EVALUATION OF MACULAR AND PERIPAPILLARY CHOROIDAL THICKNESS USING ENHANCHED DEPTH IMAGING OPTICAL COHERENCE TOMOGRAPHY IN PATIENTS WITH ESSENTIAL HYPERTENSION

DISSERTATION SUBMITED FOR
MS (Branch III) Ophthalmology

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CERTIFICATE

This is to certify that dissertation entitled "**EVALUATION OF MACULAR AND PERIPAPILLARY CHOROIDAL THICKNESS USING ENHANCHED DEPTH IMAGING OPTICAL COHERENCE TOMOGRAPHY IN PATIENTS WITH ESSENTIAL HYPERTENSION"** is a bonafide done by **Dr.Siddharth Narendran.** under our guidance and supervision in the department of Retina, Aravind Eye Hospital and Post Graduate Instuite of Ophthalmology in Madurai during his residency period from July 2013to April2016.

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DECELARATION

I**, Dr.Siddharth Narendran** solemnly declare the dissertation titled "**EVALUATION OF MACULAR AND PERIPAPILLARY CHOROIDAL THICKNESS USING ENHANCHED DEPTH IMAGING OPTICAL COHERENCE TOMOGRAPHY IN PATIENTS WITH ESSENTIAL HYPERTENSION"** has been prepared by me. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any other university board either in India or aboard

This dissertation is submitted to the **Tamil Nadu Dr. M.G.R Medical University**, Chennai in Partial Fulfilment of the rules and regulation for the award **of M.S. Ophthalmology (BranchIII**) to be held in April 2016.

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CONTENT S

INTRODUCTION

High blood pressure is considered to be the third most important risk factor for non- communicable Southern Asia (2010)(1). Hypertension causes a considerable public health burden on the cardiovascular health status of individuals and also on the healthcare providers in India.(2) It is considered to be directly responsible for 58% of all stroke deaths and 23% of coronary heart disease (CHD) related deaths in India.(3) The World Health Organization rates Hypertension as one of the most important risf factors for premature deaths in the world. A systematic analysis of population health data for attributable deaths and attributable disease burden done by The Global and Regional Burden of Disease and Risk Factors study has ranked Hypertension in Southern Asia as the second important factornext only to child underweight for age. (4) About 34% urban and 24% rural Indians are hypertensive. Among which, only 25% of the rural and 42% of the urban Indians are aware of their hypertensive status. Of this only 25% of the rural and 38% of urban Indians are being treated for hypertension.(5)

Hypertension causes end-organ damage including hypertensive retinopathy.(6) Current studies have indicated that the effects of systemic

hypertension on the retinal, optic nerve head and choroidal circulation produce three distinct and independent manifestations:

(i) hypertensive choroidopathy, (ii) hypertensive optic neuropathy, and (iii) hypertensive retinopathy.(7,8)However the classification techniques for grading hypertensive retinopathy currently in practice,are shown to have poor correlation with the degree of severity of hypertension. Large population based studies have shown that the fundus lesions described in hypertensive individuals can also occur in normal elderly indiviuals.(9–11) Poorly controlled systemic hypertension has been shown to be one of the most important comorbid factors in the worsening of microvascular disease of the eye like diabetic retinopathy.(12)Though the exact relationship has not yet been fully understood. Systemic hypertension is considered to be one be the contributing factors for several ocular diseases. Choroidal lesions secondary to elevated blood pressure are less well recognized than retinopathy in the current literature.

The choroid formsthe posteriorpart of the uveal tissue, the middle layer of the eye. The primary function of the choroid is to provide oxygen and nutrients to the retina. With the advent of Enhanced depth-imaging optical imaging ([EDI-OCT] ; as defined by Spaide et al.(13)) in-vivo imaging of the choroid has now become possible. The smooth muscle of the vessel walls of the choroid are innervated

by both the sympathetic and parasympathetic system, which form dense plexuses of fibers around the vessels ("perivascular plexus"). The choroid vasculature is principally under neurogenic control. In contrast to the retinal vasculature, the choroid does not exhibit any auto regulation. (14)Pterygopalatine ganglion provides the parasympathetic supply to the choroid.(15)They are mainly cholinergic fibers abundant in parasympathetic vasodilatory mediators like the vasoactive intestinal peptide and nitric oxide.(16) The sympathetic fibres are mainly noradrenergic fibres mediating vasoconstriction and are supplied primarily by the ciliary ganglion.(17)

In the past, many lesions attributable to hypertensive choroidopathy have been erroneously classified as being caused by hypertensive retinopathy. Hypertensive choroidopathy has been associated with toxemia of pregnancy, pheochromocytoma, renal disorders, and malignant hypertension.(18)Hayreh defined lesions attributable to hypertensive choroidopathy as initial, acute, and chronic, based on studies in rhesus monkeys. (19),(20) The circulatory levels of several endogenous vasoconstrictive mediators has been shown to increase in patients with malignant hypertension. These substances include potent vasoconstrictors such as adrenaline, angiotensin II, adrenaline, vasopressin, and endothelin-1 (ET-1). Such substances can

easily pass from the fenestrated choriocapillaris to the interstitial area of the choroid, causing severe vasoconstriction and tissue ischemia in the choriocapillaris. Thus, the choroidal lesions (Elschings spots and Siegrist's streaks) of malignant hypertension develop. Similar changes has been shown to occur in the blood and sympathetic system in patients with chronic essential hypertension.(21)

STRUCTURE AND FUNCTION OF THE CHOROID

EMBRYOLOGY OF THE CHOROID:

The choroid develops from two types of embryonic tissues: the cranial neural crest cells and the mesoderm.

The choroid is considered to develop in three stages:

i. First and second months: development of capillaries
ii. Third month: development of veins
iii. Fourth month: development of arteries.(22)

The choroidal melanocytes and the stroma are considered to develop both from the mesoderm and the neural crest cells. (23–25)

ANATOMY OF THE CHOROID:

The choroid is the posterior part of the uveal tissue, the middle covering of the eye (Fig 1). The choroid measures 0.23 to 0.30 mm in thickness in the posterior pole of the eye and 0.11 to 0.15 mm anteriorly and peripherally. This variation in diameter is due to the greater concentration of choroidal arteries and large-and medium-sized choroidal veins in the posterior choroid. The choroid can be further subdivided into

three parts from internal to external: (1) Bruch's membrane; (2) Layers of choroidal vasculature ; and (3) the suprachoroid.

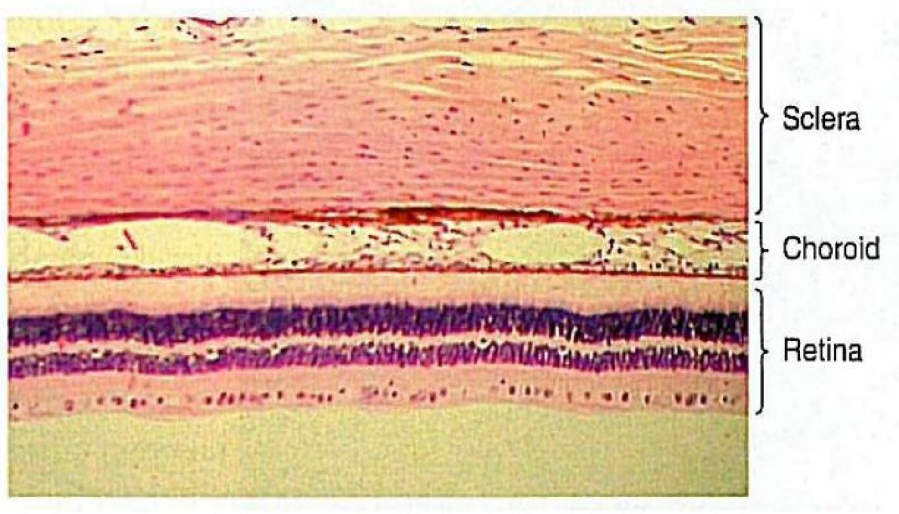


FIG 1: PHOTOMICROGRAPH OF THE THREE LAYERS AT THE BACK OF THE PRIMATE EYE.

HISTOLOGY OF THE CHOROID:

Histologically, the choroid is most commonly described as five layers:

1. Bruch’s membrane
2. Choroiocapillaries
3. Medium-sized vessels (Haller’s layer)
4. Large-sized vessels (Sattler’s layer)
5. Suprachoroid(Fig 2).(26)

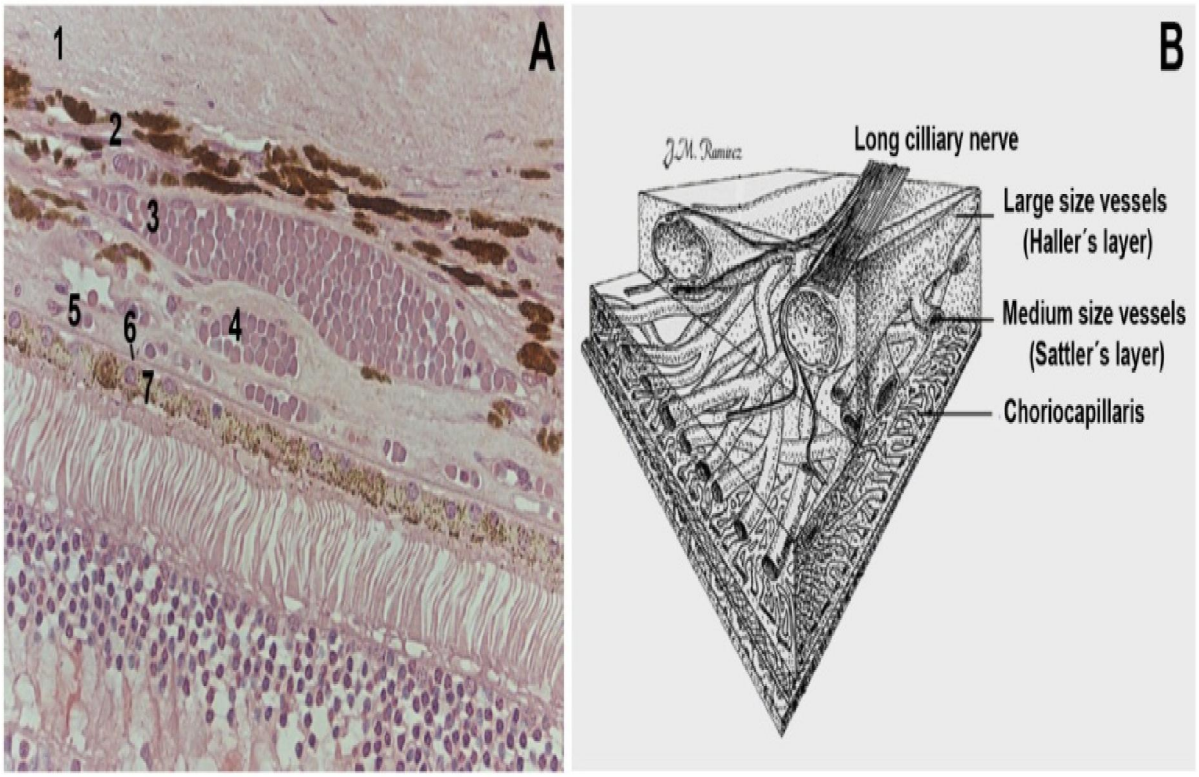


FIG 2:LAYERS OF CHOROIDAL VASCULATURE A: HISTOLOGICAL SECTION (H/E). B: THREE-DIMENSIONAL SCHEME

1: Sclera; 2: Suprachoroid; 3: Haller´s Layer; 4: Medium-sized vessel layer Sattler´s Layer ; 5Choriocapillaries; 6: Bruch´s membrane; 7: Retinal pigment epithelium

SUPRACHOROID

The suprachoroid forms the outer layer of the choroid.It is a transition zone between the innermost part of the sclera and the layer of medium-sized vessels (Haller's layer). It is formed bycollagen fibres,

fibroblasts, melanocytes, elastic fibres, nerve plexus, smooth-muscle cells, and intrinsic choroidal neurons (ICNs).(27–31)

CHOROIDAL VASCULATURE AND STROMA:

The choroid is a highly vascular structure. Most of the choroid is made up of blood vessels that gradually decrease in size from outer to inner as the vessels branch. It is composed of arteries, veins, arterioles, capillariesand a vascular stroma.The choroidal stroma contains collagen and elastic fibres, non-vascular smooth cells, numerous melanocytes, fibroblasts, mast cells, macrophages, and lymphocytes. The arterial vessels of the choroid are branches of the posterior ciliary arteries (PCAs) .It also receive blood supply from some recurring branches of the major arterial circle of the iris. The vessels become smaller in diameter in a branching hierarchy towards the capillary bed. This enables the identification of the three vessel layers of decreasing caliber: a inner layer of interconnected capillaries (the choriocapillaris), an intermediate layer of medium-sized vessels (Sattler's layer), and an outer layer of large-sized vessels (Haller's layer) outer layer of large-sized vessels (Haller's layer)(32)

BRUCH'S MEMBRANE

Bruch's membrane forms the innermost layer of the choroid. It is an acellular structure. According to electron microscopic studies, the Bruch's membrane can be divided into five layers, which, from the retinal side towards the choroid are:

1.The basal membrane of the Retinal Pigment Epithelium.

2. The inner collagen layer,

3. The elastic-fibre layer,

4. The outer collagen layer, and

5.The basement membrane of the choriocapillaries.(33,34)

INNERVATION OF THE CHOROID:

The choroidal innervation is largely made up ofnervefibre bundles from both the autonomic nervous system and the central nervous system (Fig 3). The sympathetic fibres are from the superior cervical ganglion. The parasympatheticfibres arise from the pterygopalatineand ciliary ganglion. These nerve fibres reach the choroid in three directions:i) around the Short Posterior cilairy artery, these fibres arise from the plexuses around the internal carotid and continue along with the ophthalmic artery until reaching the SPCA in the choroid; ii) through the short posterior ciliary nerves that are derived from the from the ciliary ganglion; or iii) through the long posterior ciliary nerves that come from

the nasociliary nerve .In addition to these nerve fibres, the choroid alsohas intrinsic choroidal neurons. (31,35)

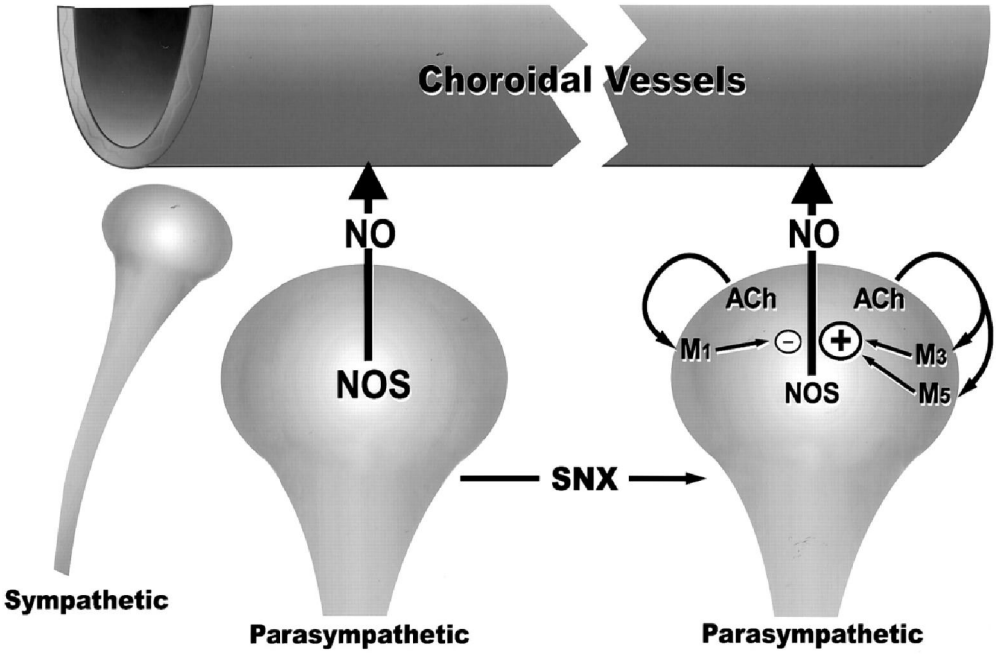


FIG 3: DEPICTING THE AUTONOMIC CONTROL OF CHOROIDAL VASCULATURE.

FUNCTIONS OF THE CHOROID

- Nutrient and oxygen supply to the outer retina especially the photoreceptors.
- Thermoregulation by the dissipationof heat
- Maintenance of intraocular pressure
- Drainage of aqueous humor
- Absorption of scattered light

CHOROIDAL HEMODYNAMICS

CHOROIDAL BLOOD SUPPLY:

The choroid receives its arterial blood from THE branches of the ophthalmic artery. The nasal and temporal short posterior ciliary arteries and the nasal and temporal long posterior ciliary arteries are branches of the posterior ciliaryartery which is a branch of the ophthalmic artery. All anterior ciliary arteries are all direct branches from the ophthalmic artery, except for the one anterior ciliary artery accompanying the lateral rectus. This anterior ciliary artery is derived from the ophthalmic artery as a branch of the lacrimal artery .Although the retinal vessels also arise from the ophthalmic artery, the retinal and choroidal blood supplies are distinct and seperate within the eye and there is little, if any, anastomosis between the two systems (Fig 4).

