CORRELATION BETWEEN MULTI MODAL IMAGING AND VISUAL PARAMETERS IN RETINITIS PIGMENTOSA

Dissertation submitted to The Tamil Nadu Dr M. G.R Medical University in partial fulfilment of the requirement for the degree of **M.S Ophthalmology**

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CERTIFICATE

This is to certify that this dissertation entitled "**CORRELATION BETWEEN MULTIMODAL IMAGING AND VISUAL PARAMETERS IN RETINITIS PIGMENTOSA"** submitted to **The Tamilnadu Dr.M.G.R.Medical University, is a bonafide work done by Dr.T.Akila, M.B.B.S,** under our guidance and supervision in the Vitreous retinal services department of Aravind Eye Hospital and Post Graduate Institute of Ophthalmology, Madurai during her residency program from January 2018 to December 2018.

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DECLARATION

I Dr.T.Akila, hereby declare that this dissertation entitled "**CORRELATION BETWEEN MULTIMODAL IMAGING AND VISUAL PARAMETERS IN RETINITIS PIGMENTOSA"** has been prepared by me. I also declare that this is my original work and the dissertation has not formed the basis for the award of any degree, associateship, fellowship, or other similar titles in any other universities board either in India or abroad . This dissertation is submitted to **The Tamil Nadu Dr.M.G.R. University,** Chennai in partial fulfilment of the rules and regulations for the award of **M.S ophthalmology (BRANCH III)** to be held in May 2020.

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CONTENTS

PART 1

PART 1

Introduction

INTRODUCTION

Retinitis pigmentosa is a group of hereditary disorders of the photoreceptors and retinal pigment epithelium which gradually causes night blindness and progressive constriction of the visual field[1],the prevalence of RP is 1 in 4000 individual. [2-4] It is a most common cause of visual loss in the world. The name retinitis pigmentosa was first described by Donder in 1857.

Mode of inheritance of RP are autosomal dominant, autosomal recessive, X-linked recessive and sporadic. Prevalance of RP inheritance includes autosomal dominant is 20-25% , autosomal recessive is 15-20%, X-linked recessive is 10-15%, or sporadic/simplex traits is 30%. Rare inheritance of RP includes X-linked dominant, mitochondrial, and digenic .The age of onset and severity depending on the inheritance pattern. Autosomal dominant RP has the best prognosis , with good central vision even till the sixth decade. X -linked recessive has the least prognosis but severe visual impairments in affected male by the fourth decade .

RP divided into three groups 1. Nonsydromic in which affecting eye alone 2.syndromic in which affecting other systems and 3.Systemic disease in which involving multiple organ.[5]

Syndromic retinitis pigmentosa

Usher syndrome: It is the most common syndromic form , typical RP is associated with neurosensory deafness define as usher syndrome. 14% of all RP cases are Usher syndrome.[6]

Bardet Biedl syndrome:It is less common than Usher syndrome, prevalence is 1 in 150,000 . This syndrome characterized by RP with childhood obesity, mental retardation , post axial polydactyly, hypogenitalism and renal abnormalities .

Senior Loken syndrome ,Alport syndrome,dysmorphic changes in Cohen syndrome,Jeune syndrome,these syndromes are less common in RP patients.

Metabolic diseases

Mucopolysaccharidoses, Abetalipoproteinemia, Zellweger syndrome, Methylmalonic acidemia with homocystinuria Neonatal adrenoleukodystrophy ,Hyperoxaluria type I with retinal atrophy in spots,Infantile Refsum disease,Adult Refsum disease.

Neurological diseases

Joubert syndrome, autosomal dominant cerebellar ataxia type II ,Hallervorden-Spatz syndrome.

Clinical features

Symptoms: Night blindness, progressive constriction of visual fields, gradually reduced visual acuity.[7]

Night blindness is the main symptom in early stage of RP ,night blindness is obvious in mid stage of disease.[8]

Visual field loss is the second most common symptom of RP. Visual field deficit occurred in RP patient usually found first and severe in the superior visual field. This indicades involvement of the inferior retina in RP,it is useful to monitoring the progressive of disease and document of the state of legal blindness.

The central vision will remain good until all the peripheral visual field lost, if RP patient having cystoid macular edema, retinal pigment epithelial defect in macular, macular epiretinal fibrosis, central vision seriously affected in early stage of RP

Signs: The Classic clinical signs of RP fundus include bone spicule retinal pigmentation, retinal arteriolar narrowing, waxy pallor of the optic disc.[6]Bone spicule due to intraretinal migration of the pigments from degenerating retinal pigment epithelium.The optic disc pallor in RP patients due to thick preretinal membrane on the disc.

RP is characterized by progressive degeneration of the retina starting in the mid periphery of the fundus and in late stage it progressing towards the macula.[5]

Macular complications includes epiretinal membrane , cystoid macular edema and macular hole lead to defective of central vision.[9]

The prevalence of ERM including vitreomacular traction syndrome in RP is 1.4%–20.3%,CME is 10%–40% and that of MH is 0.5%–10%.

Cystoid macular oedema reported in 10%-40% of RP patients,[10] Severe CME was correlated with IS/OS disruption and visual impairment,[11] it is a predictor of poor visual outcome in RP patients.

Epiretinal membrane formation, atrophy of the RPE and choriocapillaris beginning at the mid periphery of the fundus, patients with advanced stage of RP this leads to lasy choroidal vessels and disc pallor.

Prevalence of myopia, astigmatism are higher in RP patients . They may also have, vitreous degenerative changes like vitreous cells, clumps and posterior vitreous detachment.

RD incidence in RP is the same as that of the myopic patients.[1] Open-angle glaucoma incident is the same as in the general population.Posterior subcapsular cataract is the common type of cataract in RP patients, especially in autosomal dominant inheritance.

OPHTHALMOLOGIC EVALUATION FOR RP

A complete history of visual symptoms should include information regarding the nature of the earliest symptoms.

Ocular examination

The purpose of the ocular examination in a patient suspected of having one of the forms of retinitis pigmentosa is the identify those finding the support the diagnosis.The ocular examination should include

measurement of best corrected visual activity, refraction, examination of the anterior segment and measurement of intraocular pressure attention should also be given to the lens, vitreous, optic disc, retinal vessel macular and retinal periphery.

INVESTIGATION

ERG (Electroretinogram)

Electroretinography is a gold standard investigation for studying retinal function . It is an efficient techniques for diagnosis and follow-up of RP patients and also it useful for evaluation of RP prognosis.

a,b,c,waves are components of ERG: a wave produced by photoreceptor cells,b wave by muller cells and c wave by retinal pigment epithelium. Prolonged b-wave implicit times is appear in Patients with RP.[12]

EOG:(Electro oculogram)

EOG is the measurement of function of the RPE and photoreceptor.Although EOG is abnormal in RP even in early stages. In typical RP fast and slow induced oscillation of the resting potential are usually decreased in the early stage of disease

DARK ADAPTOMETRY

It measures the absolute threshold of cone and rod sensitivity,dark adaptation was slowed down in early stage of RPand the final threshold was elevated with a biphasic dark adaptation curve in progress stage of disease.The rod-mediated dark adaption was lost in advanced stage of disease and the curve showed monophasic.[13-17]

PERIMETRY

Visual field assessment is important in management of RP it used in quantifying the changes of visual field defect.Kinetic perimetry has been used to illustrate patterns and rates of visual field change in RP patients.[18-24] Static perimetry is used to quantify the viual sensitivity changes at specific locations within the central visual field.[19-21]

In early case of RP defect of visual field on kinetic perimetry are relative scotoma in the mid periphery between 30 °and 50 °from fixation. These enlarge coalesce to form ring of visual field loss. These ring scotoma enlarge towards the far periphery,normal island of visual field remain on temporal. This remnants visual field island lost before the central visual field contract.

Automated static perimetry performed with humphrey field analyzer.[25] RP patient visual field constrict to the central 10 °, the HFA 10-2 programme is most useful asses the RP progression .The HFA has been used to assess not only the extent of the central visual field but also to quantify the visual sensitivity of different areas of the central visual field.Several studies have reported a significant correlation between the presence of the IS/OS line in the OCT images and the visual field sensitivities.

Terminologies

Scotoma is a localised defect in the visual field.

Isopter is a line connecting points at the same sensitivity.

Luminance.

It is the intensity / brightness of light stimulus measured in apo stib case. This is an inverse related to sensitivity logarithmic rather than linear scale is used for stimuli intensity and sensitivity each log unit intensity changes by factor 10.

Decibel

Decibel describes retinal sensitivity less light required to be perceived by the retina of some point. More light is needed for some point of retina 1db is described as one tenth of log unit.

Variables:

HFA use 31.5 apostilb stimulus intensity of HFA can be varied over range of 5.1 log unit 51 decibels between 0.08 and 10,000 apostilbs.

Stimulus Size:

HFA is capable of testing with five standard goldmann stimulus size, but 4mm goldman size III stimulus is used exclusively,stimulus duration is 200milliseconds.

Threshold strategies:

Threshold is the minimal intensity of light at which a stimulus is perceived by visual system within visual field.

Supra threshold is any stimulus brighter than threshold.

Infra Threshold is any stimulus weaker than threshold.

Threshold strategies: supra threshold enables to detect of gross field defect.

Threshold Testing:

The objecting of threshold perimetry is to measure the differential light sensitivity of each tested location.

Full Threshold Testing:

In this test performing bracketing or stair case process every point tested.4 -2 on the HFA,4 – 2 – 1 on the octopus perimeter.

FAST PAC is a rapid thresholding strategy in the HFA .Swedish interactive thresholding strategy use continuous threshold value and measurement error through test.

Testing pattern include central field test ,macular test, temporal crescent, speciality test and custom test . central field test subdivided into 30-2,24-2,10-2.

Evaluation of HFA prinout

The HFA printout is obtained using a statpac software .

Reliability Indices

It reflects the extent to which the patients results are reliable.

1)Fixation loss: indicate steadiness of gaze during test.

2) False positive

3)False negative

Cut off value of relativity value

Three or more of the following reliable indices are consider as unreliable,Fixations loss > 20%,False positive > 33%,

False negative > 33%, Short term fluctuation > 400db

Gray scale: It provide the field defect of a glance.Darker area indicate lower differential light sensitivity and lighter area indicate higher sensitivity.

Total deviation: It provide the deviation of patient's threshold value from that of age corrected normal data.

Positive values indicate higher than normal sensitivity and negative value lower than normal.

Pattern deviation

It is derived from total deviation statpac software has corrected the result for the change caused by Cataract ,small pupil.

Global Indices is summarizes the state of visual field, **Mean deviation is** the difference between mean sensitivity and that expected.

Pattern standard deviation measure the differences between the given point and adjacent point within visual field.

Glaucoma hemi field test

Difference between corresponds superior and inferior zone as compared with the different present in the population of normal control

Actual threshold Value:

It may be inspected for any scotoma when clinical features are suspeciant and all the 7 other part of printouts are normal

MICROPERIMETRY

Microperimetry also known as fundus controlled perimetry in which images the retina during visual field testing.early method of microperimetry in which perimetry was performed with simultaneous fundus viewing,it provides precise correlation between retinal pathology and visual deficit.

Later microperimetry technique improved by the enhanced imaging capability of the scanning laser ophthalmoscope and landmark-driven perimetry techniques. It useful to evaluate visual function in patients with eccentric or unsteady fixation, and this technique is useful in the study of patients with macular disease.

Commercially available microperimetry are Nidek MP-1 and OPKO Spectral OCT/SLO and Centervue Macular Integrity Assessment technology ,these instruments feature includes registration of fundus

imaging with the visual field map and it correlates retinal morphology and function. [26-27]

MAIA is the 3rd generation of microperimetry it consist 3 techniques in the retinal function analysis.The technique includes retinal Imaging, analysis of retinal sensitivity and analysis of fixation capabilities. The retinal image is created by a Scanning Laser Ophthalmoscope in MAIA.Microperimetry, measures retinal sensitivity as the minimum light intensity that patients can perceive when spots of light stimulate specific areas of the retina.In examination MAIA covers a 10° diameter area with 37 measurement points.Goldman III the stimulus size. 4asb background luminance and, with a 36 decibels (dB) dynamic range are using in MAIA.The decibels scale is color-coded according to the MAIA normative studies green represent normal , yellow suspect, red abnormal and black represents scotoma .Fixation stability is measured by calculating the percentage of fixation points located within a distance of 1° and 2° . If more than 75% of the fixation points are located within 1°, this fixation is stable. If less than 75% of the fixation points are located within 1° but more than 75% of the fixation points are located within 2°the fixation is represented as relatively unstable. If less than 75% are located within 2° the fixation is represented as unstable.The Macular integrity index is a numerical value that describes the likelihood that a patient's responses are normal, suspect or abnormal when compared to age-adjusted normative data.

FUNDUS IMAGING

Two dimensional image of three dimensional retinal tissue called as fundus imaging, this captured by reflected light. Multiple imaging modalities useful to evaluate of pigmentary changes in RP.[28] The evaluation of RPE cells in RP is useful to the assessment of future therapeutic outcomes.RP patients exhibited classical features includes bone spicule pigment migration in varying degrees of confluence,attenuated arterioles, waxy disc pallor , these were evident on fundoscopy and color fundus photography.[29]

All fundus camera are based upon the principle of cullstrand's ophthalmoscopic ,that is the illumination and observation pathway pass through different portions of patient pupil to avoid reflection from cornea and lens.

Components of fundus camera includes illumination systems , observation and photographic system

a. **Illumination system:**

A low intensity incandescent lamp for viewing the fundus and focusing the instrument and high powered electronic flash tube for taking photograph.

The light passes through the diaphragm which controls the size of illuminants patch upon the patient's retina.

b. **Observation and photographic system:**

Between the holed mirror and the ophthalmoscopic lens the ophthalmoscopic lens produces fundus image.When the photograph is taken ,the flip mirror that direct the image into eyepiece for observation, thus permitting the image to be projected on the film for photography.Colour fundus photography include Stereo imaging and Digital fundus photography.[28]

I) **Stereo imaging:**

It creates visual sense of depth by shifting the fundus camera between sequential photograph this produce pseudo three dimensional image.

II) **Digital fundus photography**

Traditionally used fundus camera provide 30°to 45° field of view.Wide field photography provide beyond 50 degree field of view.The ultra wide field photography allowing 100° to 200°view of fundus ,These include retcam, panorex 1000^{TM} pomerantzeff camera, OPTOS camera.

OPTOS

The most widely used CSLO based ultra wide field system is OPTOS.[28]The optos system utilize an ellipsoid mirror to produce image with 200° field of view and provide high resolution imaging with multiple software and also it utilize the low powered laser wavelength that scan simultaneously.

OPTOS useful to detect the periphery pathology. In RP patients wide field FAF image is useful to evaluate the degree of retinal degeneration ,the duration of the disease. The patchy hypofluorescent was associated with age and duration of disease.[29]

III) **Confocal scanning laser ophthalmoscopy.**

This viewer imaging technique use the confocal scanning laser ophthalmoscopy principle and use the laser light to illuminate the retina.Confocality of this system is produced by pinhole placed in front of the detector,the degree of confocality is depends on the size of the pinhole.

The advantage of this CSLO are improved image quality,three dimensional imaging capability, suppression of scattered light, video capability,and this technique using in undilating eye.[28]

Fundus Autofluorescence:

Lipofuscin normally found in RPE cells as result of phagocytosis of shed photoreceptor outer segment.Imaging of this autofluorescence lipofuscin aid the diagnosis of retinal pathology,RPE dysfunction.[28] Fundus autoflouorescene images appear as hypo autofluorescence in atrophic in cells .In RP patient FAF image is useful to detect residual RPE as hyperautofluorescence.[31]

Modified fundus cameras use a single flash with excitation spectrum of 535–585 nm to produce a single image CSLO -based systems use with

excitation spectrum of 488 nm resulting in recording of multiple images with averaging to obtain a final image of high resolution.

In RP patients high density FAF ring is observed on macular .Constriction of the ring refelect the progressive visual field loss,The hyper autofluorescence ring represents an abnormal perifoveal accumulation of lipofuscin in the RPE.The constriction in diameter of the FAF ring is a sign of disease progression in patients with RP.[8]

New infrared autofluorescence

NIA imaging can be done using confocal scanning laser ophthalmoscope like spectralis HRA engineering.The image resolution is 768 X 768 pixels focusing is achieved at 815nm mode, AF produced at 787nm mode.Conventional AF imaging shows high intensity in the perifoveal area with decrease towards the fovea but in NIA has high intensity in the foveal area and decrease towards periphery. In RP FAF shows only preservation of RPE cell but NIA may correlate better with preserved cone function.

SPECTRALIS

Heidelberg spectralis is improved technique of fundus imaging by spectral domain OCT with Confocal scanning laser ophthalmoscopy**.**It provide more anatomical detail and automatic rescan at the same site.

OCT

OCT is a diagnostic tool that can produce two dimensional cross sectional images of biological tissue using light wave and axial resolution within less than 10nm. It assesses the retinal disease and correlate retinal structure and function.

Principle

OCT based on Michelson interferometer and low coherence light in near infrared (820nm) A beam of light pass through a mirror that split into probe beam and reference beam.These two beam are then thrown on two equidistant mirror reflected light from these mirror then picked up by a detector.The echo time delay of light reflected from various layers of retina is compared with echo time delay of the light reflected from reference mirror.Interferometer integrate several data point over 2mm of depth to construct a tomogram of retinal structure.The low coherence light determine the axial resolution.Axial resolution of OCT1, OCT2 - 10μ , Axial resolution of OCT3 – 7-8μ .

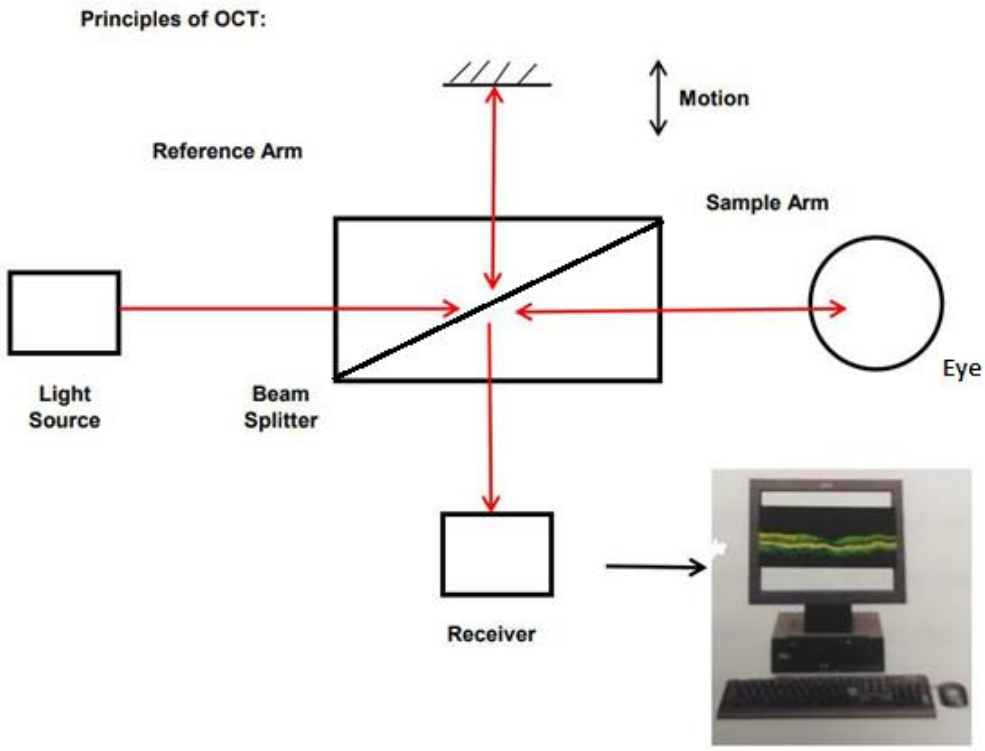


Figure 1: Image showing principal of OCT

Types of OCT

1.Time domain OCT

2. Fourier domain OCT

i) Spectrometer based

ii) swept source

OCT interpretation:

The retinal pathology detection based on the normal anatomy of line scan of imaged retina and analyzing the thickness of total retina.

MAPPING RETINAL THICKNESS.

It can be applied to macular thickness scan and fast macular scan.One map consist of color coded and other map has numerical value.Each map divided into 3 circle with diameter 1mm, 3mm and 6mm.The outer two circle are divided by radial line into four sectors.

Scanning

1.**Macular cube scan**

It is composed of six linear scan in a spoke pattern equally spaced 30° apart.

ii) **Line scan**

The length of the scan and angle can be altered to acquire multiple scan of different parameter.

iii) **Radial line**

It consist of 6 – 24 equally spaced line scans that pass through a central common axis.

The radial line are useful for acquiring macular scan and retinal thickness analysis.

iv) **Raster line**

It consist of series of line that are parallel equally spaced and are 6-24 in number.

C scan provides an overview of the morphology of the retinal surface.

Interpretation of normal retinal layer:

The axonal layer nerve fiber layer, plexiform layer are capable of potent light scatter and hence are hyperreflective.Nuclear layer has low light scattering potential it shows as hyporeflective.The fovea is recognized on cross section image by its depression due to thinning of retina with absence of inner layer at the macula.

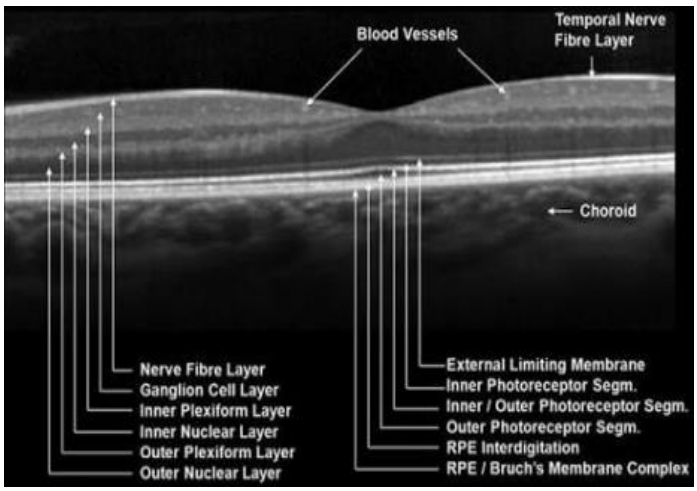


Figure2: cross sectional image of retinal layers image on OCT in healthy person

Interpretation of macular pathology:

The OCT reflects the optical properties of the imaged tissue in terms of signal intensity.The reflectivity of retinal layer is determined by the arrangement of their structure, their biological densities, degree of pigmentation.

There can be hyperreflective and hyporeflective depending upon the amount of light being reflected compared to surrounding tissues.The area of shadow and reverse shadow depends on the amount of light being absorbed by surrounding tissue .

Pathological features

Epiretinal membrane and hard exudate appear as hyperreflective area, higher fluid content area are hyporeflective like intra retinal cyst and intra retinal and sub retinal fluid accumulation.

Vitreous debris, layer retinal vessels, highly pigmented area appear as shadowing.RPE atrophy cause reverse shadowing.

OCT. Angiography:

OCT angiography detect the retinal circulation using the intrinsic motion of the blood cells in the vessels . It is based on comparison of repeated OCT scan of the eye acquired at the same position in the retina.

EDI – (Enhanced depth image)

Fourier transform decode inferometric signals into two conjugate images one of these images is shown with the retina facing toward the top

of screen.To visualize choroid, sclera, peak sensitivity placed posteriorly. The upside down conjugate image of these structures is visualized.

Changes in choroidal thickness by the help of EDI have been reported in various retinal diseases.In Rp patients ,measurement of choroidal thickness is required to understand the pathogenesis and it could be useful for future thrapies .[32-33]

In RP ultra high resolution OCT and spectral domain OCT has been used to study retinal structure .It demonstrates the decreased ONL thickness and loss of external limiting membrane and IS/OS junction.SD OCT detect macular edema, epiretinal membrane in RP.[34]OCT useful in monitoring macular function of RP ,Sandberg et al. reported that abnormal thickening or thinning of the retina and the absence of IS/OS line on OCT correlated with low VA in RP.

MANAGEMENT

Currently, there is no treatment for RP. However, there are number of therapeutic modalities aimed at slowing down the degenerating process, treating the complications and providing visual rehabilitation .[6]

Slowing down the degenerating process include Light protection and vitamin A supplementation at doses of 15,000 units per day,

Cataract: Phacoemulsification with implantation of intraocular lens is required in RP patients.

Macular edema:[35-45]In RP patients many treatment methods for CME have been tried, including intravitreal steroid ,systemic steroids, laser grid photocoagulation, anti VEGF,vitrectomy . The most effective drug for CME of RP patients is carbonic anhydrase inhibitors. Both topical and oral Carbonic anhydrase inhibitors is the mainstay of treatment for CME in RP.

Low vision Aids:

Best refraction and simple magnification,Control of glare by using dark glass,use of night vision scopes and high intensity lantern for night vision,use of field enhancement procedure.

Counseling:

The aim of genetic counseling is to educate the patient about the hereditary nature of the disease.Psychological and vocational counseling to the patient for functional and emotional well being.

Recent treatment modalities:

Retinal transplantation,Photoreceptor transplantation, Neuroprosthetic device,these controlled electrical stimulation of retina release growth factor which may delay degeneration of retina from RP.Neurotrophic factor have been tried based on their anti properties,Retinal prosthesis and intra vitreal or subretinal gene .

Review of Literature

REVIEW OF LITERATURE

Luiz H.Lima et al (2009), analyzed that retina structure underlying the hyper auto fluorescent ring visible on fundus autofluorescence in retinitis pigmentosa patients they concluded that disruption of the inner outer segment junction and decrease in outer retinal thickness were found across the central hyper auto fluorescent ring in retinitis pigmentosa.

Dilsher s Shoot et al (2012), they evaluated the choroidal thickness in retinitis pigmentosa using enhanced depth imaging in optical coherence, they concluded that sub macular choroidal thickness reduced in RP patients that did not correlate with visual acuity or retinal thickness.

Yoon Jeon Kim et al(2013), evaluated the characteristics of spectral-domain optical coherence tomography findings associated with visual outcome and compare OCT measurements according to presence of cystoid macular edema in RP patients, they concluded that the presence of CME in RP patients was not necessarily correlated with loss of visual acuity. severe CME was strongly correlated with IS/OS disruption and visual impairment.

Akio oishi et al(2013),evaluated the clinical usefulness of wide field fundus autofluorescence imaging in RP pigmentosa ,they concluded

PART 2

Aims and Objectives

AIMS AND OBJECTIVES

This study was designed to study the correlation between structural and functional changes in the retina of retinitis pigmentosa patients.

Methodology

MATERIALS AND METHODS

Study Design:

The study was conducted between January 2018 and December 2018 on 53 patients with retinitis pigmentosa at Aravind Eye Hospital and Post Graduate Institute of Ophthalmology at Madurai.

It is a cross sectional, observation study.

Informed Consent:

Informed consent was obtained from each patients, who were willing to participate in the study.

Sample size calculation:

The sample of 104 eyes was analysed the correlation of multimodal imaging and visual parameters in retinitis pigmentosa.The mean (standard deviation) of Type 3 Log Mar VA which was1.48 (0.489) taken as reference with 8 % precision and 95% confidence interval.

Data collection:

The study was approved by the Institutional Review Board and Ethical Committee. A study proforma with details of demographic data and other variables related to the study were noted in the excel sheet during data collection.

PATIENTS SELECTION CRITERIA

Inclusion criteria:

1.The Diagnosed RP patient with any age, gender and BCVA > 6/60

2.The patients willing to comply with study procedures

Exclusion criteria:

1.The patients were excluded if they are having advance stage of RP,significant cataract or other media opacity or if they had other Ocular disease.

2.The Patients not willing to comply with study procedures

METHODS

All RP patients had underwent for complete ophthalmic examination which includes:

➢ **Ocular examination:**

- Best corrected visual acuity: By snellen's chart
- Intraocular pressure: By applanation tonometer
- Slit lamp Examination: To evaluate anterior segment
- Fundus Examination: By 90 D Slit Lamp Biomicroscopy
- Indirect ophthalmoscopy(with 20 D lens): To evaluate periphery of retina.
- Visual field charting: Automated Humphrey visual field with 10-2 SITA Standard
- Visual field map: By Microperimetry (MAIA)
- OPTOS : To measure AF ring diameter.
- Spectral-Domain optical coherence tomography(SD-OCT) and Enhanced depth Imaging using (Heidelberg Engineering, Heidelberg, Germany): To evaluate sub foveal ISOS line length, AF ring diameter,macular thickness map and choroidal thickness.
- Electro physiological testing (where indicated and permissible).

