns

Thinnest pachy	Case			Control			P-value (between group) *	P-value Case (within group) *	P-value Control (within group)*
	n	Mean(SD)	Min-max	n	Mean(SD)	Min-max			
Pre-op	48	424.35(29.35)	350-486	50	454.16(47.39)	313-512	0.0001		
1 month	46	379.30(53.34)	250-451	46	452.15(48.76)	310-511	<0.001	<0.001	0.039
3 months	49	368.31(60.94)	260-472	49	454.87(44.88)	315-521	<0.001	<0.001	0.213
6 months	48	370.50(55.73)	270-475	49	448.59(51.17)	312-520	<0.001	<0.001	0.016
12 months	48	375.13(55.49)	269 – 476	49	448.76(45.76)	326-510	<0.001	<0.001	0.094

*t-test



The mean (SD) thinnest pachymetry in eyes that underwent CXL was 424.35 (29.35) microns preoperatively, 468.31(60.94) at 3 months, 370.50(55.73) at 6 months and 375.13 (55.49) at 1 year. There was a significant decrease in the thinnest pachymetry in the cases with respect to preoperative pachymetry and pachymetry at all follow-up visits (p value < 0.001) .

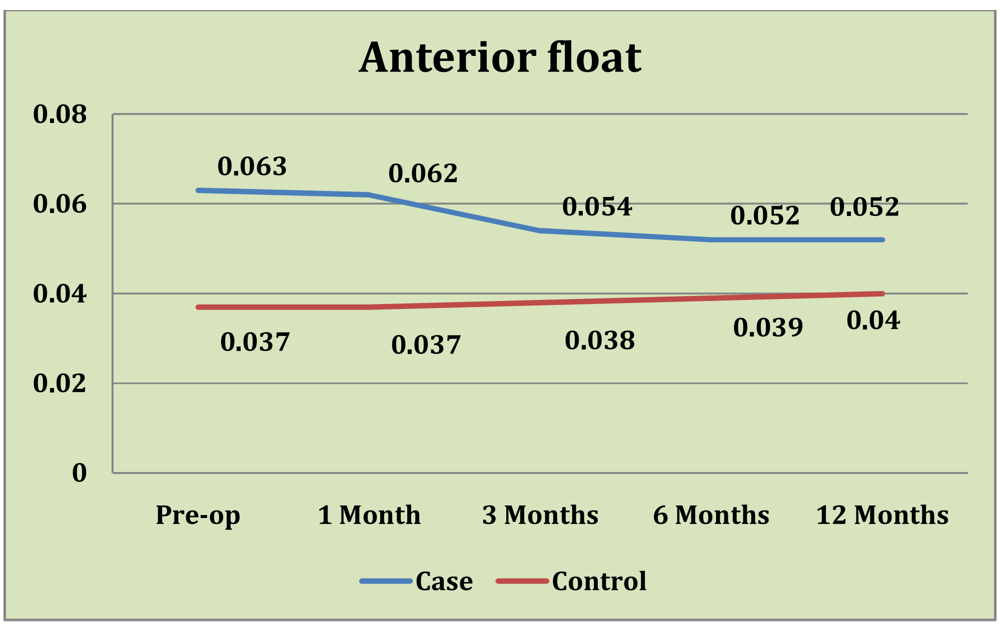
The mean (SD) thinnest pachymetry in control eyes was 454.16 (47.36) microns preoperatively, 454.87 (44.88) at 3 months, 448.59 (51.17) at 6 months and 448.76 (45.76) at 1 year. There was a significant decrease in thinnest pachymetry in the control group with respect to preoperative and postoperative values.

ANTERIOR ELEVATION (ORBSCAN)

Table – 13 Anterior elevation in millimeters

Anterior elevation	**Case**			**Control**			**P-value (between groups) ***	**P-value Case (within group)***	**P-value Control (within group)***
	n	Mean(SD)	Min-max	n	Mean(SD)	Min-max			
Pre-op	47	0.063(0.019)	0.032-0.105	49	0.037(0.018)	0.012-0.07	<0.001		
1 month	43	0.062(0.020)	0.030-0.115	41	0.037(0.018)	0.012-0.07	<0.001	0.441	0.984
3 month	46	0.054(0.020)	0.012-0.103	46	0.038(0.017)	0.012-0.07	0.0001	<0.001	0.034
6 month	42	0.052(0.018)	0.019-0.090	43	0.039(0.017)	0.006-0.069	0.0007	<0.001	0.010
12 months	48	0.052(0.018)	0.023-0.087	50	0.040(0.017)	0.009-0.076	0.0006	<0.001	0.014

*Wilcoxon signed rank test



The mean (SD) anterior float in eyes that underwent CXL was 0.063 (0.019) mm preoperatively, 0.054(0.020) at 3 months, 0.052(0.018) at 6 months and 0.052 (0.018) at 1 year. There was a significant decrease in the anterior float with respect to preoperative and postoperative values at 3 months and thereafter ($p < 0.001$).

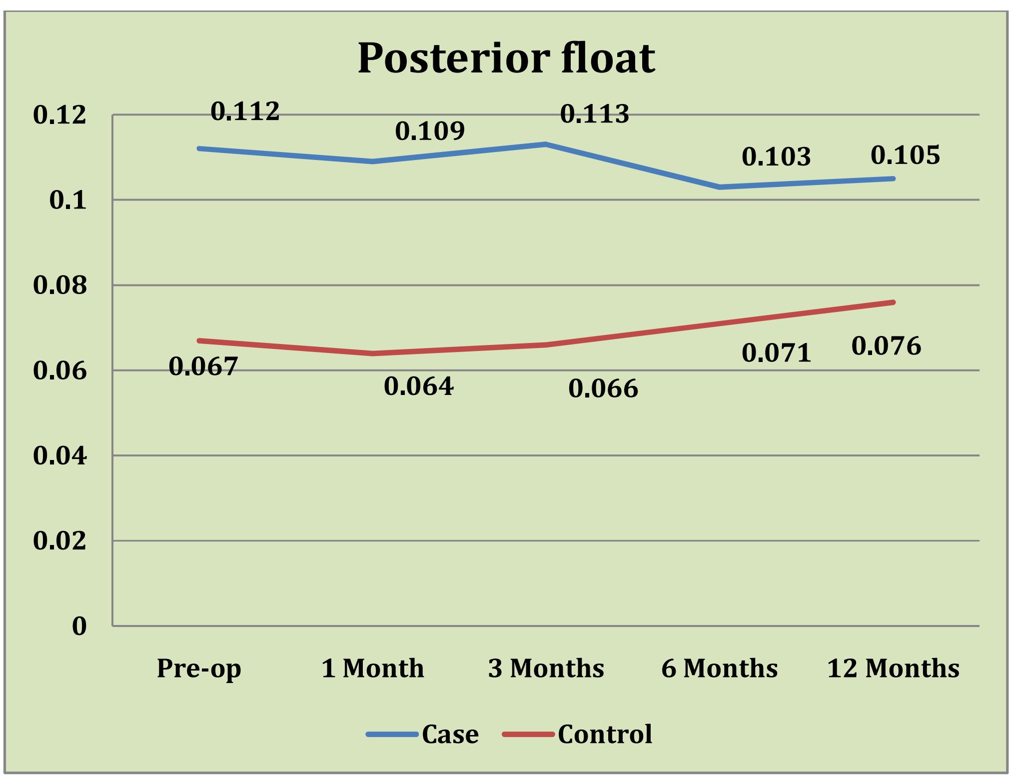
The mean (SD) anterior float in control eyes was 0.037 (0.018) mm preoperatively, 0.038 (0.017) at 3 months, 0.039(0.017) at 6 months and 0.040 (0.017) at 1 year. There was a significant increase in the anterior float in the control group at 3 months (p value = 0.034), 6 months (p value = 0.010) and 12 months (p value = 0.014) postoperatively.

POSTERIOR ELEVATION (ORBSCAN)

Table -14 Posterior elevation in millimeters

Posterior elevation	**Case**			**Control**			**P-value (between groups) ***	**P-value Case (within group)***	**P-value Control (within group)***
	n	Mean(SD)	Min-max	n	Mean(SD)	Min-max			
Pre-op	47	0.112(0.033)	0.037-0.195	48	0.067(0.040)	0.015-0.211	<0.001	-	-
1 months	43	0.109(0.036)	0.037-0.198	44	0.064(0.039)	0.015-0.211	<0.001	0.178	0.899
3 months	47	0.113(0.034)	0.038-0.197	46	0.066(0.042)	0.020-0.222	<0.001	0.569	0.075
6 months	44	0.103(0.036)	0.037-0.176	45	0.071(0.044)	0.021-0.220	0.0001	0.391	0.016
12 months	47	0.105(0.037)	0.045 – 0.176	49	0.076(0.043)	0.021-0.200	0.0003	0.584	0.002

*Wilcoxon signed rank test



The mean (SD) posterior float in eyes that underwent CXL was 0.112 (0.033) preoperatively, 0.113 (0.034) at 3 months, 0.103(0.036) at 6 months and 0.105 (0.037) at 1 year. There was no significant decrease in the posterior float of the cases.

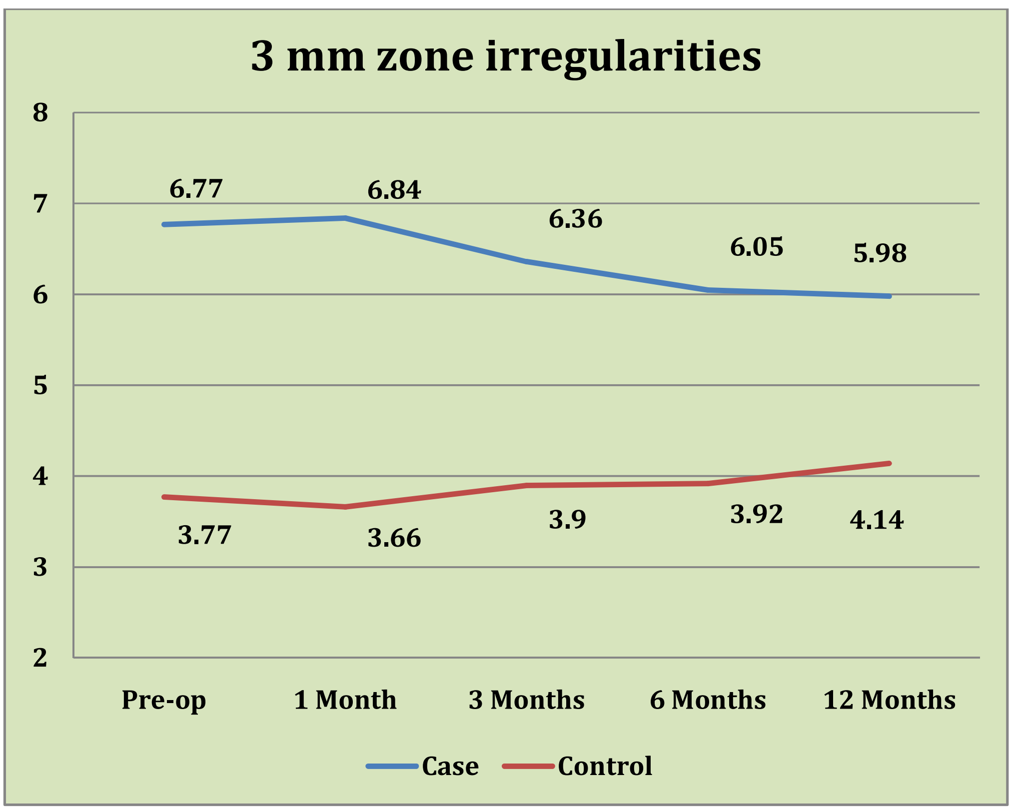
The mean (SD) posterior float in control eyes was 0.067 (0.040) preoperatively, 0.066 (0.042) at 3 months, 0.071(0.044) at 6 months and 0.076 (0.043) at 1 year. There was a significant increase in the posterior float values of the controls with respect to preoperative values and values at 6 months (p value = 0.016) and 12 months (p value =0.002)

3 MM ZONE IRREGULARITIES

Table –15 3 mm zone irregularities in Dioptre

3mm zone	Case			Control			P-value (between groups)*	P-value Case (within group)*	P-value Control (within group)*
	n	Mean(SD)	Min-max	N	Mean(SD)	Min-max			
Pre-op	47	6.77(2.89)	2.6-15.4	47	3.77(2.14)	0.8-8.3	<0.001		
1 month	42	6.84(2.82)	2.5-15.2	44	3.66(2.02)	0.8-8.2	<0.001	0.536	0.897
3 months	47	6.36(2.56)	2.1-14.6	46	3.90(2.16)	1.0-8.7	<0.001	0.0003	0.214
6 months	43	6.05(2.44)	2.2-12.2	45	3.92(1.99)	0.8-7.9	<0.001	0.0004	0.104
12 months	48	5.98(2.39)	2.2 – 12.5	50	4.14(2.18)	0.8-9.1	<0.001	<0.001	0.340

- t-test



The mean (SD) 3mm zone irregularities in eyes that underwent CXL was 6.77(2.89)D preoperatively, 6.36 (2.56) at 3 months, 6.05(2.44) at 6 months and 5.98 (2.39) at 1 year. There was a significant decrease in the 3mm zone irregularities in the cases.

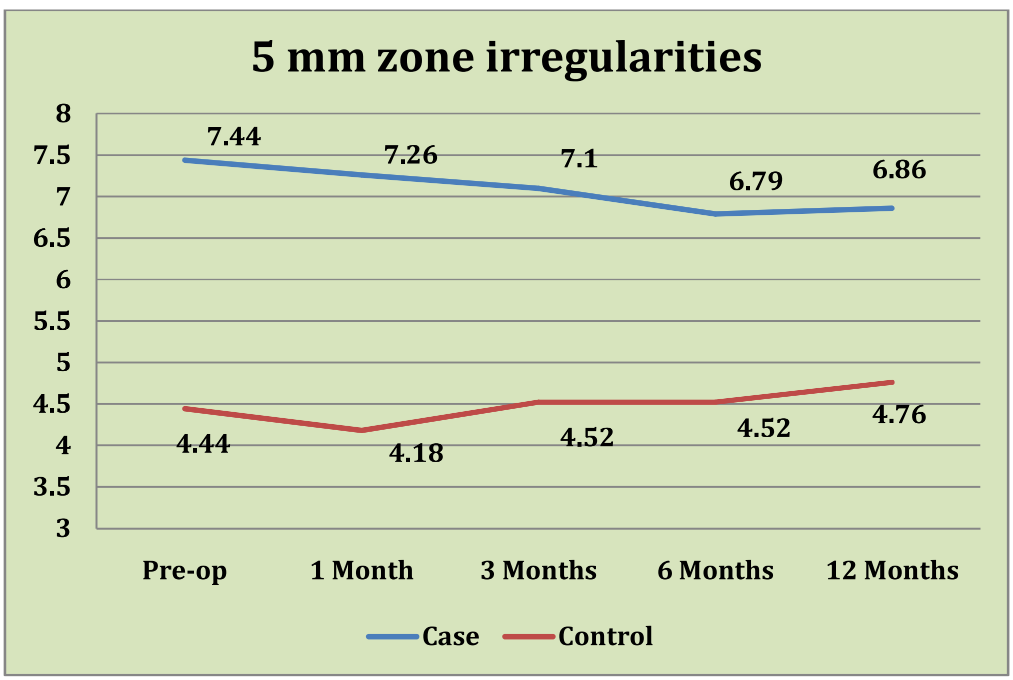
The mean (SD) 3mm zone irregularities in control eyes was 3.77(2.14)D preoperatively, 3.90 (2.16) at 3 months, 3.92(1.99) at 6 months and 4.14 (2.18) at 1 year. There was no significant increase in the 3 mm zone irregularities in the control group.

