A PROSPECTIVE OBSERVATIONAL STUDY TO ANALYZE CHANGES IN RETINAL BLOOD VESSEL DENSITY IN PRIMARY OPEN ANGLE GLAUCOMA FOLLOWING INTRA OCULAR PRESSURE REDUCTION BY SURGICAL MANAGEMENT USING OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY

DISSERTATION SUBMITTED TOWARDS FULFILLMENT OF THE RULES AND REGULATIONS FOR THE M.S. BRANCH III OPHTHALMOLOGY EXAMINATION OF THE TAMILADU

DR. M.G.R. MEDICAL UNIVERSITY TO BE HELD IN MAY 2020

Registration number:221713305


NOT TO BE MINISTERED UNTO BUT TO MINISTER
CHRISTIAN MEDICAL COLLEGE
VELLORE
INDIA

BONA FIDE CERTIFICATE

This is to certify, this dissertation entitled 'A prospective observational study to analyze changes in retinal blood vessel density in primary open angle glaucoma following intra ocular pressure reduction by surgical management using optical coherence tomography angiography' done towards fulfillment of the requirements of the Tamil Nadu Dr. MGR Medical University, Chennai, for the MS Branch III (Ophthalmology) examination to be conducted in May 2020, is the bona fide work of Dr. Sharmila. S, postgraduate student in the Department of Ophthalmology, Christian Medical College, Vellore.

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circadian fluctuation of ocular perfusion pressure and its role in various types of glaucoma.docx (D42809718)
A CROSS SECTIONAL STUDY TO MEASURE BLOOD FLOW VELOCITIES IN OPHTHALMIC ARTERY USING COLOUR DOPPLER IMAGING IN NORMOTENSIVE GLAUCOMA PATIENTS 2.docx (D57320427)
https://www.researchgate.net/publication/326014669_Peripapillary_Vessel_Density_Reversal_after_Trabeculectomy_in_Glaucoma
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INTRODUCTION

Glaucoma is an important leading cause of irreversible blindness worldwide. It is a chronic progressive optic neuropathy with multifactorial pathogenesis, raised intraocular pressure (IOP) being the most widely recognized and the only modifiable risk factor. (1)

Despite advances in technology, it has been estimated that the number of people suffering from glaucoma worldwide will increase to 76 million by the year 2020 and is estimated to increase to 111.8 million in 2040.(2) Asia is expected to have the highest number of people with glaucoma in future followed by Africa.(2) These estimates clearly indicate the need for newer strategies in glaucoma screening and management, especially in Asian countries, being a single largest contributor of glaucoma prevalence worldwide.

Since primary open angle glaucoma (POAG) progresses asymptomatically, most patients present at an advanced stage. Early diagnosis and appropriate management will delay or even prevent the progression of the disease. Mechanical, vascular and neuronal factors contribute to optic nerve damage. The clinical signs of optic nerve damage in glaucoma are very specific. They include increase in the cup disc ratio, deepening of the cup and widening of lamina cribrosa, thinning of the neuro retinal rim and nerve fiber layer defects. (3)

Given the progression of POAG despite IOP reduction and the extensive optic nerve damage seen in patients with normal tension glaucoma (NTG: glaucoma patients with IOP in the normal range), vascular factors undoubtedly have a major role to play in

the pathogenesis. Ischemia can also be considered as an independent risk factor for glaucoma and can be associated with systemic factors like hypotension, sudden blood loss, vasospasm and coagulation disorders (3)

Ocular blood flow studies have shown reduction of blood flow in the larger ocular and retinal blood vessels in glaucoma patients and improvement of ocular blood flow following IOP reduction.(1),(2).The advances in technology like the automated perimetry using Humphrey Field Analyser (HFA) and optical coherence tomography (OCT) have improved the diagnosis of glaucoma. They provide a measurement of integrity of the structure and function of the damaged neural elements, i.e., the retinal ganglion cells (RGC).

However, methods to study the blood flow in the smaller retinal vessels in the superficial layers of the retina and optic nerve head (ONH) which perfuse the RGCs and nerve fiber layers are still in the early stages. There is no gold standard yet to analyze microvascular changes. Optical coherence tomography angiography (OCT-A) is a newer investigation modality, which provides high-resolution view of the microvasculature in the optic nerve head and retina. This technology has the advantages of being rapid, reproducible and non-invasive.

Glaucoma can be managed medically and surgically. Surgical management is the treatment of choice in advanced glaucoma, for patients who are non-compliant with medical management and those with uncontrolled IOP despite maximally tolerated medical therapy.

Trabeculectomy is the commonly done surgery for glaucoma. It has been proven that trabeculectomy has been more effective in controlling IOP and preventing visual field deterioration compared to medical management in glaucoma patients. Given that cataract and glaucoma are age related diseases and occur concurrently, most of our glaucoma patients undergo combined glaucoma and cataract surgery (trabeculectomy with phacoemulsification and intraocular lens implantation- PhacoTrab) rather than a two-stage surgery which is routinely done in the developed countries. Though two-stage procedures appear to be more successful in terms of long term IOP reduction, given the expected compliance and socioeconomic status of our patients, the single combined surgery is preferred.

This study is done to analyze the optic nerve head (ONH), peripapillary and macular microvascular density and flow after trabeculectomy surgery. Since those patients who have been planned for trabeculectomy, undergo a combined procedure (PhacoTrab), to eliminate the effect of cataract extraction on our assessment of retinal vascular density using OCT-A, we thought that it would be appropriate to look at the same parameters in patients with cataract undergoing phacoemulsification with intraocular lens implantation (PhacoIOL).

We evaluated the ocular dynamics pre and post operatively using OCT-A in glaucoma and non-glaucoma patients with cataract and assessed if there was any change in the capillary density in the optic nerve head, peripapillary region and macular region in both the groups. This study has been done to see if OCT-A will help in the prognostication of the disease when used pre and post operatively and to establish the effects of surgery in altering or improving retinal vessel density.

AIM

To study the changes in retinal vascular density using swept source optical coherence tomography angiography (OCT-A) in patients with primary open angle glaucoma (POAG) and cataract, before and after combined trabeculectomy and phacoemulsification with intraocular lens implantation (PhacoTrab) and compare this to patients with cataract alone undergoing phacoemulsification with intraocular lens implantation (PhacoIOL).

OBJECTIVES

Primary Objectives:

1. To document the peripapillary, papillary and optic nerve head vascular density index by using OCT-A, in patients with POAG and cataract before and after PhacoTrab.

2. To document the peripapillary, papillary and optic nerve head vascular density index by using OCT-A, in patients with cataract alone before and after PhacoIOL.

Secondary Objectives:

1. To compare the vascular density index in the optic disc, papillary area and peripapillary area, using OCT-A in patients who have undergone PhacoIOL versus those who underwent PhacoTrab.

2. To compare the macular vessel density in these patients before and after PhacoIOL versus those who underwent PhacoTrab.

REVIEW OF LITERATURE

Glaucoma is considered as the leading cause of preventable blindness worldwide second only to cataract. Untreated glaucoma unlike cataract leads to irreversible blindness. (1) The prevalence of glaucoma worldwide among people aged 40-80 years is estimated to be 3.5%. The prevalence rises from 0.7% in the 40- 49-year age group to 7.7% among those over the age of 80. (2) The prevalence of primary open angle glaucoma (POAG) is 4.2% and that of primary angle closure glaucoma (PACG) is 1.09%. The estimated risk of blindness over 15-20 years from POAG ranges from 14.5% to 27% (unilateral) and from 6.4 to 9% (bilateral). (2)

In South India according to Aravind comprehensive eye survey the prevalence of glaucoma is 2.6% and POAG contributed to around 1.7%. In the above survey one-fifth of patients were blind in either or both eyes due to glaucoma. (3) Prevalence of POAG according to Vellore eye disease study was 0.41% .(4) Based on above studies the estimated population with glaucoma in India is around 11.2 million out of which open angle glaucoma is estimated to contribute 6.48 million, most of which go undetected or is diagnosed at an advanced stage.(5)

Definition

POAG is defined as a chronic progressive anterior optic neuropathy with characteristic changes in the optic nerve head and corresponding field defects, in which intraocular pressure (IOP) is the only modifiable risk factor. (6)

Pathophysiology:

The pathophysiology of POAG is attributed to various biomechanical, biochemical and vascular causes. No single definite pathophysiology has been explained till now.

These multiple factors ultimately lead to the damage and death of retinal ganglion cells (RGC). (7)

Various theories have been postulated as the reason for increased RGC apoptosis in glaucoma.

- It has been stated that ischemia to the retina results in the release of glutamate ions which are toxic to the RGCs. Ischemia is believed to be caused by either mechanical compression due to raised IOP or may occur due to vascular or biochemical causes without raised IOP. (8)
- Ischemia due to mechanical compression in patients with raised IOP is postulated to result in defective neurotropin transport leading to axonal death. (8)
- Mechanical theory also states that raised IOP causes stretching of lamina cribrosa leading to RGC death. (7)
- IOP related stress could also result in occlusion of capillaries in the lamina cribrosa causing ischemia and axonal damage. (9)(10)
- Failure of autoregulatory mechanism of blood flow in the retina is also postulated as a reason. (11), (7), (12)

All the above theories point to vascular dysregulation to play an important role in the pathogenesis of glaucoma. (13), (14), (15) Several studies have reported reduction in capillary beds, sclerosis of nutritional vessels, and vascular degeneration in glaucoma. (16), (17) Improving ocular blood flow has shown to reduce apoptosis of RGCs. All the above, point to abnormal ONH blood flow as a likely causative factor in the development of glaucomatous optic neuropathy (16)

Figure 1: Normal optic nerve head

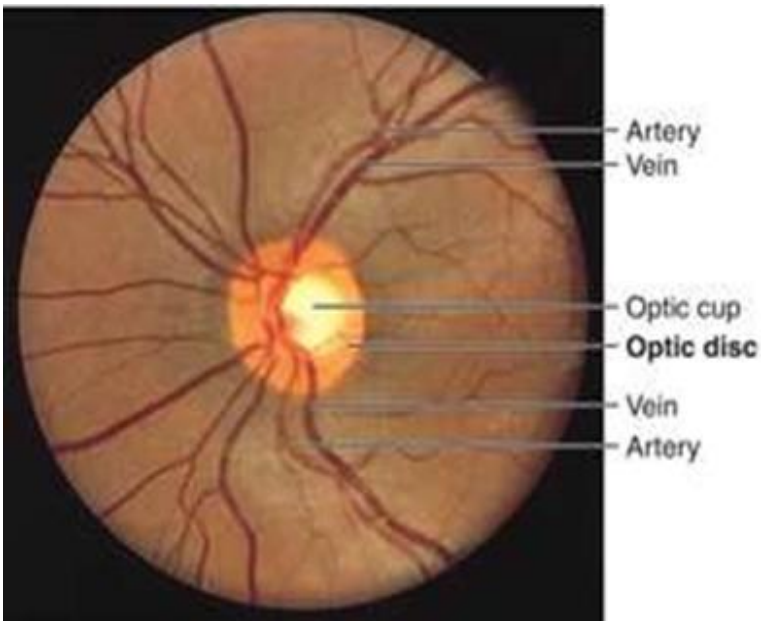
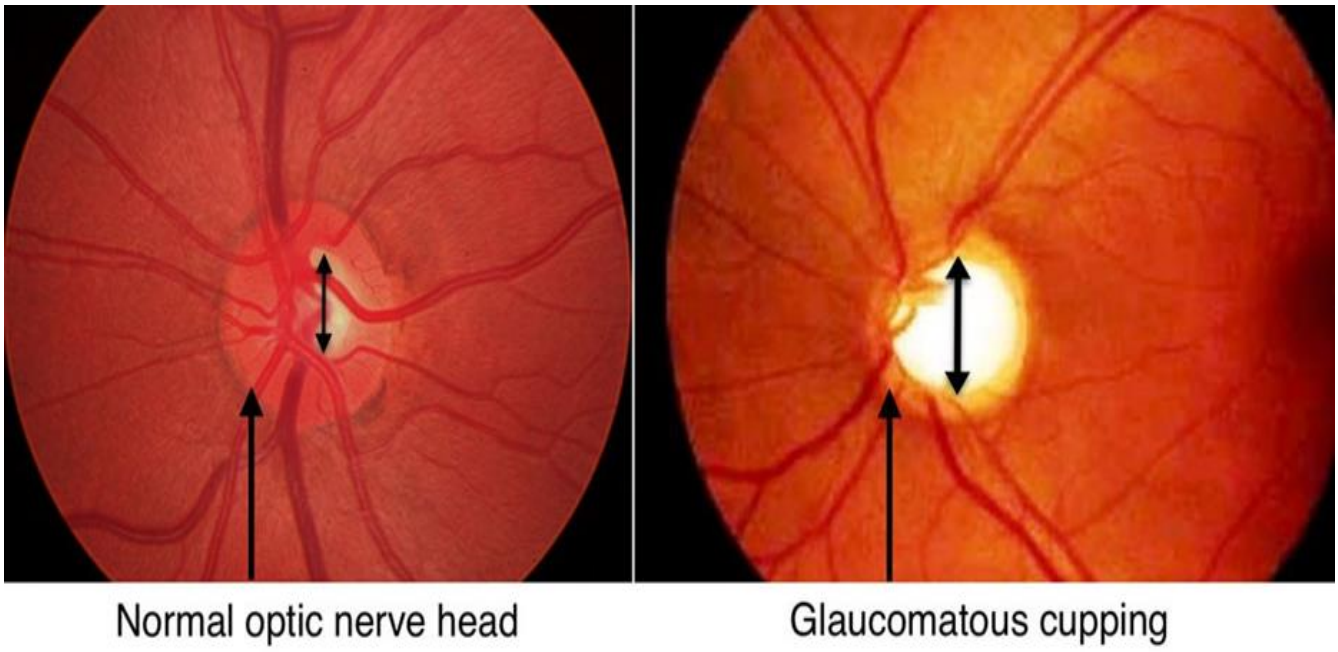


Figure 2: Progression of the ONH damage in POAG



Anatomy of ocular blood flow

The retina gets its blood supply and nutrients from both retinal and choroidal vessels. Branches of the ophthalmic artery which in turn is a branch of internal carotid artery is the main source of blood supply to the retina. The central retinal artery and the posterior ciliary arteries are the main branches. The central retinal artery divides into four divisions: arteriola nasalis retinae superior and inferior, arteriola temporalis retinae superior and inferior. It supplies mainly the inner 2/3rd of retina, retrolaminar optic nerve and superficial RNFL of the ONH. The five short posterior ciliary arteries form the "Circle of Zinn" which supplies anterior optic nerve and the peripapillary choroid.

Optic nerve vascular anatomy

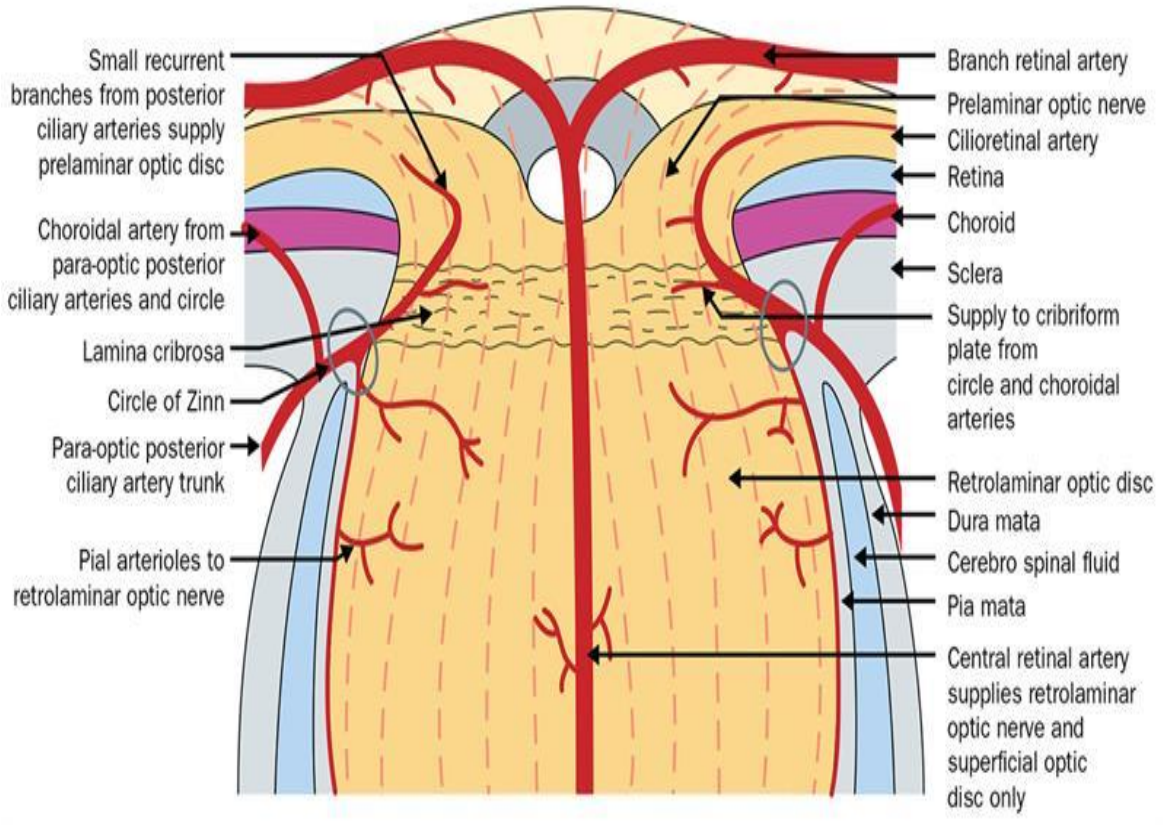
Optic nerve head has four anatomical regions:

- Superficial RNFL
- Prelaminar region
- Lamina cribrosa
- Retrolaminar region

Superficial RNFL of the ONH continues as the nerve fiber layer of the retina, the vessels arising from the surrounding RNFL reaches the center of the ONH. These are called "epipapillary vessels". Prelaminar region is supplied mainly by the branches of circle of Zinn and other short posterior ciliary arteries that course this region.

The lamina cribrosa has multiple fenestrations for the neural axons to pass through. The blood supply is same as that of prelaminar region and may receive additional supply from larger peripapillary choroidal vessels. The retrolaminar region is supplied by the central retinal artery and the pial system. The central retinal artery gives direct intraneural branches. The venous drainage is mainly via the central retinal vein.

Figure 3: Blood supply of the ONH:



Ocular perfusion pressure

Ocular perfusion pressure (OPP) is defined as the difference between arterial and venous pressure. The venous pressure is equal to or slightly higher than IOP. The OPP can therefore be defined as the difference between mean arterial blood pressure in the ocular blood vessels and IOP.

Ocular Blood Flow (OBF) = OPP ÷ Vascular Resistance (VR)

VR is controlled by autoregulation, which is thought to be impaired in glaucoma, especially in normal tension glaucoma. Accordingly, without autoregulation, there is an inverse relationship between IOP and OPP. Hence, OPP can be increased by decreasing IOP or increasing blood pressure. The higher the IOP, the lower the OPP. Therefore, blood flow in the ONH also decreases. On the other hand, decrease in IOP can augment OPP and thus increase ONH blood flow.

Various studies have reported that decreased vascular perfusion may play an important role in the development of glaucoma in addition to increased IOP. Decrease in lamina cribrosa depth following IOP reduction has been documented in glaucoma patients. (18), (19)

Investigation to assess ocular blood flow

Several new invasive and noninvasive techniques have been used to study the ONH, peripapillary and macular blood flow in glaucoma over the last few decades apart from routine standard glaucoma work up.

Invasive tests:

- Indocyanine green angiography (ICG) (20)
- Fundus fluorescein angiography (FFA) (21)

These tests have been used to assess the blood flow of choroid and retina. Both these techniques showed that glaucoma is associated with reduced peripapillary choroidal filling time but were not able to quantify it. (21), (22)

Noninvasive tests:

- Laser doppler flowmetry (23)
- Confocal scanning laser doppler flowmetry (13)
- Color doppler ultrasound imaging (14), (24), (25)
- Retinal flicker analyzer (26)
- Color doppler imaging
- Laser doppler velocimetry
- Laser speckle technique
- Retinal vessel analyzer
- Retinal oximetry
- Pulsatile ocular blood flow

These investigative methods were able to demonstrate reduced blood flow to ONH and peripapillary region in patients with glaucoma as compared to normals. However as with the invasive methods quantification of the amount of capillary network loss was not possible. (23), (13). Moreover, the reproducibility of these tests was low, and artefacts were high.

Optical Coherence Tomography Angiography

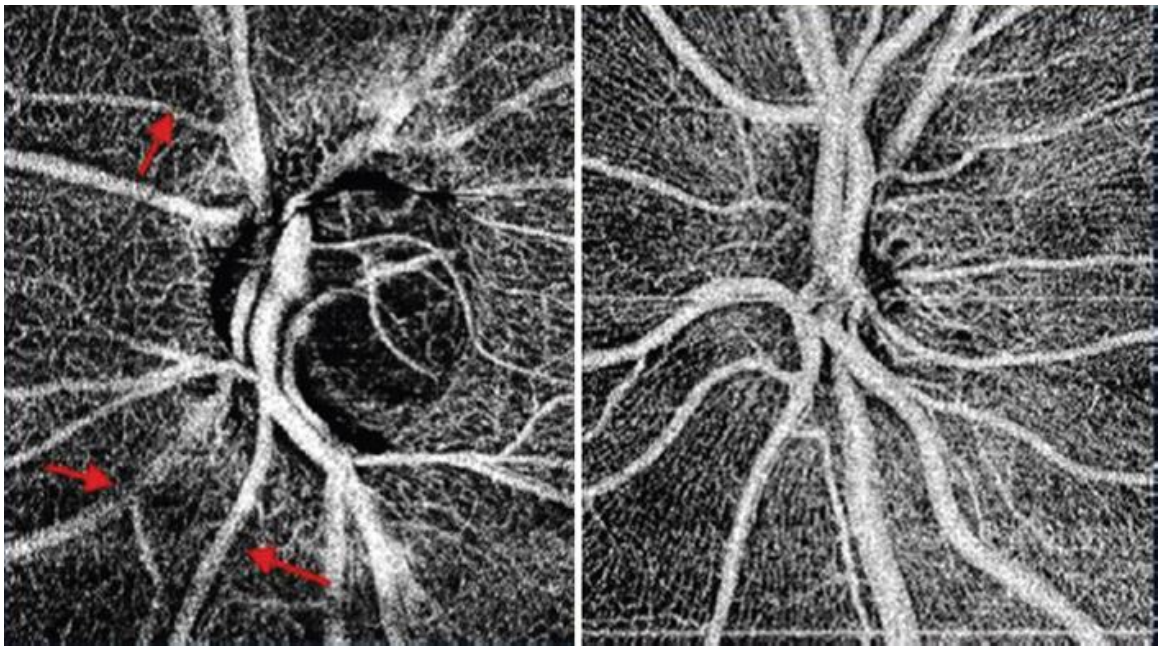
OCT is an imaging technique, analogous to B scan ultrasound. It works on the principle of low coherence interferometry. (18). Infrared light is used instead of ultrasound waves. Based on the time delay and interference of the reflected infrared light from various retinal tissues, cross sectional images of the retina are obtained. (27) The advantages of SD-OCT are 3D imaging, reproducible and advanced segmentation algorithms of ONH, peripapillary and macular region. (21), (29). OCT-A is a part of OCT imaging. It is a noninvasive technique which has emerged in the recent past as an investigation tool for the assessment of perfusion of the ONH, peripapillary region and macula in glaucoma patients and glaucoma suspects. (28), (29), (30), (31), (32), (24).

OCT-A is a non-invasive, in vivo, reproducible, non-contact, quick technique which can be done in a few seconds. Infrared light reflected from the surface of moving red blood cells as intrinsic contrast helps to depict capillaries accurately. It is sensitive to both transverse and axial flow at a time. The OCT scan consists of multiple A Scans compiled to a B-Scan. Multiple such B-Scans are obtained from the same area, providing cross sectional images of the microvascular network in the area of interest, making it possible to localize the exact region of pathology. OCT-A identifies difference in amplitude between two OCT B-Scans (amplitude deceleration). (33) As stationary structures would appear static in sequential B-scans, changes detected by OCT-A are largely attributed to erythrocyte movement in the perfused vasculatures.

A number of algorithms such as split-spectrum amplitude decorrelation angiography (SSADA), OCT-A ratio analysis, and optical microangiography (OMAG) have been developed to study blood flow measurements like vessel density, flow index and blood flux index from the sequential B-scan. Enface images of several individual vascular plexus at various depths of retina can be assessed. (11), (34) It can superimpose color coded flow information on gray scale structural information. Thus, both structural and functional information can be assessed. (29)

Many studies were able to demonstrate that the changes in the vessel density and flow index occur in early stages of glaucoma.(35), (29), (10), (36), (37), (38), (30) OCT-A can also be used as an important tool in monitoring the progression of glaucoma as there is a close correlation between flow index/vessel density and thickness of ganglion layer.(39),(40)

Figure 4: OCT-A images (Glaucoma and Normal)



Vascular factors have been correlated with RNFL thickness, functional parameters in the visual field and visual acuity. Ocular perfusion has also been evaluated in glaucomatous eyes in response to sustained therapeutic IOP reduction. The ability of anti-glaucoma medications to alter perfusion has been described using scanning laser Doppler flowmetry and color Doppler imaging methods. (14), (24), (25) Improvement of ocular perfusion has been reported following sustained IOP reduction in glaucoma patients after surgery. (31), (13)

Management of POAG

Management of POAG, medical or surgical is aimed at lowering IOP. Medical management includes systemic and topical medications. Systemic oral and intravenous medications are used for rapid control of IOP in acute elevation. Topical medications are used for long term control of IOP and can be continued for life with minimal side effects. However, the efficacy, compliance, and affordability of antiglaucoma medications have become significant in our practice. (41) Several studies have also shown that surgical procedures are capable of achieving better control of IOP and reducing disease progression in glaucoma patients compared to topical medications. (42), (43), (44)

Trabeculectomy is the treatment of choice for all patients with uncontrolled glaucoma on maximum medical therapy and in patients not tolerating medical therapy. (45) Given the socioeconomic status and compliance of patients, surgery is preferred over medical management in most of our patients. It is effective in controlling the IOP.