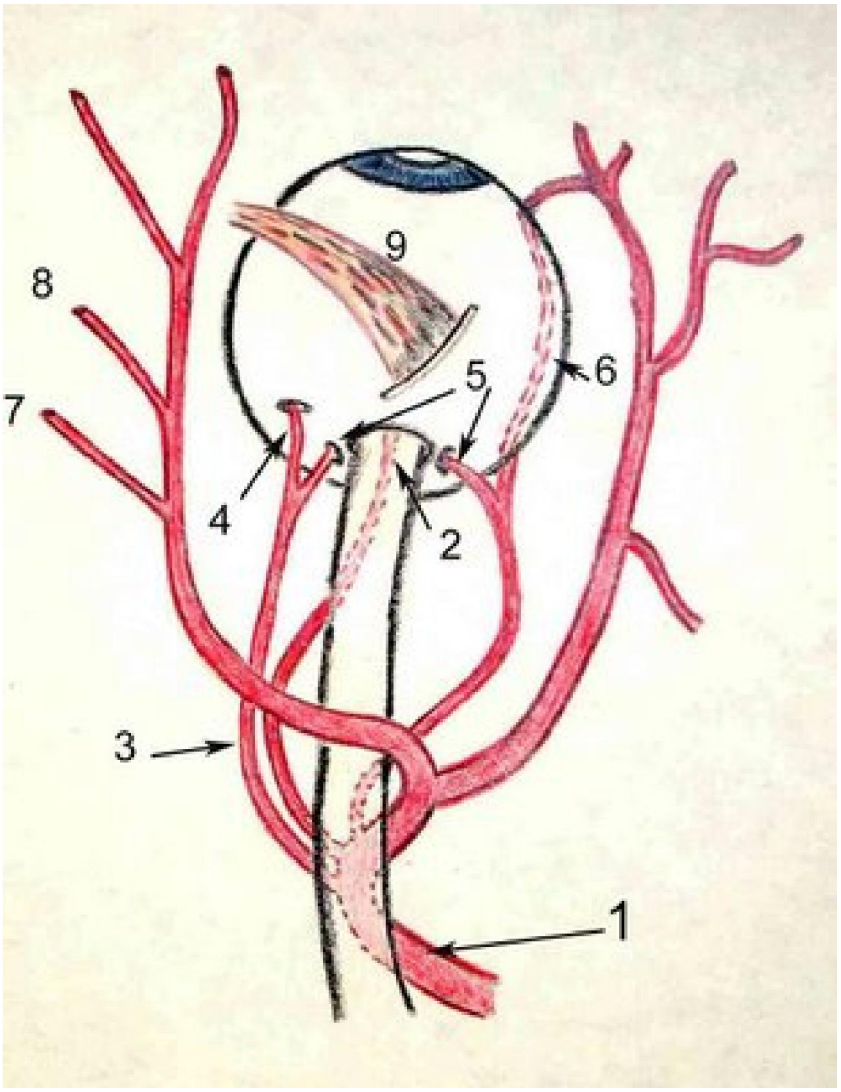


FIG4. THE BLOOD SUPPLY OF THE CHOROID

1.ophthalmic Artery 2.Central retinal artery 3.ciliary arteries 4.Long posterior ciliary artery 5.short posterior ciliary artery 6.Suprachoroidal space 7.Posterior ethmoidal arteries 8. Anterior ethmoidal arteries

CHOROIDAL BLOOD FLOW: NOURISHMENT OF THE RETINA

In spite of the conspicuous retinal blood vessels, the major blood supply to the retina is the choroidal vasculature.The photoreceptors consume more than 90-92% of the oxygen .The photoreceptors are one of the most metabolically active cells in the body. This is important especially in darkness when active ion transport is necessary to maintain ion homeostasis and to keep the ligand-gated channels open. In darkness, choroidal circulation provides 90% of the oxygen.(36) Due to presence of barriers like the Bruch's membrane and the RPE, a steep oxygen tension gradient is necessary. This is possible because of the high blood flow in the choroid, possibly the highest in the body per unit tissue weight.(37)Therefore, the arterial/venous gradient in the choroid is only 3% compared to the retinal circulation where the gradient is around 40%. In several species, the choroidal arteries supplies both the inner retina and the outer retina as the retinal blood vessels are sparse (e.g., rabbit) or absent (e.g., guinea pig) . In guinea pigs, oxygen tension shows a rapid decline, to almost 0 mm Hg, within approximately 70 μm of Bruch's membrane and so the inner retina functions in an anoxic environment which is possible only by anaerobicmetabolism. In contrast, in other vascular retinas the inner retinal oxygen tension is around 20mm maintained by the retinal vessels. (38,39) In the retina, the capillaries are

without fenestrationsforming the blood-ocular barrier, and so are impermeable to even small molecular weight molecules. Thus the role of choroidal circulation is highly crucial in supplying oxygen as well as nutrients because the capillaries of the choroid are fenestrated. These fenestrations have a high permeability not only to glucose but also to several low molecular weight substances such as albumin.

REGULATION OF CHOROIDAL BLOOD FLOW:

The smooth muscle of the vessel walls of the choroid are innervated by both the sympathetic and parasympathetic system, which form dense plexuses of fibers around the vessels ("perivascular plexus"). The choroid vasculature is principally under neurogenic control. In contrast to the retinal vasculature, the choroid does not exhibit any autoregulation. (14)Pterygopalatine ganglion provides the parasympathetic supply to the choroid.(15)They are mainly cholinergic fibres abundant in parasympathetic vasodilatory mediators like the vasoactive intestinal peptide and nitric oxide.(16) The sympathetic fibres are mainly noradrenergic fibres mediating vasoconstriction and are supplied primarily by the ciliary ganglion.(17)

CHOROIDAL HEMODYNAMICS IN EYE DISEASES:

Choroidal circulation has been found to be significantly slower in patients with normal tension glaucoma, proliferative diabetic retinopathy and age-related macular degeneration.(40–42)

CHOROIDAL WATER SHED ZONES:

The border between the areas of distribution of any two end-arteries in a tissue is called a ‘ water-shed’ zone. All choroidal arteries are end arteries.

The choroidal vasculature has several such watershed zones, which are arranged as follows:

- Between Posterior ciliary arteries (PCA) (Fig 5)
- Between short PCA
- Between the short and long PCAs
- Between the PCAs and the anterior ciliary arteries
- Between the choriocapillaris lobules
- Between the vortex veins

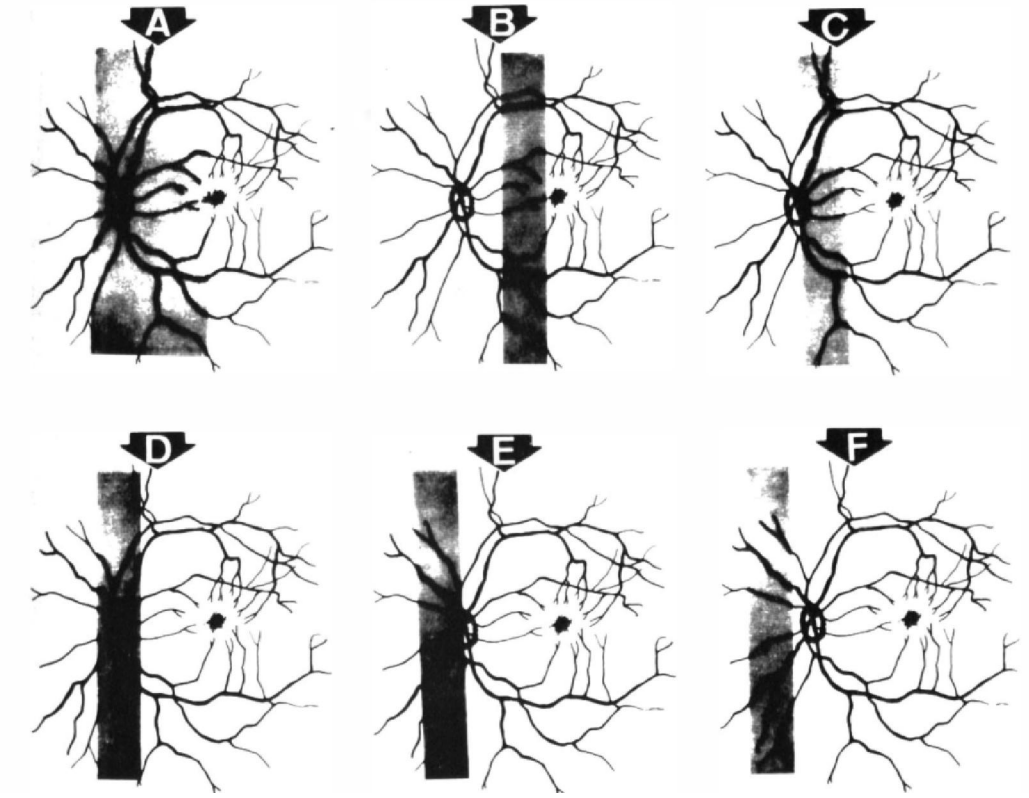


FIG 5. FIGURE DEPICTING THE PRESENCE OF WATERSHED ZONES IN THE CHOROIDAL VASCULAR BED BETWEEN THE MEDIAL AND LATERAL POSTERIOR CILIARY ARTERIES.

The close proximity of the choroidal watershed zones to the peripapillary region and the macula may prove the possible role of choroidal blood flow in ischemic optic neuropathies and in macular ischemic lesions.

PERIPAPILLARY CHOROIDAL BLOOD FLOW:

The peripapillary choroid has been reported to play a vital role in the pathophysiology of several ocular diseases including pathological myopia and glaucoma. Peripapillary choroidal blood vessels provide major part of the blood supply to the laminar and prelaminar regions of the optic nerve head.

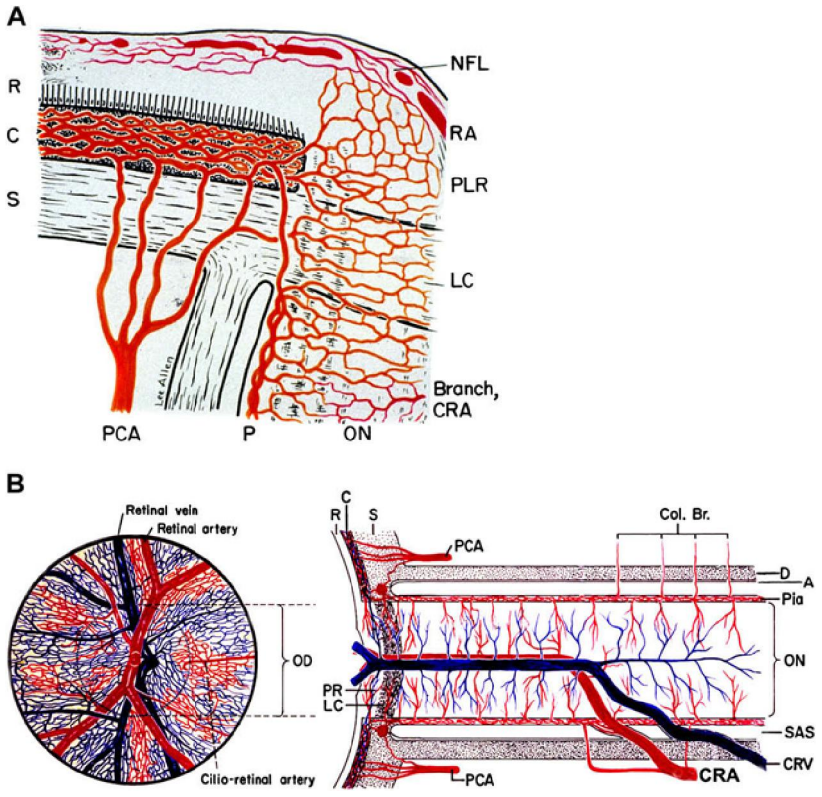


FIG. 6: DIAGRAMMATIC REPRESENTATION OF BLOOD SUPPLY OF OPTIC NERVE HEAD

ESSENTIAL HYPERTENSION

DEFINITIONAND CLASSIFICATION OF HIGH BLOOD PRESSURE (JNC 7):

According to the Seventh report of the Joint National Committee on the Prevention, Detection, Evaluation and treatment of high blood pressure, Hypertension is defined as

Blood Pressure Classification	SBP mmHg	DBP mmHg
Normal	<120	and <80
Prehypertension	120–139	or 80–89
Stage 1 Hypertension	140–159	or 90–99
Stage 2 Hypertension	≥160	or ≥100

"The diagnosis of hypertension is made when the average of two or more diastolic BP measurements on at least 2 subsequent visits is consistently greater than or equal to 90 mm Hg or when the average of multiple systolic BP readings on 2 or more subsequent visits is consistently greater than or equal to140 mm Hg. Isolated systolic hypertension is defined as systolic BP greater than or equal to140 mm Hg and diastolic BP less than 90 mm Hg."

DEFINTION OF ESSENTIAL HYPERTENSION:

Essential, idiopathic, or primary hypertension is defined as " high blood pressure in which secondary causes such as renovascular disease, renal failure, pheochromocytoma, hyperaldosteronism, or other causes of secondary hypertension or Mendelian forms are not present ".

PATHOGENESIS AND PATHOPHYSIOLOGY:

The pathogenesis of essential hypertension is a complex interplay between

1. Genetic predisposition
2. Lifestyle and environmental influences and
3. Disturbances in vascular structure and neurohumoral control mechanisms (Fig 7).

PATHOPHYSIOLOGY:

Acharacteristic feature ofprimary hypertension is an inappropriate increase in the peripheral vascular resistance of the medium-sized vessels relative to the cardiac output. This happens because of the mechanical remodelling of the arterioles, which is characterized by an increase in their media/lumen ratio. However, this is now considered to be a consequence rather than the cause for essential hypertension.Endothelial dysfunction is seen in essential hypertension along with decreased production of nitrous oxide. However the above-mentioned features are

more likely to be a consequence rather than the cause for increased blood pressure. Though the specific role of the renin-angiotensin system in the etiopathogenesis of hypertension is largely unclear, therapeutic agents acting on this system have shown good control of blood pressure. Though the blood pressure and the vascular tone is controlled by the sympathetic nervous system, its role in the maintenance of chronic hypertension is unclear.

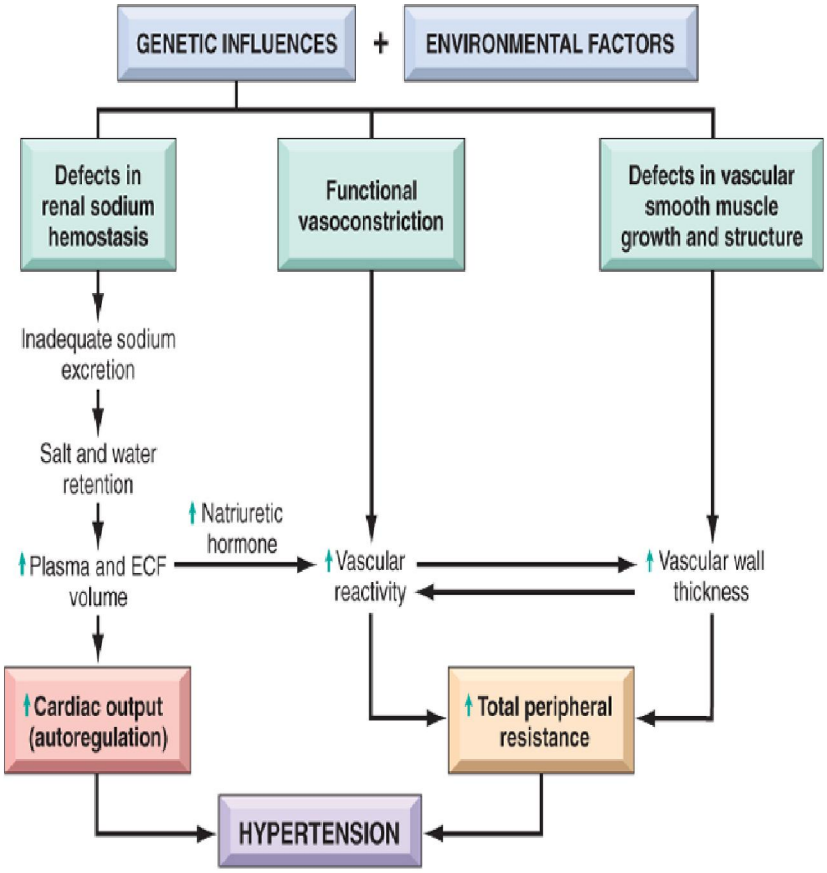


FIG 7: PATHOGENESIS OF ESSENTIAL HYPERTENSION.

