ENDOTHELIAL CELL DAMAGE AFTER CATARACT SURGERY: MANUAL SMALL INCISION CATARACT SURGERY VERSUS PHACOEMULSIFICATION

Dissertation submitted by

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In partial fulfillment of the requirements for the degree of

MASTER OF SURGERY

IN

OPHTHALMOLOGY

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY, CHENNAI

DEPARTMENT OF OPHTHALMOLOGY

PSG INSTITUTE OF MEDICAL SCIENCES&RESEARCH

COIMBATORE

APRIL 2020

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Ref: Project No. **17/375**

Date: December 26, 2017

Dear Dr Sowmiya Kalaivani,

Institutional Human Ethics Committee, PSG IMS&R reviewed and discussed your application dated 06.12.2017 to conduct the research study entitled *"Endothelial cell damage after cataract surgery: Manual small incision cataract surgery versus phacoemulsification"* during the IHEC meeting held on 15.12.2017.

.The following documents were reviewed and approved:

1. Project submission form
2. Study protocol (Version 1 dated 06.12.2017)
3. Informed consent forms (Version 1 dated 06.12.2017)
4. Data collection tool (Version 1 dated 06.12.2017)
5. Current CVs of Principal investigator, Co-investigator
6. Budget

The following members of the Institutional Human Ethics Committee (IHEC) were present at the meeting held on 15.12.2017 at IHEC Secretariat, PSG IMS & R between 10.00 am and 11.00 am:

Sl. No.	Name of the Member of IHEC	Qualification	Area of Expertise	Gender	Affiliation to the Institution Yes/No	Present at the meeting Yes/No
1	Mr R Nandakumar (Chairperson, IHEC)	BA., BL	Legal Expert	Male	No	Yes
2	Dr D Vijaya (Member – Secretary, IHEC)	M Sc., Ph D	Basic Medical Sciences (Biochemistry)	Female	Yes	Yes
3	Dr S Shanthakumari	MD	Pathology, Ethicist	Female	Yes	Yes
4	Dr Sudha Ramalingam	MD	Epidemiologist, Ethicist Alt. member-Secretary	Female	Yes	Yes
5	Dr G Subhashini	MD	Epidemiologist	Female	Yes	Yes

The study is approved in its presented form. The decision was arrived at through consensus. Neither PI nor any of proposed study team members were present during the decision making of the IHEC. The IHEC functions in accordance with the ICH-GCP/ICMR/Schedule Y guidelines. The approval is valid until one year from the date of sanction. You may make a written request for renewal / extension of the validity, along with the submission of status report as decided by the IHEC.

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1. IHEC should be informed of the date of initiation of the study
2. Status report of the study should be submitted to the IHEC every 12 months
3. PI and other investigators should co-operate fully with IHEC, who will monitor the trial from time to time
4. At the time of PI's retirement/intention to leave the institute, study responsibility should be transferred to a colleague after obtaining clearance from HOD, Status report, including accounts details should be submitted to IHEC and extramural sponsors
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   a. The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)
   b. Alteration in the budgetary status should be clearly indicated and the revised budget form should be submitted
   c. If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Ethics Committee for approval
   d. If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented
   e. If there are any amendments in the trial design, these must be incorporated in the protocol, and other study documents. These revised documents should be submitted for approval of the IHEC and only then can they be implemented
   f. Any deviation-Violation/waiver in the protocol must be informed to the IHEC within the stipulated period for review
7. Final report along with summary of findings and presentations/publications if any on closure of the study should be submitted to IHEC

Kindly note this approval is subject to ratification in the forthcoming full board review meeting of the IHEC.

Thanking You,

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Dr D Vijaya
Member - Secretary
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This is to certify that this dissertation work titled "**COMPARISON OF ENDOTHELIAL CELL DENSITY IN MANUAL SMALL INCISION CATARACT SURGERY VERSUS PHACOEMULSIFICATION"** of the candidate **Dr.T.Sowmiya Kalaivani** for the award of MASTER OF SURGERY in the branch of OPHTHALMOLOGY. I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains pages from Introduction to Conclusion and the result shows **3** percentage of plagiarism in the dissertation.

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CONTENTS

INTRODUCTION

Blindness is a severe debilitating condition to the mankind. Nearly 36 million people are blind all over the world due to various causes. [(1)]Cataract and uncorrected refractive errors are the most common cause of blindness and severe visual impairment. In India blindness is around 12 million, of which also cataract is the leading cause of preventable blindness that is around 7.75 million[(2)].

Cataract surgery is one the most frequently performed surgeries throughout the world. In India around 5 million cataract surgeries are performed annually. Manual small incision cataract surgery(MSICS) and phacoemulsification are the preferred techniques for performing cataract surgeries.

In India majority of the cataract surgeries are performed by MSICS considering the cost and prevalence. Studies have shown that visual outcome and complication rate are similar in SICS and phacoemulsification. In all types of cataract surgeries there is bound to be some amount of corneal endothelial cell loss along with morphological and functional change.

In studying the effects of cataract surgery, it is essential to understand the anatomy and functions of the cornea and crystalline lens. One also needs to have a working knowledge of the investigations used in diagnosis of corneal pathologies

and techniques of cataract surgery. In the following sections, these details are presented in a brief manner.

REVIEW OF LITERATURE

SECTION I: THE CORNEA

The cornea is a transparent avascular structure with a convex outer surface which is smooth and concave inner surface. The cornea is covered anteriorly by the tear film and posteriorly it lies in contact with the aqueous humor. A highly vascularized limbus surrounds the whole circumference of the cornea, by acting as a source of pluripotent stem cell[3].Cornea measures about 11-12 mm horizontally and10-11mm vertically[4].The cornea measures about 0.5mm thickness in the center and gradually increases in thickness towards the periphery. Its refractive index is 1.376. Cornea is a asphericstructure, with the curvature being recorded as a aspherocylinder convex mirror, with central 3 mm being the optical zone of the cornea.

Cornea has various functions. First and foremost being maintenance of the transparency for the light rays to reach the retina, secondly being optical, by refracting light forming the principal refractive surface (74%,ie +43.25 dioptric power (D) of the total+63 D of the eye). The +43.25D is obtained not only from the cornea, it is a composition of various refractive components such as air-tear fluid, fluid- cornea interface and cornea –aqueous humor interface, with each of +44D, +5D, -6D respectively thus making cornea a major astigmatic source.

The optical properties of the cornea are maintained by its transparency, smooth surfaces, contour arrangement of corneal layers and refractive index of each interface in the tissue.

1. CORNEALANATOMY

Behind the pre-corneal tear film, cornea is histopathologically composed of 5 tissue layers

a) Epithelium
b) Bowman's layer
c) Stroma
d) Descemet's membrane
e) Endothelium

a. Epithelium

A good corneal optics requires a smooth surface, which is maintained by the corneal epithelium and healthy tear film. The corneal epithelium is made of stratified squamous non keratinized epithelium, being 50-90μm thick. This forms the smooth outer surface of the cornea along the ocular tear film. The epithelium makes up to 5% of the corneal thickness and is continuous with the conjunctival bulbar epithelium, with exception of goblet cells. It is formed by 5-6 layers of

nucleated cells. These cells attached to one another by Zonula occludens. Clarity of the cornea is due to tight packing of the epithelial cells, which contributes to the uniform refractive index.

The first two or three layers of the epithelium are polyhedral shaped cells and are placed wider and flat over the surface. There is no keratinization of this surface.

The second layer is umbrella shaped cells with oval nuclei. This layer has decreased organelles compare to basal layers.

The deeper layer is basal layer formed of basal cells which are 12μm with density of approximately 6000 cells /mm^2. These cells are columnar polygonal shaped cells with an oval nucleus. The basal layer acts as the fundamental layer of epithelium. Deeper layers are formed by continuous proliferation of perilimbal basal epithelial cells and these layers subsequently differentiate into superficial cells and are moved to the superficial layer. With maturation, these cells become coated with microvilli on their outermost surface and then desquamate into the tears. This process of differentiation takes about 7 - 14 days.

The cells of basal lamina are joined laterally to other basal cells and superficial to the umbrella cells by desmosomes and macula occludes. These tight junctions maintain the corneal transparency by acting as barrier function. The basement membrane of the basal cells is made of basal lamina synthesized by the

hemidesmosomal structures. It is an irregular layer which is thicker in the periphery compared to the center. The basal lamina has collagen and glycoproteins and helps in its attachment with the bowman's layer.

Epithelial cell loss is followed by cell repair. Within hours following insult, fibrin and neutrophils appear from the tear film. The epithelial cells flatten and components of adhesion complex , which are holding the epithelial cells are disrupted resulting in sliding of cells and compensation of loss[5]

b. Bowman's Layer (Anterior Limiting Layer)

Bowman's layer, the second layer of the cornea, is a homogenous a cellular layer, measuring 8-14μm thick, lies below to the basement membrane. Anterior surface of the bowman's is smooth layer and being attached to the lamina of basement membrane and posteriorly attached to that of the stroma. Bowman's layer consists of fine collagen fibrils. In the posterior part of the bowman's the layer of collagen fibrils intertwine and attach to the stromal lamellae. The compact nature of this layer provides resistance to trauma, both mechanical and infective nature. But once destroyed, bowman's layer does not regenerate

c. Stroma (Substantia Propria):

The stroma about 500μm thick, constitutes most of the thickness of the cornea. It is made of collagen lamellae and collagen fibrils, both of which are embedded in proteoglycan ground substance. Keratocytes, wandering macrophages, histocytes and few lymphocytes are present in the lamina, which helps in production of the ground substance for the stroma.

The central part of the corneal stroma has around 200 lamella throughout thickness, with density higher in anterior part compared to posterior[(6)]. Anterior lamella are short narrow sheets and are highly interwoven with oblique orientation and also insert into the bowman's layer[(7)]whereas the posterior lamella are long wide thick lamellae and are less interwoven and is interwoven at right angles

The collagen fibrils, are very thin compared to any other connective tissue. These fibrils help in maintaining transparency of the cornea. There are about 300-400 triple helical molecules on cross section of each fibril[(8)]. Type I and Type V fibrillar collagen, intertwined with type IV fibrillar collagen form the lamellar arrangement which is parallel to each other not only in the corneal plane but also in the scleral plane. These corneal collagen acts as principal component of load barring component for the cornea.

Proteoglycans is a gel based matrix in which the collagen fibrils and corneal stroma are embedded. The stromal fibers are regularly spaced with each other with the help of this proteoglycans, which reduces scattering of light and helps in transparency of cornea. This gel like structure helps in maintaining the transparency. It contains glycosaminoglycans (GAG), keratin sulphate, dermatin sulphate and chondratin sulphate. The adult cornea has decorin, lumican, keratocan and mimeca, types of proteoglycan.

The GAGs express a swelling pressure of 60 mm Hg in the stroma, thus making stroma swell up to few folds than its normal capacity. This causes alteration in the fibrillar arrangement, which in turn causes increased scattering of light and thus loss of transparency of cornea in corneal edema.

d. Descemet's Membrane:

Descemet's membrane is a true basement membrane, measuring around 3-4μm thick and it increases with age reaching up to 10-12μm in adulthood. Descemet's membrane is rich in type IV collagen like any other basement membrane.

e. Endothelium

It is made of hexagonal cells, closely interdigitated in a single layer. It lies posterior to the Descemet's membrane with density of around 6000cells/mm^2 at birth, which reduces 26% in the first year of life as the corneal surface increases

and again a fall of 26% is lost over the next half decade. This leads to maintenance of 2700-2900cells/mm^2 in adults.[9][10]

These cells seldom divide. The cell loss and the reduction of the cell count is maintained by the enlargement of the remaining cells, that is by polymegethism. This leads to alteration of cell diameter, which is smaller around 18-20μm in early life, becoming around 40 μm in later adult life. The endothelial cells are attached to the Descemet's membrane by hemidesmosomes and by tight junctions sideward. These linkages are calcium dependent and helps maintain the barrier function of endothelium. This helps endothelium to maintain the corneal transparency and integrity by active pump mechanisms. The high metabolic activity of the endothelium is maintained by the presence of large nucleus and numerous cytoplasmicorganelles, like mitochondria, ribosome's, rough and smooth endoplasmic reticulum, golgi apparatus.

Studies have proven that there is a gradual decrease in cell density in the endothelial layer associated with increasing age. (Figure 1).[11][12][13][14]

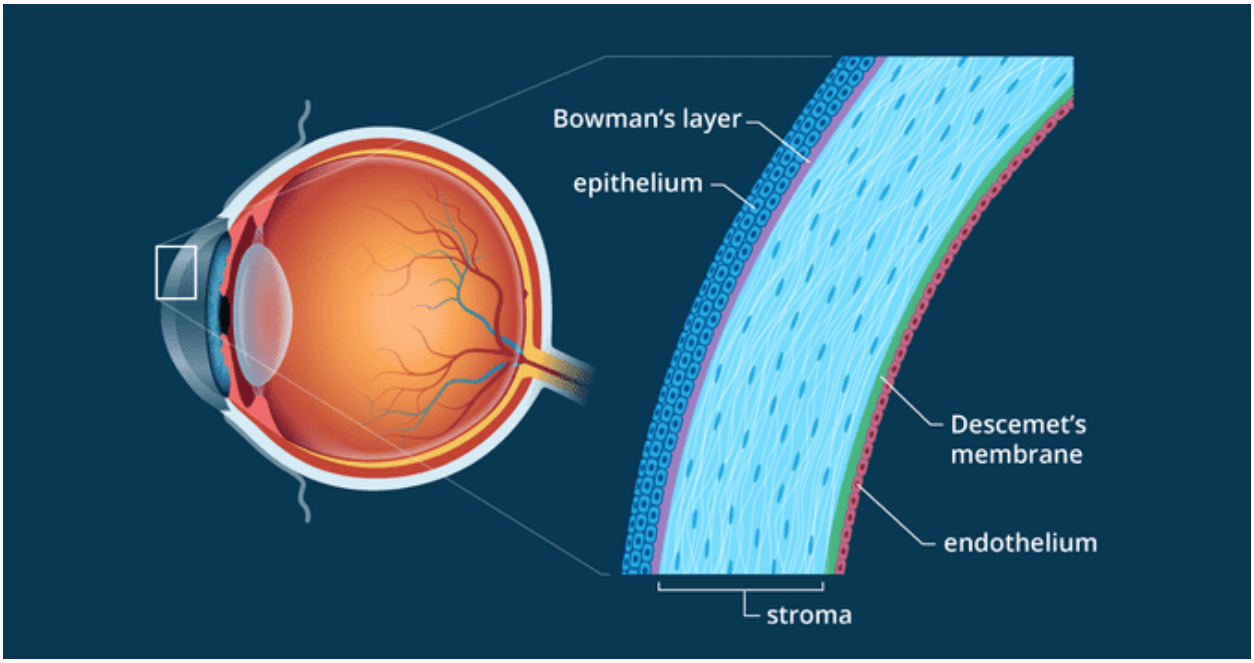


Figure-1: Layers Of Cornea

VASCULAR SYSTEM OF CORNEA:

The cornea is a vascular structure, but it obtains its nutrient from the blood derived products. These products help in corneal metabolism and healing. These source of nutrients reach the cornea from the blood components derived from the arcade of limbal region, formed by the anterior ciliary artery and facial branch of external carotid.

INNERVATION OF CORNEA:

Though an a vascular structure, cornea is highly innervated by the long posterior ciliary nerve, which is a branch of ophthalmic division of Trigerminal nerve. It

penetrates the cornea at the conjunctival, episcleral and scleral planes. These nerve endings lose their myelination, within a short distance from the corneal entry point. These nerve endings are of 300-400 times of more density compared to skin surface nerve endings.

The nerve fibers of the cornea, penetrate the corneal stroma at the periphery along the radial axis and then move on anteriorly, forming a subepithelial plexus, penetrate bowman's layer and terminate in the wing cells of epithelial layer.

2. CORNEAL PHYSIOLOGY

The physiological functions of the cornea are largely a function of its endothelium. The corneal endothelium is made up of various pumps, these help in flow of fluids and nutrients from the aqueous humor into the cornel layers. The basolateral layer of endothelium, consists of a Na^+ K^+ dependent ATPase that creates low intra cellular Na^+ and high intracellular K^+ . There are 2 more pumps in the basolateral side, Na^+/2 HCO_3^-cotransporteer and Cl^-/ HCO_3^- exchanger and Na^+/H^+ exchanger. The Na+/H+ exchanger loads the endothelium with $HCO3^-$ with removal of H^+ resulting in formation of HCO_3^-andCO_2, catalyzed by carbonic anhydrase II. TheCl^-/ HCO_3^-exchanger moves $HCO3^-$ from the cell and adds Cl[15][16](Figure 2).