(42), (43), (44), (13) and reducing the rate of progression of the visual field defect compared to medical therapy. Studies have shown that IOP reduction plays an independent role in reducing the rate of visual field progression. (46), (43), (47)

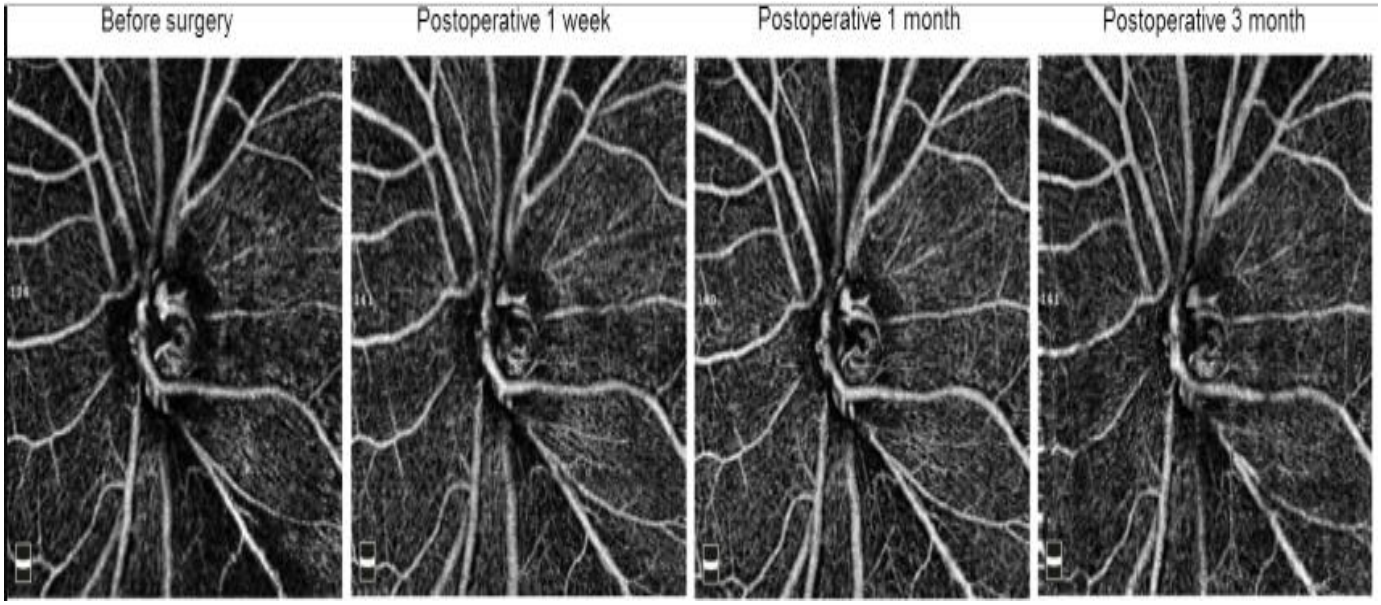
This study is done to analyze the ONH, peripapillary and macular microvascular density and flow after trabeculectomy surgery. Given the age, presence of a coexisting cataract, compliance of our patient population and socioeconomic considerations, most of our glaucoma patients who are planned for surgical management undergo combined trabeculectomy with PhacoIOL (PhacoTrab) rather than trabeculectomy. We, however, are not sure of the consequence of the cataract surgery on retinal vascular density. Hence to eliminate this potential effect of cataract extraction on our assessment of retinal vascular density using OCT-A, we thought that it would be appropriate to look at the same parameters in patients without glaucoma undergoing cataract surgery alone (PhacoIOL).

We will also evaluate the ocular dynamics preoperatively in glaucoma patients and nonglaucoma patients and see if there is an improvement in the capillary density in glaucoma patients compared to normal individuals because of lowering of IOP. There are many studies which have analyzed ONH and peripapillary perfusion and resistance index before and after trabeculectomy using different techniques. The results were variable.

Shin et al., (32) studied 31 eyes of patients with POAG who underwent trabeculectomy, with OCT-A at 3 months after trabeculectomy. There was a considerable IOP reduction along with increase in peripapillary and ONH microvascular network and statistically significant decrease in lamina cribrosa depth

after trabeculectomy. The lamina cribrosa depth significantly improved from 26.3 ± 11.8 mm to 12.5± 3.6mm ($p<0.001$). The circumpapillary vessel density increased from 44.9 ± 6.0% to 47.0 ± 7.2%. ($p=0.133$); this was not statistically significant. The peripapillary microvascular improvement was observed in 19 eyes even at 3 months after trabeculectomy.

Figure 5: OCTA before and after trabeculectomy



Berisha et al., (13) studied 30 patients with POAG who underwent trabeculectomy and followed up at 2 weeks and 10 weeks post-surgery using laser doppler flowmetry. They found a statistically significant decrease in IOP associated with increase in OPP and ONH blood flow post trabeculectomy. The mean IOP reductions were 6.8 mm Hg (4.5%) at 2 weeks and 6.8 mm Hg (4.6%) at 10 weeks respectively ($p <0.001$). There was a significant increase in OPP 18.5% and 19.0% for each postoperative visit,

respectively; (p <0.001). ONH blood flow, however, was independent of antiglaucoma therapy (p=0.583).

Kuerten et al., (48) studied thirty patients with POAG who underwent trabeculectomy using color doppler for 3 years. There was a statistically significant increase in end diastolic velocity of central retinal artery and temporal posterior ciliary artery after a successful trabeculectomy surgery. The improvement was considered to be because of a significant IOP reduction from 25 to 9 mm Hg (p < 0.0001). There was a significant improvement of end–diastolic velocities of the central retinal artery (p<0.003) and temporal posterior ciliary arteries (p< 0.003).

19 eyes of 17 patients were followed up by Cantor et al., (14) after trabeculectomy at 3 months, 6 months and 12 months using color doppler. At 3 months, the mean IOP reduction was 17.1 mm Hg (62.3%; p<.001). At 6 and 12 months, the mean IOP reduction was 15.7 mm Hg (57.3%) and 15.5 mm Hg (p<.001) respectively. But there was no significant change in ocular blood flow dynamics or ocular blood flow in ophthalmic artery, central retinal artery and posterior ciliary artery.

Zeboulon et al., in their prospective observational study of 21 eyes of 21 patients with chronic glaucoma undergoing primary filtering surgery, found a very limited effect of surgically induced IOP reduction on peripapillary and macular vessel density. The mean vessel density changes in peripapillary area was 0.065± 0.88% (p= 0.788). In the macular region, the mean change in vessel density was 0.022± 0.691% (p= 0.405). They concluded that vessel density might not be an adequate measure of blood flow. (49)

In 2012 Lee et al., studied 35 patients with POAG who underwent trabeculectomy. The amount of posterior displacement of the lamina cribrosa was significantly decreased at 6 months postoperatively (p=0.001). Both lamina cribrosa thickness and prelaminar tissue thickness significantly increased at 6 months. They also reported that lamina cribrosa reversal might give relief to the compressed nerve fibers or laminar capillaries. In 2013, the authors reported 2 year follow up of 28 patients. The significant lamina cribrosa depth that was noted at 6 months exhibited a variable course thereafter, either remaining stable, being further reversed, or increasing in depth again. The suggested that sustained reduction of the IOP is important for maintenance of the reversed lamina cribrosa displacement that occurs after trabeculectomy. (50), (51), (52).

In an article by Lee et al., 34 patients with POAG who underwent trabeculectomy and were followed up for at least 2.5 years, during which the RNFL thickness was measured using serial SDOCT. They reported that eyes with sustained lamina cribrosa depth reduction over a long period had a slow rate of progressive RNFL thinning after trabeculectomy. (53)

Alaqband et al., have shown that corneal section Phaco IOL has an effect on outflow facility and hence causes reduction in IOP. This again may affect our results and hence comparison with patients undergoing Phaco IOL is justified. (54) Lommatzsch et al., studied 19 eyes, 6 months post trabeculectomy with a mean age of 66 years and mean IOP of 21.0 mmHg and found no significant change in the vessel density and peripapillary RNFL thickness ($p = 0.88$) using OCT-A. (55)

A study by Kim et al., on 56 eyes with POAG following trabeculectomy 3 months post-operatively showed significant increase in vessel density in the lamina cribrosa ($p= 0.006$) The increase in vessel density in the lamina cribrosa was associated with larger reduction in IOP ($p = 0.040$). (56)

Lee et al., studied 25 patients with POAG following trabeculectomy. Using OCT-A vessel density was calculated at 1 week, 1 month, and 3 months postoperatively. A significant increase in the PPVD was demonstrated following trabeculectomy. The reversal was associated with greater preoperative IOP and higher IOP reduction ($p<0.05$) (57)

The main purpose of conducting this study is to evaluate the changes in peripapillary, papillary, optic nerve head and macular vessel density following reduction of IOP by surgical management in patients with POAG using OCT-A.

MATERIALS AND METHODS

STUDY DESIGN:

Prospective, observational, hospital-based study

STUDY SETTINGS:

This study was conducted in department of Ophthalmology, Christian Medical College, Vellore, a tertiary eye care centre.

STUDY DURATION:

This study was conducted between September 2018 to October 2019.

PARTICIPANTS:

Patients presenting to the glaucoma clinic and requiring combined trabeculectomy and phacoemulsification with intraocular lens (IOL) implantation (PhacoTrab) and who fulfill the inclusion and exclusion criteria as given below were recruited for the study after an informed consent. Age matched individuals with cataract, admitted for phacoemulsification with IOL implantation (PhacoIOL) and willing to take part in the study were recruited after informed consent if they satisfied all criteria.

Inclusion criteria

Inclusion criteria for PhacoTrab:

1) Baseline IOP > 21mmHg
2) Open angles on gonioscopy

3) Retinal nerve fiber layer defects or glaucomatous optic disc changes (neuroretinal rim thinning, disc excavation, or disc hemorrhage)

4) Corresponding visual field (VF) defects confirmed by reliable visual field examination. (i.e., false-positive errors <15%, false negative errors <15%, and fixation loss<20%). A glaucomatous VF defect was defined as presence of two of the three Hodapp Anderson Parrish criteria:

- Presence of a cluster of 3 non edge contiguous points on a pattern deviation plot with P < 5% (1 of which had a P < 1%)
- Pattern standard deviation with P < 5%
- Glaucoma hemifield test result outside normal limits

5) Media clear enough to obtain OCT and OCT-A images with an image quality > 40

Inclusion criteria for PhacoIOL

1) Baseline IOP of ≤ 21 mmHg

2) Normal optic nerve head and neuroretinal rim

3) Normal RNFL thickness

4) Normal standard automated perimetry according to Andersons's criteria

5) Significant cataract which warrants surgery

6) Media clear enough to obtain OCT and OCT-A images with an image quality > 40

Exclusion criteria

1. Refractive error > +3.00 D hypermetropia or − 6.00 D myopia and +/- 3D cylinder

2. Previous intraocular surgery
3. Any retinal pathology including age related macular degeneration, diabetic retinopathy, retinal vein and artery occlusions and macular edema
4. Non glaucomatous disc pathologies that cause VF defects like optic disc pit, coloboma, optic neuritis, anterior ischemic optic neuropathy, retinitis pigmentosa, optic pathway lesions.
5. History of previous intravitreal injections and retinal laser
6. History of chronic posterior uveitis.
7. Any history of drug intake that causes possible macular and retinal toxicity
8. Axial length <21mm or >26mm

Variables Tested

a) Optic nerve head area vessel density(%) (VdONH): Density of the microvasculature at the optic nerve head area, calculated by image analysis.

b) Peri-papillary area vessel density (%) (VdPPA): Density of the microvasculature at the peri-papillary area (700-micron wide elliptical annulus centered on the disc), calculated by image analysis.

c) Papillary area vessel density (%) (VdPA): Density of the microvasculature at the papillary area (3 mm circular region centered on the ONH), calculated by image analysis.

d) Macular vessel density(VdMacula) (%): Density of the microvasculature at the macular area, calculated by image analysis.

Methodology

After getting a detailed informed consent, information regarding inclusion and exclusion criteria were obtained by a thorough history and examination by the principal investigator (PI). Data regarding confounding factors was obtained using a questionnaire. The PI then did a comprehensive ophthalmic examination including best corrected visual acuity, slit lamp bio microscopy, measurement of IOP, gonioscopy and stereo biomicroscopic examination of the optic nerve head using a 78D condensing lens. If the patient is a diagnosed glaucoma patient, then anti-glaucoma medications that are being taken were noted by PI and all the data captured were entered in the proforma and stored in separate files.

IOP was measured using Goldman applanation tonometer (Model AT 900) attached to a Haag Streit slit lamp biomicroscope (BM 900). All measurements were done preoperatively and post operatively by the PI in the same machine. Gonioscopy was performed using a 4 mirror non-indentation indirect gonioscope (Volk G-2 four-Mirror Glass Gonio Lens, Germany). CCT measurement was done by using an optical biometer (Nidek AL Scan). The Humphrey Field Analyzer II (Carl Zeiss Meditec, Inc) was used for visual field assessment and RNFL thickness, was measured using SD-OCT (TOPCON DRIOCT Trion).

OCT-A was performed using the Swept source spectral domain optical coherence tomography (SSOCT-A – DRI OCT TRITON Plus, TOPCON Inc, Tokyo, Japan) with a central wavelength of 1050 nm light source and scanning speed of 100,000 A

scans/ sec. The optic disc region and macula were imaged using a 3 x 3 mm scan. The names of patients were not recorded in the spreadsheet; patients were identified with their unique hospital identification number. Examination of the patient and recording of findings were done by the PI for uniformity of diagnosis and analysis.

OCT-A scan for analysis of the optic nerve head vasculature, peripapillary, papillary and macular vessel density were done. All surgeries, i.e. PhacoTrab and PhacoIOL were done by one of the three glaucoma specialists with more than 10 years of experience in glaucoma management. Postoperatively patients are reviewed at 1 week, 1 month and 3 months. IOP was checked by the PI, OCT-A scans were done as described at the baseline visit and at 1 week, 1 month and 3month visits. After the study period, glaucoma patients were followed up and managed in the glaucoma clinic as per the standard practice in the department. The non-glaucoma patients were followed up in the general clinic.

IMAGE PROCESSING AND QUANTITATIVE ANALYSIS

En face scans that were acquired in both groups (patients who underwent PhacoTrab and those who underwent PhacoIOL) pre and post operatively were further processed and quantitative analysis of the vessel density was done using the publicly available ImageJ software. Vessel density ratio of each region of interest was calculated by using Fiji Program software (Plug-in Module for ImageJ software). This was done for 4 regions of interest: -

1) Papillary region (3 mm circular region centered on the ONH)

2) Peri-papillary region (700-micron wide elliptical annulus centered on the disc)

3) Optic nerve head

4) Central Macula (3mm area centered around the fovea)

ANALYSIS OF IMAGE USING IMAGEJ SOFTWARE

ImageJ is a free, Java-based image processing software program developed at the National Institutes of Health and the Laboratory for Optical and Computational Instrumentation (LOCI, University of Wisconsin). It can display, edit, process, analyse, save and print 8-bit color and gray scale images and can be used to manipulate these images to calculate area and pixel value statistics of user defined selections.

The vessel analysis protocol uses the below formula to calculate vessel density metrics:

$$\text{Vascular Density} = \frac{\text{Vessel Area}}{\text{Total area of image}} \times 100$$

The ImageJ software is downloaded along with the vessel analysis plugin. (available publicly, as open source). Once the plugin is installed, the vessel analysis tab will appear in the 'Plugins' drop-down menu.

Available here:

http://imagej.net/Fiji/Downloads

http://imagej.net/File:Vessel_Analysis.zip

Figure 6: ImageJ software desktop window

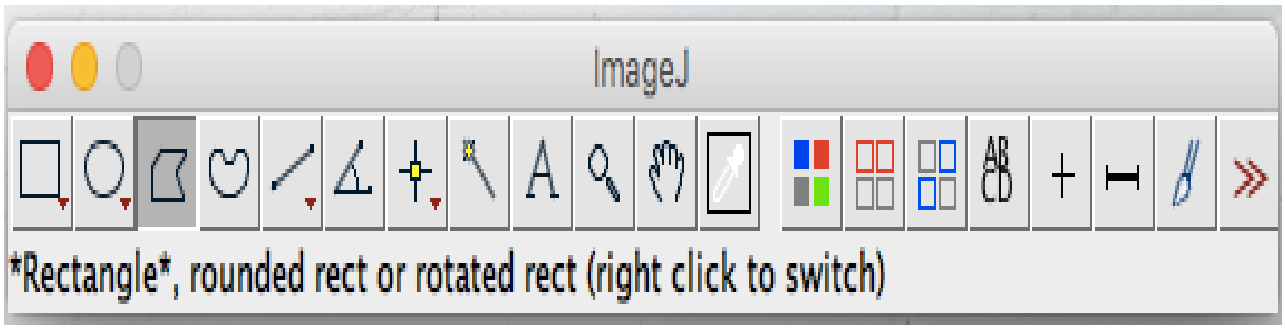


Figure 7: Vascular density tab, in the tool bar

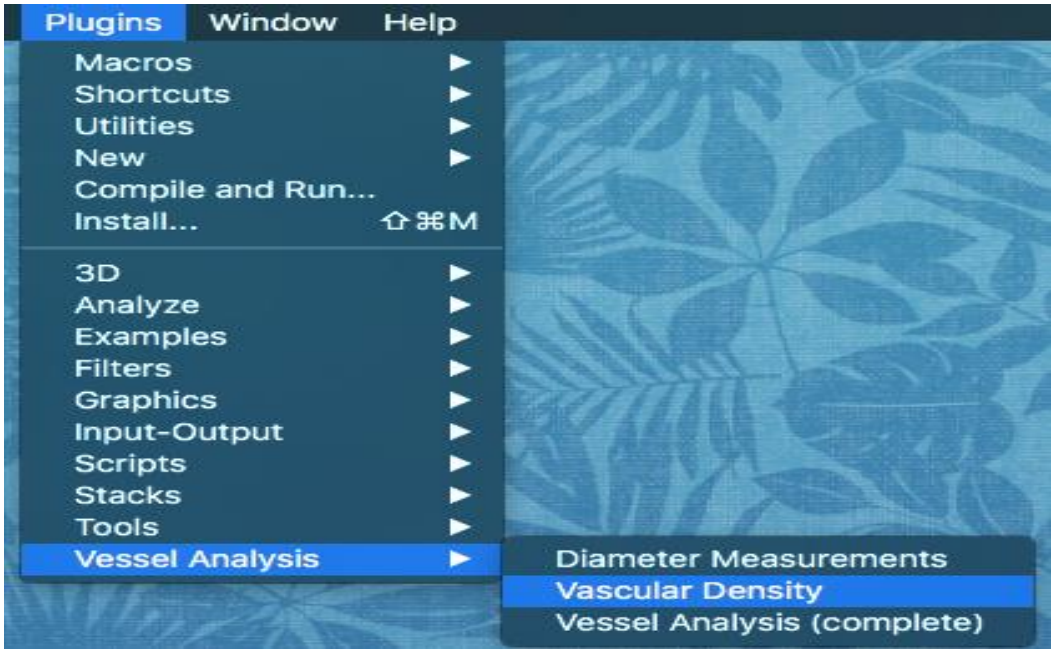
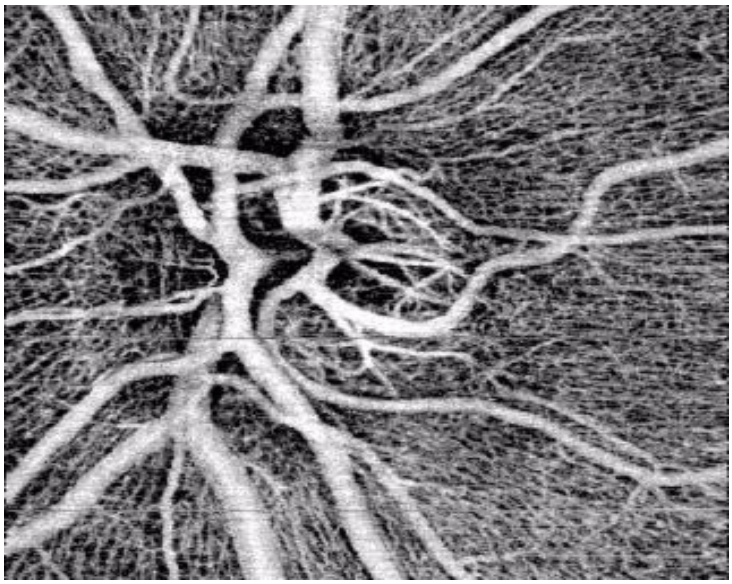


Figure 8: DRI OCT Triton plus, with microvascular network of OCT-A images at different sections, the vessel density map, disc photograph

In the first square, seen to the left, thickness from internal limiting membrane (ILM) to retinal pigment epithelium (RPE) is included, creating microvasculature maps, between the two set boundaries.

The composite image formed is like so: -

Figure 9: 2-D composite OCT-A image formed by superimposition of the microvascular network maps acquired between ILM to RPE



The above image is a 3x3 mm scan of the ONH and peri-papillary micro vascular network, with 320x320 pixel resolution. This image is transferred to the computer and opened in ImageJ software. A mesh framework of the micro vascular grid is created before vessel density analysis. This will delineate the micro vascular network by background subtraction and then, the background subtracted image is converted into an 8-bit binary (black and white) image. This is done by using the 'Binary image' under the 'Process' tab, as shown below

Figure 10: Location of Background subtraction tab and binary map tab on toolbar in ImageJ.

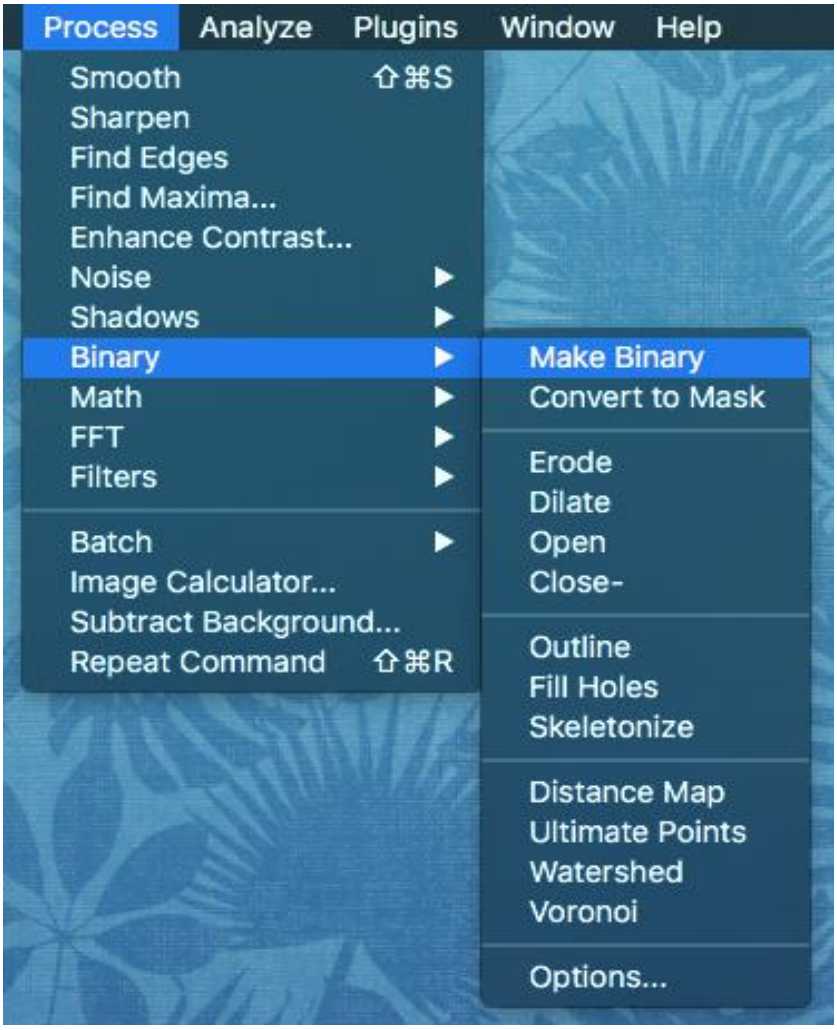
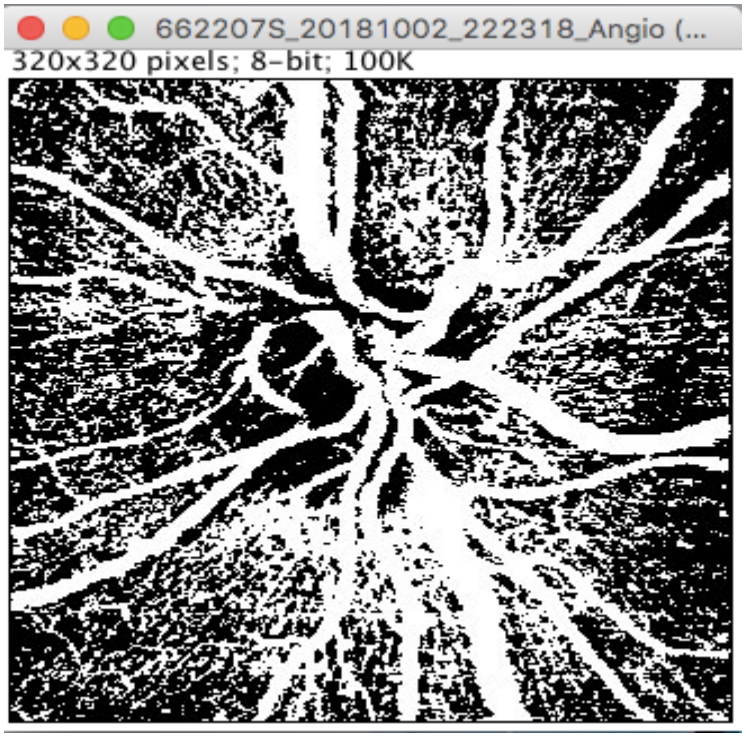


Figure 11: Composite OCT-A image, after background subtraction, and converting to binary image



The required area is selected using the 'Oval', 'Polygon' or the 'Free hand' selection tool, after measuring the proper dimensions of the area of interest. The vessel density of the area of interest, in the cropped images is calculated, by software analysis using ImageJ. The result is displayed as percentage area (%area).