HYPERTENSION AND END-ORGAN DAMAGE:

Hypertension damages blood vessels and thus causes damage to end-organs. The mechanisms causing this injury are complicated and, although studied for years in experimental animal models, are only hypothetical. The endothelial layer acts as an interface for signal transduction for the hemodynamic forces, which play a role in the regulation of vascular tone and in the chronic arterial structure remodelling. Effects of these hemodynamic mechanical forces on gene expression and signal transduction in endothelial cells have been demonstrated.(43) Mechanical stress initiates several pathways including integrin interaction of cells and matrix, tyrosine kinase activation, ion transfer,autocrine production, and growth factor release .(44) Increased blood flow through small arteries has been reported to increase the production of connective tissue and promote tunica media hypertrophy, mostly through the proliferation of thesmooth muscle cells. Increased pressure is capable of the process of induction of early response genes in thewall of the arteries. Increased Oxyradical production by endothelial cells, seen in hypertensive mammals due to xanthine oxidase, results in leukocyte-endothelial adhesion that in turnresults inthe surface expression of different cell adhesion molecules.(45)Leukocyte infiltration of the endothelium resulting in the setting up of the inflammatory cascade including the release of chemokines.

Mechanical forces alone are capable of initiating events resulting in remodeling of the vessels and subsequent end-organ damage. But, hypertension is not merely a process of mechanical events. All forms of hypertension involve mediators, which are independent of the arterial pressure.

VASOCONSTRICTIVE MEDIATORS IN ESSENTIAL HYPERTENSION:

The circulatory levels of several endogenous vasoconstrictive mediators have been shown to increase in patients with malignant hypertension. These substances include potent vasoconstrictors such as adrenaline, angiotensin II, adrenaline, vasopressin, and endothelin-1 (ET-1). Since the choriocapillaris are fenestrated, such molecules can cause vasoconstriction of the vessels.

EFFECT OF HYPERTENSION ON CHOROIDAL VESSELS:

The choroid is one of the most vascular tissues in the body. It is affected by changes in intraocular pressure, endogenous nitric oxide, vasoactive substances produced by the choroidal ganglion cells and circulating catecholamines. Studies have shown the absence of autoregulation in choroidal vasculature in contrast to the retinal vessels. A reduction in choroidal blood flow stimulates the activation of the

sympathetic nervous system and release of noradrenaline. Noradrenaline promotes vasoconstriction by its action on the alpha-1 receptors. The choroidal is capable of some autoregulation by manipulating the mean arterial pressure and IOP as reported by Riva et al who showed a increase of only 12% of choroidal blood flow with a 60% increase in ocular perfusion pressure.

The choroid is the major source of oxygen and nutrients to the outer retina. Thus, even a small change in the perfusion pressure of the choroid may impair the functioning of the retina. The increased levels of circulating vasoactive substances are now considered to be behind the pathogenesis of hypertensive choroidopathy in malignant hypertension. The circulatory levels of several endogenous vasoconstrictive mediators have been shown to increase in patients with malignant hypertension. These substances include potent vasoconstrictors such as adrenaline, angiotensin II, adrenaline, vasopressin, and endothelin-1 (ET-1). Since the choriocapillaris are fenestrated, such molecules can cause vasoconstriction of the vessels.

OCULAR MANIFESTATIONS OF HYPERTENSION

Systemic hypertension by its effect on the blood vessels of the choroid and the retina produces three characteristic manifestations in the eye

i. Hypertensivechoroidopathy
ii. Hypertensive optic neuropathy and
iii. Hypertensiveretinopathy

HYPERTENSIVE RETINOPATHY:

Hypertensive retinopathy was first described by Liebreich in 1859.(46) It represents the end-organ damage in patients with elevated systemic arterial blood pressure.

CLINICAL FEATURES:

The fundus features commonly described in hypertensive retinopathy include microaneurysms, generalized arteriolar narrowing, cotton-wool spots, intra-retinal hemorrhages, hard exudates and optic disc swelling. Changes of secondary arteriolosclerosis are, changes in the arteriolar light reflex and periarteriolar vessel sheathing, arteriovenous crossing changes and vasoconstriction.(47)

Grade	Classification
Grade I	Mild generalized retinal arteriolar narrowing or sclerosis
Grade II	Definite focal narrowing and arteriovenous crossings Moderate to marked sclerosis of the retinal arterioles Exaggerated arterial light reflex
Grade III	Retinal hemorrhages, exudates and cotton wool spots Sclerosis and spastic lesions of retinal arterioles
Grade IV	Severe grade III and papilledema

Table 1. The Keith, Wagener, and Barker hypertensive retinopathy classification (Grade I-IV), based on the level of severity of the retinal findings

HYPERTENSIVE CHOROIDOPATHY

Hypertensive choroidopathyusually occurs in young adults who experience an acute episode of hypertension associated usually with preeclampsia, pheochromocytoma, or renal hypertension.

CLINICAL MANIFESTATIONS:

Lobular nonperfusion of the choriocapillaris results in ahyper pigmented patch surrounded by a margin of hypopigmentation known as *Elschnig spots*(Fig 8).

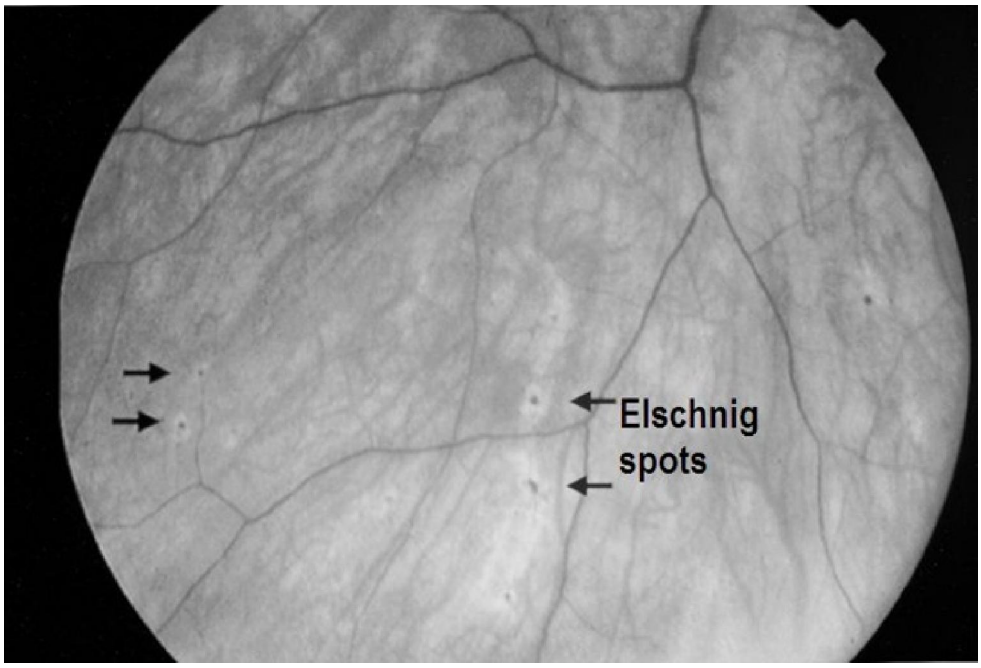


FIG 8. RED-FREE FUNDUS PHOTOGRAPH SHOWING ELSCHNIG SPOTS.

Siegrist streaks are linearhyper pigmented configurations thatusually follow the meridional course of choroidal arteries in patients with malignant hypertension (Fig 9).Fluorescein angiography reveals focal choroidal hypoperfusion in the early phases and multiple areas of subretinal fluid leakage in late phases. Though focal detachments of the retinal pigment epithelium may be seen exudative retinal detachments are extremely rare. The more commonly described features of hypertensive choroidopathy are choroidal vascular sclerosis, Elschnig spots and Siegrist's streaks.

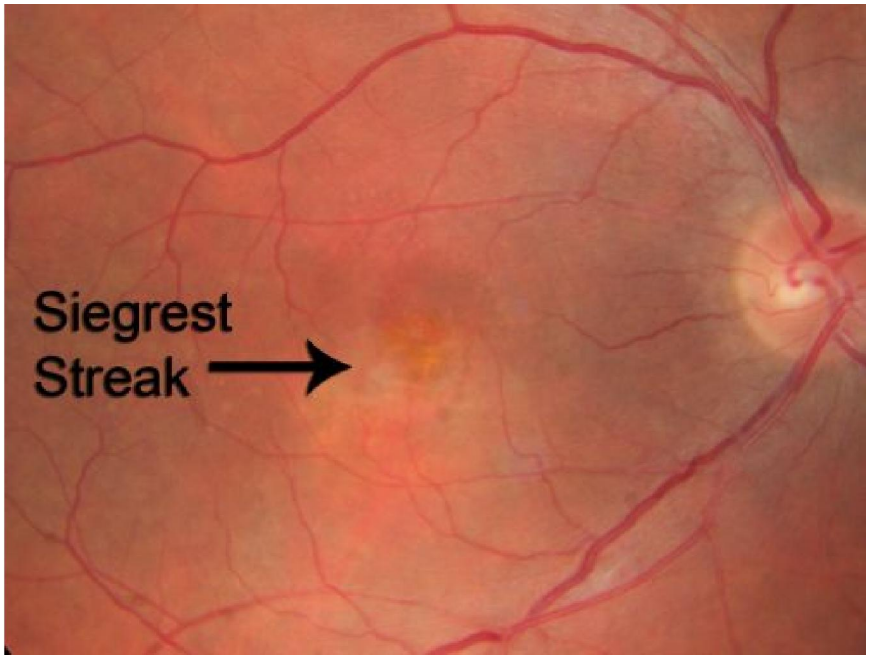
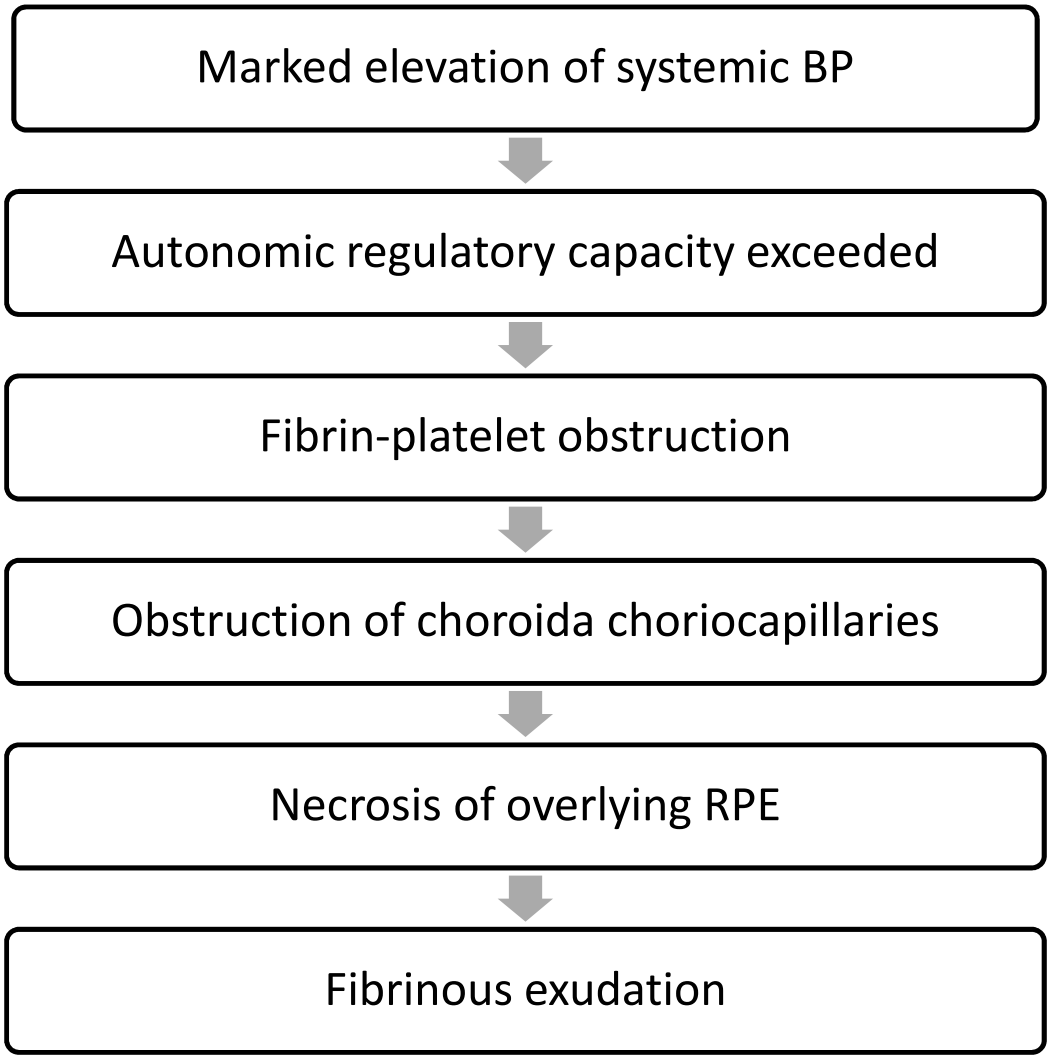


FIG 9. FUNDUS PHOTOGRAPH SHOWING SIEGREST STREAK

PATHOGENESIS:



OPTICAL COHERENCE TOMOGRAPHY

Optical coherence tomography (OCT) was first demonstrated for cross sectional retinal imaging in 1991 by a Massachusetts Institute of Technology team lead by Fujimoto.(48) Since its inception, it has become a clinically useful diagnostic toolin ophthalmology.

EVOLUTION OF OCT:

At its inception, time-domain OCT was the technique employed by commercially available OCT systems like the Stratus OCT. Time-domain OCT (TD-OCT) systems which featured an axial resolution of 8–10 μm in tissue with scan rates of 400 A-scans per second with.(49) The first commercially available spectral-domain (Fourier domain) OCT (SD-OCT) system was introduced in 2006. Spectral Domain OCT works on the principle of detection of the light echoes simultaneously by measuring the interference spectrum of the reflected light, using a high-speed spectrometer and an interferometer. This technique a resolution of 5–7 μm in tissue and scan rates of 20000 – 50000 A- scans per second.

Although OCT has been used extensively for in the diagnosis and prognosticating of many posterior segment diseases based on macular, optic nerve and RNFL images, until recently, the choroid was not able to be clearly imaged with the spectral domain OCT.

The poor visibility of the choroid in Stratus OCT is due to the presence of the hyperpigmented Retinal pigment epithelium which causes high light scattering resulting in the attenuation of the relatively weak choroidal reflection signal. Also, the relatively low signal to noise ratio of time domain OCT does not help in producing high quality images of deeper structures like the choroid. Due to the limited number of A-scans possible in time domain OCT the pixel quality is limited making visualization of the choroid difficult.

Techniques such as image averaging and enhanced depth imaging (EDI) has enabled SD-OCT systems to image the choroid. Image averaging involves increasing the signal-to-noise ratio by procuring multiple B-scans from the same location that are averaged together.(13,50) When multiple images are averaged, the software reduces the 'speckle.' This improves the image quality [Fig. 10]. Along with image averaging, Enhanced Depth Imaging involves setting the choroid adjacent to the zero delay line. This allows enhanced visualization of the choroid up to the sclera [Fig 11]. (13,51–53)

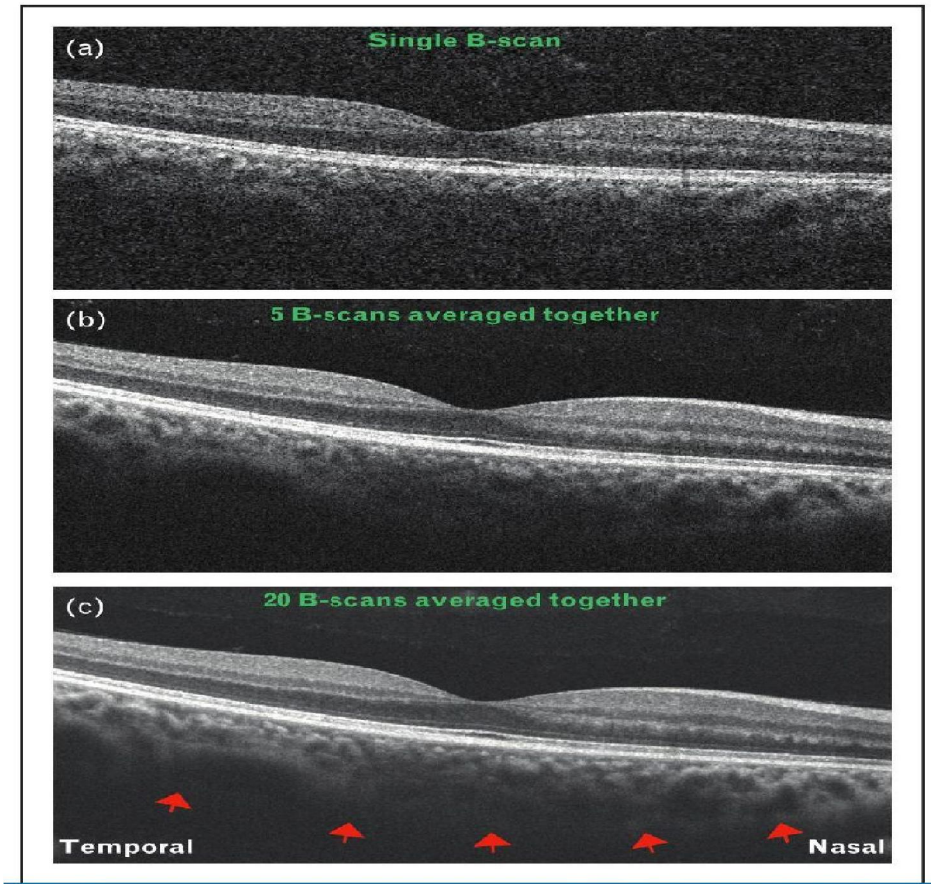


FIG 10: Optical coherence tomography (OCT) images obtained using Cirrus high definition OCT (HD-OCT) system showing the improving imaging quality with increased B-scan and image averaging. a) single B –Scan. b) 5 B-scans averaged c) 20 B-scans averaged showing the chorioscleral interface.