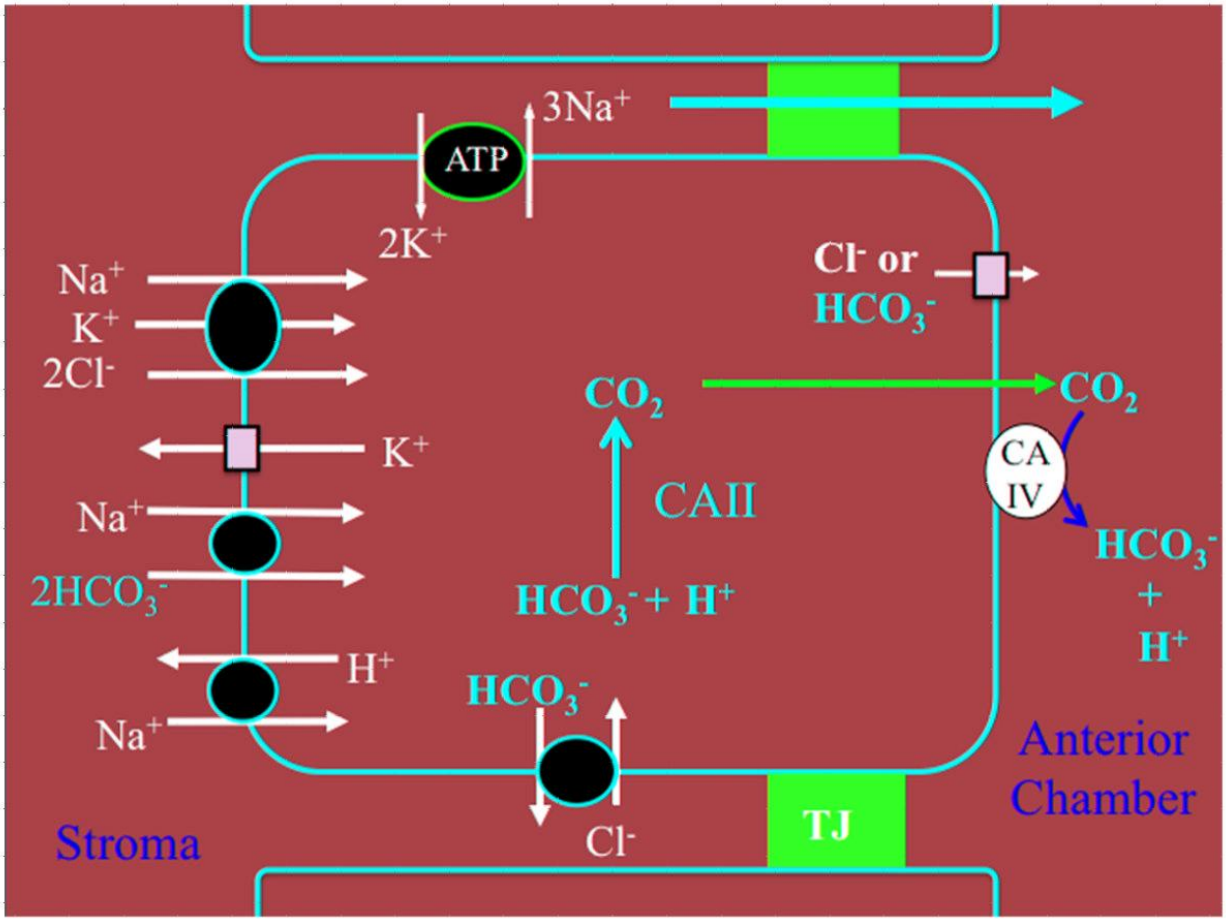


Figure -2: Illustration Of Ion Channels And Pumps On The Corneal Endothelium

3. CORNEAL BIOCHEMISTRY

Cornea is composed of 80%water and 20% solids. Epithelial cells constitutes the water, proteins, lipids and enzymes necessary for glycolysis, Krebs cycle. It also contains ATP 2000mmol/kg, glycogen10mg/g, glutathione10mg/dl and ascorbic acid 47-94mg/dl

Stroma constitutes main bulk of cornea, which is also formed by 80 % water and 20% solids. Extracellular collagen like glycosaminoglycans GAG (dermatin sulphate, chondratin sulphate A and keratin sulphates) or mucopolysaccharide forms 4% of the solid weight. These GAGs constitute to the stromal swelling pressure, that is they have the tendency to imbibe water and maintain corneal hydration. These soluble proteins of the stroma are albumin, immunoglobulin G, A and M and glycoproteins.

Glycolytic and Krebs pathway are present in the keratocytes of the stroma. Oxygen and glucose are the main nutrient source for the cornea. Oxygen is obtained from the diffusion of the tear film. Glucose is the primary metabolic substrate for the epithelium, stromal keratocytes and endothelium. The glucose is obtained from aqueous humor by carrier mediated mechanism through endothelium. Glucose transporters are present on both the apical and basolateral side of the endothelium. The glucose, via passive diffusion through stroma, reaches the epithelium.

80% of glucose utilized by the cornea is converted to lactate and it diffuses into aqueous through the endothelium.

The cornea is metabolically active layer, the metabolic activity in this layer takes place with the help of ATPs,

The 3 major biochemical pathways in cornea are:

1. Anaerobic glycolysis

2. Hexose Monophosphate shunt

3. Tricarboxylic acid pathway

Epithelium utilize the HMP shunt and breaks down approximately 35-65 % of the glucose. Under anaerobic condition that is via glycolysis and pentose phosphate shunt one molecule of glucose is converted into 2 molecules of lactic acid with 2 ATP, whereas in aerobic mechanism that is in Krebs cycle 1 molecule of glucose will utilize the pyruvic acid , producing oxygen and 36 ATP but this is very less in the stoma.

In somecases when there is decreased supply of oxygen to the cornea, the mechanism shifts from aerobic to anaerobic. The product of glycolysis, pyruvate is converted to lactic acid via anaerobic mechanism. This Lactic acid diffuses into the stroma resulting in stromal edema.

4. UNIQUE FEATURES OF THE CORNEA

CORNEAL TRANSPARENCY:

Corneal transparency is a very important feature of the cornea as it helps to maintain the clear path for light to travel and reach the neurosensory retina and formation of the image. The corneal transparency is maintained by the physical and physiological factors. The physical factors being that the arrangement of lamellae in the stroma and the physiological factor being the relative state of dehydration in

maintain the transparency. Alterations in this transparency can happen at various scenarios

Alteration of tear film happens due to various factors like , increased atmospheric exposure of the surface tear film, leads to alteration of tear film and decrease in oxygenation to the cornea. The alteration of tear film also happens in contact lens wear, prolonged use of contact lens wear causes decreased oxygen supply to the cornea

All these alterations in tear film lead to decrease in supply of oxygen to the cornea, which shifts the metabolism from aerobic to anaerobic, this metabolic alteration of cornea leads to accumulation of lactic acids, which leads to increased osmotic solute load, causing corneal edema or stromal acidosis causing endothelial pump failure.

The stroma continuously absorbs water from the aqueous via the endothelium. with the active transport of fluid in the basolateral pumps demonstrated in the endothelium helps in maintaining the corneal thickness by preventing the swelling of normal corneal stroma.

The transparency of cornea is also mainly maintained by the collagen fibrils, which have a regular and finer arrangement with homogeneity. Endothelium constantly pump out water from the cornea maintain the transparency, and homogeneity of

the corneal layers, preventing swelling and clouding[17]. The arrangement of stromal fibrils, which are embedded in the proteoglycan matrix is responsible for corneal transparency. The arrangement helps in reducing the scattering of light by destructive interface. The scattering of light rays decreases as ray passes from anterior to posterior layer, by being 1.401 at epithelium to 1.380 at the stroma. The lattice structure is so fine, compared to that of wavelength of light, thus helping in maintain the transparency of cornea.

Corneal transparency also depends on the relative state of dehydration. It is maintained by maintaining the stroma water content level. This is done with the help of intact epithelium and endothelium. Corneal hydration varies from anterior to posterior with increasing wetness closer to the endothelium and resistance of the movement of water laterally within the stroma.

ENDOTHELIAL PUMPS:

Na^+ K^+ dependent ATPase and Na^+/H^+ exchanger are present in the basolateral membrane of the endothelium. These are ion transport channels which help in maintain the corneal transparency, by preventing imbibition of water into the stroma. The Na^+ K^+ gradient, results in flow of Na^+ from the aqueous into the stroma and K^- into the opposite direction. Carbon dioxide also diffuses into the endothelial cell and there on combination with H_20 results in formation ofHCO_3^-.

ThisHCO_3^- is transported in to the aqueous, along with this HCO_3^- transport,H_20 is also transported into the aqueous.

Pump leak mechanism states that endothelium is capable of pumping fluid across the surface against pressure, where the stroma does not allow transport of water. It is suggested that any cell layer can actively transport fluids into a cell layer than into an open space

Therefore, it is evident that corneal transparency depends on lamellar collagen arrangement in the stroma and on proper endothelial function. Corneal decompensation and opacity occur when either of these is compromised. Accordingly, the treatment depends on which layer has been affected. Recent trends involve lamellar corneal grafting to optimize surgical and visual outcomes. The following surgeries are performed for specific indications:

a) Endothelial keratoplasty
b) Descemet's stripping with automated endothelial keratoplasty
c) Descemet's membrane endothelial keratoplasty

5. PATHOLOGICAL RESPONSESIN THE CORNEA

Cornea formed of 2 cellular layers, epithelium and endothelium. With each resting on the basement membrane that is epithelial basement membrane and Descemet's

membrane. These 2 layers sandwich the thin and thick a cellular and cellular connective tissue respectively.

The cornea can be subjected to variety of insults, response to these insults which can be grouped as 6 different categories of pathological response.

Each of these pathological responses are described as:

1. Defects – These are alteration in the corneal lining , it can be partial or complete, these defects usually are self-healing
2. Fibrosis and vascularization – these are the usual normal tissue repair mechanism employed by the body's defense mechanism
3. Edema and cyst – it is accumulation of fluid in between the cell spaces, which leads to alteration of the normal cellular morphology.
4. Inflammation and immune response - a starting of an pathological response, to a stimuli, causing activation of host and cellular immunity activation and finally acts as a repair process.
5. Deposits- materials getting deposited in each layer of the cornea, it may vary from exogenous and endogenous sources to degenerations and dystrophies.
6. Proliferation –
    a) Growth and maturation abnormality – hypertrophy, dysplasia, metaplasia, neoplasia

b) Ectopic migration

c) Stem cell deficiency

CHANGES IN THE ENDOTHELIUM:

Normal adult endothelium is 2500 cells/mm^3, with cell size of 250µm and a density of 500 cells/mm^2 remain clear. The adult endothelium does not divide under normal circumstances, but do divide when stimulated by injury. When endothelium is subjected to injury, the cells near to the site of injury participate to the healing.

Endothelium when subjected to defect, defect may be acute or chronic.

1. Acute
    a. accidental trauma
    b. surgical trauma – cataract surgery, most commonly in phacoemulsification and corneal transplant, in posterior lamellar endothelial keratoplasty
2. Chronic
    a. dystrophies involving the endothelium
    b. chronic irritation of endothelium by the anterior chamber IOL

Defect in the endothelium results in aqueous humor rush via the defect, resulting in formation of stromal and epithelial edema. The damaged endothelium is capable of

repairing itself with primarily with cell migration, cell division and hypertrophy. The damaged endothelium is healed by altering cell shape and size. Alteration happens by enlargement of the normal hexagonal cells. With healing normal number of hexagonal cells decrease as the hexagonal cell's near to the defect enlarge to fill it up. If the loss of endothelial cells loss continues, the remaining cells of the endothelium enlarge and flatten and try to maintain the corneal contour. But at one point cell loss is more than that of the capacity of the remaining cells to correct, resulting in stromal and epithelial edema, causing corneal decompensation

Six-sided cells are an indication of even distribution of membrane surface tension and of normal cells. The polygon that has greatest surface area relative to its perimeter is the hexagon. Thus, the most efficient cells hape to cover a given area is the hexagon; i.e. a perfect cornea should have 100% hexagons[18]

Maintenance of corneal endothelium happens with the tight junctions. These tight junctions resist flow of electrolytes and fluid into the endothelium. The most important factor for maintenance of corneal detergence is an active metabolic pump mechanism in the endothelium. These pump via active transport mechanism, makes fluid transport from corneal stroma into the aqueous humor. This process requires oxygen and energy in the form of adenosine triphosphate. Deprivation of oxygen or ATPs result in, hypoxiaof cornea, which results in corneal edema.

The corneal edema is attributed to either leak or imbibition of water from across the anterior chamber via endothelium. Water reflex across the epithelium is highly inconspicuous because of the tight junctions in it. Whereas the water flow from the anterior chamber to cornea via endothelium, due to capacity of stroma to imbibe water. Imbibition of water happens until stroma reaches a swelling pressure. For maintenance of transparent cornea, water influx into the stroma is matched with pump out from the endothelium this forms the pump leak mechanism[19]

The endothelial layer of the cornea has specialized pumps, that help in maintain the integrity of the layer. These pumps regulate fluid and ion transport under normal conditions to the cornea. These pumps also transport fluid from the corneal stroma to aqueous. This process requires oxygen and energy in the form of ATP. The depletion of these sources leads to alteration of pumps and corneal edema. Dactinomycin, ouabain and oligomycin are potent inhibitors which are present in the endothelium. Treatment with ouabain causes stromal edema[20][21]

CAUSES OF ENDOTHELIAL EDEMA:

Primary endothelial failure:

1. Congenital hereditary endothelial dystrophy
2. Fuchs dystrophy
3. Iridocorneal endothelial syndrome

4. Posterior polymorphous endothelial dystrophy

Secondary endothelial failure

1. Acute or chronic trauma
2. Chemical
3. Inflammatory
4. Hypoxia

Normal endothelial edema is caused by raised IOP and failure of endothelial pumps. The endothelium unlike the epithelium has no regenerating capacity. Thus cell damage caused by any of these factors to endothelium results in enlargement and migration of the remaining endothelial cells which are located near to the damage site.

Corneal endothelial decompensation results in blurred vision, discomfort and severe pain. Although it can be managed with medical treatment, the main stay of treatment is corneal transplantation. Selective endothelial keratoplasty has become popular in corneal endothelial dysfunction management owing to quicker visual rehabilitation and lower complication rate.

6. ENDOTHELIAL CHANGES AFTER CATARACT SURGERY

Endothelial cell loss depending upon the surgery performed. The variation is mostly dependent on the site of manipulation under the cornea. In small incision corneal damage is observed at the incision site and peripherally at the side port site. Inaba et al conducted a study on comparison of endothelial loss in intracapsular cataract extraction without IOL implantation. The results of the study state that there is decrease in post operative endothelial cell loss in 2 weeks in all quadrant. Whereas on follow up of 6 months, the loss over the surgical incision was reduced more compared to the other areas.[22]The same type of results was noted for extracapsular cataract extraction as well.[23]

7. INVESTIGATIONS FOR CORNEAL PATHOLOGY

PACHYMETRY:

Pachymetry is measurement of corneal thickness, which is an indicator of corneal endothelium[24]. It is derived from Greek word pachy, which means thick and metry being measurement. There are four various methods employed in measurement of corneal thickness

- ***a)*** Optical pachymetry
- ***b)*** Ultrasonic pachymetry
- ***c)*** Specular pachymetry
- ***d)*** Anterior segment optical coherence tomography (OCT)

a. Optical Pachymetry:

Technique used before advent of ultrasonic pachymetry. This instrument is attached to the slit lamp. By alignment of the slit image, the central corneal thickness is obtained

b. Ultrasonic Pachymetry:

Ultrasonic pachymertey was invented by a group of scientists including Wallace, DavidAFeldon, Steven whiting, Douglas in 1985. At present the most widely employed method for measuring pachymetry, is hand held ultrasound pachymetry. It operates at a frequency of 20-5- MHz, emits short acoustic pulses, these pulses reflect from anterior and posterior surface of cornea. From the time of flight of reflections from the corneal surface, thickness of cornea is calculated and the accepted speed of sound in the cornea of 1636–1640 m/s[25].

From the return of the pulse from the cornea, corneal thickness is calculated with formula

$$\text{Corneal thickness} = \frac{\text{total time travel} * \text{speed of sound in the cornea}}{2} \quad (26)$$

c. Anterior Segment OCT:

Oct measures the cornea layers by the principal of optical backscattering of light.

As light travels faster than sound, the time of returning of light to OCT is measured by low coherence interferometry.

This is a noncontact method compared to ultrasonic B scan, though both follow the same principal. Image resolution is less than or equal to 10µm, compared to UBM in which image measurement is 35-70µm.

A study conducted by Wirbelauer et al stated that comparing the central corneal measurements with OCTand pachymetry , a high degree of acceptance was noted with pachymetry and OCT . Thus making it an alternative to pachymetry[27].

d. Specular Microscopy:

The corneal endothelium was visualized by Vogt in 1918. Then specular was later then identified by David Maurice in 1960s for corneal epithelium analysis[28].Then specular was further modified for easy and conventional use by Bourne and Kaufmann.[29].The corneal endothelial cell layer is analyzed with specular microscopy. Specular microscopy is one of the non-invasive techniques to access the structure and function of the corneal endothelium. Oldest method employed in measuring corneal thickness. The specular reflex occurs ata smooth surfaced

interface of two refractive indices, with light from cornea having angle of incidence equal to angle of reflection to the observer. The endothelial cells are seen because of the varying refractive index, between the endothelium and aqueous. That is refractive index of endothelial cells is 1.336 times greater and that of aqueous humor, thus reflecting the projected light.

Further theories also state that the light reflex is caused by the proximity of the two concentric surfaces, i.e. the epithelium and the endothelium. The epithelial surface is highly reflective because of the large refractive index difference between air and the tear/epithelium. As the beam of light passes through the cornea it is reflected off the tear/epithelium interface and endothelial interface. The viewable specular area is a compromise between the beam width and the corneal thickness.

The Specular microscopy can be used to view the corneal stroma, endothelium and lens depending on the instrument used[(30)].