Figure 12: Vascular density of the selected area of interest

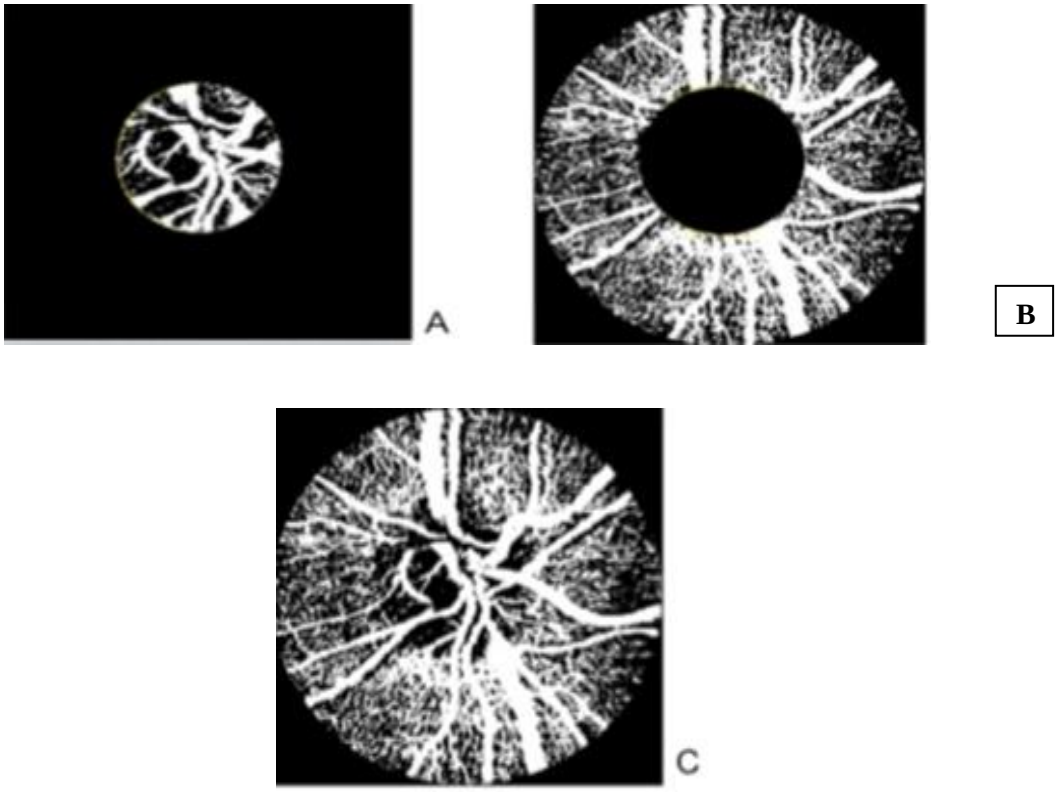


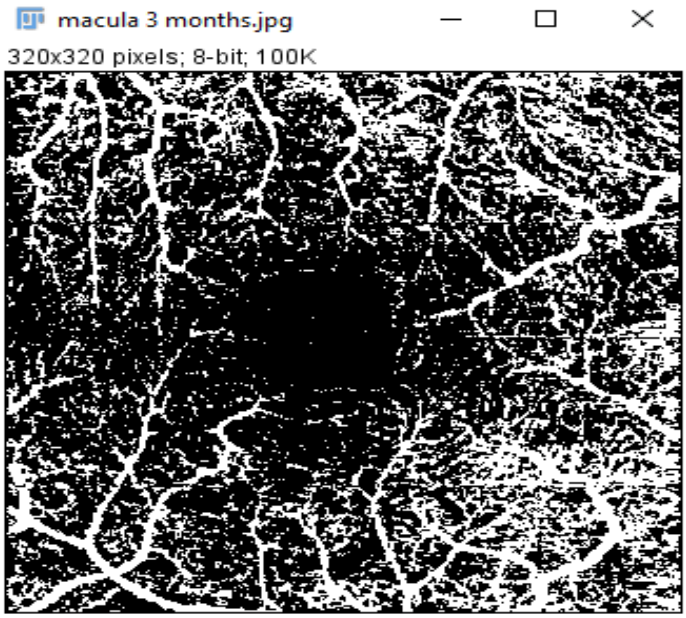
Figure A: Optic nerve head

Figure B: Peripapillary region (700µm wide elliptical annulus around ONH)

Figure C: Papillary region (3mm circular region around ONH)

Similarly, the vessel density is calculated for macular area: 3×3mm

Figure 13: Vessel density of macular area



This process is repeated for the OCT-A image of every selected eye, and the measurements are tabulated in Spreadsheet format by entering in Epidata/Excel.

STATISTICAL ANALYSIS

Sample Size Calculation

Based on the study of Shin et al., (32) the sample size calculation was done. As that study reported a wide range for vessel density, a relative precision of 20% was considered. For a relative precision of 20%, we ended having change less than 2 units for CPVD on both sides, which is acceptable. So, the sample size for CPVD is 35 considering 95% CI. If we add an attrition of 5 %, we need 2 more patients, concluding for 38 subjects. controls included were also 38.

Statistical Methods

The data was summarized using mean (SD)/ median (IQR) for continuous variables based on the normality. Categorical data was expressed as number and percentage. The continuous skewed variables were log-transformed and used for the further analysis. The continuous variables among the two groups were compared using independent-t-test and the categorical variables were compared using chi-square test. Repeated measures ANOVA was used to compare the change of variables from baseline to 3 months among the two groups. The pairwise comparison was done with TUKEY test. All the analyses were performed using STATA/ IC 15.0 software. Spearmann's correlation coefficient was used to analyse the correlation between the data.

Quantitative variables All quantitative variables will be measured as per the machine protocol and documented as raw values. Age was considered to the nearest whole number and matching was done within ±2 years.

RESULTS

A total of 73 eyes of 73 patients were studied. Of these 33 eyes were of patients with primary open angle glaucoma with immature cataract (PhacoTrab group) and 40 eyes were of patients with immature cataract (PhacoIOL group). Of the 33 patients in the PhacoTrab group, 3 patients did not complete 3-month followup.

Table 1: Distribution of patients in each group

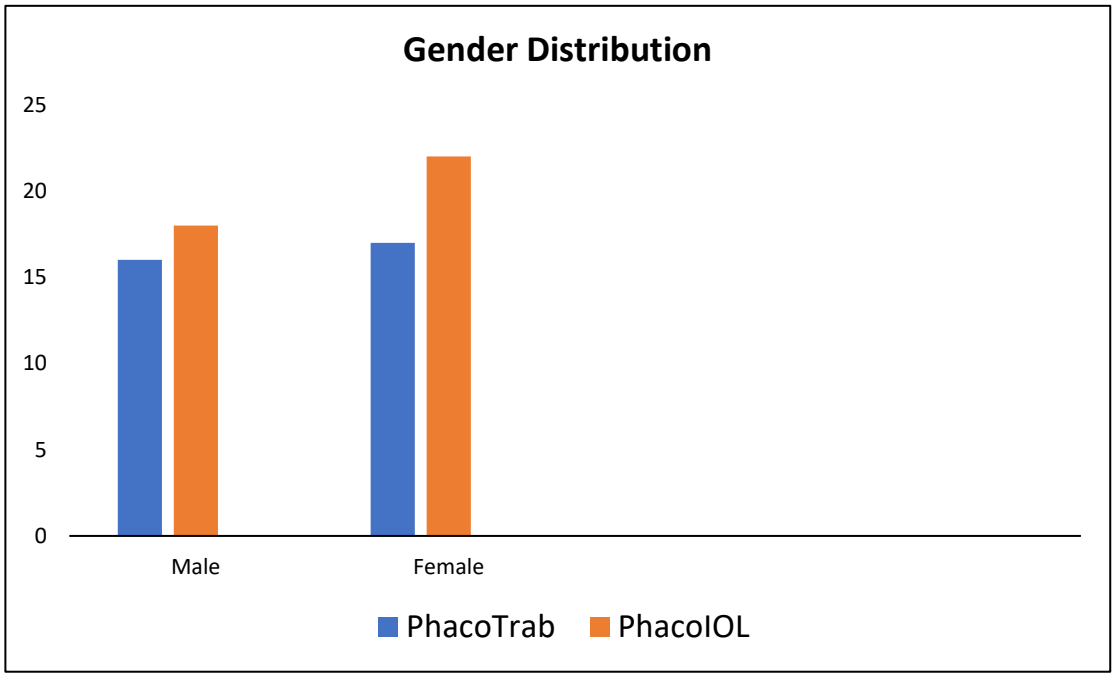
Group	PhacoTrab	PhacoIOL
Number	33	40

Of these 73 patients studied 34 (46.58%) were males and 39 were females (53.42%). There was no statistically significant difference in gender distribution between these two groups, (p=0.766). Table 2 and Graph 1 shows the gender distribution in the 2 groups.

Table2: Gender distribution

Gender	PhacoTrab (%)	PhacoIOL (%)	Total (%)
Male (%)	16(48.48)	18(45.00)	34(46.58)
Female (%)	17(51.52)	22(55.00)	39(53.42)
Total (%)	33(100)	40(100)	73(100)

Graph 1: Gender distribution



The patients in the PhacoTrab group were older (p=0.001). The age distribution in the two groups is as shown in table 3.

Table 3: Age distribution

Mean Age (SD)	PhacoTrab	PhacoIOL
64.22 (8.24)	67.61 (7.63)	61.42 (7.74)

Best corrected visual acuity was measured using Snellen's chart and was converted to LogMar for statistical analysis. The mean LogMar visual acuity of both groups is given in table 4 and graph 2.

Table 4: BCVA in the two groups

Median BCVA (quantiles)	Preop	1week	1month	3months
PhacoTrab	0.3 (0.3,0.5)	0.2 (0.2,0.2)	0.2 (0.0,0.2)	0.1 (0.0,0.2)
PhacoIOL	0.3(0.3,0.5)	0.0 (0.0,0.0)	0.0 (0.0,0.0)	0.0 (0.0,0.0)

Graph 2: Median BCVA

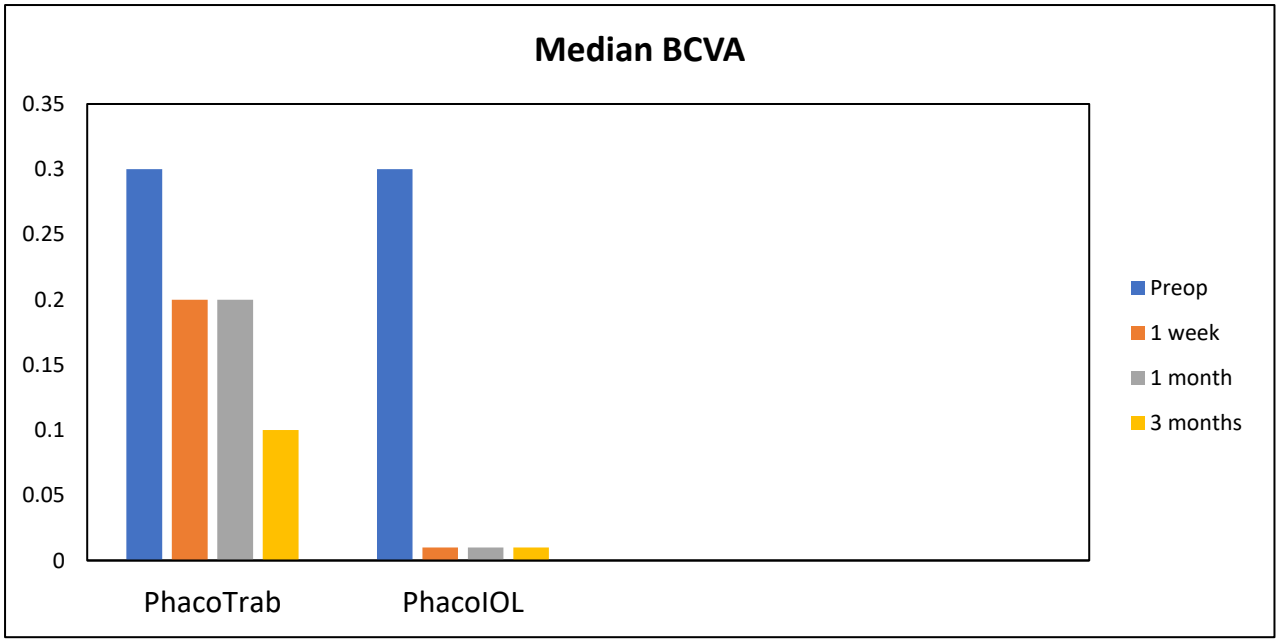
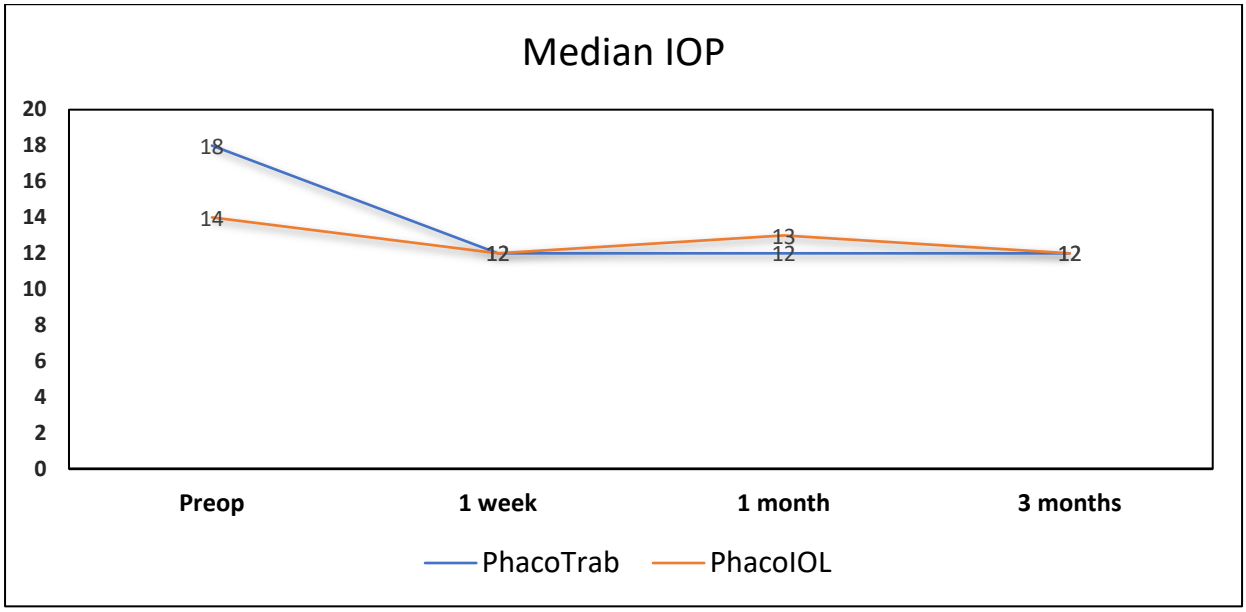


Table 5 and Graph 3 details the median IOP in both groups. Median was chosen instead of mean because of the skewed values. BCVA in the PhacoTrab group was worse than the PhacoIOL group due to advanced glaucoma.

Table 5: Median Intraocular Pressure in both groups

Median IOP (Quantiles)	PhacoTrab	PhacoIOL	p value
Baseline	28 (24,34)	14 (12,16)	<0.001
Preop	18 (18,20)	14 (12,16)	<0.001
1 week	12 (10,14)	12 (12,14)	<0.001
1 month	12 (10,16)	13 (12,14)	0.066
3 months	12 (10,14)	12 (12,14)	0.286

Graph 3: Median IOP in both groups



There was a statistically significant difference in the median IOP between the two groups preoperatively and 1 week post operatively (<0.001). However, this was not seen at 1 month (p=0.066) and 3 months post operatively (p=0.286), indicating success of trabeculectomy in the PhacoTrab group. An interesting finding was reduction in IOP in the PhacoIOL group which was also statistically significant (p=0.044)though the reduction was much lower .

Table 6 depicts the statistically significant difference in median IOP preoperative vs 1 week, 1 month and 3 months postoperative in the PhacoTrab group. The IOP was not different after 1-month post operatively.

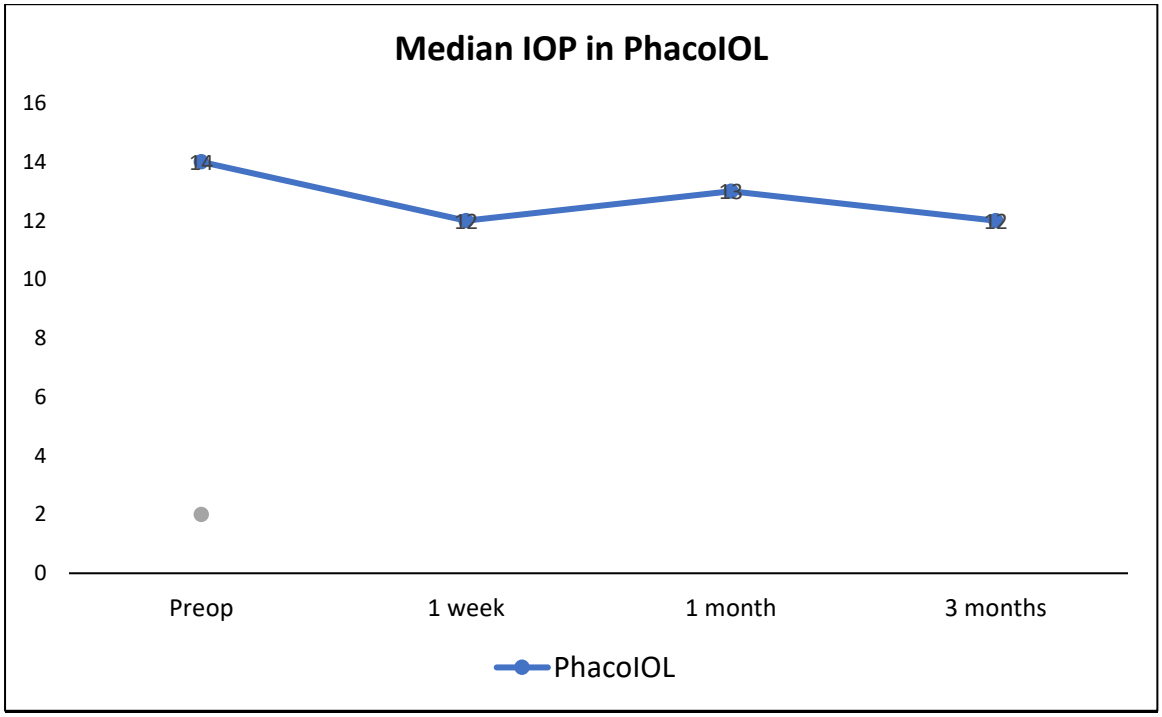
Table 6: Significant difference in the Median IOP post operatively in PhacoTrab group

Median IOP	Preop:18	1week:12	1month:12	3months:12
Preop:18	Not applicable	p = <0.001	p = <0.001	p = <0.001
1week:12	p = <0.001	Not applicable	p = 0.011	p = 0.020
1month:12	p = <0.001	p = 0.011	Not applicable	p = 0.918
3months:12	p = <0.001	p = 0.020	p = 0.918	Not applicable

Table 7: Significant change in the Median IOP post operatively in PhacoIOL group

Median IOP	Preop: 14	1week:12	1month:12	3months:12
Preop: 14	Not applicable	p = 0.053	p = 0.236	**p = 0.044**
1week: 12	p = 0.053	Not applicable	p = 0.450	p = 0.915
1month: 13	p = 0.236	p = 0.450	Not applicable	p = 0.396
3months: 12	**p = 0.044**	p = 0.915	p = 0.396	Not applicable

Graph 4: Median IOP pre and post operatively in PhacoIOL group

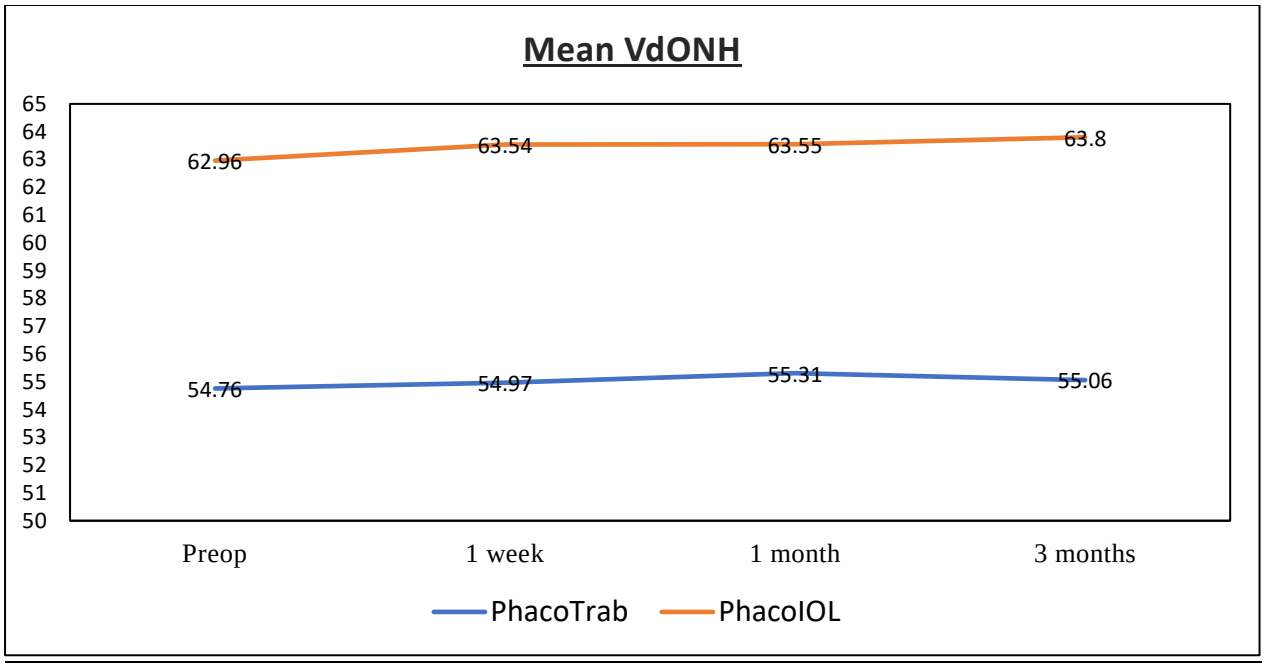


There was no statistically significant difference in the median IOP pre and post operatively at 1 week and 1 month. The respective p-values for preop vs 1 week and 1 month are 0.053 and 0.236 respectively. There was a statistically significant difference in the intraocular pressure at 3 months post operatively compared to pre-op values (p=0.044).