Apart from the already available commercially systems, newer prototype OCT systems have now started to emerge contributing greatly to this ever growing field .Some examples of such prototype OCT systems are ultra high-resolution OCT (UHR-OCT), SD-OCT systems

employing a longer-wavelength light source permitting deeper tissue penetration, and swept-source OCT (SS-OCT) systems.(54)

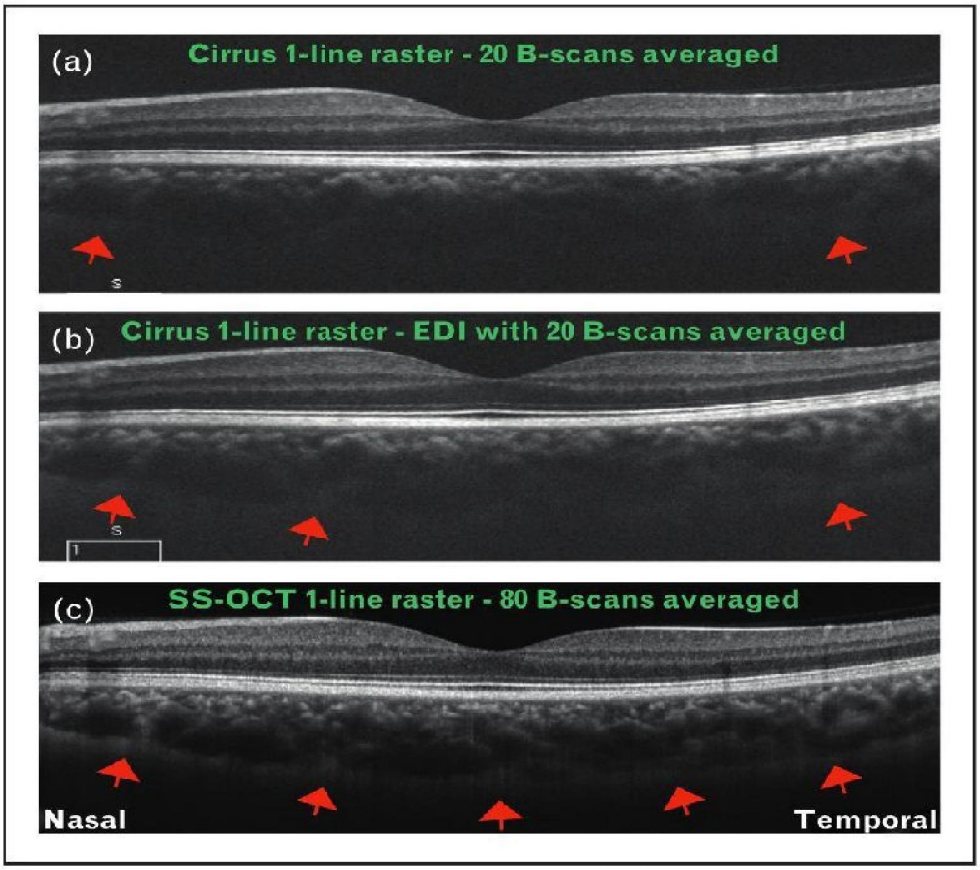


FIG 11: (a) Cirrus OCT WITHOUT EDI ; (b) OCT WITH EDI ; (c) Swept-Source OCT ; Red arrow heads indicate the choriosclera interface.

PRINCIPLES OF OPTICAL COHERENCE TOMOGRAPHY:

Optical coherence tomography is based on the principle of white light interferometry and highly sensitive to even minute changes in the refractive index of the sample. Therefore this feature helps to deliver additional information to other imaging modalities like computed tomography (CT) and magnetic resonance imaging (MRI). This principle is depicted in figure 12.Interferometry is used to compare the reflected wave from different depths of the tissue to the reference wave. The detected signal contains information on the position of the scatters within the sample, on their reflectivity, velocity and polarization properties.By this collection of depth scans from the sample three dimensional construction of cross-sectional images is possible.

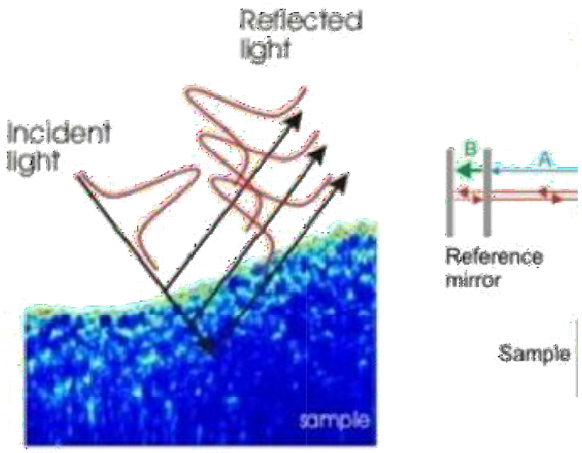


FIG 12: PRINCIPLE OF OCT: GEOMETRICAL INFORMATION IS GAINED BY PARTLY REFLECTED INFRARED LIGHT FROM VARIOUS DEPTHS WITHIN THE SAMPLE.

OCT SYSTEM DESIGNS:

Optical coherence tomography system designs.

A. Time domain OCT system: This system is based on the principle of longitudinal translation of the reference arm pathlength in time. The depth (axial) of the scan is obtained by moving the reference mirror towards and away from the beam splitter. The beam splitter directs the broadband light source into two beams. One beam is directed toward the reference mirror while the other beam is directed towards the sample. The beam splitter then combines the reflected signals from both the reference mirror and the sample and directs them to the detector. The sweep distance of the reference arm mirror gives the axial scan. 2D scan is obtained by making the sample bean move in a linear manner and a 3D scan by moving in a complex surface array.

B. Spectrally encoded Fourier domain OCT system: The reference arm is placed at a fixed distance. Similar to the Time-Domain OCT, the beam splitter directs the beam to the reference mirror and sample and redirects the reflected signals to the detector. This beam is then directed to spectrophotometer which encodes spectrally the interference signal to provide reflectance information.

C. Swept source OCT system: the source laser rapidly sweeps across the spectral frequency band. As the reflected signals from the sample and fixed reference arm are combined at the beam splitter and directed towards the detector, an axial scan is constructed from the depth resolved spectral interference signals.

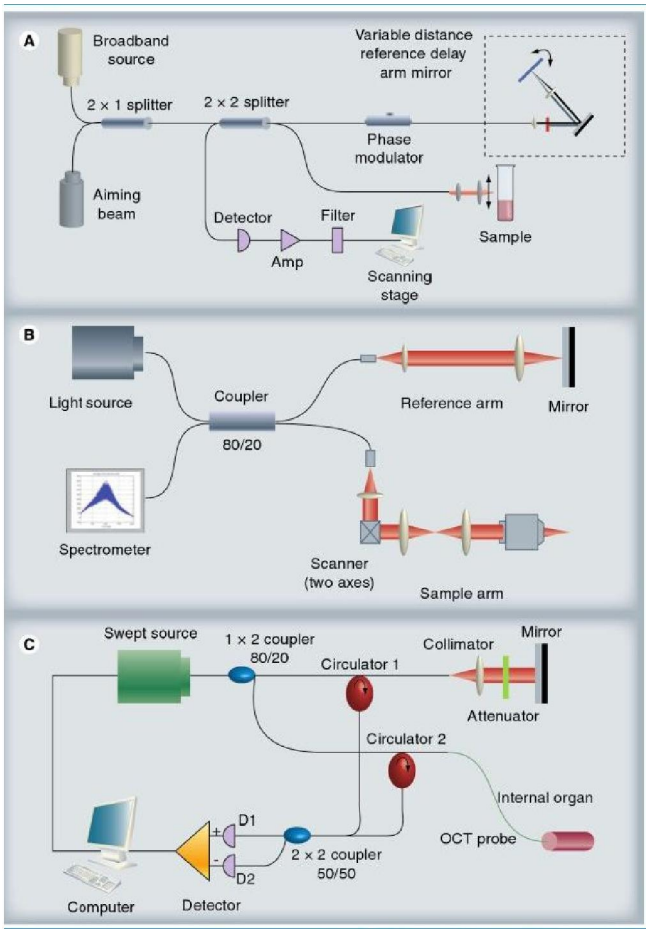


FIG 13: OCT DESIGN SYSTEMS

APPLICATIONS OF OPTICAL COHERENCE TOMOGRAPHY:

To analyze morphological changes and to quantify progression in various disease states. For example, to monitor the progress of diseases such as wet age-related macular degeneration by measuring the retinal thickness. Measuring the macular edema in retinal diseases like diabetic retinopathy and vein occlusions. Differentiating and classifying macular holes. Evaluation of the vitreoretinal surface. To measure the retinal nerve fibre layer thickness to help monitor nerve fibrelayer damage in glaucoma. It also helps in the studying the morphology of the optic nerve head.

CHOROIDAL IMAGING

The choroid until recently has been a little understood anatomical structure due to its presence behind the retinal pigment epithelium. Now with the advent of the newer OCT systems such as Enhanced Depth Imaging, imaging of the choroid is now possible enabling better understanding regarding the etiology and pathogenesis of several retinal diseases.

DEVELOPMENT OF EDI:

Enhanced Depth Imaging was pioneered in 2009 by ophthalmologists Richard Spaide, MD and Ron Margilis, MD.(55) Before this, imaging of the choroid was almost impossible .The factors responsible for this invisibility of the choroid are

- Limited axial length
- Light scatter by choroidal vasculature
- Heavily pigmented retinal pigmented epithelium
- Motion artifacts

However with the advent of the EDI technology by simply positioning the patient slightly closer to the machine imaging of the choroid is possible. This is done by inverting the image which brings the choroid/sclera interface closer to the zero delay line. This zero delay line by convention is present at the top of the imaging scree and it represents

the area of the most precise focus.[3] EDI-OCT provides an additional 500 – 800 micron tissue penetration compared to the conventional OCT.[6]

Some of the commercially available EDI-OCT models are Cirrus HD-OCT, Spectralis and RTVue.

OTHER CHOROIDAL IMAGING MODALITIES:.

The newest OCT system to be commercially available is the Swept-Source OCT system(SS-OCT) .This provides the following advantages over the Spectralis OCT

- ❖ Longer wavelength source (1050nm)
- ❖ Frequency-swept light source

The longer wavelength source enable deeper penetration of tissue.Also the presence of photodiodes compared to the spectrometer in conventional OCT systems helps in more efficient detection of interference patterns. The axial resolution of the SS-OCT is around 5.3µm with an acquisition speed of 100,000 to 400,000 A-scans per second.

CHOROIDAL THICKNESS

CHOROIDAL THICKNESS MEASUREMENTS:

The choroidal thickness is manually measured by drawing a perpendicular line from the outer edge of the retinal pigment epithelium to the chorio-scleral junction.Several studies have shown that the choroidal thickness measured in normal individuals is highly reproducible.(50,56) Shao et al. reported " very high reproducibility with a mean difference of 3.14 ± 13.1 lm between the observers ".(57)SimilarlyChabblani et al reported high reproducibility using the automated segmentation of retinal layers.(58)

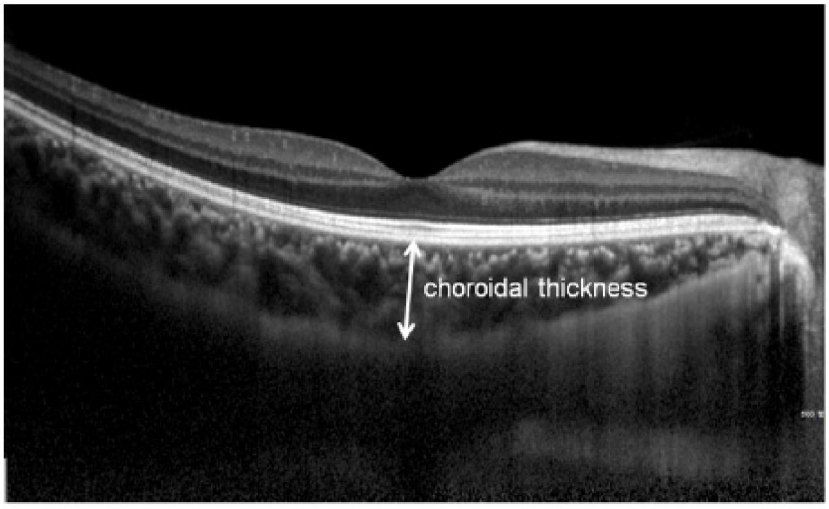


FIG 14: SPECTRALIS HD-OCT DEPICTING THE CHOROIDAL THICKNESS FROM THE HYPERREFLECTIVE RPE TO THE CHORIO-SCLERAL INTERFACE.

CHOROIDAL IMAGING IN NORMAL INDIVIUALS:

Subfoveal choroidal thickness in one study was reported to be in the normal range from 191 ± 75.2 to 354 ± 112 microns. However this is racial variations have been reported .The choroid is thickest in the subfoveal region with nasal and inferior choroid being thinner than the temporal and superior choroid respectively.(59)

FACTORS AFFECTING CHOROIDAL THICKNESS:

A. AGE:

Age is one of the established factors affecting choroidal thickness. Margolis et al and Ikuno et al reported a decrease of 15.6 micron and 14 microns for every decade respectively.(60,61)

B. AXIAL LENGTH:

Choridal thickness in inversely proportional to axial length.

C. REFRACTIVE ERROR:

Wei et al. reported that the " subfoveal thickness decreases by 15 microns for every increase in myopic refractive error of 1 D, or by 32 microns for every increase in axial length of 1mm". Fujiwara et al. reported" choroidal thickness decreases by 12.7 lm for each decade of life and by 8.7 lm for each diopter of increasing myopia".

D. DIURNAL VARIATION:

Choroidal thickness is significantly thicker in the morning.(62)

E ETHINICITY:

Studies	Place of study	Number of subjects (eyes)	Mean age±SD (years)	Ethnicity	Mean AXL±SD (mm)	Mean CT±SD (microns)
Ikuno *et al.*[11]	Japan	43 (43)	39.4±16.0	Japan	24.40±1.24 (21.76-27.35)	354±111
Ding *et al.*[9,10]	China	210 (420)	49.73±17.89	China	Not mentioned	261.93±88.42
Hirata *et al.*[10]	Japan	31 (31)	64.6±17.3	Japan	24.6±2.1 (21.35-28.66)	191.5±74.2
Rahman *et al.*[14]	United Kingdom	50 (100)	38±5	22 Caucasian, 16 Asian, 8 Oriental, and 4 Afro-Caribbean	24.46±1.12 (22.09-26.89)	332±90
Manjunath *et al.*[12]	USA	34 (34)	51.1 (22-78)	Not mentioned	Not mentioned	272±81
Margolis and Spaide[13]	USA	30 (54)	50.4 (19-85)	Not mentioned	Not mentioned	287±76
Present study	India	71 (124)	42.8 (21-80)	Indian	22.84±0.78 (20.91-25.0)	280.1±46.5

SD: Standard deviation, AXL: Axial length, CT: Choroidal thickness

TABLE 2: STUDIES DEPICTING ETHNIC DIFFERENCE IN CHOROIDAL THICKNESS

CHOROIDAL THICKNESS IN VARIOUS DISEASES :

HIGH MYOPIA:

Choroid thickness decreases with increase in axial length. Flores-Moreno et al. had reported a decrease in choroidal thickness by 25.9 ± 2.1 microns for every additional millimeter in myopia.(63)

CENTRAL SEROUS CHORIORETINOPATHY:

Indocyanine green angiography studies have shown increased choroidal permeability in Central serous chorioretinopathy (CSCR). Increased choroidal thickness has been reported in patients with acute central serous chorioretinopathy. Studies have also reported bilateral increase in choroidal thickness patients with unilateral CSCR.(55,64,65)Markuno et al by measuring the choroidal thickness before and after treatment in CSCR reported a decrease in choroidal thickness in patients treated with photodynamic therapy while o difference was reported in patients treated with laser photocoagulation. (66)

AGE-RELATED MACULAR DEGENERATION (AMD):

Age-related macular degeneration is a multifactorial disease where the choroidal blood flow may play a role in the pathogenesis of the disesase. SD-OCT has improved the understanding and management of

AMD. Manjunath et al. reported that eyes with AMD on an average had a thinner choroid than that of normalcontrols. Furthermore, eyes with exudative AMD had thinner choroids than eyes with nonexudative AMD.