In recently a study conducted on comparing various methods to measure corneal thickness using non contact specular microscopy, ultrasonic, orbscan and contact specular microscopy. The mean thickness values differed significantly, and increased thickness was observed with the noncontact specular microscopic. The results indicate that these instruments cannot be simply used interchangeably[(31)].

Figure 3: Specular Microscopy

SPECULAR MICROSCOPY FOR MORPHOLOGY:

Endothelial cell loss happens due to various factors such as disease, trauma, chemical toxicity, post intraocular surgery. Any pathology that causes damage to the endothelial cell causes it to decrease in density meanwhile with an increase in cell surface area.

The endothelial cell alteration is studied using specular under:

1. cell surface area in μm ± standard deviation in μm^2
2. coefficient of variation of cell surface (CV)

a. Cell Density:

Corneal endothelium consists of 130μm^2 cells in the surface. Endothelial cell density reduces with age as age progresses. At birth endothelial cell density is around 6000 cells/mm^2 which gradually reduces with 26% over the course of years and reach 3500-4000 cells/mm^2 by 4 years of age[32].On reaching the adult life it furthermore reduces to 2400-3000 cells/mm^2.

b. Polymegethism:

It Is the Description of variation in cell surface area. When there is alteration in the hexagonal shape of the cell, resulting in enlargement of the nearby cell structures causing alteration of the cell surface area. The cell density has an inverse

relationship with the standard deviation of cell surface area. Thus and increased polymegethism leads to decrease in average cell surface area.

c. Cell Morphology:

Hexagonal, this structural arrangement has equally distributed surface area and tension .These hexagonal shaped cells have equal sized sides with each at an angle of 120° with each other[33].

Normal cornea is arranged with equally sized hexagonal cells. Any alteration in normal cornea would lead to alteration in the hexagonal shape of the cells.

Any damage to endothelial cell is compensated by the enlargement of nearby endothelial cells which result in alteration of hexagonal cells at that area.

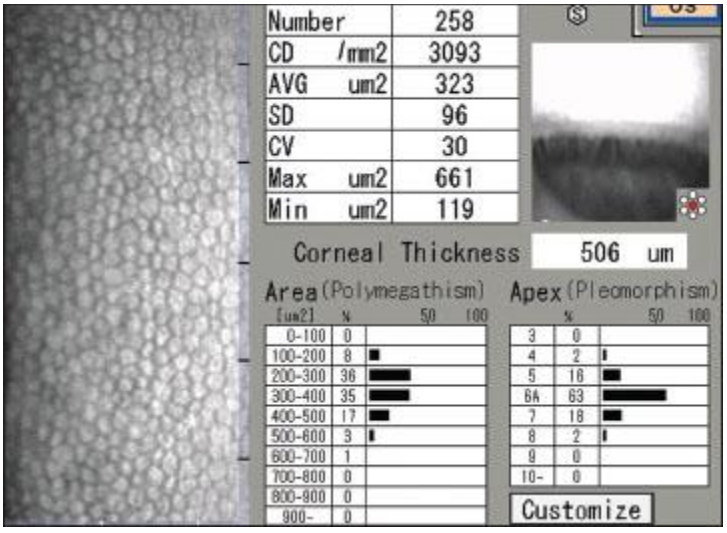


Figure 4: Corneal Endothelial Analysis In Specular

SECTION II: CRYSTALLINE LENS

The human crystalline lens isa asymmetric oblate spheroid, avascular structure, that lack nerves which is a transparent structure, which is biconvex in nature.

It lies anterior to the vitreous body and posterior to the iris and is suspended by the zonules of Zinn. The anterior surface is in contact with the aqueous humor and posterior surface in contact with vitreous. It lies in the vitreous in a saucer shaped depression called patella fossa. These are delicate fibrils that attach the lens to the ciliary body. The lens has no blood supply and it receives its nutrient only from the aqueous humor.

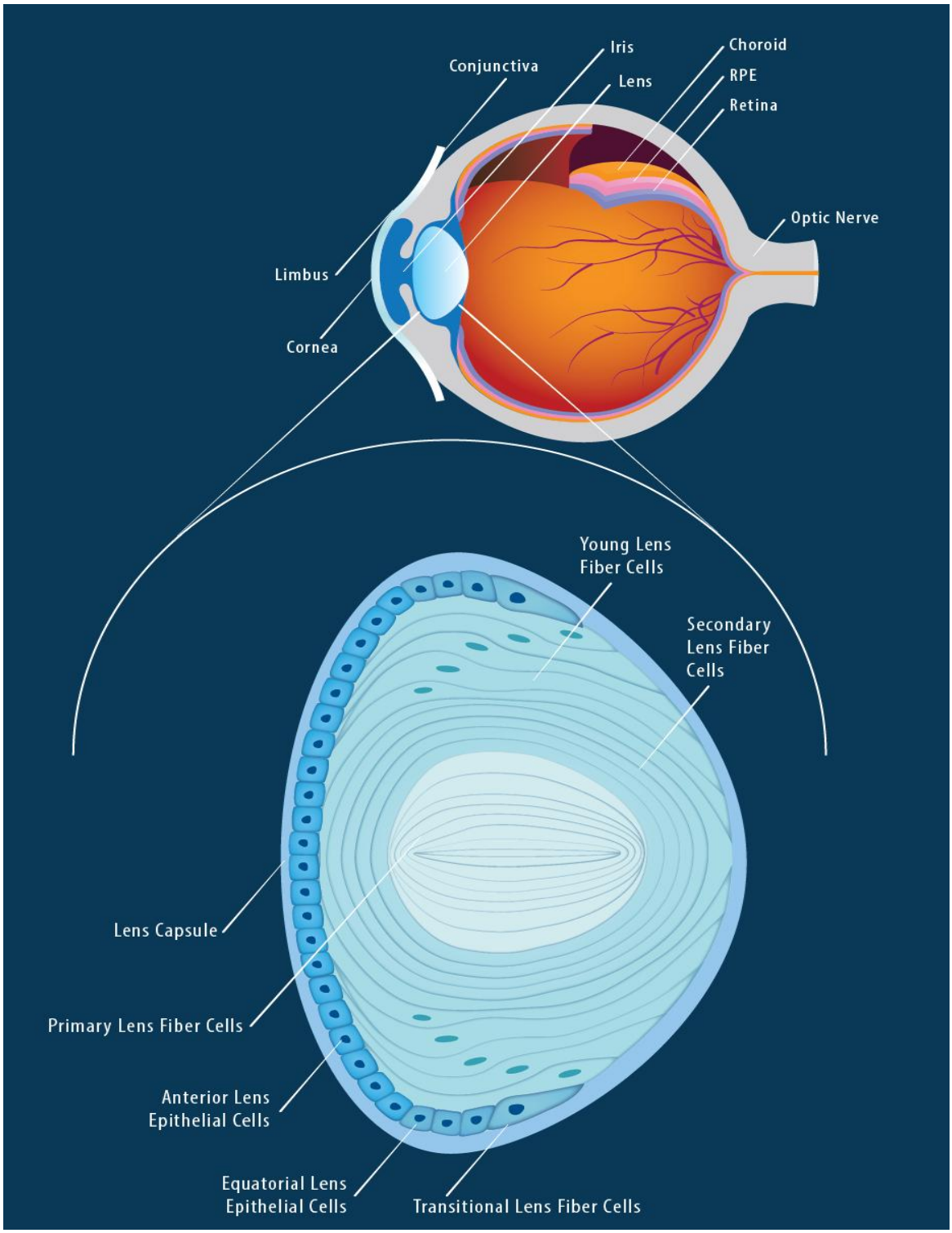


Figure 5: Anatomy Of Crystalline Lens

1. CRYSTALLINE LENS ANATOMY

The lens diameter is around 9-10 mm. the thickness of lens varies with age, It is around 3.5 mm at birth and to 5 mm at older age. As the thickness weight of the lens also varies 135mg upto adolescent and 255 mg from adolescence to old age.

The crystalline lens has an anterior and posterior surface. They are joined to each other by an imaginary line called optical axis. The anterior surface is less convex compared to the posterior surface. The refractive index of the lens 1.39, with total dioptre power of 15-16D.

Histologically, the crystalline lens components are

1. Lens capsule
2. Lens epithelium
3. Lens substance

a. Lens Capsule:

It is a acellular thin transparent hyaline membrane, made of type IV collagen surrounding the anterior and posterior surface of the lens. It is synthesized by the lens epithelium anteriorly and lens fibers posterior. The outer layer of lens capsule is zonular lamella and it helps in attaching lens strongly to the zonules which in turn attached to the ciliary body. Capsule is thick at the anterior surface compared

to the posterior surface. Capsule is thickest at pre-equator regions (14 μ) andthinnest at the posterior pole (3 μ).

b. Anterior Epithelium:

It has a single layer of cuboidal cells lying immediately beneath the anterior capsule**.** Anterior epithelial layer is metabolically active including the biosynthesis of DNA, RNA, protein, and lipid; they also generate adenosine triphosphate to meet the energy demands of the lens. These cells undergo mitosis and that is how they become columnar layer become from cuboidal at the equatorial region, by active dividing and elongation. There is no posterior epithelium

c. Lens Fibres:

The epithelial layer of the lens, becomes columnar at the periphery. These columnar epithelial cells elongate even more to form the lens fibres. These fibres are formed throughout the life and they are compactly arranged. These fibres move towards the centre as the age increases thus forming the nucleus and cortex of the lens. The arrangement is as that the foetal nucleus surrounds the embryonic nucleus. They terminate into two Y shaped sutures. Anterior upright Y and posterior inverted Y. The lens fibres are laid down in a dendrite pattern throughout lifetime. They are laid down and the oldest fibres in the centre and the newer fibres surrounding it. It contains different zones depending on the period of development.

Nucleus is the innermost part of central embryonic nucleus. The outer layers of lens being foetal, infantile, adult respectively surrounding the embryonic part. Cortex is formed by the newest fibres and are in the peripheral most part of the lens

2. AGE RELATED LENTICULAR CHANGES

The main age related change of lens is cataractous change. As the ageing process, epithelial cells become flatter with flat nuclei, and the lens increases with density and thickness along thus decrease in accommodation. As aging process, there is increase in mass and dimension of lens compared to younger age. This is because of proliferation of lens epithelial cells.

The oldest lens fibres migrate and are found in the centre of the lens behind the anterior pole. The newer formed cells are formed around this central part, thus oldest fibres are in the centre and newer one at the periphery. As aging process epithelial cells become falter with flattened nuclei, increase in density

Lens fibres show loss in plasma membrane and cytoskeleton component with age. The biochemical properties such as total level of proteins, amino acids and potassium are altered along with increased concentration of sodium. The cholesterol-phospholipid ratios of the plasma membrane alter in plasma membrane throughout life causing decrease in membrane fluidity and increase in structural

integrity. This causes coagulation of proteins causing opacification of cortex. This process increases with age, greater in nuclear, resulting in nuclear sclerosis

The nuclear sclerosis at middle age is yellowish and it usually does not cause any visual impairment. As aging progresses an excessive amount of scattering and yellowing is called nuclear cataract. In case of cortical cataract, it is caused due to local disruption of structure of mature lens fibre cells. Alteration in cytoskeletal component, increases the number of furrowed membranes and microvilli on fibre surface. This alteration results in formation of ruptures in the cortical fibres of the crystalline lens resulting in cortical cataract.

3. INDICATIONS FOR CRYSTALLINE LENS REMOVAL

Removal of crystalline lens is performed for many indications. They may be grouped under two heads. They are:

1. Optical
2. Medical

OPTICAL INDICATION

1. Lenticular opacification (cataract)

MEDICAL INDICATIONS

1. Lenticular malformation
    a. Coloboma
    b. Lenticonus
    c. Lentiglobus
    d. Spherophakia
2. Lenticular malposition
    a. Subluxation
    b. Dislocation
3. Lens-induced inflammation
    a. Phacolytic glaucoma.
    b. Phacomorphic glaucoma
    c. Phacotoxic uveitis (phacoanaphylaxis)
4. Lenticular tumor
    a. Epithelioma.
    b. Epitheliocarcinoma
5. Facilitatory (surgical access)
    a. Vitreous base
    b. Ciliary body
    c. Ora serrata

The most common indication for removal of crystalline lens is optical rehabilitation of cataract.

4. METHODS OF CATARACT SURGERY

There are various methods employed for cataract extraction.They range from the ancient technique of couching to the modern femtosecond laser cataract surgery. A short summary of the different techniques that are employed is as follows:

1. Lens repositioning (‘couching’)
2. Extracapsular
3. Intracapsular

a. Physical (instrumental) zonulysis

b. Pharmacological (enzymatic) zonulysis

4. Lens removal

    - Partial (extracapsular)

a. Anterior capsulotomy / capsulectomy

    i. Discontinuous

    ii. Continuous (capsulorrhexis)

    iii. Linear

b. Nucleus removal

    i. Assembled delivery (large incision)

1. Expression (‘push’)
2. Extraction (‘pull’)

ii. Disassembled extraction

1. Phacosection
2. Phacoemulsification-aspiration

a. Ultrasound

i. linear

ii. torsional

b. Laser

c. Water jet

d. Impeller

- Total (intracapsular)

a. Capsule forceps

b. Suction erysiphake

c. Cryoextraction

5. Cortex removal

i. Irrigation

ii. Aspiration[34]

5. A BRIEF HISTORY OF CATARACT SURGERY:

Since ancient of times, cataract has been a dominant cause of vision loss. The removal of the crystalline lens has been standard care of treatment since the dawn of time. Cataract surgery has undergone hundreds of innovative technologies in the recent years. Techniques have be developed and abandoned over the years. The first surgical removal of lens is dated back around 2000 years, by an Indian scientist names Sushruta samhitha, couching a method implied in dislodging the crystalline lens with a needle[35].A needle was introduced into the anterior chamber and the capsule was disrupted, causing lens hydration and absorption of lens. Later stages as couching was considered dangerous and causing blindness at higher rate, newer methods were developed by European scientists. In 1895, Colonel Henry Smith, implicated a method in which he loosened the zonules of the lens by applying external pressure on the inferior cornea with muscle hook. He disclosed the lens by tumbling as the zonules were still attached at the superior quadrant[36].

In 1902 a suction device for lifting of the lens out of the eye[37].Removal of cataract surgery by suction method , using vacuum pump with erysiphake handle for suction and removal of cataract and also a method for cataract extraction with chemical alpha chymotrpsin causing zonular dialysis was employed[38].

Another method was invention of a cryoextractor , with no pressure a small cold probe was applied to the surface of the lens forming ice ball ,causing union of all the lens components and extraction of lens[39].

In 1949 Harold Ridley performed the first artificial lens implantation using ICCE, but as there was no support for placement of lens in ICCE, so the modification to ECCE was started on from then

Demerits of ICCE, which made the shift of ECCE were

1. Large incision, which led to complications such as delayed wound healing, iris, vitreous incarceration, suture abscess
2. Cataractous lens extraction can touch the cornea and causes endothelial damage

On shifting to ECCE, Cornelius Binkhorst of Holland, refined ECCE, using toothed forceps to remove the anterior capsule, and aspiration of soft nucleus and expressed hard nucleus followed with irrigation and aspiration of cortex

By 1967,Kelman modified and established the ultrasound method for nucleus delivery followed by the aspiration irrigation of cortex technique . this led to the advent of phacoemulsification[40].

Manual small incision cataract surgery (MSICS) a very common and accepted eye surgery performed all over the world with low cost making it a not burdensome technique . MSICS is preferred by many surgeons over phacoemulsification in hard brown or black cataracts.

6. ANESTHESIA FOR CATARACT SURGERY

Different types of anesthesia have been employed in the cataract surgery. The retrobulbar and peribulbar anesthetic techniques can be supplemented with facial blocks as well.

1. Retro bulbar anesthesia gives best ocular akinesis and ocular anesthesia. It is injection of local anesthetic agent in the intra conal space, the area behind the globe of the eye that is between the optic nerve and extra ocular muscle using Atkinson or retro bulbar needle (23- or 25-gauge and 1.5 inches (38 mm) in length)but retro bulbar injection has high level of complications include retrobulbar hemorrhage, globe perforation, optic nerve injury, extra ocular muscle toxicity
2. Peribulbar on the other hand, has a slow and minimally effective compared to retro bulbar, but comes with fewer complications
3. Topical anesthesia is at present being widely employed for phacoemulsification with foldable IOL implantation. As this method

includes no lid spasm patient can leave the operation theatre with no bandage. But even this method comes with few complications like increased ocular motility while performing surgery, blephrospasm and pain discomfort[41].

4. Intracameral lidocaine 1% or 2% can be used in addition with topical anesthesia for phacoemulsification with foldable IOL[42].
5. Subconjunctival lignocaine can be used in as an addition with topical anesthesia, in patient who have pain even with intracameral and topical anesthesia

7. SURGICAL STEPS OF MANUAL SMALL INCISION CATARACT SURGERY (MSICS)

BRIDLE SUTURE

Bridle sutures are applied over any one or two of the extraocular muscle to obtain transportability and fixation of the globe during surgery. It is also used for applying counter force in nucleus delivery in MSICS along with tunneling. It is done to the muscle near the site of incision. It is done by rotation of globe with muscle hook, and catching the muscle with Dastoor Superior Rectus Forceps and with at the insertion of the suture below the muscle. This step includes scleral perforation as a complication.