Table 8: Mean Optic nerve head vessel density (VdONH) in both groups

Mean VdONH (SD)	PhacoTrab	PhacoIOL	p-VALUE
Preop	54.76 (3.67)	62.96 (1.76)	<0.001
1 week	54.97 (3.69)	63.54 (2.24)	<0.001
1 month	55.31 (3.93)	63.55 (1.95)	<0.001
3 months	55.06 (4.09)	63.80 (1.84)	<0.001

Graph 5: Mean VdONH in both groups

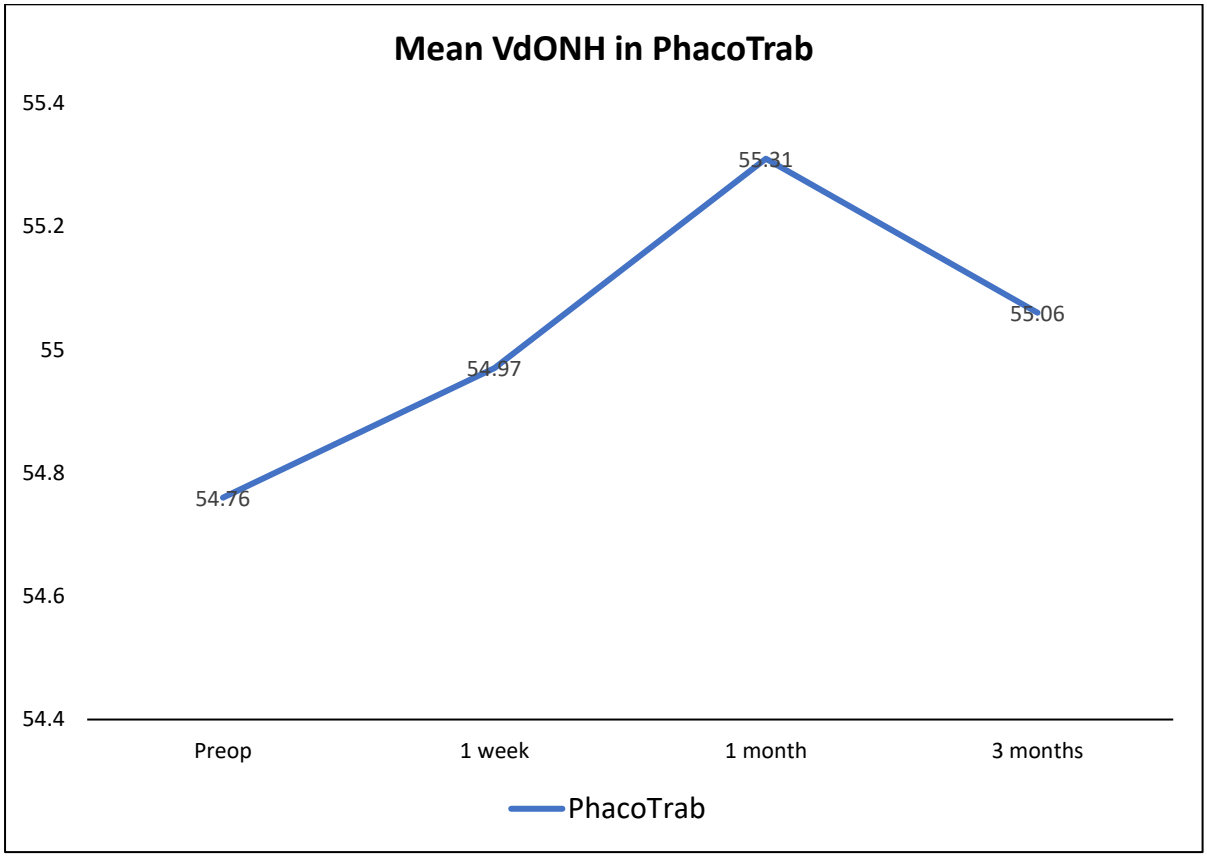


The optic nerve head vessel density in the PhacoTrab group was statistically significantly lower than the PhacoIOL group ($p<0.001$)

Table 9: Difference in mean VdONH Pre and post operatively in PhacoTrab group

Mean VdONH (SD)	Preop: 54.76 (3.67)	1 week: 54.97 (3.69)	1 month: 55.31 (3.93)	3 months: 55.06 (4.09)
Preop: 54.76 (3.67)	Not applicable	p = 0.476	p = 0.061	**p = 0.008**
1 week: 54.97 (3.69)	p = 0.476	Not applicable	p = 0.245	**p = 0.046**
1 month: 55.31 (3.93)	p = 0.061	p = 0.245	Not applicable	p = 0.375
3months: 55.06 (4.09)	**p = 0.008**	**p = 0.046**	p = 0.375	Not applicable

Graph 6: Mean VdONH in PhacoTrab group pre and post-surgery

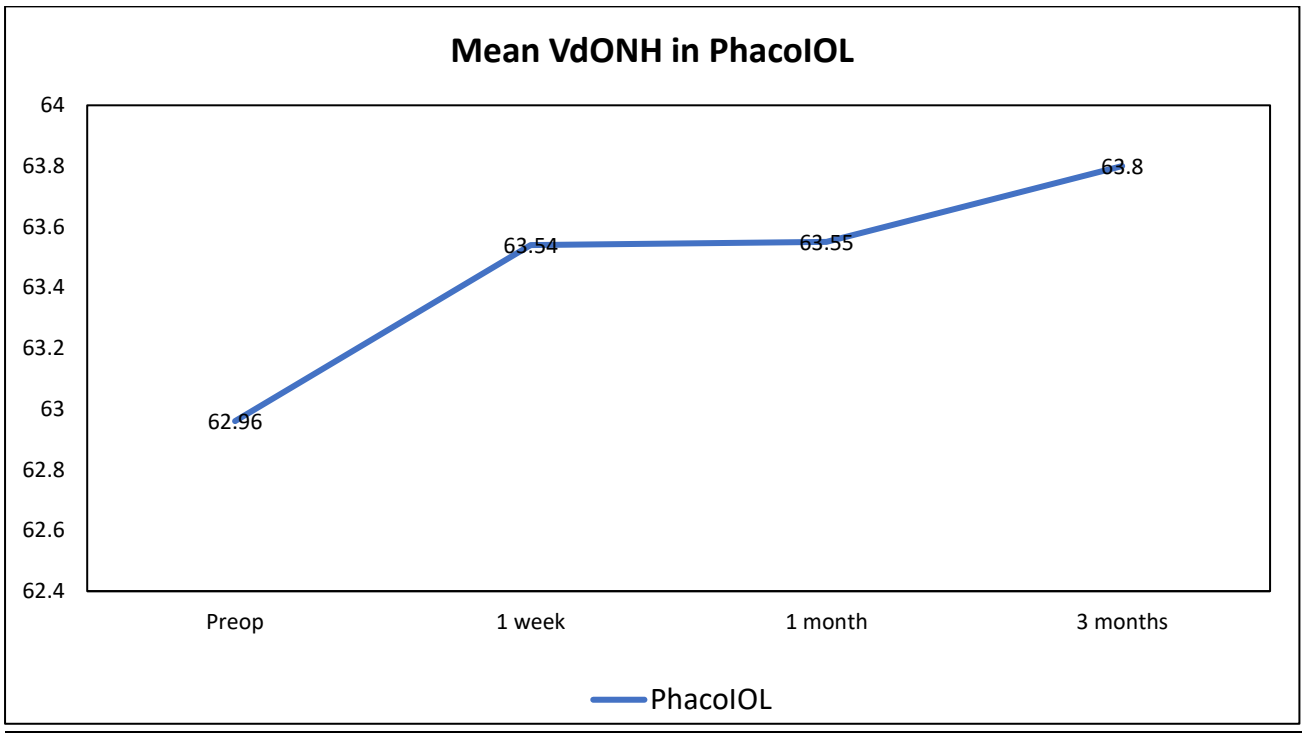


There was no statistically significant difference in the mean optic nerve head vessel density preoperatively vs 1 week and 1month post operatively. The respective p-values for preop vs 1 week and 1 month are 0.476 and 0.061 respectively. But there was a statistically significant difference in the mean optic nerve head vessel density at 3 months (p=0.046).

Table 10: Difference in Mean VdONH Pre and post operatively in PhacoIOL group

Mean VdONH	Preop: 62.96 (1.76)	1 week: 63.54 (2.24)	1 month: 63.55 (1.95)	3months: 63.80 (1.84)
Preop: 62.96 (1.76)	Not applicable	p = 0.031	p = 0.030	p = 0.009
1 week: 63.54 (2.24)	p = 0.031	Not applicable	p = 0.994	p = 0.624
1 month: 63.55 (1.95)	p = 0.030	p = 0.994	Not applicable	p = 0.629
3 months: 63.80 (1.84)	p = 0.009	p = 0.624	p = 0.629	Not applicable

Graph 7: Mean VdONH pre and post-surgery in PhacoIOL group

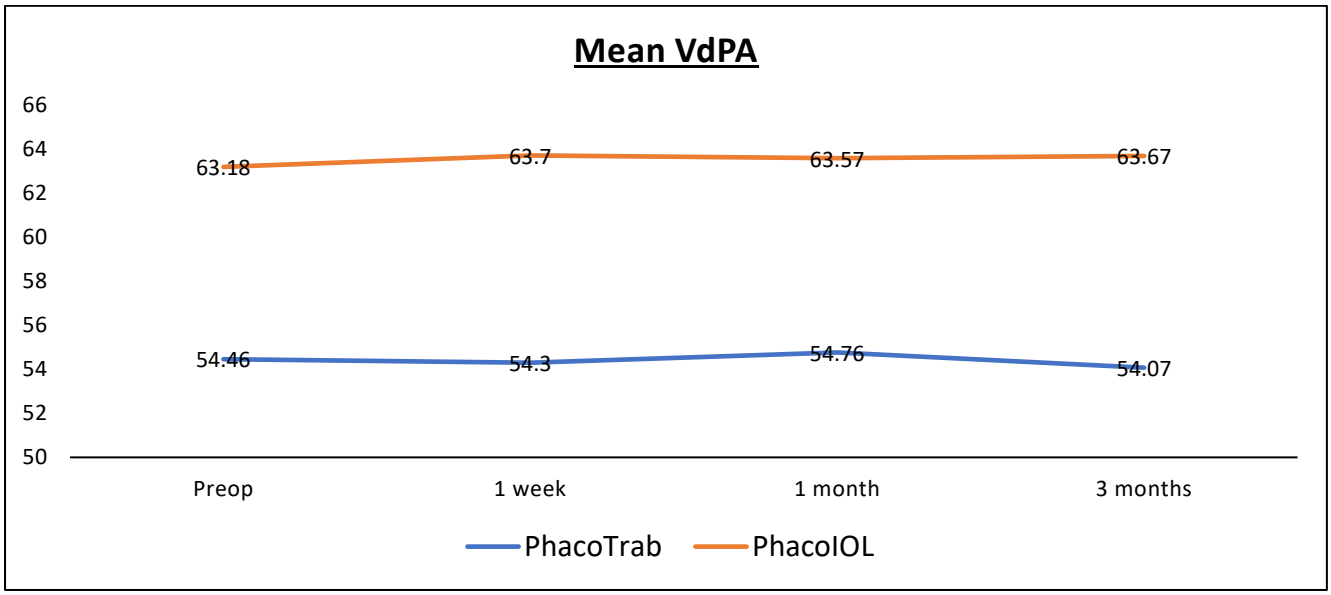


There was a statistically significant difference in the mean optic nerve head vessel density pre and post operatively. The respective p-values for preop vs 1 week,1 month and 3 months are 0.031, 0.030 and 0.009 respectively. So both groups had improvement in mean optic nerve head vessel density post operatively.

Table 11: Mean Papillary area vessel density (VdPA) in both groups

Mean VdPA	PhacoTrab	PhacoIOL	p value
Pre op	54.46 (4.11)	63.18 (2.15)	<0.001
1 week	54.30 (4.73)	63.70 (2.33)	<0.001
1 month	54.76 (4.25)	63.57 (2.33)	<0.001
3 months	54.07 (4.33)	63.67 (1.92)	<0.001

Graph 8: Mean VdPA in both groups

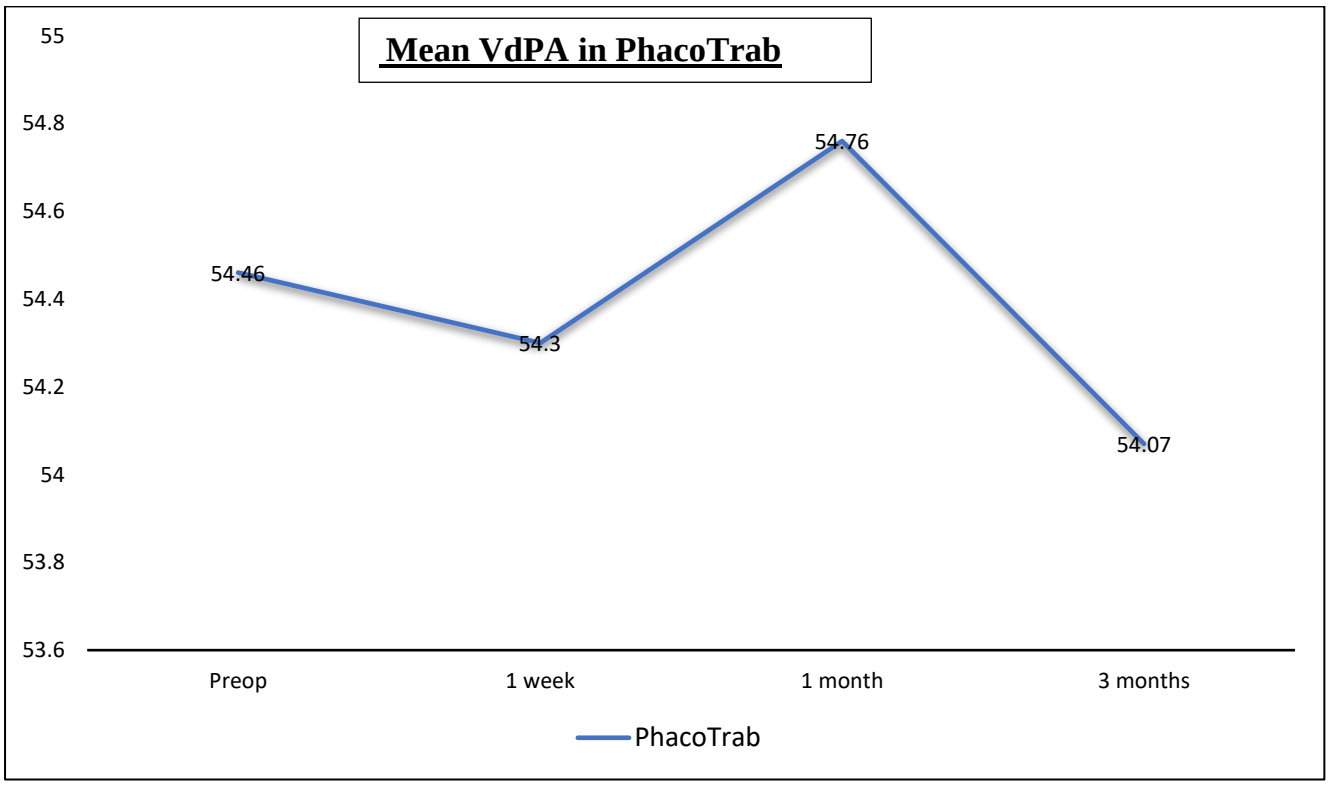


The difference in the mean papillary area vessel density (VdPA) between the PhacoTrab group and the PhacoIOL group was always statistically significant ($p<0.001$) (Table 6, Graph 4). However, there is no significant change in VdPA postoperatively even up to 3 months after PhacoTrab ($p=0.410$) or PhacoIOL ($p=0.471$)

Table 12: Difference in Mean VdPA Pre and post operatively in PhacoTrab group

Mean VdPA (SD)	Preop: 54.46 (4.11)	1 week: 54.30 (4.73)	1 month: 54.76 (4.25)	3 months: 54.07 (4.33)
Preop: 54.46 (4.11)	Not applicable	p = 0.554	p = 0.262	p = 0.410
1 week: 54.30 (4.73)	p = 0.554	Not applicable	p = 0.08	p = 0.165
1 month: 54.76 (4.25)	p = 0.262	p = 0.08	Not applicable	p = 0.802
3 months: 54.07 (4.33)	p = 0.410	p = 0.165	p = 0.802	Not applicable

Graph 9: Mean VdPA pre and post-surgery in PhacoTrab group

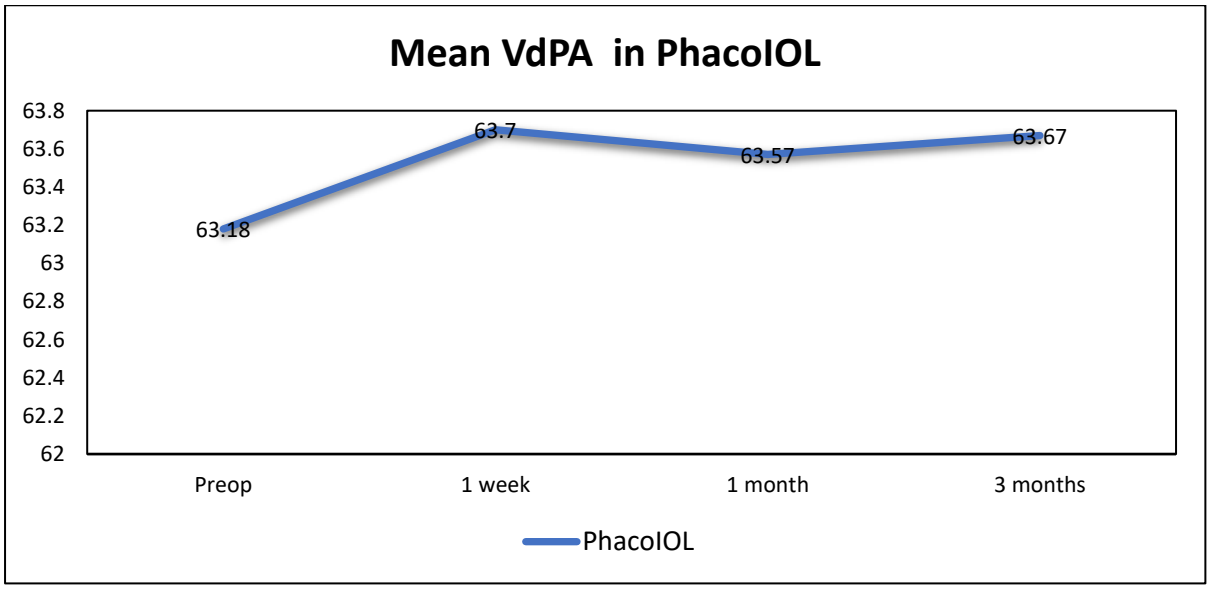


There was no statistically significant improvement in the mean papillary vessel density pre and post operatively.

Table 13: Difference in Mean VdPA Pre and post operatively in PhacoIOL group

Mean VdPA	Preop: 63.18 (2.15)	1 week: 63.70 (2.33)	1 month: 63.57 (2.33)	3 months: 63.67 (1.92)
Preop: 63.18 (2.15)	Not applicable	p = 0.031	p = 0.099	p = 0.114
1 week: 63.70 (2.33)	p = 0.031	Not applicable	p = 0.605	p = 0.582
1 month: 63.5 (72.33)	p = 0.099	p = 0.605	Not applicable	p = 0.966
3 months: 63.67 (1.92)	p = 0.114	p = 0.582	P = 0.966	Not applicable

Graph 10: Mean VdPA pre and post-surgery in PhacoIOL group



The mean papillary vessel density pre and post operatively were not statistically different.

Table 14: Mean peripapilary vessel density (VdPPA) in both groups

Mean VdPPA (SD)	PhacoTrab	PhacoIOL	p value
Preop	54.06 (4.69)	63.36 (2.08)	<0.001
1 week	54.11 (4.83)	64.00 (2.39)	<0.001
1 month	54.56 (4.53)	63.97 (2.40)	<0.001
3 months	53.69 (4.36)	64.23 (2.07)	<0.001

The mean peripapillay vessel density (VdPPA) in the PhacoTrab group was statistically significantly different from the PhacoIOL group pre and post operatively ($p<0.001$). Successful trabeculectomy did not show any statistically significant change in the VdPPA ($p=0.471$)

Graph 11: Mean VdPPA in both groups

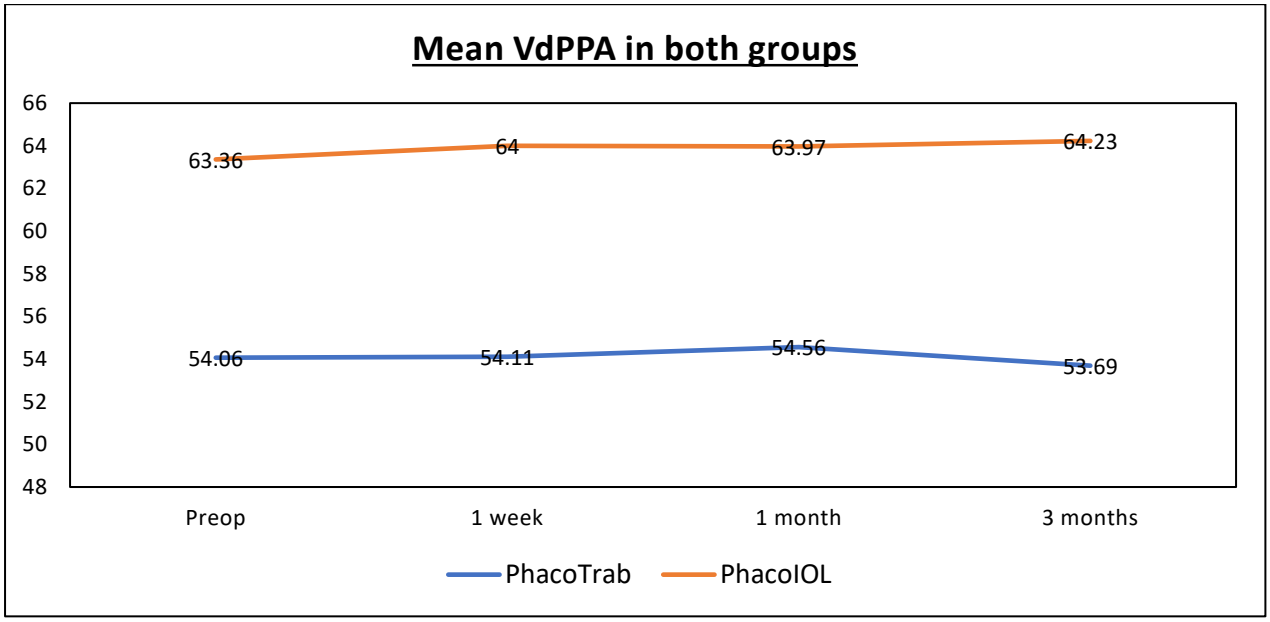
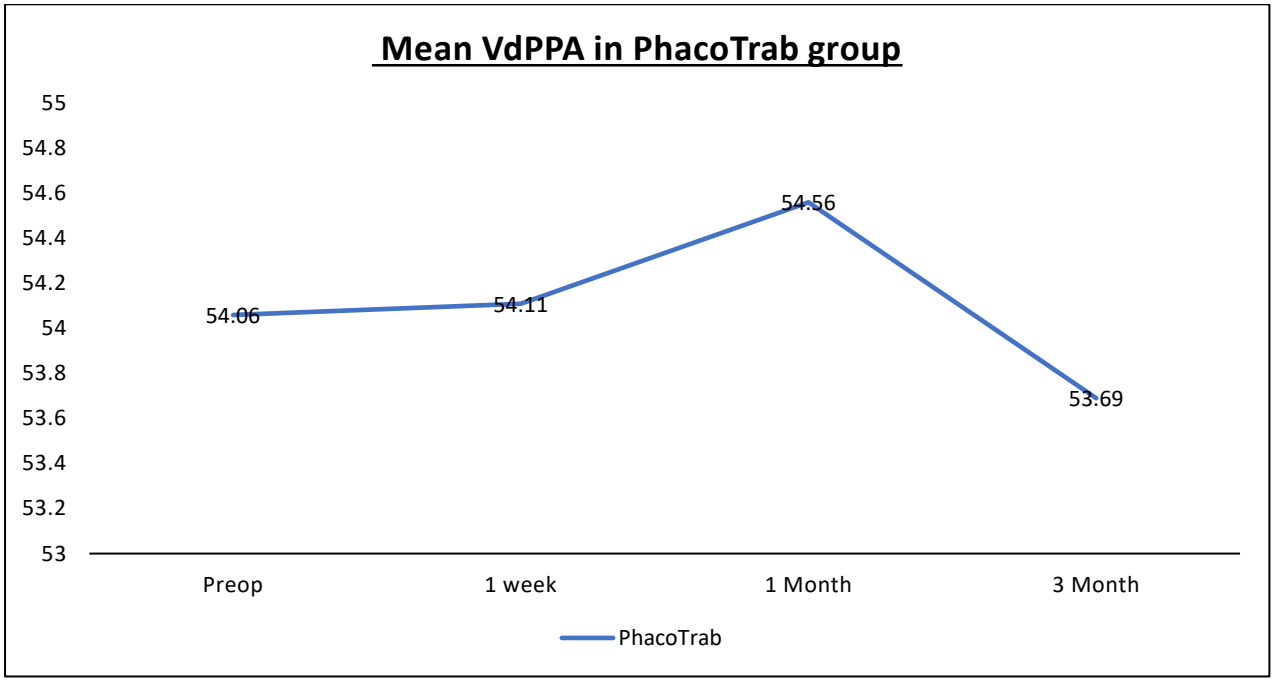


Table 15: Difference in Mean VdPPA Pre and post operatively in PhacoTrab group

MeanVdPPA	Preop: 54.06(4.69)	1week: 54.11(4.83)	1month: 54.56(4.53)	3months: 53.69(4.36)
Preop: 54.06(4.69)	Not applicable	p = 0.876	p = 0.072	p = 0.471
1week: 54.11(4.83)	p = 0.876	Not applicable	p = 0.100	p = 0.567
1month: 54.56(4.53)	p = 0.072	p = 0.100	Not applicable	p = 0.314
3month: 53.69(4.36)	p = 0.471	p = 0.567	P = 0.314	Not applicable

Graph 12: Mean VdPPA in PhacoTrab group pre and post surgery

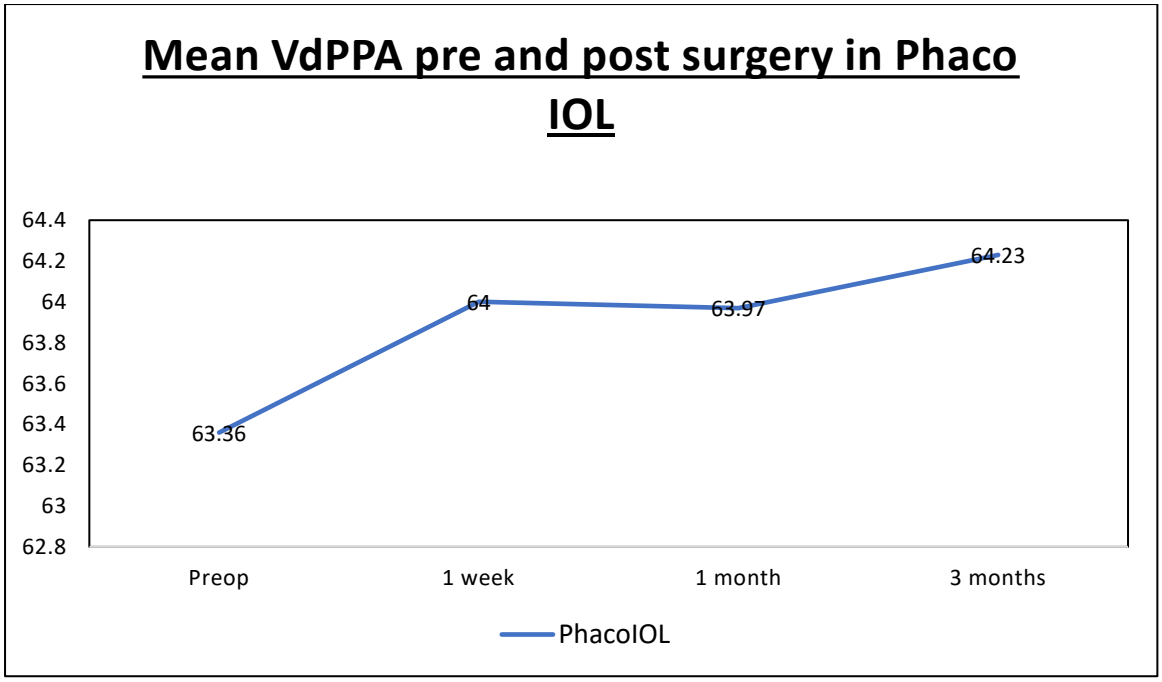


There was no statistically significant difference in the mean peripapillary vessel density pre and post operatively. The respective p-values for preop vs 1 week,1 month and 3 months are 0.876, 0.07 and 0.471 respectively.

