Ho Chi Yun Doreen (Orcid ID: 0000-0001-7707-0267)

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Relationship between reticular pseudodrusen and choroidal thickness in intermediate age-related macular degeneration

Chi Yun Doreen Ho MBBS, Jia Jia Lek BOptom, Khin Zaw Aung MBBS, Myra B McGuinness MBiostat, Chi D Luu PhD and Robyn H Guymer PhD FRANZCO

Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital; Department of Surgery (Ophthalmology), The University of Melbourne, Melbourne, Australia.

Correspondence: Chi Yun Doreen Ho, Macular Research, Centre for Eye Research Australia, Level 8, 32 Gisborne Street, East Melbourne, VIC 3002, Australia.
Email: cy.doreen.ho@gmail.com

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ABSTRACT

Importance: Reticular pseudodrusen (RPD) is strongly associated with late age-related macular degeneration (AMD) but their etiology remains unknown. RPD have been associated with reduced choroidal thickness but most studies are limited by small sample size and varying severity of AMD.

Background: To investigate the relationship between choroidal thickness (ChT) and RPD in eyes with intermediate AMD (iAMD), controlling for variables known to influence ChT.

Design: Retrospective cohort study

Participants: Participants were recruited from Centre for Eye Research Australia.

Methods: Colour fundus photographs, fundus auto fluorescence, near infrared and spectral-domain optical coherence tomography (OCT) were graded for RPD. ChT was measured from enhanced depth imaging OCT scans at the centre of fovea, 1500 µm and 3000 µm nasal, temporal, superior and inferior from centre of fovea.

Main outcome measures: ChT between RPD and non-RPD group

Results: 297 eyes from 152 subjects were included. 84 (28%) had RPD and were older than non-RPD group (75.1 ± 5.4 years and 68.7 ± 6.9 years, respectively; $p < 0.001$). In unadjusted analysis, the RPD group was significantly associated with thinner choroids across all measured locations ($p \leq 0.022$). After adjustment for variables, the presence of RPD was no longer associated with ChT ($p \geq 0.132$ for all locations) but age ($p < 0.001$) and refractive error ($p = 0.002$) remained significantly associated with ChT.

Conclusions: Age and refractive error, rather than RPD, was significantly associated with reduced choroidal thickness in eyes with iAMD. Choroidal insufficiency may be a less important variable in RPD etiology than previously considered.

Keywords: Age-related macular degeneration (AMD), choroidal thickness, reticular pseudodrusen

INTRODUCTION

Multimodal imaging of eyes with age-related macular degeneration (AMD) have revealed a far greater prevalence of reticular pseudodrusen (RPD) than had originally been described.[1] With this has come increasing evidence that RPD are associated with late AMD and risk of progressing to late AMD, in particular to geographic atrophy (GA), independent of conventional drusen and focal pigmentary abnormalities.[2, 3] Evidence suggests that there is a four to sixfold higher risk of progression to late AMD in AMD eyes with RPD than those without RPD in cohorts with late AMD in the fellow eye,.[3, 4]

Understandably, interest in the pathogenesis and the role that RPD plays in the natural history of AMD has grown.[5-7] In the first histopathologic study of an eye with clinically confirmed RPD, Arnold et al reported loss of medium sized vessels in the choroid along with increased stromal fibrosis, suggesting a possible role of the choroid in RPD pathogenesis.[2] Further reports followed suggested that the underlying etiology may involve choroidal vascular abnormalities.[8] For example the distribution of evolving RPD seems to be related to sites of choroidal watershed zones, suggesting choroidal hypoxia may have a role in their pathogenesis.[9] Using optical coherence tomography and choroidal maps, several groups have reported reduced choroidal thickness (ChT) in eyes with various stages of AMD with RPD compared to eyes without RPD.[10-14] Furthermore, en face images through the choroid have shown predominantly narrow and sparse choroidal vessels in eyes with RPD.[11, 13] These studies however are often limited either by a small sample size, a cohort with various stages of AMD or had elements of selection bias, or did not adequately adjust for variables known to influence ChT such as age and refractive error.[10-12, 14] There has also been one study that did not find a clear association between ChT and RPD.[15]

As we seek answers about the etiology of RPD due to their profound influence on AMD outcomes, it is important that the relationship with the choroid be determined. ChT is known to be influenced by many factors[16], therefore it is of utmost importance that variables known to influence choroidal thickness be taken into account when aiming to determine relevant associations.