VOGT–KOYANAGI–HARADA (VKH) DISEASE:

Like central seous retinopathy, choroidal hyperpermeability is shown to be the main factor in the development of VKH. Studies have shown the increase in choroidal thickness in acute stages of VKH. Choroidal thickness is reported to decrease with treatment and increase with recurrence.

DIABETIC RETINOPATHY:

However several studies have reported conflicting results of choroidal thickness in diabetic retinopathy. . A large population-based study from China reported choroidal thickening in diabetic patients, however, diabetic retinopathy did not appear to associate with increased choroidal thickness.(67) A recent retrospective study from Korea, demonstrated increasing choroidal thickness with increasing severity of retinopathy.(52) These conflicting reports may reflect dynamic nature of natural history of diabetes and its effect on the eye.

REVIEW OF LITERATURE

1. **Hayreh et al** in 1986 based on his studies on rhesus monkeys first reported the morphological and physiological changes in hypertensive choroidopathy. Experimental accelerated hypertension was produced by modified Glodblatt procedures in 60 rhesus monkeys. The changes were studied using serial ophthalmoscopy and fundus fluorescein angiography in all monkeys on a long-term followup.Pathological examination was done in 30 eyes. The most common clinical presentations of hypertensive choroidopathy were RPE abnormalities and serous retinal detachment.Histopathological and angiographic studies revealed impaired choroidal circulation with extensive ischemic and occlusive changes .These studies revealed that hypertensive choroidopathy and retinopathy are two unrelated and independent manifestations of accelerated hypertension. (20)

2. **Kur et al** reported that " The ability of the retinal vasculature to regulate its blood flow is contrasted with the far more restricted ability of the choroidal circulation to regulate its blood flow by virtue of the absence of glial cells, the markedly reduced

pericyteensheathment of the choroidal vasculature, and the lack of intermediate filaments in choroidal pericytes". The authors reviewed the cellualar and physiological responses responsible for the choroidal and retinal blood flow. (68)

3. **Yakugaku et al** by their work on the blood vessels in spontaneously hypertensive rats demonstrated the impairment of endothelium derived relaxation in hypertension.This impairment was a result of decreased production of nitric oxide and endothelium-derived relaxing factor and increased production of endothelium-derived contracting factor. This imbalance in the vasocactive mediators in hypertension may be due to the increased production of superoxide.The structural damage to the endothelium was shown by scanning electron microscopy. The authors concluded that in chronic hypertension there is impairment of endothelium-dependent relaxation which can be prevented by early initiation of anti-hypertensive treatment.(69)

4. **Head GA et al** reported the increase of several vasoactive mediators and also the role of sympathetic system in chronic essential hypertension by ganglionic blockade alone and coupled with low-frequency oscillations of systolic blood pressure.(21)

5. **Lütjen-Drecoll et al** in 2006 reported the mechanosensory properties of the choroidal gaglion cells.He also reported that these cells stain positive for several vasomotor mediators like Nitric oxide synthetase and Vasoactive intestinal peptide. Immunohistochemical staining of choroidal mounts of 21 donor eyes was done. Microscopy revealed the presence of a contractile smooth muscle unit in the choroid.(70)

6. **Chou et al in 2001** demonstrated the presence of choroidal vessel denervation super senstivity thus demonstrating the effect of circulating catecholamines on choroidal blood vessels. The study was conducted in 24 albino rats divided into two groups. 12 rabbits received bilateral superior cervical sympathectomy while twelve rabbits served as controls. Four different concentrations of 0.1 ml phenylephrine, 0.05%, 0.025%, 0.013%, and 0.007% were slowly injected into the vitreous body near the retina. The choroidal blood flow was measured simultaneously by laser Doppler flowmetry Velocity decreased similarly in both group rabbits except for the 0.007% phenylephrine, concentration in which velocity decreased significantly in group containing the sympathized rabbits. This study emphasized the choroidal denervation supersentivity thus

demonstrating the effect of catecholamines on choroidal vasculature.

7. **Sugiyama et al** reported a decrease in peripapillary choroidal circulation in normal–tension glaucoma. They also found that a decrease in blood pressure was related to reduced blood flow in the choroid. 16 patients with normal-tension glaucoma underwent computerized image analysis and fluorescein angiography. These measurements were correlted with visual fields, retinal vessel width, optic disc pallor and blood pressure. (71)

8. **Polak et al** in 2007 reported the response of the choroidal vasculatue to systemic nitric oxide.(72)This was an in-vivo study in 16 patients with glaucoma whose were compared to 16 age-matched controls. All patients underwent subfoveal choroidal flow, ocular fundus pulsation amplitude and optic nerve head blood flow measurement at baseline and after inhibition of nitric oxide synthase by intravenous administration of NG-monomethyl-L-. A decrese in choroidal blood flow was seen with inhibition of nitric oxide syntetase.

9. **Leitgeb et al** first reported the superiority of the Fourier Domain Optical Coherence Tomography systems. They compared it with the standard time-domain OCT systems using a charge coupled device camera. They reported the larger sensitivity of the Fourier-Domain OCT systems even in low light with faster detection rates.

10. **Ron Margolis et al** in 2009 reported his pioneering work on Enhanced Depth Imaging Optical Coherence tomography enabling choroidal imaging. (60): "The images were obtained by positioning the SD OCT device close enough to the eye to obtain an inverted representation of the fundus in healthy volunteers who did not have pupillary dilation. Seven sections, each comprised of 100 averaged scans, were obtained within a 5- x 15-degree rectangle centered on the fovea. The choroidal thickness could be evaluated in every subject's choroidal image. The mean choroidal thickness under the fovea was 318 microm in the right eye and 335 microm in the left eye. The choroidal thickness showed a high correlation in both eyes The correlation between the measurements performed by the independent observers was highly significant. This method provides detailed, measurable images from the choroid, a structure that heretofore has been difficult to image in clinical practice."

11. **Masís et al.** studied 112 patients with systemic hypertension and 15 healthy controls. The mean ages of the two groups were 67 and 51 years, respectively. The choroidal thickness was significantly thinner in hypertensive patients compared to controls.

12. **V. Mustafa et al** studied a total of 228 eyes of 116 patients with essential hypertension and compared them with age-matched controls. 89 patients underwent ambulatory blood pressure monitoring. These patients were divided into two groups depending upon the mean fall of systolic and diastolic pressure at night. Those in whom the mean systolic and diastolic blood pressures fell by at least 10% at night (compared to day) were "dippers," and the others "nondippers." All patients underwent standard trans thoracic echocardiography and the aortic wall distensibility was measured. The authors reported no significant difference in sub-foveal choroidal thickness between the test and the control group and also between the sub-groups. (73)

AIM AND OBJECTIVE

AIM

To measure and compare macular and peripapillay choroidal thickness between patients with essential systemic hypertension and normal control participants.

OBJECTIVE

To measure and compare macular and peripapillay choroidal thickness between patients with essential systemic hypertension and normal control participants and to correlate the choroidal thickness in hypertensive patients with age, grade of hypertension and hypertensive retinopathy.

MATERIALS AND METHODS

This was a case–control, cross-sectional prospective study. This study was conducted with the approval of our Local Ethics Committee and in accordance with the tenets of the Declaration of Helsinki. A total of 25 (46 eyes) patients with systemic hypertension, and 25 (46 eyes) healthy controls over 30 years of age, were included. 4 eyes of 2 patients in each group were excluded due to the poor image quality .Two eyes of 2 patients in the hypertension group were excluded due to branch vein occlusion while two eyes of two patients in the control group were excluded due to prior history of IOL implantation in the past 6 months. Illustrated consent forms were given to all participants and were explained and signed. Comprehensive ophthalmic examinations were performed on all groups. All study participants had best corrected visual acuities of 20/25 or more, a refractive error in the range +3.0 to –3.0 diopters and intraocular pressure (IOP) lower than 21 mmHg. Those with systemic or ocular disease (glaucoma, uveitis, high myopia, age-related macular degeneration, diabetes mellitus, etc.) or a history of ophthalmic surgery that may have affected the choroidal vascular network were excluded. All participants in the patient group included in the study were hypertensive patients receiving medical treatment and newly diagnosed hypertensive patients and with cardiology follow-up. All these patients

were diagnosed according to the criterias of the seventh report of the Joint Committee on the diagnosis, evaluation and management of hypertension (JNC 7). All hypertensive patients were graded into three stages based on the World Health Organization guidelines on systemic hypertension. All participants were subjected to a thorough medical workup and fasting blood sugar, serum cholesterol, blood urea and creatinine were done in both groups of participants to rule out secondary hypertension, diabetes and hypercholesterolemia.

INCLUSION CRITERIA	EXCLUSION CRITERIA
AGE between 30 - 85 years	Age <30 or > 85
Systemic hypertension (under treatment)	Any retinal/ macular diseases (Except Grades 1- 3 hypertensive retinopathy) H/O ocular inflammation/ intraocular surgery (except cataract surgery with intact posterior capsule before 6 months from the date of enrollment in the study)/ intraocular procedure including YAG capsulotomy
Newly diagnosed hypertension BP systolic > 140 Diastolic > 90 Or > 140/90	BCVA < 6/9 IOP < 11 or > 20 REFRACTIVE ERROR < + or - 3D
	Any H/O systemic illness other than essential hypertension. H/O of smoking

INSTRUMENTATION

All choroidal thickness measurements were done using the SPECTRALIS HRA + OCT platform (Heidelberg Engineering Inc., Heidelberg, Germany). All patients also underwent Autofluorescence and fundus photography

SPECIFICATIONS:

Scanning Laser Specifications (30°/ 20°/ 15°)	Transversal field of view Scan angle: 30°x30°, 20°x20°, 15°x15° Wide field composite image to 120° High resolution mode Digital image size: 1536x1536 / 1024x1024 / 768x768. Lateral resolution 5 µm/pixel digital Image Acquisition Frequency 5 Hz / 7 Hz / 9 Hz Maximum Scan Depth 8 mm
OCT Scanner Specifications	A-Scans Scan rate: 40 kHz; Scan depth: 1.8 mm Scan size: 512 pixels;Axial resolution: 7 µm optical B-Scans Scan angle: 30 / 15 / 10 degrees Scan width: up to 9 mm High resolution mode Scan width: 1,536 A-Scans

IMAGING PROTOCOL

The same clinician performed EDI-OCT imaging of all subjects in the morning (between 9 am and 12 pm) with Heidelberg Spectralis equipment (Heidelberg Engineering Inc, Heidelberg, Germany) .

FOR MACULAR CHOROIDAL THICKNESS MEASUREMENT:

Scan Angle: 30°x15°

Sections : 19

ART: 100

Mode: Enhanced-Depth imaging

HIGH-RESOLUTION MODE

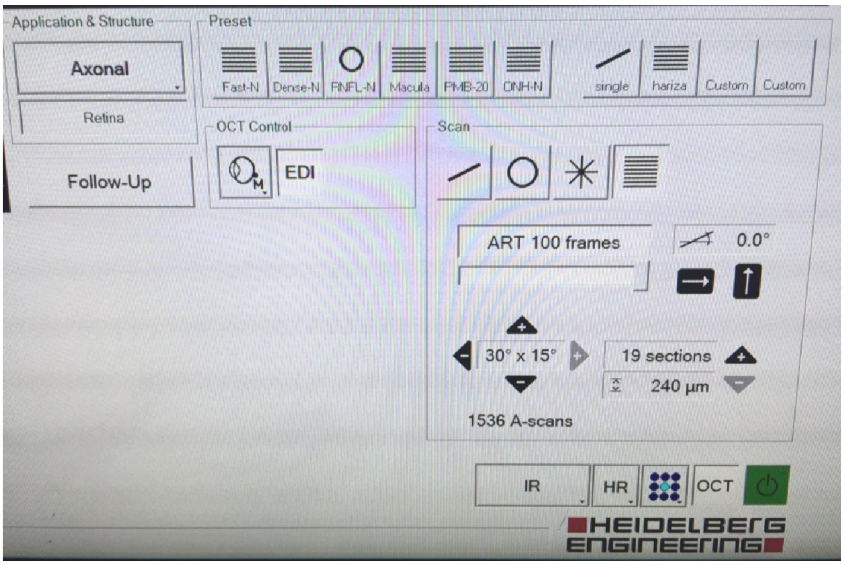


FIG 15: PROTOCOL FOR MACULAR CHOROIDAL THICKNESS

IMAGING PROTOCOL FOR PERIPAPILLARY CHOROIDAL THICKNESS MEASUREMNT:

Scan Area: 3.4 mm peripapillary circle centered on the disc

ART: 100 scans/second

Mode: Enhanced-Depth imaging

HIGH-RESOLUTION MODE

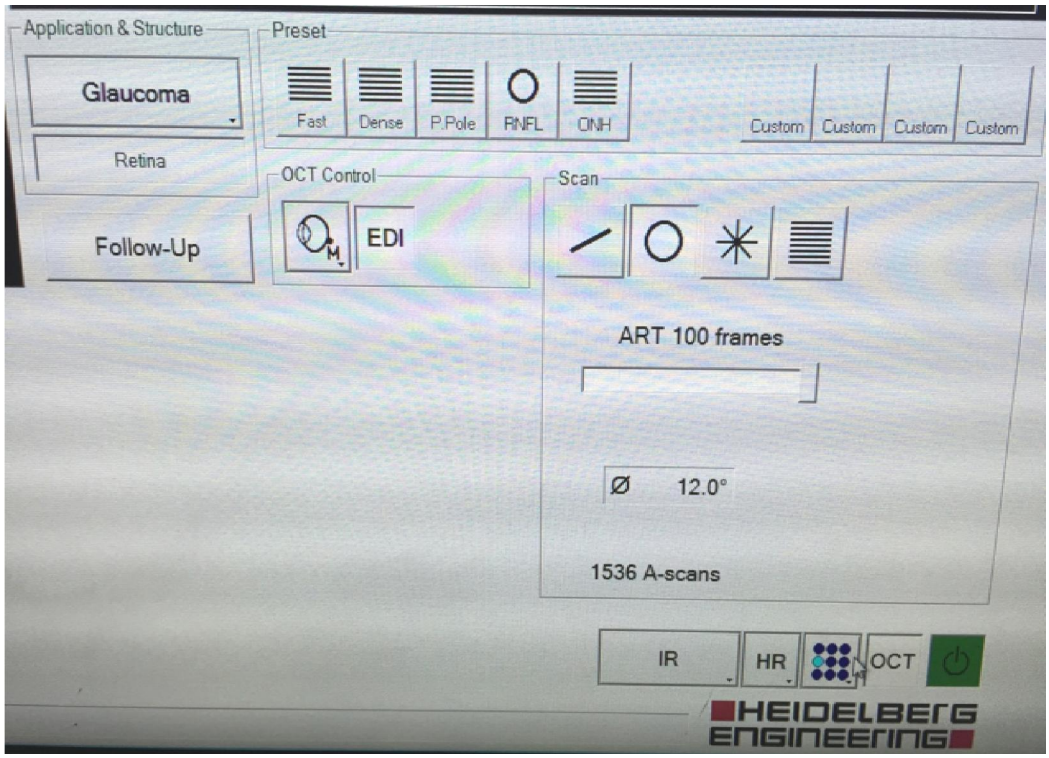


FIG 16: PROTOCOL FOR PERIPAPILLARY CHOROIDAL THICKNESS

CHOROIDAL THICKNESS MEASUREMENT:

The chorioscleral interface is identified. The anterior boundary of the choroid in each image was defined as the hyper-reflective band corresponding to the RPE-Bruch's membrane complex. The posterior boundary was defined as the outer boundary of the chorioscleral interface. All OCT images were classified and measured by two masked trained retinal physicians. After manual delineation of the boundaries, the choroidal thickness was measured using the caliper tool available in the Spectralis platform.