Table 16: Difference in Mean VdPPA Pre and post operatively in PhacoIOL group

MeanVdPPA	Preop: 63.36(2.08)	1week: 64.00(2.39)	1month: 63.97(2.40)	3months: 53.69(4.36)
Preop: 63.36(2.08)	Not applicable	p = 0.011	p = 0.015	**p = 0.001**
1week: 64.00(2.39)	p = 0.011	Not applicable	p = 0.907	p = 0.361
1month: 63.97(2.40)	p = 0.015	p = 0.907	Not applicable	p = 0.304
3month:64.23(2.07)	**p = 0.001**	p = 0.361	p = 0.304	Not applicable

Graph 13: Mean VdPPA pre and post surgery in Phaco IOL group

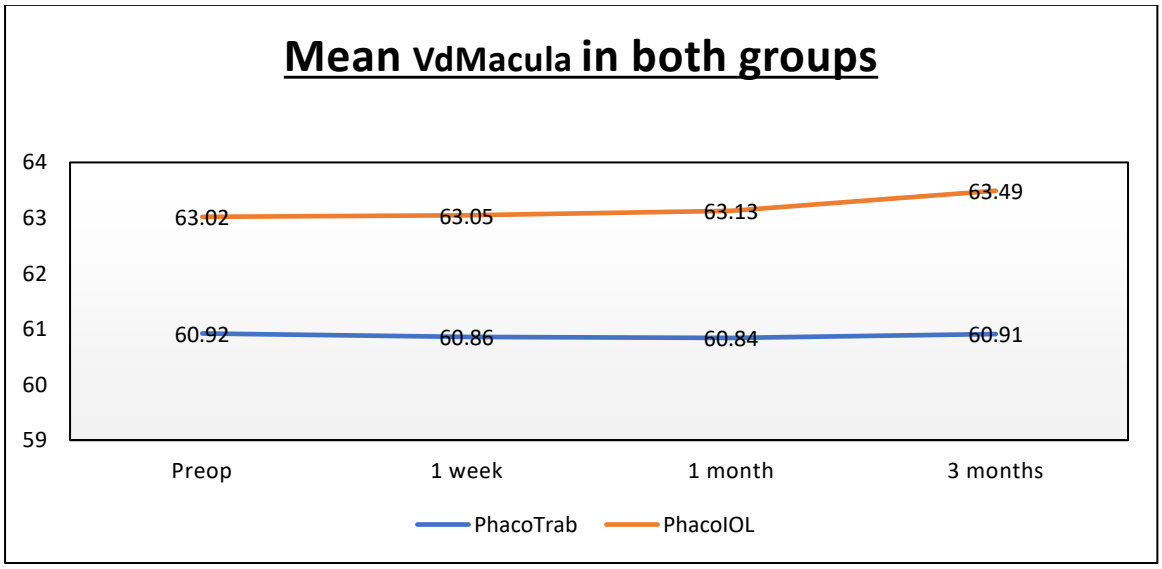


There was statistically significant difference in the mean peripapillary vessel density pre and post operatively. The respective p-values for preop vs 1 week,1 month and 3 months are 0.011, 0.015 and 0.001 respectively.

Table 17: Mean Macular vessel density(VdMacula) in both groups

Mean VdMacula (SD)	PhacoTrab	PhacoIOL	p-value
Preop	60.92(2.31)	63.02(2.14)	<0.001
1 week	60.86(2.29)	63.05(2.13)	<0.001
1 month	60.84(2.05)	63.13(2.05)	<0.001
3 months	60.91(1.94)	63.49(1.74)	<0.001

Graph 14: Mean VdMacula in both groups

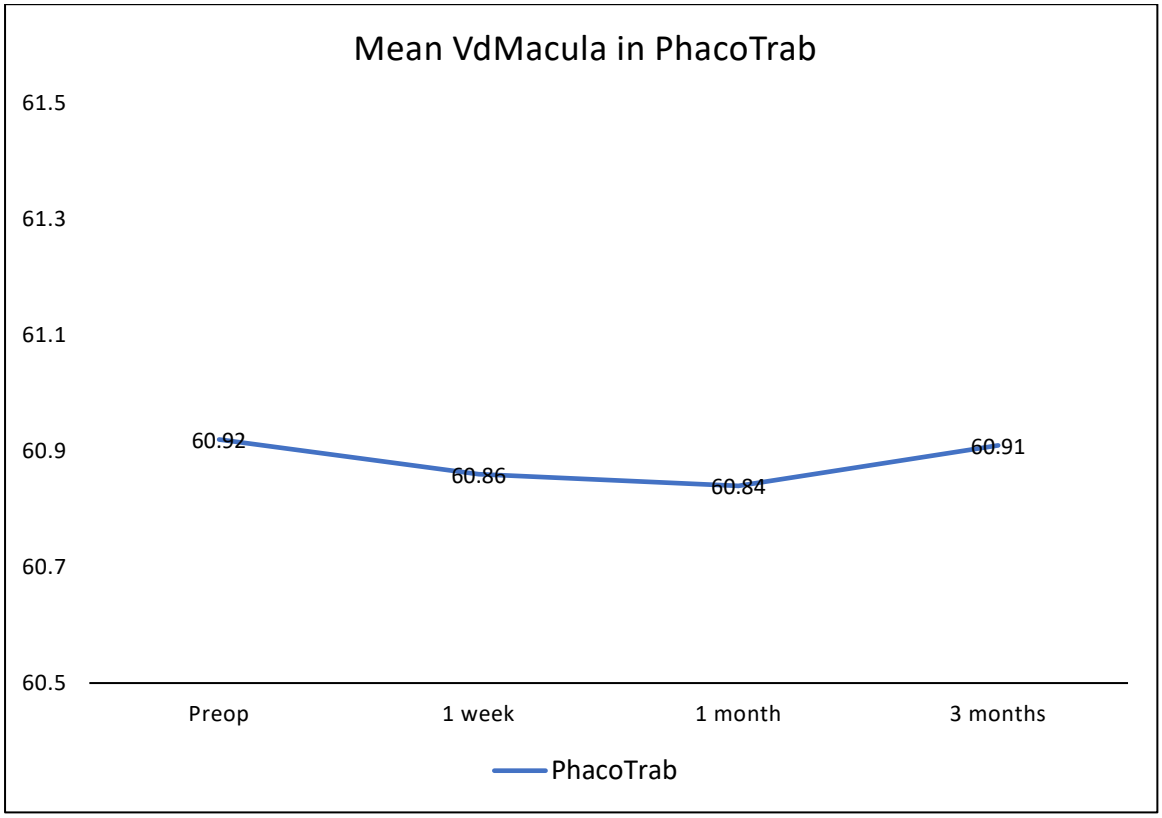


There was a statistically significant difference in the mean macular vessel density between both the groups ($p<0.001$).

Table 18: Difference in VdMacula Pre and post operatively in PhacoTrab group

Mean VdMacula	Preop: 60.92(2.31)	1week: 60.86(2.29)	1month: 60.84(2.05)	3months: 60.91(1.94)
Preop: 60.92(2.31)	Not applicable	p = 0.792	p = 0.716	p = 0.193
1week: 60.86(2.29)	p = 0.792	Not applicable	p = 0.920	p = 0.121
1month: 60.84(2.05)	p = 0.716	p = 0.920	Not applicable	p = 0.100
3month: 60.91(1.94)	p = 0.193	p = 0.121	p = 0.100	Not applicable

Graph 15: Mean VdMacula pre and post operatively in PhacoTrab group

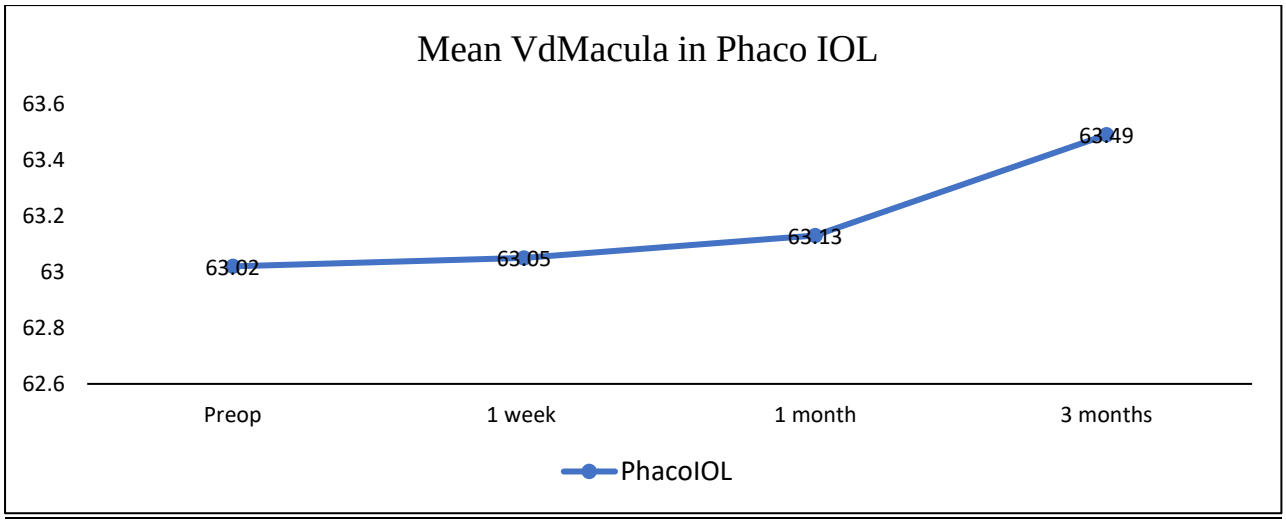


There was no statistically significant difference in the mean macular vessel density pre and post operatively. The respective p-values for preop vs 1 week,1 month and 3 months are 0.792, 0.716 and 0.193 respectively

Table 19: Difference in Mean VdMacula Pre and post operatively in PhacoIOL group

Mean VdMacula	Preop: 63.02(2.14)	1week: 63.05(2.13)	1month: 63.13(2.05)	3months: 63.49(1.74)
Preop: 63.02(2.14)	Not applicable	p value = 0.849	p value = 0.538	p value = 0.055
1week: 63.05(2.13)	p value = 0.849	Not applicable	p value = 0.670	p value = 0.083
1month: 63.13(2.05)	p value = 0.538	p value = 0.670	Not applicable	p value = 0.187
3month: 63.49(1.74)	p value = 0.055	p value = 0.083	p value = 0.187	Not applicable

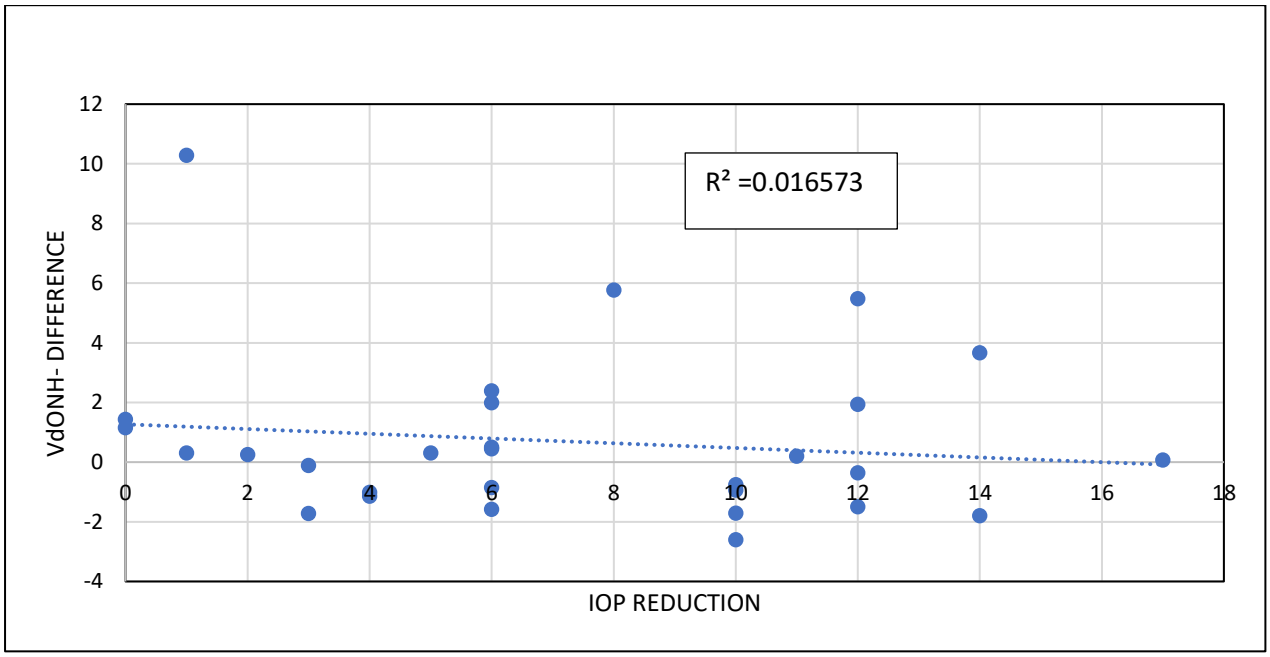
Graph 16: Mean VdMacula pre and post surgery in Phaco IOL group



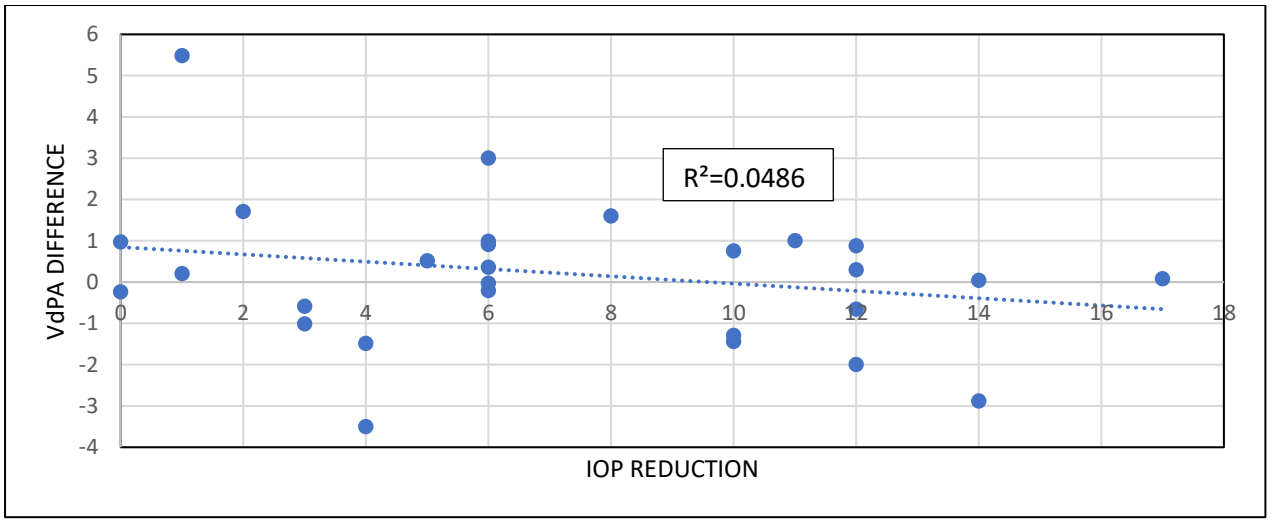
There was no statistically significant difference in the mean macular vessel density pre and post operatively. The respective p-values for preop vs 1 week, 1 month and 3 months are 0.849, 0.538 and 0.055 respectively.

Given the adequate IOP reduction postoperatively at 3 months in 29 out of 30 patients in the PhacoTrab group we looked at correlation between reduction IOP and OCT-A variables.

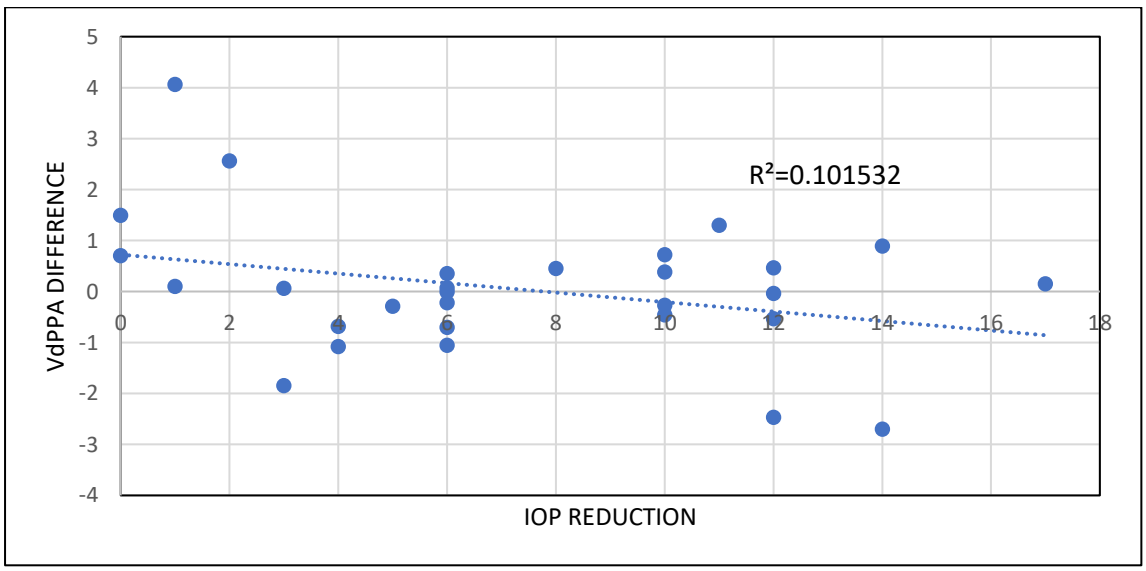
Graph 17: Correlation between reduction in IOP and change in VdONH at 3 months in PhacoTrab



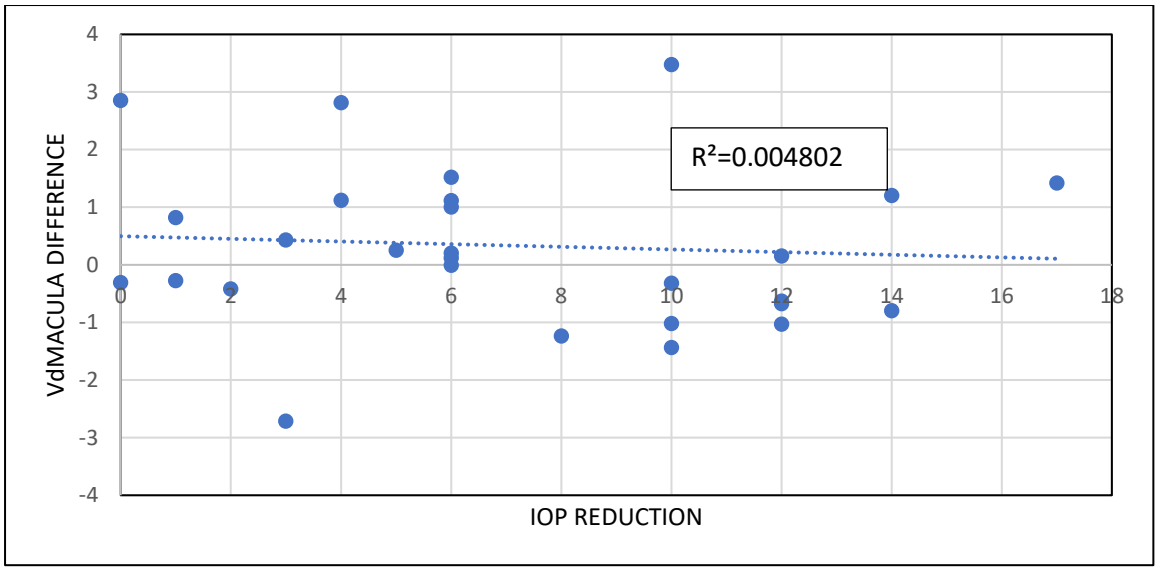
Graph 18: Correlation between reduction in IOP and change in VdPA at 3 months in PhacoTrab



Graph 19: Correlation between reduction in IOP and change in VdPPA at 3 months in PhacoTrab



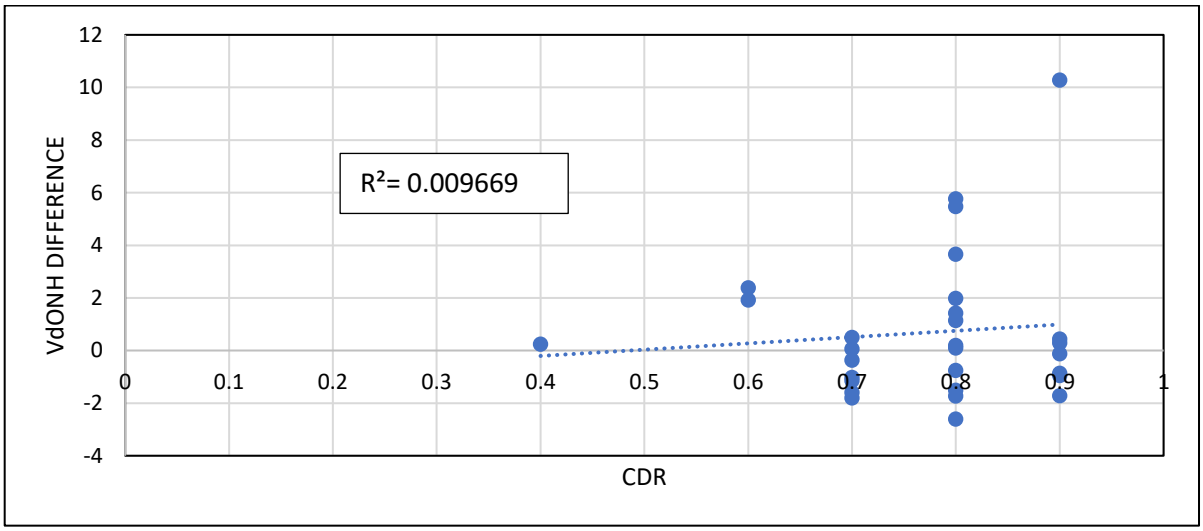
Graph 20: Correlation between reduction in IOP and change in VdMacula at 3 months in PhacoTrab



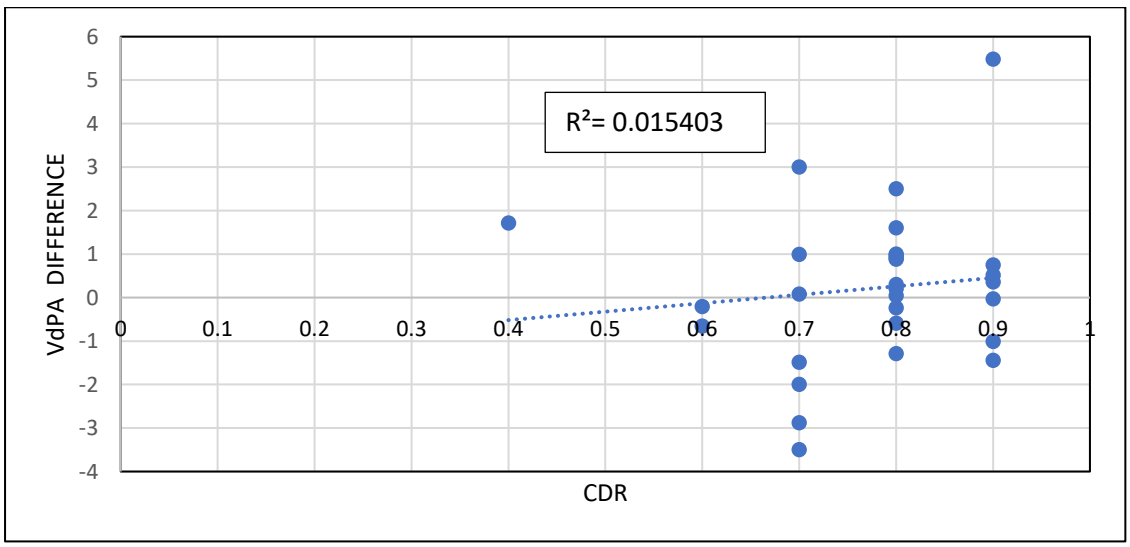
There was no correlation between IOP reduction and change in VdONH, VdPA, VdPPA and VdMacula post operatively at 3 months. The Spearman correlation coefficient (R^2) was 0.016573, 0.048623, 0.101532, 0.004802 respectively.