5 MM ZONE IRREGULARITIES

Table –16 5 mm zone irregularities in Dioptre

5mm zone	Case			Control			P-value (between groups) *	P-value Case (within group)*	P-value Control (within group)*
	n	Mean(SD)	Min-max	n	Mean(SD)	Min-max			
Pre-op	47	7.44(3.10)	3.4-16.4	47	4.44(2.50)	1.3-15.2	<0.001	-	-
1 month	42	7.26(2.89)	3.6-15.8	43	4.18(1.96)	1.3-8.9	<0.001	0.367	0.780
3 months	47	7.10(2.66)	3.8-14.4	46	4.52(2.63)	1.3-15.5	<0.001	0.009	0.598
6 months	43	6.79(2.54)	2.5-13.3	44	4.52(2.06)	1.2-10.4	<0.001	0.006	0.022
12 months	47	6.86(2.41)	2.9-13.0	50	4.76(2.24)	1.3-11.20	<0.001	0.010	0.602

- t-test



The mean (SD) 5 mm zone irregularities in eyes that underwent CXL was 7.44(3.10) D preoperatively, 7.10 (2.66) at 3 months, 6.79 (2.54) at 6 months and 6.86 (2.41) at 1 year. There was a significant decrease in 5mm zone irregularities in the cases with respect to preoperative values and values at 3 months (p value = 0.009) , 6 months (p = 0.006) and 12 months (p value = 0.010)

The mean (SD) 5 mm zone irregularities in control eyes was 4.44(2.50) D preoperatively, 4.52 (2.63) at 3 months, 4.52(2.06) at 6 months and 4.76 (2.24) at 1 year. There was no significant increase in the 5mm zone irregularities in the control group.

SPECULAR MICROSCOPY

Table –17 Specular count in cells/mm^3

Parameters	**Case**			**Control**		
	n	Mean(SD)	Min-Max	n	Mean(SD)	Min-Max
CD	10	2610.80(299.34)	2162 – 3030	18	2572.61(281.61)	2008 – 2990
SD	7	126.00(26.76)	76 – 160	15	117.27(31.94)	75 – 200
CV	10	31.20(5.55)	23 – 42	18	33.06(12.93)	22 – 62
HEX	9	69.00(13.55)	46 – 82	17	60.65(21.34)	0 – 90

There was no significant change in the specular count of the eyes that could be measured, between case and control group. However, values could not be obtained on a majority of cases as specular could not be captured due to the advanced stage of the disease. This was one of the major limitations noted in our study.

INTRAOCULAR PRESSURE

Table –18 Intraocular pressure in mmHg

IOP	Cases	Control	% difference	Case median (min-max)	Control median (min-max)	P value between groups
	Mean +/- SD	Mean +/- SD				
Preop (1)	12.8 +/- 1.2	12.8 +/- 1.2				0.74
1 month (2)	12.8 +/- 1.3	12.7 +/- 1.2	IOP 1-2	0(-16.7 – (16.7))	0(-20-(28.6))	0.97
3 months (3)	12.7 +/- 1.2	12.6 +/- 1.4	IOP 1 -3	0(-16.7 – (14.3))	0(-20-(16.7))	0.69
6 months (4)	12.4 +/- 1.2	12.3 +/- 0.9	IOP 1-4	0(-16.7 – (28.6))	0(-20-(28.6))	0.83
12 months (5)	12.4 +/- 1.0	12.6 +/- 0.9	IOP 1-5	0(-16.7 – (16.7))	0(-20-(14.3))	0.71
P value within group	0.3	0.5				

The mean (SD) intraocular pressure in eyes that underwent CXL was 12.8(1.2) mmHg preoperatively, 12.7 (1.2) at 3 months, 12.4(1.2) at 6 months and 12.4 (1.0) at 1 year. There was a significant change in intraocular pressure in the cases.

The mean (SD) intraocular pressure in control eyes was 12.8(1.2) D preoperatively, 12.6 (1.4) at 3 months, 12.3(0.9) at 6 months and 12.6 (0.9) at 1 year. There was no significant change in intraocular pressure in the control group.

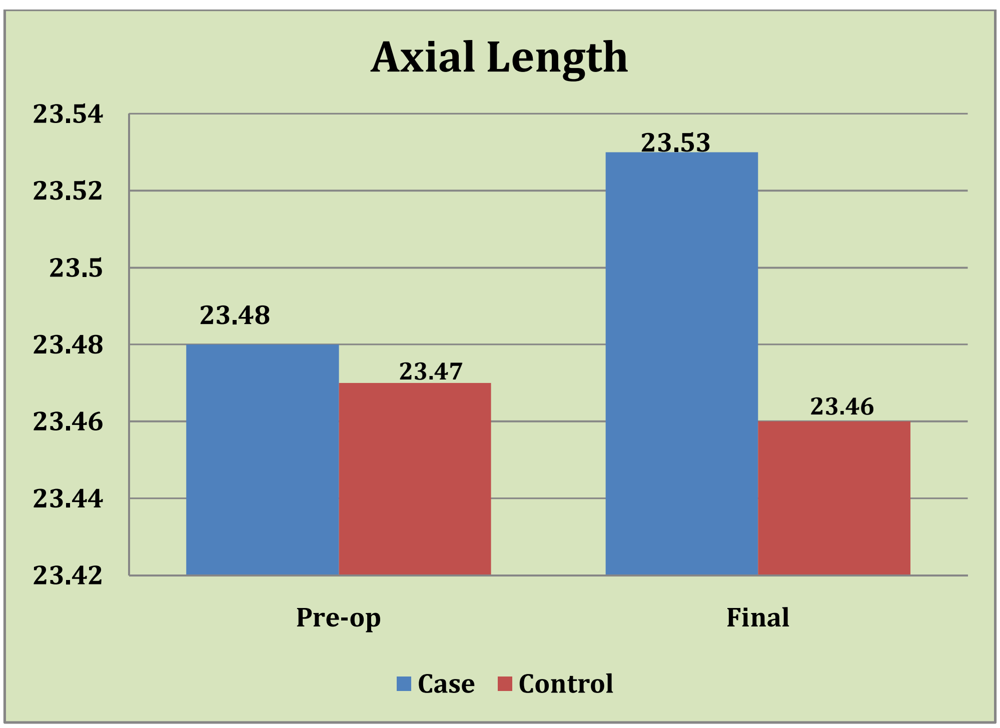
There was no significant change in the intraocular pressure between the case and control group.

AXIAL LENGTH

Table -19 Axial length in millimeters

Axial length	Case			Control			P-value*
	n	Mean(SD)	Min-Max	n	Mean(SD)	Min-Max	
Pre-op	34	23.48(0.79)	21.71-25.11	34	23.47(0.82)	21.57-25.2	0.98
Final	34	23.53(0.75)	21.72-25.10	35	23.46(0.81)	21.59-25.2	0.44
P-Value*	0.51			0.004			

*t-test



The mean axial length of the eyes undergoing CXL was 23.48 mm preoperatively and 23.53 mm at 1 year follow-up. The mean axial length in control eyes preoperatively was 23.47mm and 23.46 mm at 1-year postoperative follow-up.

SCARRING AND PERSISTENT STROMAL HAZE

Table -20

	Scarring	**Persistent stromal haze**
Present (%)	13 (26 %)	30 (60 %)
Absent (%)	37 (74 %)	20 (40 %)
Total	50	50

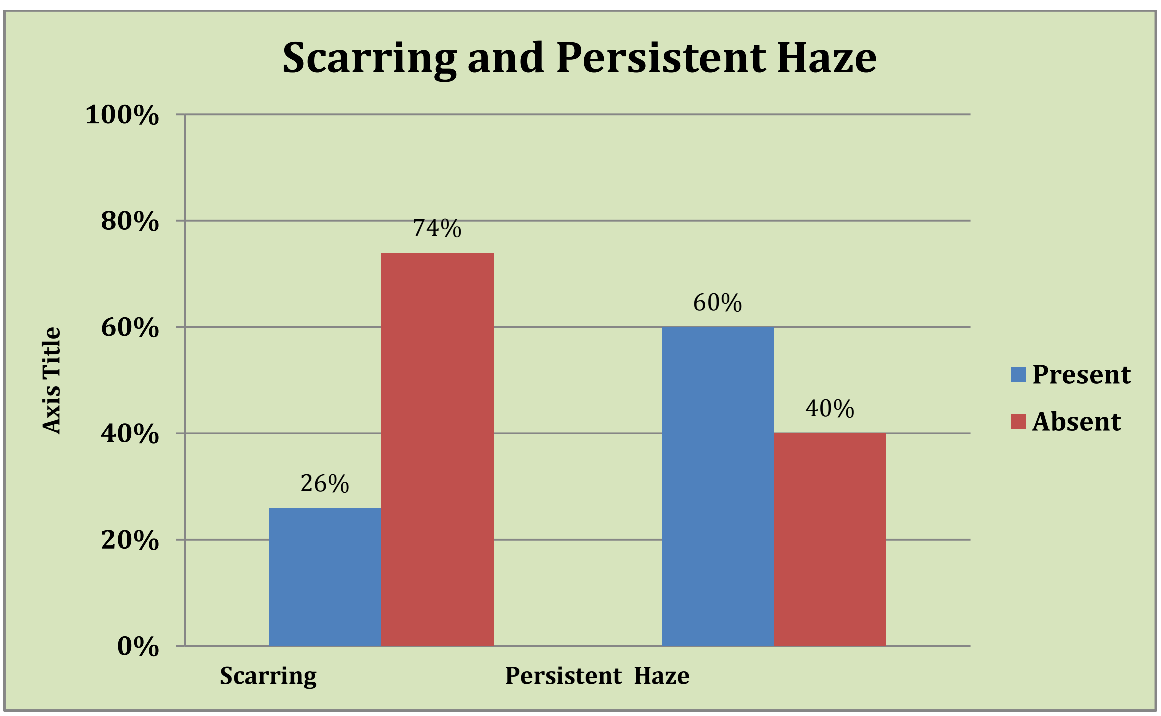
Postoperative scarring was seen in 13 patients (26%) and persistent stromal haze (beyond 3 months) was present in 30 patients (60%).

Table -21

K max	Total number of patients	Scarring present	percentage
Upto 56 D	27	3	11.11 %
More than 56 D	23	10	43.48 %

P value = 0.002 (chi square test)

Stromal haze was seen more commonly in patients with advanced keratoconus.



INTERGROUP COMPARISION

Table -22

Preoperative values	CASE MEAN (SD)	CONTROL MEAN (SD)	P-VALUE BETWEEN GROUPS
UDVA	1.04(0.28)	0.63(0.46)	<0.001
BSCVA	0.36(0.26)	0.17(0.22)	<0.001
SPHERICAL EQUIVALENT	-5.60(3.28)	-3.57(2.92)	0.0002
K MAX	56.34(5.13)	50.35(4.96)	<0.001
THINNEST PACHYMETRY	424.35(29.35)	454.16(47.39)	0.0001
ANTERIOR ELEVATION	0.063(0.019)	0.037(0.018)	<0.001

The preoperative uncorrected visual acuity and best spectacle corrected visual acuity in the cases was significantly worse than the control group. Also the preoperative spherical equivalent, k max and anterior elevation were significantly higher in the case group. This intergroup disparity was due to the fact that the eye that has progressed further in the disease was chosen as the case, while the fellow eye served as the control.

DISCUSSION

Demographic results

This was a prospective interventional clinical trial undertaken to evaluate the safety and efficacy of collagen cross-linking with ultraviolet –A and riboflavin in the treatment of progressive keratoconus. A total of 50 eyes were treated with cross-linking with epithelial debridement, while the fellow eyes served as the control group.

The mean age of presentation was 17.72+/- 2.98 years. Amongst the patients 62 % were males (n=31) and 38% were females (n=19). Wiitig-Silva et al[32] conducted a randomized control trial with 66 eyes randomized to treatment and control group. The mean age was 26.9 +/- 6.22 years. In the study by Agarwal et al[44] the mean age was lowest at 16.9 +/-3.5. In other studies by Koller et al[42] and Vinciguerra et al[43], the fellow eyes of the patients served as controls.

Visual acuity

In our study, we found a significant improvement in uncorrected visual acuity (UDVA) at 12 months follow up visit by 0.11 log MAR units which was significant with respect to the controls where no significant change was observed.

In the corrected distance visual acuity, no significant improvement was observed at 6 months and 12 months in both the case and the control group.

The improvement in uncorrected visual acuity is due to reduction in keratometry and astigmatism as demonstrated by previous studies.

In the pilot study by Wollensak et al[27] in 23 eyes, the BCVA improved statistically in 65 % of the patients by 1.26 lines. Vinciguerra et al[43] studied 28 eyes with mean increase in UCVA from 0.77 +/- 0.18 to 0.51 +/- 0.20 at 6 months, 0.57 +/- 0.16 at 12 months and BSCVA from 0.28 +/- 0.09 to 0.17 +/- 0.11 at 6 months, 0.14 +/- 0.08 at 12 months. A study by Caporrosi et al[29] including 10 eyes showed improvement of 3.6 lines for UCVA and 1.66 for BSCVA at 6 months. In a randomized controlled trial by Wittig-Silva et al[32], improvement in BCVA of average 0.07 log MAR at 6 months and 0.12 log MAR at 12 months was observed. In a study by Raiskup-Wolf et al [36](241 eyes), BCVA improved by at least one line in 53% and remained stable in 20 % at one year follow up. In a study by Agarwal et al[44], the BCVA improved by at least one line in 54 % and remained stable in 28 % eyes. In another Indian study by Grewal et al[45], no significant change was observed in BCVA at one year post-operative visit, indicating stabilization but no improvement.

Refractive results

In our study, a mean decrease in refractive cylinder by 0.44D was observed at 6 months and 0.50D at 1 year, which however was not significant with respect to the control group. The spherical equivalent showed no significant change in the cases but a significant increase in the control group at 6 months and 12 months. There was no significant change in refractive sphere in either group. The improvement in astigmatism is due to reduction in keratometry, increased rigidity of cross-linked collagen and regularization of the shape of the cornea as demonstrated by previous studies. Wollensak et al[20] observed significant increase in corneal rigidity by rise in stress by 71.9 % in porcine enucleated corneas and by 328.9 % in human enucleated corneas. Koller et al [37] observed significant reduction in 4 out of 7 keratoconic indices, Caporossi et al[29] found a trend towards increasing corneal symmetry with a reduction in topographically calculated symmetry index at 3 months. In the pilot study by Wollensak et al[27] (23 eyes), the refractive correction improved significantly by an average of 1.14 D in spherical equivalent. Vinciguerra et al [43](28 eyes) reported significant decrease in cylinder and spherical equivalent by 0.41D of spherical equivalent at 12 months. Caporossi et al[29] reported a mean reduction in spherical equivalent by 2,5 D at 6 months. Raiskup-Wolf et al[36] (241 eyes) observed a mean reduction of 0.93D in 50% eyes and remained stable in 36% at one year, reduced by 1.20D in 43% and remained stable in 42% and after 3 years decreased by a mean of 1.45D in 54% eyes. Grewal et al[45] (102 eyes) found no significant change in astigmatism over a period of one year. Agarwal et al[44] (37 eyes) found a mean reduction of 1.20D in 47% eyes and stabilization in 42%.

Thinnest pachymetry

In our study we found a significant decrease in the thinnest pachymetry by a mean of 56.04 microns at 3 months and 49.22 microns at one year postoperative, which was significant in relation to the control group. The cross linking process makes the stroma compact by chemically induced crosslinks in the stroma thereby causing a reduction in the pachymetry. In a study by Caporossi et al [29] (10 eyes), no significant increase in central corneal thickness up to 3 months follow up was observed which was explained on the basis of corneal edema. Vinciguerra et al [43] (28 eyes) observed that the central corneal thickness decreased significantly at 12 months by 20 microns and pachymetry at thinnest point by 15 microns, Grewal et al [45] (102 eyes) found no significant change in corneal thickness after one year of treatment. The compression effect was explained either as a measurement artifact or due to chemical bonds by the authors.

Keratometry

In our study there was a reduction in maximum keratometry by 0.67D which was significant in relation to the controls at 1 year follow up. The simulated keratometry showed a decrease of 0.54D at 1 year follow up. The flattening effect of the cornea following crosslinking is similar to the other studies.