Visual field analysis by HFA 10-2

A static perimetry was performed for all subjects using the Humphrey visual field analyser 10-2 (ZEISS).

Perimetry data were considered reliable if the false responses were lower than 20% and fixation losses lower than 20%.The numerical value of HFA represents the retinal sensitivity. The numerical value was obtained by using HFA software. Average of central 4 point of numerical value represented as S4,central 12 points represented as S12,central 20 points represented as S20.

Visual field map by Microperimetry

The patients Visual field map was obtained by using microperimetry (Macular Integrity Assessment Technology). The average threshold value represents retinal sensitivity. The average threshold value was obtained by using microperimetry software. The visual field map illustrate a decibel scale for average threshold. It describes green color for normal patients, yellow color for suspected patients and red color for abnormal patients.In this study it is graded 0,1 and 2 for normal patients, suspected patients and abnormal patients respectively.

OPTOS

OPTOS (Daytona plus) was used to obtain Wide field fundus ring and fundus autoflouorescene ring.Fundus autofluorescence ring was measured manually along outer hyperfluorescent area using the calibers of the OPTOS software.

OCT image acquisition

RP patients were imaged by spectralis HRA OCT(Heidelberg Engineering, Heidelberg, Germany).All subjects had their pupils dilated with 1% Tropicamide and 2.5% Phenylephrine hydrochloride.

In this study macular thickness values were measured by SD-OCT, we used fast mode macular thickness map protocol. From the retinal thickness map print out Macular thickness calculation was noticed. The map was consists of a sector in three concentric circles. Outer, middle and inner circle with a diameter of 6mm, 3mm,1mm respectively. Outer and middle circles were formed the perifoveal area, middle and inner circles were formed the parafoveal area.The parafoveal and perifoveal area were divided into superior inferior, nasal, temporal quadrant.

The 1mm central thickness area corresponding to the CMT was used in our study. Scanning results were analysed by OCT software. All quadrants measurement were obtained from this thickness map.

Fundus autofluorescence imaging was done with confocal laser ophthalmoscope (Spectral OCT Heidelberg Engineering). Fundus

autofluorescence imaging was obtained using a 30° field of view and used solid laser 488nm for excitation and >500 nm for barrier filter.

Fundus autofluorescence imaging was recorded through dilated pupil. In these image AF Ring diameter was measured. AF ring is a border between functional and dysfunctional retina in FAF image .It represented as hyper fluorescent area, this AF ring measurement was done by calipers available on the Heidelberg software.

IS/OS line was described as hyper reflective area after the retinal pigment epithelium layer on OCT. IS/OS line measurements were recorded from SD OCT at the subfoveal area using the calipers of the Heidelberg reader software. Patients were classified into two groups according to the IS/OS line length as follows: IS/OS line length was <2mm,length was >2mm.

The choroidal thickness measurement was done using spectral HRA +OCT (Heidelberg Engineering ,Heidelberg ,Germany techniques) can image choroid, using techniques such as image averaging and enhanced depth imaging (EDI). In EDI involves setting the choroid adjacent to the Zero delay line, which allows enhanced visualization of choroid up to the sclera. Choroidal thickness was measured manually from the inner borer of the sclera to outer border of the RPE vertically at the subfoveal area using caliber of the Heidelberg reader software.

Protocol for choroidal thickness measurement

Mode:Enhanced Depth imaging

Scan Angle 30°×15°

ART(Automatic real time Tracking):100

Section :19

All patients also underwent fundus photography.

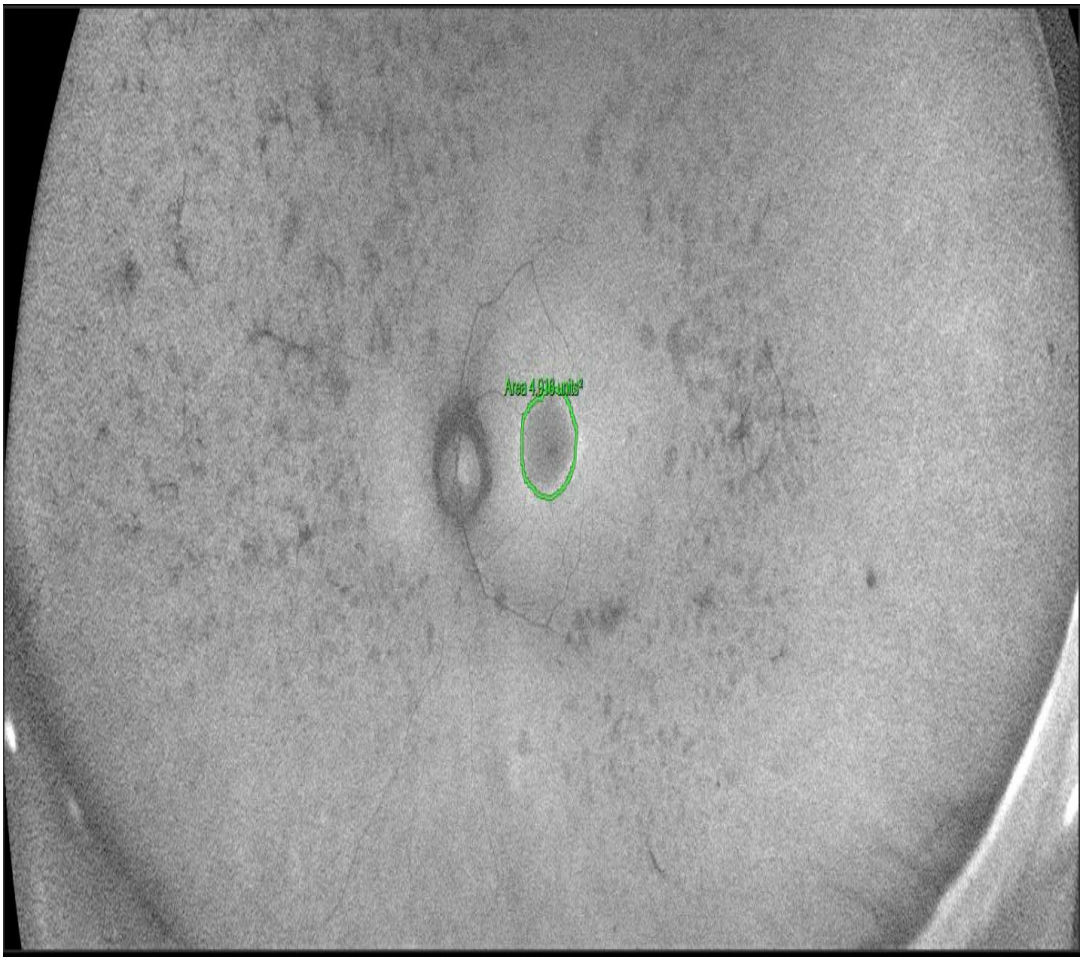


Figure 3: OPTOS image of RP patient showing hyper auto fluorescent ring on OPTOS

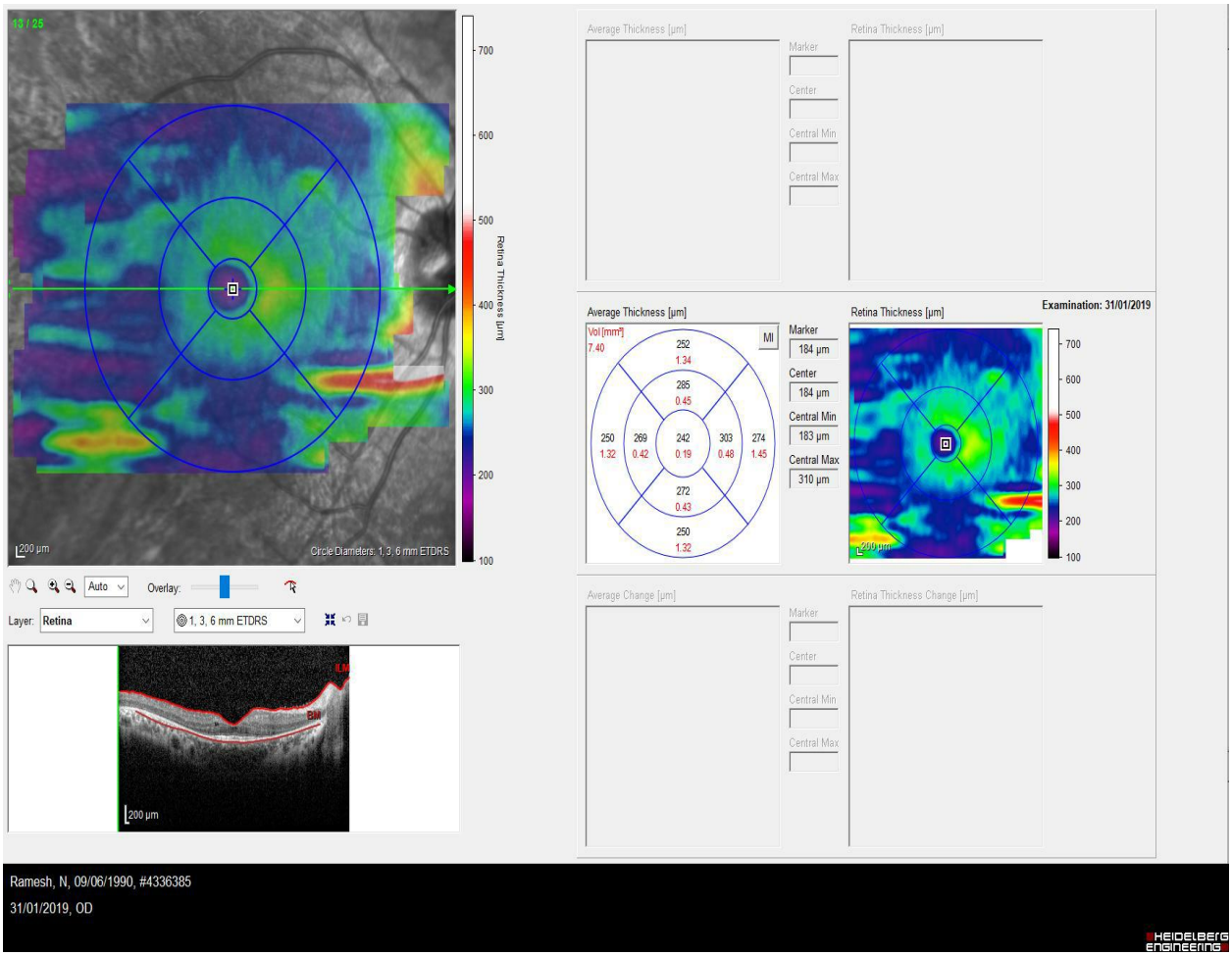


Figure 4: Image depicting macular thickness measurement with scan (RP patient)

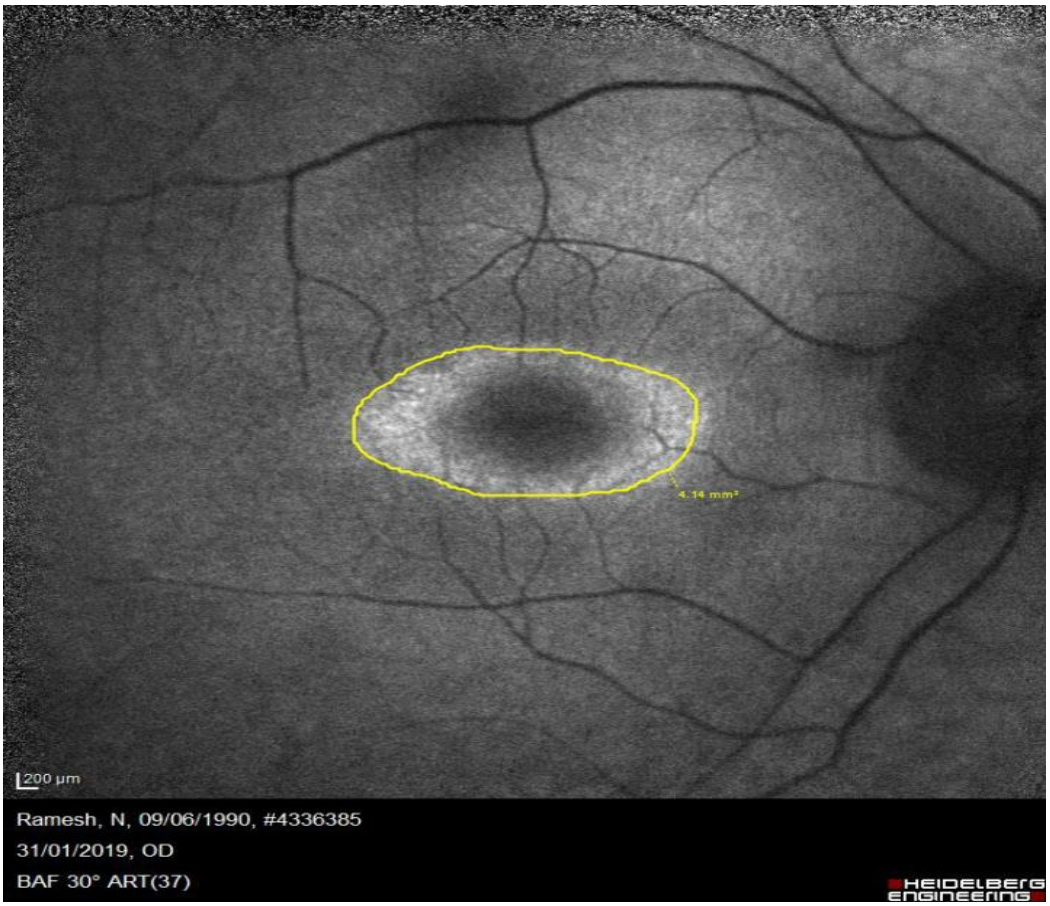


Figure 5:SD OCT image of RP patient showing hyper auto fluorescent ring measurement.

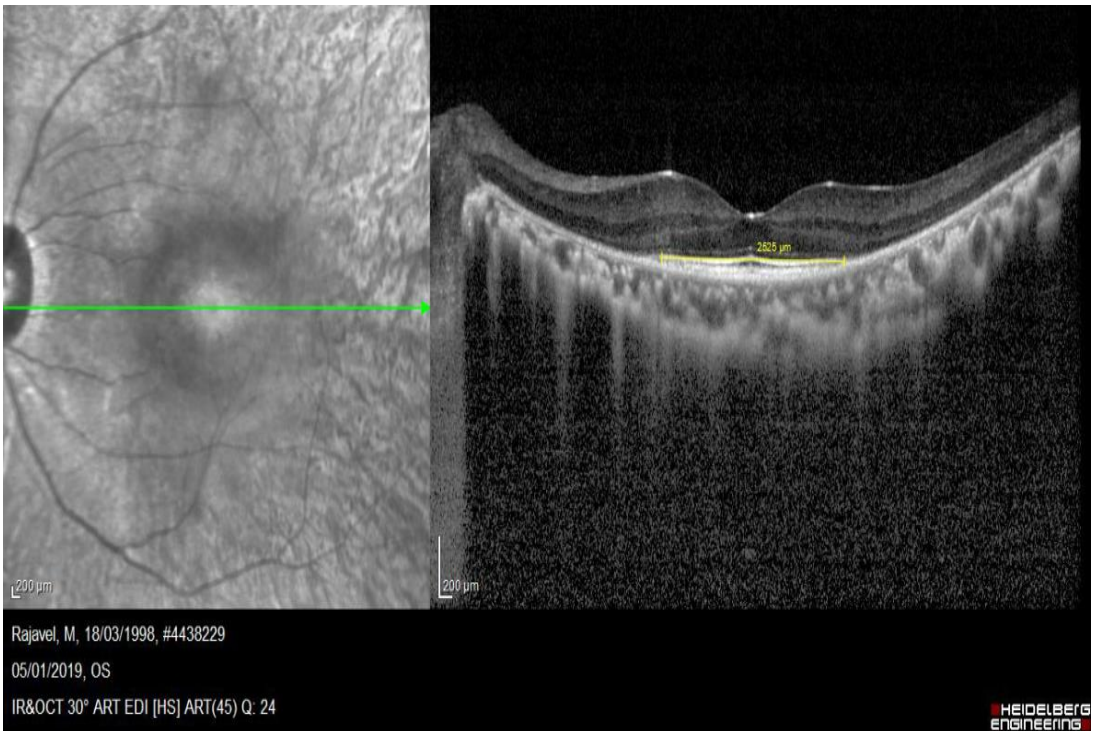


Figure 6:SD OCT image of RP patient showing subfoveal IS/OS line measurement

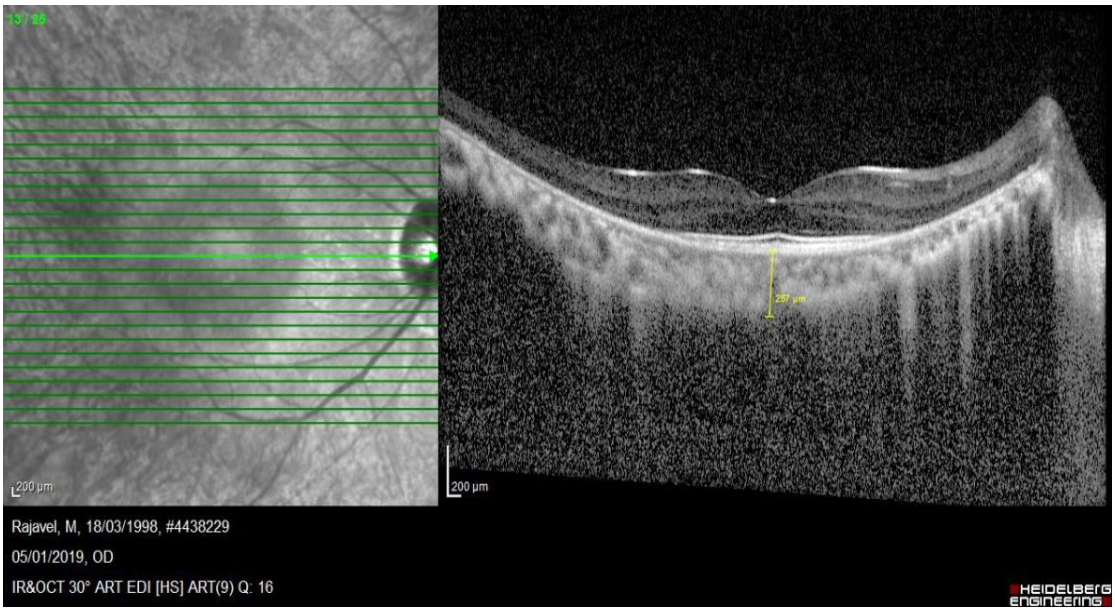


Figure 7: SD OCT(EDI) image of RP patient showing the choroidal thickness measurement.

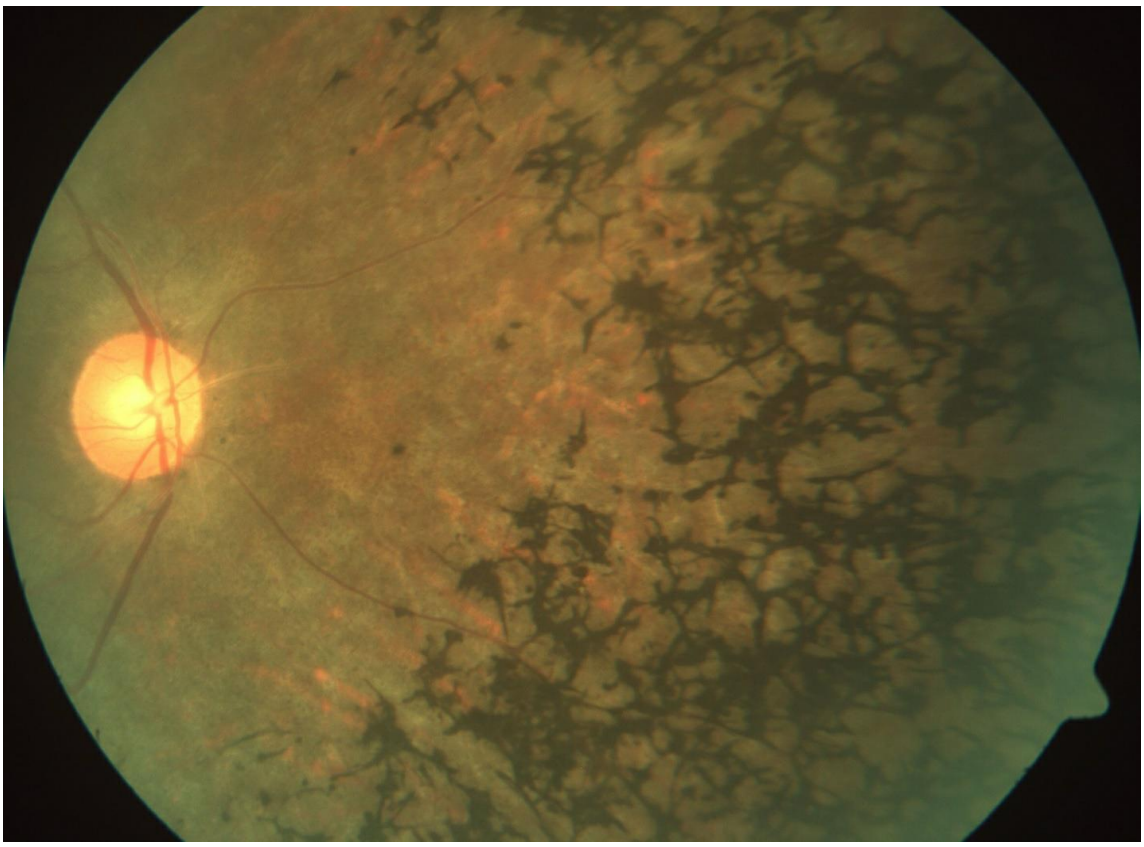


Figure 8:color fundus photographic image of RP patients showing bony spicules, attenuated arterioles

Results

RESULTS

The study evaluated 104 eyes of 53 case clinically diagnosed RP patients.

Statistical Analysis

Descriptive statistics like mean (SD) were given for continuous variables and frequency (percentage) for categorical variables. Wilcoxon Rank sum test was used to compare the difference between the two groups. Spearman rank correlation was used to find correlation between two continuous variables. P-value < 0.05 was considered statistically significant. All the statistical analysis were done by using statistical software STATA version 14.0 (Texas, USA).

DEMOGRAPHIC PROFILE

Age distribution:

The RP patients in this study ranged from 13 to 71 years of age with a mean age of 35.43(13.65) years.

Table 1: Age distribution

Age(years)-Range	Mean(SD)-years	n
13- 71	35.43	53

Gender distribution.

The study was carried out with 53 RP patients. In 53 RP patients 69.8%(n=37)were males and 30.2%(n=16) were females.

Table 2: Gender distribution in RP

Gender	n (%)	Total
Male	37(69.8%)	53
Female	16(30.2%)	53

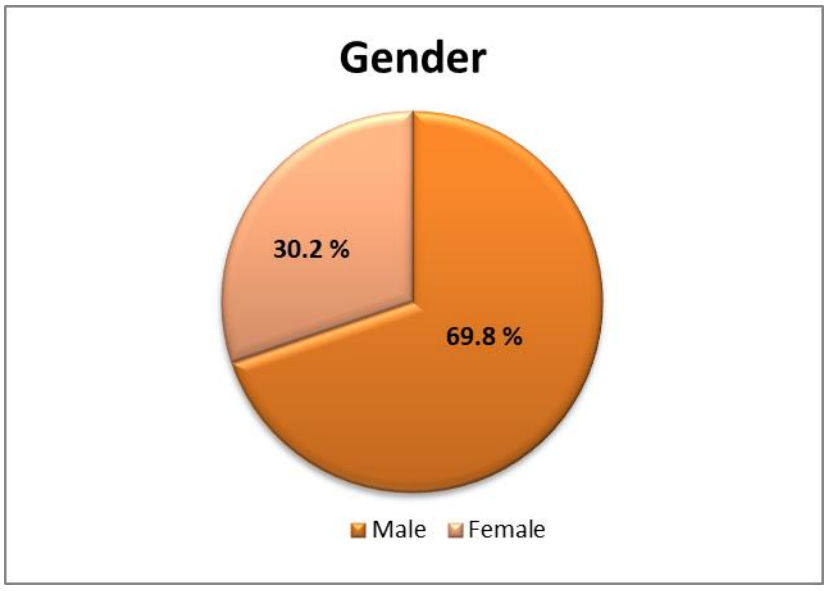


Figure 9: Gender distribution in RP

Basic ocular examination

The Mean BCVA of participants were 0.20+/-0.18.

Table 3: showing mean, median of BCVA in RP

BCVA	n	Mean (SD)	Median (Snellen's equivalent)	Interquartile Range
	104	0.20(0.18)	0.18(6/9)	0.00-0.30

The best corrected visual acuity was measured with Snellen's chart that was converted to the logarithm of the minimal angle of resolution units.

In anterior segment examination 16 eyes revealed posterior subcapsular cataract, intraocular pressure was within normal limits in all subjects.

Affected Eyes

In this study 53 RP patients were participated which includes 104 eyes were included out of them BE were 51 96.2% and with one eye(LE) was 2 3.8%.

Table 4: Showing affected eyes in RP patients

Affected eye	N	%	Total no. of eyes
BE	51	96.2	102
LE	2	3.8	2
Total	53	100	104

CME (cystoid maclar edema)

In 104 eyes of RP patients observed 96(92.3%) eyes without CME and 8 eye(7.7 %) with CME .

Table 5: CME in RP

CME	n	%
Present	8	7.7
Absent	96	92.3
Total	104	100

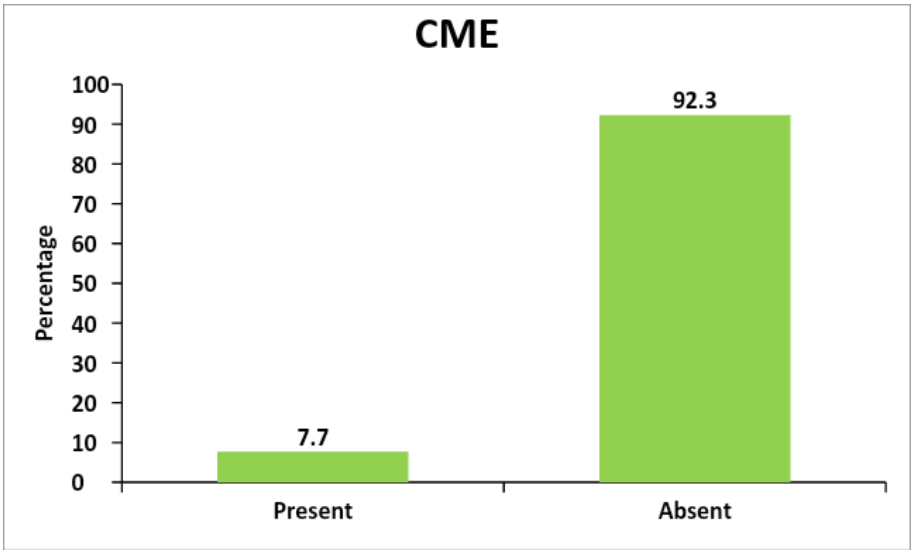


Figure 10: showing CME in RP patients

Fundus photo

All RP patients exhibited attenuated arterioles , bony spicules. Bone spicules observed varying degree of migration ,it was evident on colour fundus photography.Optic disc pallor was observed in 50 eyes .

Structural and functional Parameters used in this study .

Table 6: Structural and functional Parameters used in RP patients.