CONJUNCTIVAL FLAP

In MSCIS, a fornix based conjunctival flap is raised. a small conjunctival button hole like incision is made radially to the cornea. The conjunctiva is separated from the underlying tenons capsule in both directions up to about 4mm from the limbus using a conjunctival scissors. The incision is extended now along the limbus circumferentially for about 8mm length. Thus, raising a conjunctival flap of 8*4mm

SCLEROCORNEAL TUNNEL

Paul ernest was the first to describe the sclerocorneal tunnel with internal corneal lip, to prevent the aqueous seeping from the anterior chamber. The three-step internal corneal lip incision consists of perpendicular incision through the sclera, a horizontal incision through the clear cornea and sclera and angelled beveled incision into the clear anterior chamber. Each of these steps acts as a plane, forming a three planar incision. Advantages of this incision is, in case of any emergency like interoperative collapse of chroidal hemorrhage the eye can be closed as such without any suturing. Surgery can be done once the emergency situation is dealt with. This incision also has a decrease incidence of iris prolapse, faster wound healing and no suture requirement as it being a self-sealing wound.

The ideal location for this incision is 2-3 mm from the limbus with one third thickness in the sclera which is obtained with a crescent or diamond blade. The sclera corneal tunnel is obtained by wriggling with bevel up crescent blade with tip raised an heal depressed along the incision length.

The internal corneal incision is done with a keratome of sharp 3.2mm. The heal of keratome is raised resulting in a dimple on corneal surface. The keratome is then advanced into the corneal plane causing entry into the anterior chamber

Side port:

It is performed before the internal corneal incision; it is made at 10'0 clock position perpendicular to the tunnel. The side port is used for viscoelastic injection to maintain eyeball. Sometimes it can also be used for cortex aspiration and reforming anterior chamber

CAPSULAR STAINING

It is employed when red reflex is absent and performing a Continuous curvilinear capsulorhexis is difficult. It is done using one of the following, trypan blue 0.1%,[43][44][45]indocyanine green 0.5% units or sodiumfluorescein 0.25% units. The dye can be injected either subcapsular, under the airbubble or under the viscoelastic.

CAPSULOTOMY

It is a procedure in which an incision is made on the capsule of the crystalline lens of the eye. The normal crystalline lens is 9 mm in equatorial region, with zonular adhesionsin 1.5mm on the anterior surface. Thus capsular opening is made in the zonular free area 5.5-6mm in the centre. Capsulotomy can be performed with various techniques

a) Can opener capsulotomy
b) Continuous curvilinear capsulorhexis (CCC)
c) Envelop capsulotomy

Continuous curvilinear capsulorhexis most commonly performed and preferred capsulotomy procedure in both MSCICS and phacoemulsification .With the help of a good CCC the nucleus can easily prolapsed from the bag and IOL can be easily placed inside the bag with minimum damage to the capsule. This procedure can be done with either a bend 26G needle or with utarata or caporessi forceps. The steps involve first an incision over the capsule at the center and a capsular flap is raised. The flap is enrolled with the cystitome and capsulorhexis is created with either shearing or ripping force. The rhexis is completed outside in.

Can opener capsulotomy is performed where CCC cannot be or difficult to perform that is for mature cataracts with small pupils, grade III or grade IV nuclear

sclerosis. This is done under viscoelastic cover, to prevent corneal damage. A bent 26 G needle is used, needle is bend a 70 degrees at hub and 90 degree at bevel. Multiple radial cuts or punctures made over the capsule. Nearly 60 cuts with 15 in each quadrant is made, these are made equatorially to avoid damage to zonules. This technique is prone for tears in anterior capsule which may get attached to the simcoe canula during aspiration.

Envelop ecapsulotomy is another technique that is ideal for morgagnian cataracts.

HYDROPROCEUDRES

It is removal of nucleus from the cortex, epinuclus and cortex without zonular loss.

Two techniques are employed

a) Hydrodissection
b) Hydrodelineation

Hydrodissection is separation of cortex from lens capsule by using balanced salt solution (BSS)or ringer lactate(RL). It is done using 2 techniques cortical cleaving hydrodissection and conventional hydrodissection. Cortical cleaving hydrodissection is done by advancing the hydro cannula 1 mm under the anterior capsule and with steady flow of BSS into the lens results in separation of cortex and capsule. The dissection can be visualized by a wave. This fluid pass behind the

equator, posterior pole of the nucleus and cortex and reach the other end of equator thus separating the capsule and cortex in all zones.

Hydrodelineation debulking nucleus between epinucleus and nucleus using fluid the simcoe canulae is used to inject the BSS/RL into the cortex and the nucleus separating both.

PROPLAPSE OF THE NUCLEUS:

After a satisfying hydrodissection , nucleus lifts and tilts into the anterior chamber . the simcoe canula is moved under the rhexis and fluid is injected and thus resulting in prolapsed of the nucleus into the anterior chamber . If this fails to move out the whole nucleus, a sinskey hook is used to remove the nucleus out of the bag.

NUCLEUS DELIVERY:

There are various method employed in delivery of nucleus and over the years these step have evolved

In SICS, the nucleus is brought out of the capsular bag into the anterior chamber and extracted outside the eye using and one of the techniques

a) Blumenthal`s method
b) Ruit technique
c) Malik technique

d) Phacosandwich orphacosection.

e) Phacofracture technique

f) Fish hook technique

a. Blumenthal Technique

The Blumenthal's ‘Mininuc’ technique states the removal of nucleus through the 5 to 7 mm scleral or limbal incision. Firstly the bridle suture is applied and conjunctival flap is created. A 5-7mm sclerocorneal tunnel created. Two small entries are made using a 19 or 20G microvitreoretinal (MVR) knife adjacent to the limbus in the cornea. The side port at 10 o'clock can be used for performing capsulotomy, hydrodissection, nuclear manipulation, aspiration of cortex and dialling of intraocular lens (IOL) in the bag. Another port is created for introducing the anterior chamber maintainer (ACM) into the anterior chamber connected to the balanced salt solution (BSS) bottle 50 to 60 cm above the eye for building up sufficient hydropressure. A CCC under viscoelastic or canopener under fluid cover is done. Hydrodissection and hydrodelination are done, thus separating the nucleus. The free nucleus is rotated and lifted out of the bag. The nucleus is mounted on lens guide and is between nucleus and iris. The ACM is on flow and applied over the lens guide. The nucleus moves and get engaged into the ACM, and with increase in height of the BSS bottle, the nucleus removal is fastened.

This continuous flow from ACM to anterior chamber keeps the eye under positive pressure physiological state besides clearing the chamber of cortex, blood and pigments offering excellent visualization[46].

b. Ruit Technique

After administration of peribulbar anesthesia, and prepped with iodine based antiseptic and drapes laden, superior rectus bridle suture is placed. A fornix based conjunctival flap is created 10-2'o clock position. Exposure of the bare sclera and diathermy used to blanch the vessels. A sclerocorneal tunnel is made and a tissue plane parallel to the incision is made extending upto and into the cornea. A triangular capsulotomy falp is made at 12'0 clock position with 26G Needle. In cases of immature cataract, irrigation fluid is injected into the lens to separate the nucleus from other lens components and the nucleus is prolapsed into the anterior chamber. In cases of mature cataract hydro dissection is not employed, just by tilting and rotating the nucleus is delivered into the anterior chamber. The nucleus can be delivered from the anterior chamber either with simcoe canula, creating hydrostatic pressure or with irrigation vectis creating the same. Air is injected into the anterior chamber. A polymethyl methacrylate intraocular lens is passed into the eye and placed in the bag. Using the Simcoe cannula anterior chamber air is removed and replaced with irrigation fluid. Subconjunctival injection of antibiotic and steroid is given just above the cut edge of conjunctiva.

c. Malik`s Technique

Under local peribulbar anesthesia, after painting and draped with povidoneiodine. Conjunctival flap raised and sclerocorneal tunnel is created, with the size depending on the nucleus stage and size. Two sided ports are then made with microvitreoretinal blade, with one at 10o clock and other at 5 o clock in case of right eye and 7o clock in case of left eye, for anterior chamber maintainer fixation. Capsulotomy is performed followed with hydrodissection with the prolapsed of nucleus into the anterior chamber. ACM is attached to the a syringe containing 2% hydroxy methylcellulose (HPMC) and is injected into the anterior chamber. As the pressure of the anterior chamber increases, the nucleus progresses towards the section. the internal opening is first enlarged using a keratome. With pressure given over the inner lip of the section the nucleus is delivered[47]

d. Phacosandwich:

Luther L Fry first describe this technique in 1985. It can be performed in incision sizes I 5.5mm-6mm. In phacosandwich, a vectis is placed below the nucleus. The nucleus is sandwiched between the vectis and Sinskys hook and the nucleus is removed being sandwiched between the vectis and Sinskys hook

e. Phacofracture:

In phaco fracture the manual fracturing of nucleus. This technique is employedfor soft and mild hard cataracts. It is done using various methods

1. Phacofracture with bisector
2. Nucleus trisector
3. Phacofracture at exit of tunnel
4. Phacofracture with wire loop
5. Phacosalute and fracture

Phacofracture with wire loop most commonly employed . Vectis is applied below the nucleus and Sinski is placed above the nucleus. Vectis and Sinskys hook are moved towards each other, fragmenting the nucleus, the separated parts are removed with forceps

f. Fish Hook Technique:

A 30 G disposable needle is bent in fish hook form and entered into the anterior chamber with side way stilt. Using this hook, nucleus is hooked and is slided out with mild pressure

REMOVAL OF EPINUCLEUS:

After removal of the nucleus in any of the above stated techniques. The retained epinucleus can be either aspirated with simcoe or removed with viscoelastic injection into the anterior chamber. They can also be removed by minimal pressure on the posterior scleral lip of wound

CORTICAL ASPIRATION:

Removal of cortex can either be by aspiration or by viscolestic. In case of intact epiucleus it is flipped out of the bag with irrigation cannula. The cannula is placed in the bag and irrigated lifting the epinucleus outside into the anterior chamber. This is expressed out by depressing the scleral lip.

This can also be done by viscoelastic, that is viscodisection. Viscoelastic is injected into or under the capsular rim, between capsular and cortex. Thus separating the epinuleus and prolapsing it into the anterior chamber. The prolapsed epinucleus can be extracted through the incision

IOL IMPLANTATION:

In 1949, Sir Harold Ridley implanted the first Intra ocular lens (IOL) at Saint Thomas' Hospital in London[48].

Depending upon the size of the wound, IOL size is chosen 6mm/6.5mm rigid Polymethylmethacrylate (PMMA)is placed in the bag

The bag is filled with viscoelastic, IOL is held with Shepards or Kratz forceps and passed through the tunnel, IOL is tilted upward while entering the anterior chamber and made horizontal after entering anterior chamber. The leading haptic is now pushed under the rhexis, once leading haptic is inside the bag the forceps is released and lens is dialed into the bag in anticlockwise direction by Sinskis hook. After IOL placed, thorough was is given to remove the remaining viscoelastic.

WOUND CLOSURE:

A good sclerocorneal tunnel is self sealing. The side port sealed with stroma hydration. The conjunctiva is apposed back and cauterized.

A subconjunctival injection of dexamethasone 2mg (0.3ml) is given and eye is patched

8. STEPS OF PHACOEMULSIFICATION SURGERY

Phacoemulsification (phaco) an exemplary technique developed by Kelmer in 1967[(49)]. It employs an ultrasonically driven tip to fragment the nucleus and emulsify them. This is achieved through a surgeon controlled automated aspiration system. Earlier there were problems with phacoemulsification needle as related to

the level of proximity of need with the cornea, later this problem was conquered with the invention of coaxial irrigation sleeve. Even though with the invention of co-axial sleeve, the incision created was large as to fit a rigid IOL. This was later overcome by Mazzocco who developed and placed foldable IOL made of silicone.[50]

Foldable IOLs became a ground breaking development in field of cataract surgery causing shift from large to small incision. Similar to conventional surgery, pupil is pharmacologically dilated and mostly a topical anesthesia is applied. Initial steps are similar to MSICS. A bridle suture is placed and a conjunctival flap is raised.

CLEAR CORNEAL INCISION:

From this step phacoemulsification and MMSICS vary Globe fixation is obtained by using fixation rings or toothed forceps are used instead of bridle suture. clear corneal incision is mostly preferred for phacoemulsification. A small 2.5-2.8 mm clear corneal incision is made superior or temporal or at steepest corneal meridian. There are various methods of clear corneal

1. Multiplanar incision
2. Near clear incision

Multiplanar incision invented by Langermann, a diamond knife is used to create a vertical groove in the cornea, perpendicular to corneal surface. Another groove is

created tangentially to the corneal surface by creating a 1.5mm tunnel through the cornea into the anterior chamber.

Next method was introduced by Shimuzu and Fina beveled method. The blade is advanced tangentially to corneal surface, until its shoulders are buried fully into the stroma. Various blades can be used for this incision newer beveled, trapezoid diamond blade are employed in this.

Near clear incision is made in the vascular arcade.

CONTINOUS CURVILINEAR CAPSULORHEXIS(CCC):

After incision, opening of the capsule is the next step. CCC is the most preferred method of capsulotomy, as it provides wider range of opening with less radial tears for the phacoemulsification probe to operate. It also helps in stabilizing the nucleus in the bag which helps in easy fragmentation of the nucleus. This fragmentation in the capsule bag helps in decrease damage to cornea.

CCC is carried out by first making an incision on the anterior capsule withcystitome needle and tip is holded by either the cystitome or capsulorhexis forceps. The tip of the capsular is either pushed away or pulled in the direction of desired tear. This causes anterior capsule to fold onto itself. The folded end of the flap is captured and carried around in circular manner. the tear should neither be inward or outward. Inward fore causes small CCC resulting in capsular phimosis

post-surgery. Whereas too large incision can result in extension and tear in posterior capsule and may allow IOL dislocation anteriorly into sulcus.

HYDRODISSECTION:

It is used to separate the cortex from the posterior lens capsule along with loosening of nucleus of the lens. A blunt tipped 25-30 gauge cannula is used , it is placed under the anterior capsule of the lens, balanced salt solution is injected in radial fashion. While injecting fluid a mild pressure is given on the nucleus to prevent posterior fluid collection and rupture of posterior capsule. Hydrodissection is to be continued until nucleus is rotatable inside the capsule

HYDRODELINEATION:

This is injection of BSS into the nucleus separating various layers of nucleus. In this the fluid wave can be seen as it separates the epinucleus and the endonucleus. This is known as a golden ring sign.

NUCLEUS ROTATION:

If hydrodissection successfully breaks the attachment between the posterior cortex and posterior capsule, we should be able to rotate the nucleus in the capsular bag. This rotation of nucleus favor's the fragmentation of nucleus in phacoemulsification.

NUCLEUS FRAGMENTATION:

This involves various steps sculpting, cracking, grasping and emulsifying.

Sculpting is a process that debulks the nucleus using the phaco tip. It is performed with low aspiration and high power and with a modest vacuum. As the phaco needle moves forward, it comes in contact with the lens material and lens material is removed in controlled aspiration. Through the aspiration port the nuclear particles are aspirated out. After sculping , nucleus fragments are grasped with the help of vacuum at the phaco tip. The nucleus fragments are pulled between the posterior capsule and endothelium. The vacuum allows the material to be held at the tip and the ultrasonic power at the tip emulsifies the material into the fragments. The whole process happens under a low flow rate as to maintain the anterior chamber. With low flow, emulsification and aspiration occur at a slow and controlled manner.

After removal of nucleus the epinucleus and cortical matter aspirated with phaco handpiece or irrigation aspiration cannula

Nucleus emulsification:

The nucleus emulsification can happen at various places

a. Anterior chamber

b. Iris

c. Posterior chamber

d. Supracapsular

a. Anterior chamber:

This was the first described technique in phacoemulsification, in which emulsification of lens in the anterior chamber. This process involved less complication like posterior capsular rupture and also provided excellent visibility. But this method increases endothelial trauma and corneal edema.

b. Iris:

The next later developed method was performing phacoemulsification at iris plane. This is indicated in cases of small pupil, zonular weakness and compromised capsule. Here the superior pole of nucleus is prolapsed anteriorly and emulsification is done. In small pupil, nucleus is held midway between in the pupillary zone and emulsified which gives better visualization of the nucleus. This technique causes less damage to endothelium and gives less stress to zonules and posterior capsule.

c. Posterior chamber:

This is at present the most common preferred site. Removing of the nucleus after capsulorhexis, hydrodissection and nuclear rotation. The emulsification when

performed in the posterior chamber causes less damage to the endothelium. But emulsification at the posterior capsule involves damage to the posterior capsule by causing increased stress on the zonules and capsular bag. It is hard to be performed in a small pupil.

d. Supracapsular technique:

This technique involves prolapsing the nucleus from the capsular bag and positioning and placing the nucleus above the capsular bag and the emulsification is done. This is not widely employed as it causes increase tension on the capsular bag and high chances of damage to the iris while aspiration.

NUCLEUS DISSEMBLY:

Nucleus dissemble employs 2 instruments that subdivide the nucleus prior to emulsification.

There are various technique employed in nucleus disassembly

a. Divide and conquer
b. Chopping

Divide and conquer:

This method is employed for soft cataracts. Post hydrodissection and delineation, using a continuous ultrasound phaco probe, a deep sculpting is done and a linear

groove is made in the nucleus. The groove is then deepened, deep enough to allow cracking of the nucleus. A good groove is made out with brightening of the red reflex and smoothening of situations of the groove. After this nucleus is cracked into two parts and it each part is further cracked, forming four parts. The phaco tip and Sinskey hook is inserted inside each grove and is separated creating four separate pieces. The separated pieces are presented to the phaco tip at the center of the bag, and with adequate vacuum the parts are captured by the phaco tip and emulsified. Each separated quadrant of the nucleus is sequentially removed.