The aim of this cross-sectional study was to examine the association, if any, between RPD and ChT in a large uniform cohort all of whom had a diagnosis of iAMD, controlling for important variables that are known to influence the ChT such as age, gender, refractive error and smoking status.

METHODS

This study was approved by the Human Research Ethics Committee of the Royal Victorian Eye and Ear Hospital and conducted in adherence with the Declaration of Helsinki. Written informed consent was obtained from all participating subjects after providing an explanation of all the test procedures.

Participants

Participants were recruited from the Macular Research Unit at the Centre for Eye Research Australia. The inclusion criteria for all participants in this study included being over 50 years of age, and having a subset of intermediate AMD; bilateral drusen ≥125 μm with or without pigmentary changes, according to the Beckman's classification.[17] Eligible participants also had to have images of sufficient quality to determine the presence of RPD and with entire choroidal thickness measurable on enhanced-depth imaging spectral domain optical coherence tomography (EDI SD-OCT). The exclusion criteria included having in either eye GA, CNV, significant

cataracts or any corneal pathology that could obscure the fundus. Participants were also excluded if they had any physical and/or mental impairment preventing them from participating in this study or an inability to sign the consent form. Participants with myopia (≥ - 5.00D), other retinal conditions that might affect choroidal thickness and those graded with questionable RPD were excluded from this study.

Procedure

A questionnaire was conducted to obtain demographic information, medical history including smoking history and best corrected visual acuity (BCVA) measurements were performed. Refractive error measurements represented in spherical equivalent was calculated as the sum of the value of the sphere and half the cylindrical value.

Multimodal Imaging Acquisition

Multimodal imaging was performed at the baseline visit and included colour fundus photography using a nonmydriatic fundus camera (Canon CR6-45NM; Canon, Saitama, Japan). Near-infrared reflectance (NIR), fundus autofluorescence (FAF), spectral-domain optical coherence tomography (SD-OCT) volume scans and EDI SD-OCT scans were obtained using a Spectralis HRA+OCT device (Heidelberg Engineering, Heidelberg, Germany). Volume scans were performed over the central 20 x 20º area, with 49 equally spaced horizontal B-scans used. For EDI SD-OCT images, two 9 mm high quality line scans through the fovea (one horizontal and one vertical) were obtained for each eye set to average 100 frames each.

AMD grading

Participant AMD status was determined by a senior grader using CFP and OptomizePro (Digital Healthcare Image Management System; Digital Healthcare Ltd., Cambridge, UK).[18] For this study, all eligible eyes were graded as having at

least one drusen > 125 μm without any GA or CNV and as such were within the grade of iAMD as defined by the Beckman classification.[17]

RPD Grading

Our definition for the presence of RPD was informed by previous studies and modified with the emphasis on ensuring that RPD were definitely present when they were graded as such.[19, 20] Two graders and one senior retinal specialist graded all images. RPD were graded at an image type level, then at an eye level. At an image level and an eye level, RPD were graded as being either definitely present, questionable or definitely absent on each modality; CFP, FAF, NIR and OCT.

The grading of CFP was performed using OptomizePro (Digital Healthcare Image Management System; Digital Healthcare Ltd., Cambridge, UK). RPD were defined as being present on CFP when pale, ill-defined networks of broad, interlacing ribbons and/or multiple light yellowish-pale or grayish discrete dots grouped in a pattern that appear slightly whiter or greyish compared with soft drusen were present.[21]

RPD were defined on FAF imaging as typical multiple discrete or interlacing hypoautofluorescent foci against a mildly elevated FAF background and grouped in a pattern. RPD were recognised as either dot; discrete solitary hypoautofluorescent foci correlating with the same location of RPD on IR or SD-OCT, or target; discrete dots of any size with isoautofluorescence center surrounded by reduced autofluorescence ring.[22]

RPD were defined as present on NIR as typical multiple discrete or interlacing hyporeflective foci of ≥25 μm in size and grouped in a pattern correlating with the same location of RPD within macular SD-OCT.