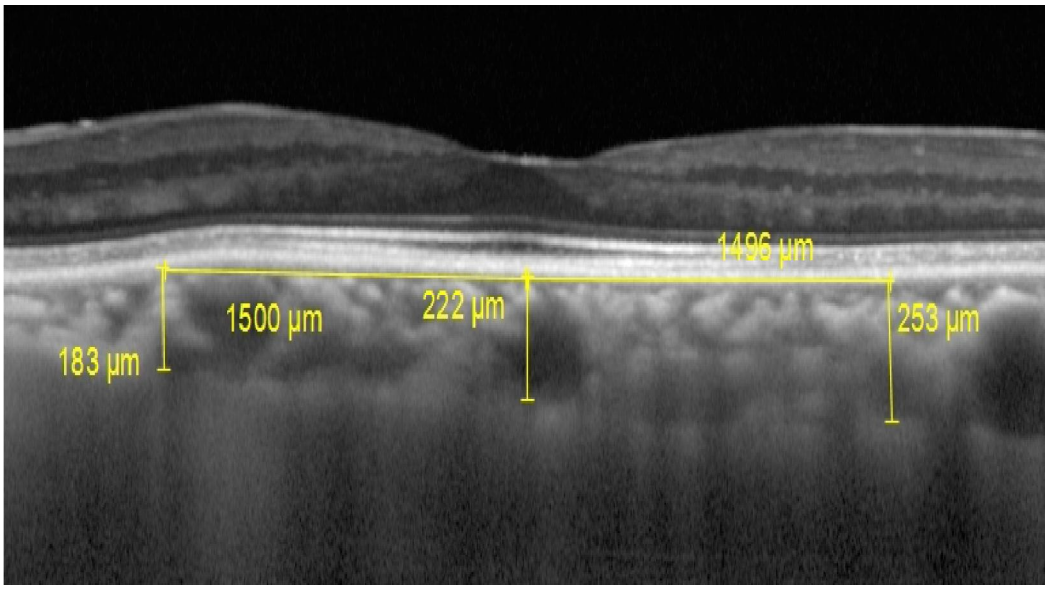


FIG 17: OCT IMAGE DEPICTING THE MANUAL MEASUREMENT OF THE CHOROIDAL THICKNESS AFTER DELINEATING THE ANTERIOR AND POSTERIOR BOUNDARIES

MACULAR CHOROIDAL THICKNESS MEASUREMENT:

The choroidal thickness was measured at the subfoveal region and at 1500 microns nasal, temporal, superior and inferior to the centre of the fovea. The centre of the fovea was identified as the region of maximum depression.

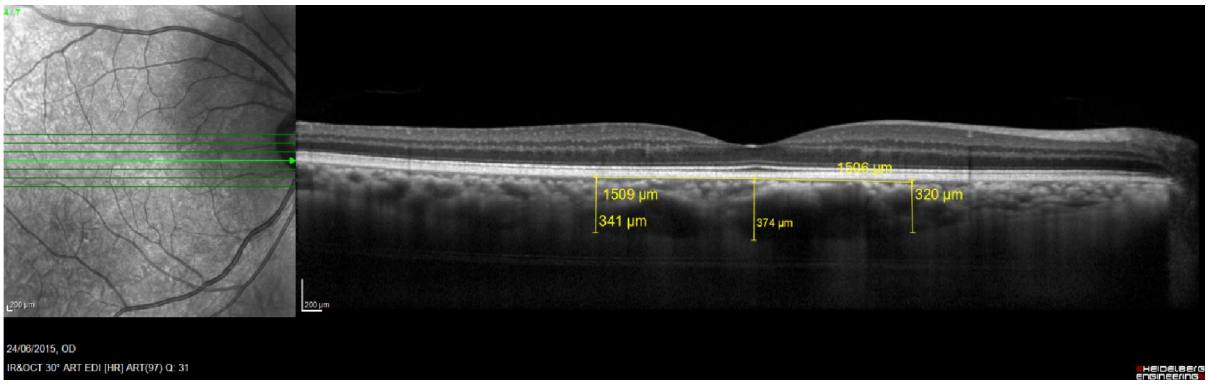


FIG 18: SUB-FOVEAL, NASAL AND TEMPORAL MACULAR CHOROIDAL THICKNESS

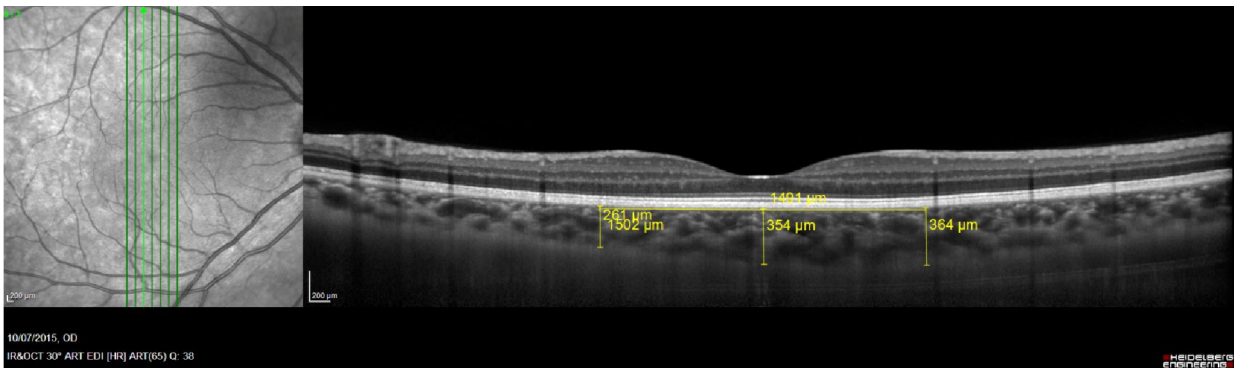


FIG 19: SUPERIOR AND INFERIOR MACULAR CHOROIDAL THICKNESS

PERIPAPILLARY CHOROIDAL THICKNESS MEASUREMENT:

The choroidal thickness was measured at the edge of the 3.4 mm peripapillary circle at the nasal, temporal, superior and inferior quadrants by drawing perpendicular lines from the centre of the disc using the caliper tool.

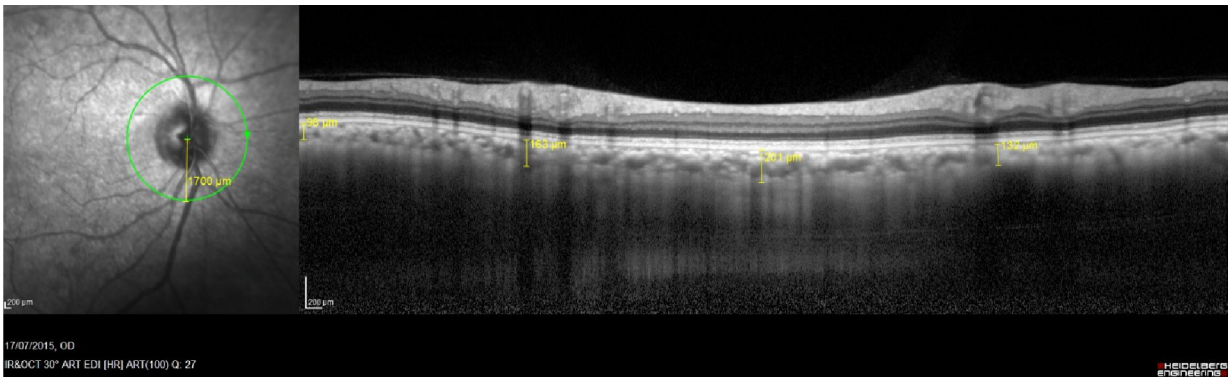
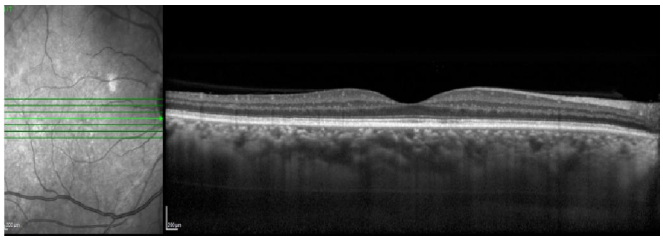
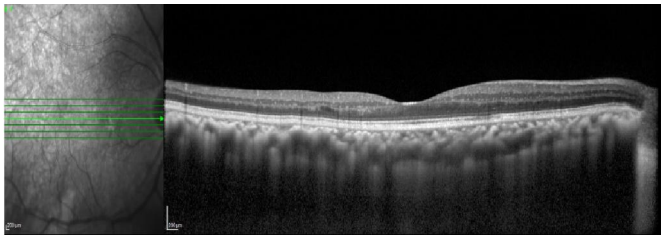
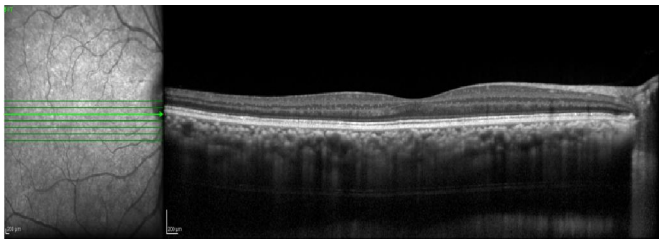
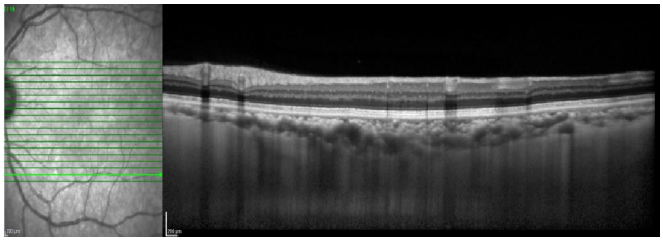


FIG 20: OCT IMAGE SHOWING THE MEASUREMENT OF CHOROIDAL THICKNESS IN ALL FOUR QUADRANTS

CHORIOSCLERAL INTERFACE GRADING:

All OCT images were graded into four categories based on the visibility of the chorioscleral interface along the entire length of the scan. OCT images with signal strength less than 6 dB and CSI grade less than one were excluded from the study.

CHORIOSCLERAL INTERFACE GRADING:

OCT	CSI GRADE
	1- < 25 % of CSI visible
	2- 25-50% of CSI visible
	3- 50-75 % of CSI visible
	4- > 75% of CSI visible

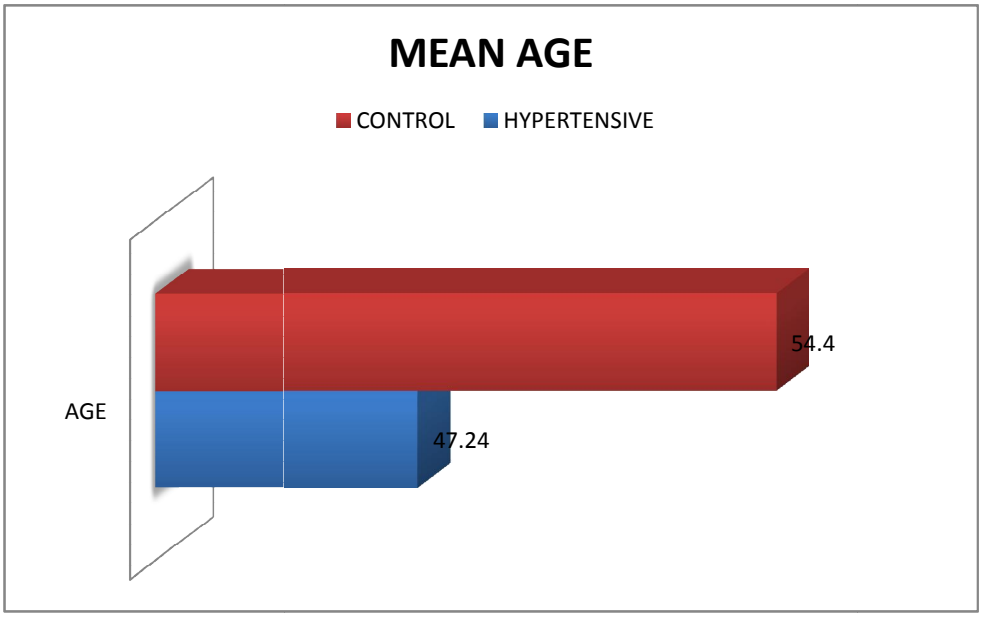
STATISTICAL ANALYSIS

Mean (SD) or Frequency (Percentage) was used to describe summary information. Student's t-test was used to assess the difference of continuous variable. Chi-square test or Fisher's exact test was used to assess the association between categorical variables. P-value is less than 0.05 considered as statistically significant. All statistical analysis was done by STATA 11.1 (Texas, USA).

RESULTS

DEMOGRAPHICS:

Variable	Normal (n=25*patient*)	Hypertension (n=25*patient*)	Total	p-value
Age				
Mean(SD)	47.24(8.28)	54.4(9.71)	50.82(9.63)	0.007†
Min - Max	33 - 67	37 - 76	33 – 76	
Gender				
Male	12(48.0)	15(60.0)	27(54.0)	0.72††
Female	13(52.0)	10(40.0)	23(46.0)	



CHOROIOSCLERAL INTERFACE GRADING:

Macular CSI grade	**Normal** (n=44 *eyes*)	**HTN** (n=44 *eyes*)	**Total** (n=88)
2	7(15.9)	19(43.2)	26(29.5)
3	14(31.8)	15(34.1)	29(33.0)
4	23(52.3)	10(22.7)	33(37.5)

Perpapillary CSI grade	**Normal** (n=42 *eyes*)	**HTN** (n=41 *eyes*)	**Total** (n=83)
2	2(4.8)	2(4.9)	4(4.8)
3	4(9.5)	13(31.7)	17(20.5)
4	36(85.7)	26(63.4)	62(74.7)

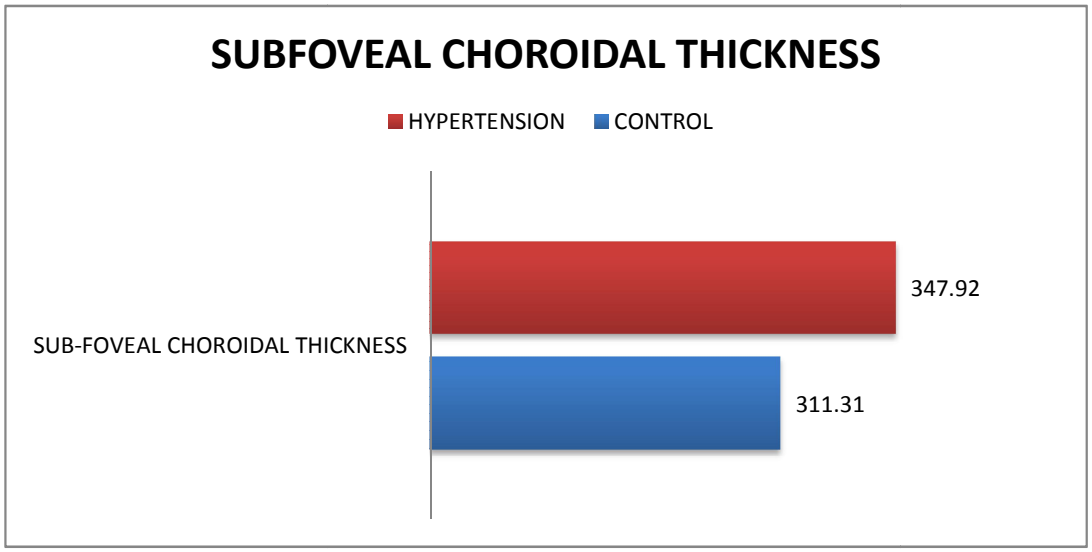
INTEROBSERVER VARIATION:

Inter Observer Variability	HTN		Normal	
	RE	**LE**	**RE**	**LE**
Macular Choroid Thickness	0.485	0.951	0.666	0.262
Superior	0.112	0.217	0.333	0.186
Inferior	0.241	0.754	0.379	0.221
Nasal	0.400	0.368	0.407	0.232
Temporal				
Average	2.02(0.078)	5.92(0.298)	0.93(0.076)	0.98(0.324)
Mean difference(p-value)				
Peripapillary Choroid Thickness	0.857	0.256	0.599	0.187
Superior	0.633	0.019	0.656	0.343
Inferior	0.127	0.346	0.275	0.782
Nasal	0.196	0.906	0.068	0.283
Temporal				
Average	1.14(0.257)	4.16(0.180)	0.18(0.782)	0.52(0.374)
Mean difference(p-value)				

SUBFOVEAL CHOROIDAL THICKNESS:

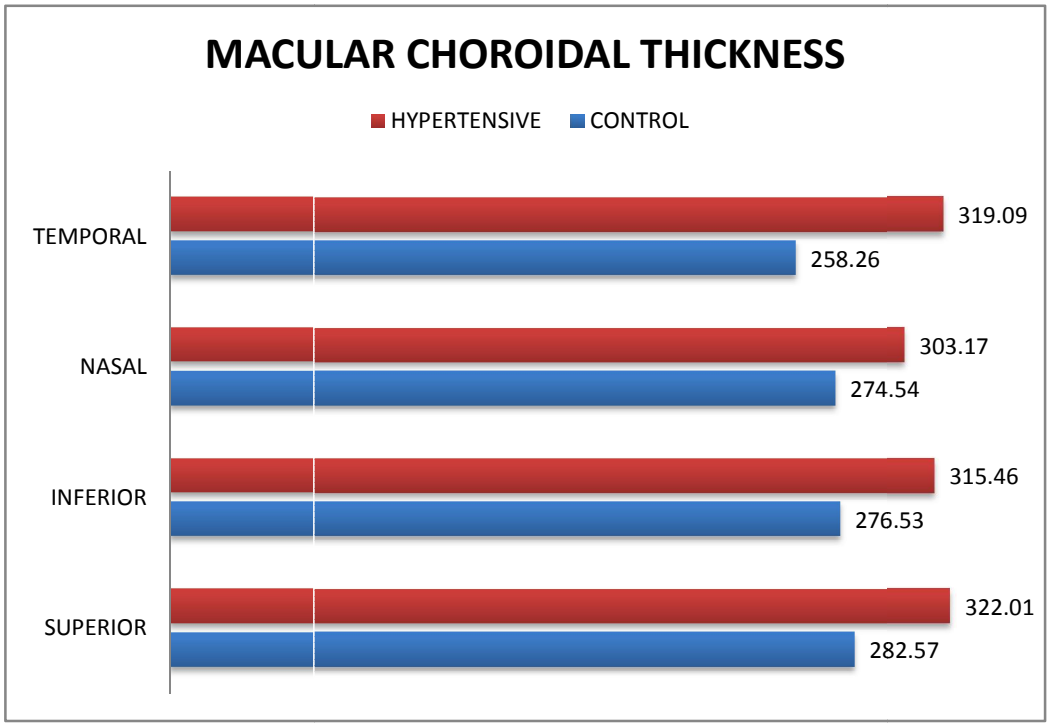
The mean subfoveal thickness was significantly thicker in the hypertensive group.