The pilot study by Wollensak et al[27] (23 eyes) showed a mean reduction by 2.01 D in 70 % and stabilization in 22 %. Caporossi et al [29] (10 eyes) showed a mean k reduction of 2.1D with a reduction of 2.4 in K min and 1.9D in K max. Vinciguerra et al [43] reported a mean reduction of K max, K min and K average by 6.16D, 4D and 6.07D respectively at 12 months. Raiskup –Wolf et al[36] (241 eyes) found that the k value at the apex decreased by a mean of 2.68 D in 62% of the eyes and remained stable in 17%. Maximum keratometry decreased by a mean of 1.46 D in 56 % and remained stable in 30% eyes at one year. At 3 years follow up, K value at apex decreased by 4.84D in 78 % and remained stable in 2% of the eyes. K max decreased by a mean of 2.57D in 57% and remained stable in 9%. In an Indian population study by Agarwal et al [44] the k value at apex decreased by a mean of 2.73D in 66% eyes and remained stable in 22%. K max decreased by mean of 2.47D in 54% and remained stable in 38% at 1 year. In another Indian study by Grewal et al[45] no significant change was seen in keratometry at one year. In a randomized control trial by Wittig Silva[32] there was a significant flattening of K max by a mean of 92 D at 6 months and 1.45 D at one year.

Anterior and posterior elevation changes

In our study, we observed a significant reduction in the anterior float by 110 microns at 1 year postoperative visit. Koller et al [42] however noticed a reduction in the anterior elevation peak after treatment that was not statistically significant. There was a reduction of 70 microns in the posterior float, which was significant compared to the control group. This however could be a measured artifact as the posterior surface parameters may be fallacious, for they are derived from the anterior surface parameters. Grewal et al[45] showed no significant change in the anterior or posterior elevation post crosslinking.

Complications

In our study we could not measure changes in endothelial cell count, as a significant number of specular microscopy could not be captured due to advanced nature of disease. There was no significant change the intraocular pressure at follow up visits in either group. Similar findings were observed in other studies as well. In one study by Goldich et al[46] (10 eyes), the IOP measurement by Goldmann Applanation tonometer showed a significant increase at one week, one and three months postoperatively which may be a measurement artifact due to changes in corneal parameters like increased CCT. We also observed transient stromal haze in a majority of our patients, which persisted beyond 3 months in 30 patients (60%). The animal studies also show crosslinking effect limited to the anterior part of the stroma. Kohlhaas et al [25] found that the stiffening effect is limited to the anterior treated flaps in enucleated porcine eyes. Wollensak et al [23] found that in rabbit eyes with corneal thickness less than 400 microns, the endothelial UVA dose reached cytotoxic levels.

We found mild scarring in 13(26%) of our patients. Koller at al[42] found that out of 117 eyes ,failure rate was 7.6%. Sterile infiltrates were seen in 7.6% of the eyes and 2.8% showed central stromal scars. There are various case reports of postoperative infections in literature.

No cases of keratitis, inflliltrate or corneal melting were seen in our study. Kymionis et al[50] reported a case of herpetic keratitis, Rama et al[39] reported a case of acanthamoeba keratitis, Sharma N[40] et al reported a case of pseudomonas keratits, and Perez-Santinja et al[38] reported a case of staphylococcal keratitis after crosslinking. Koeppen et al[41] reported 4 cases of severe keratitis after crosslinking, 2 of which had persistent decrease in visual acuity.

Two patients in our study had a decrease in best spectacle corrected visual acuity (by two Snellen's lines) at one year postoperative. This could be attributed to persistent stromal haze in one patient and apical scarring in another. We observed no lens changes or induced retinal pathologies in our study.

CONCLUSION

Collagen crosslinking is a safe and effective procedure to halt the progression of disease in cases of mild to moderate keratoconus.

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PROFORMA

SERIAL NUMBER:	MR NUMBER:
NAME:	DATE OF SURGERY:
AGE:	TELEPHONE NUMBER:
SEX:	ADDRESS:

BRIEF HISTORY

2.Known keratoconus YES/NO, Years __
3.Contact lens use YES/NO,Years __
4.Spectacle use YES/NO, Years __
5.Comfort with refraction
6.Eye rubbing/ VKC or ocular allergy
7.Hormone Therapy
8.Pregnancy/Lactation
9.Lasik Surgery/Zyoptix surgery
10.Family History

SYSTEMIC HISTORY

10. Diabetes mellitus YES/NO,duration-
11. Hypertension YES/NO,duration-
12. Asthma YES/NO,duration-

OCULAR EXAMINATION

13. Visual acuity

	RIGHT EYE	LEFT EYE
UCVA		
BCVA		
CLVA		
CL TRIAL		

3. Slit lamp examination

	RIGHT EYE	**LEFT EYE**
LIDS		
CONJUNCTIVA		
CORNEA 1.scarring 2.striae 3.endothelial changes		
ANTERIOR CHAMBER		
IRIS		
PUPIL		
LENS		

- Fundus

RIGHT EYE	**LEFT EYE**

- Previous refraction / ORBSCAN,if any

	RIGHT EYE	LEFT EYE
Sim K		
K max		
Thinnest Pachy		
Anterior Float		
Posterior Float		

- Refraction

	SPHERICAL	CYLINDRICAL	AXIS	MEAN SPHERICAL EQUIVALENT
RIGHT EYE				
LEFT EYE				

- Intraocular pressure

RIGHT EYE	
LEFT EYE	

	RIGHT EYE	LEFT EYE
ORBSCAN 1. Sim K 2. K max 3. Thinnest pachy 4. Anterior float 5. Posterior float		
MANUAL KERATOMETRY		
AXIAL LENGTH		
SPECULAR MICROSCOPY 1.ECD 2. CV 3.% hexagonality		

DIAGNOSIS

RIGHT EYE______________ LEFT EYE______________

TREATMENT ADVISED

SURGICAL DETAILS

- Date of surgery :
- Surgeon : Dr.M.S./Dr. N.V.P./Dr. J.M./Dr. M.R.D./Dr. S.S
- Anaesthesia : Topical anaesthesia / general anaesthesia
- Intraoperative complications :
- Post-operative complications :

1.Non healing/ Persistent epithelial defect

a) < 2mm
b) 2-5 mm
c) > 5mm

2. Permanent stromal haze
   a)mild
   b)moderate
   c)severe
3. Corneal scarring
   a)nebular
   b)macular
   c)leucomatous
4. Infective Keratitis
5. Corneal melting
6. Corneal Infiltrate
   a)single/multiple
   b) < 2mm, 2-5 mm, > 5mm
   c) bacterial/fungal/sterile
7. Endothelial cell loss
8. Cataract formation
9. Retinal pathology
10. Loss of 2 or more lines in BCVA

FOLLOW UP

DATE OF SURGERY ------------------	PREOPERATIVE	F-U 1 (1-5 DAYS)	F-U 2 (1 MONTH)	F -U 3 (3 MONTHS)	F-U 4 (6 MONTHS)	F-U 5 (12 MONTHS)
DATE						
BCVA						

- Slit Lamp Examination

	PREOPERATIVE	F-U 1 (1-5 DAYS)	F-U 2 (1 MONTH)	F -U 3 (3 MONTHS)	F-U 4 (6 MONTHS)	F-U 5 (12 MONTHS)
CONJUNCTIVA						
EPITHELIAL DEFECT						
STROMAL HAZE						
DM FOLDS						
ANTERIOR CHAMBER						
LENS						
FUNDUS						

	PREOPERATIVE	F-U 1 (1-5 DAYS)	F-U 2 (1 MONTH)	F -U 3 (3 MONTHS)	F-U 4 (6 MONTHS)	F-U 5 (12 MONTHS)
CLVA						
CL TRIAL						
NCT						
KERATOMETRY						

- Refractive Astigmatism -RIGHT EYE

	spherical	cylinder	axis	mean spherical equivalent
Preoperative				
F-U 1(1-5 days)				
F-U 2(1 month)				
F-U 3(3 months)				
F-U 4(6 months)				
F-U 5(12 months)				

LEFT EYE

	spherical	cylinder	axis	mean spherical equivalent
Preoperative				
F-U 1(1-5 days)				
F-U 2(1 month)				
F-U 3(3 months)				
F-U 4(6 months)				
F-U 5(12 months)				

- ORBSCAN/OCULUS - RIGHT EYE

	PREOPERATIVE	**F-U 1 (1-5 DAYS)**	**F-U 2 (1 MONTH)**	**F -U 3 (3 MONTHS)**	**F-U 4 (6 MONTHS)**	**F-U 5 (12 MONTHS)**
Sim K						
K max						
Thinnest pachy						
Anterior float						
Posterior float						

LEFT EYE

	PREOPERATIVE	**F-U 1 (1-5 DAYS)**	**F-U 2 (1 MONTH)**	**F-U 3 (3 MONTHS)**	**F-U 4 (6 MONTHS)**	**F-U 5 (12 MONTHS)**
Sim K						
K max						
Thinnest pachy						
Anterior float						
Posterior float						

	PREOPERATIVE	F-U 1 (1-5 DAYS)	F-U 2 (1 MONTH)	F -U 3 (3 MONTHS)	F-U 4 (6 MONTHS)	F-U 5 (12 MONTHS)
SPECULAR MICROSCOPY						

ABBREVIATIONS

DALK	-	Deep anterior Lamellar Keratoplasty
ALTK	-	Automated Lamellar Therapeutic Keratoplasty
CDVA	-	Corrected Distance Visual Acuity
UDVA	-	Uncorrected Distance Visual Acuity
BCVA	-	Best-corrected Visual Acuity
BSCVA	-	Best Spectacle Corrected Visual Acuity
SE	-	Spherical Equivalent
Kmax	-	Maximum Keratometry
Kmin	-	Minimum Keratometry
IOP	-	Intraocular Pressure
CXL	-	Corneal Collagen Crosslinking
UV-A	-	UltraViolet A