We also looked at the cup disc ratio (CDR) and its correlation with change in OCT-A variables at 3 months post operatively.

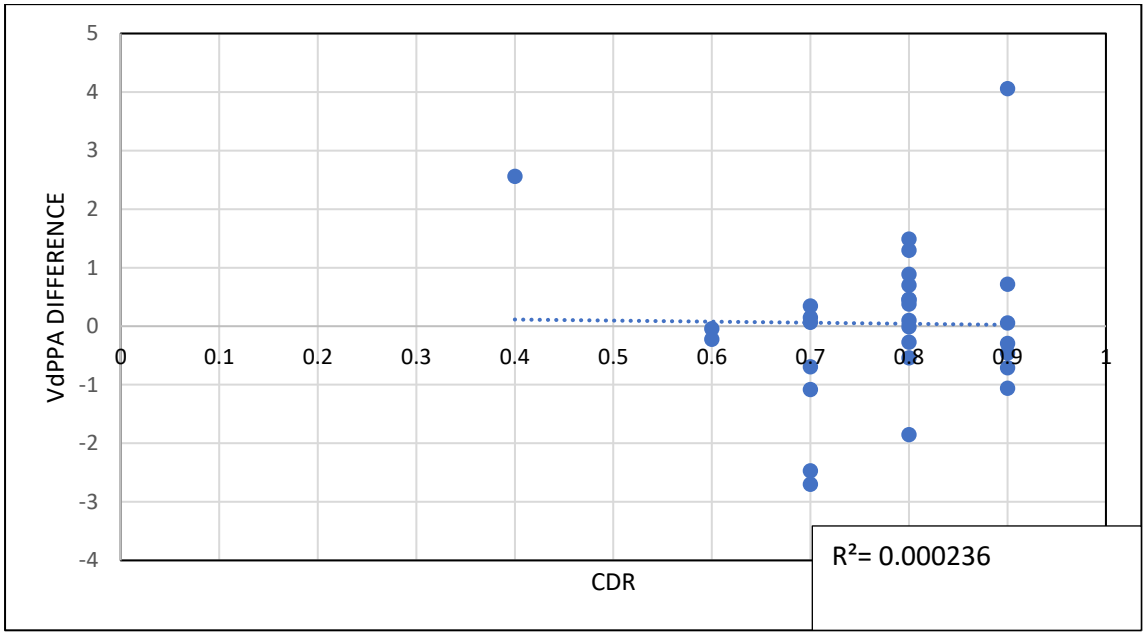
Graph 21: Correlation between CDR and VdONH at 3 months in PhacoTrab



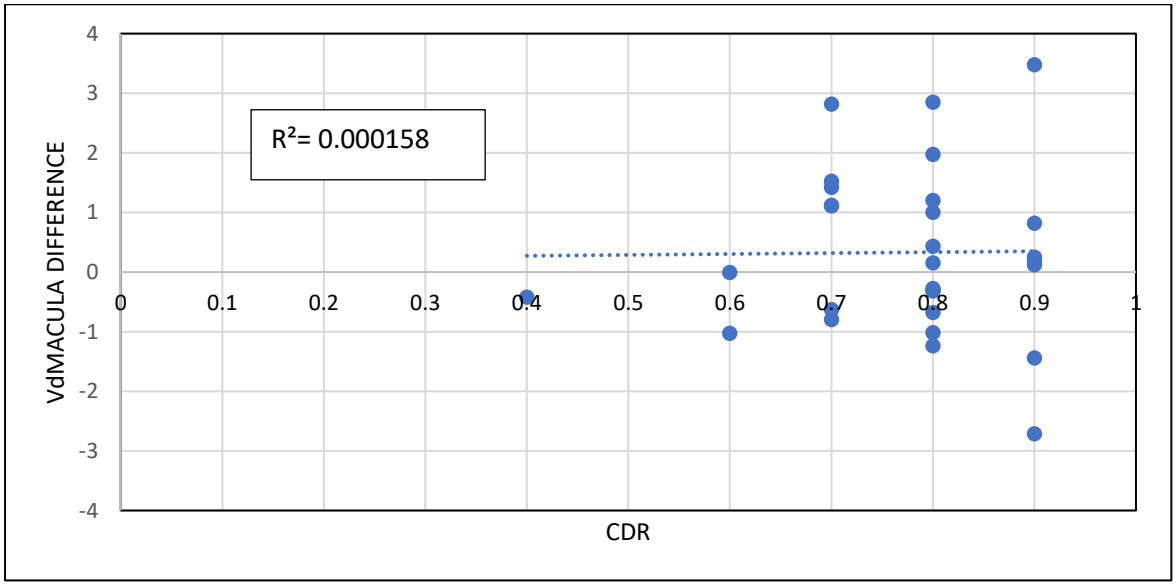
Graph 22: Correlation between CDR and VdPA at 3 months in PhacoTrab



Graph 23: Correlation between CDR and VdPPA at 3 months in PhacoTrab



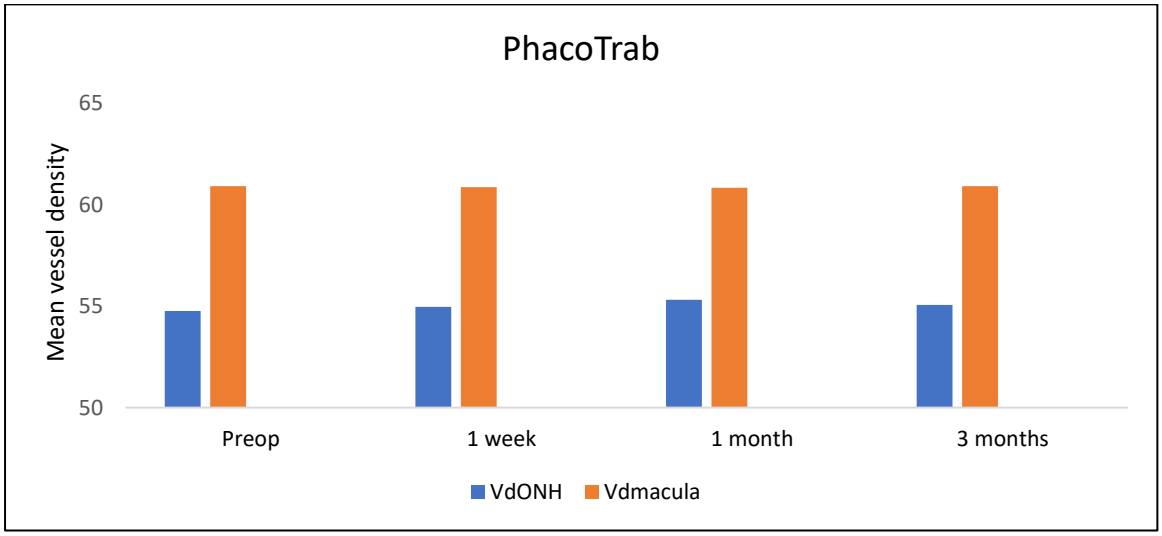
Graph 24: Correlation between CDR and VdMacula at 3 months in PhacoTrab



There was no correlation between CDR and change in VdONH, VdPA, VdPPA and VdMacula post operatively at 3 months. The Spearmann correlation coefficient (R^2) was 0.009669, 0.015403, 0.000236, 0.000158 respectively.

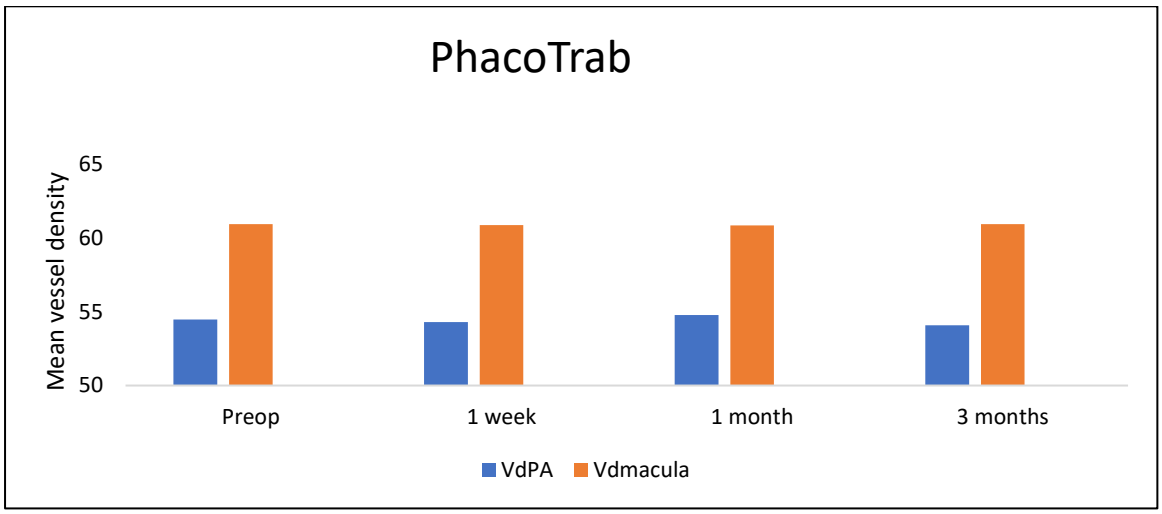
Though there was a statistically significant difference between VdMacula in both groups pre and post operatively, the VdMacula in the PhacoTrab group was significantly more than other vascular parameters.

Graph 29: Mean VdONH VS VdMacula in PhacoTrab pre and post operatively.



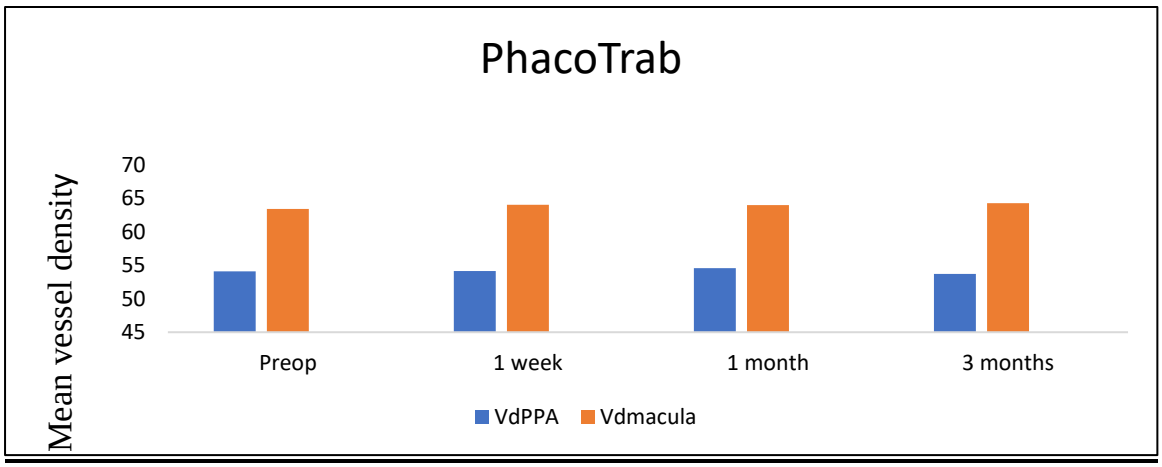
There was a statistically significant difference in the meanVdONH and VdMacula pre and post operatively ($p<0.001$).

Graph 30: Mean VdPA VS VdMacula in PhacoTrab pre and post operatively



There was a statistically significant difference in the meanVdPA and VdMacula pre and post operatively ($p<0.001$).

Graph 31: Mean VdPPA VS VdMacula in PhacoTrab pre and post operatively



There was a statistically significant difference in the meanVdPPA and VdMacula pre and post operatively ($p<0.001$).

DISCUSSION

Primary open angle glaucoma (POAG) is caused by apoptosis of the RGCs resulting in characteristic visual field defects. POAG is a silent threat to vision as the disease is asymptomatic till the late stages when the field defects become very advanced. A better understanding of the pathogenesis, methods for early diagnosis, appropriate medical or surgical treatment, monitoring and preventing progression is critical in the management of POAG. HFA and OCT are two investigations which play an indispensable role in diagnosis, prognosis and management of glaucoma.

OCT has altered the management of various ocular diseases over the last 1-2 decades. Advances in OCT technology have enabled the formation of original OCT-based methods for improving diagnosis. The recent OCT uses swept source technology using which high-resolution images of all layers of retina can be obtained. OCT-A is another technology that has quickly gained clinical acceptance. OCT-A is a newer non-invasive technique that generates angiography images, by detecting motion contrast. Images delineating individual vascular plexus, providing information about the perfusion at each layer of the retina can be obtained.

Recent studies have assessed the glaucoma diagnostic ability of OCT-A because it can provide a reproducible and quantitative assessment of the microvasculature in the peripapillary retina, optic nerve head (ONH), and macula (31). Studies using OCT-A have reported reduced vessel density (VD) in the ONH and peripapillary retina in glaucomatous eyes, which is correlated with glaucoma severity. (31)(56)(57).

According to the vascular theory of glaucoma, vascular dysregulation leading to alterations in the retinal microcirculation, derangement of perfusion to the optic nerve

head and peri-papillary retina are important in the pathogenesis of glaucoma.(4),(5),(6) Various studies have analyzed retinal vascular bed, using various non-invasive and invasive techniques before and after surgical management. Laser doppler flowmetry and other non-invasive techniques have demonstrated significant reduction in the blood flow at the ONH in glaucomatous eyes (24), (25), (26) and further studies have demonstrated improved vessel density in POAG patients post trabeculectomy. (13), (14), (49-52).

The purpose of our study was to explore the use of OCT-A in POAG before and after combined phacoemulsification with IOL implantation and trabeculectomy (PhacoTrab) which is the most commonly done glaucoma surgery in patients with age related cataract and glaucoma. By doing this we wanted to compare the vessel dynamics around the optic nerve head and macula pre and post operatively in glaucoma patients. Given that cataract surgery could be a potential confounder, we performed the same evaluation in age matched individuals undergoing cataract surgery alone (PhacoIOL) using the TRITON swept source OCT.

Shin et al., have shown a significant increase in vessel density at the level of the lamina cribrosa 3 months after trabeculectomy, which was moderately associated with IOP reduction. (32) A significant increase in the peripapillary vessel density after trabeculectomy using OCT-A was reported in 25 Korean eyes which underwent trabeculectomy. The reversal of peripapillary vessel density was associated with higher preoperative IOP and greater IOP reduction. (57). However, Lommatzsch et al., in a 6month prospective study on 19 patients with POAG, found no significant change in papillary and macular vessel density after successful trabeculectomy (55).

Various other studies also did not reveal any changes in the vessel density post trabeculectomy. (14). All these studies have used OCT-A images of different area measurements with either machine inbuilt analysis protocols or have used external third party software applications, by different techniques, to analyze the images.

The two groups in our study were age and gender matched. Among the participants, we found that patients belonging to the PhacoTrab group were older. This is in agreement with several previous studies, where glaucoma was found to occur in a slightly older population (4).We compared the images and data from the two groups; to search for any significant differences, by performing paired analysis between the groups, for each of the specific areas of interest preoperatively and post operatively.

There was a significant reduction in IOP in the PhacoTrab group in 32 out of 33 eyes at 1 month and 29 out of 30 patients 3 months post operatively. The IOP difference between the two groups was statistically significant preoperatively ($p<0.001$) and at 1 week post operatively ($p<0.001$). This difference between the two groups did not exist thereafter, indicating successful trabeculectomy. This reduction in IOP postoperatively was evident in the PhacoIOL group as well ($p=0.044$) though not to the same extent.

The mean optic nerve head vessel density, peripapillary vessel density, papillary vessel density and macular vessel density($p<0.001$) was statistically significantly lesser in the PhacoTrab group compared to the other group. A very recent OCT-A study by Lee et al., (57) showed that even in early POAG, significant microvascular damage was present in both macular and peripapillary areas. Vessel density parameters in OCT-A showed good diagnostic capability in early glaucoma. (58). This

difference in the vessel density persisted post operatively at 1week($p<0.001$), 1month($p<0.001$) and 3 months($p<0.001$) undoubtedly verifying the vascular theory of etiopathogenesis of glaucoma and also opening possibilities for OCT-A to be an imperative investigation for the diagnosis of glaucoma. Serial assessments of vessel density over a period will help to assess progression of the disease and subsequent prognostication.

The main aim of our study was to assess the changes in the vessel dynamics of patients after successful trabeculectomy when combined with cataract surgery (PhacoTrab) that is more commonly performed than trabeculectomy alone in glaucoma associated with cataract in our institution. Inspite of significant IOP reduction postoperatively, the mean VdPA and VdPPA did not show any statistically significant improvement at each follow-up visit upto 3 months. Even in a small subset of 11 patients who had IOP reduction of $\geq$ 10mmHg there was no consistent or significant improvement in vessel density. In fact, 6 out of those 11 patients showed a decrease in vessel density.

However, the mean VdONH showed statistically significant improvement in the 3month follow up visit ($p<0.04$), though this was not seen at 1 week and 1 month follow up. This finding may be comparable to the vessel improvement in the vessel density at the lamina cribrosa level after trabeculectomy that was reported by Shin et al.(32) We, however, could not assess the lamina cribrosa depth or the optic nerve volume due to poor image quality. Our study demonstrates that even in advanced glaucoma, adequate IOP reduction causes improvement in VdONH. From this one

could assume that IOP reduction following trabeculectomy will reduce the severity of further progression in optic neuropathy associated with POAG.

When we looked at the mean macular vessel density (VdMacula) in the PhacoTrab vs Phaco IOL group, we found that though there was a statistically significant difference between the two, the magnitude was not as much as the difference in VdONH, VdPA or VdPPA. The VdMacula in the PhacoTrab group was much higher than the VdONH ($p<0.001$), VdPA($p<0.001$) and VdPPA($p<0.001$). The VdMacula showed no change at 3 month follow up. This preservation of vessel density at the macula even in advanced glaucoma is probably the reason why RGCs at the macula are preserved till the late stages in POAG.

The significant improvement in the VdONH and VdPPA post operatively in the Phaco IOL group may be related to the significant IOP reduction that was seen postoperatively even in this group. It is probably worthwhile to note that most of our patients in the PhacoTrab group had advanced glaucoma in which the blood flow would have been severely compromised to start with and hence the re-establishment of blood flow after surgery was not possible in spite of significant IOP reduction. The VdPA and VdMacula in the PhacoIOL group showed no increase in vessel density.

Our study clearly emphasizes the role of OCT-A as a diagnostic and prognostic tool in the management and follow up of glaucoma patients. OCT-A substantiates the vascular dysregulation theory in the pathogenesis of POAG.

CONCLUSIONS

- There was a significant difference in retinal vascular density in the optic nerve head, papillary, peripapillary and macular areas between patients in the PhacoTrab group and PhacoIOL group using Swept source OCTA

- There was a significant improvement in optic nerve head vessel density using Swept source OCT after significant IOP reduction following phacotrabeculectomy

- Significant IOP reduction after phacotrabeculectomy did not improve vessel density in papillary, peripapillary and macular areas

- Macular vessel density was preserved even in advanced glaucoma

- There was a significant reduction in IOP in the PhacoIOL group as well

- Though the magnitude in IOP reduction was less in the Phaco IOL group, there was improvement in the optic nerve head and macular vessel density

- Further studies on patients with mild and moderate POAG alone may help us to determine whether adequate IOP reduction following phacotrabeculectomy will improve retinal vascular density

LIMITATIONS

- Visual acuity was recorded using a Snellens chart and had to be converted into LogMar for calculations.

- Motion artifacts due to blinking or eye movement during image acquisition, caused a problem by producing poor quality images and the images had to be captured multiple times to get good quality images

- Majority of patients in the PhacoTrab group had advanced glaucoma with probably compromised vessels

- Our study population in both groups included diabetics and hypertensives, diseases that are known to cause changes in the microvasculature and may have influenced the outcome.

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ANNEXURES

PROFORMA

Study title*:* A prospective observational study to analyze changes in retinal blood vessel density in primary open angle glaucoma following intra ocular pressure reduction by surgical management using optical coherence tomography angiography

DATE : SERIAL NO :

NAME : HOSPITAL No:

AGE : SEX :

PHONE NO :

HTN/ DM / IHD/ASTHMA/ if on any anticoagulants:

Systemic medications:

Steroid Drop use: Yes/No

Any recent ocular surgery/ retinal laser -

CLINICAL EVALUATION – EXAMINATION AT BASELINE

OCULAR EXAMINATION	RIGHT EYE	LEFT EYE
BCVA		
IOP (In mm Hg)		
Gonioscopy (RP center grading)		
Fundus disc and macula		

Diagnosis-

Details of surgery-

Intra ocular pressure

	Date of examination	Right eye	Left eye
Baseline			
1 week			
1 month			
3 months			

Data Table:

	Baseline		1 week		1 month		3 months	
	RE	LE	RE	LE	RE	LE	RE	LE
Optic nerve head vessel density (%)								
Peripapillary area vessel density (%)								
Papillary area vessel density (%)								
Lamina cribrosa Depth (mm)								
Optic cup volume (μ)								
Macular vessel Density (mm)								

This data will be entered to excel from the machine.

PATIENT INFORMATION (ENGLISH)

STUDY TITLE:

A prospective observational study to analyze changes in retinal blood vessel density in primary open angle glaucoma following intra ocular pressure reduction by surgical management using optical coherence tomography angiography

You are being invited to take part in this research study carried out in the Department of Ophthalmology, Schell Eye Hospital, Christian Medical College, Vellore. The information in this document is meant to help you decide whether or not to take part in this study.

Before you decide whether or not you wish to take part, you should read the information provided below carefully and, if you wish, discuss it with your relatives. Take time to ask questions – do not feel rushed or under pressure to make a quick decision.

You should clearly understand the risks and benefits of taking part in this study so that you can make a decision that is right for you. This process is known as 'Informed Consent'.

You do not have to take part in this study and a decision not to take part will not effect on your future medical care.

You can change your mind about taking part in the study any time you like. Even if the study has started, you can still opt out. You do not have to give us a reason. If you do opt out, it will not affect the quality of treatment you get in the future.

What is the purpose of the study?

Our study will assess the differences in microscopic circulation in the retina (the nerve of the eye), using a non-invasive investigative test, Optical coherence tomography angiography, between glaucoma patients who undergo combined glaucoma and cataract surgery (trabeculectomy and phacoemulsification), and age matched normal (controls) patients who undergo only cataract surgery. This angiography test is done with a machine, which takes pictures of the retina from outside (without any dye of injection being required to be given from outside). It is a painless and completely risk-free test.

The volunteers with also be undergoing the routine, full eye examination and also the following additional tests for glaucoma evaluation, all of which are completely, noninvasive. All these are routinely used tests in the evaluation of glaucoma.
They will also undergo their routine investigations for cataract surgery.

Why have I been invited?

You have been chosen because you have fit one of the following criteria: -

- You are either a diagnosed patient of glaucoma
- You are chosen as a healthy volunteer, to be included in the control group who has been planned for cataract surgery for cataract.

What will happen if I take part?

If you take part in the study, you will be requested to provide the required clinical information and then undergo the routine eye examination and the required clinical investigations, which are non-invasive.

Expenses and payments?

There are no additional expenses or payments.

What are the possible benefits of taking part?

If you are a diagnosed glaucoma patient, then, the clinical testing and investigations will be part of the regular follow up care both before and after the routine Glaucoma surgery is performed. No additional investigations, other than those needed for routine follow up care, will be performed, and no extra cost will be levied on you. Additionally, by participating in this study, you will be helping future patients by helping to advance our understanding of the disease, which currently ails many others like yourself.

If you are a normal patient, recruited as a control, then you will be helping future patients, for whom newer treatment strategies may be developed as a result of better understanding of this disease.

What are the possible risks of taking part?