Parameter	n	Mean(SD)	Range
OCT			
ISOS length	104	1954.99 (1639.59)	0 – 7159
AF ring	98	9.74 (5.69)	1 – 23.3
CMT	104	264.11 (87.26)	101 - 822
CT	104	239.93 (41.18)	106 – 400
Parafoveal thickness-(S)	104	299.41 (56.72	208 – 640
Parafoveal thickness (I)	104	299.17 (53.35)	214 – 490
Parafoveal thickness-(N)	104	306.77 (61.34)	218 – 640

Parafoveal thickness-(T)	104	286.83 (57.11)	211 – 604
Perifoveal thickness(S)	104	245.12 (46.27)	23 – 462
Perifoveal thickness(I)	104	257.51 (55.99)	28 – 493
Perifoveal thickness(N)	104	274.51 (44.49)	213 – 436
Perifoveal thickness(T)	104	241.96 (46.87)	176 – 417

Parameters	**n**	**Mean(SD)**	**Range**
HFA			
S4	100	24.21 (7.68)	0.5 – 40
S12	100	20.71 (10.06)	0 – 34
S20	100	17.04 (9.86)	0 – 36.05
Microperimetry			
Average threshold	102	15.67 (8.14)	0.0 – 28.9
OPTOS			
OPTOS AF ring	101	9.83 (6.46)	1.08 – 27.37

In this study few patients were not fully cooperative for all investigation.

ISOS line length grading:

Table 7: showing ISOS line length grading in RP

Grading	n	%
< 2mm	60	57.7
> 2mm	44	42.3
Total	104	100

The length of ISOS line was measured in OCT images at the sub foveal area.The ISOS line length graded in to less than 2mm and more than 2mm. The analyses revealed that the ISOS line length was less than 2 mm in 57.7% of the eyes and more than 2mm in 42.3 % of the eyes.

Correlation of structural and functional parameters in RP

We analysed whether a significant correlation was present between the structural and functional Parameters in 104 eyes of 53 patients with RP .

Correlation between BCVA and structural parameters in RP

The visual acuity is the conventional parameter to assess the visual function of patients.

We have analysed whether a significant correlation was present between the visual acuity and structural parameters observed on OCT images and OPTOS in 104 eyes of 53 RP patients.

Table 8: Correlation between BCVA and structural parameters in RP.

Parameter	n	Rho	P-value[s]
BCVA Vs CMT	104	-0.2115	0.031
BCVA Vs CT	104	-0.1770	0.072
BCVA Vs AF ring	98	-0.2269	0.025
BCVA Vs Optos AF ring	101	-0.3215	0.001
BCVA Vs Perifoveal thickness (S)	104	-0.0433	0.663
BCVA Vs Perifoveal thickness (l)	104	0.2275	0.020
BCVA Vs Perifoveal thickness (N)	104	0.0899	0.364
BCVA Vs Perifoveal thickness (T)	104	0.1206	0.300

BCVA Vs Parafoveal thickness (S)	104	-0.0959	0.333
BCVA Vs Parafoveal thickness (I)	104	-0.1098	0.267
BCVA Vs Parafoveal thickness (N)	104	-0.1147	0.246
BCVA Vs Parafoveal thickness (T)	104	-0.1022	0.302
BCVA Vs ISOS line length	104	-0.4977	<0.001

The analyses revealed that the visual acuity was negatively correlated with central macular thickness. Visual Acuity did not correlate with choroidal thickness and all quadrant of para foveal thickness and superior, nasal, temporal quadrant of Perifoveal thickness ($p>0.05$).Visual acuity was weakly correlated with inferior quadrant of Perifoveal thickness ($p<0.05$). Visual acuity was negatively correlated with the AF ring diameter ($p<0.05$).This AF ring(autofluorescent) observed on OCT images, AF ring diameter was negatively correlated with visual acuity .The recently introduced OPTOS shows AF ring,

visual acuity was negatively correlated with OPTOS AF Ring ($p<0.05$). Visual acuity was negatively correlated with ISOS line length ($p<0.05$).

Correlation between retinal sensitivity and structural parameters in RP Patients.

The retinal sensitivity is a better indicator of macular function, it represents the sensitivity of a larger retinal area, therefore there tinal sensitivity used as better indicator of visual function of patients.

The average central retinal sensitivity calculated by the HFA 10-2 program. We analysed whether a significant correlation was present between the retinal sensitivity and structural parameters in RP patients.

Correlation between HFA S4 and structural parameters in RP.

We analysed whether a significant correlation was present between average sensitivity of central 4 points on the HFA 10-2 and Structural parameters.

Table 9: Correlation between HFA S4 and structural parameters in RP

Parameter	n	Rho	P-value[s]
HFA S4 Vs CMT	100	0.4148	<0.001
HFA S4 Vs CT	100	-0.0546	0.589
HFA S4 Vs AF ring	96	0.2191	0032
HFAS4 OPTOS ring	99	0.3029	0.002
HFA S4 Vs Perifoveal thickness (S)	100	0.2229	0.026
HFA S4 Vs Perifoveal thickness (I)	100	-0.0284	0.917
HFA S4 VsPerifoveal thickness (N)	100	0.2281	0.022
HFA S4 Vs Perifoveal thickness (T)	100	0.1288	0.202
HFA S4 Vs Parafoveal thickness (S)	100	0.359	0.0002
HFA S4 VsParafoveal thickness (I)	100	0.3823	0.0001

HFA S4 Vs Parafoveal thickness (N)	100	0.3480	0.0004
HFA S4 Vs Parafoveal thickness (T)	100	0.3447	0.0004
HFA S4 Vs ISOS length	100	0.4838	<0.001

HFA S4 was moderately correlated with central macular thickness ($p<0.05$).HFA S4 was weakly correlated with AF ring , OPTOS AF ring ($p<0.05$) .HFAS4 was weakly correlated with superior and ,nasal quadrant of Perifoveal thickness p(<0.05). HFAS4 was weakly correlated with all quadrants of parafoveal thickness.HFAS4 was moderately correlated with ISOS line($p<0.05$).The correlation between HFAS4 and Perifoveal inferior, HFA S4 and perifoveal temporal thickness, HFA S4 and choroidal thickness were not significant ($p >0.05$).

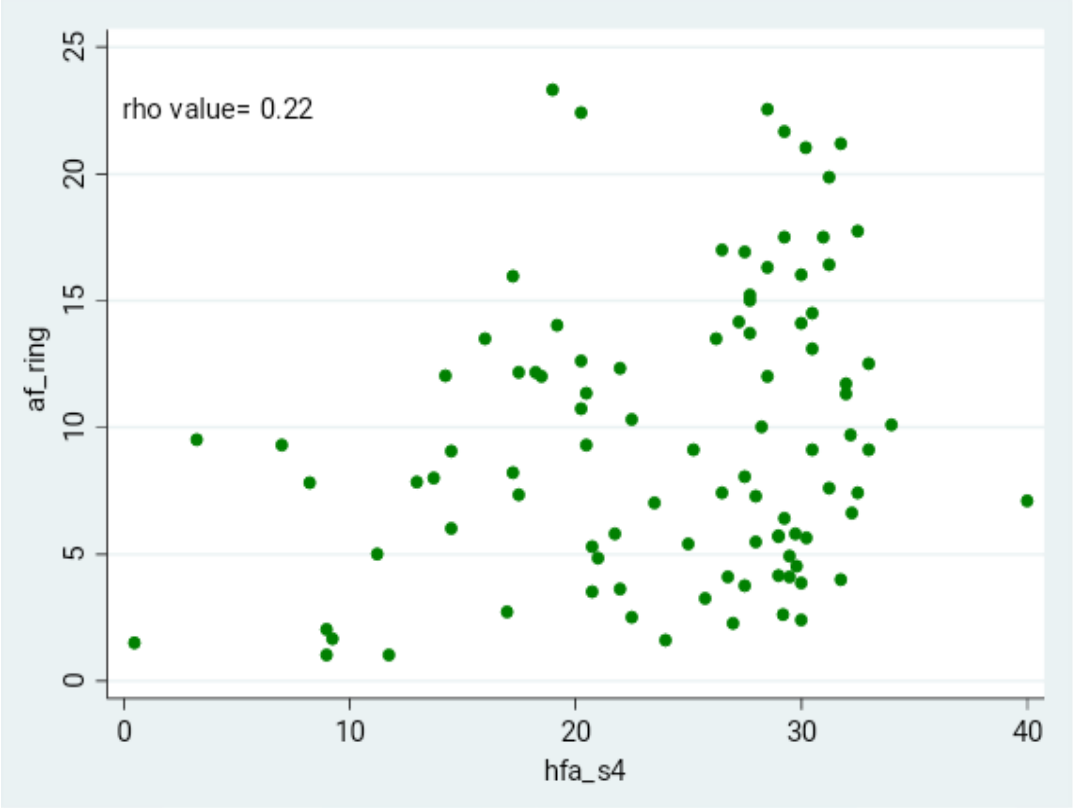


Figure 11:Scatter plot showing the correlation between HFA S4 and AF ring of SD-OCT in RP

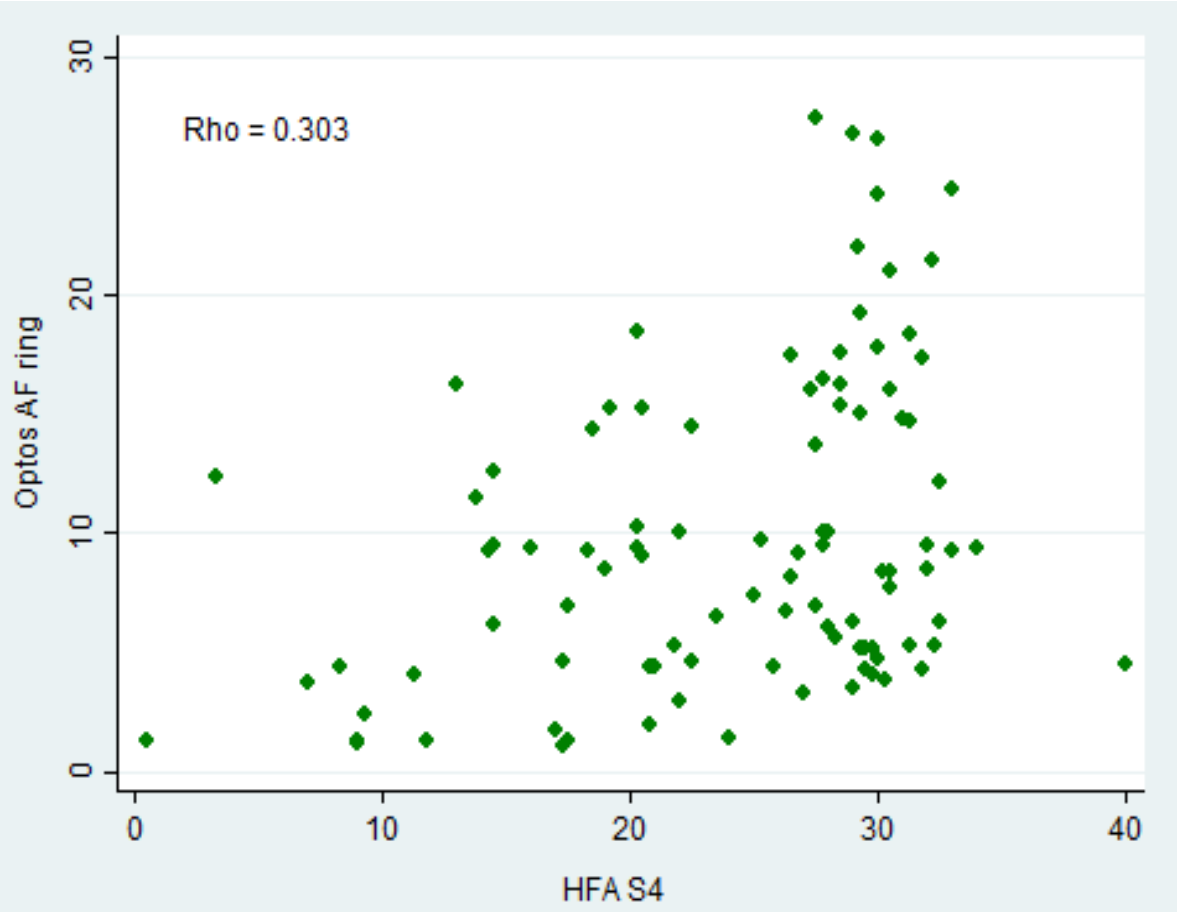


Figure 12:Scatter plot showing the correlation between HFA S4 Optos AF Ring in RP.

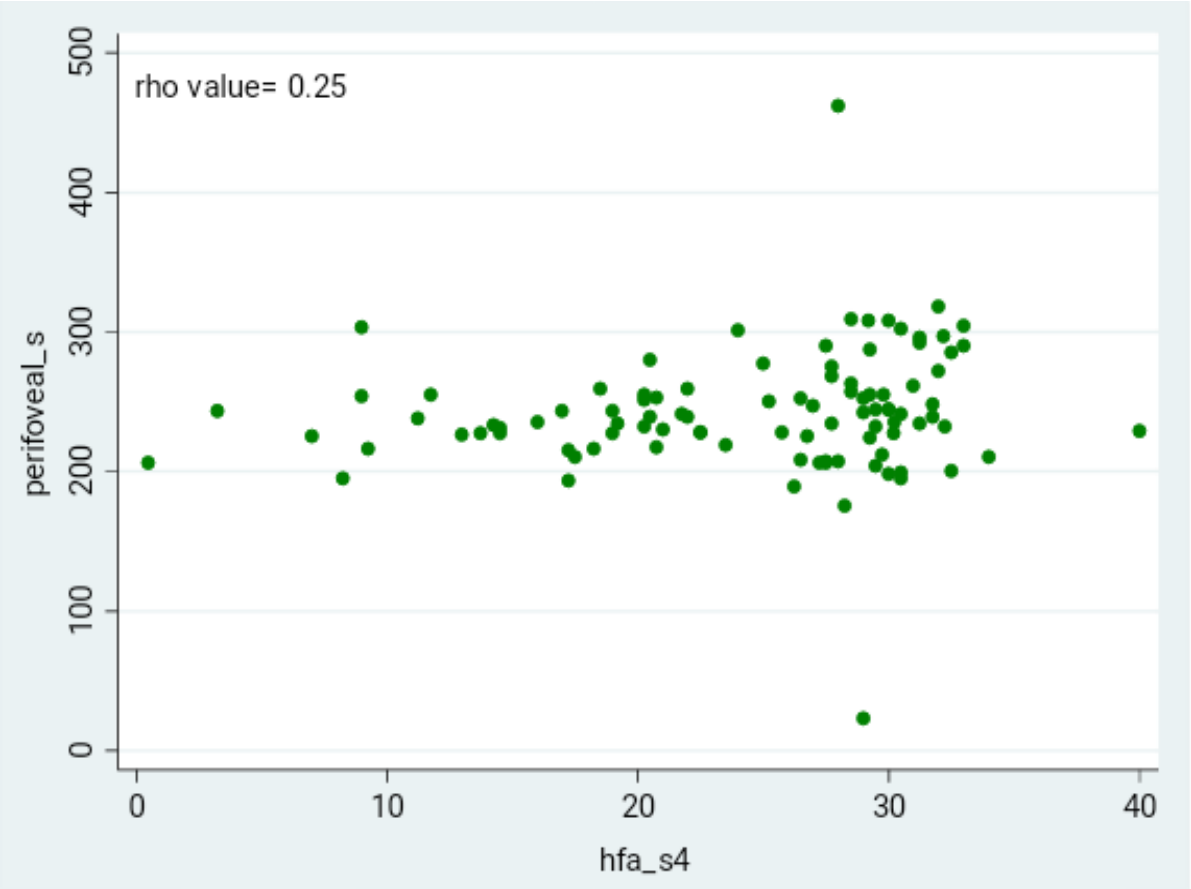


Figure 13: Scatter plot showing the correlation between HFA S4 and Perifoveal thickness (Superior) in RP.

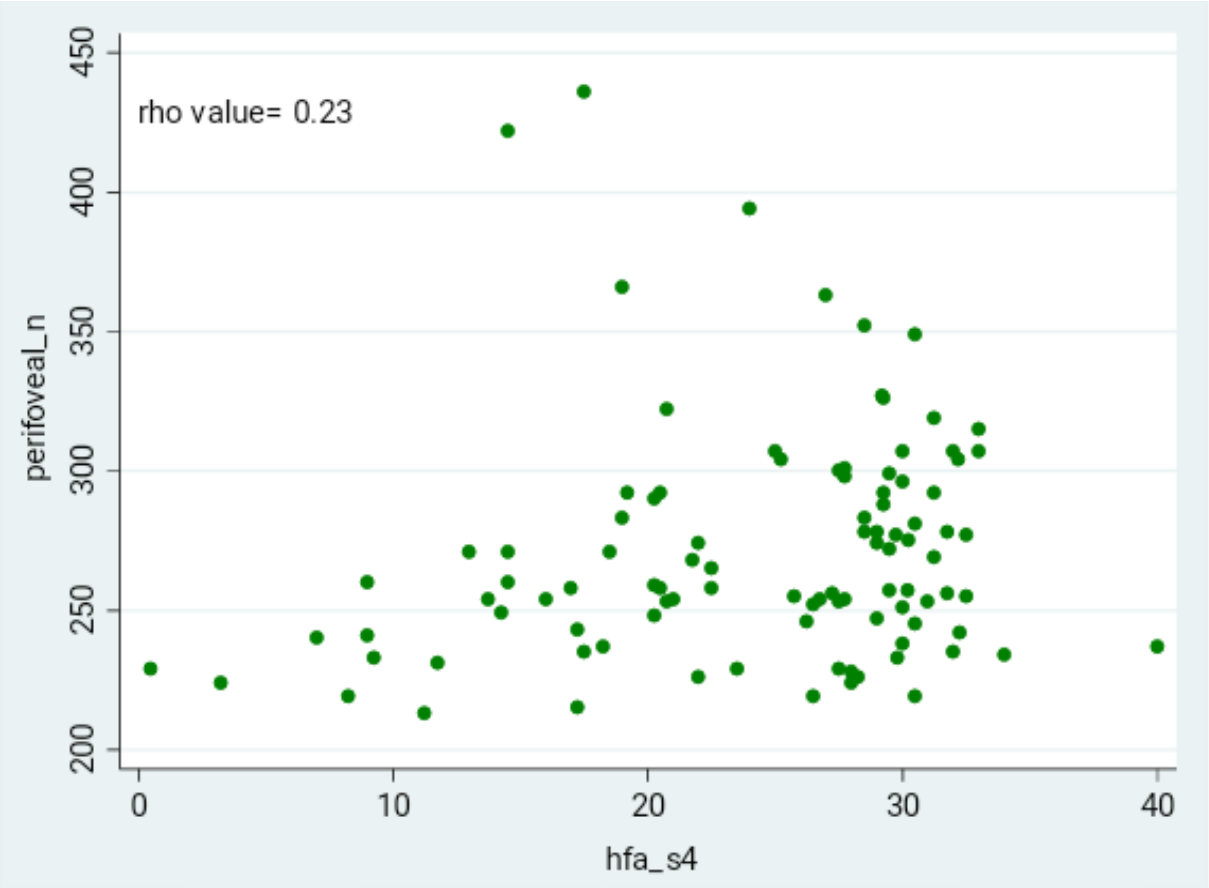


Figure 14: Scatter plot showing the correlation between HFA S4 Perifoveal thickness (Nasal) in RP.

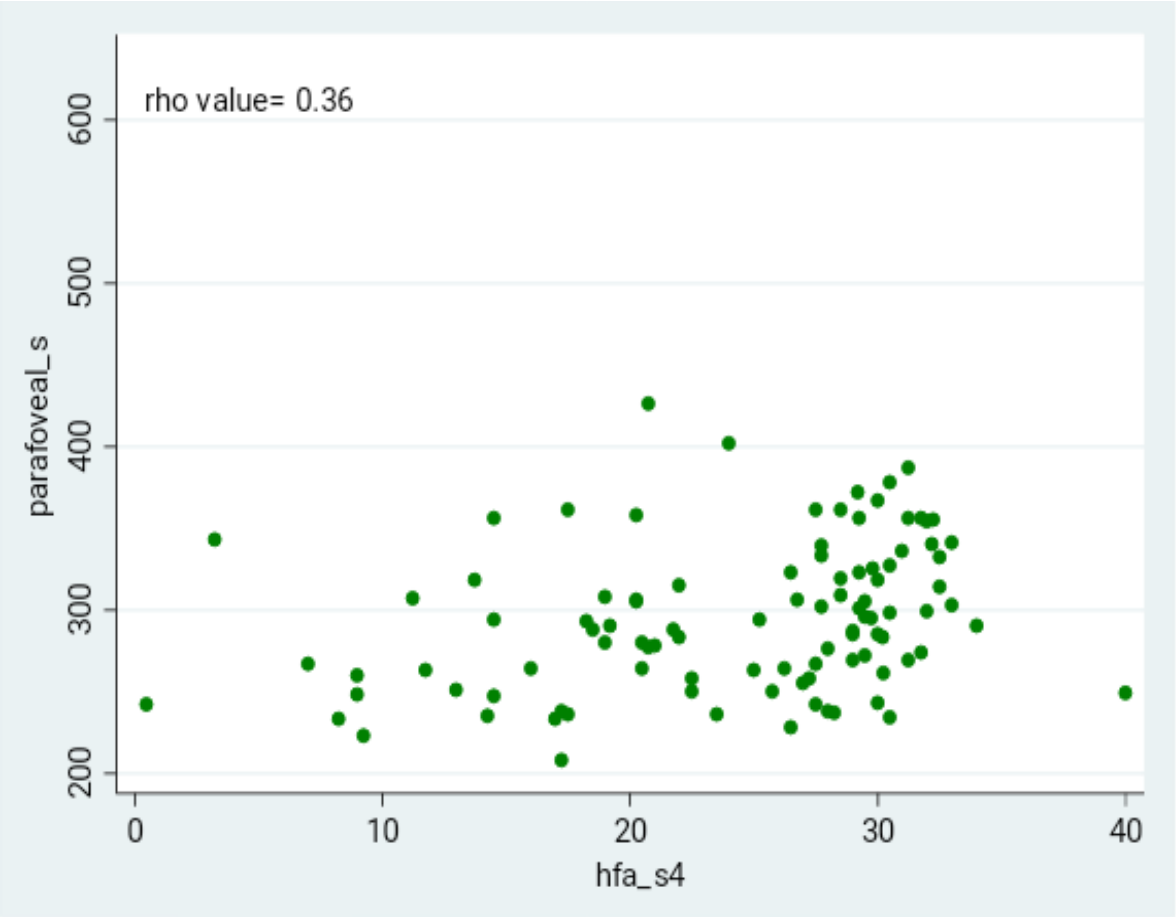


Figure 15:Scatter plot showing the correlation between HFA S4 and Parafoveal thickness (superior) in RP.

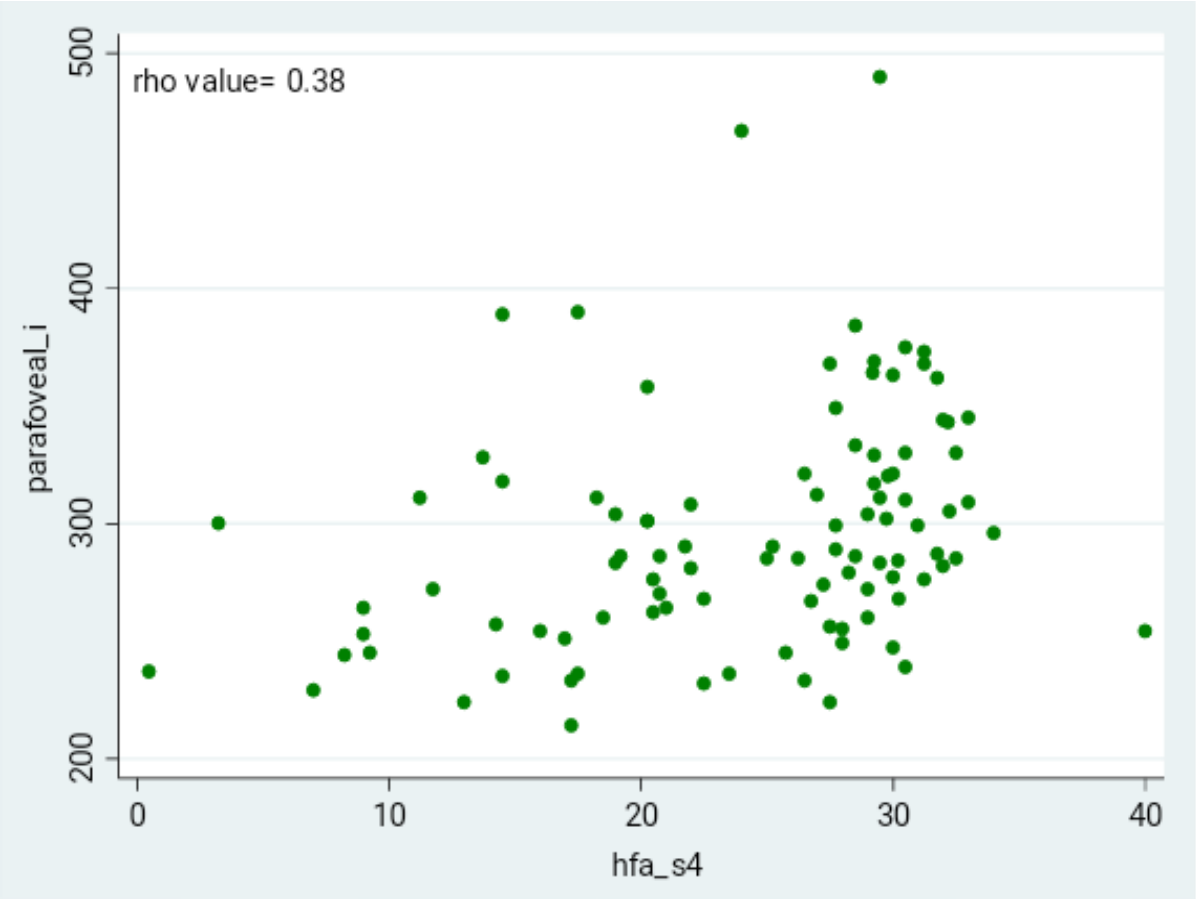


Figure 16 :Scatter plot showing the correlation between HFAS4 and Parafoveal thickness (inferior) in RP.

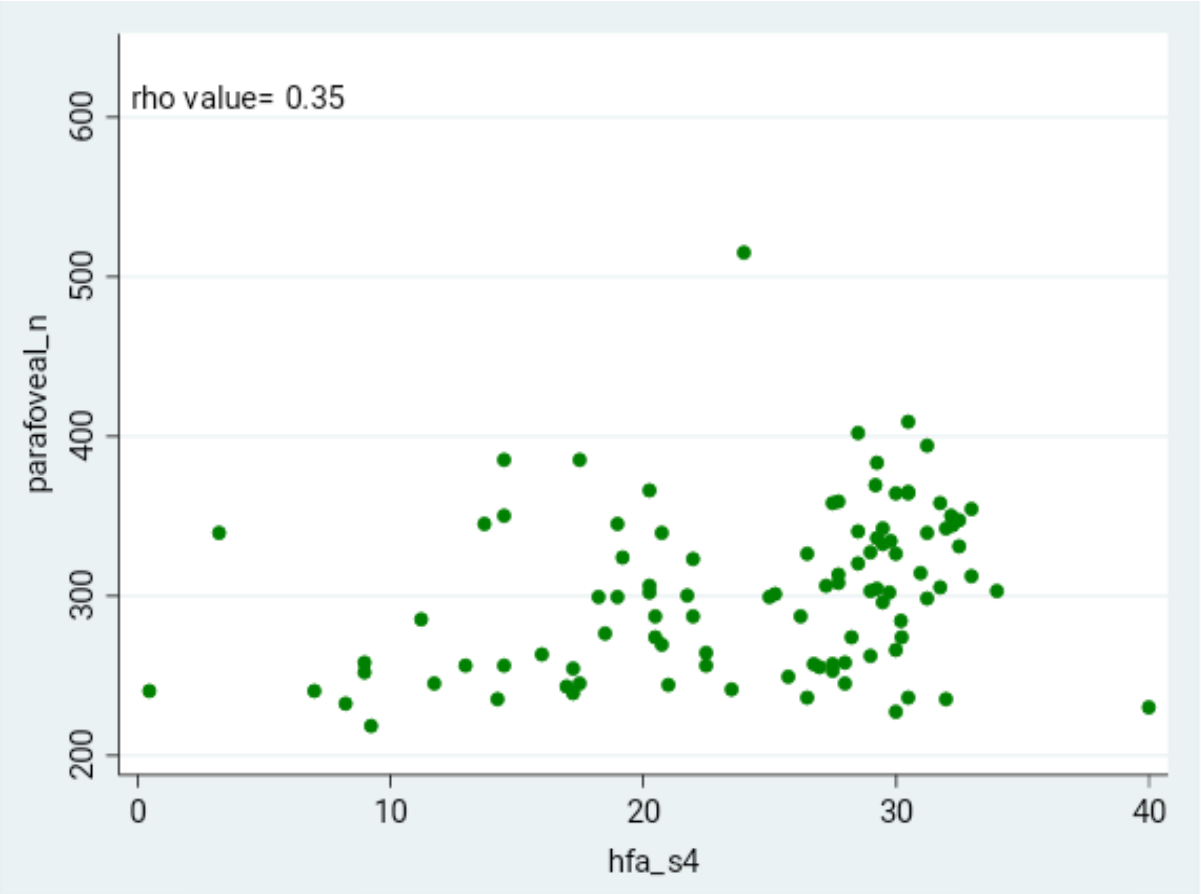


Figure 17:Scatter plot showing the correlation between HFA S4 and Parafoveal thickness (Nasal) in RP.