S NO	MR NUMBER	AGE	SEX	EYE	UCVA CONTROL PREOP	POSTOPERATIVE 1 WEEK	1 MONTH	3 MONTHS	6 MONTHS	12 MONTHS	UCVA CASE PREOP	1 WEEK	POSTOPERATIVE 1 MONTH	3 MONTHS	6 MONTHS	12 MONTHS	BCVA CONTROL PREOP	1 WEEK	1 MONTH	3 MONTHS	6 MONTHS	12 MONTHS	BCVA CASE PREOP	1 WEEK	1 MONTH
1	3045050	14	F	RE	6/12p	6/12p; -1.0 @ 105	6/12P	6/12	6/12	6/18p;	6/60	4/60	6/60P	6/36	6/36	6/36p	6/9	6/9	6/9	6/9	6/9	6/9	6/18	6/36	6/18
					-1.0 DC @ 105		-1.0 @ 105	-1.0 @ 105	-1.0 @ 105	-1.25 @ 90	-2.0DS , -2.0 @ 20	-2.0,-3.0@10	-2.0DS , -3.0 @ 180	-2.0DS , -2.50 @ 180	2.0 DS , -2.50 @ 180	-2.25 DS /-2.5 @15									
2	3110370	16	M	LE	5/60	5/60; -3.5 , -2.5 @20	5/60	4/60	4/60	5/60	3/60	2/60 ;	5/60 P	4/60	4/60	6/60	6/6	6/6	6/6	6/6	6/6	6/6P	6/6P	6/18	6/9P
					-3.50 DS , -2.50 @ 20		-3.50 DS , -2.50 @ 20	-3.50 DS , -2.50 @ 20	-3.50 DS , -2.50 @ 20	-3.50 DS , -2.5 @ 20	-3.50 DS , -3.50 @160	- 4.0DS; -1.5 @180	-3.50 DS, -1.0 @ 160	-3.50 DS , -2.0 @ 160	-3.50 DS, -2.0 @ 160	-3.50 DS, -2.0 @ 160									
3	2938361	16	M	RE	5/60	4/60	5/60	5/60	5/60	5/60	5/60	3/60	5/60	5/60	5/60	5/60	6/12P	6/12p	6/12p	6/12P	6/12	6/12P	6/12P	6/18	,6/12
					-3.0DS , -6.0 @ 140	-3.5DS , -5.0 @ 135	-3.0DS , -6.0 @ 135	-3.0DS , -6.0 @ 135	-2.0DS , -6.0 @ 140	-2.0 DS , -6.0 @ 140	-2.0 DS , -5.50 @ 20	-2.5 DS , -4.50 @ 30	-2.0 DS , -5.50 @ 30	-2.0 DS , -5.50 @ 30	-2.0 DS , -5.50 @ 30	-2.0 DS , -5.50 @ 30									
4	3166135	17	F	RE	6/60	6/60	6/60	4/60	5/60	5/60	2/60	6/60	6/60	5/60	6/60	4/60	6/12P	6/12	6/12	6/12	6/12	6/12P	6/36P	6/24P	6/24P
					-3.0 DS , -1.0 @ 90	-3.0 DS	-3.0 DS	-3.0 DS , -1.0 @ 180	-3.0 DS , -2.0 @ 180	-4.0 DS ,-2.50 @ 180	-8.0 DS , -3.0 @ 180	-4.0 DS	-4.0 DS	-4.0 DS , -1.50 @ 65	-4.0 DS , -2.0 @ 180	-4.0 DS , -2.50 @ 180									
5	2832987	18	M	LE	5/60	5/60	4/60	4/60	4/60	4/60	4/60	4/60	4/60	4/60	4/60	3/60	6/24	6/18	6/18	6/24P	6/12p	6/18	6/60	2/60	2/60
					-2.0 DS , - 4.0 @45	-2.0DS/-4.0 @45	-2.0 DS , - 4.0 @55	-2.0 DS , - 4.0 @55	-2.0 DS , - 4.0 @55	-2.0 DS , -4.0 @ 65	-5.0 DS , -6.0 @ 135	-4.50 DS , -6.0 @ 135	-4.50 DS , -6.0 @ 135	-5.0 DS , - 6.0 @ 90	-4.0 DS , - 6.0 @ 80	-5.0 DS , -4.0 @ 60									
6	3070189	22	M	LE	6/36	6/36	6/36	6/60	6/60	6/60	5/60	5/60	5/60	4/60	3/60	4/60	6/6	6/6	6/6	6/6	6/6	6/6	6/9P	6/12	6/9
					-2.50 DS	-2.50 DS	-2.50 DS	-2.50 DS	-2.50 DS	-2.50 DS	-5.50 DS	-5.50 DS	-5.50 DS	-5.50 DS ,-2.50 @ 120	-5.50 DS ,-2.50 @ 120	-5.50 DS , -2.50 @ 120									
7	3090172	20	M	RE	6/60	5/60	4/60	5/60	6/60	5/60		6/36	6/36P	6/60	6/60	6/60	6/12P	6/18P	6/18P	6/18P	6/18P	6/18	6/6P	6/18	6/12P
					-2.0 DS , -2.50 @ 150	-2.50 DS ,-3.0 @ 160	-2.50 DS , -3.5 @ 165	-2.50 DS , - 3.5 @ 165	-2.50 DS , - 3.0 @ 165	-2.50 DS , -3.5 @ 160		-2.0 DS , -3.50 @ 30	-2.0DS , -3.50 @ 45	-2.0 DS , -3.50 DS @ 35	-2.0 DS, -3.50 DS @ 35	-2.0DS , -3.50 @ 35									
8	2615781	21	M	RE	6/60	5/60	5/60	4/60	4/60	5/60	5/60	4/60	5/60	5/60	5/60	5/60	6/12	6/12	6/12	6/12	6/12	6/12	6/12p	6/18	6/12
					-7.0 DS , -4.0 @ 180	-7.0 DS , -4.0 @ 180	-7.0 DS , -4.0 @ 180	-6.75 DS , -3.50 @ 180	-6.75 DS , -3.50 @ 180	-6.75 DS , -3.50 @ 180	-6.0 DS , -5.0 @ 180	-6.0 DS , -5.0 @ 180	-6.0 DS , -5.0 @ 180	-6.0 DS , -4.0 @ 20	-6.0 DS , -4.0 @ 20	-5.0 DS , -4.50 @ 20									
9	3198888	16	F	RE	6/18	6/18P	6/18P	6/18P	6/18	6/24	1/60	1/60	1/60	1/60	1/60	3/60	6/6	6/6	6/6	6/6	6/6	6/6	6/60	6/60	6/60
					-1.0 DS , -0.50 @ 90	-1.0 DS , -0.50 @ 90	-1.0 DS , -0.50 @ 90	-1.0 DS , -0.50 @ 90	-1.25 DS	-1.50 DS	-13.0 DS , -3.50 @ 15	-13.0 DS , -3.50 @ 15	-13.0 DS , -3.50 @ 15	-13.0 DS , -3.50 @ 15	13.0 DS , -4.0 @ 15	-6.0 DS , -4.0 @15									
10	2756895	20	M	RE	6/60	6/60	6/60	6/60	4/60	4/60	4/60	4/60	4/60	4/60	4/60	6/60	6/9	6/9	6/9	6/9	6/9	6/9	6/9P	6/18	6/12
					-2.0 DS , -2.0 @ 150	-2.0 DS , -2.0 @ 150	-2.50 DS , -2.0 @ 105	-2.50 DS , -2.0 @ 105	-4.0 DS , -2.0 DS @ 165	-4.0 DS , -2.0 DS @ 165	-4.0 DS , -4.0 @ 50	-4.0 DS , -4.0 @ 50	-4.0 DS , -4.0 @ 50	-4.0 DS , - 3.0 @ 45	-4.0 DS , - 3.0 @ 45	-4.0 DS , -3.0 @ 15									
11	3199871	21	F	RE	6/6P	6/6P	6/9p	6/12p	6/12p	6/12p	4/60	4/60	6/60	5/60	5/60	5/60	6/6	6/6	6/6	6/6	6/6	6/6	6/6	6/9p	6/6P
					-0.50 @ 90	-0.50 @ 90	-0.75 DS,-0.50 @ 90	-0.75 DS,-0.50 @ 90	-0.75 DS,-0.50 @ 90	-0.50 DS , -0.75 @ 90	-3.50 DS , -2.50 @ 90	-3.50 DS , -1.50 @ 90	-4.25 DS	-4.5 DS	-3.0 DS, -2.75 @70	-3.0 DS, 3.25 @70									
12	2707294	18	F	LE	6/60	6/60	6/60	6/60	6/60	6/60	5/60	5/60	6/60	6/60	6/60	5/60	6/9	6/6P	6/6P	6/6p	6/6P	6/6p	6/9	6/9	6/9
					-2.50 DS , -3.0 @ 20	-2.50 DS , -3.0 @ 20	-3.0 DS , -3.0 @ 20	-3.0 DS , -3.0 @ 15	-3.0 DS , -3.0 @ 15	-3.0DS , -3.0 @ 15	-4.0 DS , -3.50 @ 165	-4.0 DS , -3.50 @ 150	-4.0 DS , -3.50 @ 150	-4.0 DS , -3.50 @ 150	-4.0 DS , -3.50 @ 165	-4.0 DS , -4.0 @ 170									
13	3229418	17	M	LE	6/36	6/36	6/36	6/36	6/36		5/60	5/60	6/60	6/60	6/60	6/60	6/9	6/9	6/9	6/6P	6/6P	6/6p	6/12	6/12p	6/12P
					-1.50 DS , -1.50 @ 40	-1.50 DS , -1.50 @ 40	-1.50 DS , -1.50 @ 45	-1.50 DS , -1.50 @ 30	-1.50 DS , -1.50 @ 30		-2.0 DS , -6.0 @ 165	-2.0 DS , -4.0 @ 150	-2.0 DS , -4.0 @ 150	-2/0 DS , -2.0 @ 170	-2.0 DS , -2.0 @ 170	-2.0 DS , -2.0 @ 170									
14	3244064	17	M	LE	6/12P	6/12P	6/12	6/12P	6/12P	6/12P	6/36P	6/36P	6/18P	6/18	6/18	6/18	6/6	6/6	6/6	6/6	6/6	6/6	6/9	6/9p	6/9p
					-1.0 @ 180	-1.0 @ 180	-1.0 @ 180	-1.0 @ 180	-1.0 @ 180	-1.0 @ 180	-2.50 @ 165	-2.50 @ 165	-2.0 @ 165	-1.0 @ 165	-1.50 @ 140	-1.50 @ 140									
15	32331052	21	M	LE	6/24	6/24	6/36	6/36	6/24	6/24	5/60	5/60	5/60	6/60	6/60	4/60	6/6	6/6	6/6	6/6	6/6	6/6	6/6P	6/12	6/12
					-0.75 DS , -1.50 @ 30	-0.75 DS , -1.50 @ 30	-1.0 DS , -1.25 @ 30	-1.0 DS , -1.25 @ 30	-1.0 DS , -1.50 @ 30	-1.0 DS , -1.50 @ 30	-2.0 DS , -5.0 @ 135	-2.0 DS , -5.0 @ 135	-3.50 DS , -5.50 @ 130	-3.50 DS , -4.00 @ 130	-3.50 DS , -4.50 @ 130	-3.50 DS , -5.50 @ 130									
16	3264972	16	F	RE	6/6	6/6	6/6	6/6	6/6	6/6	6/60	6/60	6/60	6/60	6/60	6/60	6/6	6/6	6/6	6/6	6/6	6/6	6/60	6/60	6/60
					NIL GLASS	NIL GLASS	NIL GLASS	NIL GLASS	NIL GLASS	NIL GLASS	NIG	NIG	NIG	-5.0 DS, -6.0 @ 20	NIG	NIG									
17	3214792	13	M	LE	6/60	6/60	6/60	5/60	5/60	5/60	3/60	1/60	4/60	4/60	4/60	4/60	6/6	6/6	6/6	6/6	6/6	6/6	6/36	6/36p	6/24
					-2.50 DS	-2.50 DS	-2.50 DS	-2.50 DS	-2.50 DS	-3.0 DS	-5.50 DS , -2.0 @ 150	-5.50 DS , -2.50 @ 150	-5.50 DS , -2.0 @ 150	-4.50 DS,-3.0 @ 165	-4.50 DS,-3.0 @ 165	-4.50 DS , -3.0 @ 165									
18	3282660	12	F	RE	6/6	6/6	6/6	6/6	6/6	6/6	3/60	3/60	3/60	2/60	3/60	3/60	6/6	6/6	6/6	6/6	6/6	6/6	6/24P	6/36	6/24
					NIL GLASS	NIL GLASS	NIL GLASS	NIL GLASS	NIL GLASS	NIL GLASS	-8.0 DS , -2.50 @ 180	-8.0 DS , -2.50 @ 180	-8.0 DS , -2.50 @ 180	-8.0 DS , -2.00 @ 176	-8.0 DS , -2.75 @ 180	-8.0 DS , -2.50 @ 180									
19	3084612	18	F	LE	6/24	6/24	6/36	6/36	6/24P	6/24P	6/24	6/36	6/60	6/60	6/36P	6/36	6/6P	6/9	6/9	6/9P	6/12	6/12	6/9P	6/9	6/9
					-1.50 DS , -0.5 @ 105	-1.50 DS , -0.5 @ 100	-1.0 DS ,-1.0 @ 100	-1.0 DS , -1.0 @ 100	-1.0 DS , -1.0 @ 100	-1.50 DS , -1.0 @150	-050 DS , -2.25 @ 120	-050 DS , -2.0 @ 120	-0.75 DS , -2.25 @ 90	-0.75 DS , -2.25 @ 90	-0.75 DS , -2.25 @ 90	-1.25 DS , -2.0 @ 86									
20	3164281	17	M	LE	4/60	1/60	2/60	3/60	3/60	4/60	5/60	1/60	2/60	3/60	3/60	4/60	6/18	6/12P	6/18P	6/18	6/18	6/18	6/12	6/12	6/12
					-8.0 DS, -2.0 @ 60	-8.0 DS, -2.0 @ 60	-8.0 DS, -2.0 @ 60	-8.0 DS, -2.0 @ 60	-8.0 DS, -2.0 @ 60	-8.0 DS , -1.75 @ 65	-4.0DS, -1.75 @ 90	-8.0 DS , -1.50 @90	-8.0 DS , -1.50 @90	-8.0 DS , -1.50 @90	-8.0 DS , -1.50 @160	-8.0 DS , -1.25 @ 150									
21	3093568	20	M	LE	6/9	6/9	6/9	6/9P	6/9	6/9p	4/60	6/60	6/60	6/60	6/60	6/60	6/9	6/9	6/9P	6/9P	6/9p	6/9p	6/12P	6/12	6/18
					NIG	NIG	-1.50 @ 15	NIG	NIG	NIG	-2.0 DS , -6.0 @ 160		-2.0 DS , -5.0 @ 160	-2.0 DS , -5.50 @ 160											
22	3290456	12	F	LE	6/36	6/36	6/36	6/36	6/24p	6/24P	6/60	6/60	6/60	6/60	6/60	6/60	6/18	6/18	6/12P	6/12P	6/12P	6/12P	6/36P	6/36P	6/36P
					-3.0 @ 15	-3.0 @ 15	-2.0 DS , -2.0 @ 180	-2.0 DS ,-2.0 @ 10	-2.0 DS ,-2.0 @ 10	-2.0 DS ,-2.0 @ 10	-3.0DS , -2.0 @180		-3.0DS , -3.0@ 165	-3.0DS , -3.25@ 160	-3.0DS , -3.0@ 165	-3.0 DS ,-3.0 @165									
23	3167038	12	M	RE	6/36	6/60	4/60	4/60	4/60	4/60	6/60	6/60	4/60	4/60	4/60	4/60	6/12	6/12P	6/9	6/9P	6/12P	6/12P	6/18P	6/18	6/12P
					-0.75 DS , -2.0 @ 120	-1.25 DS , -2.0 @ 112	-2.0 DS , -2.0 @ 135	-2.50 DS , -2.25 @ 130	-3.0 DS , -2.50 @ 160	-3.0 DS , -2.50 @ 160	-3.50 DS , - 2.0 @ 15		-6.0 DS , -4.0 @ 180	-6.0 DS , -3.50 @ 2	-6.0 DS , -4.50 @ 180	-6.0 DS , - 4.50 @ 180									
24	3230538	18	F	LE	6/60	6/60	6/60	6/60	6/60	4/60	6/60	6/60	6/60	6/60	6/60	6/60	6/18P	6/18P	6/12P	6/12P	6/9P	6/9	6/9P	6/9P	6/9P
					-4.0 DS , -4.0 @ 10	-4.0 DS , -3.75 @ 8	-4.0 DS , -3.75 @ 8	-3.75 DS , -4.O @ 180	-4.0 DS , -4.50 @ 50	-4.0DS , -3.50 @ 180	-4.0 DS , -4.0 @ 140		-4.0 DS , -4.0 @ 150	-4.0 DS , -4.0 @ 150	-4.0 DS , -4.0 @ 150	-3.0 DS , -2.0 @ 180									
25	3213158	16	M	RE	3/60	3/60	3/60	3/60	3/60	1/60	5/60	5/60	6/36	6/12	6/18	6/24	6/24P	6/24P	6/24	6/18	6/18	6/18	6/12	6/12P	6/9
					-9.0 DS , -5.0 @ 150	-9.0 DS , -5.0 @ 150	-9.0 DS , -5.0 @ 150	-9.0 DS , -5.0 @ 150	-9.0 DS , -4.0 @ 156	-9.0 DS , -3.75 @ 125	-3.50 DS , -2.0 @18		-1.0DS,-2.0 @ 15	-2.0 @ 120	-0.75 DS, -1.50 @ 5	-2.0 @ 130									
26	3301899	14	F	LE	6/18	6/24	6/36	6/9P	6/12p	6/12	4/60	4/60	4/60	6/60	6/60	6/60	6/12P	6/12P	6/12P	6/9P	6/12	6/12	6/18P		6/24P
					-2.0 @ 30	-1.75 D @ 35	-1.0 ds , -2.0 @ 30	NIG	NIG	NIG	-10.0DS , -2.0 @165		-10.0DS, -2.0 @ 165	-5.0 DS , -4.0 @ 135	-3.0 DS , -6.0 @ 140	-3.0 DS , -6.0 @ 140									
27	3312163	20	F	RE	6/12P	6/18P	6/18P	6/18P	6/24	6/24	4/60	4/60	4/60	4/60	4/60	4/60	6/6P	6/6P	6/6P	6/9	6/9	6/9P	6/18	6/18	6/18
					-1.50 DS , -0.75 @165	-1.50 DS , -0.75 @165	-1.50 DS , -0.75 @165	-1.50 DS , -1.0 @165	-1.50 DS , -0.75 @160	-1.50 DS , -1.0 @ 165	-4.50 DS , - 3.0 @ 180	-5.0 DS , - 3.0 @ 180	-5.0 DS , - 3.0 @ 180	-5.0 DS , - 3250 @ 180	-5.0 DS , - 3.25 @ 5	-5.0 DS , -3.0 @ 10									