There are no risks involved in taking part in this study. All the examination procedures and investigations to be done are completely non-invasive and pain free and no radiation hazard.

Will my taking part be kept confidential?

All patient information is stored on password protected computer databases and in locked filing cabinets and will only be accessible to the research team.

What if there is a problem?

If you wish to complaint about any aspect of the way in which you have been approached or treated during the course of this study, you should contact the Principal investigator or you may contact Research Office, Carman Block, Bagayam, Vellore, 632002, email - research@cmcvellore.ac.in or researchothers@cmcvellore.ac.in, phone - 0416 2284294.

What will happen to any of my test results/samples I give?

The test results will be kept safe in the hospital's patient information databases, which are password protected and accessible to only the members of the research team, who are medical professionals.

How will the information I provide be used?

We plan to analyze the information collected and understand the disease condition, that is, glaucoma, in a better way and the effect of surgery in altering the progression of disease. We will then publish the results in a health journal so others can read about

it and learn from the results of the study, so that the new-found information may be used to benefit others, The personal information collected will still remain strictly confidential, and only the interpretations of the data will be published.

Who has reviewed this study?

The Institutional Review Board (IRB) of the Christian Medical College, Vellore, has reviewed this study.

You have the right to confidentiality regarding the privacy of your medical information (personal details, results of physical examinations, investigations, and your medical history). By signing this document, you will be allowing the research team investigators, if required to access your medical information.

The results of clinical tests and therapy performed as part of this research may be included in your medical record. The information from this study, if published in scientific journals or presented at scientific meetings, will not reveal your identity.

Thank you for reading this.

If you agree to enter the study, please sign the attached consent form.

Contact Person (Principal Investigator)

Dr. Sharmila. S

Department of Ophthalmology, Schell Campus,

Christian Medical College, Vellore.

Phone: 8973454594, sharmi2193sunder@gmail.com

INFORMED CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY

Study Title:

A prospective observational study to analyze changes in retinal blood vessel density in primary open angle glaucoma following intra ocular pressure reduction by surgical management using optical coherence tomography angiography.

Study Number : _____

Subject's Initials : _____

Subject's Name : _____

Date of Birth / Age : _____

(Subject)

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that ***the Sponsor of the clinical trial, others working on the Sponsor's behalf (delete as appropriate)***, the Ethics Committee and the

regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). [ ]

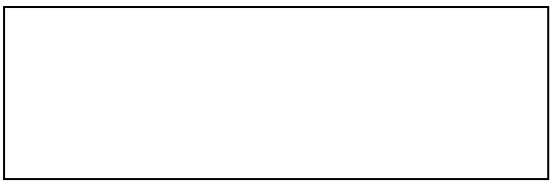
(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date: _____/_____/_____

Signatory's Name: _____ Signature:

Or



Representative : _____

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature or thumb impression of the Witness: _____

Date: _____/_____/_____

Name & Address of the Witness: _____

PATIENT INFORMATION (Tamil)

தகவல் படிவம்:

தலைப்பு: கண்ணில் உயர் அழுத்தம் (Glaucoma) வியாதி உள்ளவர்கள் மற்றும் கண்ணில் புரை (Cataract) உள்ளவர்களின் கண் நரம்பு இரத்த ஓட்டத்தை அறுவை சிகிச்சைக்கு முன்னும், பின்னும் ஆராய்தல்.

எங்கள் சி.எம்.சி கண் மருத்துவமனையில் நடக்கும் ஆராய்ச்சியில் பங்கு பெறுவதற்காக தங்களை அன்புடன் அழைக்கிறோம். இந்த படிவம், தங்களுக்கு இந்த ஆராய்ச்சியைப் பற்றி தெரிவிப்பதற்கான படிவம். இதை படித்த பின்பு நீங்கள் இந்த ஆராய்ச்சியில் பங்குபெற வேண்டுமா, வேண்டாமா என்பதை முடிவு செய்துக் கொள்ளலாம். வேண்டுமானால் தங்கள் உறவினரிடம் இதைப் பற்றி பேசி, பின்பு முடிவு செய்யவும். ஏதாவது சந்தேகம் இருந்தால் கேட்டு தெளிவு பெற்று பின்னர் பங்கு கொள்ளலாம்.

இந்த ஆராய்ச்சியில், தாங்கள் பங்கு பெறுவதற்கு முன் இதில் உள்ள நன்மை தீமைகளை நன்கு அறிந்த பின், தங்களுக்குப் பிடித்த முடிவை எடுத்துக்கொள்ளலாம். இதற்கு பெயர் ("Informed Consent") ஒப்புதல் தகவல் படிவம். இதில் தாங்கள் கலந்து கொள்ள வேண்டுமென்ற கட்டாயமில்லை. இதில் கலந்து கொள்ளவில்லையென்றாலும் தங்களுக்கு வழக்கமாக அளிக்கும் மருத்துவத்தில் எந்த பாதுபாடும் இருக்காது.

இந்த ஆராய்ச்சியின் நடுவில் தங்களுக்கு விலகவேண்டும் என்று தோன்றினால் தாங்கள் விலகிக்கொள்ளலாம். இதற்கு நீங்கள் காரணம் தெரிவிக்கவேண்டும் என்ற அவசியமில்லை. இதனால் தங்களுக்கு இங்கு கிடைக்கும் மருத்துவத்தில் எந்த மாற்றமும் இருக்காது.

1) என்னை இந்த ஆய்விற்கு தேர்ந்தெடுத்ததன் காரணம்?

தங்களுக்கு குளேக்கோமா (Glaucoma) வியாதி இருந்தால்

அல்லது கண்ணில் புரை (Cataract) இருந்தால் இந்த ஆய்வில்சேர்த்துக்கொள்ளப்படுவார்கள்.

2) இதில் பங்குகொள்வதற்கு நான் என்ன செய்யவேண்டும்?

இதில் பங்குபெறுவதாக இருந்தால் விருப்ப படிவத்தில் கையொப்பமிட வேண்டும். வழக்கமாக நடைபெறும் கண் பரிசோதனைகளுடன் "ஓ.சி.டி. ஏன்ஜியோகிரபி" (OCT Angiography) பரிசோதனை செய்யப்படும். இந்த பரிசோதனைகள் அனைத்தும் முற்றிலும் பாதுகாப்பான பரிசோதனைகள்.

3) இதில் பங்குபெறுவதால் வரும் செலவுகள் என்ன?

இந்த ஆராய்ச்சியில் பங்குபெறுவதால் தங்களுக்கு எந்த அதிகப்படியான செலவும் இல்லை .

4) இதில் பங்குபெறவதால் ஏற்படும் தன்மைகள் என்ன?

இந்த ஆய்வின் மூலம் நோயைப் பற்றி நன்கு அறிய முடியும். இதனால் நோயின் தீவிரம் மற்றும் சிகிச்சையால் ஏற்படும் நன்மைகளைப் பற்றி நன்கு அறிந்து, அதனால் தங்களுக்கு அளிக்கும் மருத்துவத்தை மேன்மைபடுத்த முடியும். இந்த ஆராய்ச்சியின் மூலம் மற்ற நோயாளிகளுக்கும் தாங்கள் உதவ முடியும்.

5) இந்த ஆராய்ச்சியால் ஏற்படும் தீமைகள் என்ன?

இந்த ஆராய்ச்சியால் எந்த தீமைகளும் இல்லை.

6) இந்த ஆராய்ச்சியில் பங்குபெறுவதால் என்னுடைய இரகசியங்கள் **பாதுகாக்கப்படுமா?**

நோயாளியின் அனைத்து இரகசியங்களும் பாதுகாக்கப்படும். நோயாளியின் அனைத்து விவரங்களும் ரகசிய சொல் மூலம் கணினியில் பாதுகாப்பாக வைக்கப்படும். ஆராயச்சியாளார் மட்டுமே இதை பார்க்க

முடியும்.

7) ஏதாவது பிரச்சனை ஏற்பட்டால் என்ன செய்வது?

ஏதாவது புகார் தெரிவிக்க வேண்டுமென்றால் அதை ஆராய்ச்சியாளரிடமோ

அல்லது ஆராய்ச்சி அலுவலகத்திலோ தெரிவிக்கலாம். ஆராய்ச்சி அலுவலகம்,

கார்மன் ப்ளாக், பாகாயம், வேலூர். - 632002. Ph: 0416-2284294. E.mail:

research@cmcvellore.ac.in (or) cmcvellore.ac.in.

8) இந்த ஆராய்ச்சியை அங்கீகரித்தது யார்?

நிறுவன மறு சீராய்வுக்குழு ஒப்புதல். அளித்துள்ளது தங்களது அனைத்து தகவல்களையும் இரகசியமாக வைப்பதற்கான உரிமை தங்களுக்கு உண்டு.

இந்த ஆராய்ச்சிக்கு ஒப்புதல் தருவதன் மூலம் தாங்கள் தங்கள் அனைத்து மருத்துவ தகவல்கள் மற்றும் பரிசோதனைகளை பார்ப்பதற்கு ஆராய்ச்சியாளருக்கு அனுமதியளிக்கிறீர்கள்.

இந்த ஆராய்ச்சியின் முடிவுகள் தங்களது மருத்துவ பதிவேட்டில் சேர்க்கப்படும். இந்த ஆராய்ச்சியின் முடிவுகள் ஏதாவது கருத்தரங்கத்தில் வெளியிடப்பட்டாலும். தங்களது விபரங்கள் வெளியிடப்படமாட்டாது இரகசியம் பாதுகாக்கப்படும்.

படித்தமைக்கு நன்றி.

இந்த ஆராய்ச்சியில் பங்குபெற விருப்பம் இருந்தால், இதனுடன் உள்ள ஒப்புதல் படிவத்தில் கையெழுத்திடவும்.

தகவல் தொடர்புக்கு:

(ஆராய்ச்சியாளர்) டாக்டர். ஷர்மிளா, கண்மருத்துவ பிரிவு, கிருஸ்துவ மருத்துவ கல்லூரி, வேலூர் - 632001. செல்: 8838520513

மின்அஞ்சல்:sharmi2193sunder@gmail.com

INFORMED CONSENT (TAMIL)

தலைப்பு:

கண்ணில் உயர் அழுத்தம் (glaucoma) வியாதி உள்ளவர்கள் மற்றும் கண்ணில் புரை (Cataract) உள்ளவர்களின் கண் நரம்பு இரத்த

ஓட்டத்தை அறுவை சிகிச்சைக்கு முன்னும், பின்னும் ஆராய்தல்.

ஆய்வில் பங்கேற்பதற்கான தகவலறிந்த ஒப்புதல் வடிவம்

ஆய்வு எண்:

ஆய்வில் பங்கு பெறுவரின் முன்னெழுத்துக்கள் (Initials):

ஆய்வில் பங்குபெறுவரின் பெயர்:

பிறந்த தேதி / வயது:

1. தேதி அன்று நான் மேற்கூறிய ஆய்விற்கான தகவல் தாளைப் படித்து

அதை புரிந்துகொண்டேன் என்று உறுதி அளிக்கிறேன். அது தொடர்பான கேள்விகள் கேட்க எனக்கு முழு வாய்ப்பு இருந்தது.

2. இந்த ஆய்வில் கலந்து கொள்வது ஒரு கட்டாயம் இல்லை என்பதையும், எந்த நிலையிலும் நான் இந்த ஆய்விலிருந்து எந்த காரணமும் அளிக்காமல் விலகிக் கொள்ளலாம் என்பதையும் தான் அறிவேன்

3. இந்த ஆய்வை நடத்தும் அதிகாரிகள் மற்றும் இது தொடர்பான பிறஅதிகாரிகள் என்னுடைய மருத்துவ விவரங்களை எனது அனுமதி இல்லாமலே கையாள உரிமை உள்ளவர்கள் என்பதை தான் அறிவேன். ஒரு வேளை நான் இந்த ஆய்விலிருந்து விலகிக்கொண்டாலும் இது பொருந்தும் என்பதையும் நான் அறிவேன். இதற்கு நான் ஒப்புதல் அளிக்கிறேன். ஆனால் இதன் மூலம் என்னுடைய அடையாளம் வெளியாட்களுக்குத் தெரிவிக்கப்படமாட்டாது என்பதை அறிவேன்

. 4. இந்த ஆய்வினால் வெளிவரக்கூடிய தகவல்கள் மற்றும் விளைவுகளை அறிவியல் காரணங்களுக்காகப் பயன்படுத்துவதை நான் தடுக்க மாட்டேன்.

5. மேற்கூறிய ஆய்வில் பங்குகொள்ள நான் ஒப்புதல் அளிக்கிறேன்.

ஆய்வில் பங்குபெறுபவரின் கையொப்பம் (அல்லது கைநாட்டை_):

தேதி :–

_

_

பெயர் :

கையொப்பம்:

அல்லது

பெற்றோர் :

_

பெயர் :

கையொப்பம்:

அல்லது

தேதி: __/__

பெயர்: ஆய்வு ஆராய்ச்சியாளரின் கையொப்பம் : தேதி: – – –

ஆய்வு ஆராய்ச்சியாளரின் கையொப்பம் :

சாட்சி கையொப்பம் :

தேதி: –

–

–

சாட்சியின் பெயர் & முகவரி:

INSTITUTIONAL REVIEW BOARD APPROVAL

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

September 27, 2018

Dr. Sharmila.S,
PG Registrar,
Department of Ophthalmology,
Christian Medical College,
Vellore – 632 002.

Sub: **Fluid Research Grant: New Proposal:**
A prospective observational study to analyze changes in retinal blood vessel density in primary open angle glaucoma following intra ocular pressure reduction by surgical management using optical coherence tomography angiography.
Dr. Sharmila.S, Employment Number: 21451, PG registrar, Ophthalmology, Dr.Lekha Mary Abraham, Employment Number: 20086, Ophthalmology,Dr. Andrew David BraganzaEmployment Number: 14092, Ophthalmology, Dr. Arathi Simha. R, Employment number: 20217, Ophthalmology, Mr. John Michael Employment Number: 52234, Optometrist.

Ref: IRB Min. No. 11465 [OBSERVE] dated 16.08.2018

Dear Dr. Sharmila.S,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Biju George, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS., MD., DM.,
SECRETARY (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

Cc: Dr.Lekha Mary Abraham, Dept. of Ophthalmology, CMC, Vellore

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

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Ref: IRB Min. No. 11465 [OBSERVE] dated 16.08.2018

Dear Dr. Sharmila.S,

The Institutional Review Board (**Blue**, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "A prospective observational study to analyze changes in retinal blood vessel density in primary open angle glaucoma following intra ocular pressure reduction by surgical management using optical coherence tomography angiography" on August 16th 2018.

The Committee reviewed the following documents:

1. IRB application format
2. Consent form and Information sheet (English, Tamil)
3. Data Collection Form
4. Cvs of Drs. Sharmila, john Michael, Andrew David Braganza, Arathi simha and Lekha Mary Abraham.
5. No. of documents 1- 4.

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on August 16th 2018 in the New IRB Room, Bagayam, Christian Medical College, Vellore 632 004.

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Name	Qualification	Designation	Affiliation
Dr. Biju George	MBBS, MD, DM	Professor, Haematology, Research), Additional Vice Principal , Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC, Vellore	Internal, Clinician
Dr. B. J. Prashantham	MA(Counseling Psychology), MA(Theology), Dr. Min(Clinical Counselling)	Chairperson, Ethics Committee, IRB. Director, Christian Counseling Centre, Vellore	External, Social Scientist
Mr. C. Sampath	BSc, BL	Advocate, Vellore	External, Legal Expert
Ms. Grace Rebekha	M.Sc., (Biostatistics)	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Mr. Samuel Abraham	MA, PGDBA, PGDPM, M. Phil, BL.	Sr. Legal Officer, CMC, Vellore	Internal, Legal Expert
Dr. Ratna Prabha	MBBS, MD (Pharma)	Associate Professor, Clinical Pharmacology, CMC, Vellore	Internal, Pharmacologist
Mrs. Sheela Durai	MSc Nursing	Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse
Dr. Sathish Kumar	MBBS, MD, DCH	Professor, Child Health, CMC, Vellore	Internal, Clinician
Dr. Winsely Rose	MBBS, MD (Paed)	Professor, Paediatrics, CMC Vellore	Internal, Clinician
Dr. John Antony Jude Prakash	MBBS, MD	Professor, Clinical Microbiology, CMC, Vellore.	Internal, Clinician.
Dr Sneha Varkki	MBBS, DCH, DNB	Professor, Paediatrics, CMC, Vellore	Internal, Clinician

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
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Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

We approve the project to be conducted as presented.

Kindly provide the total number of patients enrolled in your study and the total number of Withdrawals for the study entitled: "A prospective observational study to analyze changes in retinal blood vessel density in primary open angle glaucoma following intra ocular pressure reduction by surgical management using optical coherence tomography angiography" on a monthly basis. Please send copies of this to the Research Office (research@cmcvellore.ac.in).

Fluid Grant Allocation:

A sum of 50,000/- INR (Rupees Fifty Thousand Only) will be granted for 13 Months.

Yours sincerely,

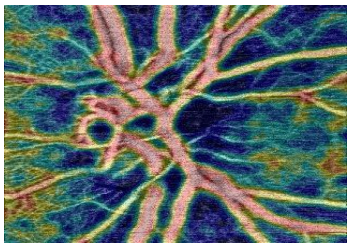
Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

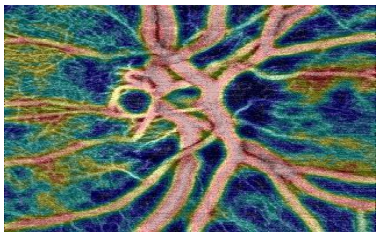
Dr. BIJU GEORGE
MBBS., MD., DM.,
SECRETARY - (Ethics Committee)
Institutional Review Board
Christian Medical College, Vellore - 632 004

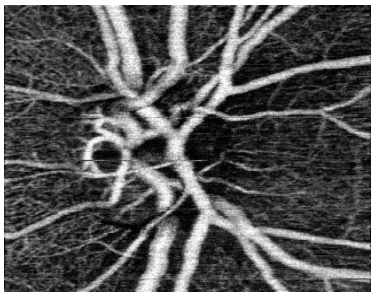
OCT-A OF OUR STUDY PATIENT PRE AND POST OP-PhacoTrab

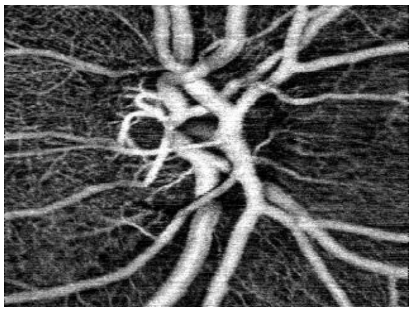
OCT-A PREOP - PhacoTrab **OCT-A 3 MONTHS PhacoTrab**

Optic Disc:

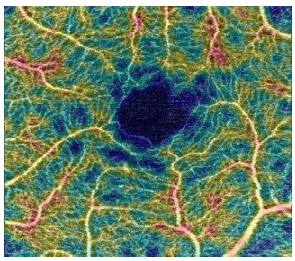


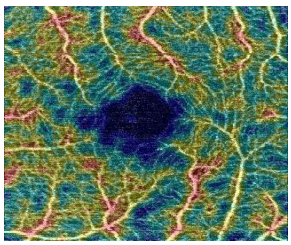


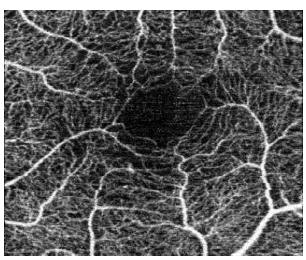


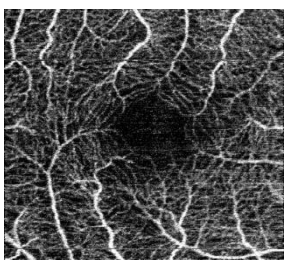


Macula:





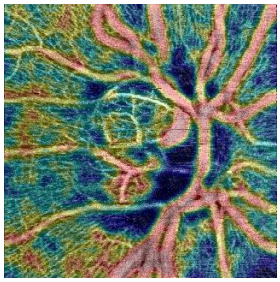
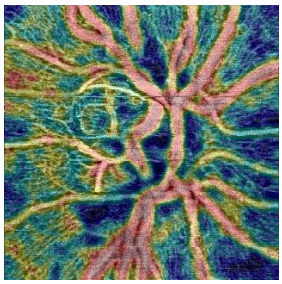
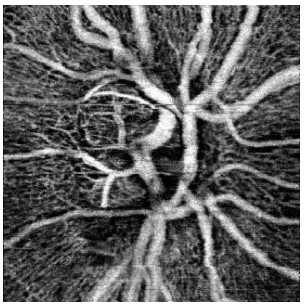
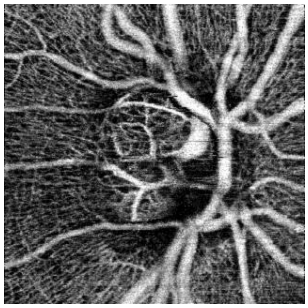




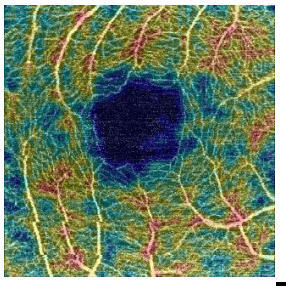
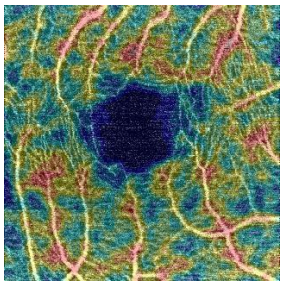
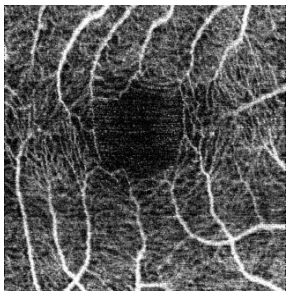
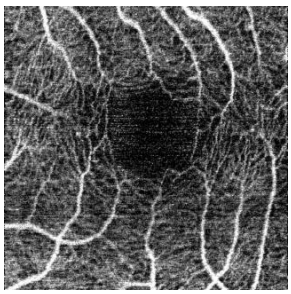
OCT-A OF OUR STUDY PATIENT PRE AND POST OP-PhacoIOL

OCT-A PREOP - PhacoIOL **OCT-A 3 MONTHS PhacoIOL**

Optic Disc

Macula

DATA SHEET LEGEND

GROUP	1 – PhacoTrab 2 – PhacoIOL
EYE	1 – RIGHT 2 – LEFT
SEX	1 – MALE 2 – FEMALE
DM	1 – PRESENT 2 – ABSENT
HTN	1 – PRESENT 2 – ABSENT
IHD	1 – PRESENT 2 – ABSENT
BRONCHIAL ASTHMA	1 – PRESENT 2 – ABSENT
GONIOSCOPY	0 – NO DIPPING 1 – DIPPING PRESENT 2 – SCHWALBE'S LINE AND ANT 1/3rd OF TRAB MESHWORK SEEN 3 – MID 1/3RD OF TRAB MESHWORK 4 – POST 1/3RD OF TRAB MESHWORK 5 – SCLERAL SPUR 6 – CILIARY BODY BAND SEEN

OCT-A	OCT ANGIOGRAPHY
BCVA	BEST CORRECTED VISUAL ACUITY
IOP	INTRAOCULAR PRESSURE (mm hg)
VDD	VERTICAL DISC DIAMETER (millimeters)
CDR	CUP DISC RATIO
CCT	CENTRAL CORNEAL THICKNESS (micrometers)
VdONH	VESSEL DENSITY – OPTIC NERVE HEAD (%)
VdPPA	VESSEL DENSITY – PERIPAPILLARY AREA (%)
VdPA	VESSEL DENSITY – PAPILLARY AREA (%)
VdMacula	VESSEL DENSITY – Macular AREA (%)