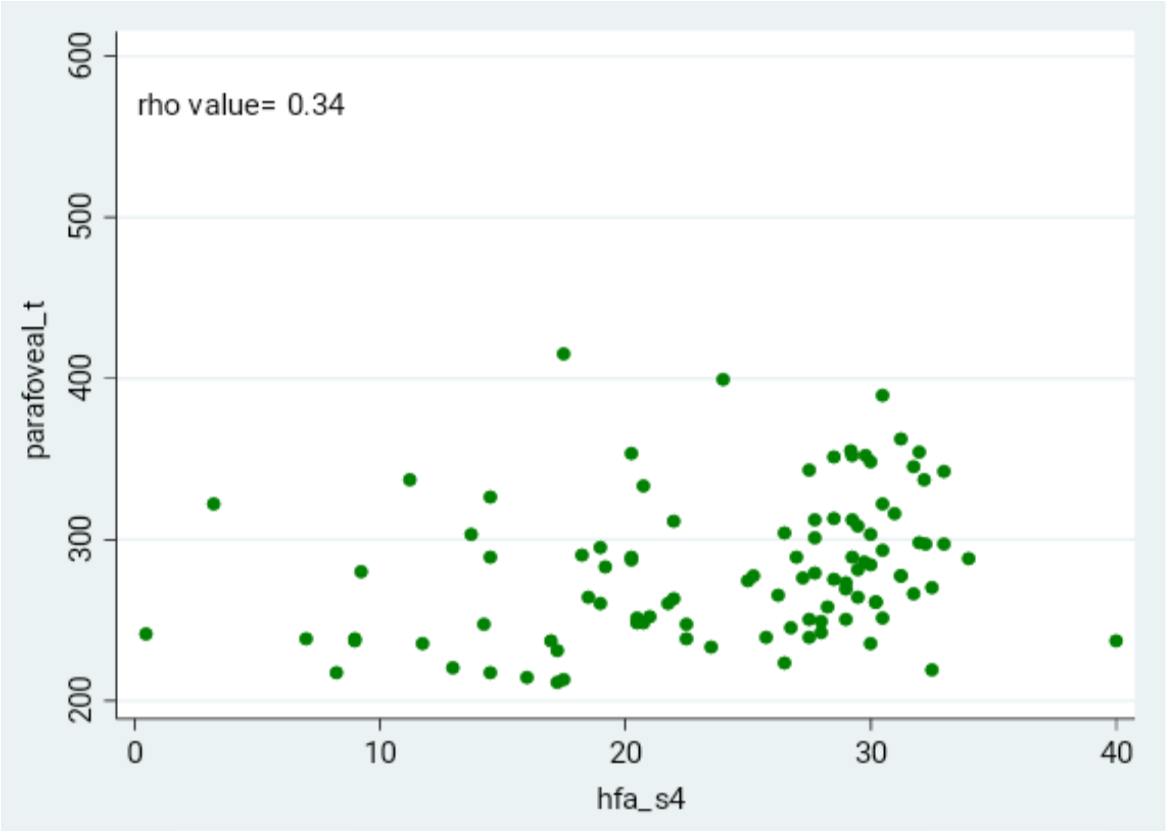


Figure 18;Scatter plot showing the correlation between HFA S4 and Parafoveal thickness (Temporal) in RP.

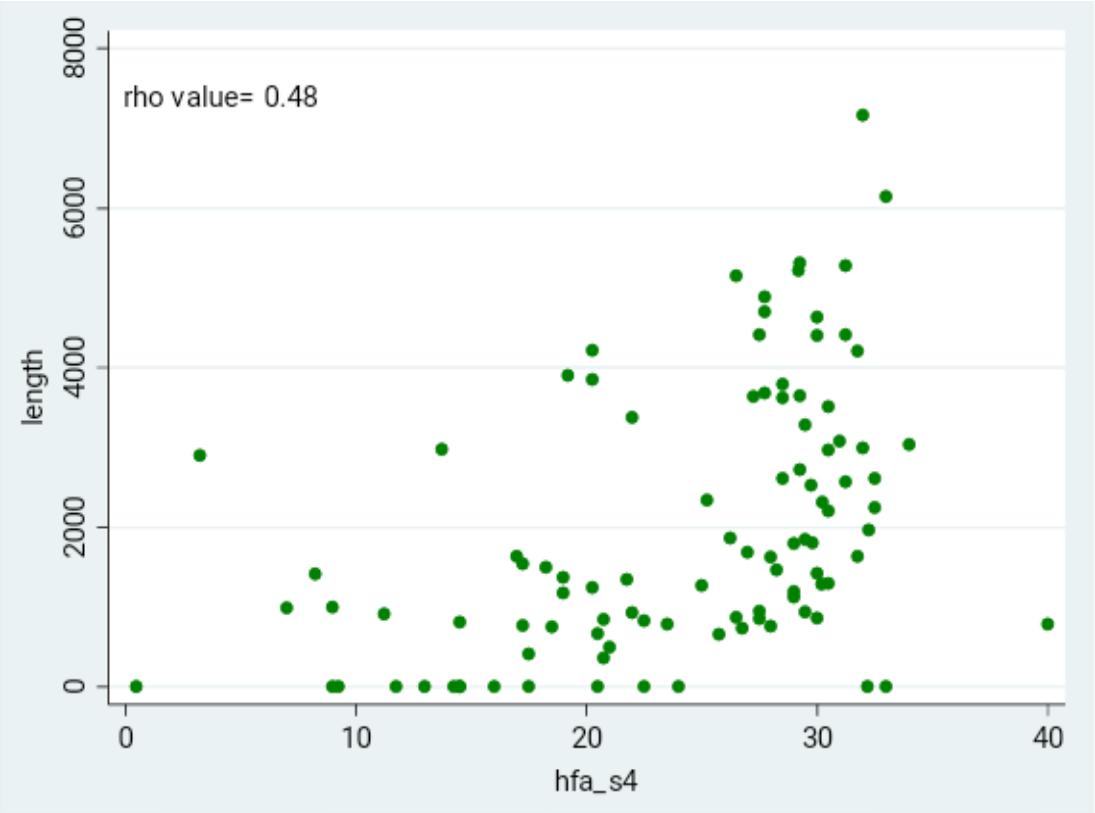


Figure 19;Scatter plot showing the correlation between HFA S4 and IS/OS line in RP.

Correlation between HFA S12 and structural parameters in RP.

We analysed whether a significant correlation was present between average sensitivity of central 12 points on the HFA 10-2 and structural parameters in RP patients.

Table10: Correlation between HFA S12 and structural parameters in RP.

Parameter	n	Rho	P-value[s]
HFA S12 Vs CMT	100	0.4871	<0.001
HFA S12 Vs CT	100	0.0320	0.7520
HFA S12 Vs AF ring	96	0.3134	0.002
HFA S12 Vs Optos AF ring	99	0.4405	<0.001
HFA S12 Vs Perifoveal thickness (S)	100	0.3189	0.0012
HFA S12 Vs Perifoveal thickness (I)	100	0.0599	0.554
HFA S12 Vs Perifoveal thickness (N)	100	0.3282	0.0009
HFA S12 Vs Perifoveal thickness (T)	100	0.2052	0.041
HFA S12 Vs Parafoveal thickness(S)	100	0.4427	<0.001

HFA S12 Vs Parafoveal thickness (l)	100	0.5019	<0.001
HFA S12 Vs Parafoveal thickness (N)	100	0.4330	<0.001
HFA S12 Vs Parafoveal thickness (T)	100	0.4625	<0.001
HFAS12 Vs ISOS line length	100	0.5695	<0.001

HFA S12 was moderately correlated with central macular thickness($p<0.05$).HFA S12 was weakly correlated with AF ring. HFA S12 moderately correlated with OPTOS AF ring ($p<0.05$) .HFAS 12 was weakly correlated with superior , nasal, temporal quadrant of Perifoveal thickness ,moderately correlated with all quadrants of parafoveal thickness p(<0.05). HFAS12 was moderately correlated with ISOS line($p<0.05$).HFAS12 did not correlate with Perifoveal inferior thickness and choroidal thickness ($p >0.05$).

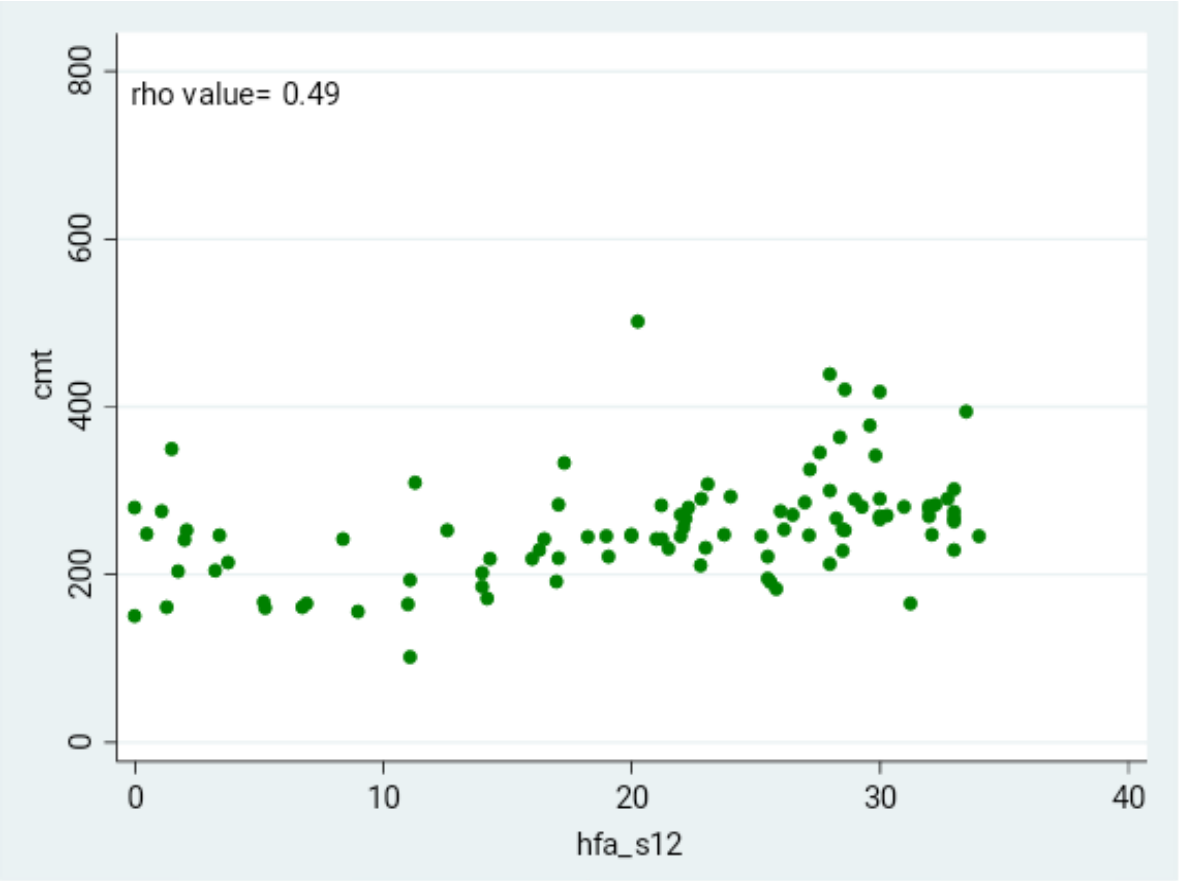


Figure :20 Scatter plot showing the correlation between HFA S12 and CMT in RP.

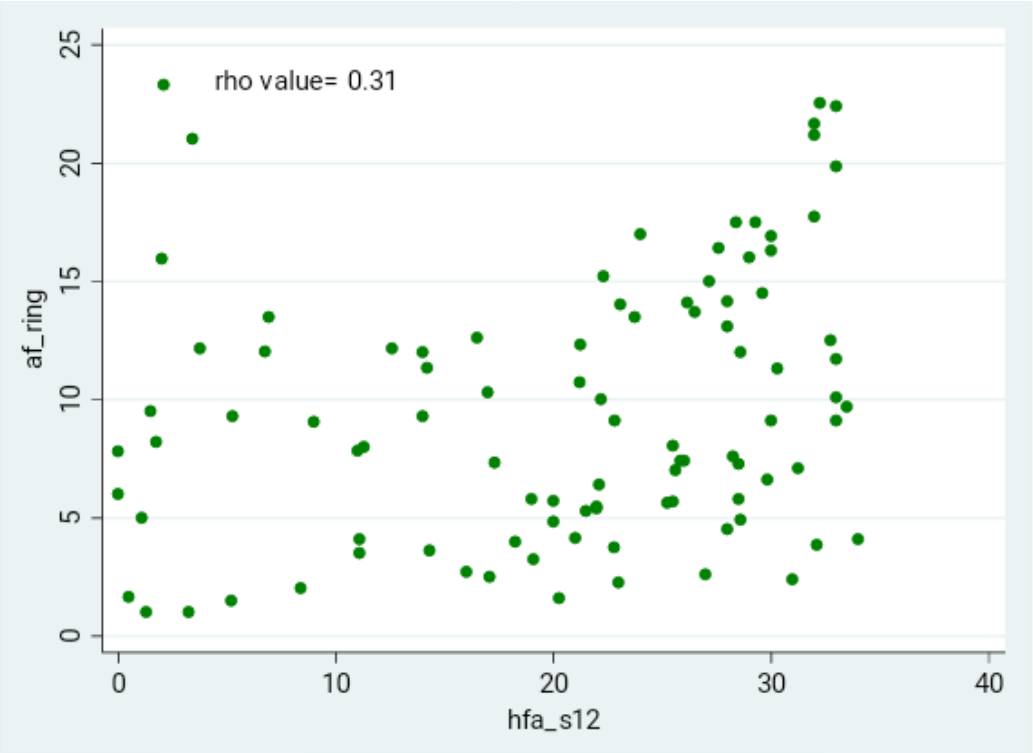


Figure 21:Scatter plot showing the correlation between HFA S12 and AF ring of SD-OCT in RP

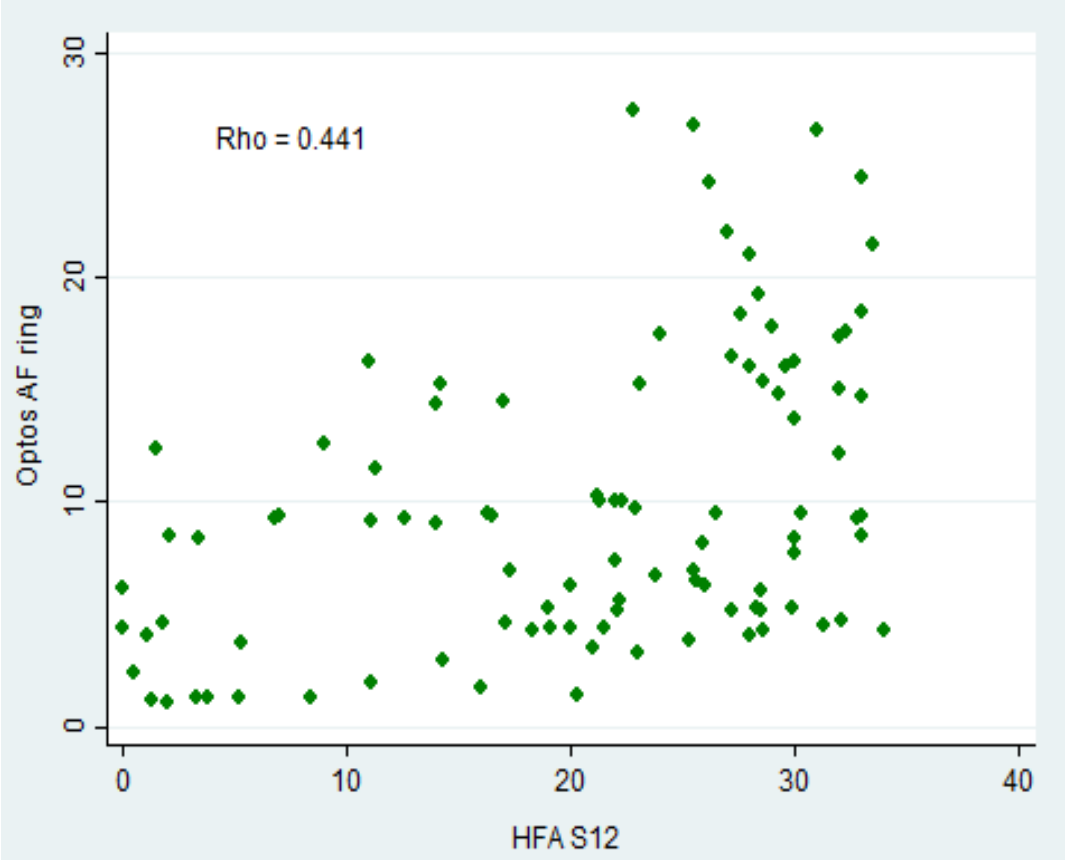


Figure22:Scatter plot showing the correlation between HFA S12 and Optos AF ring in RP

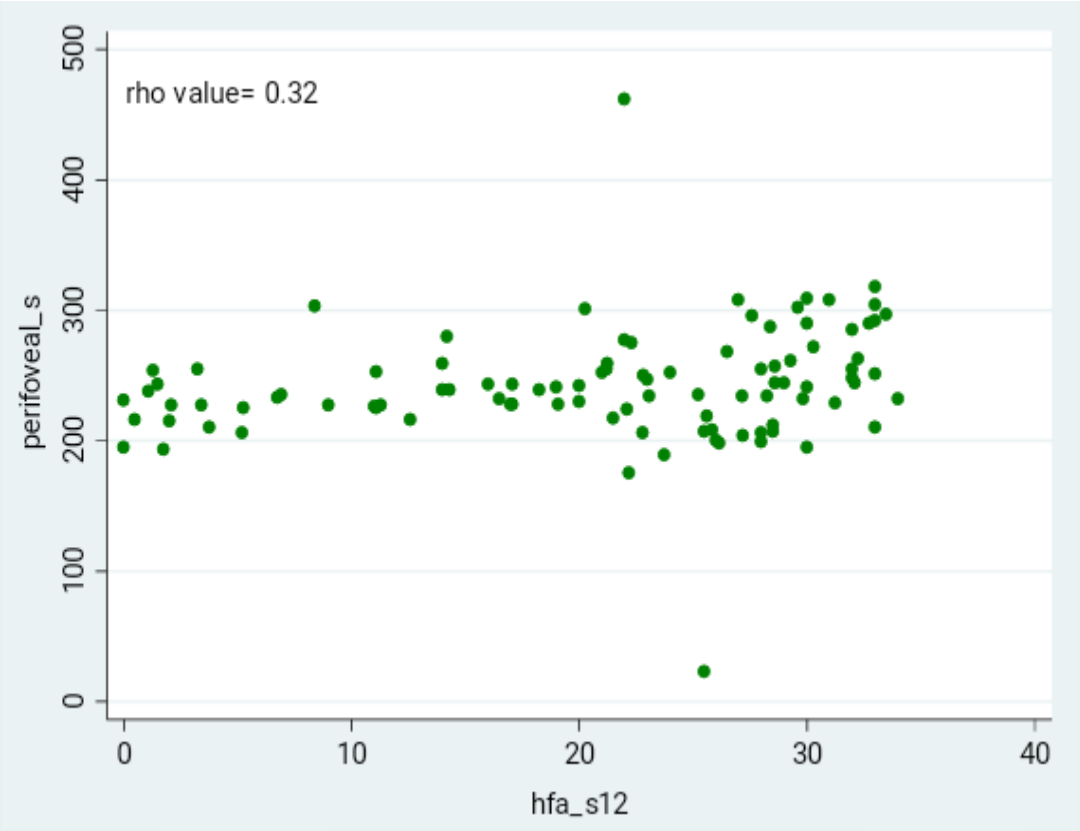


Figure23:Scatter plot showing the correlation between HFA S12 and Perifoveal thickness(superior) in Rp

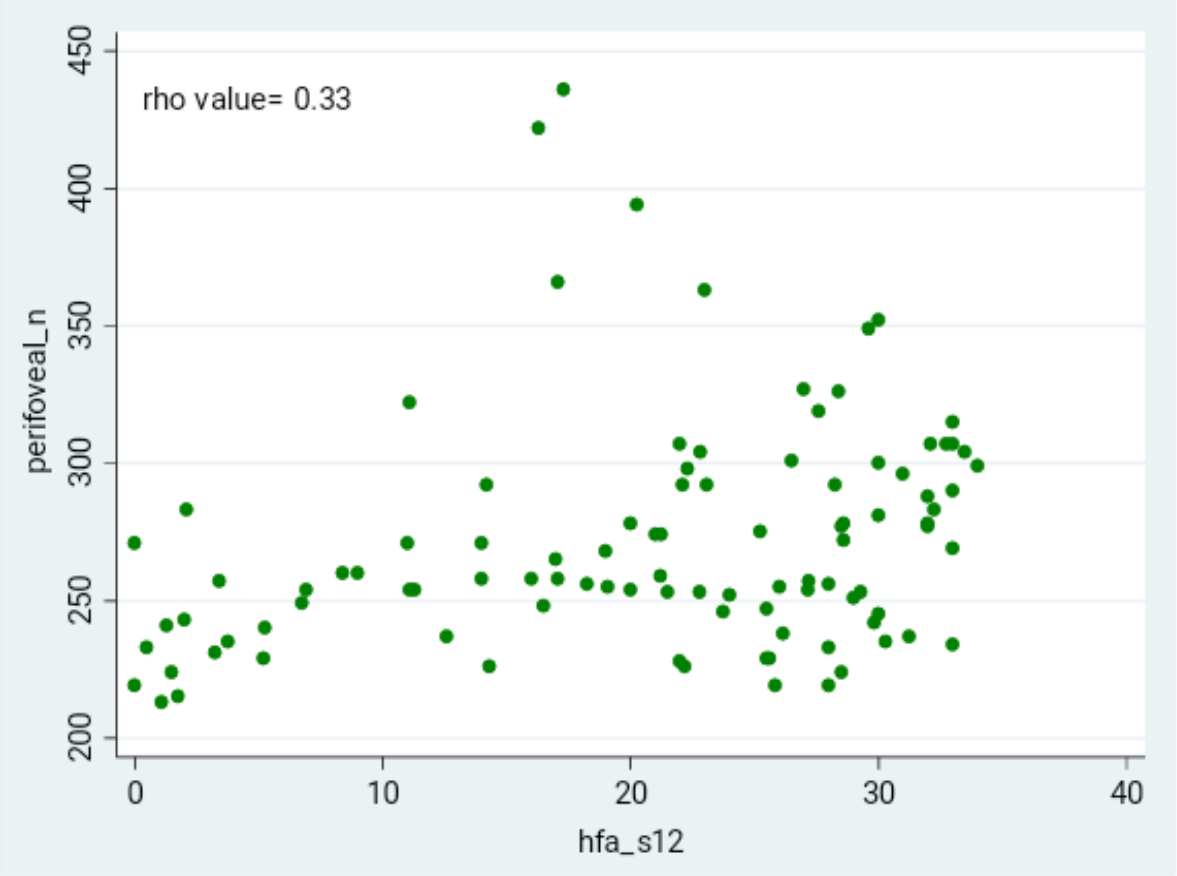


Figure:24 Scatter plot showing the correlation between HFA S12 and Perifoveal thickness (Nasal)in RP

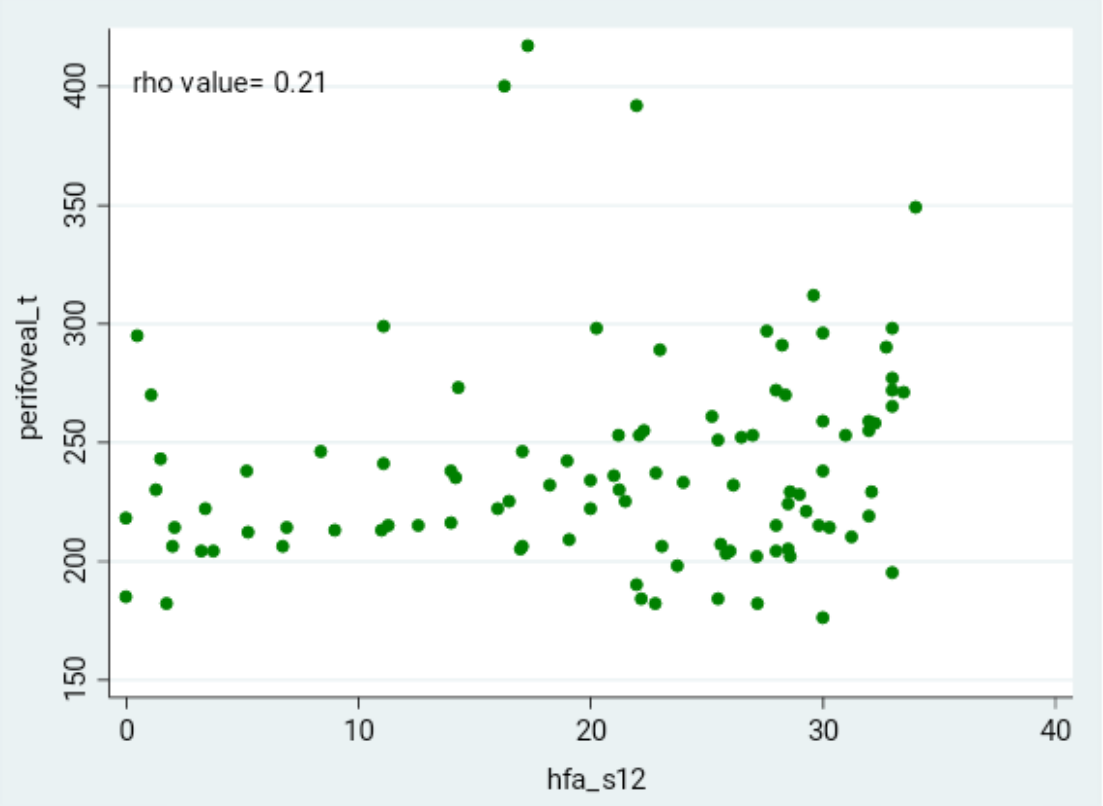


Figure 25:Scatter plot showing the correlation between HFA S12 and Perifoveal thickness (temporal) in RP.