Subfoveal Choroid Thickness	Normal	Hypertension	Total	p-value
Sub foveal				
Mean(SD)	311.31(68.15)	347.92(71.89)	329.11(71.99)	0.015
Min – Max	207.0 – 476.5	195 – 491.5	195 – 491.5	



MACULAR CHOROIDAL THICKNESS:

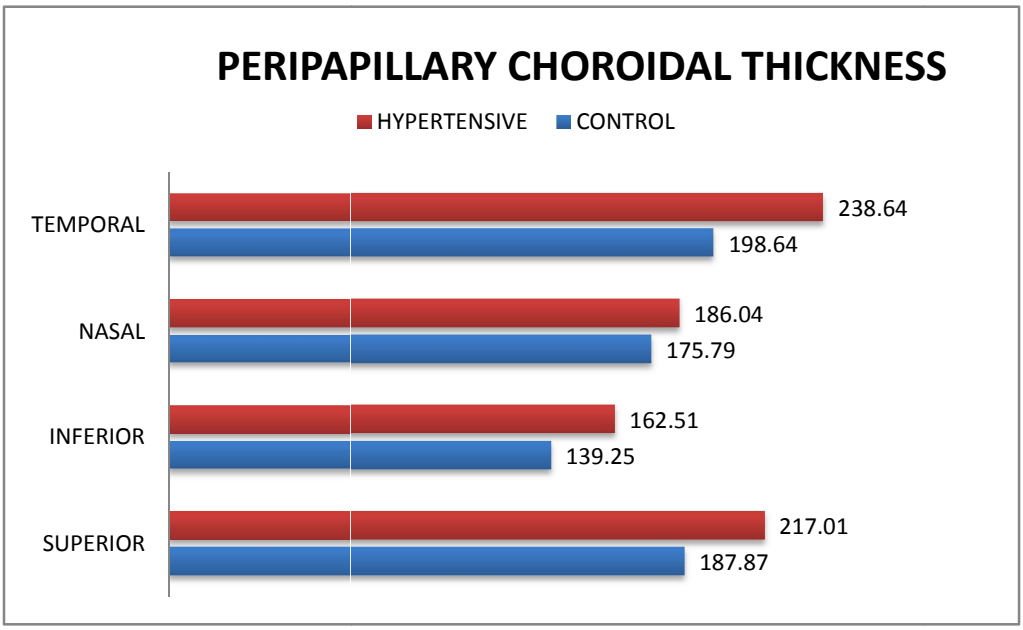
Macular Choroid Thickness	Normal	Hypertension	Total	p-value
Superior Mean(SD) Min - Max	 282.57(64.04) 168.5 – 406.0	 322.01(62.41) 172.0 – 432.0	 303.81(65.80) 168.5 – 432.0	 0.008
Inferior Mean(SD) Min - Max	 276.53(70.30) 153.5 – 418.5	 315.46(66.23) 184.0 – 471.5	 297.49(70.45) 153.5 – 471.5	 0.014
Nasal Mean(SD) Min - Max	 274.54(71.87) 147.0 – 456.5	 303.17(73.92) 156.0 – 440.0	 288.70(73.89) 147.0 – 456.5	 0.067
Temporal Mean(SD) Min - Max	 258.26(70.69) 147.0 – 432	 319.09(80.37) 140.0 – 494.5	 288.33(81.18) 140.0 – 494.5	 0.0003



The subfoveal and the macular choroidal thickness 1500 microns superior, inferior and temporal to the center of the fovea was significantly thicker in the hypertension group compared to normal individuals. The sub-foveal choroidal thickness was the highest followed by the temporal macular choroidal thickness.

PERIPAPILLARY CHOROIDAL THICKNESS:

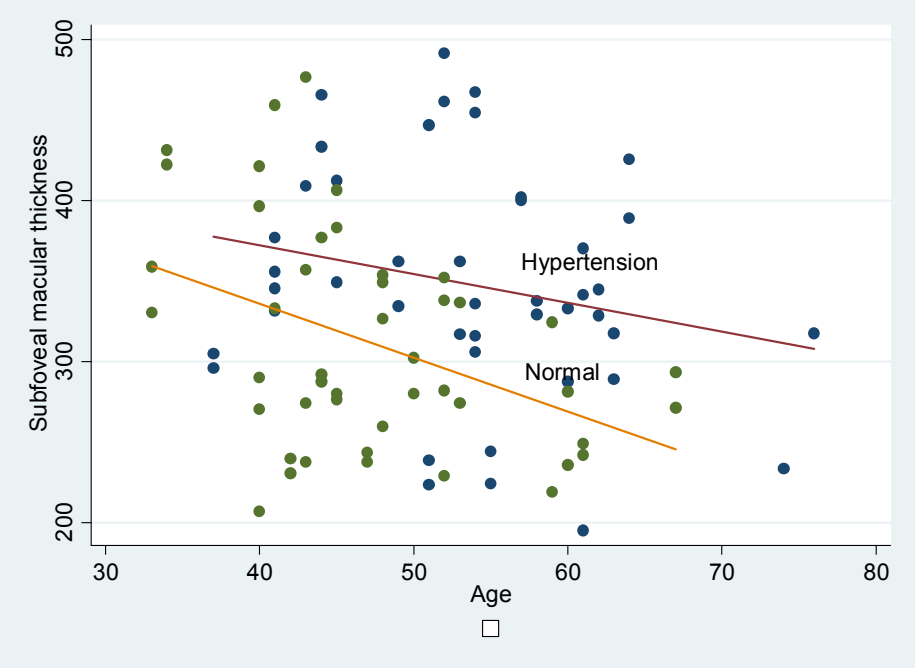
	Normal	Hypertension	Total	p-value
Superior				
Mean(SD)	187.87(46.69)	217.01(65.96)	202.26(58.54)	0.023
Min - Max	87.5 – 268.5	87.5 – 357.5	87.5 – 357.5	
Inferior				
Mean(SD)	139.25(38.99)	162.51(56.81)	150.74(49.71)	0.033
Min - Max	62.0 – 202.5	62.5 – 290.0	62.0 – 290.0	
Nasal				
Mean(SD)	175.79(60.53)	186.04(61.61)	180.85(60.91)	0.447
Min - Max	78.0 – 325.5	50.5 – 293.0	50.5 – 325.5	
Temporal				
Mean(SD)	198.64(61.48)	238.64(72.05)	218.40(69.48)	0.008
Min - Max	87.0 – 317.5	58.5 – 379.5	58.5 – 379.5	



Like the macular choroidal thickness, the peripapillary choroidal thickness was significantly thicker in the hypertensive group compared to the normal participants. The peripapillary choroidal thickness was thinnest in the inferior quadrant and thickest in the temporal quadrant.

SUB-FOVEAL CHOROIDAL THICKNESS AND AGE:

Variable	Regression coefficient (95% CI)	P-value
Normal		
<=40	-	-
41 – 50	-31.88(-84.10, 20.33)	0.225
51 – 60	-60.42(-121.44, 0.61)	0.052
>60	-83.67(-163.48, -3.86)	0.040
Hypertension		
<=40	-	-
41 – 50	79.18(-30.61, 188.97)	0.153
51 – 60	48.43(-57.50, 154.35)	0.361
>60	22.45(-87.34, 132.24)	0.382



DISCUSSION

The choroid is a highly vascular tissue. The choroid has one of the highest blood flow probably the highest in terms of per unit tissue. The choroidal blood flow in terms of per unit tissue is almost ten times of that of the brain.(37) The choroidal circulation provides major supply of nutrients and oxygen to the outer retina especially the photoreceptos. Unlike the retinal circulation, autoregulation in the choroidal circulation is believed to be limited. The choroid is largely under the control of the autonomic nervous system.(70) The role of the choroid in the pathophysiology of several diseases including age-related macular degeneration, Vogt-Koyanagi Harada disease and central serous retinopathy has been proved.(65,74,75) Hypertension is the third most common risk factor for non-communicable diseases in South Asia and about thirty percent of Indians are hypertensive patients.(5) Considering the high vascularity of the choroid, the changes induced by hypertension on the choroid has been studied sparsely. This may be largely because of the inaccessibility of the choroidal tissue for in vivo investigations in the past. Postmortem examinations of the choroid have been proven to have little clinical value .Postmortem fixation and absence of circulation in postmortem samples may not provide accurate data for correlation with in vivo mechanisms. However with the advent of Enhanced depth imaging

Optical Coherence Tomography , the till now inaccessible choroid is made available for extensive research. (13) The choroidal tissue is also made up of several unique anatomical features .The choroid consists of intrinsic choroidal neurons which are largely responsible for the vasomotor control of the choroid.(68) The choroid also consists on non-vascular smooth muscle tissue which are arranged as a single layer parallel to the bruch membrane. Several vasoactive mediators such as endothelin-1 and catecholamines have been proven to increase in the blood of patients with hypertension.(21,76) The large fenestrations of the choriocapillaries have cause easy transduation of these mediators resulting in morphological and physiological changes to the choroidal tissue. The morphological and physiological changes in the choroid to accelerated malignant hypertension has been extensively studied. Hayreh was the first to perform extensive research on this subject. Following his study on sixty rhesus monkeys with malignant hypertension produced by Goldbatt technique, Hayreh was the first to recognize hypertensive choroidopathy as an independent and important clinical entity different from hypertensive retinopathy. (20) The choroid has been proven to be a highly dynamic structure capable of modulating its thickness. The choroidal thickness has been reported to vary with several factors including age, axial length and ethnicity. (77) The age-related choroidal thinning has been also shown in several postmortem studies. OCT studies

have also demonstrated a gradual decline in choroidal thickness with age.(55,61) This decline in choroidal thickness with age is usually greater after the sixth decade.(78) Though the choroid has been reported to increase in thickness in acute hypertension, the pathophysiology of malignant hypertension is totally different from that of chronic systemic hypertension. The choroidal vasculature changes in chronic hypertension was reported by Imran Bhutto in spontaneously hypertensive rats.(79) Scanning electron microscopy of the choroid in the hypertensive rats revealed a decrease in the number of choroidal arteries and venules .Transmission electron microscopy studies revealed hypertrophy of the smooth vessels of the vascular wall. M Gok et al reported no change in the choroidal thickness between hypertensive and normal patients. (80) However, the increase in the choroidal thickness in hypertensive patients can be explained by several theories. The choroidal thickness has been shown to change both as a transient and permanent response to several stimuli. Transient changes in choroidal thickness have been reported in chick embryos to myopic and hyperopic defocus. (81) Though several mechanism for this transient change in choroidal thickness have been proposed, the most accepted is the filling up of the large lacunae present in the choroidal stroma. This happens because of the contraction of the choroidal nonvascular smooth muscle. These smooth muscles are arranged parallel and not perpendicular to the choroidal tissue thus

causing filling up of the lacunae in response to the constriction. The smooth muscle hypertrophy is one of the most consistent reported morphological changes in chronic hypertension.(82) Thus chronic hypertension may cause choroidal vascular smooth muscle contraction resulting in an increase in the choroidal thickness. The permanent increase in choroidal thickness as a response to prolonged refractive defocus has been reported in several studies thus highlighting the role of the choroid in emmetropization. These studies report the ability of the choroid in secreting several growth factors such as transforming growth factor, fibroblast growth factor and several other mediators affecting smooth muscle proliferation and vasomotor tone.(77) Schindler et al reported an augmentation of growth factors in chronic hypertension. (83) The increased expression of growth factors in chronic hypertension and the intrinsic ability of the choroid to secrete growth factors may also cause morphological changes in the choroidal tissue thus explaining the increase in choroidal thickness in hypertensive patients.

LIMITATIONS

- Small sample size
- There was a significant difference in the mean age of the control group and the hypertensive patients, which may have played a confounding role in the choroidal thickness measurements.
- Water and caffeine intake were not regulated in our participants and these are reported to influence choroidal thickness.
- The chorioscleral interface grading was done considering the visibility of the interface along the length of the entire scan. The visibility of this interface at the sub-foveal region was not included in the criteria for the grading.
- The image quality of the OCT images in the hypertensive group was less than the control group, which could have hampered accurate measurement of the choroidal thickness.

CONCLUSION

The advent of newer Optical Coherence Tomography systems like the Enhanced Depth Imaging technology has made the previously inaccessible choroid available for in-vivo imaging in several disease states. The role of essential hypertension as a co morbid factor in several retinal and choroidal diseases is still largely unclear. Several population studies and hospital based studies are required for better understanding of the choroid and the role elevated blood pressure plays in the pathophysiology of glaucoma and several retinal diseases.

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PROFORMA

NAME: DATE:

STUDY NO: MR NO:

AGE:

GENDER:

BLOOD PRESSURE: (2 MEASUREMENTS FOR HYPERTENSIVES)

	SYSTOLIC	DIASTOLIC	TIME
1ST MEASUREMENT			
2ND MEASUREMENT			

BLOOD INVESTIGATIONS:

Fasting blood sugar:

Blood urea:

Serum creatinine:

Total cholesterol:

STUDY EYE: RE/LE/BE

	RE	LE
UCVA		
BCVA		
MANIFEST REFRACTION		
SPHERICAL EQUIVALENT		
ANTERIOR SEGMENT		
IOP		
FUNDUS		

MACULAR CHOROIDAL THICKNSS				
	RE		LE	
SUBFOVEAL				
SUPERIOR				
INFERIOR				
NASAL				
TEMPORAL				

PERIPAPILLARY CHOROIDAL THICKNSS				
	RE		LE	
SUPERIOR				
INFERIOR				
NASAL				
TEMPORAL				

CSI GRADE	RE	LE
MACULAR		
PERIPAPILLARY		

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6th February 2015

To

Dr. Siddharth Narendran
MS Resident
Aravind Eye Hospital
Madurai

Dear Dr.Siddharth Narendran,

Thesis Title: Evaluation of Macular and Peripapillary Choroidal Thickness Using Enhanced Depth Imaging Optical Coherence Tomography in Patients with essential Hypertension

IRB Code: IRB201500171

Thank you for submitting your thesis and seeking the approval from the ethics committee. The documents provided by you for consideration which include the thesis protocol and informed consent forms were reviewed for the research methodology and scientific content. The Ethical committee did not find any correction and has recommended the thesis to go ahead in the present form.