B-scan SD-OCT criteria of RPD were defined as ≥1 dome-shaped or oval hyper-reflective material of any size internal to and adjacent to the RPE with or without various-degrees of disturbance of Ellipsoid zone.

At an eye level, RPD were defined as definitely present when there was the presence of ≥5 RPD on SD-OCT in >1 B-scan and on at least one en face modality (CFP, FAF, NIR) or present on two en face modalities in the absence of SD-OCT findings (including outside the SD-OCT grid). RPD were graded questionable when questionably present in two modalities or if RPD was only definitely present on SD-OCT but not on any other en face image**.** RPD were grade absent if they were not present or did not reach the criteria for being present on any modality.

Only eyes with definite RPD were considered to have RPD. Those graded as having questionable RPD were excluded from further analysis. Those with definite RPD were compared to those with definitely absent RPD.

Distribution and Extent of RPD

Three graders determined the distribution of the RPD within the 1500 μm and 3000 μm radius circle centred on the fovea by indicating the extent of RPD found in each quadrant (superior, inferior, temporal and nasal as determined by the Early Treatment Diabetic Retinopathy Study [EDTRS] grid). Extent of RPD was determined by the area in μm^2 of RPD involvement as measured by two en face modalities, NIR and FAF. We divided the groups into three relatively equally represented groups based upon the area of RPD measured. Small area of RPD was defined as a RPD area between 0-30 μm^2, medium between >30-60 μm^2, and large between >60-95 μm^2.

EDI SD-OCT Analysis

EDI SD-OCT images were viewed and measured using Heidelberg Eye Explorer interactive software's manual calipers tool (Heidelberg Eye Explorer software; Heidelberg Engineering, Heidelberg, Germany) and resized to a 1:1 aspect ratio before measurements were undertaken. The choroid was measured from the outer portion of the hyper-reflective line corresponding to the RPE/Bruch's membrane to the inner surface of the sclera.[23] These measurements were obtained at the fovea and at 1500 μm and 3000 μm from centre of fovea in nasal, superior, temporal and inferior directions (Figure 1). The ChT measurements were performed by one grader, measured twice in 10% of our cohort and analysed for intra-grading variability using Bland and Altman.[24]

Figure 1: EDI SD-OCT images of choroid measurements at the fovea, 1500 μm nasal, 1500 μm temporal, 1500 μm superior, 1500 μm inferior, 3000 μm nasal, 3000 μm temporal, 3000 μm superior and 3000 μm inferior from centre of fovea.

Statistical Analysis

Statistical calculations were performed using a commercial package, SPSS (Statistical Package for Social Sciences, version 23.0; SPSS Inc., Chicago, IL). Given that both eyes were used in this study, Pearson's correlation was used to determine correlation between right and left eye. ChT at each point along horizontal and vertical meridians for RPD and non-RPD group in iAMD participants was compared using a generalised estimation equation model factoring in age, gender, smoking status, refractive error and BCVA. For stratification analysis, we stratified all locations by median age ($\leq$ 70 or > 70 years old) to subgroup ChT difference estimates. Further sub-analysis between ChT and extent of RPD was evaluated by using generalised estimation equation. To determine whether the ChT was preferentially reduced in the superior retina in eyes with RPD, ChT measurements of the superior and inferior retina of the RPD eyes were converted into a Z-score to adjust for the

physiological variations in ChT. Using the mean and standard deviation data of non-RPD eyes as reference, the Z-score was calculated for each ChT measurement along the vertical meridian of the RPD eyes, representing the number of standard deviation from the mean ChT of the non-RPD eyes. A Z-score of more than 2 was considered equivalent to an alpha value of <0.05 and thus that measurement was deemed as significantly differing from the non-RPD group.

RESULTS

One-hundred and sixty-two participants with iAMD were eligible to be included in this study. However, 10 participants (20 eyes in total; 6 eyes with RPD, 14 eyes with no RPD) were excluded as the entire choroid was not visualised on EDI SD-OCT (see Figure 2). A total of 152 subjects (304 eyes) were included in the study.