28	3127492	15	M	LE	3/60	3/60	3/60	4/60	3/60	3/60	2/60	2/60	3/60	4/60	3/60	3/60	6/24	6/36	6/18	6/12P	6/12P	6/12P	6/24	6/24p	6/24
					-7.0 DS , -3.0 @ 15	-7.25 DS, -3.0 @ 10	-7.50 ds , -3.0 @ 15	-5.0 DS , -3.0 @ 30	-7.50 DS , - 3.0 @ 30	-7.50 DS , - 3.0 @ 30	-10.0DS , -3.0 @ 180		-10.50DS,-3.0 @ 180	-8.0 DS,-3.50@165	-8.0 DS , -3.50 @ 165	-8.0 DS , -3.50 @ 165									
29	2739126	18	F	RE	6/18					6/18P	6/24	6/24	6/24	6/18p	6/18p	6/18P	6/6	6/6	6/6	6/6	6/6	6/6	6/24	6/24	6/18
					-2.0 DS					-2.0 DS	NIG	NIG	NIG	NIG	NIG	-0.50 DS,-1.50 @ 90									
30	3103212	18	M	LE	1/60	6/60	6/60	1/60	1/60	3/60	1/60	1/60	1/60	1/60		3/60	6/60	6/60		6/60		6/60	6/9	6/12P	6/12
					-8.0 DS , -1.50 @ 165	-8.0 DS , -4.50 @ 165	-8.0 DS , -4.50 @ 165	-8.0 DS , -4.50 @ 165	-8.0 DS , -4.50 @ 165	-8.50 DS, -4.0 @ 165	-7.50 DS , -3.50 @ 15	-8.50 DS , -4.0 @ 15	-8.50 DS , -4.25 @ 12	-8.50 DS , -3.50 @ 15		-8.0 DS , -3.50 @ 15									
31	2530718	21	M	RE	5/60		6/24	6/24	6/24	6/24	5/60	5/60	5/60	5/60	5/60	5/60	6/12		6/12	6/12	6/12	6/12	6/12P		6/18
					-1.0 DS, -3.0 @ 135		-3.0 D @ 105	-3.0 D @ 105	-3.0 @ 105	-3.0 @ 105	-2.0 DS , -3.0 @ 50	-2.0 DS , -4.50 @ 60	-2.0 DS , -4.50 @ 60	-2.0 DS , -4.0 @ 60	-2.0 DS , - 4.0 @ 60	-2.0 DS , - 4.0 @ 60									
32	3347360	17	F	LE	3/60	3/60	3/60	3/60	3/60		3/60	3/60	3/60	3/60	3/60		6/18		6/9	6/9	6/9		6/24P		6/9
					-7.50 DS , -6.0 @ 10	-7.50 DS , -6.0 @ 10	-5.50 DS , -6.0 @ 10	-5.50 DS , -5.5 @ 10	-7.50 DS, -6.0 @ 10		-8.75 DS , -5.50 @ 145	-8.75 DS , -5.50 @ 145	-8.50 DS, -5.0 @ 145	-8.50 DS, -4.0 @ 145	-8.50 DS, -3.0 @ 145										
33	3345656	21	M	RE	6/9P	6/12	6/12	6/12	6/12	6/12P	6/24P	6/24P	6/24P	6/24	6/24	6/36	6/6			6/6	6/6	6/6	6/9		6/6P
					-0.50DS , -0.50 @ 120	-0.75 DS , -0.75 @ 120	-0.75 DS , -0.75 @ 120	-0.75 DS , -0.75 @ 120	-0.75 DS , -0.75 @ 120	-0.75 DS , -0.75 @ 120	-1.50DS, -1.0 @ 60	-1.50DS, -1.0 @ 60	-1.50DS, -1.0 @ 60	-1.50DS, -1.0 @ 60	-1.50DS, -1.0 @ 60	-1.50 DS,-1.0 @ 60									
34	3150032	22	M	LE	6/9P		6/9P	6/9P	6/12	6/12	6/24	6/24	6/24	6/24	6/24P	6/24	6/6P		6/6P	6/6P	6/6P	6/6P	6/6P		6/9
					-0.75 @ 90		-0.75 @ 90	-0.75 @ 90	-1.0 @ 90	-1.0 @ 90	-2.25@ 135	-2.25@ 135	-2.25@ 135	-2.25@ 135	-2.50@ 135	-2.50 @ 135									
35	2926039	17	F	RE	6/6p		6/6	6/6	6/6	6/6	6/24P		6/24	6/24	6/24	6/24	6/6		6/6	6/6	6/6	6/6	6/9		6/9
					NIL GLASS		NIL GLASS				-3.0 @ 30		-2.0 @ 30	-2.0 @30	-2.0 @30	-2.0 @30									
36	3348364	21	M	RE	6/36P		6/60	6/60	6/60	6/36	6/36		6/60	6/36	6/36	6/36	6/12P		6/12	6/12	6/12	6/18	6/12P		6/12P
					-1.50DS, -5.50 @ 140		-1.50DS, -5.50 @ 140	-1.50DS, -5.50 @ 140	-1.50DS, -5.50 @ 136	-1.50 DS , -5.50 @ 120	-1.0DS , -5.50 @30		-1.50DS , -4.0 @ 15	-1.0 DS , -3.5 @ 30	-1.0 DS , -4.0 @ 40	-1.0 DS , -4.0 @ 30									
37	2519220	19	M	RE	6/36		6/36	6/36	6/36	6/18P	6/60		4/60	4/60	4/60	4/60	6/6	6/6	6/6	6/6	6/6	6/6	6/24		6/18
					-2.50 @ 160		-2.50 @ 165	-2.50 @ 165	-2.50 @ 170	-2.50 @ 180	-14.0 DS , -2.50 @ 165		-15.0 DS , -2.50 @ 150	-15.0 DS , -2.50 @ 150	-14.0 DS , -2.50 @ 150	-14.0DS , -2.50 @ 165									
38	3122795	20	M	LE	6/60		6/36	6/60		6/60	6/36		6/60	6/36P		6/60	6/6P		6/6	6/6	6/6	6/6	6/9P		6/18
					-3.0 @ 70		-3.0 @ 70	-3.0 @ 70		-3.50 @ 70	-1.0DS , -3.50 @ 120		-1.0 DS ,-6.0 @ 130	-1.0 DS , -3.0 @ 120		-1.0 DS , -3.0 @ 120									
39	3278809	13	M	LE	6/6			6/6	6/9P	6/9	6/24		6/24	6/60	6/60	6/60	6/6		6/6	6/6	6/6	6/6P	6/12P		
					NIG			NIG	-1.0DS	-1.0DS	-3.0 @ 120		-3.0 @ 120	-3.0 @ 130	-3.0 @ 130	-3.0 @ 120									
40	3300452	16	M	RE	6/9P		6/9P	6/9P	6/9P	6/9P	6/60		5/60	6/60	6/60	6/60	6/9		6/9	6/9	6/9	6/9	6/12P		6/12P
					NIG		NIG	NIG		NIG	-3.50 @ 70		-3.50 @ 70	-4.0 @ 75	-4.0 @ 70	-4.0 @ 75									
41	33677961	18	F	LE	6/6		6/6	6/6	6/6	6/6	6/60		6/60	6/36P	6/36P	6/60	6/6		6/6	6/6	6/6	6/6	6/9P		6/12
					NIL GLASS		NIL GLASS	NIL GLASS		NIL GLASS	-1.50 DS , -4.0 @ 90		-1.50 ds, -4.0 @ 100	-1.40 DS , -4.50 @ 100	-1.50 DS , -4.25 @ 110	-1.50 DS , -4.50 @ 100									
42	3368590	16	F	LE	6/6		6/9	6/9	6/9	6/12	5/60		6/60	6/60	6/60	5/60	6/6		6/6	6/6	6/6	6/6	6/12P		6/12
					NIL GLASS		-05.50@ 50	-05.50@ 50	-05.00@ 50	-5.25 D C @ 60	-5.50 @ 120		-6.00 @ 120	-4.50 @ 120	-5.50 @ 120	-5.50 @ 120									
43	3371821	16	F	LE	6/36		6/36	6/36	6/24	6/24	6/60		6/60	6/60	6/36	6/36	6/9P		6/9P	6/6P	6/6P	6/9	6/12P		6/12P
					-1/0DS , -2.0 @ 45		-1/0DS , -2.0 @ 45	-1.25 DS , -2@60	-1.0DS , -2.0 @60	-1.0DS , -2.0 @60	-0.75 DS , -3.50 @ 120		-1.50 DS , -4.0 @ 120	-2.50 DS,-4.50 @ 120	-1.50 DS , -2.50 @ 120	-1.50 DS , -2.50 @ 120									
44	2962144	26	M	LE	6/36		6/36	6/36	6/24	6/24	6/60		6/60	6/60	6/36	6/36	6/9P		6/9P	6/6P	6/6P	6/9	6/12P		6/12P
					-1/0DS , -2.0 @ 45		-1/0DS , -2.0 @ 45	-1.25 DS , -2@60	-1.0DS , -2.0 @60	-1.0DS , -2.0 @60	-0.75 DS , -3.50 @ 120		-1.50 DS , -4.0 @ 120	-2.50 DS,-4.50 @ 120	-1.50 DS , -2.50 @ 120	-1.50 DS , -2.50 @ 120									
45	3373628	15	F	RE	6/60		6/36	6/36	6/36	6/36P	4/60		5/60	5/60	5/60	5/60	6/6P		6/6P	6/9	6/9	6/9P	6/24		6/12
					-1.50 DS, -4.0 @ 150		-1.50 DS , -3.50 @ 150	-1.50 DS , -3.50 @ 150	-1.50 DS , -3.50 @ 150	-1.50 DS , -3.50 @ 150	-3/0 DS , -6.0 @ 30		-5.0 DS , -3.50 @ 30	-5.0 DS , -3.50 @ 30	-5.0 DS , -3.00 @ 30	-5.0 DS, -3.0 @ 30									
46	3321732	21	M	RE	6/18	6/18	6/12	6/12P		6/18	6/36	6/12	6/12	6/12P		6/6	6/6	6/6	6/6	6/6		6/9	6/12P	6/9	6/9
					-0.50 DS , -1.0 @ 180	-0.50 DS , -1.25 @ 180	-1.50 @ 180	-1.50 @ 180		-1.0 @ 90	-3.50 @ 90	-1.25@90	-0.75 @ 90	-0.75 @ 90											
47	3372689	16	M	RE	6/6		6/6	6/6	6/6	6/6	4/60		4/60	5/60	5/60	5/60	6/6		6/6	6/6	6/6	6/6	6/18	6/18	6/18
					NIL GLASS		NIL GLASS	NIL GLASS	NIL GLASS	NIL GLASS	-6.0 DS , -5.0 @ 50		-7.0 DS , -5.5 @ 50	-5.0 DS , -2.0 @ 40	-5.5 DS , -2.0 @ 40	-5.0 DS , -2.0 @ 40									
48	3343417	21	M	LE	6/6		6/6	6/6	6/6	6/6	6./60		6/18	6/18	6/12P	6/12P	6/6		6/6	6/6	6/6	6/6	6/9		6/18
					NIL GLASS		NIL GLASS	NIL GLASS	NIL GLASS	NIL GLASS	-4.0 @ 45		NIG	-1.50 @ 30	-1.50 @ 30	-1.50 @ 30									
49	3288551	18	M	LE	6/6		6/6	6/6	6/6	6/6	6./60		6/18	6/18	6/12P	6/12P	6/6		6/6	6/6	6/6	6/6	6/9		6/18
					NIL GLASS		NIL GLASS	NIL GLASS	NIL GLASS	NIL GLASS	-4.0 @ 45		NIG	-1.50 @ 30	-1.50 @ 30	-1.50 @ 30									
50	3349161	19	M	RE	6/18		6/18	6/18	6/12	6/12P	6/18		6/36	6/12	6/12	6/12P	6/6		6/6	6/6	6/6	6/6	6/9		6/12P
					-0.50 DS , -1.0 @ 180		-0.50 DS , -1.0 @ 180	-0.50 DS , -1.25 @ 180	-1.50 @ 180	-1.50 @ 180	-1.0 @ 90		-3.50 @ 90	-1.25@90	-0.75 @ 90	-0.75 @ 90									