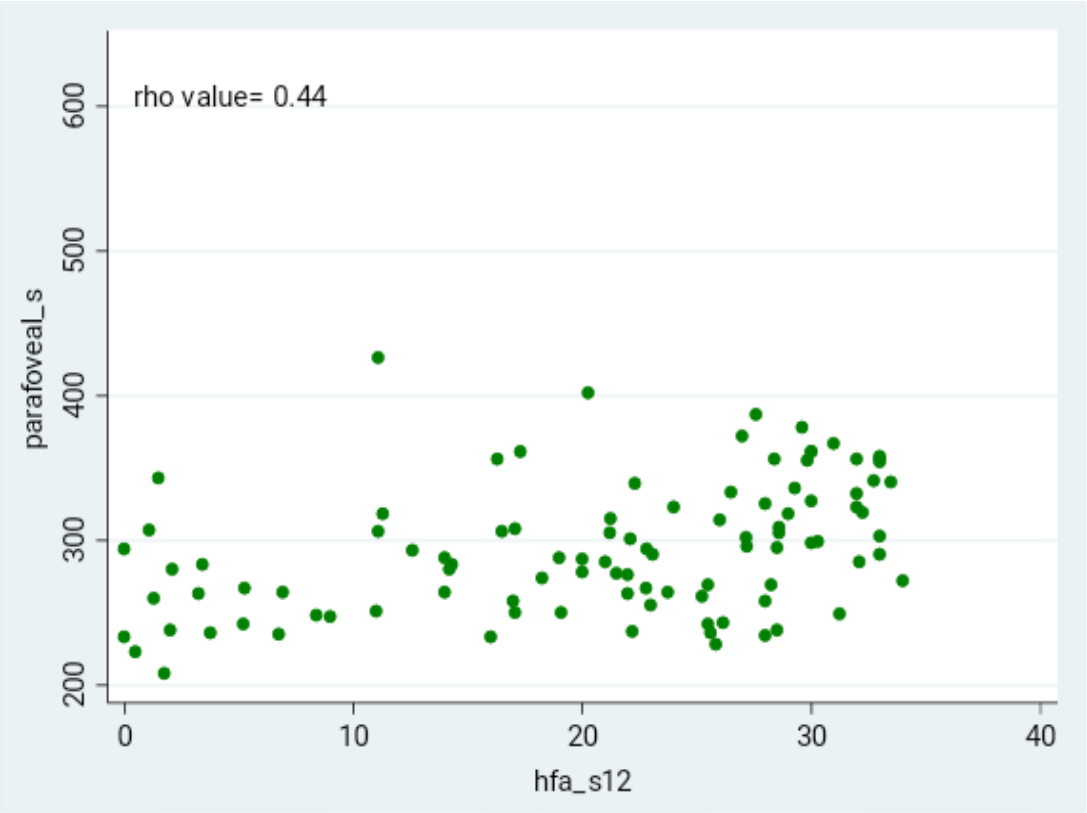


Figure 26:Scatter plot showing the correlation between HFA S12 and Parafoveal thickness (Superior) in RP

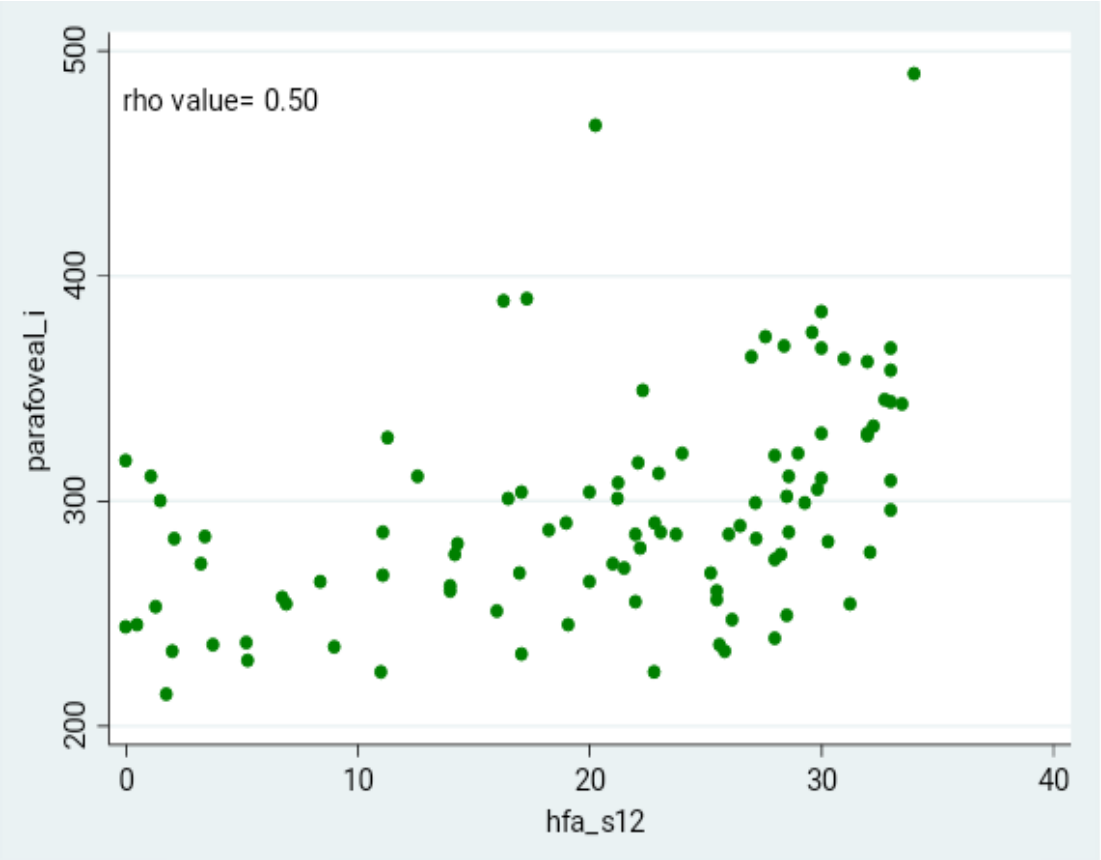


Figure 27:Scatter plot showing the correlation between HFA S12 and Parafoveal thickness (inferior) in RP.

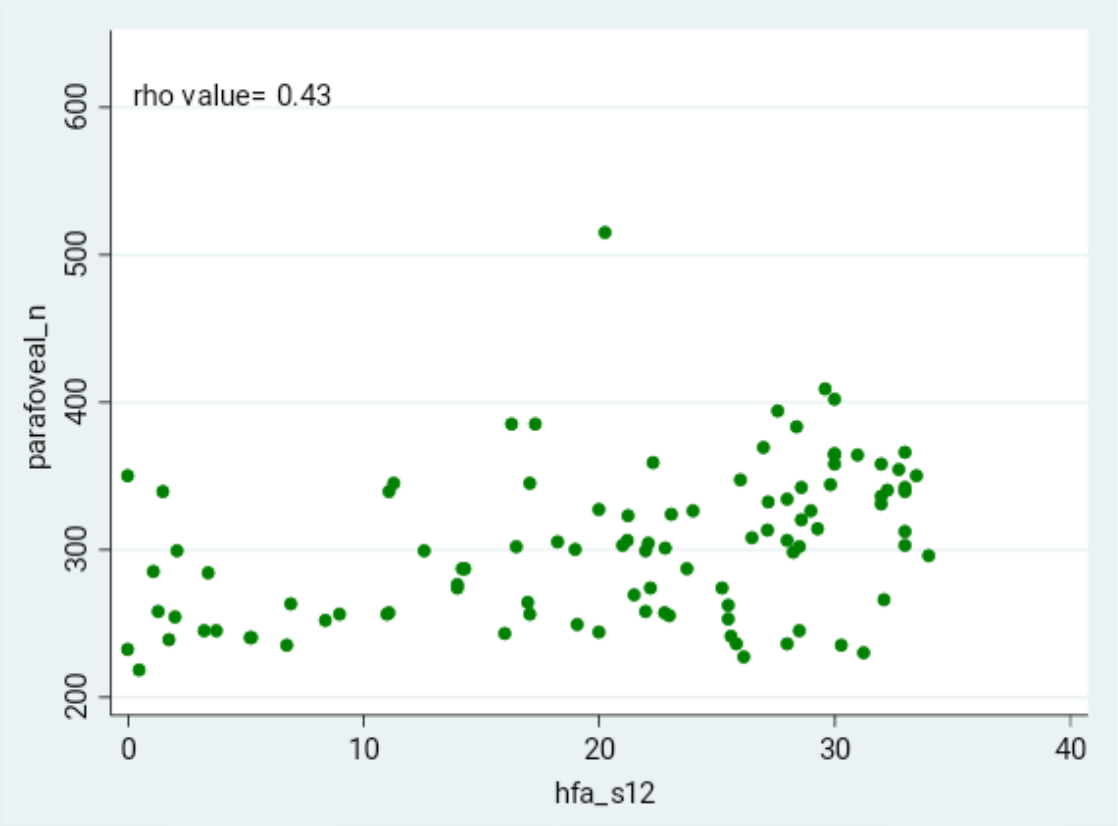


Figure28:**Scatter plot showing the correlation between HFA S12 and Parafoveal thickness (nasal) in RP**

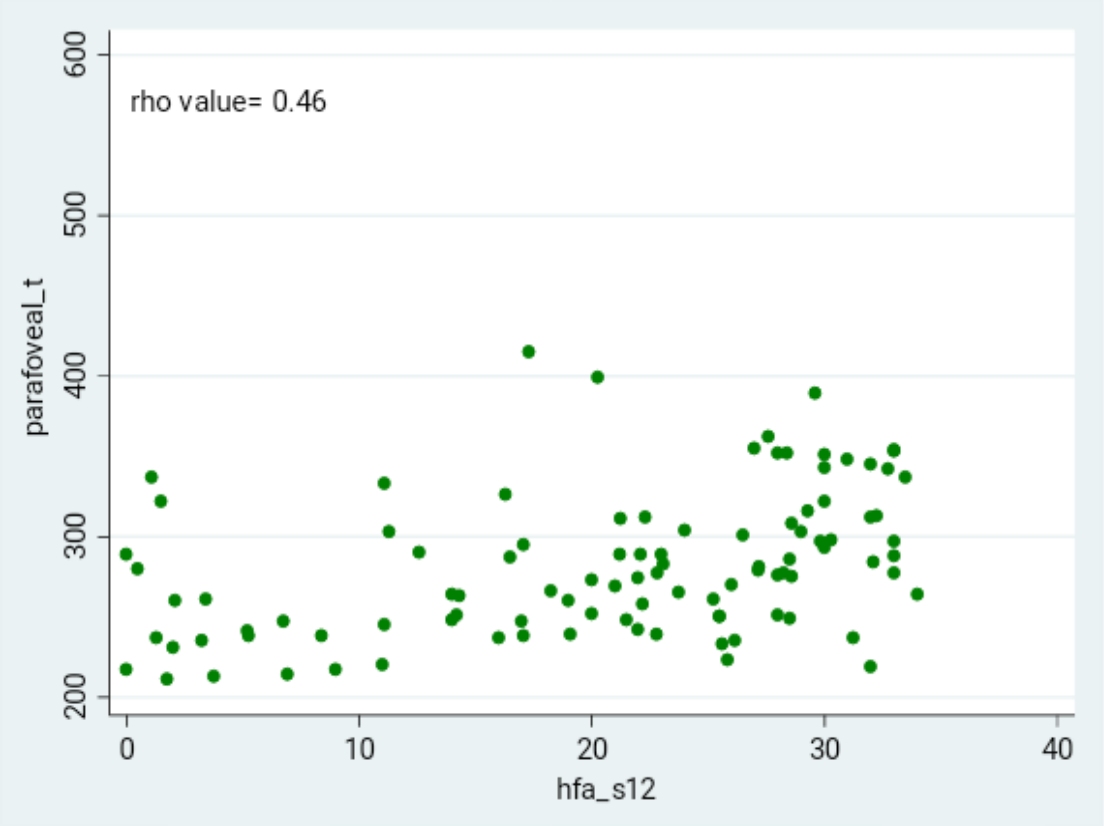


Figure29:Scatter plot showing the correlation between HFA S12 and Parafoveal thickness (Temporal) in RP

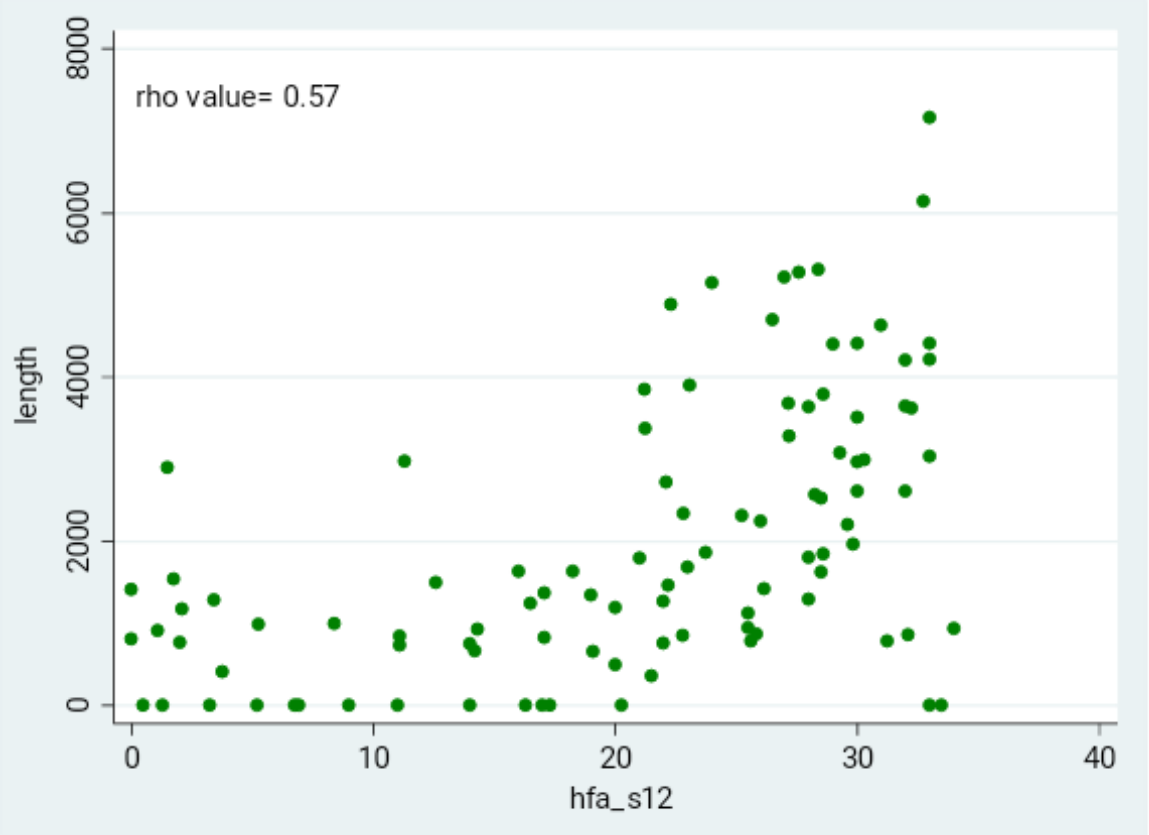


Figure 30:Scatter plot showing the correlation between HFA S12 and IS/OS line length in RP

Correlation between HFA S20 and structural parameters in RP Patients.

We analysed whether a significant correlation was present between average sensitivity of central 20 points on the HFA 10-2 and Structural parameters.

Table11:Correlation between HFA S20 and structural parameters in RP

Parameter	n	Rho	P-value[s]
HFA S20 Vs CMT	100	0.4227	<0.001
HFA S20 Vs CT	100	-0.0004	0.996
HFA S20 Vs AF ring	96	0.3274	0.001
HFA S20 Vs Optos AF ring	99	0.4664	<0.001
HFA S20 Vs Perifoveal thickness (S)	100	0.3334	0.0007
HFA S20 Vs Perifoveal thickness (I)	100	0.0637	0.5290
HFAS20Vs Perifoveal thickness (N)	100	0.3682	0.0002
HFA S20Vs Perifoveal thickness (T)	100	0.2146	0.032
HFA S20 Vs Parafoveal thickness (S)	100	0.4261	<0.001

HFAS20 Vs Parafoveal thickness (I)	100	0.5012	<0.001
HFA S20 Vs Parafoveal thickness (N)	100	0.4143	<0.001
HFAS20 Vs Parafoveal thickness (T)	100	0.4489	<0.001
HFAS20 Vs ISOS line length	100	0.5150	<0.001

HFA S 20 was moderatly correlated with central macular thickness($p<0.05$).HFA S20was weakly correlated with AF ring ,but moderately correlated with OPTOS AF ring ($p<0.05$) .HFAS 20 was weakly correlated with superior , nasal, temporalquadrant of Perifoveal thickness, moderately correlated with all quatrant s of parafoveal thickness ($p<0.05$).HFAS12 was moderately correlated with ISOS line ($p<0.05$).HFAS12 did not correlate with Perifoveal inferior thickness and choroidal thickness.

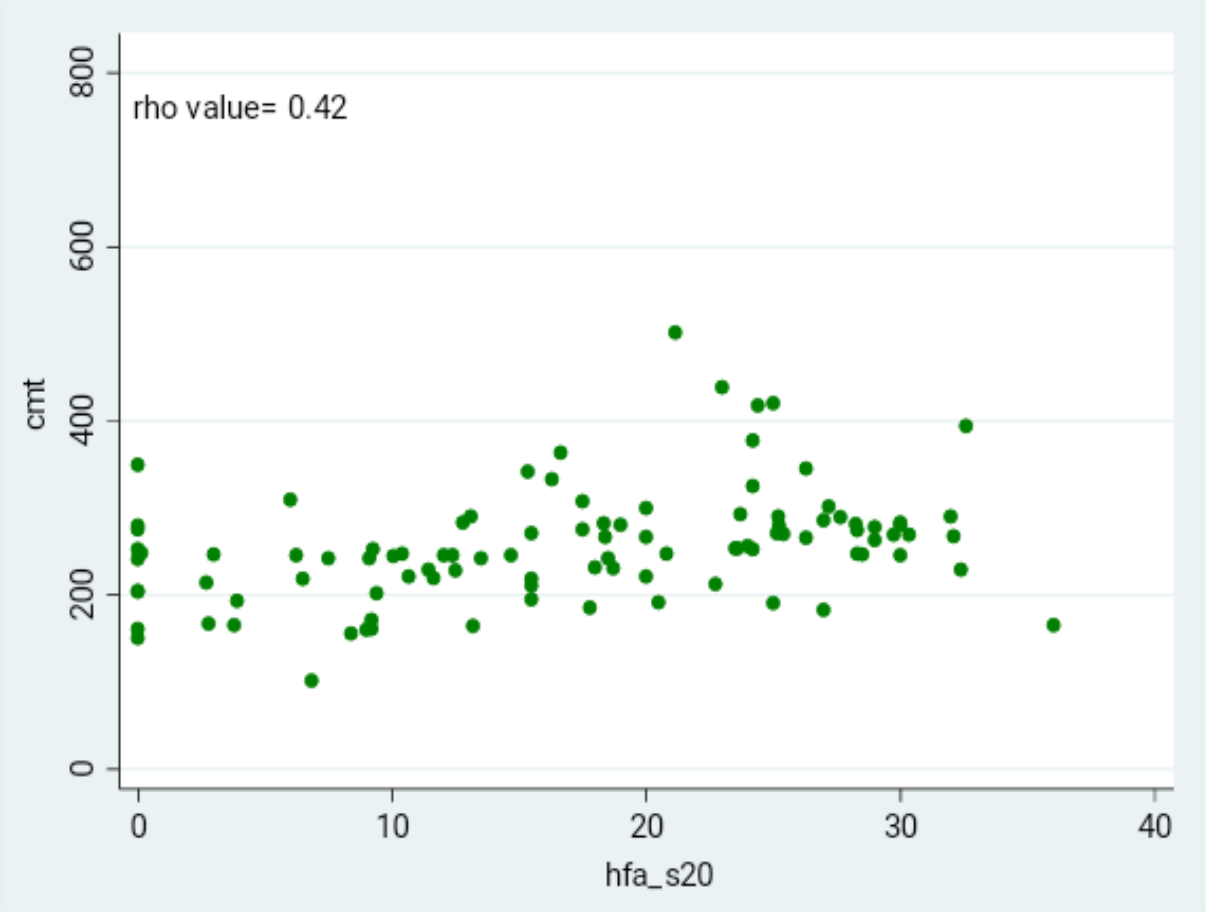


Figure 31:Scatter plot showing the correlation between HFA S20 and CMT in RP.

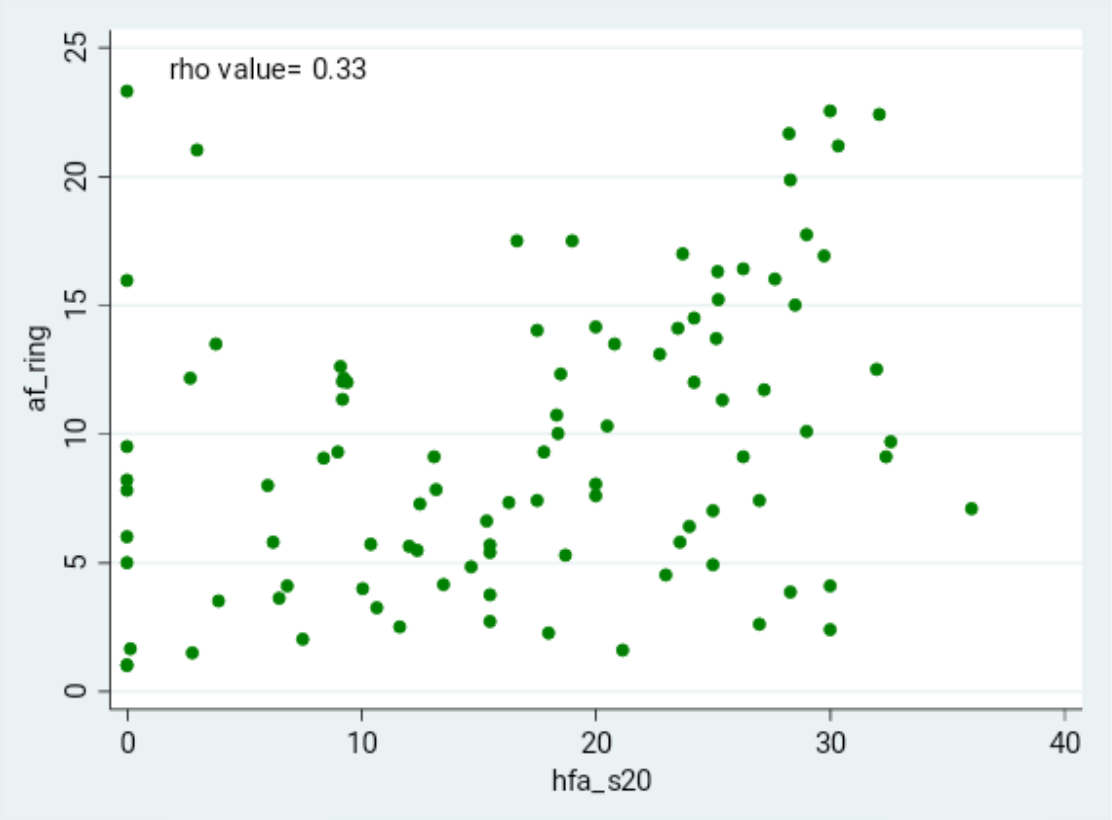


Table 32:Scatter plot showing the correlation between HFA S20 and AF ring of SD-OCT in RP.

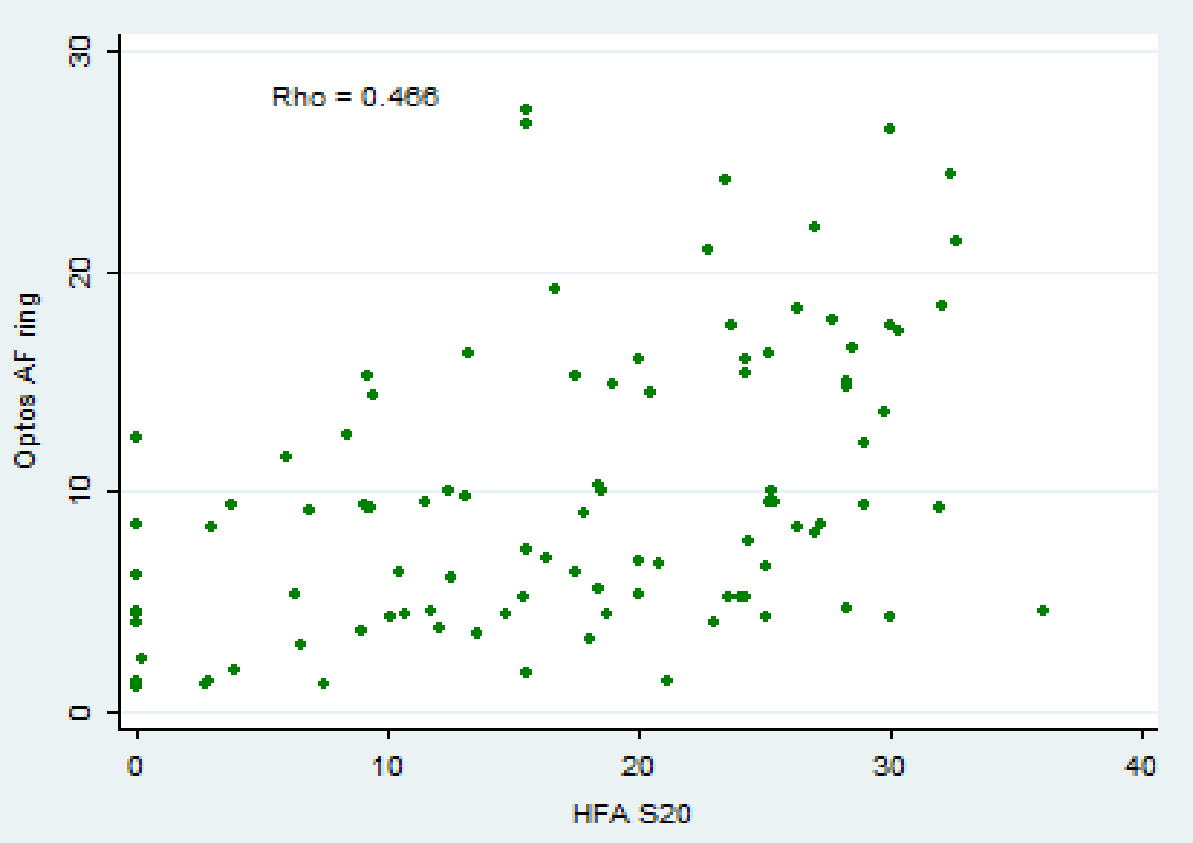


Figure 33:Scatter plot showing the correlation between HFA S20 and Optos AF ring in RP

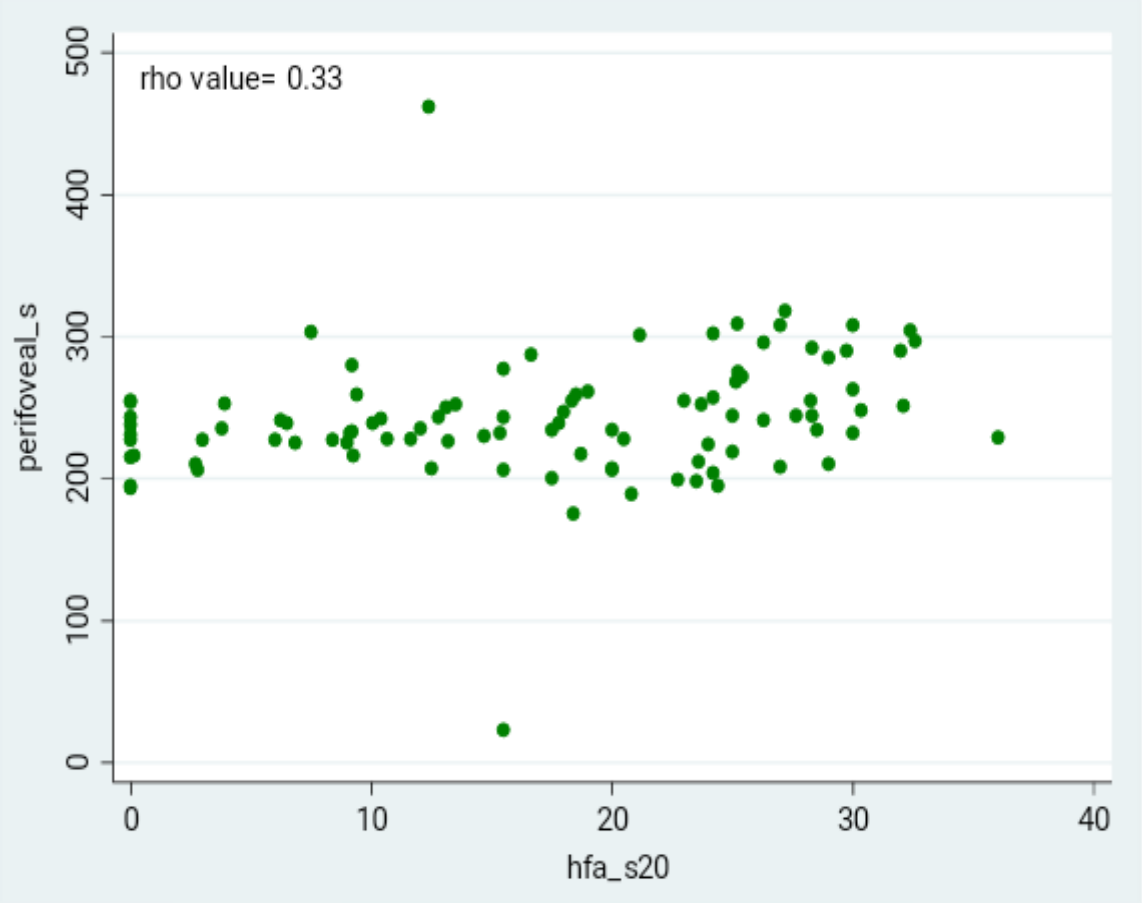


Figure 34: Scatter plot showing the correlation between HFA S20 and Perifoveal thickness (superior) in RP