Thanking you

Yours Sincerely,

S. Lalitha

Dr.Lalitha Prajna
Member Secretary
Institutional Ethics Committee

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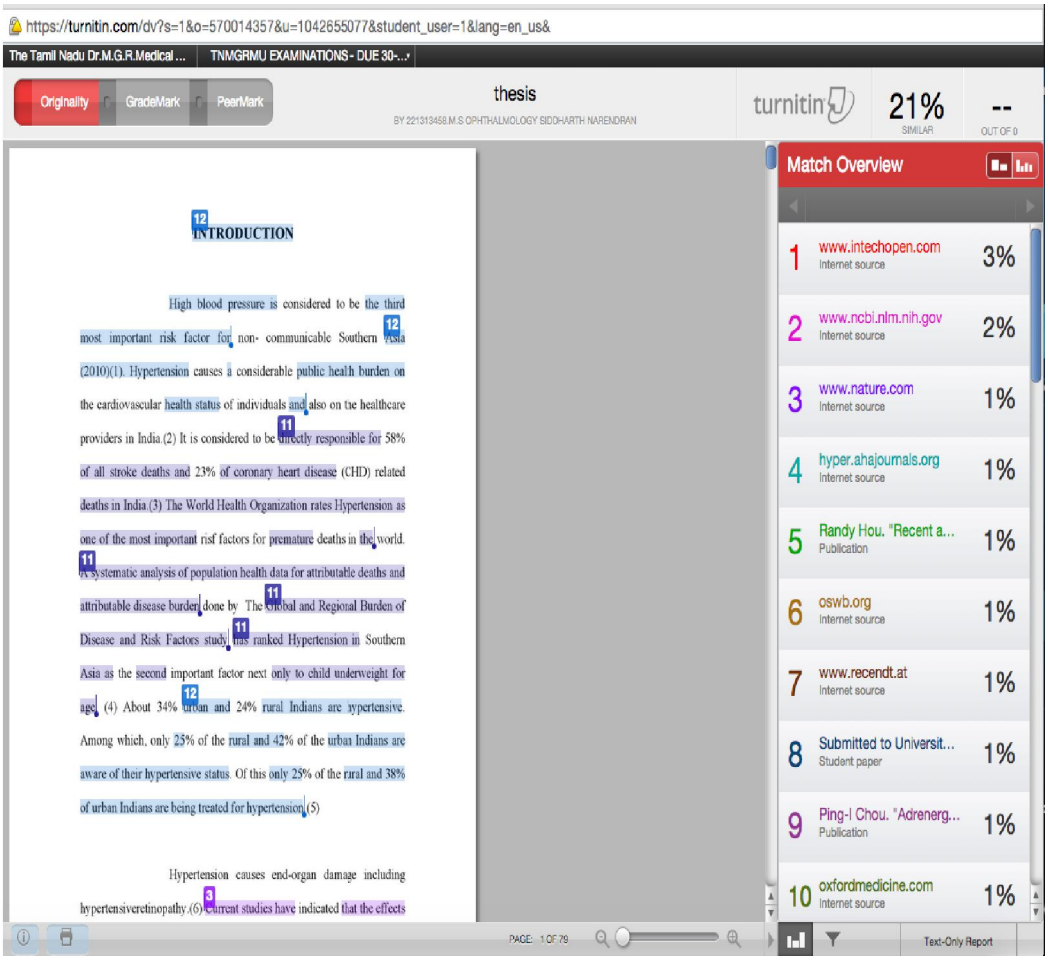
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INTRODUCTION
High blood pressure is considered to be the third most important risk factor for non- communicable Southern Asia (2010)(1). Hypertension causes a considerable public health burden on the cardiovascular health status of individuals and also on the healthcare providers in India.(2) It is considered to be directly responsible for 58% of all stroke deaths and 23% of coronary heart disease (CHD) related deaths in India.(3) The World Health Organization rates Hypertension as one of the most important risf factors for premature deaths in the world. A systematic analysis of population health data for attributatle deaths and attributable disease burden done by The Global and Regional Burden of Disease and Risk Factors study has ranked Hypertension in Southern Asia as the second important factor next only to child underweight for age. (4) About 34% urban and 24% rural Indians are hypertensive. Among which, only 25% of the rural and 42% of the urban Indians are aware of their hypertensive status. Of this only 25% of the rural and 38% of urban Indians are being treated for hypertension.(5)
Hypertension causes end-organ damage including hypertensiveretinopathy.(6) Current studies have indicated that the effects
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INTRODUCTION

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Study No	MR NO	NAME	Age	Gender	STUDY EYE	Spherical equivalent		MACULAR CHOROIDAL THICKNESS (micrometer)																	
								SUBFOVEAL				NASAL				TEMPORAL				INFERIOR				SUPERIOR			
								RE		LE		RE		LE		RE		LE		RE		LE		RE		LE	
						RE	LE	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2
1	1976238	PREMALATHA	50	F	RE	0.35		279	281			253	245			256	260			240	238			221	230		
2	840830	GANESAN	45	M	BE	0	0	413	400	386	380	382	375	340	342	220	230	289	287	300	310	300	310	345	343	289	288
3	1976231	DHANBAK	53	F	BE	1.25	0.75	338	335	275	273	261	270	240	235	284	280	230	224	245	242	236	239	250	244	256	259
4	1683059	PALANISAMY	47	M	BE	-0.35	0	242	245	240	235	230	234	163	165	217	220	235	223	170	166	157	160	230	223	232	222
5	1977982	rengaraj	44	M	RE	0.25		284	291			232	234			186	190			294	290			281	275		
6	1977917	SHABEER ALI	34	M	BE	-1.25	-0.75	430	433	420	425	374	377	395	399	385	376	191	198	416	421	369	372	372	377	343	341
7	1977943	CHANDRASEKAR	44	M	BE	0.25	0.25	374	380	289	295	320	315	295	290	341	347	268	271	307	310	302	305	268	275	273	275
8	1977927	RAJAGOPALAN	61	M	BE	0.3	0.3	253	245	240	244	176	170	191	195	145	150	179	174	240	243	196	200	222	225	258	253
9	1977919	SARASWATHI	52	F	BE	1	1.25	343	333	233	225	281	283	408	400	258	266	219	224	310	304	344	345	245	255	366	369
10	1978719	CHANDRASEKAR S	43	M	BE	0.25	0.25	235	240	273	275	145	149	204	208	217	220	207	210	222	225	222	223	190	198	207	208
11	1436019	LOGAMBAL	41	F	BE	0	0	336	330	460	459	382	274	399	394	382	384	400	395								
12	1980374	S BABY	40	F	BE	0	0	269	272	292	288	235	240	226	230	331	335	248	244								
13	1980340	KANAMMAL	48	F	BE	-2	-0.75	325	328	263	256	311	301	274	277	238	242	199	190								
14	1980342	SHANMUGAM	67	M	BE	0	0	292	295	274	269	285	289	250	245	274	270	173	180								
15	1980359	CHINNAPONNU	45	F	BE	0.75	0	276	277	279	281	176	180	274	270	178	180	200	199								
16	1981179	chandrika	60	F	BE	2	2	281	282	240	232	302	298	279	281	289	294	222	226	227	230	237	230	295	290	222	219
17	1981192	AMUTHA	48	F	BE	1.25	1.25	356	352	348	351		315	318	281	285	260	305	300	331	335	333	331	323	330	330	334
18	1981219	REJINI	40	F	BE	0	0	395	398	426	417	301	296	341	345	264	270	346	341	377	385	346	350	410	402	390	395
19	1981520	SRINIVASAN	50	M	LE		0.75			300	305	235	238			250	255					261	265			285	280
20	1984402	NALINI	52	F	BE	1.5	1.5	354	350	279	285	274	277	227	231	346	350	287	283	313	316	240	245	271	275	274	274
21	1759415	S K SUDHA	33	F	BE	-1	-1	357	361	328	333	314	320	348	345	348	345	294	300	343	339	387	385	395	390	284	287
22	1981594	BALAKRISHNAN	42	M	BE	0	0	236	243	232	229	166	170	206	210	214	218	173	175	181	185	152	155	227	230	272	270
23	1984391	SAIDALI	59	M	BE	0	0.5	330	319	220	218	233	230	218	210	237	230	150	144	280	284	232	228	200	210	225	220
24	1984424	NALLASAMY	40	M	RE	0	0	204	210			192	200			160	155			180	177			172	165		
25	1984413	NIRMALADEVI	43	F	BE	0.5	0	354	360	483	470	235	230	462	451	320	329	434	430	261	257	382	377	364	357	390	380

PERIPAPILLARY CHOROIDAL THICKNESS (micrometer)																CSI GRADING			
NASAL				TEMPORAL				INFERIOR				SUPERIOR							
RE		LE		RE		LE		RE		LE		RE		LE		MACUAR		PERIPAPILLARY	
OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	RE	LE	RE	LE
114	117			227	220			140	147			240	246			2		3	
253	245	225	230	315	320	292	284	196	190	147	150	205	210	204	210	2	3	4	4
155	150	136	137	176	180	188	190	145	140	158	152	230	224	176	170	3	3	4	4
106	110	77	79	111	120	85	90	60	64	77	75	85	90	121	115	4	4	4	4
264	257			294	286			155	160			269	264			3		4	
176	180	209	205	310	319	292	296	168	177	145	142	194	199	261	267	2	2	3	4
119	121	121	122	214	222	212	221	137	135	124	120	178	182	153	157	3	4	4	4
106	105	168	165	119	123	147	150	83	80	90	88	111	115	161	165	2	3	4	4
209	214	255	250	294	290	300	310	199	190	188	180	238	233	244	250	2	2	2	2
																4	4		
93	89	114	110	88	86	122	124	80	78	96	98	132	131	109	115	4	4	4	4
201	204	199	201	222	224	203	206	191	183	190	185	204	210	230	228	4	4	4	4
140	145	106	100	170	176	159	155	98	100	88	92	184	180	114	122	3	3	3	3
103	105	145	150	145	150	180	175	100	101	130	120	230	225	197	202	3	3	4	4
266	260	215	213	232	235	212	220	126	130	109	112	271	266	214	219	4	4	4	4
186	180	191	188	189	188	201	205	200	192	160	162	217	215	204	200	4	4	4	4
194	196	150	155	222	225	227	225	150	155	174	170	186	188	186	189	4	3	4	4
		116	119			186	180			122	120			194	191		4		4
183	189	171	175	217	222	201	205	170	169	155	160	160	158	176	180	3	4	4	4
168	162	250	251	142	145	279	274	139	133	200	205	145	150	266	260	4	4	4	4
176	170	266	260	127	130	173	175	90	92	98	100	145	142	205	210	4	4	4	4
333	318	305	310	204	210	183	190	194	190	152	160	204	210	178	185	3	3	4	4
142	140			121	118			120	129			111	118			4		4	
121	122	168	172	150	145	176	170	134	128	188	177	155	150	181	172	4	4	4	4

mr no	name	study no	eye	Age	Gender	Spherical equivalent		YEARS OF HTN	BP GRADE	HTR GRADE	MACULAR CHOROIDAL THICKNESS (micrometer)																PERIPAPILLARY CHOROIDA							
											SUBFOVEAL				NASAL				TEMPORAL				SUPERIOR				INFERIOR				SUPERIOR				INFERIOR			
						RE	LE				RE		LE		RE		LE		RE		LE		RE		LE		RE		LE		RE		LE		RE		LE	
											OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2
1613928	durairaj	1	LE	74	m	0	0	3	0	0			232	235			195	198			272	273			219	222			222	226			147	150			89	92
1969211	RANGARAJ	2	BE	58	M	0.25	O.50	10	0	0	326	333	336	339	335	343	279	285	320	312	295	300	372	363	357	363	320	311	269	674	289	291	243	247	140	145	170	167
1628093	chandar	3	BE	52	M	-2	-2	10	0	1	490	493	460	463	337	380	330	332	501	488	485	470	372	379	434	430	433	438	377	379	279	283	192	195	243	247	140	145
1969914	rajani	4	BE	41	F	0	0	3	1	0	379	375	360	352	325	315	310	320	351	342	340	332	270	280	292	270	333	320	310	300	338	330	353	362	266	259	265	269
1976221	ANTHONY CRUZ	5	BE	63	M	1	1.25	2	2	1	291	287	315	320	240	232	305	310	256	262	328	320	380	372	370	377	227	225	358	364	217	209	248	250	140	136	119	128
1969948	SAVITHRI	6	BE	54	F	0	0	10	0	2	460	449	475	460	400	421	411	390	430	421	426	418	399	385	420	411	415	405	431	450	276	270	248	241	199	195	190	199
1788636	PERIYASAMY	7	RE	76	M	0		10	1	2	315	320			300	290			343	338			305	310			346	349			140	141			90	95		
1969221	RAJESHWARI	8	BE	49	F	-0.25	-0.5	3	0	0	330	339	364	360	248	253	261	270	263	270	328	334	294	300	305	310	310	316	370	362	160	165	199	190	145	138	156	150
1970083	SAROJINI	9	BE	51	F	1.5	1	6	0	0	240	237	227	220	163	167	180	185	261	269	212	220	384	390	274	280	292	299	250	260	150	141	165	160	75	80	91	99
1969325	REGIYA	10	BE	37	F	-1.5	-1.5	5	2	1	292	300	302	308	232	227	245	250	277	280	225	237	366	377	314	330	372	370	323	338	143	150	204	410	121	130	124	129
1969475	PRADEEP	11	LE	51	M		0	0	1	2			454	440			382	370			440	421			405	390			304	320			290	275			147	140
1938021	mohammed	12	RE	61	M	0		4	1	2	190	200			177	185			142	150			175	180			180	188										
1719752	CHANDRAN	13	BE	60	M	0	0	3	1	0	336	330	292	283	261	255	269	260	310	300	400	407	325	329	392	400	369	360	410	399								
1976815	MURUGAN	14	BE	41	M	-0.3	-0.3	0	2	1	351	340	330	333	310	300	222	213	372	368	152	149	395	390	252	259	207	218	328	333	147	155	222	229	169	160	145	152
1336387	SAKTHIVEL	15	RE	43	M	0	0	5	0	0	410	408			346	350			343	337			236	230			245	256			250	246			210	204		
1977921	?	16	BE	44	F	0.5	-0.5	2	0	0	446	421	501	430	421	400	430	405	407	391	462	447									246	250	293	301	292	288	220	229
1977964	USHA NAIR	17	BE	62	F	2.25	2	9	0	0	320	337	336	354	304	297	379	385	290	288	373	370	288	300	340	328	272	290	318	330	225	220	207	210	142	144	121	124
1728873	NAGARAJ	18	BE	64	M	0	0.5	20	1	0	390	388	430	421	361	379	369	385	330	339	376	385	290	301	340	356	300	301	270	277	238	240	263	270	243	250	171	180
1981582	?	19	BE	61	M	0	0	10	0	0	374	367	338	345	383	388	431	449	243	249	130	150	310	313	280	290	284	295	250	260	225	230	221	229	232	240	205	213
1970147	?	20	RE	54	M	0		2	1	1	302	310			280	287			292	294			285	287			288	290			127	125			109	112		
1987097	sivakumar	21	be	53	m	1.25	1.25	1	0	0	314	320	404	320	280	290	333	339	300	294	308	331	333	311	329	320	254	270	304	318	183	190	190	200	130	134	150	151
1987106	VASANTHAMANI	22	BE	45	F	0.75	0.3	5	0	0	354	345	406	419	256	270	335	350	284	270	364	355	284	279	383	372	348	340	352	341	132	140	204	210	152	155	157	160
1989828	?	23	BE	54	F	1.5	1.75	2	0	0	341	331	320	312	326	320	315	320	300	309	380	287	330	341	300	304	300	305	272	280	175	177	163	167	122	130	132	138
1392683	MANOHAR	24	BE	57	M	2	1.75	4	1	2	390	410	394	410	328	340	360	350	323	335	369	351	350	352	380	371	299	310	405	415	276	266	333	326	230	225	235	230
1989413	BANUMATHI	25	BE	55	F	1	1.5	3	3	1	243	245	222	226	155	157	183	175	251	248	253	262	170	174	209	215	212	218	230	240	88	90	85	90	83	79	65	60

L THICKNESS (micrometer)								CSI GRADING			
NASAL				TEMPORAL							
RE		LE		RE		LE		MACULAR		PERIPAPILLARY	
OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	OBV 1	OBV 2	RE	LE	RE	LE
		171	175			85	90		4		4
233	235	232	240	316	321	238	233	3	3	4	4
217	220	213	222	269	275	238	229	3	3	3	4
279	268	275	265	291	283	292	285	2	2	2	3
160	167	229	219	194	196	243	245	4	3	4	4
297	289	225	230	364	360	284	290	2	2	3	3
137	140			199	202			2		4	
165	159	260	250	183	178	219	210	4	4	4	4
101	108	111	118	163	167	145	141	4	4	4	4
145	150	137	149	178	184	227	236	2	2	3	3
		154	160			294	280		2		2
								4			
								3	3		
215	220	235	240	287	294	266	274	3	3	4	4
212	210			269	272			3		4	
210	219	200	190	196	188	310	315	2	2	3	3
176	180	227	220	248	253	233	238	2	2	3	3
240	249	201	210	279	287	334	340	3	3	4	4
160	165	134	140	281	288	302	306	3	3	4	4
124	130			201	198			4		4	
180	182	190	194	200	210	220	211	2	2	3	3
98	102	170	174	201	211	250	239	2	2	4	4
109	111	100	103	225	220	200	210	3	2	4	4
287	280	281	275	341	333	379	380	2	2	3	4
52	54	49	52	67	69	57	60	4	4	4	4