Chopping techniques:

This technique does not create a central groove. After aspiration of cortex the phaco tip is buried inside the nucleus. Then the phaco chopper is inserted and placed at the other end of the nucleus. These two instruments are moved in opposite directions and divide the nucleus. The fragmented nucleus is emulsified and aspirated.

There is a modified type of chopping identified by Koch and Katzen , This process involves of dividing the nucleus into two by sculpting and cracking and then the hemi nuclei are chopped. This is termed as the stop and chop technique. High levels of vacuum are needed for this process to maintain the fragmented nuclei.

There are two methods of chopping

1. Horizontal
2. Vertical

Horizontal methods of chopping, the phaco probe is placed below the anterior capsule and nucleus is engaged from the periphery. This provides better visualization.

Vertical method of chopping, the phaco tip is placed in the center of the nucleus, which tightly holds the nucleus and the chopper with sharp tip is placed below the phaco tip inside the nucleus. The phaco tip lifts and chopper depress the nuclei causing separation of nucleus.

IRRIGATION AND ASPIRATION:

The cortical material can be removed with phaconeedleforirrigation aspiration without ultrasound. Reduced vacuum can be used to aspirate the cortical matter from capsular fornix. The cortical material should be engaged to the probe dragged to the center and stripped by suction.in alteration, cortex is captured with mild suction to the cannula tip, stripped to the center and released by irrigation into anterior chamber.

Cortex resistance to aspiration can be separated with ocular viscoelastic devices(OVD), which allows easier access of the capsule to the tip of probe. This enhances removal of the cortical material.

IOL IMPLANTATION :

The posterior capsule bag is filled with OVD and with a lens inserter a foldable hydrophilic acrylic posterior chamber IOL is placed in the bag

After cortical aspiration and IOL implantation, OVD is be removed from the bag.

WOUND CLOSURE:

BSS is used for reforming the anterior chamber and the corneal incision is hydrated with BSS. Hydration of corneal incision causes temporary stromal swelling and increased wound apposition.

A subconjunctival injection of dexamethasone 2mg (0.3ml) is given and eye is patched

STUDIES:

Thakur et al evaluated the loss of endothelial cells after MSICS in 100 patients. A gradual decrease in endothelial cell count was evident, there was a 15.83% decrease in endothelial cell at 1 month postoperative period. [51]

Walkow et al from Germany analysed the effect of preoperative and intraoperative parameters and location of corneo-scleral tunnel incision on total and localized endothelial loss in 50consecutive patients who underwent phacoemulsification. After a study period of 12 months they found no significant difference between superior and temporal surgical approaches in endothelial cell density intraoperative parameters like surgical time and relative intensity of phacoemulsification. The only risk factors found significant for higher endothelial cell loss were shorter axial length and longer phacoemulsification time.**[52]**

Philipet al conducted a study in relationship between the change in endothelial cell density in the central corneal thickness before and after surgery in MSICS versus Phacoemulsification of total 120 patients amoung which 60 had undergone MSICS and 60 had undergone phacoemulsification cataract surgery. They found there was no statistical difference in endothelial cell loss in MSICS versus phacoemulsification patients after1 month of postoperative period. But the study had some limitations as there was no age and sex matched comparisons between

the groups, and other relative factors like diabetes pseudo exfoliation, nuclear sclerosis which would alter the postoperative outcome between the groups have not been included. [53]

Gogate et al compared the endothelial cell loss in cataract surgery by MSICS and phacoemulsification(stop and chop) in 200 patients by a randomized control trial. There was no statistically significant difference in endothelial cell loss in both groups. However the study was limited by the short follow up of 6 weeks.[54]

Kohlhaa et al., conducted study on comparision of "Reversed Tip and Snip" technique compared with "Divide and Conquer"-technique. The corneal endothelial cell count was measured before surgery and was measured post operative at 4 weeks and 3 months . It stated that the endothelial cell count was reduced significantly about 10% in the "Reversed Tip and Snip" group and about 15% in "Divide and Conquer"-Technique, thus stating that The "Reversed Tip and Snip" phakoemulsification technique causes less endothelial cell loss than the "Divide and Conquer"-technique.[55]

JUSTIFICATION OF STUDY:

Although cataract surgery by both MSICS and phacoemulsification are claimed to provide equally good results, there is concern that MSICS may be more harmful to the endothelium than phacoemulsification because more maneuvering is performed

manually in the anterior chamber in MSICS. In phacoemulsification maneuvering is performed mechanically in the capsular bag far from the endothelium. Few studies from India have compared the morphological and functional endothelial changes after MSICS versus phacoemulsification using the chop technique. The divide and conquer technique of nuclear disassembly in phacoemulsification is the technique recommended for beginners/ surgeons in transition phase from MSICS to phacoemulsification. This technique has been said to consume a higher effective phacoemulsification time because of more sculpting.[56]. The heat production at tip of ultrasonic probe and ultrasound vibration can result in greater intraoperative mechanical damage to the endothelium. There is paucity of literature comparing the endothelial cell loss after cataract surgery by MSICS versus divide and conquer phacoemulsification. Hence this study aims to compare the endothelial cell loss after MSICS versus divide and conquer phacoemulsification technique. Only few studies have done long term follow up on postoperative endothelial cell density after cataract surgery, so we would like to justify our study by doing a long term follow up.

AIM AND OBJECTIVE

To study the corneal endothelial alteration in postoperative MSICS and phacoemulsification patients visiting PSG IMS&R

MATERIALS AND METHODS

STUDY DESIGN:

Longitudinal study.

STUDY POPULATION:

Patients willing for cataract surgery MSICS/phacoemulsification aged between 45-75 years in PSGIMSR, Coimbatore, during the time period of 2017- 2019.

SAMPLE SIZE:

The sample size estimation was based on an 80% power to detect 20% difference in endothelial cell loss at a 5% level of significance and with a 20% loss of follow up. The sample size meeting this requirement was 100 for each surgical technique (MSICS and phacoemulsification)

MATERIALS AND METHODS

1) This was a hospital-based study which included patients who were attending the Ophthalmology Department for cataract surgery in PSG Institute of Medical Sciences and Research, Coimbatore.
2) The study was done spanning over a period of 18 months from January 2018 to June 2019.

3) A convenient sample of 200 patients cataractous lens change were selected

INCLUSION CRITERIA:

1) Study population between the age of 45 - 75 years
2) Patients diagnosed with age related cortical or nuclear cataract and scheduled for cataract surgery.

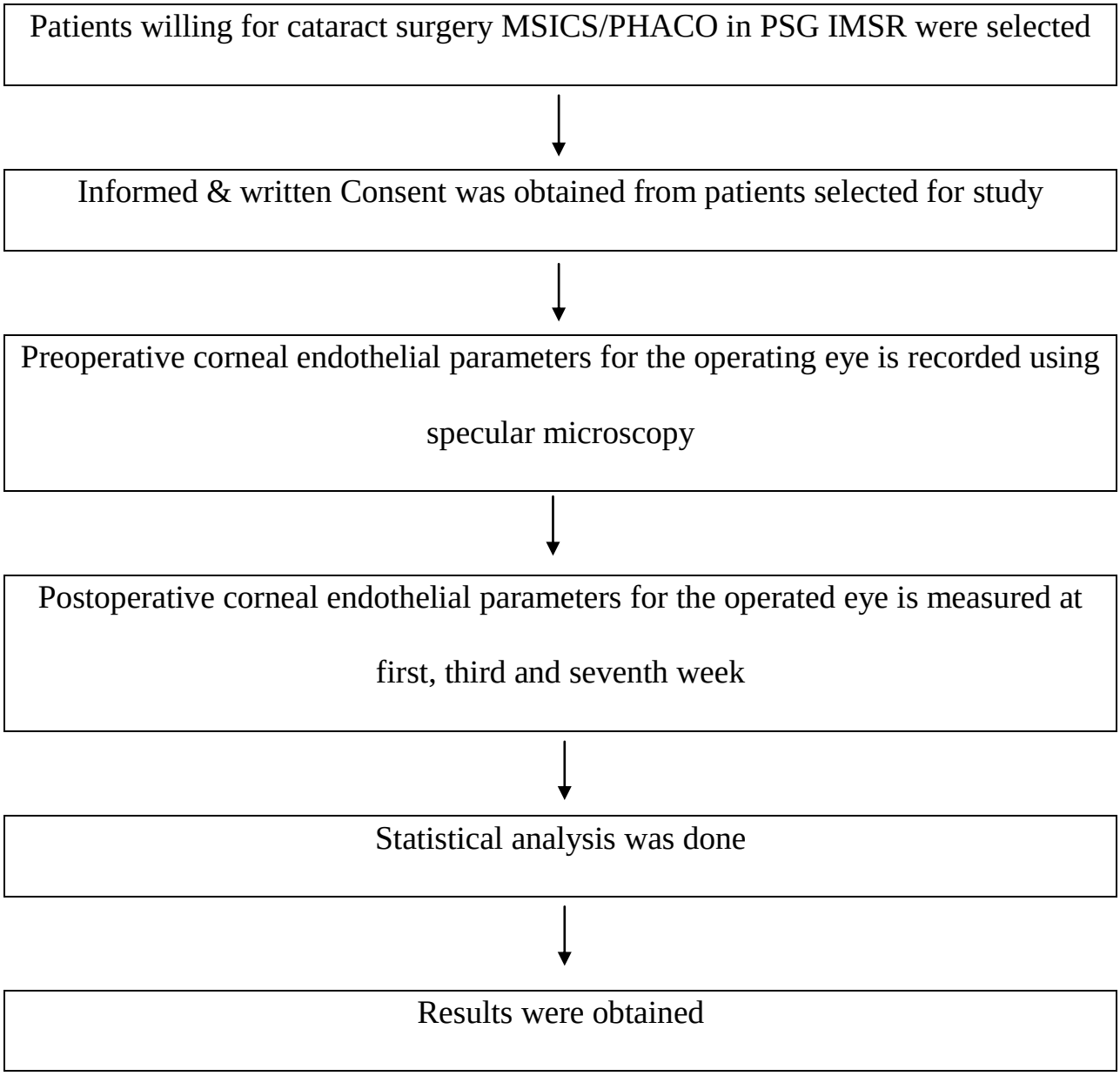
EXCLUSION CRITERIA:

1) Patients with traumatic/complicated cataract, pseudo exfoliation, glaucoma and retinal pathology.
2) Patients with past history of other ocular surgeries.
3) Patients with intra-operative complications like posterior capsular rupture, vitreous loss during cataract surgery.
4) Patients with preoperative endothelial cell density of less than 2000/mm square.

METHODOLOGY:

After clearance from the Institutional Ethical Committee, Patients visiting Ophthalmology OPD for cataract surgery were selected and detailed history was obtained regarding the age, sex, occupation and presenting symptoms, duration, progression and about associated systemic and ocular conditions. Patients were

then selected based on inclusion and exclusion criteria. Informed consent was obtained. Preopertaive and postoperative (first, third and seventh week) corneal endothelial parameters were noted. The final data was compared with each other. Statistical analysis was done and results are obtained.



RESULTS

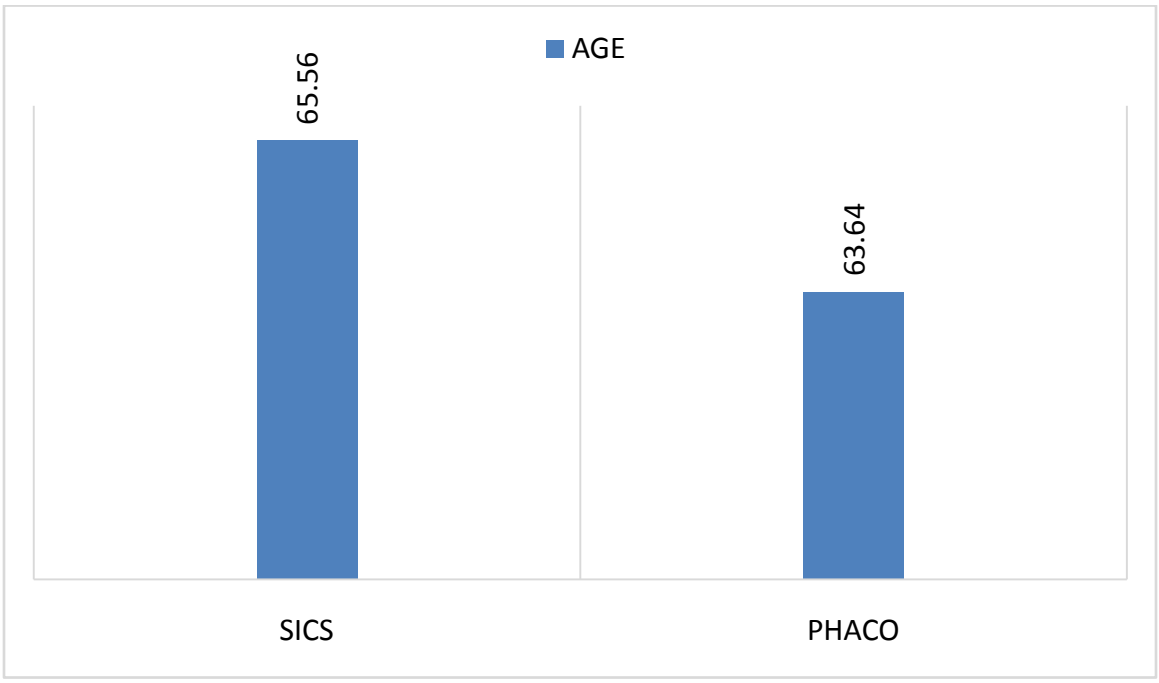
I. AGE COMPARISON

The demographic data of the patients included in the study was analyzed. Out of the two hundred patients included in the study, hundred patients underwent MSICS and hundred patients underwent phacoemulsification. The mean age in MSICS group was 65.56 years ± 8.61 and the mean age of phacoemulsification group was 63.64 years ± 8.52 (Table 1 and Figure 6).

Table 1: Comparison Of Age In Both MSICS And Phacoemulsification

Group	N	Mean	Std. Deviation	P value
SICS	100	65.5600	8.61092	0.114
Phaco group	101	63.6436	8.52477	

Figure 6: Comparison Of Age In Both MSICS And Phacoemulsification

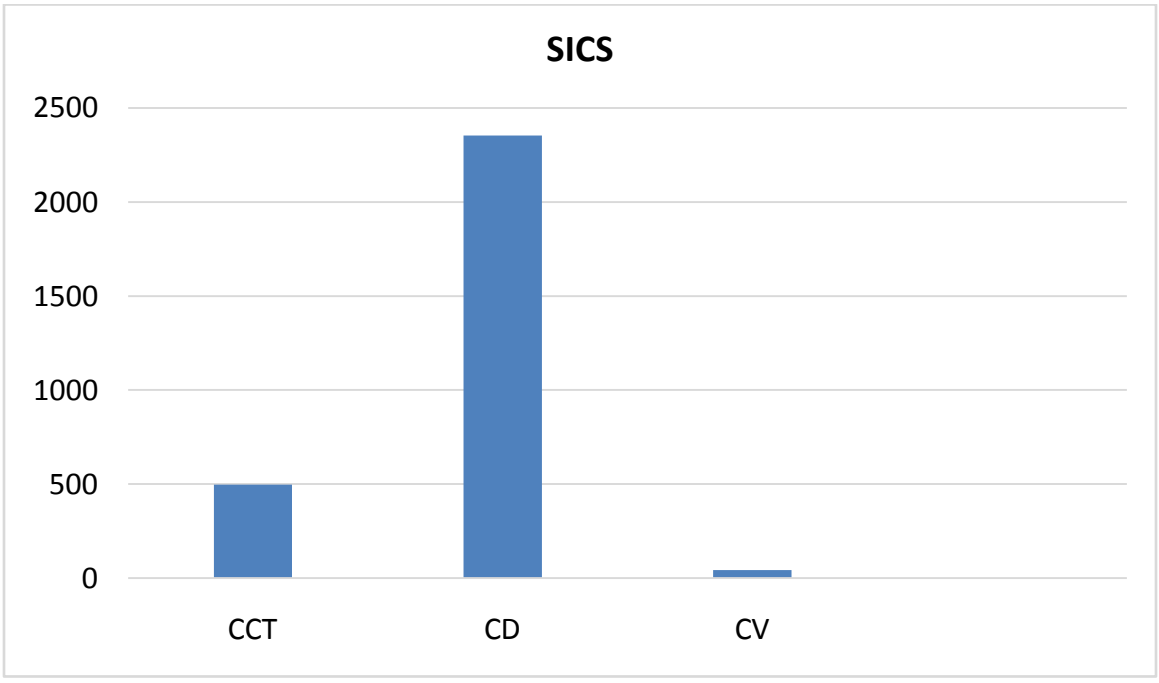


II. CCT AND ENDOTHELIAL PARAMERTES PREOPERATIVELY IN MSICS

Table 2: Preoperative CCT And Endothelial Parameters In MSICS

	N	Mean	Std.Deviation
CCT -Pre OP	100	496.3100	32.46683
CD-Pre OP	100	2354.2400	276.15766
CV-Pre OP	100	42.9400	9.71183

Figure 7:Preoperative CCT And Endothelial Parameters In MSICS



In MSICS group, the mean preoperative CCT was 496.31± 32.46 µm and CD 2354.24±276.15 cells/m^2 and CV being 42.94±9.7 %.