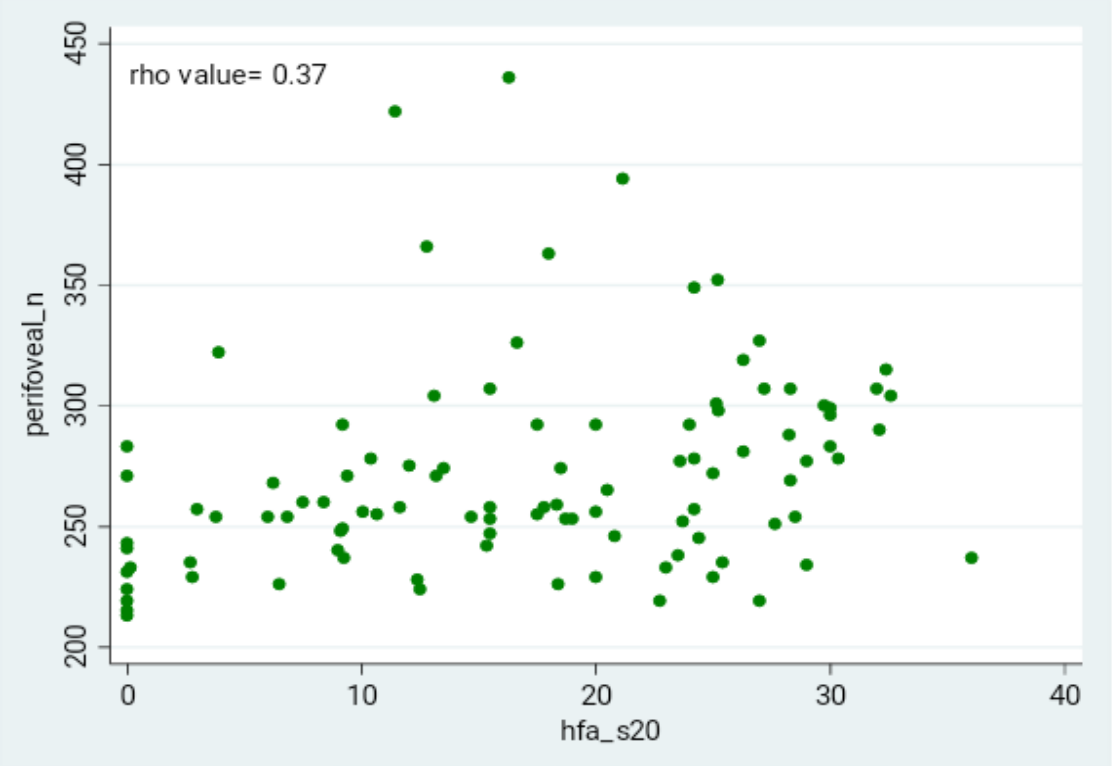


Figure 35:Scatter plot showing the correlation between HFA S20 and Perifoveal thickness(Nasal) in RP

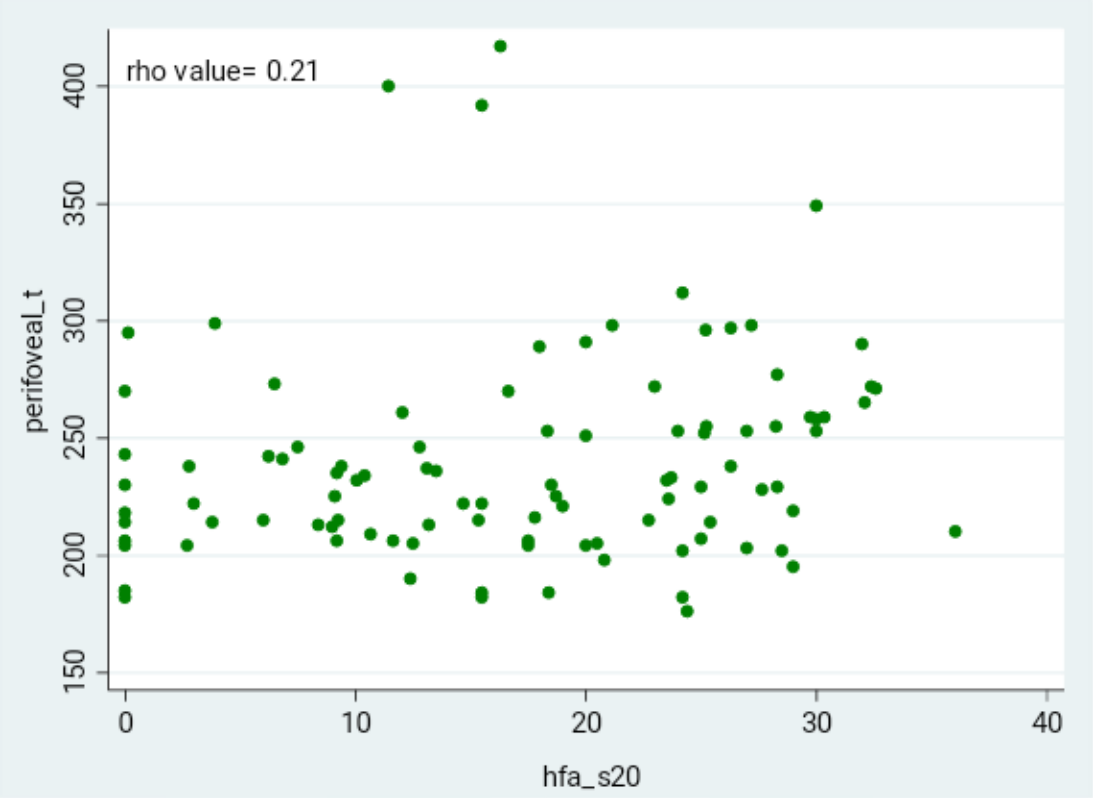


Figure36:Scatter plot showing the correlation between HFA S20 and Perifoveal thickness(Temporal) in RP

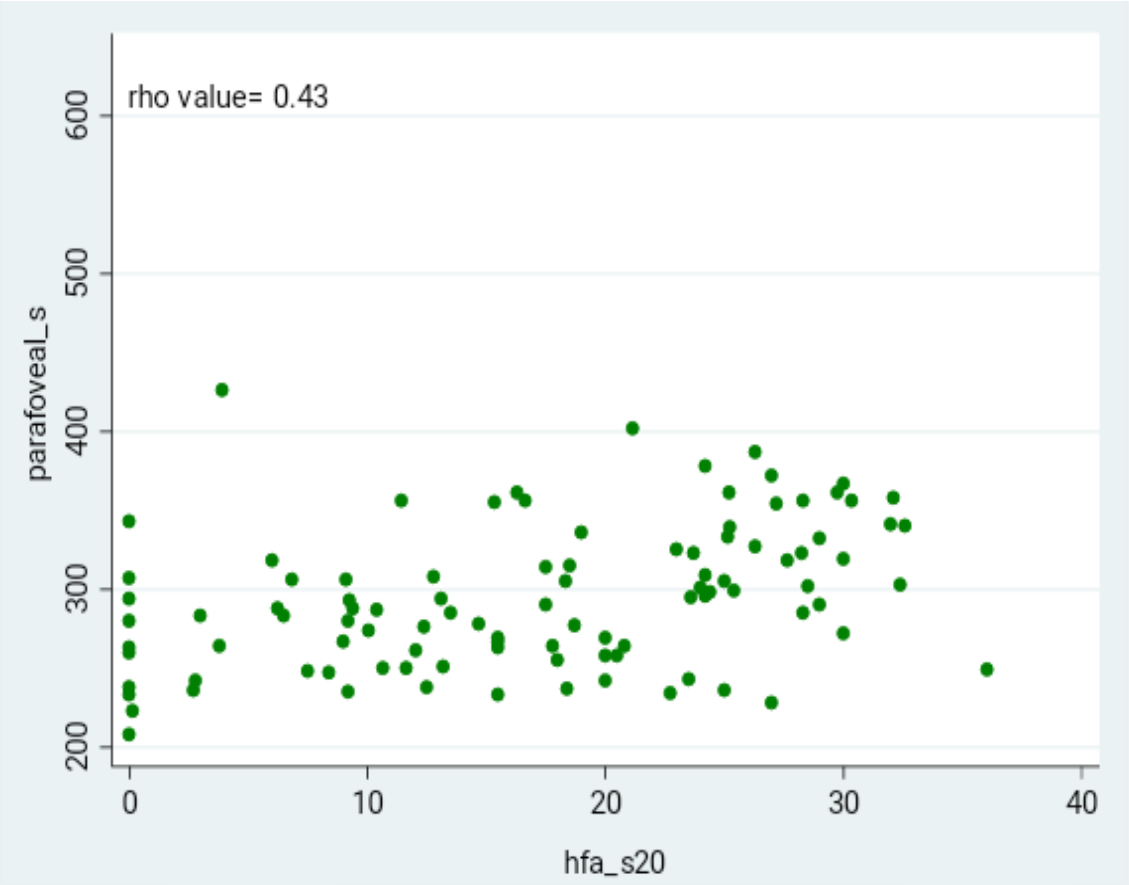


Figure37:Scatter plot showing the correlation between HFA S20 and Parafoveal thickness (Superior) in RP.

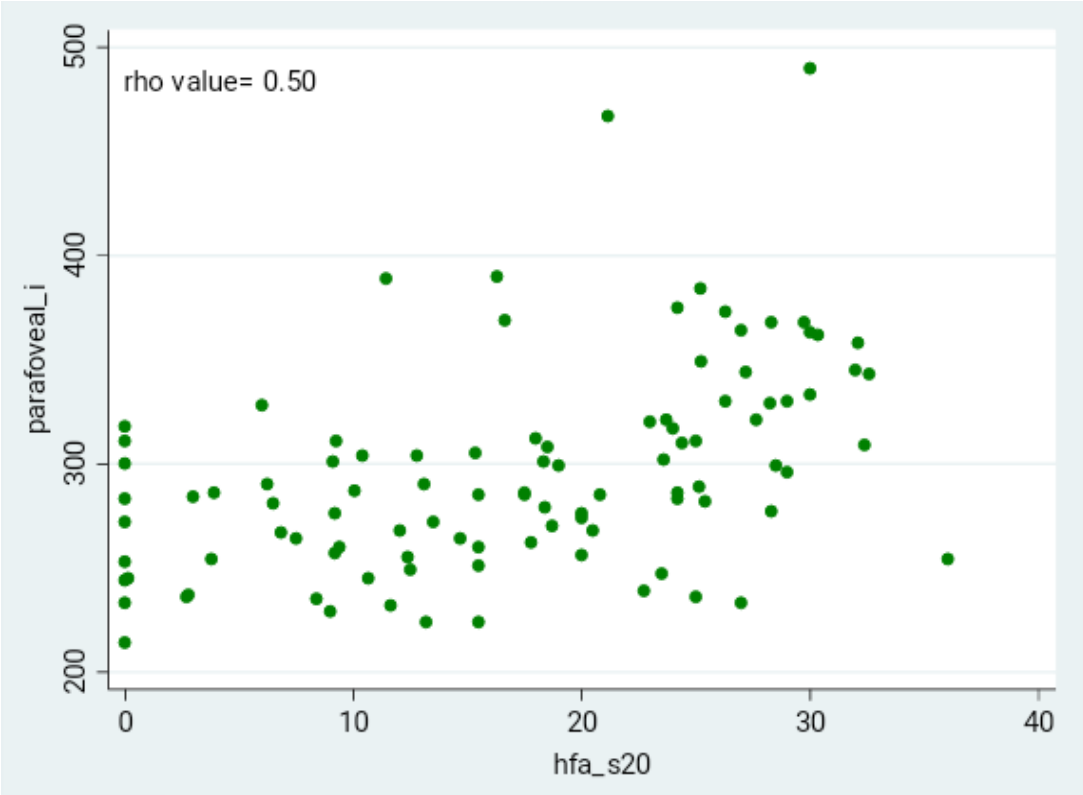


Figure 38:Scatter plot showing the correlation between HFA S20 and Parafoveal thickness (Inferior) in RP.

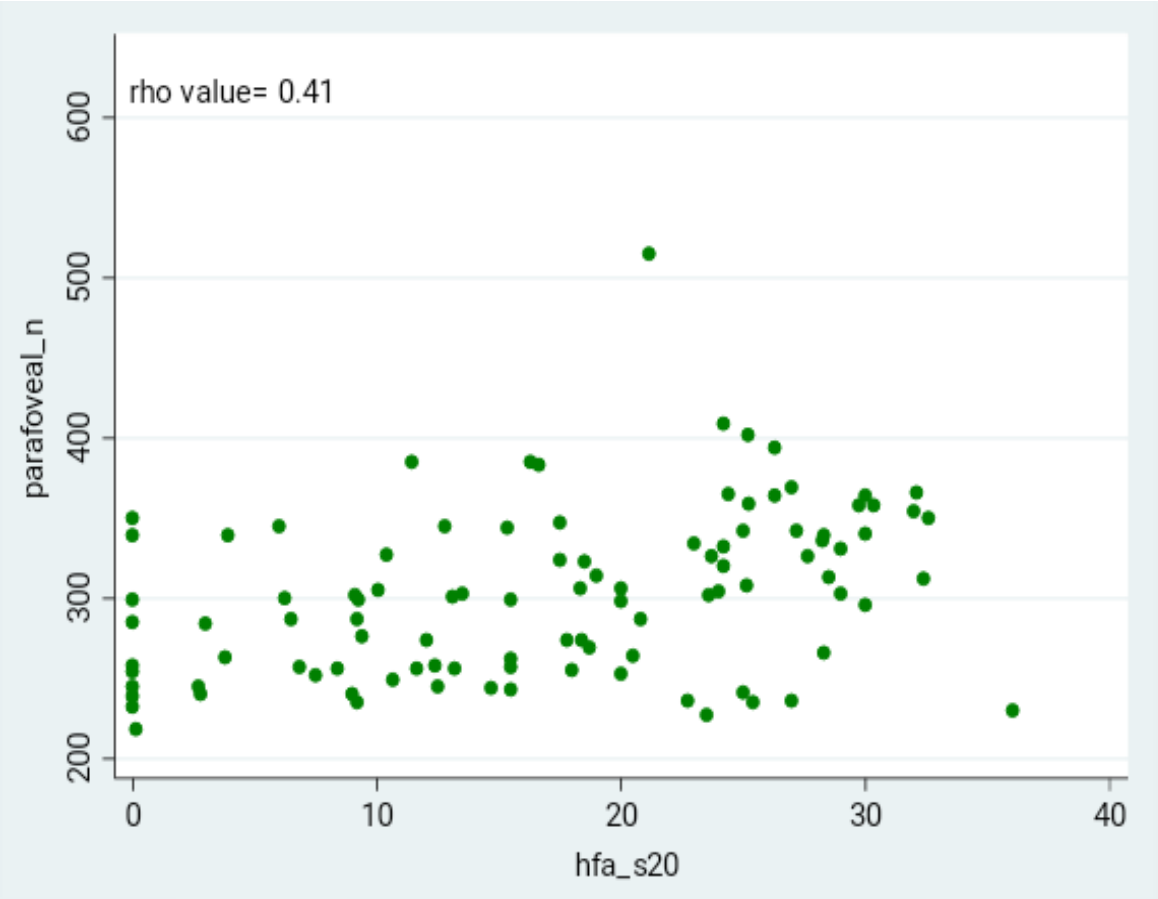


Figure 39:Scatter plot showing the correlation between HFA S20 and Parafoveal thickness (Nasal) in RP

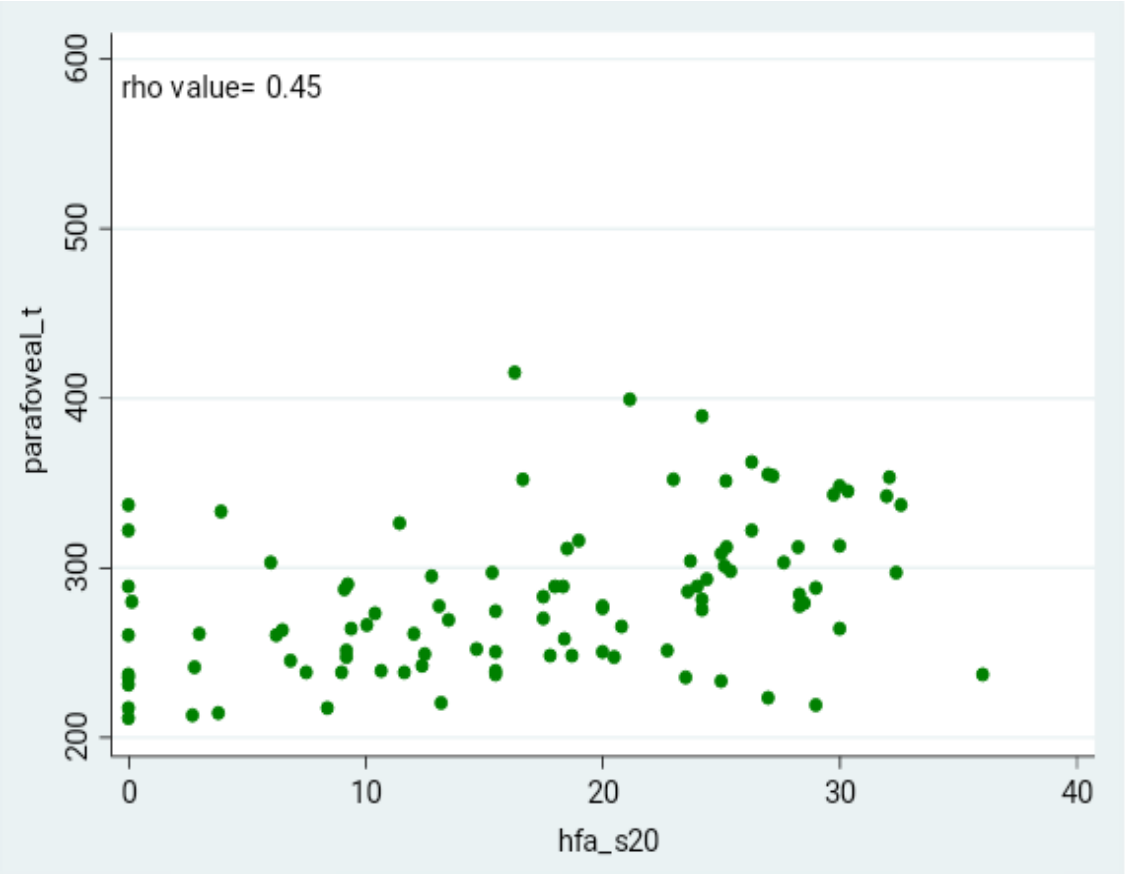


Figure 40:Scatter plot showing the correlation between HFA S20 and Parafoveal thickness (Temporal) in RP

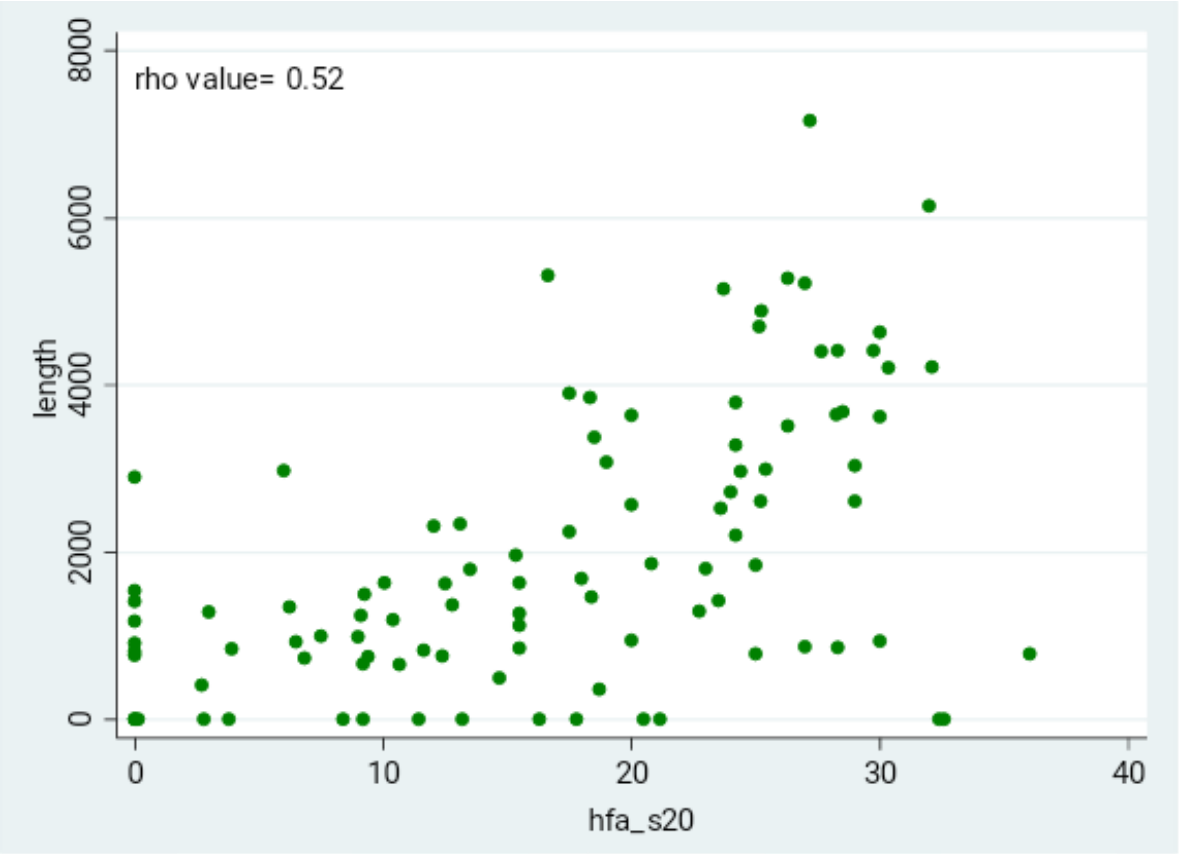


Figure41:Scatter plot showing the correlation between HFA S20 and IS/OS line Length in RP.

Correlation between average threshold and structural parameters in RP

The average retinal sensitivity calculated by the recently introduced micro perimetery , these retinal sensitivity observed as average threshold.

We analysed whether a significant correlation was present between the average threshold and structural parameters in RPpatients.

Table12:**Correlation between average threshold and structural parameters in RP.**

Parameter	n	Rho	P-value[s]
Average threshold Vs CMT	102	0.5412	<0.001
Average threshold Vs CT	102	0.0774	0.4394
Average threshold Vs af ring	96	0.4869	<0.001
Average threshold Vs Optos af ring	99	0.5309	<0.001
Average threshold Vs Perifoveal S	102	0.3432	0.0004
Average threshold Vs Perifoveal I	102	0.0427	0.670
Average threshold Vs Perifoveal N	102	0.2899	0.003

Average threshold Vs Perifoveal T	102	0.1578	0.113
Average threshold Vs Parafoveal S	102	0.5348	<0.001
Average threshold Vs Parafoveal I	102	0.4950	<0.001
Average threshold Vs Parafoveal N	102	0.5276	<0.001
Average threshold Vs Parafoveal T	102	0.4828	<0.001
Average threshold Vs ISOS line length	102	0.6211	<0.001

Average threshold was moderately correlated with central macular thickness($p<0.05$).Average threshold was moderatly correlated with AF ring ,OPTOS AF ring ($p<0.05$) . Average threshold was Moderately correlated with all quadrants of parafoveal thickness and weakly correlated with superior , nasal quadrant of perifoveal thickness p(<0.05).Average threshold was strongly correlated with ISOS line($p<0.05$).Average threshold did not correlate with perifoveal inferior ,temporal quadrant thickness and choroidal thickness ($p >0.05$).