3 MONTHS	6 MONTHS	12 MONTHS	CLVA CONTROL PREOP	3 MONTHS	6 MONTHS	12 MONTHS	CASE PREOP	3 MONTHS	6 MONTHS	12 MONTHS	SCARRING	persistent haze (>3 months)	ORBSCAN SIM K CONTROL PREOP	1 MONTH	3 MONTHS	6 MONTHS	12 MONTHS	CASE PREOP	1 MONTH	3 MONTHS	6 MONTHS	12 MONTHS	K MAX CONTROL PREOP	1 MONTH	3 MONTHS	6 MONTHS	12 MONTHS	CASE PREOP	1 MONTH	3 MONTHS	6 MONTHS	12 MONTHS	THINNEST PACHY CONTROL PREOP	1 MONTH	3 MONTHS	6 MONTHS
6/12P	6/12P	6/12	6/6	6/6	6/6	6/6	6/9	6/6P	6/9	6/6		+	-1.3D @ 119	-1.4D @ 119	-1.40D @ 133	-1.6D @123	-1.8 @110	-5.5 D @ 24	-4.5 D @ 30	-4.3 D @ 36	-3.8 D @ 28	-4.2 D @25	45.5D @ 29	45.5D @ 43	45.5D @ 43	45.8D @ 33	46.2 D @ 24	53.6D @ 114	52.4D @ 124	51.3 D @ 126	52.5 D @ 118	52.1 @121	436	432	438	435
6/9P	6/9P	6/9	6/6	6/6	6/6	6/6p	6/6P	6/6	6/6	6/6p		+	-4.0 D @ 13	-4.0 D @ 15	-4.0 D @ 15	-3.9 D @ 17	-4.4 D @ 11	-4.2D @154		-4.6 D @ 155	-4.7 D @ 152	-4.8 D @156	50.1 D @ 105	49.9 D @ 105	49.9 D @ 105	50.7 D @ 107	50.2 D @ 101	51.4 D @ 64	51.6 @ 64	51.7 D @ 65	51.7 D @ 62	61.0 D@ 66	411	322	414	435
6/12	6/9	6/9	6/6	6/6	6/6	6/6	6/6P	6/9	6/6P	6/6	+		-5.9D @ 157	-5.6@154	-5.6@154	-5.4 @ 151	-5.4 @ 151	-6.4D @ 30	-6.1@26	-5.8 D @ 21	-5.3 D @ 25	-4.9 @ 28	56.1D @ 67	56.4 D @ 61	56.1 D @ 61	56.1 D @ 61	56.5 @ 69	54.6 D @ 120	52.5@112	51.7 D @ 111	51.6 D @ 115	49.7 @ 118	370	372	377	377
6/24P	6/18	6/18p	6/6P	6/6P	6/6P	6/6P	6/12P	6/9	6/6P	6/6P		+	-1.5 D @ 105	-1.5 D @ 112	-1.5 D @ 119	-1.3 D @ 144	-4.1 D @ 167	-11.2 D @ 21	7.8@14	-7.2 D @ 20	-7.8 D @ 20	-6.1 D@ 21	49.7 D @ 25	50.4@26	52.3 D @ 29	52.4 D @ 54	57.9 D @ 77	64.8 D @ 111	59.2@ 110	60.8 D @ 110	60.5 D @ 110	60.7 D @ 111	468	456	465	432
6/60	6/36P	6/60	6/6	6/6	6/6p	6/6p	6/9	6/12	6/12	6/9	+		-7.2 D @ 10	-7.4D 2@ 10	-6.8D @ 2	-7.5D @ 2	-8.4D@ 4	-10.9 @ 160	-9.1@ 160	-8.5 D @ 157	-6.3D @ 172	-7.6@165	53.7 D @ 100	53.8 @ 92	53.8 @ 92	55.2 D @ 92	56.2@91	66.5 D @ 70	63.1 @ 67	63.1 @ 67	65.3D @ 82	65.5@82	476	477	480	480
6/9	6/9	6/9P	6/6	6/6	6/6	6/6	6/6	6/6	6/6	6/6	+		-0.6 D @ 10	-0.6 D @ 10	-0.6 D @ 10	-0.7D @ 20	-0.7D @ 176	-5.6 D @ 159	-4.6@ 160	-4.2@ 160	-4.6 D @ 164	-5.3 D @ 168	46.3 D @ 100	46.3 D @100	46.7 D @ 110	46.7 D @ 110	46.2 D @ 86	52.6 D @ 69	53.1 D @ 71	51.6 D @ 74	51.6 D @ 74	48.6 D @ 78	466	461	465	460
6/12	6/12	6/12	6/6	6/6	6/6	6/6	6/6	6/6	6/6	6/6		+	-4.7 D @ 151	'-4.7 D @ 151	-5.4D @ 151	-6.3 D @ 156	-6.6 D @ 154	-8.2 D @ 37	-8.4 D @ 37	-7.4 D @ 37	-7.4 D @ 37	-7.3 D @ 37	54.1 D @ 61	54.1 D @ 61	55.1 D @ 61	55.4 D @ 65	56.8 D @ 64	54.7 D @ 127	55.1 D @ 127	54.2 D @ 127	54.0 D @ 127	53 D @ 127	432	432	414	412
6/9P	6/9P	6/12	6/6	6/6	6/6	6/6	6/6	6/6	6/6	6/6		+	-4.7 D @ 32	-4.7 D @ 32	-4.8 D @ 23	-4.8 D @ 23	-4.8 D @ 23	-7.3 D @ 170	-8.3 @ 171	-7.7 D @ 168	-3.9 @ 141	-3.3 @ 141	56.6 D @ 122	56.6 D @ 122	56.3 D @ 113	56.5 D @ 118	56.5 D @ 118	58.2 D @ 80	58.9 D @ 80	57.8 D @ 78	55.1 D @ 51	55.1 D @ 51	455	456	460	454
6/60	6/36	6/24p	6/6	6/6	6/6	6/6	6/12	6/18	6/6P	6/6P	+		-0.6 D @ 40	-0.6 D @ 40	-0.6 D @ 40	-0.7 @ 40	-0.7 D @ 37	-13.4 D @ 7	-13.8@180	-12.9@2	-13.1@7	-12.6 D @ 17	45.5 D @130	45.5 D @130	45.1 D @130	45.1 D @130	45.3 @127	66.5 @ 97	66.8 @ 97	66.3 @ 97	64.5 @ 97	62.3 D @ 107	512	505	504	509
6/12	6/12	6/9p	6/6	6/6	6/6	6/6	6/6	6/6	6/6	6/6		+	-4.7 D @ 161	-4.6 D @ 161	-4.8 D @ 165	-6.1 D @ 12	-6.4 D @ 12	-4.5 D @ 21	-5.6@17	-5.7 D @ 20	-2.7@176	-2.2 @ 164	53.7 D @ 71	53.7 D @ 71	53.7 D @ 75	55.7 D @ 71	57.4 D @ 120	52.9 D @ 111	56.8 D @ 110	56.1 D @ 110	55.2 D @ 102	53.1 D @ 84	438	437	435	418
6/9	6/6p	6/12P	6/6	6/6	6/6	6/6	6/6	6/9P	6/9p	6/9P		+	-0.7D @ 89	-0.7D @ 89	-0.5D@ 86	-0.7D @ 84	-0.6D@ 86	-2.8 D @ 37	-2.9 D @ 38	-3.1 D @ 38	-3.9 D @ 38	-4.3 D @ 58	47.7 D @ 179	47.7 D @ 179	47.6@177	47.7 D @ 177	47.6 D @ 176	54.6 @ 127	54.6 @ 127	54.4 D @ 128	56.4 D @ 128	59.6 D @ 148	464	460	460	
6/9	6/9	6/9	6/6	6/6	6/6	6/6	6/6P	6/6p	6/6	6/6			-5.4 D @ 22	-5.5 D @ 22	-5.4 D @ 22	-5.3 D @ 24	-5.5 D @ 22	-3.7 D @ 147	-4.7 D @ 147	-4.1 D @ 147	-4.1 D @ 147	-4.1 D @ 147	51.5 D @ 112	51.5 D @ 112	51.5 D @ 112	51.8 D @ 114	51.8 D @ 114	52.9 D @ 57	53.3 D @ 57	51.9 D @ 57	50.7 D @ 57	51.8 D @ 57	422	421	423	428
6/18	6/18	6/12	6/6P	6/6P	6/6P	6/6P	6/6P	6/6	6/6	6/6				-2.0 DS @ 33	-2.0 DS @ 33	-2.0 DS @ 33	-2.0 DS @ 33	-6.1 D @ 159	-6.1 D @ 159	-6.3D @160	-5.0 D @ 163	-4.2 D @ 163	46.3 D @ 121	46.3 D @ 121	46.5 D @ 121	46.9 D @ 123	46.3 D @ 121	52.8D @ 69	52.8D @ 69	53.6D @ 70	52.3 D @ 73	52.1D @ 76	507	507	507	509
6/9	6/6	6/6	6/6	6/6	6/6	6/6	6/9	6/6P	6/6	6/6		+	-3.1 D @ 14	-3.1 D @ 14	-3.1 D @ 14	-3.4 D @ 16	-3.4 D @ 16	-4.4 D @ 164	-4.5D @ 135	-4.3D @ 135	-4.1D @ 135	-3.7D @ 135	47.7D @ 104	47.7D @ 104	47.7D @ 104	48.3D@106	48.3D@106	53.6 D @ 74	53.8 D @ 45	53.2 D @ 45	52.5 D @ 45	52.1 D @ 45	442	442	441	444
6/9	6/9p	6/12	6/6	6/6	6/6	6/6	6/6P	6/6P	6/6P	6/9p	+		-2.6 D @ 35	-2.6 D @ 35	-2.8 D @ 35	-3.1 D @39	-3.1 D @39	-6.0 D @ 146	-6.2 D @ 139	-6.0 D @ 130	-6.8 D @ 130	-7.6 D @ 132	45.8 D @ 125	45.8 D @ 125	45.8 D @ 125	46.4 @ 129	46.4 @ 129	51.8 @ 56	52.8 @ 61	51.9 @ 60	53.8 @ 56	60.6 @ 49	472	471	477	462
6/60	6/60	6/60	6/6	6/6	6/6	6/6	6/9	6/6	6/6	6/6		+	-2.1 D @ 151	-2.1 D @ 151	-2.2 D @ 153	-2.1 D @ 151	-1.8 D @ 150	-10.0 D @ 25		-14.0 D @ 19	-12.0 D @ 10	-11.5 D @ 7	46.9 D @ 61	46.9 D @ 61	47.2 D @ 63	47.0 D @ 74	47.2 D @ 80	62 @ 115	62.3 D @110	63.8 D @ 109	63.7 D @ 112	63.9 D @ 104	484	480	491	486
6/18	6/18	6/18P	6/6	6/6	6/6	6/6	6/6P	6/6P	6/6P	6/6P		+	-0.7 D @ 164	-0.7 @ 160	-0.75 @ 154	-0.80 @ 154	-0.80 @ 154	-3.3D @ 151		-3.3D @ 155	-3.4 D @ 160	-3.3 D @ 150	45.4 D @ 76	45.4 D @ 70	45.6D @ 72	45.6 D @ 64	45.6 D @ 68	53.3 D @ 61	52.9 D @ 62	53.0 D @ 68	52.8 D@70	52.7 D @ 71	505	500	510	508
6/24p	6/24p	6/24	6/6	6/6	6/6	6/6	6/6P	6/6P	6/6P	6/6P			-0.7 D @ 4	-0.7 D @ 6	-0.75 D @ 2	-0.75 D @ 164	-0.8 D @ 158	-4.1 D @ 177		-4.3 D @ 174	-4.5 D @ 180	-5.0 D @ 178	45.5 D @ 94	45.5 D @ 94	45.2 D @ 98	45.0 D @ 78	45.0 D @ 70	56.9 D @87	56.9 D @87	57.1 D @90	57.5 D@87	57.5 D @82	492	490	490	487
6/9P	6/9P	6/9p	6/6	6/6	6/6	6/6	6/6	6/6P	6/6	6/6		+	-0.50D @ 92	-0.75 D @ 90	-1.6 D @104	-0.6 D @ 18	-0.7 D @ 140	-3.7 D @139		-3.9D @ 132	-3.8D @132	-3.7D @130	51.1 D @ 2	51.1 D @ 2	51.2 D @14	51.8 D @ 108	50.5 D @ 50	52.1 D @ 49	52.1 D @ 49	52.2 D @ 42	51.8 D @ 42	51.2 D @ 47	409	412	412	355
6/9	6/9	6/9p	6/9	6/6p	6/6P	6/9	6/6	6/6	6/6P	6/6		+	-5.0 D @ 110	-5.0 D @ 110	-5.2 D @115	-5.0 D @ 110	-5.0 D @ 110	-0.7 D @ 171		-1.0D @ 151	-1.0D @ 151	-1.0D @ 151	58.0 D @ 20	58.0 D @ 10	58.6 D @ 22	55.6 D @ 20	53.0 D @ 20	52.2 D @ 81	52.8D @ 81	53.0D @ 61	55.0D @ 67	57.2D @ 94	313	310	315	320
6/18	6/18	6/18	6/6		6/6	6/6	6/6	6/6	6/6	6/6		+	-2.8 D @ 16	-3.0 D @ 20	-3.8D @ 23	-4.2 D @ 20	-4.7 D @ 19	-6.8 D @ 159		-7.4 D @ 159	-7.2 D @ 148	-7.0 D @ 152	46.3 D @ 106	46.5 D @ 126	47.6 D @ 113	48 D @ 100	48.2 D @ 100	53.5 @ 69	53.7 D @ 69	54.6 @ 69	54 D @ 72	54 D @ 72	453	450	463	460
6/36	6/24P	6/24										+	-6.5 D @ 25	-6.7 D @ 25	-6.7 D @ 25	-6.9 D @ 20	-7.2 D @ 19	-9.7 D @ 166	-9.7 D @ 166	-9.8 D @ 160	-10.2 D @ 17	-10.9 D @174	55.3 D @ 115	55.2 D @ 115	55.7 D @ 112	56 D @ 109	56.4 D @ 109	65.5 D @76	66 D @ 80	66.2 D @ 80	66.7 D @ 84	67.0 D @84	437	435	431	427
6/18	6/18P	6/18	6/6	6/6	6/6	6/6	6/9P	6/9P	6/9P	6/9P		+	-4.25 D @ 148	-4.25 D @ 145	-4.5 D @ 152	-4.5 D @ 152	-4.0 D @149				NOT RECORDABLE					54.7 D @ 62	56.6 D @ 59				NOT RECORDABLE		452	425	440	446
6/9P	6/9P	6/9	6/6P	6/6P	6/6P	6/6P	6/6P	6/6P	6/6P	6/6P		+	-8.2 D @11	-8.3 D @ 10	-8.5 D @ 15	-8.9 D @ 23	-9.0 D @ 20	-6.8 D @ 108	-7.2 D @ 145	-8.3 D @ 148	-8.7 D @ 157	-8.7 D @ 157	63.8 D @ 101	63.8 D @ 101	62 D @ 110	62.1 D @ 113	62 D @ 110	59.8 D @ 18	58 D @ 25	58 D @ 65	57.4 D @ 67	57.6 D @ 70	411	410	403	372
6/6P	6/6	6/6	6/12P	6/12P	6/12	6/9	6/9	6/9	6/9P	6/6P	+		-5.3 D @ 148	-5.5 D @ 145	-6.0 D @ 51	-5.8 D @ 140	-5.6 D @ 122	-4.2D @ 26	-4.8 D @ 54	-5.9 D @ 97	-4.8 D @ 54	-3.8 D @ 45	60.2D @ 58		60.6D @ 51			56.2 D @ 116		50.8 D @ 97			347	347	347	345
6/24P	6/24	6/18	6/6	6/6	6/6P	6/6P	6/6	6/6P	6/6	6/6		+	-4.3 D @ 41				-6.0 D @ 35	-8.3 D @ 134				-8.6 D @ 196	52.1 D @ 131				53.0 D @ 125	59.6 D @ 94				63.4 D @ 56	499	500	500	500
6/24	6/24	6/24	6/6	6/6	6/6	6/6	6/6P	6/6P	6/6	6/6		+	-2.4 D @ 179		-3.2 D @ 178		-4.8 D @ 7	-7.1 D @2		-5.1 D @ 2		NOT RECORDA	48.8 D @ 89		48.9 D @ 88		53.1 D @ 97	59.2D @ 92		57.2 D @ 92		NOT RECORDA	470	462	458	452