EXCEL DATA SPREAD SHEET

														BCVA					IOP			
					HYPERTENSIO							DIAGNOS										
s.no	GROUP	hospital number	age	sex	DIABETES	N	ASTHMA	IHD	EYE	GONIO	VDD	CDR	IS	BCVA PRE OP	One week post op	1 month post op	3 months post op	BASELINE IOP	PRE OP	ONE WEEK POST OP	ONE MONTH POST OP	3 MONTH POST OP
1	1	595126s	71	1	1	1	1	1	1	5	2.6	0.7	1	0.2	0	0	0	0	26	19	18	18	15
2	1	650150S	70	2	1	1	2	1	1	5	2.2	0.9	1	0.5	0	0	0	0	28	18	4	18	17
3	1	565666S	77	2	2	1	2	1	2	1	5	2.2	0.9	1	0.3	0.2	0.2	0.2	26	16	6	10	11
4	1	547481s	61	2	1	1	1	1	2	5	1.65	0.6	1	0.2	0.2	0	0	0	30	20	13	15	8
5	1	622823s	60	2	1	1	1	1	1	2	5	1.8	0.9	1	0.3	0.2	0.2	0.2	28	18	12	12	15
6	1	631215s	58	2	1	2	1	1	2	5	2.6	0.8	1	0.2	0.2	0	0	0	23	20	10	7	9
7	1	632114S	57	1	2	1	1	1	2	5	1.76	0.9	1	0.3	0.2	0	0	0	31	22	3	17	12
8	1	129371s	71	1	2	1	1	1	2	5	1.9	0.7	1	0.3	0.2	0.2	0.2	0.2	38	30	16	18	16
9	1	969477e	73	1	1	1	1	1	1	5	1.8	0.8	1	0.3	0	0	0	0	25	19	14	18	16
10	1	674674s	74	1	1	1	1	1	1	5	1.7	0.8	1	0.2	0.2	0.2	0.2	0	36	14	12	8	13
11	1	573232s	77	1	1	1	1	2	1	5	2.08	0.8	1	0.7	0.2	0.3	0.3	0.3	46	15	10	12	15
12	1	480211s	72	2	1	2	1	1	1	5	1.98	0.8	1	0.3	0.2	0.2	0.2	0.2	24	22	16	14	12
13	1	669353s	51	2	2	2	1	1	1	5	1.8	0.7	1	0.3	0.2	0.2	0.2	0.2	55	20	16	18	14
14	1	682629s	56	2	2	2	1	1	1	5	1.76	0.7	1	0.2	0.2	0.2	0.2	0.2	37	22	18	16	10
15	1	685532s	80	2	2	2	1	1	1	5	1.76	0.7	1	0.3	0.3	0.3	0.3	0.2	22	18	14	12	14
16	1	688126s	60	2	1	1	1	1	1	5	1.8	0.8	1	0.5	0.2	0.2	0.2	0.2	24	26	6	16	14
17	1	432420s	65	2	2	2	1	1	2	5	1.9	0.9	1	0.5	0.3	0.2	0.2	0.2	23	18	14	12	12
18	1	320241s	73	2	1	2	1	1	2	5	1.9	0.8	1	0.4	0.1	0.1	0.1	0.1	26	18	14	6	10
20	1	691047s	75	2	1	2	1	1	2	5	2.34	0.8	1	0.5	0.2	0.2	0	0	22	14	15	10	14
21	1	681116s	65	2	2	2	1	1	1	5	1.76	0.9	1	0.3	0	0	0	0	24	16	10	10	10
22	1	650150s	73	2	1	2	1	1	2	5	2.21	0.8	1	0.6	0.3	0.2	0.2		23	18	10	16	
23	1	660154s	64	2	2	2	1	1	2	5	2.2	0.8	1	0.3	0.2	0	0	0	22	18	7	4	6
24	1	697193s	55	1	1	1	1	1	1	5	1.89	0.6	1	0.4	0.2	0.2	0.2	0.2	38	20	8	10	10
25	1	652077s	71	1	2	2	1	1	2	5	1.76	0.7	1	0.3	0.2	0.2	0.2	0.2	30	18	10	12	12
26	1	691412s	71	2	1	1	1	1	2	5	1.89	0.8	1	0.5	0.3	0.3	0.3	0.2	34	29	12	16	12
27	1	364431s	61	1	1	1	1	1	1	5	1.54	0.4	1	0.3	0.2	0	0		30	18	12	10	
28	1	696013s	72	1	1	1	1	1	2	5	1.87	0.8	1	0.3	0	0	0	0	46	24	8	8	10
29	1	292915s	78	1	1	2	2	1	1	5	1.98	0.9	1	0.5	0	0	0	0	24	12	12	10	10
30	1	688335s	66	1	1	2	1	1	1	5	1.87	0.7	1	0.4	0.2	0.2	0.2		36	20	12	16	
31	1	699972s	78	1	1	1	1	1	2	5	1.43	0.7	1	0.3	0.2	0.2	0	0	34	18	10	12	12
32	1	694240s	63	1	2	2	1	1	1	5	1.76	0.9	1	0.3	0.2	0	0	0	30	24	10	14	14
33	1	700718s	64	1	1	1	1	1	1	5	2.1	0.9	1	0.5	0.2	0.2	0.2	0.1	24	16	8	10	10

					VESSEL DENSITY ONH				VESSEL DENSITY PERIPAPILLARY REGION				VESSEL DENSITY PAPILLARY REGION				VESSEL DENSITY MACULA			
s.no	GROUP	hospital number	age	sex	PRE OP	ONE WEEK POST OP	ONE MONTH POST OP	3 MONTHS POST OP	PRE OP	ONE WEEK POST OP	ONE MONTH POST OP	3 MONTHS POST OP	PRE OP	ONE WEEK POST OP	ONE MONTH POST OP	3 MONTHS POST OP	PRE OP	ONE WEEK POST OP	ONE MONTH POST OP	3 MONTHS POST OP
1	1	595126s	71	1	59.585	58.131	58.347	58.443	58.3	56.451	58.812	57.611	59.88	56.811	59.8	58.393	58.462	63.775	59.302	61.277
2	1	650150S	70	2	53.16	58.13	58.67	63.44	51.9	54.63	54.92	55.96	54.73	58.42	56.85	60.21	63.01	64.01	63.3	63.83
3	1	565666S	77	2	53.98	54.31	54.42	54.28	57.8	57.02	57.89	57.51	56.1	56.42	56.65	56.61	63.01	62.57	62.28	63.26
4	1	547481s	61	2	59.64	59.61	58.91	61.57	61.52	59.81	61.47	61.48	62.18	58.61	61.98	61.52	62.92	61.81	61.87	61.89
5	1	622823s	60	2	56.822	56.912	56.584	56.703	56.06	56.1	57.65	56.12	56.93	56.56	54.93	55.92	61.971	60.94	59.245	59.256
6	1	631215s	58	2	54.42	56.12	56.12	54.62	53.61	54.62	54.21	54.91	52.61	52.62	53.62	53.61	61.13	59.33	59.18	63.1
7	1	632114S	57	1	46.818	47.096	45.389	45.107	47.221	43.675	49.409	46.762	47.492	42.301	47.627	46.049	54.583	56.527	59.798	58.059
8	1	129371s	71	1	58.01	56.01	56.02	56.21	57.9	55.2	55.22	55.2	57.98	55.1	56.91	55.1	60.02	60.2	60.27	59.22
9	1	969477e	73	1	61.01	56.69	61.04	59.29	56.47	54.09	54.73	54.62	56.7	54.09	57.03	56.11	58.58	56.59	56.59	59.01
10	1	674674s	74	1	54.39	54.39	54.89	54.69	50.359	50.369	50.459	50.569	51.158	51.138	51.168	51.108	60.969	60.15	60.62	60.69
11	1	573232s	77	1	52.1	52.93	53	53.53	50.12	51.26	51.56	50.82	48.13	48.29	49.56	49.1	59.29	59.16	61.67	62.14
12	1	480211s	72	2	53.19	51.17	51.17	50.59	50.18	49.82	50.12	49.91	51.48	49.89	50.12	50.19	62.16	62.74	62.56	61.14
13	1	669353s	51	2	55.707	55.801	56.884	54.12	52.391	52.691	52.461	52.951	54.133	54.123	54.163	54.163	62.865	62.855	62.885	62.885
14	1	682629s	56	2	52.17	52.1	52.6	51.81	54.81	54.12	51.801	52.34	54.23	55.16	52.89	52.23	61.75	61.25	61.38	61.12
15	1	685532s	80	2	56.02	55.62	55.61	55	50.62	50.67	51.91	49.54	53.04	52.12	52.97	49.54	58.14	60.12	58.26	59.26
16	1	688126s	60	2	52.13	49.38	51.89	50.63	49.56	50.04	48.96	50.02	49.56	48.69	49.69	49.86	63.14	62.31	63.96	63.29
17	1	432420s	65	2	51.171	51.71	51.161	51.61	46.358	45.358	46.358	45.65	47.563	47.663	47.693	47.92	57.8	57.46	58.963	57.92
18	1	320241s	73	2	52.641	55.921	54.721	58.41	56.16	56.04	57.119	56.61	57.01	57.35	56.58	58.61	62.61	62.5	62.61	61.37
20	1	691047s	75	2	55.021	56.739	56.448	56.17	54.02	55.49	54.811	55.51	54.43	54.13	54.13	54.19	59.74	58.8	58.96	59.43
21	1	681116s	65	2	52.42	50.59	50.49	51.56	52.62	49.14	51.65	51.56	52.62	50.56	51.68	52.59	60.45	60.65	60.56	60.65
22	1	650150s	73	2	54.16	58.18	58.14		56.12	58.12	58.12		58.16	58.69	58.96		62.16	63.18	63.22	
23	1	660154s	64	2	54.639	56.85	56.515	60.119	54.697	54.19	55.375	54.16	56.083	56.21	56.492	56.96	64.639	63.19	63.079	63.96
24	1	697193s	55	1	57.563	58.204	56.781	56.81	59.582	60.518	59.794	59.96	56.108	58.628	58.08	58.61	59.419	59.74	59.74	59.1
25	1	652077s	71	1	58.06	58.16	57.06	60.45	56.84	56.13	56.28	56.62	58.12	58.8	56.12	57.91	62.87	62.8	63.41	62.86
26	1	691412s	71	2	50.12	49.12	50.35	50.19	50.04	51.19	50.18	50.19	50.04	49.87	50.06	50.12	60.89	60.86	60.18	62.31
27	1	364431s	61	1	62.4	62.16	62.72		62.71	63.28	62.55		59.45	62.86	61.07		62.82	62.16	60.48	
28	1	696013s	72	1	48.9	49.1	49.5	52.56	48.63	48.73	48.18	49.52	49.12	49.5	50	49.16	58.91	58.46	58.11	60.11
29	1	292915s	78	1	54.01	54.92	53.65	54.26	43.13	45.78	45.18	45.69	46.15	46.76	46.96	47.86	56.63	55.68	56.82	56.21
30	1	688335s	66	1	59.251	59.365	59.96		59.489	61.922	61.16		58.846	59.413	59.46		65.275	65.366	65.25	
31	1	699972s	78	1	53.16	53.09	56.16	55.15	60.16	60.09	60.06	60.15	57.65	57.09	59.37	58.56	60.16	61.14	60.26	61.16
32	1	694240s	63	1	60.5	59.56	62.03	59.56	59.43	61.46	60.12	60.15	59.41	62.56	60.42	60.16	61.56	59.77	60.73	60.12
33	1	700718s	64	1	49.67	49.67	49.76	50.17	55.21	55.21	56.49	55.56	54.64	54.76	55.49	55.63	60.14	60.16	60.52	61.66

															BCVA				IOP				
s.no	GROUP	hospital number	age	sex	DIABETES	HYPERTENSION	ASTHMA	IHD	EYE	GONIO	VDD	CDR	DIAGNOSIS	BCVA PRE OP	One week post op	1 month post op	3 months post op	BASELINE IOP	PRE OP	ONE WEEK POST OP	ONE MONTH POST OP	3 MONTH POST OP
1	2	673184s	68	1	1	1	1	1	2	5		0.4	2	0.5	0	0	0	16	16	10	12	10
2	2	897883e	68	1	1	1	1	1	2	5		0.3	2	0.5	0	0	0	16	16	12	18	16
3	2	639344s	57	1	2	1	1	1	1	5		0.3	2	0.2	0	0	0	20	20	10	16	16
4	2	678082s	67	1	2	2	1	1	1	5		0.3	2	0.5	0	0	0	14	14	12	14	14
5	2	664743s	58	2	1	1	1	1	1	5		0.4	2	0.6	0	0	0	12	12	12	12	14
6	2	322039s	75	2	1	1	1	1	2	5		0.3	2	0.3	0	0	0	12	12	12	14	12
7	2	618297s	68	1	2	2	1	2	2	5		0.3	2	0.3	0	0	0	16	16	13	14	12
8	2	469593s	54	1	2	2	1	1	2	5		0.4	2	0.3	0	0	0	14	14	16	14	16
9	2	298178s	68	1	1	2	1	1	1	5		0.3	2	0.2	0	0	0	16	16	10	12	14
10	2	553234s	67	1	2	1	1	1	2	5		0.3	2	0.5	0	0	0	10	10	12	14	14
11	2	540618s	51	2	1	1	1	1	1	5		0.5	2	0.3	0	0	0	14	14	14	14	14
12	2	681722s	66	1	1	1	1	1	1	5		0.3	2	0.5	0	0	0	16	16	12	14	12
13	2	683568s	58	2	1	1	1	1	1	5		0.4	2	0.5	0	0	0	18	18	16	12	14
14	2	684147s	59	2	1	1	1	1	1	5		0.3	2	0.5	0	0	0	12	12	14	14	14
15	2	541433s	51	1	1	1	1	1	2	5		0.2	2	0.5	0	0	0	18	18	14	14	14
16	2	686482s	69	2	1	1	1	1	2	5		0.3	2	0.2	0	0	0	16	16	16	12	12
17	2	580740s	59	2	1	1	1	1	2	5		0.4	2	0.6	0	0	0	14	14	14	12	12
18	2	689948s	59	2	1	1	1	1	1	5		0.3	2	0.3	0	0	0	10	10	12	10	12
19	2	637134s	74	2	1	1	1	1	2	5		0.3	2	0.2	0	0	0	16	16	10	10	12
20	2	691726s	69	2	1	1	1	1	2	5		0.4	2	0.3	0	0	0	12	12	14	12	12
21	2	694241s	63	2	1	1	1	1	1	5		0.4	2	0.6	0	0	0	12	12	12	12	12
22	2	510801s	63	1	1	1	1	1	1	5		0.5	2	0.5	0	0	0	14	14	14	12	8
23	2	682648s	60	2	2	1	1	1	2	5		0.4	2	0.3	0	0	0	16	16	12	16	14
24	2	685741s	50	1	2	2	1	1	2	5		0.3	2	0.3	0	0	0	18	18	14	12	12
25	2	679540s	67	2	1	1	1	1	2	5		0.3	2	0.2	0	0	0	14	14	12	12	12
26	2	622894s	59	2	1	2	1	1	1	5		0.4	2	0.5	0	0	0	12	12	14	12	12
27	2	393033s	54	1	1	1	1	1	2	5		0.3	2	0.3	0	0	0	12	12	14	14	12
28	2	694399s	59	2	1	1	1	1	2	5		0.3	2	0.5	0	0	0	14	14	14	12	12
29	2	552954s	65	2	2	2	1	1	1	5		0.3	2	0.5	0	0	0	16	16	12	14	12
30	2	344753s	64	2	1	1	1	1	2	5		0.3	2	0.3	0	0	0	12	12	10	12	12
31	2	741850e	78	1	2	2	1	2	1	5	1.65	0.5	2	0.2	0	0	0	12	12	12	12	12
32	2	681722s	66	1	1	1	1	1	2	5		0.3	2	0.2	0	0	0	14	14	12	14	12
33	2	698694s	52	2	1	1	1	1	2	5		0.2	2	0.3	0	0	0	14	14	14	14	12
34	2	691998s	57	1	2	1	1	1	1	5		0.4	2	0.6	0	0	0	14	14	12	12	12
35	2	652599s	51	2	1	2	1	1	1	5		0.5	2	0.2	0	0	0	10	10	12	12	12
36	2	610312e	60	2	1	1	1	1	1	5		0.3	2	0.3	0	0		10	10	12	14	
37	2	696578s	56	1	1	1	1	1	2	5		0.4	2	0.6	0	0	0	14	14	14	14	16
38	2	271217s	72	1	1	2	2	1	2	5		0.4	2	0.3	0	0	0	14	14	14	14	14
39	2	219799s	45	2	1	1	1	1	2	5		0.3	2	0.5	0	0	0	14	14	12	12	10
40	2	352912s	51	2	1	1	1	1	1	5		0.4	2	0.6	0	0		10	10	10	14	

					VESSEL DENSITY ONH				VESSEL DENSITY PERIPAPILLARY REGION				VESSEL DENSITY PAPILLARY REGION				VESSEL DENSITY MACULA			
s.no	GROUP	hospital number	age	sex	PRE OP	ONE WEEK POST OP	ONE MONTH POST OP	3 MONTHS POST OP	PRE OP	ONE WEEK POST OP	ONE MONTH POST OP	3 MONTHS POST OP	PRE OP	ONE WEEK POST OP	ONE MONTH POST OP	3 MONTHS POST OP	PRE OP	ONE WEEK POST OP	ONE MONTH POST OP	3 MONTHS POST OP
1	2	673184s	68	1	64.42	65.4	65.13	65.41	64.96	64.01	64.41	64.39	64.83	64.51	64.33	64.96	65.73	65.77	65.93	65.85
2	2	897883e	68	1	62.33	64.34	61.21	61.19	61.31	62.95	62.95	61.2	60.27	60.18	60.19	60.68	61.57	63	63.02	65.16
3	2	639344s	57	1	64.06	67.38	65.74	64.27	63.09	63.93	62.05	62.98	61.03	61.66	61.71	61.85	63.09	62.4	63.07	63.94
4	2	678082s	67	1	62.49	62.24	63.01	65.24	64.42	63.61	67.03	68.94	63.79	63.82	64.93	66.07	63.77	63.51	63.12	63.4
5	2	664743s	58	2	62.53	64.66	63.22	64.57	60.12	61.54	61.24	64.92	60.56	62.04	61.37	64.68	61.97	60.86	60.98	61.95
6	2	322039s	75	2	61.66	61.56	61.63	61.96	61.85	63.33	64.08	62.92	61.51	62.23	62.89	61.36	62.86	62.37	63.53	62.53
7	2	618297s	68	1	64.46	67.36	67.14	64.47	64.94	63.89	64.56	63.49	62.1	62.89	63.79	61.39	64.89	64.28	65.08	64.94
8	2	469593s	54	1	64.38	64.1	64.42	67.72	65.57	66.12	64.98	66.7	66.81	66.36	64.01	67.01	63.47	63.21	63.38	62.06
9	2	298178s	68	1	65.27	65.49	65.66	65.57	64.31	63.25	64.06	64.81	64.81	64.79	64.59	65.34	63.75	63.74	63.16	63.54
10	2	553234s	67	1	61.96	61.37	62.24	62.93	62.48	62.96	63.26	63.82	61.36	61.48	61.24	61.98	61.86	61.54	61.93	61.56
11	2	540618s	51	2	61.45	61.62	61.76	63.72	61.26	61.01	62.64	61.04	61.77	61.43	61.62	61.53	62.73	63.53	62.91	63.04
12	2	681722s	66	1	63.51	62.62	63.91	63.12	63.85	62.29	62.87	63.19	62.52	62.61	62.86	62.09	63.87	64.09	64.45	64.33
13	2	683568s	58	2	63.14	62.98	63.63	64.08	64.69	62.47	64.06	66.03	65.33	62.84	63.91	65.51	63	62.82	62.9	61.81
14	2	684147s	59	2	62.98	63.68	63.38	65.19	61.42	63.29	62.04	63.32	63.23	62.89	63.57	64.19	62.01	62	63.2	63.62
15	2	541433s	51	1	62.82	62.03	62.31	62.15	62.89	62.55	62.54	64.61	62.39	62.83	62.41	62.55	61.83	62.88	61.88	61.89
16	2	686482s	69	2	62.18	64.71	64.45	63.62	61.18	62.61	63.05	61.52	61.18	62.98	62.84	62.52	62.59	62.38	64.65	64.65
17	2	580740s	59	2	60.16	60.58	60.1	60.19	62.98	63.93	64.62	64.62	61.98	61.84	61.86	62.63	60.17	60.17	60.15	60.24
18	2	689948s	59	2	61.19	61.94	62.03	64.54	62.89	62.19	65.1	66.7	61.19	63.29	64.64	63.81	65.02	63.09	63.9	64.52
19	2	637134s	74	2	62.97	61.35	61.97	62.93	59.91	59.61	60.12	61.12	60.12	60.61	60.12	61.21	60.19	61.19	61.28	61.92
20	2	691726s	69	2	61.12	61.57	64.91	63.87	61.53	61.92	61.85	63.22	63.77	62.447	61.1	62.96	61.92	61.84	60.05	60.09
21	2	694241s	63	2	64.26	66.49	66.49	65.49	61.56	61.92	62.36	64.42	62.12	62.35	63.29	63.93	61.23	61.93	62.99	63.19
22	2	510801s	63	1	61.91	62.94	61.49	61.01	62.84	62.191	61.29	61.19	61.84	63.09	60.89	61.15	62.31	62.32	61.19	62.24
23	2	682648s	60	2	62.46	62.43	61.95	61.29	64.21	64.35	63.21	62.29	62.71	63.86	62.78	61.29	61.46	62.14	61.92	62.32
24	2	685741s	50	1	63.68	66.26	64.48	64.28	67.56	66.45	66.66	66.96	65.116	65.78	65.89	65.28	67.84	67.51	65.28	66.82
25	2	679540s	67	2	64.63	65.04	64.15	64.06	64.64	63.01	66.29	64.2	65.51	64.9	63.42	64.69	62.29	62.92	61.25	62.59
26	2	622894s	59	2	61.59	62.47	61.9	61.14	62.39	64.93	62.39	62.46	62.93	64.93	62.19	61.02	61.37	61.94	62.63	63.25
27	2	393033s	54	1	68.43	68.16	64.22	64.46	66.82	71.82	68.83	68.48	65.23	71.56	66.56	66.39	65.57	65.95	65.23	65.81
28	2	694399s	59	2	62.05	62.52	63.98	64.79	65.08	66.4	69.93	65.33	68.17	66.7	69.86	65.1	68.19	67.95	68.18	66.2
29	2	552954s	65	2	61.84	61.13	62.92	62.67	66.31	68.99	66.26	66.53	66.62	66.65	69.42	66.3	67.96	67.94	68.4	66.17
30	2	344753s	64	2	62.68	62.46	61.95	62.69	64.21	64.35	63.21	64.21	62.21	63.86	62.71	63.26	62.47	61.14	61.92	62.45
31	2	741850e	78	1	64.1	61.87	61.95	62.19	68.36	67.7	68.09	68.12	67.36	67.7	68.09	67.66	65.39	66.3	65.37	65.89
32	2	681722s	66	1	61.19	61.45	64.37	62.53	65.05	66.56	68.23	65.56	67.05	65.6	66.27	66.17	65.32	66.78	66.18	66.16
33	2	698694s	52	2	62.16	62.98	64.26	64.21	62.13	65.19	66.5	65.61	63.67	63.64	65.51	64.61	63.82	63.18	64.26	64.65
34	2	691998s	57	1	63.45	66.26	65.68	65.89	64.56	65.96	63.01	63.52	63.86	66.26	64.37	64.95	60.15	60.12	61.52	61.65
35	2	652599s	51	2	64.54	65.54	67.53	65.96	62.56	62.88	62.72	62.98	63.18	63.18	64.86	64.45	61.88	61.88	61.02	62.88
36	2	610312e	60	2	62.01	62.01	63.39		65.3	65.65	65.28		62.44	64.25	64.92		61.65	61.92	61.65	
37	2	696578s	56	1	68.09	68.87	68.09	68.96	63.42	66.92	63.21	63.65	63.42	66.72	63.08	63.65	60.21	60.75	60.12	61.52
38	2	271217s	72	1	62.12	64.26	62.58	63.56	59.61	59.81	58.92	61.69	62.12	62.19	62.18	62.78	60.12	60.16	63.17	63.59
39	2	219799s	45	2	62.49	61.69	63.38	62.36	61.06	64.25	63.5	64.16	61.82	61.96	63.38	62.36	64.34	64.44	64.34	64.28
40	2	352912s	51	2	59.8	59.91	59.19		61.11	63.03	61.26		59.16	59.05	59.34		60.81	60.16	60.12	

SNELLEN VISUAL ACUITY TO LOGMAR VISUAL ACUITY CONVERSION TABLE

Snellen	LogMAR
6/60	1
6/48	0.9
6/38	0.8
6/30	0.7
6/24	0.6
6/19	0.5
6/15	0.4
6/12	0.3
6/9.5	0.2
6/7.5	0.1
6/6	0.0
6/4.8	-0.1
6/3.8	-0.2
6/3	-0.3

ABSTRACT

TITLE OF THE ABSTRACT :

A prospective observational study to analyze changes in retinal blood vessel density in primary open angle glaucoma following intra ocular pressure reduction by surgical management using optical coherence tomography angiography.

DEPARTMENT :

This study was conducted in department of Ophthalmology, Christian Medical College, Vellore, a tertiary eye care centre.

NAME OF THE CANDIDATE :DR.Sharmila.S

DEGREE AND SUBJECT :MS OPHTHALMOLOGY

NAME OF THE GUIDE :DR.Lekha Mary Abraham

OBJECTIVES:

1. To document the peripapillary, papillary and optic nerve head vascular density index by using OCT-A, in patients with POAG and cataract before and after PhacoTrab.

2. To document the peripapillary, papillary and optic nerve head vascular density index by using OCT-A, in patients with cataract alone before and after PhacoIOL.

METHODS:

. OCT-A(using the Swept source spectral domain optical coherence tomography) scan for analysis of the optic nerve head vasculature, peripapillary, papillary and macular vessel density were done at preop,1 week,1month and 3 months. All surgeries (PhacoTrab and PhacoIOL) were done by glaucoma specialists. The continuous variables among the two groups were compared using independent-t-test and the

categorical variables were compared using chi-square test. Repeated measures ANOVA was used to compare the change of variables from baseline to 3 months among the two groups. The pairwise comparison was done with TUKEY test. All the analyses were performed using STATA/ IC 15.0 software.

RESULTS:

- There is a significant difference in optic nerve head, papillary and peripapillary vessel density between patients in the PhacoTrab group and Phaco IOL group using Swept source OCT
- There was no difference in macular vessel density between patients in both the groups
- There was an improvement in optic nerve head vessel density using swept source OCT after significant IOP reduction following PhacoTrab
- There was no improvement in papillary, peripapillary and macular vessel density using swept source OCT after significant IOP reduction following PhacoTrab