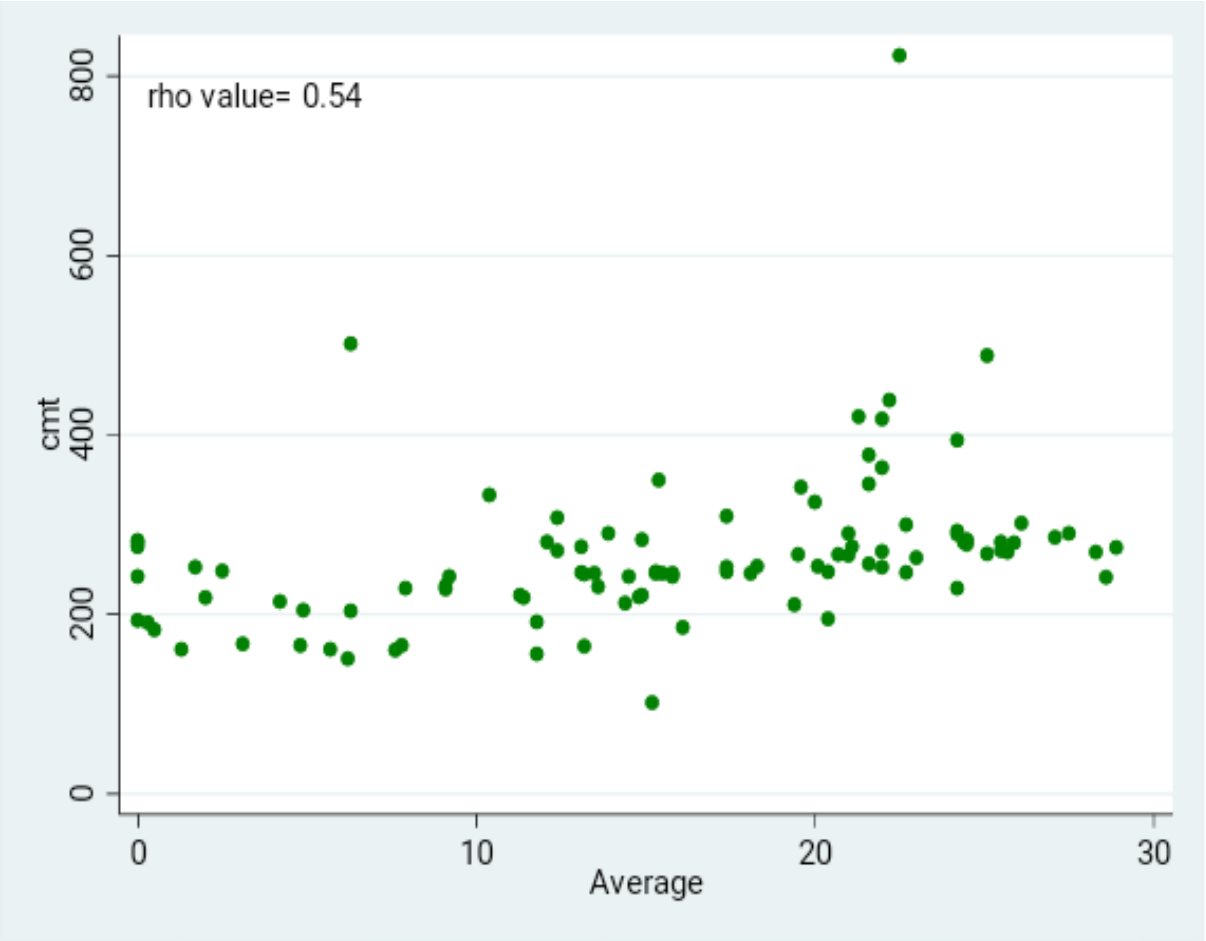
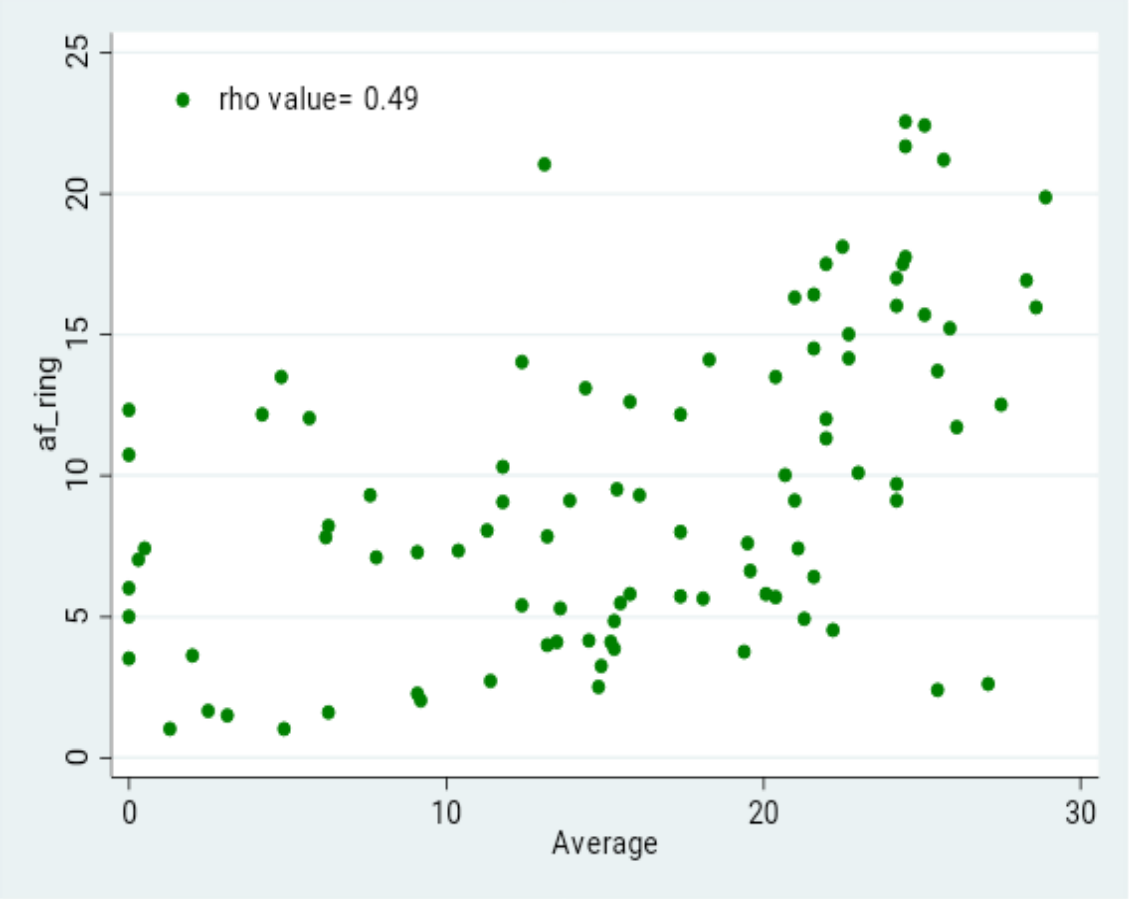


Figure42:Scatter plot showing the correlation between average threshold of microperimetry and CMT in RP



Figire43:Scatter plot showing the correlation between average threshold of microperimetry and AF ring of SD-OCTin RP

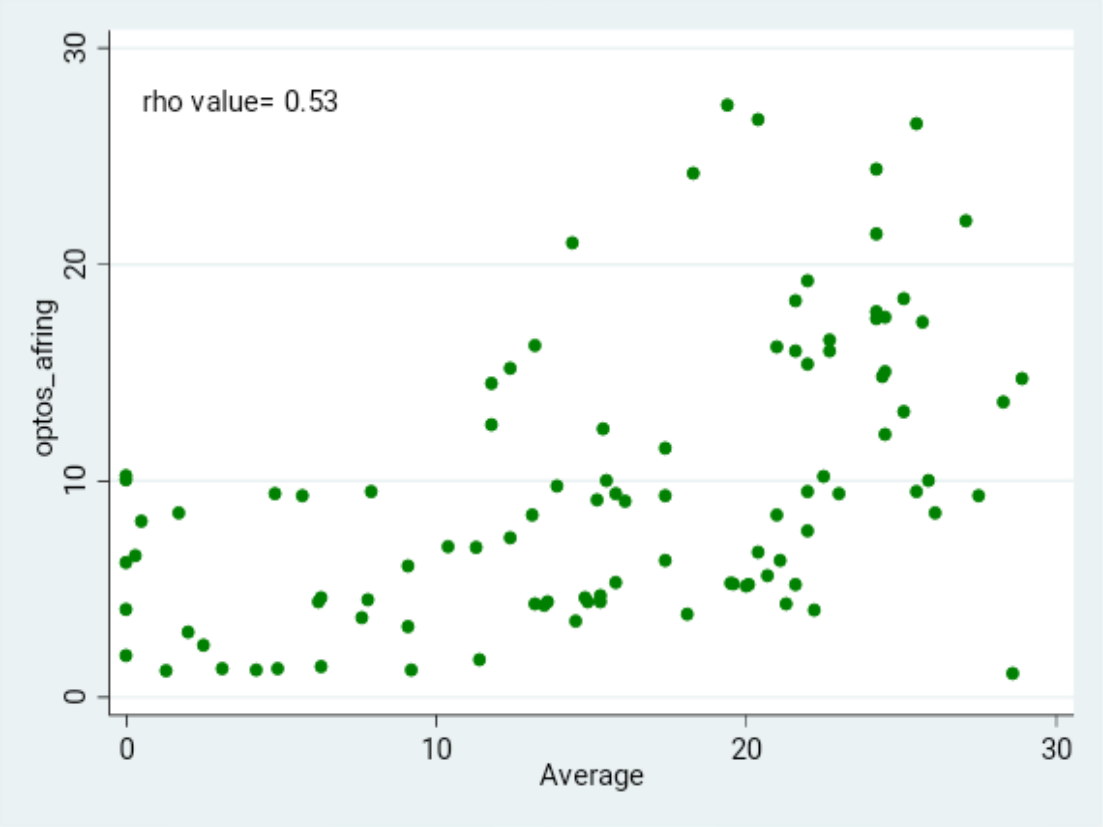


Figure 44:Scatter plot showing the correlation between average threshold of microperimetry and OPTOS AF ring in RP

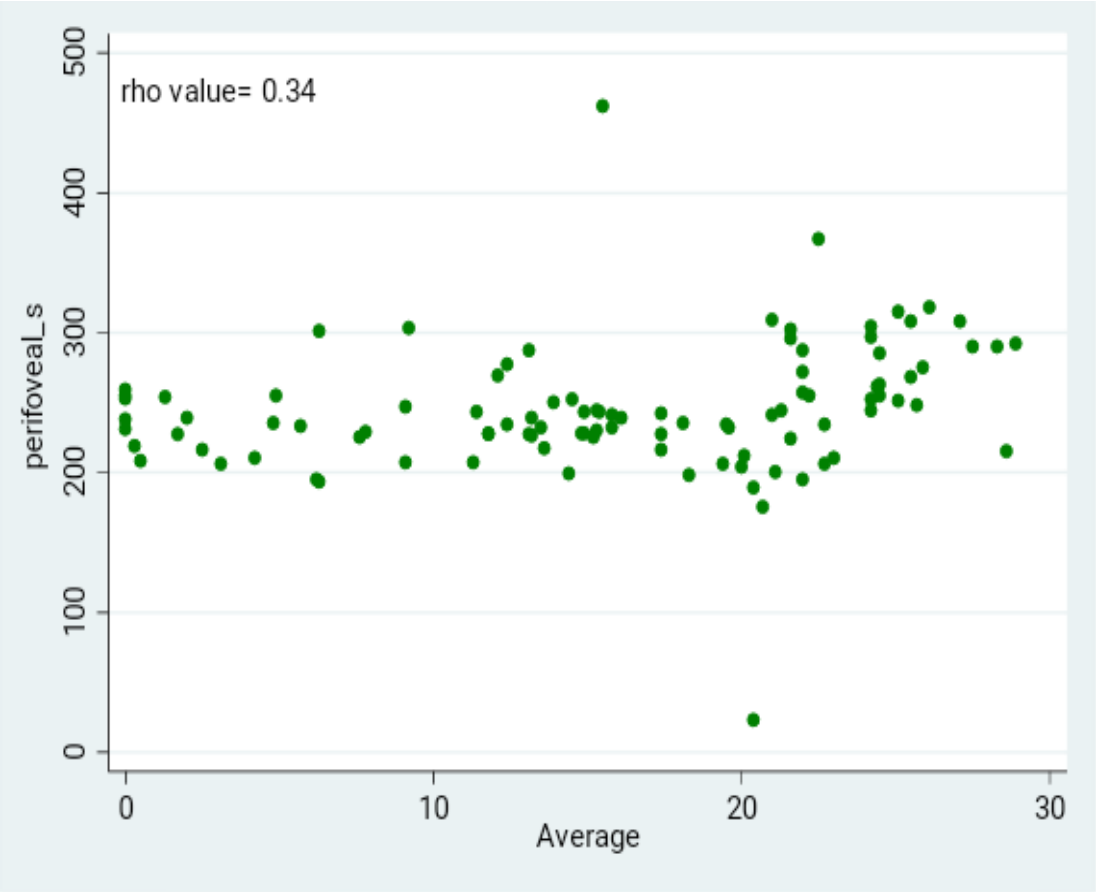


Figure45:Scatter plot showing the correlation between average threshold of microperimetry and perifoveal thickness(superior) in RP

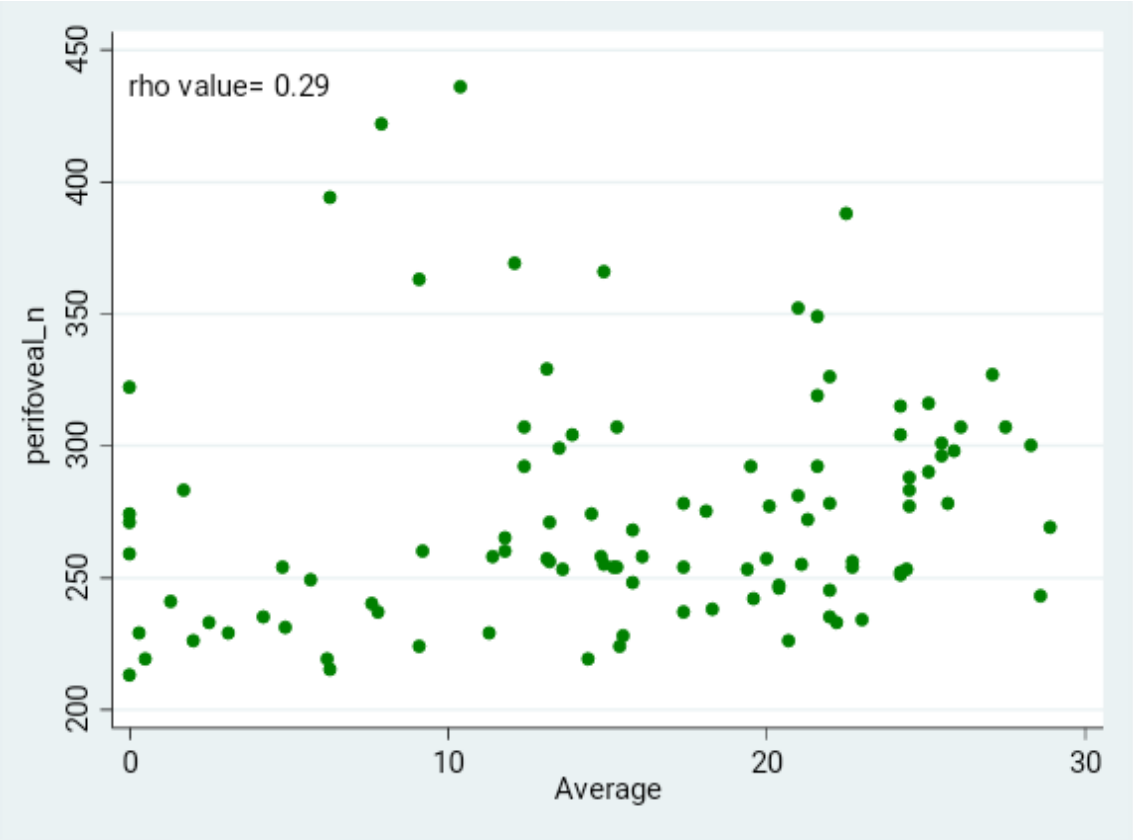


Figure 46:Scatter plot showing the correlation between average threshold of microperimetry and Perifoveal thickness(Nasal)

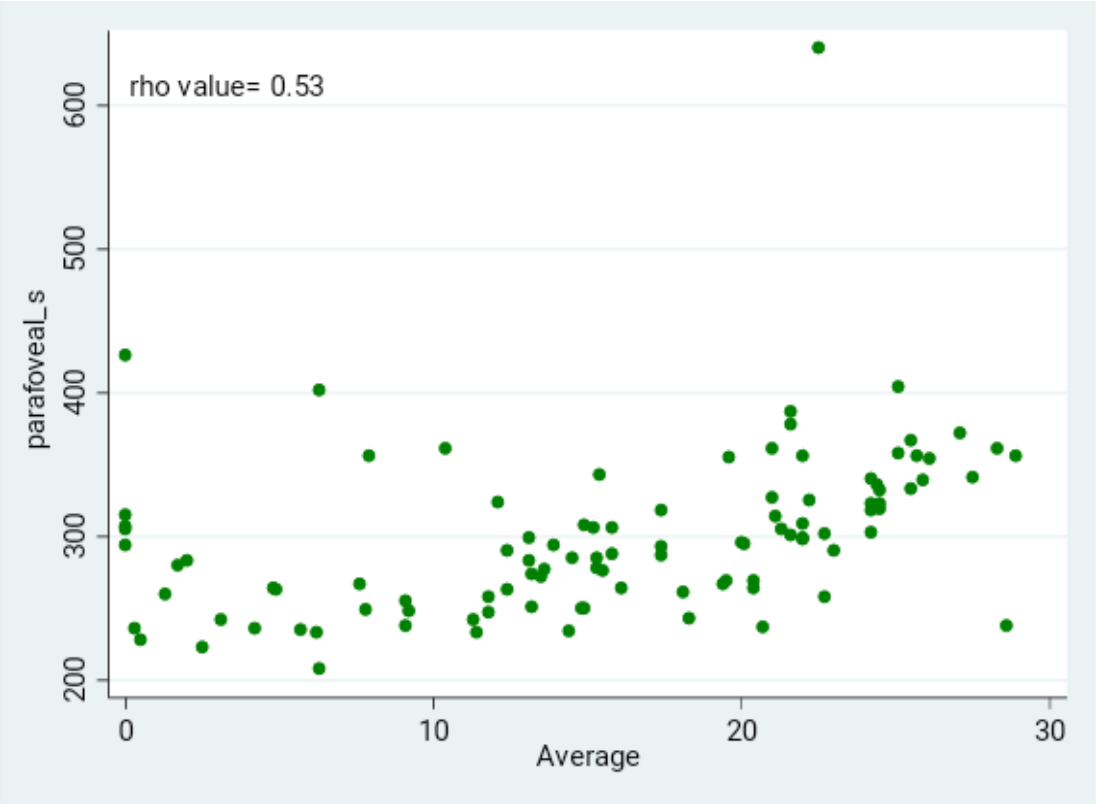


Figure 47:Scatter plot showing the correlation between average threshold of microperimetry and Parafoveal thickness(Superior) in RP

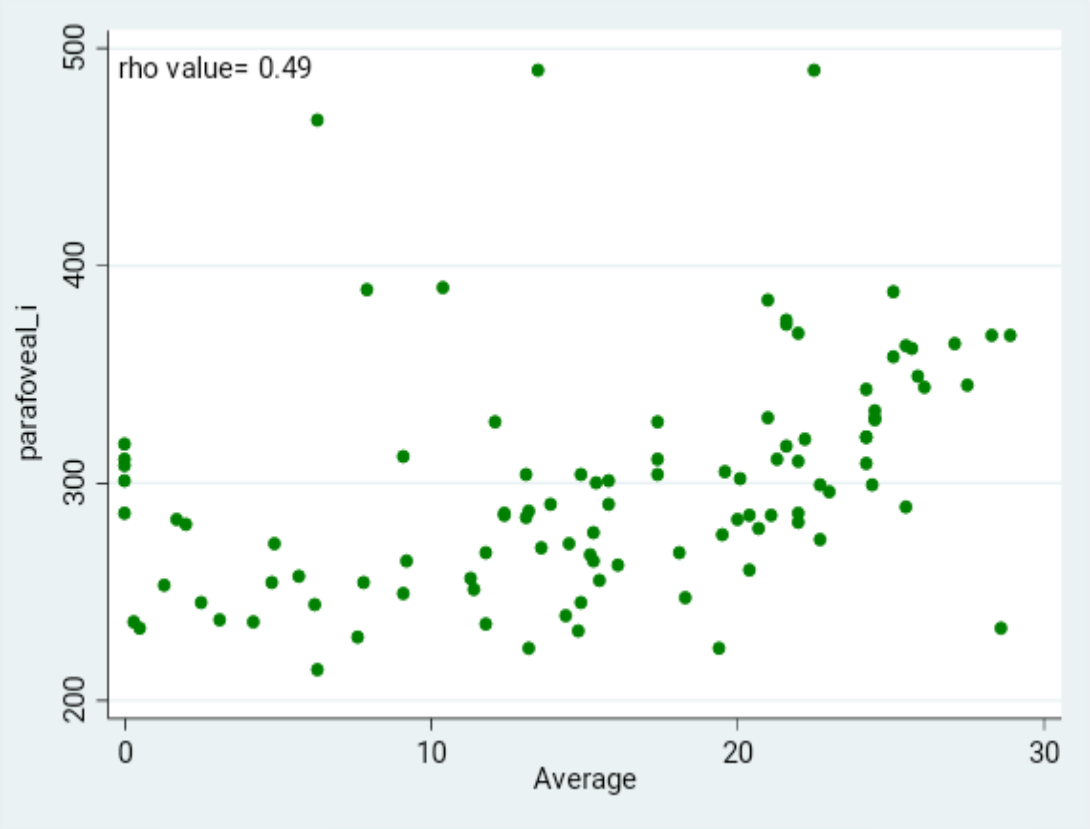


Figure 48:Scatter plot showing the correlation between average threshold of microperimetry and Parafoveal thickness (Inferior) in RP

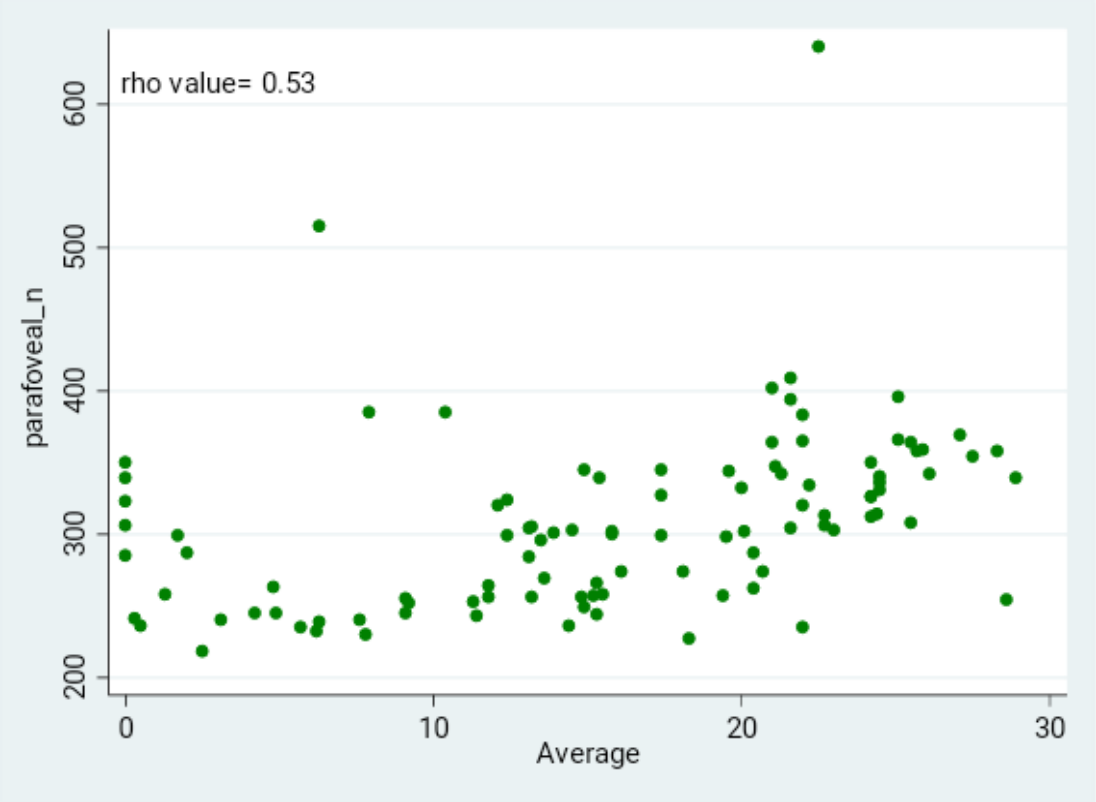


Figure 49:Scatter plot showing the correlation between average threshold of microperimetryand Parafoveal (Nasal) in RP

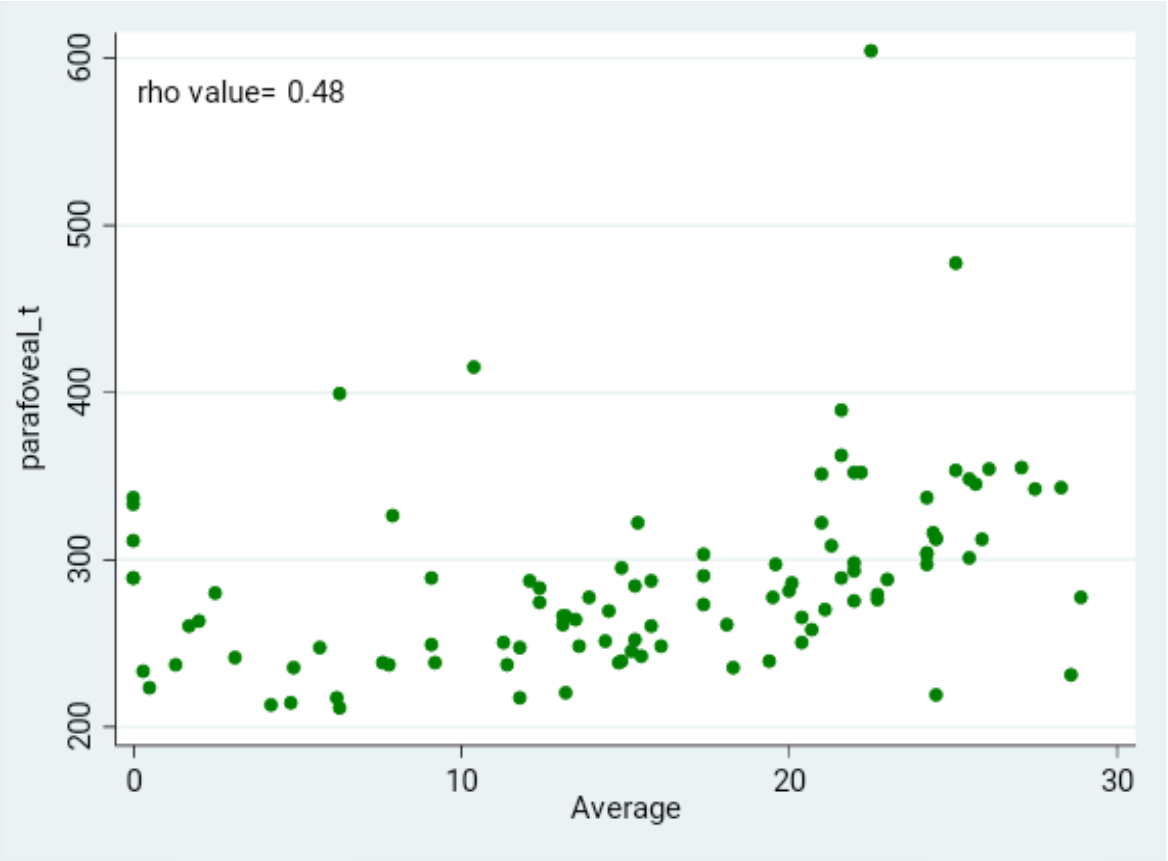


Figure 50:Scatter plot showing the correlation between average threshold of microperimetry and Parafoveal thickness (Temporal) in RP

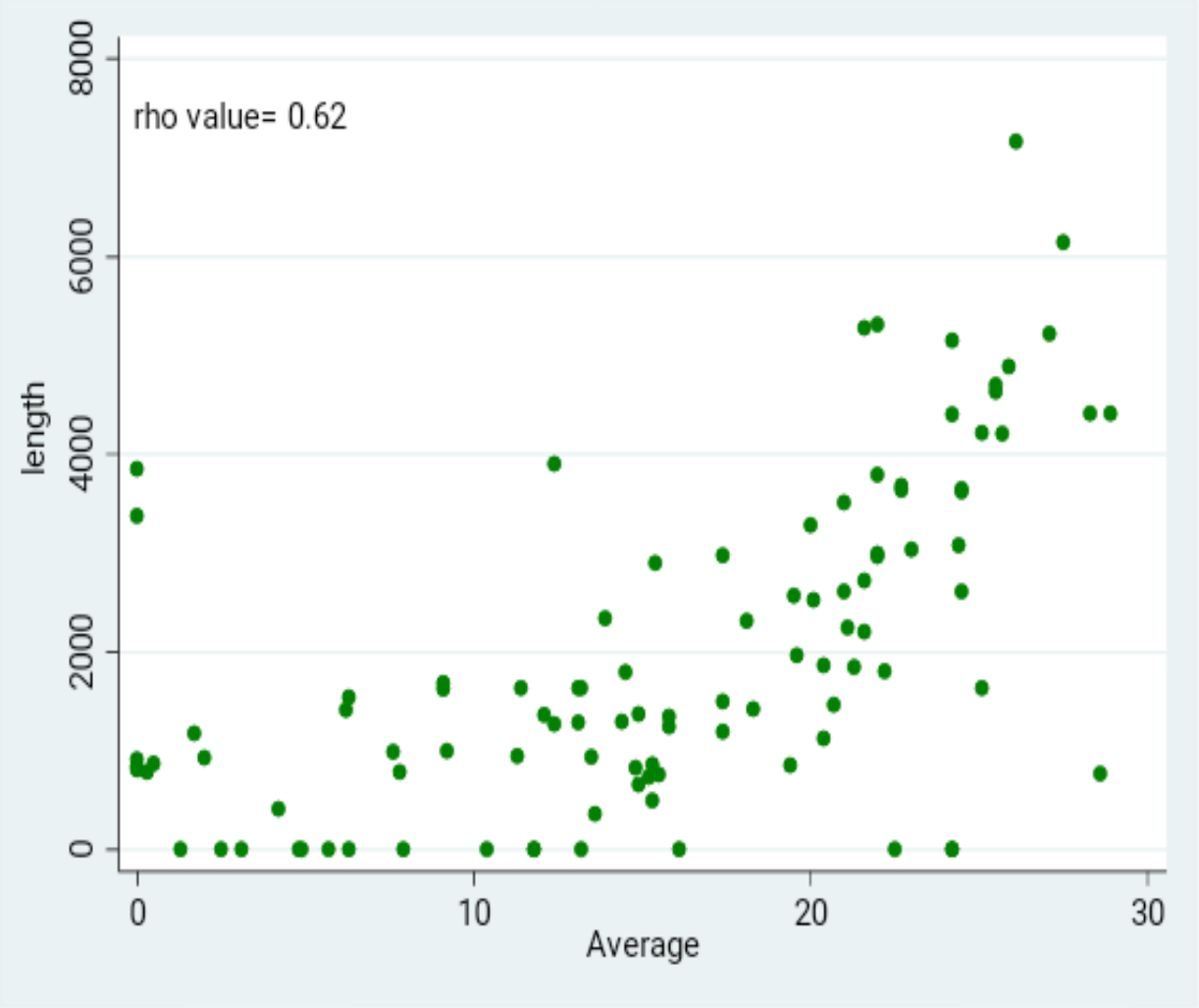


Figure51:Scatter plot showing the correlation between average threshold of microperimetry and IS/OS line Length in RP

Discussion

DISCUSSION

This cross-sectional observational study evaluated 104 eyes of 53 patients suffering from RP. We studied the correlation between structural and functional changes in the retina in RP patients.