6/18	6/18	6/18	6/6P	6/6P	6/6	6/6	6/6P	6/6P	6/6P	6/6P		+	-6.7D @ 11	-7.8 D @ 12	-8.2 D @ 10	-9.4 D @ 7	-8.4 D @ 6	-10.8 D @ 10	-10.8 D @ 17	-10.9D @ 180	-9.7D @ 184	-8.1 D @ 164	64.8 D @ 101		66.2D @ 97	63.2D @ 90	60.8 D @ 96	69.5 D @ 100		68.2 D @ 90		60 D @ 74	390		389	372
6/18	6/18	6/18	6/6	6/6	6/6	6/6	6/12	6/9	6/9	6/6			-1.9 D @ 176	-1.9 D @ 176	-2.0 D @ 180	-2.0 D @ 172	-2.2 D @174	-6.9D @ 24	-6.9D @ 24	-6.8D @ 20	-6.7D @ 25	-6.5 D @27	51.4 D @86		51.1 D @90	50.4 D @86	49.8 D @ 84	58.1 D @ 114		58.0 D @ 110		56.8 D @ 117	485		482	480
6/18	6/18	6/18	6/9P	6/9	6/9p	6/12	6/6	6/6P	6/6p	6/9		+			NOT REC		-0.9 D@145	-4.8 D @ 25	-4.8 D @ 20	-4.5 D @ 22	-4.0 D @ 20	-3.2 D @ 17	55.7 D @ 50		NOT REC		55.2 D @ 55			56.2 D @ 112		52.0 D @ 107	346		NOT R	312
6/18P	6/18P	6/18P	6/6	6/6	6/6	6/6	6/6	6/6	6/6	6/6		+	-4.6 D @ 128	-4.6 D @ 128	-4.5 D @ 128	-4.4 @ 122	-4.4 @ 122	-6.9 D @ 47	-6.0 D @ 47	-5.5 D @ 47	-3.8 D @ 53	-3.8 D @ 53	50.8 D @ 38	50.8 D @ 38	50.5 D @ 38	50.9 D @ 32	51.5 D @ 30	57.2 @ 137	53.1 D @ 143	53.1 D @ 143	53.1 D @ 143	53.1 D @ 143	484		485	487
6/9	6/9		6/9	6/9	6/9	6/9	6/9P	6/12	6/12			+	-5.5 D @ 33	-5.5 D @ 33	-6.0 D @ 33	-6.3 D @ 33	-6.5 D @ 33	-6.0 D @ 155	-6.0 D @ 155	-5.5 D @ 155	-5.1 D @ 147		55.8 D @ 123	55.8 D @ 123	56.6 D @ 123	57.8 D @ 123		58.7 D @ 57	58.6 D @ 57	57.7 D @ 57	57.7 D @ 57	56.9 D @ 57	450	440	435	432
6/6P	6/9	6/9P	6/6	6/6	6/6	6/6	6/6		6/6	6/6P			-0.5D @ 159	-0.8D @ 159	-0.8D @ 159		-0.8 D @ 149	-2.0D @ 41	-2.0D @ 41	-1.8D @ 41	-1.2D @ 41	-1.1D @ 56	48.5 D @ 69	48.7 D @ 69	48.7 D @ 69	48.8 D @ 69	48.9D @ 59	52.8 D @ 131	51.6 D @ 131	51.6 D @ 131	48.2 D @146	48.2 D @146	430	450	460	459
											+																									
6/9	6/9	6/9	6/6P	6/6P	6/6P	6/6P	6/6P	6/6	6/6P	6/6P		+	-1.7 D @ 30	-2.5.0 D @ 30	-2.5 D @ 30	-2.1 D @ 29	-2.9 D @ 27	-3.6 D @ 166	-3.6 D @ 166	-3.5 D @ 166	-4D @ 164	-3.7 D @ 160	47.6 D @ 120	47.6 D @ 120	48.6 D @ 120	48.2D @ 119	48.8 D @ 117	50.2 D @ 76	50.2 D @ 76	49.2 D @ 76	48.7 D @ 74	47.7 D @ 70	440	435	436	428
6/9	6/9	6/9	6/6	6/6	6/6	6/6	6/6	6/6	6/6	6/6		+	-2.9 D @ 163	-2.9 D @ 163	-2.9 D @ 163	-2.9 D @ 163	-3.0 D @ 162	-7.9 D @ 39	-7.9 D @ 39	-7.5 D @ 39	-7.0 D @ 39	-6.5 D @ 39	49.8 D @ 73	49.8 D @ 73	49.7 D @ 73	49.9 D @ 63		55.2 @ 129	54.2 @ 129	54.0 @ 129	54.0@ 129	53.8 @ 129	465	465	460	460
6/9	6/9	6/9	6/6	6/6	6/6	6/6	6/6	6/6	6/6	6/6	+		-7.0 D @ 147	-7.0 D @ 147	-6.5 D @ 147	-6.5 D @ 147	-5.8 D @ 150	-5.4 D @ 25	-5.4 D @ 25	-5.0 D @ 25	-5.0 D @ 25	-5.3 D @ 28	55.7 D @ 57	55.7 D @ 57	55.5 D @ 57	55.0 D @ 57	54.6 D @ 60	53.9 @ 115	52.8 D @ 118	51.8 D @ 118	51.8 D @ 118	51.8 D @ 118	412	412	410	412
6/18	6/18	6/24P	6/6	6/6		6/6	6/9	6/9	6/9	6/9			-1.3D @ 76	-1.3D @ 76	-1.5D @ 150	-2.5D @ 176	-2.5 D @ 167	not recordable		-10.3 @ 3	-8.5 @ 6	-7.1 D @ 10	45.3 D @166	45.3 D @166	46.0 D @166	46.7 D @166	48.5D @ 77	not recordable		68.2 d @ 93	65.2	63.4D @ 100	492	490	495	495
6/12P	6/12	6/9P	6/6	6/6	6/6	6/6P	6/6P	6/6P	6/6P	6/6P	+			-3.6 D @ 56	-4.0 D @ 68	-4.0 D @ 78	-4.8 D @ 68	-5.5D @120	-5.5D @120	-5.0D @120	-5.0D @120	-4.8 D @ 134	49.7 D @ 120	49.7 D @ 130	49.7 D @ 140	49.9 D @ 146	50.2 D @ 158	55.8 D @ 44	55.8 D @ 44	53.8 D @ 44	53.8 D @ 44	52.8 D @ 44	512	510	500	498
6/12P	6/12P	6/18P	6/6	6/6	6/6	6/6	6/12P	6/12P	6/12P	6/9P	+		-3.6 D @ 146	-3.6 D @ 146	-4.0 D @ 143	-4.0 D @ 142	-4.5 D @ 140	-4.8 D @33	-5.0@30	-4.5 D @ 26	-4.0@40	-4.0 D @ 35	49.7 D @ 56	49.7 D @ 53	49.7 D @ 53	49.9 D @ 53	50.5 D @ 50	59.2 D @ 123	60.2 D @ 123	59.1 D @ 116	58.2 D @ 120	57.6 D @ 125	511	510	495	490
6/12P	6/12	6/12	6/6	6/6	6/6	6/6	6/6	6/6	6/6	6/6			-3.6 D @ 146	-3.6 D @ 146	-4.0 D @ 143	-4.0 D @ 142	-4.5 D @ 140	-11.8 D @33	-12.0@30	-11.9 D @ 26	-10.5@40	-10.5 D @ 35	49.7 D @ 56	49.7 D @ 53	49.7 D @ 53	49.9 D @ 53	50.5 D @ 50	59.2 D @ 123	60.2 D @ 123	59.1 D @ 116	58.2 D @ 120	57.6 D @ 125	511	510	495	490
6/18	6/12P	6/12P	6/6	6/6	6/6	6/6	6/6P	6/9	6/6	6/6	+		-2.8 D @ 36	-2.8 D @ 38	-2.8 D @ 37	-2.9 D @ 39	-2.9 D @ 36	-11.9D @ 177	-11.9D @ 17	-11.2 D @ 179	-11.25 D @ 18	-11.4 D @ 2	46.5 D @ 126	46.5 D @ 126	46.2D @ 127	46.5 D @130	46.4D @ 126	68.8D @ 87	69.0 D @ 89	68.4D @ 89	68.4D @ 90	68.3 D @ 92	498	496	499	495
6/12	6/12	6/12	6/6	6/6	6/6	6/6	6/12	6/12	6/12	6/12		+	-1.0 @ 39	-1.0 @ 39	-1.5 @ 40	-1.5 @ 40	-1.7 D @ 54	-9.5 D @ 124	-9.4 D @ 126	-9.6 D @ 136	-9.0 D @ 130	-8.4 D @ 126	45.2 @ 129	45.4 @ 130	45.6 @ 132	46.0 @ 129	46.3 D @149	55.2 D @ 34	55.2 D @ 34	55.2 D @ 40	55.0 D @ 36	55.4 @ 36	481	480	478	476
6/12	6/12	6/9P	6/6	6/6	6/6	6/6	6/6P	6/6P	6/6	6/6		+	-3.7 D @ 44		-2.4 D @ 64	-3.9 D @ 54		-6.8 D @ 152		-6.2 D @ 144	-6.3 D @ 144	-5.5 D @ 146	48.3D @ 134		47 D @ 154	47.7 D @ 141	48.6 D @ 142	55.6 D @ 62	55.8 D @ 60	53.3 D @ 54	53.1 D @ 59	53.0 D @ 60	511	511	521	520
6/12	6/12	6/9P	6/6	6/6	6/6	6/6	6/6P	6/6P	6/6	6/6		+	-3.7 D @ 44		-2.4 D @ 64	-3.9 D @ 54		-6.8 D @ 152		-6.2 D @ 144	-6.3 D @ 144	-5.5 D @ 146	48.3D @ 134		47 D @ 154	47.7 D @ 141	48.6 D @ 142	55.6 D @ 62	55.8 D @ 60	53.3 D @ 54	53.1 D @ 59	53.0 D @ 60	511	511	521	520
6/12	6/12	6/12P	6/6	6/6	6/6	6/6P	6/9	6/9	6/9	6/9			-4.6 D @ 154	-4.6 D @ 154	-4.6 D @ 150	-4.25 D @ 148	-4.2 @ 147	-5.9 D @ 54	-5.9 D @ 54	-5.6 D @ 52	-5.5 D @ 50	-5.1 D @ 44	53.1 D @ 64	53.1 D @ 64	53.0 D @ 60	52.8 D @ 64	52.6 D @ 57	58.0 D @ 144	59.0 D @ 144	55.7 D @ 140	56.0 D @ 146	55.7 D @ 134	401	401	400	411
6/9		6/6	6/6	6/6		6/6	6/6P	6/6P		+	+		-1.2 D@180	-1.1D @ 177	-1.1D @ 179		-2.8D @ 21	-2.5@30	-2.2D @ 23	-2.6 D @ 25		46.3 D@ 93	46.4 D@ 90	46.4D @ 87	46.4D @ 89		49.6D @ 111	49.8@112	48.6D @ 113	49 D @ 115		434	424	429	443	
6/12	6/12	6/12	6/6	6/6	6/6	6/6	6/6	6/6	6/6	6/6		+	-0.7 D @ 1	-0.7D @ 1	-0.3 D @ 33	-0.5 D @ 33	-0.4 D @ 21	-6.1 D @ 67	-6.5 D @ 67	-6.0 D @ 65	-6.0 D @ 65	-6.0 D @65	43.9 D @ 91		43.9D @ 123	43.5 D @ 91	43.2 D @ 121	55.7 D @ 157	56.0 D @155	54 D @155	54.0 D @ 157	54.3 D @ 154	511	506	503	505
6/12	6/9	6/9	6/6		6/6	6/6	6/6P	6/6P	6/6	6/6	+		-1.3D @ 3	-1.50D@6		-1.1 D @ 4	-1.4D @ 1	-2.2D @ 70	-2.8D @ 70	-2.8D @ 70	-2.6D @ 71	-2.9D @ 61	45.5D @ 93	45.5D @ 93	45.6D @ 93	45.3 D @ 94	45.7D@ 91	49.1 D @ 160	49.2 D@160	49.1 D @ 160	48.9 D @ 161	49.4 D @ 151	478	478	476	477
6/12	6/9	6/9	6/6		6/6	6/6	6/6P	6/6P	6/6	6/6	+		-1.3D @ 3	-1.50D@6		-1.1 D @ 4	-1.4D @ 1	-2.2D @ 70	-2.8D @ 70	-2.8D @ 70	-2.6D @ 71	-2.9D @ 61	45.5D @ 93	45.5D @ 93	45.6D @ 93	45.3 D @ 94	45.7D@ 91	49.1 D @ 160	49.2 D@160	49.1 D @ 160	48.9 D @ 161	49.4 D @ 151	478	478	476	477
6/9	6/9	6/9	6/6	6/6	6/6	6/6	6/6	6/6P	6/6P	6/6P		+	-1.2 D @ 3		-1.2 D@180	-1.1D @ 177	-1.1D @ 179	-2.8D @ 21	-3.0@30	-2.5@30	-2.2D @ 23	-2.6 D @ 25	46.3 D@ 93	46.8 D@ 90	46.4 D@ 90	46.4D @ 87	46.4D @ 89	49.6D @ 111	50.4@110	49.8@112	48.6D @ 113	49 D @ 115	434	420	424	429

12 MONTHS	CASE PREOP	1 MONTH	3 MONTHS	6 MONTHS	12 MONTHS	ANTERIOR FLOAT CONTROL PREOP	1 MONTH	3 MONTHS	6 MONTHS	12 MONTHS	CASE PREOP	1 MONTH	3 MONTHS	6 MONTHS	12 MONTHS	POSTERIOR FLOAT CONTROL PREOP	1 MONTH	3 MONTHS	6 MONTHS	12 MONTHS	CASE PREOP	1 MONTH	3 MONTHS	6 MONTHS	12 MONTHS	3MM CONTROL PREOP	1 MONTH	3 MONTHS	6 MONTHS	12 MONTHS	CASE PREOP	1 MONTH	3 MONTHS	6 MONTHS	12 MONTHS	5 MM CONTROL PREOP	1 MONTH	3 MONTHS	6 MONTHS	12 MONTHS	CASE PREOP	1 MONTH	3 MONTHS	6 MONTHS	12 MONTHS	AXIAL LENGTH PREOP CONTROL	CASE	FINAL REVIEW CONTROL	CASE	SPECULAR CONTROL CD	SD	CV	HEX	CASE CD	SD	CV	HEX
422	406	342	339	354	367	0.033	0.034	0.037	0.037	0.039	0.066	0.062	0.059	0.06	0.06	0.073	0.073	0.077	0.077	0.082	0.102	0.09	0.083	0.085	0.092	3.2	3.2	3.4	4.7	4.8	6.4	6.7	6.6	6.1	5.7	3.2	3.2	3.2	4.3	4.8	6.5	6.6	6.8	6.5	6.2	22.91	23.18	22.91	23.18	NOT CAPTURED				NOT CAPTURED			
414	404		277	319	335	0.025	0.025	0.025		0.026	0.032		0.036		0.026	0.05	0.05	0.056	0.046	0.059	0.069		0.089	0.115	0.097		2.6	2	3.6	1.7	3.1		3.1	3.2	2.8	2.4	2.4	2.4	2.4	2.3	3.4	3.6	3.9	4.1	3.3	24.05	23.67	24.05	23.67	NOT CAPTURED				NOT CAPTURED			
377	402		324	345	368	0.065	0.064	0.061	0.067	0.067	0.051	0.043	0.041	0.034	0.029	0.097	0.09	0.09	0.118	0.098	0.093	0.09	0.09	0.107	0.096	4.7	4.5	4.6	4.2	4.7	4.1	3.9	3.7	2.9	3.2	6.3	5.9	5.9	5.7	6	5.2	4.8	4.2	4.2	3.8	24.76	24.46	24.77	24.4	NOT CAPTURED				NOT CAPTURED			
441	427	321	312	298	326	0.030	0.03	0.034	0.043	0.061	0.087	0.08	0.087	0.076	0.062	0.05	0.048	0.057	0.078	0.097	0.157	0.098	0.087	0.082	0.062	2.9	3.8	4.2	5.4	7.6	11.8	10.2	8.2	7.3	7.6	4.3	4.5	4.5	6.3	7.7	15	11.6	10.9	8.4	9.1	24	24.02	24	24.02	NOT CAPTURED				NOT CAPTURED			
451	422	310	295	352	362	0.055	0.05	0.05	0.05	0.06	0.105	0.101	0.103	0.086	0.086	0.099	0.1	0.11	0.107	0.107	0.175	0.175	0.177	0.155	0.155	5.9	5.4	5.4	5.6	6.1	10.1	9.9	9.2	10	10.1	5.6	5.6	6.2	6.8	7.1	12	11.1	10.1	10.3	11.2	25.2	25.11	25.2	25.1	2308	96	22	50	NOT CAPTURED			
454	407	275	299	321	321	0.027	0.027	0.029	0.032	0.026	0.049	0.046	0.044	0.042	0.033	0.036	0.036	0.039	0.047	0.043	0.09	0.086	0.084	0.078	0.073	2.4	2.4	2.4	2.4	2.2	6.6	6.4	6.4	5.9	4.5	2.4	2.6	2.6	3.2	3.2	6.2	6.1	5.8	5.8	4.4	23.32	23.4	23.32	23.4	2470	99	24	83	NOT CAPTURED			
374	402	302	295	311	323	0.066	0.066	0.06	0.06	0.068	0.057	0.056	0.058	0.057	0.057	0.141	0.129	0.132	0.144	0.149	0.113	0.123	0.122	0.134	0.12	6.7	6.7	6.7	6.9	7.4	7.3	7.2	6.7	6.4	5.7	7.1	7.5	8.7	10.4	11.2	6.8	6.6	6.9	7.4	5.9	22.8	22.69	22.82	22.7	NOT CAPTURED				NOT CAPTURED			
453	447	311	316	322	342	0.064	0.062	0.059	0.061	0.061	0.068	0.059	0.054	0.056	0.056	0.125	0.118	0.125	0.123	0.123	0.136	0.153	0.132	0.121	0.112	4.5	4.5	4.8	4.6	5.1	3.5	4.1	3.8	3.8	3.8	6.5	6.4	6.6	6.5	6.5	6.4	6.5	6.1	5.9	6.1	24.92	24.59	24.92	24.5	NOT CAPTURED				NOT CAPTURED			
506	486	354	332	322	308	0.013	0.012	0.012	0.012	0.012	0.08	0.083	0.076	0.076	0.078	0.019	0.02	0.023	0.029	0.025	0.094	0.1	0.112	0.11	0.132	1.5	1.5	1.6	1.6	1.5	15.4	15.2	14.6	11	10.4	3	3.1	2.7	2.9	3	16	15.8	14.4	13.1	12	23.47	23.32	23.5	23.35	NOT CAPTURED				NOT CAPTURED			
397	414	325	287	293	398	0.057	0.057	0.066	0.06	0.061	0.048	0.054	0.03	0.03	0.05	0.143	0.15	0.14	0.15	0.159	0.118	0.18	0.197	0.162	0.133	5.3	5.3	7	6.5	6.9	5.9	7.2	6.5	6.4	5.9	6	6.2	6.5	7.6	8.2	6.4	7.4	7.7	6.7	6	24.12	24.22	24.12	24.18	NOT CAPTURED				DONE			
459	405	328	297	284	283	0.014	0.013	0.013	0.013	0.013	0.038	0.038	0.041	0.052	0.057	0.042	0.042	0.043	0.044	0.044	0.098	0.1	0.153	0.151	0.155	1.5	1.3	1.3	1.4	1.1	2.6	2.8	3.2	4.1	4.5	2.1	2	2	2	2.1	3.8	3.9	3.9	4.3	5	23.57	23.63	23.55	23.71	2377	157	37	90	2926		25	72
432	398	343	354	349	322	0.049	0.047	0.047	0.047	0.047	0.058	0.051	0.051	0.051	0.038	0.085	0.085	0.085	0.093	0.093	0.115	0.112	0.123	0.103	0.102	5.7	5.5	5.4	5.6	5.8	5.8	6.2	6	5.9	5.6	5.5	5.3	5.8	5.8	5.8	6.2	6.4	6.3	6.2	6.3	23.43	23.51	23.44	23.53	2688	200	54		NOT CAPTURED			
505	480	435	448	470	476	0.015	0.015	0.016	0.015	0.018	0.048	0.051	0.055	0.048	0.039	0.027	0.025	0.027	0.028	0.027	0.086	0.085	0.085	0.092	0.085	4.3	4.3	4.4	4.4	4.5	5.6	5.6	5.8	5.2	5.1	3.8	4.1	3.8	3.9	4.1	5.6	5.7	5.7	5.1	5.1	23.37	23.13	23.37	23.14	2660	125	33	55	NOT CAPTURED			
																																																		2830	94	27	30	2503	133	33	40
444	419	376	398	401	409	0.04	0.04	0.04	0.044	0.044	0.086	0.088	0.08	0.08	0.078	0.079	0.079	0.079	0.085	0.085	0.128	0.144	0.134	0.14	0.14	4.5	4.4	4.5	4.5	4.5	7.6	7	6.9	6.4	6	5	5.2	5.1	5	5	9.5	9.5	9.3	8.8	8.8	23.94	23.99	23.95	23.99	2792		23	70	NOT CAPTURED			
																																																		2631	122	32	73				
452	485	402	389	381	340	0.026	0.026	0.026	0.026	0.026	0.042	0.039	0.027	0.043	0.067	0.048	0.048	0.049	0.05	0.052	0.09	0.08	0.06	0.09	0.125	1.4	1.4	1.6	1.8	1.8	3.8	4.1	4.4	5.1	6.3	2	2	2	2.2	2.2	4.7	5.1	4.6	6.8	10	24.47	24.6	24.48	24.62	NOT RECORDED							
486	441	440	438	431	423	0.046		0.05	0.05	0.04	0.103	0.115	0.012	0.032	0.045	0.078	0.075	0.073	0.07	0.068	0.14	0.14	0.15	0.15	0.15	6.7	6.5	6.4	6.2	6.2	13.2	13	11.9	12	12.5	5.9	5.8	5.8	5.7	5.7	12	11.2	11	11.2	11	22.98	23.55	22.99	23.57	NOT CAPTURED							
504	449	435	426	387	392	0.012		0.012	0.014	0.014	0.061	0.06	0.057	0.055	0.056	0.026	0.027	0.027	0.029	0.025	0.107	0.107	0.109	0.111	0.107	0.8	0.8	1	1.3	1.7	5.8	5.7	5.2	4.4	4.4	1.3	1.3	1.3	1.4	1.7	6	6	5.8	5.4	5.4					2849	89	25	62	NOT CAPTURED			
487	423	410	386	342	321	0.031		0.03	0.027	0.025	0.059	0.06	0.055	0.052	0.042	0.045	0.04	0.042	0.042	0.048	0.123	0.12	0.102	0.076	0.076	1.8	1.7	1.7	1.9	1.9	4.5	4.5	4.5	4.6	4.6	2.8	2.7	2.6	2.6	2.5	6.7	6.7	6.7	6.7	6.7					NOT CAPTURED				3030	76	23	60
326	403	395	298	301	320	0.042		0.035	0.032	0.03	0.046	0.038	0.029	0.019	0.023	0.07	0.07	0.075	0.046	0.025	0.076	0.07	0.038	0.049	0.058	3.1	3	8.7	3.8	3.3	3.4	3.4	3.5	3	3.5	3.4	3.2	15.5	4.6	4.2	3.6	4	4.4	3.7	3.7	22.62	22.48	22.63	22.5	2990	82	25	0	NOT CAPTURED			
357	427	398	268	355	386	0.065	0.07	0.071	0.067	0.063	0.054	0.05	0.062	0.051	0.048	0.211	0.211	0.222	0.22	0.2	0.113	0.1	0.135	0.13	0.128	8.2	8.2	8.1	7.8	7.8	5.4	5.5	6	5.5	5.1	7.7	7.7	7.9	7.7	7.7	6.7	7	7	6.2	6.1	24.3	24.07	24.3	24.07	NOT CAPTURED				NOT CAPTURED			
461	418	400	306	309	320	0.02	0.02	0.029	0.03	0.035	0.07	0.07	0.056	0.056	0.054	0.057	0.058	0.062	0.063	0.065	0.131	0.13	0.146	0.15	0.15	1.4	1.8	3.5	3.8	3.8	6.1	6	5.8	5.8	5.8	3.7	3.5	3.4	3.8	3.9	6.2	6.2	6.1	6	5.9	23.92	23.94	23.93	23.94	2981		29	62	NOT CAPTURED			
449	388	382	380	385	385	0.066	0.065	0.065	0.064	0.063	0.086	0.086	0.086	0.087	0.087	0.09	0.1	0.1	0.102	0.102	0.138	0.135	0.136	0.136	0.14	8.3	8	7.9	7.9	7.7	10.7	10	10	10	10	7.6	7.4	7.2	7.2	7.1	12	11.7	11.5	11.2	11	22.26	22.35	22.27	22.38	NOT CAPTURED							
425				NOT RECORI		0.066	0.065	0.065	0.068	0.076				NOT RECORDABLE					0.122	0.134				NOT RECORDABLE					7.2	8.7				NOT RECORDABLE					6.9	8.3				NOT RECORI		23.6	23.41	23.62	23.44	NOT CAPTURED				NOT CAPTURED			
424	414	410	382	323	320	0.061	0.06	0.064	0.069	0.067	0.063	0.06	0.057	0.037	0.033	0.121	0.1	0.16	0.176	0.172	0.128	0.125	0.087	0.063	0.063	6.8	6.5	6.3	6	6	9.2	9	8.3	6.2	6.6	7.4	7.2	7	6.9	7	15	14.2	13.8	13.3	13					NOT CAPTURED				NOT CAPTURED			
345	456	428	392	390	393	0.048	0.05	0.047	0.05	0.04	0.057	0.05	0.042	0.04	0.04	0.113	0.1	0.099	0.1	0.15	0.077	0.11	0.137	0.08	0.08	2.9	2.9	3	3	2.5	4.9	4.8	4.3	4.5	4.5	5.7	5.4	5.1	5.5	5.4	5.7	5.4	4.8	6.2	6.2					NOT CAPTURED							
497	447	440	423	418	334	0.033				0.037	0.089				0.086	0.07				0.074	0.177				0.171	4				4.1	9.2				9.1	4.1				4	8.8				8.5	21.57	21.71	21.59	21.72	NOT CAPTURED				NOT CAPTURED			
447	424	420	410		NOT R	0.033		0.037		0.043	0.085		0.093		NOT RE	0.059		0.063		0.079	0.141		0.102		NOT RE	2.7		2.7		4	7.4		7.4		NOT F	3.7		2.7		4	8		8.2		NOT	23.32	23.29	23.32	23.29	2491	109	27	72	2456	119	29	50