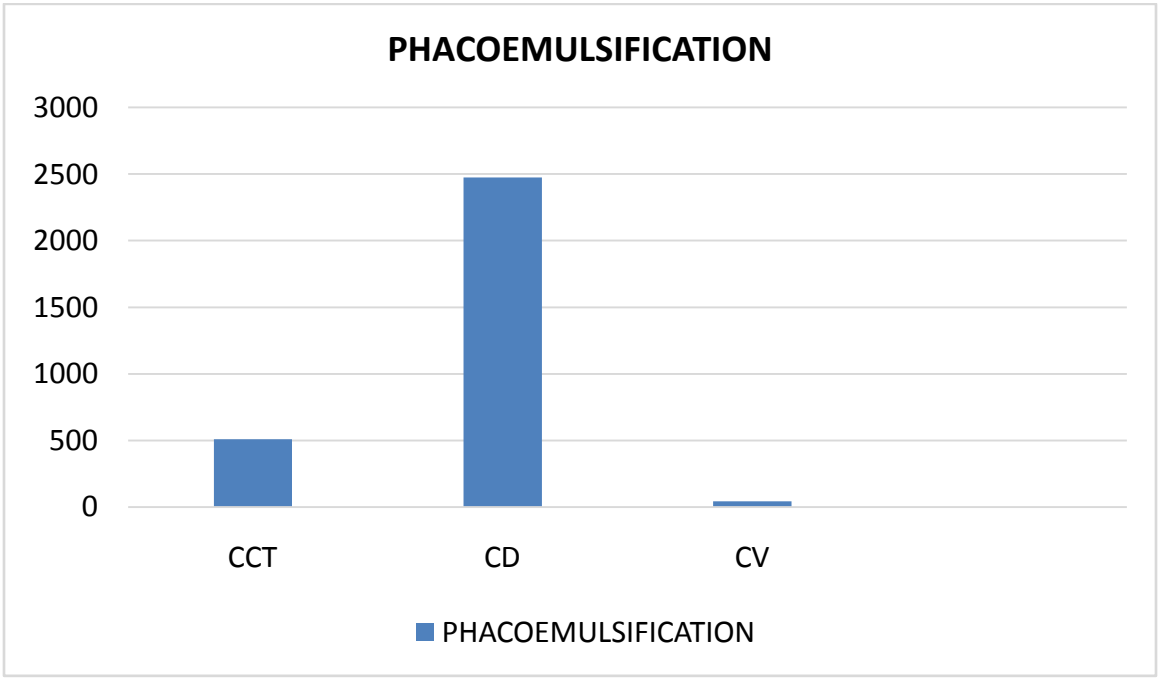
III. CCT AND ENDOTHELIAL PARAMERTES PREOPERATIVELY IN PHACOEMULSIFICATION

In phacoemulsification the mean preoperative CCT being 508.79±39.10 µm. The mean CD being and 2473.74 ±173.13 cells/m^2. The mean CV being 43.48±7.9 %

Table 3: Preoperative CCT And Endothelial Parameters In Phacoemulsification

	N	Mean	Std. Deviation
CCT -Pre OP	100	508.7900	39.10418
CD-Pre OP	100	2473.7426	173.13617
CV-Pre OP	100	43.4800	7.91174

Figure 8:Preoperative CCT And Endothelial Parameters In Phacoemulsification



IV. CCT COMPARISON BETWEEN THE TWO GROUPS

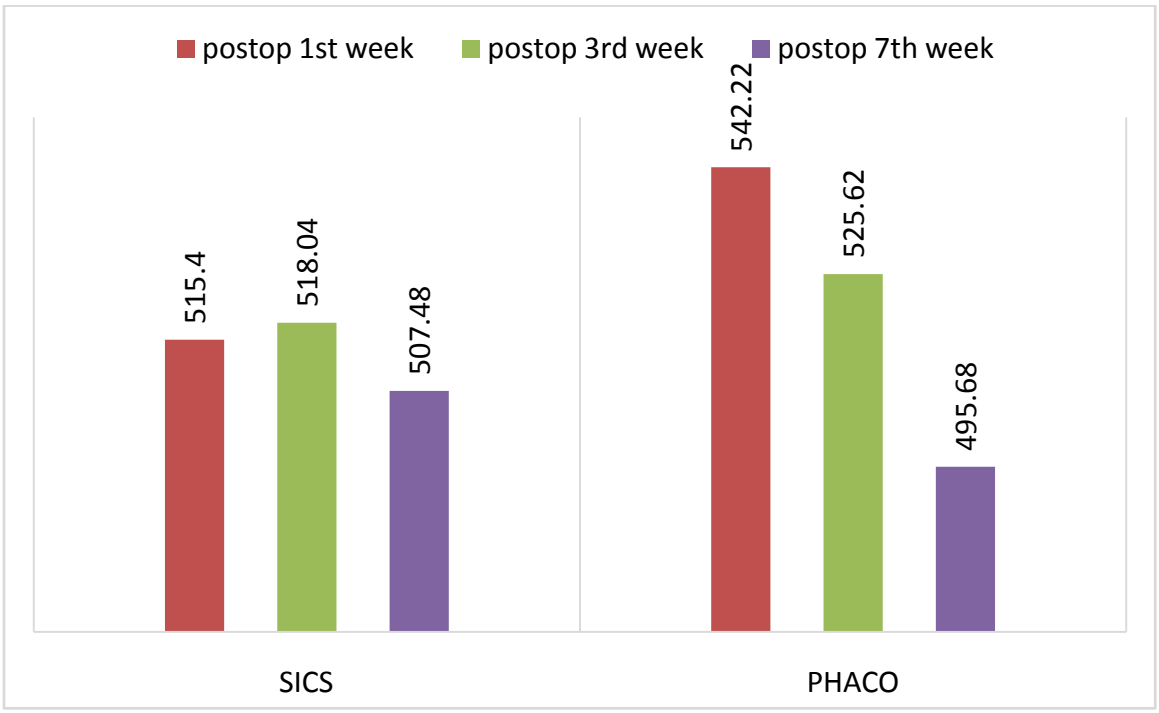
Central corneal thickness (CCT) was compared in MSICS and phacoemulsification groups (Table 4 and Figure 9). The mean postoperative CCT of patients who underwent MSICS in first, third and seventh visits were, 515.40±32.45 µm, 518.04±32.96 µm, 507.480± 37.93µm respectively.

In phacoemulsification the mean value of CCT postoperatively in the first, third and seventh week showed 542.22±45.32 µm, 525.62 ± 41.19µm , 495.68±39.24µm respectively. The comparison between MSICS and phacoemulsification groups postoperatively first, third and seventh week, showed statistically significant difference in CCT in first and seventh week (p value 0.00 and 0.032). The mean value of CCT in phacoemulsification reduced, stating there is a decrease in CCT in seventh week of postoperative period when compared to MSICS.

Table 4: Comparison Of CCT In MSICS And Phacoemulsification Groups

	Group	**N**	**Mean**	**Std. Deviation**	**P value**
CCT-Post OP 1st week	SICS	100	515.4000	32.45759	0.000
	Phaco group	100	542.2200	45.32277	
CCT-Post OP 3rd week	SICS	100	518.0400	32.96001	0.152
	Phaco group	100	525.6200	41.19130	
CCT-Post OP 7th week	SICS	100	507.4800	37.93654	0.032
	Phaco group	100	495.6800	39.24383	

Figure 9: Comparison Of CCT In Both MSICS And Phacoemulsification



V. ENDOTHELIAL CELL DENSITY COMPARISON BETWEEN THE TWO GROUPS

In MSICS and phacoemulsification groups, the endothelial cell density was compared and results are shown in Table 5 and Figure 10.

The mean value of endothelial cell density (CD) in patients who underwent MSICS postoperatively in the first, third and seventh week showed, 1736.85± 648.82 cells/m^2, 1653.72 ±546.27 cells/m^2, 1559.71±599. 14cells/m^2 respectively. The mean value of CD in patients who underwent phacoemulsification, postoperatively in the first, third and seventh week postoperatively showed 2161.66± 405.59cells/m^2, 1836.70± 391.61cells/m^2, 1759.47±377.69 cells/m^2 respectively.

The comparison between both groups first, third and seventh week postoperative, showed statistically significant alteration in cell density of endothelial cells in cornea in all three post operative weeks. (p value 0.00, 0.005, 0.007 respectively).

Table5*: *Comparison Of Cell Density In MSICS And Phacoemulsification

	Group	**N**	**Mean**	**Std. Deviation**	**P Value**
CD /mm2 -Post OP 1st week	MSICS	100	1736.8500	648.82337	0.000
	Phaco	100	2161.6634	405.59956	
CD /mm2 -Post OP 3rd week	MSICS	100	1653.7200	546.27567	0.005
	Phaco	100	1836.7030	391.61942	
CD /mm2 -Post OP 7th week	MSICS	100	1559.7100	599.14905	0.007
	Phaco	100	1759.4752	377.69068	

Figure 10: Comparison Of Cell Density In MSICS And Phacoemulsification

VI. COEFFICIENT OF VARIATION COMPARISON BETWEEN THE TWO GROUPS

The coefficient of variation (CV) of cells in the cornea was compared between groups at different time intervals. These details are given in Table 6 and Figure11.

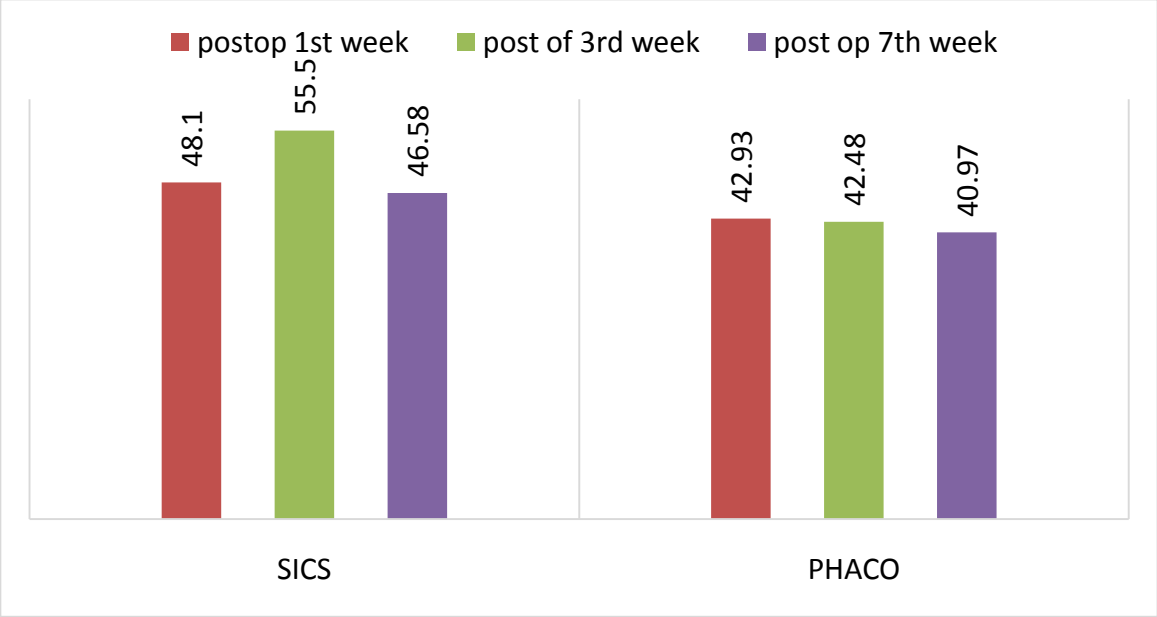
The mean value of CV in patients who underwent MSICS, postoperatively in the first, third and seventh week showed, 48.10± 11.45cells/m^2 , 55.50±53.55cells/m^2, 46.58 ±8.98cells/m^2respectively. The mean value of CV in patients who underwent phacoemulsification, postoperatively in the first, third and seventh week showed 42.93± 7.87cells/m^2, 42.48± 10.45cells/m^2, 40.97±8.05 cells/m^2 respectively.

The comparison of CV in both MSICS and phacoemulsification groups in the first, third and seventh week postoperatively, showed statistically significant alteration in CV in all three postoperative visit(p value 0.00, 0,018 and 0,00).

Table 6: Comparison Of Coefficient Of Variation In Cells In MSCIS And Phacoemulsification

	Group	N	Mean	Std. Deviation	P value
CV % -Post OP 1st week	SICS	100	48.1000	11.45963	0.000
	Phaco	100	42.9300	7.87305	
CV % -Post OP 3rd week	SICS	100	55.5000	53.55456	0.018
	Phaco	100	42.4800	10.45672	
CV % -Post OP 7th week	SICS	100	46.5800	8.98391	0.000
	Phaco	100	40.9700	8.05217	

Figure 11: Comparison Of Coefficient Of Variation In Cells In MSCIS And Phacoemulsification



VII. COMPARISON OF PARAMETERS WITHIN THE MSICS GROUP

Within the MSICS group, on comparing CCT preoperative with postoperative third week and seventh week, showed a increase of 21.73 (4.3%), and 11.17(2.25%) respectively. Stating that there is an increase in CCT in third week and seventh week post operatively compared to preoperative. There was statistically significant variation in CCT when preoperative was compared with the third and seventh week postoperative (p Value = 0.00)

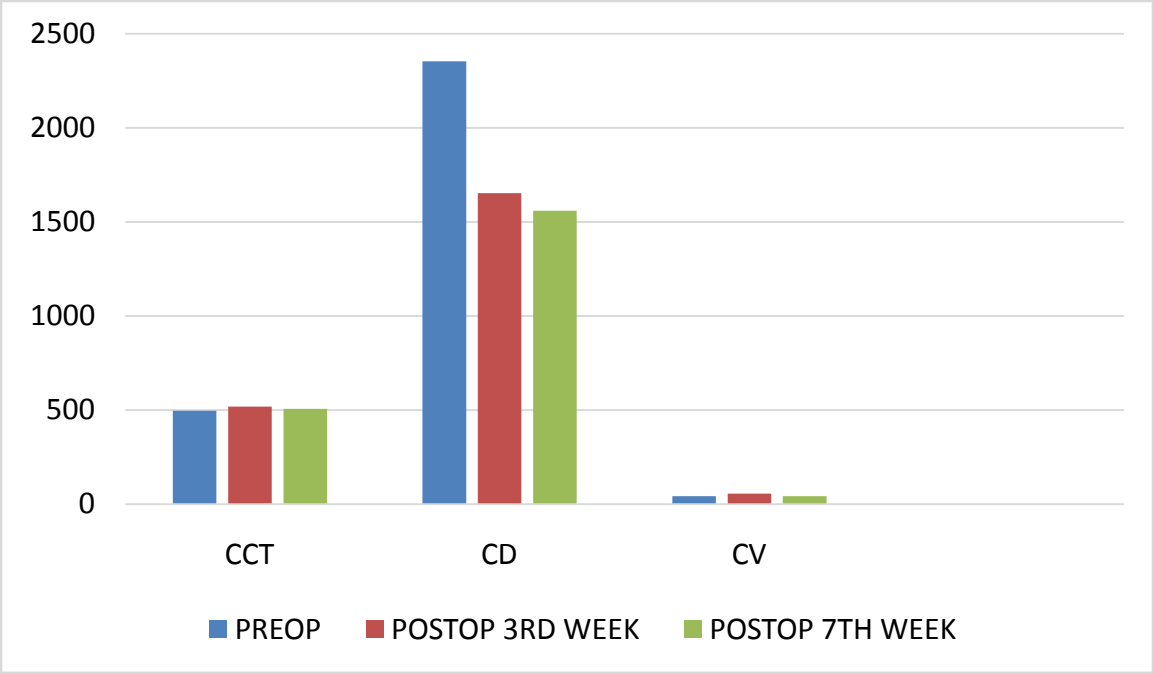
On comparing CD preoperative with post operative third and seventh week, showed a decrease of 700.52 cells/mm^2(29.75%) and 794.53 cells/mm^2(33.74%) respectively. Thus stating there is a decrease of CD in postoperative third and seventh week. There was statistically significant variation in CD when preoperative was compared with the, third and seventh week postoperative (p Value = 0.00)

On comparing CV preoperative with post operative third week and seventh week, showed a increase of 12.56% (29.2%) and 3.64%(8.47%). Stating that there is an increase in CV post operatively. There was statistically significant variation in CV when preoperative is compared with, third and seventh week postoperative(p Value =0.021). These changes are described in Table 7 and Figure 12.

Table 7: Comparison Of Various Endothelial Cell Parameters In Preoperative With Third And Seventh Week Postoperative In MSICS group.

	Mean	**Mean diff**	**Mean diff %**	**Std. Deviation**	**P value**
CCT-Pre OP	496.31			32.46683	0.000
CCT-Post OP 3rd week	518.04	21.73	4.378312	32.96001	
CCT-Post OP 7th week	507.48	11.17	2.250609	37.93	
CD /mm2-Pre OP	2354.24			276.1577	0.000
CD /mm2 -Post OP 3rd week	1653.72	-700.52	-29.7557	546.2757	
CD /mm2 -Post OP 7th week	1559.71	-794.53	-33.7489	599.1491	
CV %-Pre OP	42.94			9.71183	
CV % -Post OP 3rd week	55.5	12.56	29.25012	53.55456	0.021
CV % -Post OP 7th week	46.58	3.64	8.476945	8.98391	
				0.00	

Figure 12: Comparison Of Various Endothelial Cell Parameters In Preoperative With Third And Seventh Week Postoperative In MSICS group.