Structural parameters in this study included central macular thickness, choroidal thickness, peri foveal and parafoveal thickness in four quadrants and IS/OS line length (all recorded using OCT on Spectralis HRA), size of autofluorescence ring measured by Spectralis HRA and size of autofluorescence ring measured by OPTOS pseudo-colour, wide-field imaging device.

Functional parameters included visual acuity measured with Snellen's chart, visual field measured by HFA 10-2 automated static perimetry and average retinal sensitivity measured by microperimetry.

Our results showed that visual acuity of RP eyes correlated negatively with increasing central macular thickness. In previous studies however, presence of CME in RP patients has not been found to correlate with loss of visual acuity.[11]

In literature, sub-foveal choroidal thickness has been found to be reduced in RP patients, which again has not been noted to correlate with visual acuity or retinal thickness.[33] Similarly, we observed that visual acuity did not correlate with sub-foveal choroidal thickness. However,

since we have not taken any control group, we could not compare the absolute values of choroidal thickness.

The autofluorescent ring observed in Spectralis HRA images in RP patients represents the border between functional and dysfunctional retina. Hyper autofluorescence is generally observed in this area and an association with between the size of this hyper-autofluorescent zone and functional or structural changes of photoreceptors has been descirbed in previous studies. [30,46-54] In RP patients, this AF ring size has been observed to decrease with the progression of disease.[31] Moreover, RP patients with larger AF ring may have better central vision. Hence, the AF ring size seems to have a prognostic value of indicating visual loss in RP patients.[8] The recently introduced wide field fundus imaging technique using OPTOS is useful to evaluate the fundus autofluorescence images in a broader area of retina.[30] The fundus image of RP shows a similar ring-shaped hyperautofluorescence area on OPTOS. Again, constriction of this AF ring has been seen to be associated with macular function changes in RP patients.[30,55-59] Our study has found that size of the AF ring measured on Spectralis HRA and OPTOS both correlated with visual acuity, indicating that a larger AF ring diameter correlated with better visual acuity in RP. It was weakly corelating with visual acuity.

Macular thickness calculation in our study was done based on the 6 mm retinal thickness map as has been previously done.[60] The para- and peri-foveal area was divided by the software's automatic algorithm into superior, inferior, nasal and temporal quadrants. The centre macular thickness in our RP study eyes was thinner. The macular thickness was thicker in all the quadrants within the 3 mm ring, and thickness was reduced in the quadrants in the 6 mm zone. Overall thickest quadrants were superior and nasal, with temporal being the thinnest. In RP, retinal degeneration starts in the mid-periphery of the fundus and at a later stage progresses towards the macula.[5] The inferior thickness of parafoveal macular area has been found to remained unchanged in RP patients, while the inner temporal area has been found to be most commonly affected.[61]

We noted that perifoveal inferior quadrant thickness and parafoveal thicknesses weakly correlated with foveal visual acuity. However, perifoveal thickness in our study eyes did not directly correlate with foveal vision. Perifoveal macular thickness correlated with the size of AF ring on OPTOS and Spectralis both. Since the AF ring size measured both on Spectralis and OPTOS also correlated with visual acuity, it may be concluded that perifoveal thickness may in fact be an indirect prognostic indicator of central vision.

IS/OS line measured in the OCT image represents inner/ outer segment junction of the photoreceptors.[62] An intact IS/OS line indicates

the presence of functioning anatomically normal photoreceptors. Hence, normal IS/OS line indicates good visual function. Shortening of IS/OS line length may indicate pathological changes in photoreceptors.[31] Our study revealed that IS/OS line was negatively correlated with central visual acuity. From this observation, we can say that that ultrastructural morphological changes detected on OCT, apart from macular thickness can also reflect the functional changes in RP patients.

In our RP study eyes, macular thinning was found to be associated with reduction in visual acuity and retinal sensitivity. We found that retinal sensitivity moderately correlated with macular thickness. with the correlation decreasing towards periphery of the macula.

Our findings showed that AF ring sizes on Spectralis HRA and OPTOS were moderately correlated with threshold values on visual fields of RP patients. In RP patients, hyper-autofluorescent ring has been shown to be associated with measures of retinal function, namely visual field and microperimetry.[28,63-65] Automated static perimetry has been previously demonstrated to show significant deterioration in the 10°central field. [28,66] Hyperfluorescent ring constriction may also be associated with the progression of visual field loss.[8,67] This indicates that larger AF ring is associated with better retinal sensitivity. During the progression of RP, constriction of AF ring may be associated with a decrease in retinal sensitivity.

IS/OS line length has been previously found to be significantly correlated with mean retinal sensitivity observed by microperimetry.[62] We also found that average threshold on microperimetry was moderately correlated with structural changes in the IS/OS line. IS/OS line length strongly correlated with average threshold. This association indicates that a short IS/OS line may be associated with reduced retinal sensitivity. The size of AF ring decreases during progression of RP and this may be associated with shortening of IS/OS line length, thereby decreasing the retinal sensitivity. Hence, a large diameter of AF ring and long and intact IS/OS line may be associated with good retinal function.

Limitation

LIMITATION

The limitations of this study were that the sample size was relatively small, and this was a cross-sectional study. The patients were not followed up to study the progression patterns of the structural and functional changes measured using the different modalities. Future longitudinal studies may be planned to look into this further.

Conclusion

CONCLUSION

Multi-modal imaging to detect structural (OCT, OPTOS and reflectance imaging on Spectralis) and functional changes (microperimetry, static automated perimetry) in the retina may be useful to study RP patients. All of these modalities may give us more insight into degenerative nature of the disease, apart from simply detecting visual loss in these patients. Apart from adding on to the diagnostic staging of the disease at a current date, these changes may reflect the future progression pattern of the disease and help us in prognosticating the patients regarding future risk of visual loss and the rate at which it might happen. Moreover, these structural and functional changes may also be useful for staging and selecting the patients for any future clinical trials that may begin, using newer modalities of therapy like immunomodulation, gene therapy, etc.

BIBLIOGRAPHY

REFERENCES:

1. Natarajan S. Retinitis pigmentosa: a brief overview. Indian J Ophthalmol. 2011;59:343–6. Vinchurkar MS, Sathye SM, Dikshit M. Retinitis pigmentosa genetics: a study in Indian population. Indian J Ophthalmol. 1996;44:77–82.
2. Vinchurkar MS,sathye SM, Dikshit M.Retinitis pigmentosa genetics:a study in Indian population. Indian J ophthalmology.1996,44:77-82
3. BoughmanJA,FishmanGA. A genetic analysis of retinitis pigmentosa. Br J Ophthalmol. 1983;67:449–54.
4. Bundey S, Crews SJ. A study of retinitis mentosa in the City of Birmingham. I Prevalence. J Med Genet. 1984;21:417–20.
5. Ferrari S, Di Iorio E, Barbaro V, Ponzin D, Sorrentino FS, Parmeggiani F. Retinitis pigmentosa: genes and disease mechanisms. Curr Genomics. 2011;12:238–49.
6. Hamel C. Retinitis pigmentosa. Orphanet J Rare Dis. 2006;1:40
7. Zhang Q. Retinitis Pigmentosa: Progress and Perspective. Asia Pac J Ophthalmol (Phila). 2016;5:265–71.
8. Lima LH, Cella W, Greenstein VC, Wang N-K, Busuioc M, Smith RT, et al. Structural assessment of hyperautofluorescent ring in

patients with retinitis pigmentosa. Retina (Philadelphia, Pa). 2009;29:1025–31.

9. Ikeda Y, Yoshida N, Murakami Y, Nakatake S, Notomi S, Hisatomi T, et al. Long-term Surgical Outcomes of Epiretinal Membrane in Patients with Retinitis Pigmentosa. Sci Rep. 2015;5:13078.

10. Strong S, Liew G, Michaelides M. Retinitis pigmentosa-associated cystoid macular oedema: pathogenesis and avenues of intervention. Br J Ophthalmol. 2017;101:31–7.

11. Kim YJ, Joe SG, Lee D-H, Lee JY, Kim J-G, Yoon YH. Correlations between spectral-domain OCT measurements and visual acuity in cystoid macular edema associated with retinitis pigmentosa. Invest Ophthalmol Vis Sci. 2013;54:1303–9.

12. Hassan-Karimi H, Jafarzadehpur E, Blouri B, Hashemi H, Sadeghi AZ, Mirzajani A. Frequency Domain Electroretinography in Retinitis Pigmentosa versus Normal Eyes. J Ophthalmic Vis Res. 2012 ;7:34-8.

13. Yang GQ, Chen T, Tao Y, Zhang ZM. Recent advances in the dark adaptation investigations. Int J Ophthalmol. 2015 Dec 18;8(6):1245-52.

14. Haim M. Epidemiology of retinitis pigmentosa in Denmark. Acta Ophthalmol Scand Suppl. 2002;(233):1–34.

15. Herse P. Retinitis pigmentosa: visual function and multidisciplinary management. Clin Exp Optom. 2005;88(5):335–350.
16. Alexander KR, Fishman GA. Prolonged rod dark adaptation in retinitis pigmentosa. Br J Ophthalmol. 1984;68:561–569.
17. Konieczka K, Flammer AJ, Todorova M, Meyer P, Flammer J. Retinitis pigmentosa and ocular blood flow. EPMA J. 2012;3(1):17.
18. Kim LS, McAnany JJ, Alexander KR, Fishman GA. Intersession repeatability of humphrey perimetry measurements in patients with retinitis pigmentosa. Invest Ophthalmol Vis Sci. 2007;48:4720–4.
19. Grover S, Fishman GA, Anderson RJ, Alexander KR, Derlacki DJ. Rate of visual field loss in retinitis pigmentosa. Ophthalmology. 1997;104:460-5.
20. Grover S, Fishman GA, Brown J Jr. Patterns of visual field progression in patients with retinitis pigmentosa. Ophthalmology. 1998;105:1069-75.
21. Ross DF, Fishman GA, Gilbert LD, Anderson RJ. Variability of visual field measurements in normal subjects and patients with retinitis pigmentosa. Arch Ophthalmol. 1984;102:1004-10.

22. Holopigian K, Greenstein V, Seiple W, Carr RE. Rates of change differ among measures of visual function in patients with retinitis pigmentosa. Ophthalmology. 1996;103:398-405.

23. Berson EL, Sandberg MA, Rosner B, Birch DG, Hanson AH. Natural course of retinitis pigmentosa over a three-year interval. Am J Ophthalmol. 1985;99:240-51.

24. Massof RW, Dagnelie G, Benzschawel T, Palmer RW, Stein DF. First order dynamics of visual field loss in retinitis pigmentosa. Clin Vision Sci .1990 ;5:1-26.

25. Sayo A, Ueno S, Kominami T, Nishida K, Inooka D, Nakanishi A, et al. Longitudinal study of visual field changes determined by Humphrey Field Analyzer 10-2 in patients with Retinitis Pigmentosa. Sci Rep. 2017;7:16383.

26. Crossland, M., Jackson, M.-L., & Seiple, W. Microperimetry: a review of fundus related perimetry. Optometry Reports, (2012). , e2. https://doi.org/10.4081/optometry.2012.e2

27. Acton JH, Smith RT, Greenberg JP, Greenstein VC. Comparison between MP-1 and Humphrey visual field defects in glaucoma and retinitis pigmentosa. Optom Vis Sci. 2012;89:1050–8.

28. Jain AB, Prakash VJ, Bhende M. Techniques of fundus imaging. Medical & Vision Research Foundations. 2015;33:100.

29. Schuerch K, Marsiglia M, Lee W, Tsang SH, Sparrow JR. Multimodal imaging of disease-associated pigmentary changes in retinitis pigmentosa. Retina (Philadelphia, Pa). 2016;36 Suppl 1:S147–58.

30. Oishi A, Oishi M, Ogino K, Morooka S, Yoshimura N. Wide-Field Fundus Autofluorescence for Retinitis Pigmentosa and Cone/Cone-Rod Dystrophy. Adv Exp Med Biol. 2016;854:307–13

31. Iriyama A, Yanagi Y. Fundus autofluorescence and retinal structure as determined by spectral domain optical coherence tomography, and retinal function in retinitis pigmentosa. Graefes Arch Clin Exp Ophthalmol. 2012;250:333–9.

32. Chhablani J, Jonnadula GB, Srinivasa Rao P, Venkata A, Jalali S. Choroidal thickness profile in Retinitis Pigmentosa - Correlation with outer retinal structures. Saudi J Ophthalmol. 2016;30:9–13

33. Dhoot DS, Huo S, Yuan A, Xu D, Srivistava S, Ehlers JP, et al. Evaluation of choroidal thickness in retinitis pigmentosa using enhanced depth imaging optical coherence tomography. Br J Ophthalmol. 2013;97:66–9.

34. Oishi A, Nakamura H, Tatsumi I, Sasahara M, Kojima H, Kurimoto M, et al. Optical coherence tomographic pattern and focal electroretinogram in patients with retinitis pigmentosa

35. Schachat AP, Sadda SR, editors. Ryan's Retina. 6th ed. Vol. 2. Edinburgh: Elsevier; 2018. p. 911.

36. Cox SN, Hay E, Bird AC. Treatment of chronic macular edema with acetazolamide. Arch Ophthalmol. 1988;106:1190–5.

37. García-Arumí J, Martinez V, Sararols L, Corcostegui B. Vitreoretinal surgery for cystoid macular edema associated with retinitis pigmentosa. Ophthalmology. 2003;110:1164–9.

38. Newsome DA, Blacharski PA. Grid photocoagulation for macular edema in patients with retinitis pigmentosa. Am J Ophthalmol. 1987;103:161–6.

39. Saraiva VS, Sallum JMF, Farah ME. Treatment of cystoid macular edema related to retinitis pigmentosa with intravitreal triamcinolone acetonide. Ophthalmic Surg Lasers Imaging. 2003;34:398–400.

40. Scorolli L, Morara M, Meduri A, Reggiani LB, Ferreri G, Scalinci SZ, et al. Treatment of cystoid macular edema in retinitis pigmentosa with intravitreal triamcinolone. Arch Ophthalmol. 2007;125:759–64.

41. Forte R, Pannarale L, Iannaccone A, Vingolo EM, Santi G, Pannarale MR. Cystoid macular edema in retinitis pigmentosa – clinical and functional evaluation of patients treated with deflazacort. Invest Ophthalmol Vis Sci. 1994;35:1958.

42. Artunay O, Yuzbasioglu E, Rasier R, Sengul A, Bahcecioglu H. Intravitreal ranibizumab in the treatment of cystoid macular edema associated with retinitis pigmentosa. J Ocul Pharmacol Ther. 2009;25:545–50.

43. Fishman GA, Gilbert LD, Fiscella RG, Kimura AE, Jampol LM. Acetazolamide for treatment of chronic macular edema in retinitis pigmentosa. Arch Ophthalmol. 1989;107:1445–52.

44. Melo GB, Farah ME, Aggio FB. Intravitreal injection of bevacizumab for cystoid macular edema in retinitis pigmentosa. Acta Ophthalmol Scand. 2007;85:461–3.

45. Yuzbasioglu E, Artunay O, Rasier R, Sengul A, Bahcecioglu H. Intravitreal bevacizumab (Avastin) injection in retinitis pigmentosa. Curr Eye Res. 2009;34:231–7.

46. Robson AG, El-Amir A, Bailey C, Egan CA, Fitzke FW, Webster AR, et al. Pattern ERG correlates of abnormal fundus autofluorescence in patients with retinitis pigmentosa and normal visual acuity. Invest Ophthalmol Vis Sci. 2003;44:3544-50.

47. Robson AG, Egan C, Holder GE, Bird AC, Fitzke FW. Comparing rod and cone function with fundus autofluorescence images in retinitis pigmentosa. Adv Exp Med Biol. 2003;533:41-7. P

48. Robson AG, Egan CA, Luong VA, Bird AC, Holder GE, Fitzke FW. Comparison of fundus autofluorescence with photopic and

scotopic fine-matrix mapping in patients with retinitis pigmentosa and normal visual acuity. Invest Ophthalmol Vis Sci. 2004;45:4119-25.

49. Popović P, Jarc-Vidmar M, Hawlina M. Abnormal fundus autofluorescence in relation to retinal function in patients with retinitis pigmentosa. Graefes Arch Clin Exp Ophthalmol. 2005;243:1018-27.

50. Murakami T, Akimoto M, Ooto S, Suzuki T, Ikeda H, Kawagoe N, et al. Association between abnormal autofluorescence and photoreceptor disorganization in retinitis pigmentosa. Am J Ophthalmol. 2008;145:687-94.

51. Robson AG, Michaelides M, Luong VA, Holder GE, Bird AC, Webster AR, et al. Functional correlates of fundus autofluorescence abnormalities in patients with RPGR or RIMS1 mutations causing cone or cone rod dystrophy. Br J Ophthalmol. 2008;92:95-102.

52. Fleckenstein M, Charbel Issa P, Fuchs HA, Finger RP, Helb HM, Scholl HP, et al. Discrete arcs of increased fundus autofluorescence in retinal dystrophies and functional correlate on microperimetry. Eye (Lond). 2009;23:567-75.

53. Greenstein VC, Duncker T, Holopigian K, Carr RE, Greenberg JP, Tsang SH, et al. Structural and functional changes associated with

normal and abnormal fundus autofluorescence in patients with retinitis pigmentosa. Retina. 2012 ;32:349-57.

54. Iriyama A, Yanagi Y. Fundus autofluorescence and retinal structure as determined by spectral domain optical coherence tomography, and retinal function in retinitis pigmentosa. Graefes Arch Clin Exp Ophthalmol. 2012;250:333-9.

55. Robson AG, Saihan Z, Jenkins SA, Fitzke FW, Bird AC, Webster AR, et al.Functional characterisation and serial imaging of abnormal fundus autofluorescence in patients with retinitis pigmentosa and normal visual acuity. Br J Ophthalmol. 2006;90:472-9.

56. Aizawa S, Mitamura Y, Hagiwara A, Sugawara T, Yamamoto S. Changes of fundus autofluorescence, photoreceptor inner and outer segment junction line, and visual function in patients with retinitis pigmentosa. Clin Exp Ophthalmol. 2010;38:597-604.

57. Wakabayashi T, Sawa M, Gomi F, Tsujikawa M. Correlation of fundus autofluorescence with photoreceptor morphology and functional changes in eyes with retinitis pigmentosa. Acta Ophthalmol. 2010;88:e177-83.

58. Robson AG, Tufail A, Fitzke F, Bird AC, Moore AT, Holder GE, et al. Serial imaging and structure-function correlates of high-

density rings of fundus autofluorescence in retinitis pigmentosa. Retina. 2011;31:1670-9.

59. Robson AG, Lenassi E, Saihan Z, Luong VA, Fitzke FW, Holder GE, Webster AR. Comparison of fundus autofluorescence with photopic and scotopic fine matrix mapping in patients with retinitis pigmentosa: 4- to 8-year follow-up. Invest Ophthalmol Vis Sci. 2012;53:6187-95.

60. Waris A, Asghar A, Yunus SM, Malakar M. Normal macular thickness measurements in normal eyes using fourier domain optical coherence tomography. IOSR Journal of Dental and Medical Sciences. 2015;14:63-66.

61. Chen YF, Wang IJ, Su CC, Chen MS. Macular thickness and aging in retinitis pigmentosa. Optom Vis Sci. 2012;89:471-82.

62. Mitamura Y, Mitamura-Aizawa S, Nagasawa T, Katome T, Eguchi H, Naito T. Diagnostic imaging in patients with retinitis pigmentosa. The Journal of Medical Investigation. 2012;59:1-11.

63. Fleckenstein M, Charbel Issa P, Fuchs HA, Finger RP, Helb HM, Scholl HP, et al. Discrete arcs of increased fundus autofluorescence in retinal dystrophies and functional correlate on microperimetry. Eye (Lond). 2009;23:567-75.

64. Robson AG, Saihan Z, Jenkins SA, Fitzke FW, Bird AC, Webster AR, et al. Functional characterisation and serial imaging of

abnormal fundus autofluorescence in patients with retinitis pigmentosa and normal visual acuity. Br J Ophthalmol. 2006;90:472-9.

65. Robson AG, El-Amir A, Bailey C, Egan CA, Fitzke FW, Webster AR, et al. Pattern ERG correlates of abnormal fundus autofluorescence in patientswith retinitis pigmentosa and normal visual acuity. Invest Ophthalmol Vis Sci. 2003;44:3544-50.

66. Hirakawa H, Iijima H, Gohdo T, Imai M, Tsukahara S. Progression of defects in the central 10-degree visual field of patients with retinitis pigmentosa and choroideremia. Am J Ophthalmol. 1999;127:436-42.

67. Srinivasan VJ, Wojtkowski M, Witkin AJ, Duker JS, Ko TH, Carvalho M, et al. High-definition and 3-dimensional imaging of macular pathologies with high-speed ultrahigh-resolution optical coherence tomography. Ophthalmology. 2006;113:2054.e1-14.

LIST OF ABBREVIATIONS

AF ring	-	Autofluorescence ring
BCV	-	Best corrected visual acuity
CT	-	Choroidal thickness
CME	-	Cystoid Macular edema
CMT	-	Central macular thickness
ERG	-	Electroretinogram
EOG	-	Electrooculography
ERM	-	Epiretinal membrane
FAF	-	Fundus autofluorescence
HFA	-	Humphrey Field Analyzer
IS/OS	-	Inner segment / outer segment
OCT	-	Optical coherence Tomography
MH	-	Macular hole
MAIA	-	Macular Integrity Assessment
NIR	-	Near infrared autofluorescence
RP	-	Retinitis pigmentosa
RPE	-	Retinal pigmentary epithelium
RD	-	Retinal detachment
SD OCT	-	spectral Domain optical coherence Tomography
SD	-	Standard deviation

CONSENT FORM

Informed Consent form to participate in a clinical study.

Study Title: **CORRELATION BETWEEN MULTI MODAL IMAGING AND VISUAL PARAMETERS IN RETINITIS PIGMENTOSA**

Protocol Number:

Subject's Name: _____

Subject's Initials: _____

Subject ID No: _____

		Please put initial in the box (Subject)
(i)	I confirm that I have understood the information about the study, procedures and treatments for the above study and have had the opportunity to ask questions and I received satisfactory answers to all of my questions. I have been given a copy of the informed consent form to take home	[ ]
(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. However, this is may not be possible for certain surgical procedures	[ ]
(iii)	I understand that the Investigator of the study to access my health records	[ ]

	for the research purpose. 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:

Subject's Name:

Date:

Signature (or Thumb impression) of

Legally Acceptable Representative (LAR):

Date:

Signature of the Investigator:

Investigator's Name:

Date:

Signature of the Witness:

Name of the Witness:

Date:

PROFORMA

Correlation between Multimodal imaging visual parameters in Retinitis Pigmentosa

Name : Date :

Age : Study No :

Male : ☐ Female : ☐ MR No :

RE LE UID No :

1. Microperimetry finding

0. Normal

1.Suspect

2. Abnormal

Mascular integrity RE: Value ____ ☐

LE: Value ____ ☐

Average thershold RE: Value ____ ☐

LE: Value ____ ☐

Fixalion RE: Value ____ ☐

LE: Value ____ ☐

2. Optical Coherence Tomography

CMT RE ____ LE ____

Subfield

	Perifoveal		Parafoveal	
	RE	LE	RE	LE
S				
I				
N				
T				

I SOS Distruption

1 length - < 2mm

2 length - > 2 mm

Grading RE ☐

LE ☐

Length RE _____

LE _____

Choroidal

Thickness RE _____

LE _____

AF ring Size RE _____

LE _____

3. OPTOS

AF ring size RE _____

LE _____

4. Fundus Photograph finding

Bone Spioules		Attenuated Arterioles	
RE	LE	RE	LE

HFA (Humphrey field analyzer

5.HFA finding

	RE	LE
S4		
S12		
S20		

ARAVIND MEDICAL RESEARCH FOUNDATION
Institutional Ethics Committee
(REGISTRATION NO. ECR/182/INST/TN/2013 DATED 20.04.2013)

20th December 2017

To
Dr.T.Akila
MS Resident
Aravind Eye Hospital
Madurai

Dear Dr. Akila,

Thesis Title: CORRELATION BETWEEN MUILIMODAL IMAGING AND VISUAL PARAMETERS IN RETINITIS PIGMENTOSA

IEC Code: IEC201800259

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,

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
ARAVIND MEDICAL RESEARCH FOUNDATION
No.1, Anna Nagar, Madurai-625 020

Dr.R.Sharmila
Member Secretary
Institutional Ethics Committee

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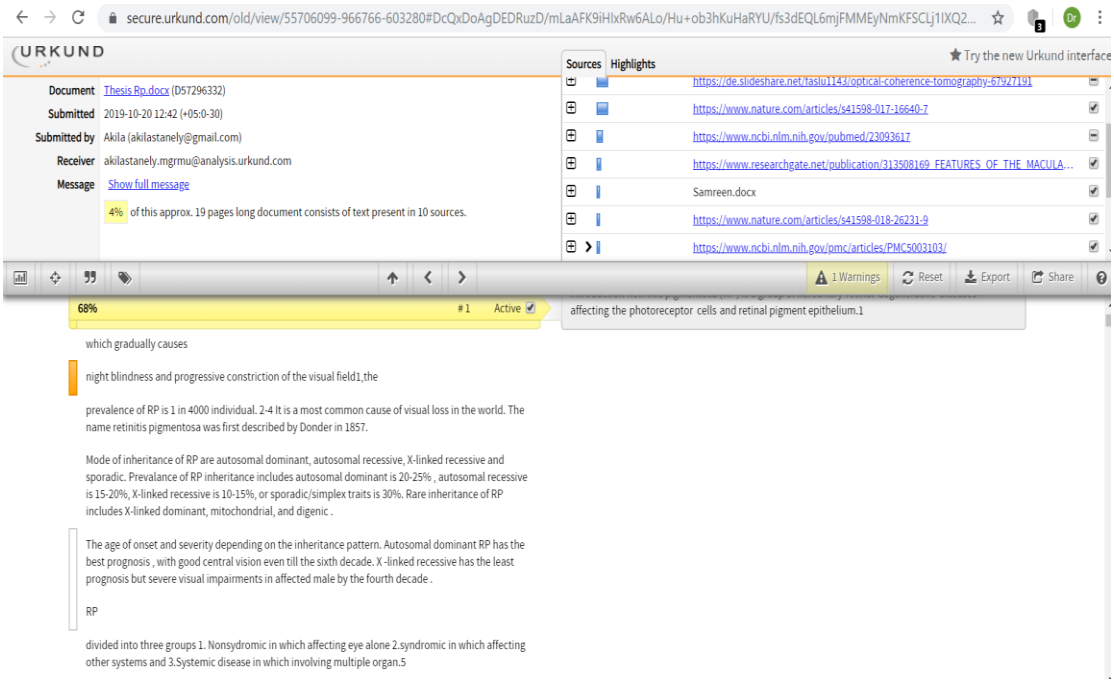
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1 Warnings
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#1
Active
affecting the photoreceptor cells and retinal pigment epithelium.1
which gradually causes
night blindness and progressive constriction of the visual field1,the
prevalence of RP is 1 in 4000 individual. 2-4 It is a most common cause of visual loss in the world. The name retinitis pigmentosa was first described by Donder in 1857.
Mode of inheritance of RP are autosomal dominant, autosomal recessive, X-linked recessive and sporadic. Prevalance of RP inheritance includes autosomal dominant is 20-25% , autosomal recessive is 15-20%, X-linked recessive is 10-15%, or sporadic/simplex traits is 30%. Rare inheritance of RP includes X-linked dominant, mitochondrial, and digenic .
The age of onset and severity depending on the inheritance pattern. Autosomal dominant RP has the best prognosis , with good central vision even till the sixth decade. X -linked recessive has the least prognosis but severe visual impairments in affected male by the fourth decade .
RP
divided into three groups 1. Nonsydromic in which affecting eye alone 2.syndromic in which affecting other systems and 3.Systemic disease in which involving multiple organ.5