367	394	370	338	321	293	0.07				0.061	0.089				0.065	0.129		0.024		0.141	0.139		0.132		0.16	8.2		6.8		5.2	7.7		7.3		5.2	15		8.4		7.3	9.8		9.4		8	22.48	22.5	22.48	22.5	NOT CAPTURED							
474	443	440	440	436	434	0.035				0.026	0.051				0.049	0.069				0.054	0.099				0.097	4.1				3.9	8				5.9	6.3				3.4	9.6				5.7					2924	123	36		2907	144	42	
0	450	451	457	443	422			NOT REC		0.026			0.062		0.043			NOT REC		0.069			0.107		0.108			NOT REC		9.1			6.4		5.3			NOT REC		9.1			6.4		5.3	24.37	24.25	24.37	24.26	NOT CAPTURED				NOT CAPTURED			
																																																		NOT CAPTURED				2141	190	41	66
480	455	400	390	384	415	0.056	0.056	0.056	0.047	0.05	0.085	0.085	0.076	0.071	0.07	0.097	0.097	0.097	0.087	0.09	0.141	0.141	0.142	0.176	0.15	8.3	8	7.5	7.2	7	12	11.5	11	10	10	8.9	8.9	8	7	7.5	12	11	10.5	9.4	9	23.8	22.29	23.8	22.29	NOT CAPTURED				2681	115	31	75
420	425	420	424	420	420	0.045	0.046	0.056	0.056	0.06	0.04	0.03	0.035	0.025	0.025	0.09	0.095	0.1	0.108	0.11	0.058	0.057	0.06	0.057	0.05	3.5	3.6	3.8	4	4.2	5	4.6	4.2	4	3.5	5	5.2	5.4	5.7	6	6.5	6.3	6.2	6.1	5.5	23.8	22.29	23.8		NOT CAPTURED				NOT CAPTURED			
458	350	320	326	325	317	0.033	0.032	0.04	0.035	0.036	0.042	0.04	0.035	0.032	0.029	0.033	0.033	0.03	0.035	0.036	0.112	0.11	0.09	0.085	0.076	1.7	1.7	1.6	1.7	1.75	2.6	2.5	2.1	2.2	2.2			2.1		2.7	5.5	4.5	5.2	2.5	2.9	23	24.5	23	24	2379	109	26	53	not captured			
436	412	315	320	313	299	0.033	0.032	0.04	0.035	0.036	0.046	0.046	0.04	0.036	0.043	0.067	0.068	0.072	0.074	0.077	0.083	0.076	0.08	0.073	0.086	4.1	4.2	4.5	4.9	4.4	5.7	6	6.5	7	7	4	4.2	4.5	4.5	4.6	5.6	5.8	6	6.4	6.3	22	24	22	24	2268	113	26	73	2162	131	28	82
																																																		2302	131	30	50	2174	160	35	63
462	435	420	430	415	412	0.019	0.02	0.025	0.035	0.035	0.042	0.04	0.035	0.032	0.029	0.033	0.033	0.03	0.035	0.036	0.072	0.075	0.078	0.08	0.086	1.7	1.7	1.6	1.7	1.75	4.5		4.2	3.8	3.8	2.2	2.2	2	2.5	2.3	5		4.6	4.5	4.5					NOT CAPTURED							
414	428	380	380	382	381	0.041	0.044	0.044	0.044	0.042	0.063	0.054	0.065	0.078	0.031	0.078	0.08	0.08	0.084	0.094	0.112	0.11	0.09	0.085	0.076	3.8	3.5	3.8	3.8	3.4	4.1	4	4	4	3.8	5.1	5	4.8	4.8	4.5	4.8	4.6	4.8	5.2	5.6					NOT CAPTURED							
502	not r	350	380	380	417	0.029	0.03	0.035	0.035	0.041	not rec	0.05	0.05	0.045	0.043	0.035	0.04	0.05	0.056	0.057	not rec	0.186	0.189	0.09	0.064	3.8	3.8	4	3.5	3.1	not re	10.5	10.1	10	9.5	4.6	4.6	4.5	4	3.3	not record		10.4	10	9.9	23.56	23.43	23.57	23.45	NOT CAPTURED							
497	460	440	462	462	464	0.029	0.03	0.033	0.036	0.042	0.06	0.08	0.04	0.05	0.056	0.042	0.046	0.056	0.06	0.085	0.133	0.092	0.124	0.126	0.128	3.5	3.6	3.8	4.2	4.4	6.5	6.8	6.2	5.5	5	3.5	3.6	4.2	4.4	4.4	6.5	6.2	5.5	5	5.4	23.46	23.57	23.45	23.57	2008	129	26	80	2246	137	31	46
																																																			112	26	63	2309	not captured		
480	388	320	320	350	393	0.029	0.03	0.033	0.036	0.042	0.06	0.08	0.04	0.05	0.056	0.042	0.046	0.056	0.06	0.062	0.133	0.092	0.124	0.056	0.045	4.8	4.9	4.6	4.4	4.2	8.4	8.2	7.3	7.6	7.6	4.6	4.5	4.5	4.8	4.9	8.3	8.2	7.6	7.4	7.3					NOT RECORDABLE							
																																																			3077	95	29	60	2899	139	40	49
480	388	320	320	350	393	0.029	0.03	0.033	0.036	0.042	0.06	0.08	0.04	0.05	0.056	0.042	0.046	0.056	0.06	0.062	0.133	0.092	0.124	0.056	0.045	4.8	4.9	4.6	4.4	4.2	8.4	8.2	7.3	7.6	7.6	4.6	4.5	4.5	4.8	4.9	8.3	8.2	7.6	7.4	7.3					NOT RECORDABLE							
494	397	320	314	330	354	0.023	0.023	0.022	0.03	0.033	0.101	0.105	0.101	0.09	0.084	0.053	0.057	0.056	0.056	0.058	0.195	0.198	0.177	0.165	0.152	4.3	4.5	5	5	4.8	10.4	10	9	8.8	8.5	4.1	4.2	4.6	4.4	4.6	11	10.8	10.6	10	9.8					NOT CAPTURED							
472	453	440	442	440	443	0.015	0.015	0.016	0.018	0.026	0.08	0.08	0.082	0.082	0.085	0.02	0.02	0.02	0.03	0.04	0.115	0.125	0.13	0.132	0.134	1.3	1.3	1.5	1.5	1.9	10.1	10.2	9.6	9.5	9.6	1.5	1.5	2	2	2.3	9.6	9.8	9.5	9	9.1					NOT RECORDABLE							
510	459	435	472	475	470	0.035	0.035	0.031	0.037	0.04	0.071	0.072	0.053	0.055	0.05	0.06	0.05	0.035	0.041	0.051	0.105	0.095	0.091	0.089	0.075	3.6	3.8	3.7	3.7	3.5	7.4	7.5	6.6	6.7	6	3.9	4	4.3	4.4	4.6	7.1	7.5	7	7	6.5					NOT CAPTURED							
510	459	435	472	475	470	0.035	0.035	0.031	0.037	0.04	0.071	0.072	0.053	0.055	0.05	0.06	0.05	0.035	0.041	0.051	0.105	0.095	0.091	0.089	0.075	3.6	3.8	3.7	3.7	3.5	7.4	7.5	6.6	6.7	6	3.9	4	4.3	4.4	4.6	7.1	7.5	7	7	6.5					NOT CAPTURED							
420	376	250	260	270	269	0.063	0.063	0.065	0.06	0.059	0.076	0.078	0.069	0.07	0.072	0.102	0.1	0.1	0.1	0.1	0.132	0.14	0.14	0.145	0.176	4.6	4.4	4.4	4.6	4.4	7.8	7	7.2	6.8	6.7	4.9	4.9	4.8	5	5	7.8	7.9	7.4	7.2	6.9					NOT CAPTURED							
395	390	383	381		0.013	0.014	0.016	0.012		0.044	0.04	0.035	0.039		0.025	0.03	0.032	0.021		0.086	0.08	0.078	0.099		1	1	1	0.8		4.4	4.4	3.8	3.5		1.3	1.4	1.6	1.6		4	4	3.8	3.8					2298	145	33	75						
507	417	380	376	390	398	0.014	0.014	0.016	0.006	0.009	0.059	0.06	0.056	0.058	0.056	0.015	0.015	0.022	0.022	0.023	0.124	0.13	0.102	0.116	0.117	1	1	1.13	1.11	1.12	5.9	6	5.9	5.8	5.9	1.4	1.6	1.3	1.2	1.3	6	6.2	5.9	5.8	6	23.24	23.21	23.24	23.21	2371	108	25	47	2344	160	37	80
476	448	435	440	448	456	0.019	0.019	0.02	0.023	0.023	0.045	0.048	0.042	0.041	0.038	0.031	0.031	0.031	0.032	0.031	0.037	0.037	0.04	0.037	0.059	1.6	2	1.4	1.6	1.3	4.1	4.4	3.5	3.3	2.8	2	2	2.2	2.2	1.9	4.1	4.4	4.1	3.8	5.1	22.75	22.92	22.76	22.94	2727		62	42	2678		33	78
																																																		2604	145	38	51	3017	128	39	25
476	448	435	440	448	456	0.019	0.019	0.02	0.023	0.023	0.045	0.048	0.042	0.041	0.038	0.031	0.031	0.031	0.032	0.031	0.037	0.037	0.04	0.037	0.059	1.6	2	1.4	1.6	1.3	4.1	4.4	3.5	3.3	2.8	2	2	2.2	2.2	1.9	4.1	4.4	4.1	3.8	5.1	22.75	22.92	22.76	22.94	2727		62	42	2678		33	78
																																																		2604	145	38	51	3017	128	39	25
443	395		390	383	381	0.013	0.013	0.014	0.016	0.012	0.044	0.046	0.04	0.035	0.039	0.025	0.025	0.03	0.032	0.021	0.086	0.085	0.08	0.078	0.099	1	1	1	1	0.8	4.4	5	4.4	3.8	3.5	1.3	1.3	1.4	1.6	1.6	4	4.5	4	3.8	3.8					2298	145	33	75				

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SAFETY AND EFFICACY OF CORNEAL COLLAGEN CROSSLINKING WITH RIBOFLAVIN AND ULTRAVIOLET-A IN THE TREATMENT OF PROGRESSIVE KERATOCONUS DISSERTATION SUBMITTED FOR MS (Branch III) Ophthalmology THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY CHENNAI APRIL – 2014 CERTIFICATE This is to certify that the thesis entitled "SAFETY AND EFFICACY OF CORNEAL COLLAGEN CROSSLINKING WITH RIBOFLAVIN AND ULTRAVIOLET-A IN THE TREATMENT OF PROGRESSIVE KERATOCONUS" is the original work of Dr. Gitansha Sachdev and was conducted under our direct supervision and guidance at Aravind Eye Hospitals and Postgraduate Institute of Ophthalmology, Madurai Dr.Mano Ranjan Das Dr. N.Venkatesh Prajna Guide, Chief Medical Officer &...