VIII. COMPARISON OF PARAMETERS WITHIN THE PHACOEMULSIFICATION GROUP

In the phaco group, on comparing CCT preoperative with post operative, third week and seventh week , 16.79 (3.29%), and 13.25%(2.60%) respectively. Stating that there is an increase in CCT in third week and decrease in CCT in the seventh week post operatively, the reduction was below the baseline CCT. There was statistically significant variation in CCT preoperative, third and seventh week postoperative (p Value 0.00 and 0.00 for third and seventh week respectively)

On comparing CD preoperative with post operative third week and seventh week, showed a decrease of 637cells/mm^2(25.75%) and 714.26 cells/mm^2 (28.87%) respectively. Thus stating there is a decrease in CD in postoperative third and seventh week. There was statistically significant variation in CD preoperative, third and seventh week postoperative (p Value 0.00 and 0.00 for third and seventh week respectively)

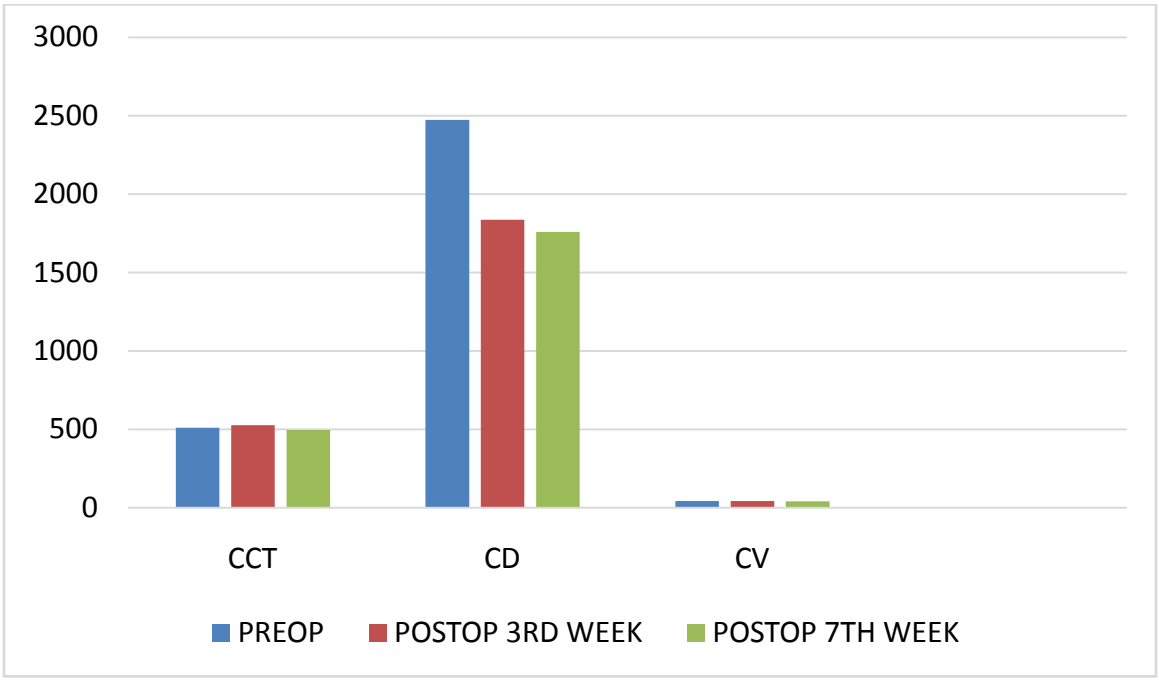
On comparing CV preoperative with post operative third week and seventh week, showed a decrease of 1.01%(2.34%) and 2.47%(5.6%). Stating that there is and decrease in CV in third and seventh week post operatively. They were statistically insignificant difference in CV in the third week with p Value being 0.184and statistically significant difference in the seventh week with p value 0.00.

These changes are described in Table 8 and Figure 13.

Table 8: Comparison Of Various Endothelial Cell Parameters In Preoperative With Third And Seventh week Postoperative In Phacoemulsification.

	Mean	Mean diff	Mean diff %	Std. Deviation	P value
CCT-Pre OP	509.2079			39.13421	
CCT-Post OP 3rd week	526	16.7921	3.29769	41.16236	0.000
CCT -Post OP 7th week	495.9505	-13.2574	-2.60353	39.141	0.000
CD /mm2-Pre OP	2473.743			173.1362	
CD /mm2 -Post OP 3rd week	1836.703	-637.04	-25.7521	391.6194	0.000
CD /mm2 -Post OP 7th week	1759.475	-714.267	-28.874	377.6907	0.000
CV %-Pre OP	43.4257			7.89094	
CV % -Post OP 3rd week	42.4059	-1.0198	-2.34838	10.43089	0.184
CV % -Post OP 7th week	40.9505	-2.4752	-5.69985	8.01421	0.000

Figure 13: Comparison Of Various Endothelial Cell Parameters In Preoperative With Third And Seventh week Postoperative In Phacoemulsification.



DISCUSSION

In our study conducted in a tertiary care hospital, a sample of 200 patients who were willing for cataract surgery were selected based on the inclusion and exclusion criteria. 2 groups of each 100 patients were selected based on patient's surgery preference as MSICS or phacoemulsification. All patients underwent specular microscopy before the surgery and postoperatively in the first , third and seventh week.

In our study, patients who underwent MSICS had increased CCT and CV and decreased CD values post operatively. Whereas there was an increase and consecutive fall in CCT, with decrease in both CD and CV noted in patients who underwent phacoemulsification.

The mean age of MSICS patients is 65.56 years ± 8.61. The mean age of phacoemulsification patients being 63.64 years±8.52 .

In MSICS the mean preoperative CCT was 496.31 and third week and seventh week postoperative CCT being 518.04 and 507.48. The difference of CCT with preoperative with postoperative third week and seventh week , showed a increase of 21.73 , and 11.17 respectively.

In phacoemulsification the mean preoperative CCT was 509.20, third week and seventh week postoperative CCT being 526 and 495.95. The difference between

preoperative and postoperative CCT in the third week and seventh week was 16.79 and 13.25 respectively.

On comparing preoperative with postoperative CCT values of MSICS and phacoemulsification, there was increase in CCT in both groups in the third post operative week followed by decrease at seven weeks follow up.

This inference in our study is similar to study by Deshpande et al stating that there is increase in CCT in MSICS and phacoemulsification post operatively. They compared the CCT values in patients who underwent cataract surgery (50 MSICS and 50 phacoemulsification). There was significant increase in CCT in both 7^{th} day and 30^{th} day postoperatively. CCT in $7^{th}$and 30^{th}postoperative day in MSICS patients were 528.96 and 514.15 respectively and in phacoemulsification being 533.78 and 524.9. this states that there is an increase in CCT in both MSICS and phacoemulsification postoperatively.[57]

Micheali et al also conducted a study comparing CCT and endothelial change after, in 51 patients who underwent phacoemulsification with clear cornea and scleral tunnel incision and their central corneal thickness measured preoperatively and on post-op days 1, 7, 30 and 90. Their corneal thickness increased significantly in all measurements post-op, and returned to baseline by 3 months. As stated in the study the CCT may reach the baseline by the end of third month. But in our study we

have not analyzed post operative CCT up to third month, thus we are unable to conclude the restoration of corneal thickness to the baseline value.[58]

Kosrirukvongs et al compared study of CCT and endothelial cell loss in divide and conquer with chip and flip in 41 eyes, specular microscopy was done at one week, one and third month postoperatively. This study noted there was increase in corneal thickness and greater endothelial loss in chip and flip compared to divide and conquer[59]

In MSICS the mean preoperative CD was 2354.24, the postoperative CD for third week and seventh week being 1653.72 and 1559.71. The difference in CD preoperative with post-operative third week and seventh week, showed a decrease of 700.52 cells/mm^2(29.75%)and 794.53 cells/mm^2 (33.74%) respectively.

In phacoemulsification the mean preoperative CD was 2473.74 and third- and seventh-week postoperative values was 1836.73 and 1759.47 respectively. While comparing preoperative CD with post-operative CD for third week and seventh week, the CD showed a decrease of 637cells/mm^2(25.75%)and 714.26 cells/mm^2(28.8%)respectively.

On comparing MSICS and phacoemulsification the CD values decrease in both the groups. Cataract surgery has been known to be associated with decrease in endothelial cell density and alteration of cell morphology. The percentage of

endothelial cell loss was found to be significantly less with phacoemulsification compared to MSICS.

In correlation with our study, a study by Ganekal et al, where they compared the morphological and functional endothelial cell changes after MSICS versus phacoemulsification cataract surgery(chop technique) in around 200 patients using non-contact specular microscope. They found a statistically significant difference in endothelial cell density at 1 week and 6 weeks between the 2 groups. [60]

Storr-Paulsen et al compared endothelial cell damage after phacoemulsification using divide and conquer or phacoemulsification chop nuclear fracturing technique in 60 patients. Endothelial cell loss was measured postoperatively and at 3rdand 12th month. Both groups had a significant but equal decrease in cell density contradicting the popular hypothesis that phacoemulsification chop technique is less harmful to the corneal endothelium than divide and conquer.[61]

In MSICS the mean preoperative CV was 42.94 %, postoperative third week and seventh week were 55.5 %and 46.58 %. On comparing the CV preoperative with post-operative for the third week and seventh week, CV showed an increase of 12.56% and 3.64%. Thus, showing a significant increase in CV for third week postoperative when compared to the seventh week postoperative values.

In phacoemulsification the mean preoperative CV 43.42 and third and seventh week postoperative being 42.40 and 40.95. While comparing CV preoperative with post operative third week and seventh week, showed a decrease of 1.01% and 2.47%.

On comparing MSICS and phacoemulsification, there was an increase of CV in MSICS compared to phacoemulsification surgeries

Ganesan et al conducted a study to assess the corneal endothelium, CCT after phacoemulsification. On comparing preoperative, 1st week, 6th week and 3rd month postoperative endothelial cell density (ECD), coefficient of variation (CV), hexagonality and central corneal thickness (CCT). There was a significant increase in CV after phacoemulsification. In contrast we did not observe a similar increase in CV in phacoemulsification group.[62]

CONCLUSION

Our longitudinal comparative study has shown that there is increase in CCT in MSICS compared to phacoemulsification surgeries.

The study also showed that there is a significant percentage of cell loss in MSICS compared to phacoemulsification.

Polymegethism was noted to be increased in MSICS group than phacoemulsification.

Our study demonstrates that phacoemulsification using divide and conquer technique was superior compared to MSICS in terms of postoperative corneal endothelial alterations.

LIMITATIONS

- Lack of sample size in each group
- Lack of consideration of effective phaco time and ultrasound time
- Comparison of single technique of phaco and MSICS, other techniques may give rise to various results.
- Surgery by trainee surgeons

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CASE PROFOMA

NAME:

AGE:

SEX:

HOSPITAL NUMBER:

DIAGNOSIS :

RIGHT EYE:

LEFT EYE:

PREOPERATIVE SPECULAR MICROSCOPY:

S.NO	PREOPERTAIVE SPECULAR

TYPE OF SURGERY:

POSTOPERATIVE SPECULAR MICROSCOPY:

S.NO	1ST POSTOPERTIVE WEEK	3rd POSTOPERATIVE WEEK	7thPOSTOPERATIVE WEEK

PSG Institute of Medical Science and Research, Coimbatore
Institutional Human Ethics Committee
INFORMED CONSENT FORMAT FOR RESEARCH PROJECTS

I , Dr. T.Sowmiya Kalaivani am carrying out a study on the topic: **ENDOTHELIAL CELL DAMAGE AFTER CATARACT SURGERY: MANUAL SMALL INCISION CATARACT SURGERY VERSUS PHACOEMULSIFICATION,** as part of my research project being carried out under the aegis of the Department of OPHTHALMOLOGY

My research guide is: Dr.K.Divya MBBS, MS,DNB,FICO

The justification for this study is:

Although cataract surgery by both MSICS and phacoemulsification are claimed to provide equally good results, there is concern that MSICS may be more harmful to the endothelium than phacoemulsification because more maneuvering is performed manually in the anterior chamber in MSICS. In phacoemulsification maneuvering is performed mechanically in the capsular bag far from the endothelium. Few studies from India have compared the morphological and functional endothelial changes after MSICS versus phacoemulsification using the chop technique. The divide and conquer technique of nuclear disassembly in phacoemulsification is the technique recommended for beginners/ surgeons in transition phase from MSICS to phacoemulsification. This technique has been said to consume a higher effective phacoemulsification time because of more sculpting.(9). The heat production at tip of ultrasonic probe and ultrasound vibration can result in greater intra operative mechanical damage to the endothelium. There is paucity of literature comparing the endothelial cell loss after cataract surgery by MSICS versus divide and conquer phacoemulsification. Hence this study aims to compare the endothelial cell loss after MSICS versus divide and conquer phacoemulsification technique. Only few studies have done long term follow up on postoperative endothelial cell density after cataract surgery, so we would like to justify our study by doing a long term follow up.

The objectives of this study are:

To study the comparison of endothelial cell loss in post manual small incision cataract surgery and phacoemulsification

Sample size: 200 subjects.

Study volunteers / participants are : Patients attending out patient department of Ophthalmology between age group of 45-75 years

Location: PSG IMS&R Hospital, Coimbatore.

We request you to kindly cooperate with us in this study. We propose collect background information and other relevant details related to this study. We will be carrying out:

Initial interview (specify approximate duration) : 10 minutes

Data collected will be stored for a period of 5 years. We will not use the data as part of another study.

Health education sessions: Number of sessions : **Not applicable.**
Approximate **duration** of each session : **Not applicable**

Clinical examination :

1. Preoperative corneal endothelial cell density measurement
2. Surgical procedure (SICS/ phacoemulsification)
3. Postoperative corneal endothelial cell density measurement at 1^{st} ,6^{th} and 3^{rd} month

Blood sample collection:
Specify quantity of blood being drawn **: Not applicable.**
No. of times it will be collected **: Not applicable**.

Whether blood sample collection is part of routine procedure or for research (study) purpose: Not applicable

1. Routine procedure 2. Research purpose

Specify **purpose**, discomfort likely to be felt and side effects, if any **: Not applicable**
Whether blood sample collected will be stored after study period: Yes / No, it will be destroyed

Whether blood sample collected will be sold: Yes / No

Whether blood sample collected will be shared with persons from another institution: Yes / No

Medication given, if any, duration, side effects, purpose, benefits : **Not applicable**

Whether medication given is part of routine procedure : Yes / No (If not, state reasons for giving this medication)

Whether alternatives are available for medication given: Yes / No (If not, state reasons for giving this particular medication)

Final interview : **Not applicable**

If **photograph** is taken, purpose : **Not applicable**

Benefits from this study: Endothelial cell loss measured between the 2 procedures helps us to identify which technique is useful for the patient and helps us to prevent endothelial loss in the future patients by choosing the appropriate method.

Risks involved by participating in this study : **Nil**

How the **results** will be used : **For research purpose only**

If you are uncomfortable in answering any of our questions during the course of the interview / biological sample collection, **you have the right to withdraw from the interview / study at anytime.** You have the freedom to withdraw from the study at any point of time. Kindly be assured that your refusal to participate or withdrawal at any stage, if you so decide, will not result in any form of compromise or discrimination in the services offered nor would it attract any penalty. You will continue to have access to the regular services offered to a patient. You will **NOT** be paid any remuneration for the time you spend with us for this interview / study. The information provided by you will be kept in strict confidence. Under no circumstances shall we reveal the identity of the respondent or their families to anyone. The information that we collect shall be used for approved research purposes only. You will be informed about any significant new findings - including adverse events, if any, – whether directly related to you or to other participants of this study, developed during the course of this research which may relate to your willingness to continue participation.

Consent: The above information regarding the study, has been read by me/ read to me, and has been explained to me by the investigator/s. Having understood the same, I hereby give my consent to them to interview me. I am affixing my signature / left thumb impression to indicate my consent and willingness to participate in this study (i.e., willingly abide by the project requirements).

Signature / Left thumb impression of the Study Volunteer / Legal Representative:

Signature of the Interviewer with date: Witness:

Contact number of PI:
Contact number of Ethics Committee Office: 0422 4345818

பூ சா கோ மருத்துவக் கல்லூரி மற்றும் ஆராய்ச்சி நிறுவனம், கோவை
மனித நெறிமுறைக் குழு
ஒப்புதல் படிவம்

டாக்டர் <u>த. சௌம்யா கலைவாணி</u> ஆகிய நான். பூ சா கோ மருத்துவக் கல்லூரியின் / மருத்துவ மனையின் **<u>கண் மருத்துவ</u>** துறையின் கீழ்,

எண்டோதீலியல் செல் இழப்பீடு கண் புரை அறுவை சிகிச்சைக்குப் பின்னர் : சிறு கீறல் கண் புரை அறுவை சிகிக்சை எதிர் நிலையில் நுண் துளை அறுவை சிகிச்சை

என் ஆய்வு வழிகாட்டி : **<u>டாக்டர் திவ்யா கா.</u>**

<u>ஆய்வு மேற்கொள்வதன் அடிப்படை</u>:

கண்புரை அறுவை சிக்கிச்சையை கை முறை சிறு கீறல் முறையிலும், நுண் துளை முறையில் செய்தாலும் முடிவு நல்ல பலனை தரும். ஏனெனில் கைமுறையாக செய்யும் சிறு கீறல் கண் புரை அறுவை சிகிக்சை எண்டோதீலியத்தின் அருகில் செய்யப்படுவதால் எண்டோதீலியில் செல்லில் நிறைய சேதம் ஏற்பட்டு அதன் அடர்த்தியில் மாற்றம் ஏற்படலாம்.

ஆனால் நுண் துளை அறுவை சிகிச்சை முறையில் கேப்சுலார் பையில் செய்யப்படுகிறது. இதில் ஏற்படும் சேதம் சற்று குறைவாகவே இருக்கும். புரையிலுள்ள நியூக்ளியஸை சிறு சிறு துண்டுகளாக்கி வெளியேற்றும் முறை கையாளப்படுகிறது எண்டோதீலியத்தில் இருந்து சிறிது தொலைவில் இது செய்யப்படுகிறது. இந்த இரு வகை அறுவைச் சிகிக்சை முறையிலும் எண்டோதீலியம் செல்லின் உருவத்திலும், செயல்பாடுகளிலும் ஏற்படும் மாற்றங்கள் குறித்து இந்தியாவில் சில ஆய்வுக் கட்டுரைகளே உள்ளன.புதிதாக அறுவை சிகிக்சை செய்ய ஆரம்பிப்போர் கை முறை நுண் துளை கண் புரை அறுவை சிகிக்சை முறையில் நியூக்ளியஸை சிறு சிறு துண்டுகளாக பிரித்து கைப்பற்றும் முறையைத்தான் உபயோகிக்கின்றனர். இம்முறையில் நிறைய நேரம் எடுப்பதோடு அல்ட்ரோசோனிக் ப்ரோப் வெப்பமடைகிறது இதனால் எண்டோதீலியம் செல்லில் நிறைய சேதம் ஏற்பட வாய்ப்புஉள்ளது.

இவ்விரு அறுவைச் சிகிக்சை முறையிலும் எண்டோதீலியம் செல்லில் ஏற்படும் பாதிப்புகளைக் குறித்து வெகு சில ஆய்வுகளே வந்துள்ளன. ஆகையால் நாங்கள் கைமுறை கண்புரை அறுவை சிகிச்சையும் நுண் துளை கண் புரை அறுவை சிகிச்சையில் நியூக்கிலியஸை சிறு சிறு துண்டுகளாய் பிரித்து கைப்பற்றும் முறையில் ஏற்படும் எண்டோதீலியல் மாற்றத்தை ஒப்பிடுகிறோம். மேலும் இதில் உள்ள ஆய்வுகள் அனைத்தும் குறுகிய காலக் கட்டத்திலேயே முடிக்கப்பட்டன. அதனால் நாங்கள் இந்த ஆய்வுகளை மேற்கொள்வதோடு நீண்டகால ஆய்வாகவும் இதனை செய்கிறோம்.

ஆய்வின் நோக்கம்:
எண்டோதீலியத்தின் அடர்த்தியை கை முறை சிறு கீறல் கண்புரை அறுவை சிகிச்சை மற்றும் நுண் துளை கண் புரை அறுவை சிகிச்சைக்குப் பின்னும் ஒப்பிடுதல்.

ஆய்வில் பங்கு பெறும் நபர்களின் எண்ணிக்கை : 200

ஆய்வில் பங்கு பெறுவோர் மற்றும் வயது : **கண் மருத்துவ துறைக்குவரும் 45-75 வயதிற்கு உட்பட்டோர்.**

ஆய்வு மேற்கொள்ளும் இடம்: **பூ சா கோ மருத்துவக் கல்லூரி**

இந்த ஆய்வில் எங்களுடன் ஒத்துழைக்குக்குமாறு கேட்டுக்கொள்கிறோம். நாங்கள் சில தகவல்களை இந்த ஆய்விற்காக சேகரிக்க உள்ளோம்.

ஆய்வு செய்யப்படும் முறை : நீளமான ஆய்வு

முதன்மை நேர்காணல் : **10** நிமிடங்கள்.

இந்த ஆய்வில் கிடைக்கும் தகவல்கள் **ஐந்து** வருடங்கள் பாதுகாக்கப்படும்.
இந்தத் தகவல்கள் வேறு ஆய்விற்குப் பயன்படுத்ததப்படமாட்டாது.

சுகாதாரக் கல்வி : பொருந்தாது

ஒரு அமர்வுக்கான நேரம் : பொருந்தாது

மருத்துவ பரிசோதனைகள் :

இரத்த மாதிரி சேகரிப்பு - : பொருந்தாது

இரத்த மாதிரி எடுப்பது வழக்கமான சிகிக்சைக்காகவா அல்லது இந்த ஆய்விற்க்காகவா ?

1. வழக்கமான சிகிக்சைக்காக 2.. குறிப்பிட்ட ஆய்விற்க்காக : **பொருந்தாது**

இதனால் ஏற்படக்கூடிய அசௌகரியங்கள் / பக்கவிளைவுகள் **பொருந்தாது**

இரத்த மாதிரிகள் ஆய்விற்குப் பின் பாதுகாத்து வைக்கப்படுமா ? பொருந்தாது

சேகரிக்கப்பட்ட இரத்தம் விற்கப்படுமா ? : **பொருந்தாது**

சேகரிக்கப்பட்ட இரத்தம் வேறு நிறுவனத்துடன் பகிர்ந்து கொள்ளப்படுமா? : **பொருந்தாது**

மருந்துகள் ஏதேனும் கொடுக்கப்படவிருந்தால் அவை பற்றிய விவரம் :

: **பொருந்தாது**

மருந்துகள் கொடுக்கப்படுவது வழக்கமான சிகிக்சை முறையா ? :

:பொருந்தாது

கொடுக்கப்படும் மருந்துகளுக்கு மாற்று உள்ளதா ? : **பொருந்தாது**

ஆய்வில் பங்கு பெறுவதால் ஏற்படும் பலன்கள் :

இவ்விரு முறைகளில் செய்யப்படும் கண்புரை அறுவை சிகிச்சையினால் எண்டோதீலியம் செல்லில் ஏற்படும் பாதிப்புகளை அளவிடுதல் மூலமாக பிற்காலத்தில் நோயாளிகளுக்கு எந்த முறையில் அறுவை சிகிக்சை செய்வது பலனளிக்கும் என்பதைக் கண்டறியலாம்.

ஆய்வில் பங்கேற்பதால் ஏற்படும் அசௌகரியங்கள் / பக்க விளைவுகள்

: பொருந்தாது

ஆய்வின் முடிவுகள் எந்த முறையில் பயன்படுத்தப்படும் ?

இந்த தகவல்களை நாங்கள் எங்களுடைய ஆய்வுக்கு மட்டுமே பயன்படுத்துவோம் என உறுதி அளிக்கிறோம்.

இந்த ஆய்வின் கேள்விகளுக்கு பதிலளிப்பதிலோ , இரத்த மாதிரிகள் அல்லது திசு மாதிரிகள் அல்லது எடுப்பதிலோ உங்களுக்கு ஏதேனும் அசௌகரியங்கள் இருந்தால், எந்த நேரத்தில் வேண்டுமானாலும் ஆய்விலிருந்து விலகிக்கொள்ளும் உரிமை உங்களுக்கு உள்ளது. எப்பொழுது வேண்டுமானாலும் ஆய்விலிருந்து விலகிக்கொள்ளும் உரிமை உங்களுக்கு உள்ளது. ஆய்விலிருந்து விலகிக்கொள்வதால் உங்களுக்கு அளிக்கப்படும் சிகிச்சை முறையில் எந்த வித பாதிப்பும் இருக்காது என்று உங்களுக்கு உறுதியளிக்கிறோம். மருத்துவமனையில் நோயாளிகளுக்கு அளிக்கப்படும் சேவைகளை நீங்கள் தொடர்ந்து பெறலாம். இந்த ஆய்வில் பங்கேற்க ஒப்புக்கொள்ளுவதால் வேறு எந்த விதமான கூடுதலான பலனும் உங்களுக்கு கிடைக்காது. நீங்கள் அளிக்கும் தகவல்கள் இரகசியமாக வைக்கப்படும். ஆய்வில் பங்கேற்பவர்கள் பற்றியோ அவர்கள் குடும்பத்தைப் பற்றியோ எந்த தகவலும் எக்காரணம் கொண்டும் வெளியிடப்படாது என்று உறுதியளிக்கிறோம். நீங்கள் அளிக்கும் தகவல்கள் /இரத்த மாதிரிகள் /திசு மாதிரிகள் அங்கீகரிக்கப்பட்ட ஆய்விற்கு மட்டுமே பயன்படுத்தப் படும். இந்த ஆய்வு நடைபெறும் காலத்தில் குறிப்பிடத்தகுந்த புதிய கண்டுபிடுப்புகள் அல்லது பக்க விளைவுகள் ஏதும் ஏற்பட்டால் உங்களுக்கு தெரிவிக்கப்படும். இதனால் ஆய்வில் தொடர்ந்து பங்கு பெறுவது பற்றிய உங்கள் நிலைப்பாட்டை நீங்கள் தெரிவிக்க ஏதுவாகும்.

ஆய்வுக்குட்படுத்துபவரின் ஒப்புதல்: இந்த ஆய்வைப் பற்றிய மேற்கூறிய தகவல்களை நான் படித்து அறிந்து கொண்டேன் /ஆய்வாளர் படிக்கக் கேட்டுத் தெரிந்து கொண்டேன். ஆய்வினைப் பற்றி நன்றாகப் புரிந்து கொண்டு இந்த ஆய்வில் பங்கு பெற ஒப்புக்கொள்கிறேன். இந்த ஆய்வில் பங்கேற்பதற்கான எனது ஒப்புதலை கீழே கையொப்பமிட்டு /கை ரேகை பதித்து நான் தெரிவித்துக் கொள்கிறேன் .

பங்கேற்பாளரின் பெயர் ,முகவரி :

பங்கேற்பாளரின் கையொப்பம் /கை ரேகை / சட்டபூர்வ பிரதிநிதியின் கையொப்பம் :

தேதி :

ஆய்வாளரின் கையொப்பம் :
தேதி :

ஆய்வாளரின் தொலைபேசி எண் :

மனித நெறிமுறைக் குழு அலுவலகத்தின் தொலைபேசி எண்: 0422 4345818

MASTER CHART

S.No	O			Pre-Op SICS						SICS 1 ST Week Post-OP							SICS 3RD Week Post-OP							SICS 7 TH Weeks Post-OP					
	op number	age	sex	CCT	CCT (US)	Number	CD /mm²	AVG µm²	SD µm²	CV %	CCT	CCT (US)	Number	CD /mm²	AVG µm²	SD µm²	CV %	CCT	CCT (US)	Number	CD /mm²	AVG µm²	SD µm²	CV %	CCT	CCT (US)	Number	CD /mm²	AVG µm²	SS	CV %
1	01201433	53	M	512	522	209	2313	446	151	36	532	554	180	2214	459	155	40	542	544	174	2314	467	159	45	532	537	169	2214	441	145	40
2	01804136	61	M	508	521	291	2614	383	118	31	525	540	245	2478	390	142	35	545	527	263	2343	410	149	29	542	552	257	2254	391	167	32
3	00503495	68	F	468	481	242	2265	442	167	38	486	510	220	2065	478	169	42	506	509	215	1987	498	171	45	500	512	210	2164	423	165	44
4	00705930	55	M	508	521	257	2621	390	140	35	524	551	245	2415	431	145	41	530	533	237	2314	441	151	44	524	532	231	2218	400	148	41
5	01806503	57	F	500	513	253	2314	432	162	38	516	542	249	2014	456	169	45	524	527	245	2111	487	174	47	518	528	240	1998	410	170	45
6	01801843	59	F	501	514	251	2403	416	130	31	521	555	270	2410	446	137	33	521	531	227	2444	450	142	37	515	517	222	2310	411	140	35
7	01801316	61	M	498	519	245	2341	383	154	41	513	561	226	2141	402	159	44	523	527	220	2243	412	164	45	517	527	216	2018	399	160	44
8	01801838	62	M	479	520	255	2413	413	135	39	502	542	231	2210	427	140	43	512	513	228	2345	431	146	47	512	523	224	2134	409	147	45
9	01804136	67	M	487	574	280	2571	389	147	38	507	514	232	2235	475	498	111	517	528	241	2341	510	505	101	511	512	235	2145	390	500	99
10	01901263	68	F	489	502	186	2203	454	180	40	508	497	164	2073	486	268	56	516	531	172	2134	512	274	59	510	524	164	1934	412	265	57
11	01800553	69	F	501	512	241	2265	421	152	42	522	492	234	2014	436	160	48	530	542	230	2136	458	165	47	522	534	225	1987	412	156	42
12	01805007	64	F	419	432	213	2267	441	203	46	441	492	200	2094	467	210	49	451	461	196	2176	490	215	52	445	465	189	1956	410	201	50
13	01001474	65	M	511	528	253	2486	445	124	41	530	570	224	2146	487	125	44	538	541	220	2276	495	130	54	529	510	214	1873	435	127	51
14	01804293	61	F	523	536	261	2468	405	154	38	543	540	241	2314	443	159	41	553	561	238	2375	451	164	57	546	572	231	2109	390	157	54
15	01902643	62	F	529	542	263	2626	381	136	36	549	560	249	2465	413	140	42	558	561	245	2145	428	146	45	498	522	237	2311	377	140	46
16	01800875	63	F	480	493	274	2688	372	140	38	497	510	260	2566	389	154	41	507	508	256	2413	414	160	47	539	537	250	2390	364	155	48
17	01902643	59	F	520	533	273	2620	382	131	34	537	574	249	2476	409	135	43	547	531	241	2512	428	140	50	480	491	236	2156	374	132	51
18	01601717	56	F	459	472	194	2007	498	169	34	480	510	180	2495	502	174	42	488	509	176	2315	516	180	43	538	537	171	2398	473	175	44
19	01804564	55	M	515	548	192	2415	416	162	38	534	550	165	1864	419	175	41	544	564	159	1984	448	180	40	586	591	152	2189	401	176	42
20	01802312	53	F	560	573	242	2393	418	161	38	582	600	231	2175	427	170	45	591	611	227	2276	435	175	47	586	592	221	2098	411	165	45
21	01705602	58	F	534	561	193	2356	419	157	31	552	601	200	2176	429	160	42	560	576	196	2265	456	177	45	552	562	190	2012	403	166	41
22	01704779	57	F	512	525	277	2577	388	146	38	532	599	246	2143	399	151	41	542	531	240	2198	428	165	42	538	542	236	2009	400	142	42
23	01800875	54	F	480	493	256	2601	384	152	39	502	542	231	2571	410	153	42	511	527	224	2612	467	157	48	506	513	219	2310	415	143	41
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31	01805473	76	F	462	475	252	2418	414	143	34	479	501	158	2368	487	152	37	479	596	218	2453	509	158	41	470	482	212	2087	405	162	39
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33	01109193	72	F	507	520	194	2187	457	166	36	527	541	174	2008	499	167	40	527	561	171	2315	515	172	42	516	528	167	1989	427	184	39
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35	01800938	61	M	547	560	163	2029	493	197	40	567	590	154	1785	601	201	41	567	598	150	1897	612	157	49	558	562	146	1698	428	137	39
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37	01206153	62	M	515	528	302	2771	361	116	32	534	550	287	2476	401	124	43	534	521	282	2564	435	141	47	528	548	276	2123	343	131	43
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43	01804845	69	M	476	489	215	2252	436	178	41	494	501	207	2018	467	182	39	494	501	201	2067	498	188	51	587	591	196	1953	423	200	49
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53	00804440	73	M	512	525	216	2109	474	212	45	532	555	201	1176	490	218	49	532	545	199	1350	501	221	52	441	482	191	961	465	212	50
54	00606409	75	M	493	506	226	2229	449	240	54	513	546	219	2384	467	245	55	513	526	215	2468	478	254	59	501	523	210	1320	432	214	51
55	01800938	76	F	508	518	245	2451	324	240	51	522	521	231	2314	379	249	54	522	534	228	2365	401	251	59	511	519	225	1390	345	243	54
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63	01304542	63	M	447	460	249	2495	401	172	43	465	506	228	1084	447	183	55	465	486	222	1134	498	194	51	454	461	216	989	420	175	41
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67	01800715	54	F	478	491	245	2536	384	140	35	498	509	219	617	419	145	37	498	475	211	734	467	164	54	471	461	207	542	410	154	59
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74	00606563	77	M	482	502	231	2481	461	211	51	501	521	127	1398	487	219	59	501	509	209	1430	501	326	42	476	462	205	1105	454	314	45
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77	01901068	74	F	512	539	123	2468	419	241	46	531	541	109	722	473	250	54	531	542	106	884	501	254	51	524	471	101	623	420	231	59
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79	01608665	76	M	532	560	245	2165	433	214	61	551	561	232	1762	497	224	67	551	568	227	1893	507	231	61	541	571	223	1523	412	221	60
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81	00902464	56	F	485	507	245	2654	500	213	55	508	463	231	2347	453	221	37	508	511	226	2490	498	227	46	498	527	213	2265	488	214	44
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83	01900999	57	F	539	552	251	2375	421	148	35	560	542	263	911	498	153	33	560	546	225	1009	510	167	47	546	543	219	894	451	160	42
84	01804295	58	F	575	588	249	2570	389	159	41	595	601	235	854	412	161	42	595	612	229	972	453	174	43	561	541	224	746	399	176	40
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87	01901574	71	F	512	525	243	2345	426	161	38	533	549	228	1027	456	261	45	533	555	224	1190	499	275	48	503	509	215	934	435	241	37
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