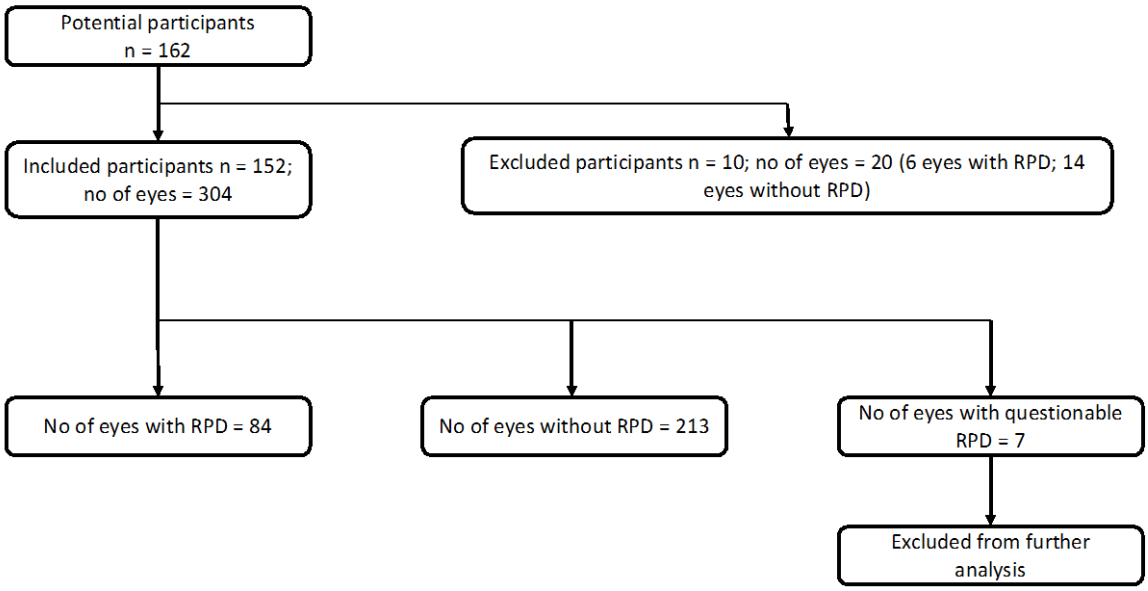

Figure 2: Flow diagram of eligible and excluded participants

Demographics and clinical characteristics of participants

Table 1 summarises demographics of the studied groups. Of the 304 eyes with intermediate AMD, 84 (28%) had RPD and 213 (70%) had no RPD. Seven eyes (2%) were graded as questionable RPD and were excluded from further analysis. The average age of the RPD group (75.1 ± 5.4 years) was significantly older than those of the non-RPD group (68.7 ± 6.9, p <0.001) and had worse BCVA (p < 0.001).

Table 1: Demographics and clinical characteristics of the study participants

	RPD	**Non-RPD**	**P Value**
Number of eyes	84	213	
Number of participants	46	107	
Age (Mean ± SD, range), years	75.1 ± 5.4, 52 - 86	68.7 ± 6.9, 53 – 83	<0.001*
Gender (Female %)	76%	75%	0.479**
Smoking History Current or Previous Never	 41 (49%) 43 (51%)	 111 (52%) 102 (48%)	0.735**
BCVA (Mean ± SD number of letters), Snellen equivalent	83.0 ± 5.0, 20/25	85.4 ± 4.9, 20/20	<0.001*
Refractive error (Mean ± SD of spherical equivalent), diopters	+0.76 ± 1.3	+0.88 ± 1.4	0.489*

*p value based on independent t-test

**p value based on chi-squared test.

SD, standard deviation; BCVA, best corrected visual acuity

There was a strong, positive correlation between right and left eyes (r = 0.82, p <0.001). As such we used the generalised estimation equation to correct for the use of both eyes. To determine the accuracy of the ChT measurement, the ChT were measured twice in randomly selected 10% (15 participants) of the study cohort. The 95% limit of agreement of the two measurements was ±21 μm.

Choroidal thickness in iAMD eyes with and without RPD

Unadjusted analysis showed that the RPD group had on average thinner choroids (184.5 µm ± 58.1) across all measured locations when compared to non-RPD group (209.4 µm ± 76.4, $p \leq 0.022$) except at the 3000 µm temporal location ($p = 0.711$) (Figure 3A).

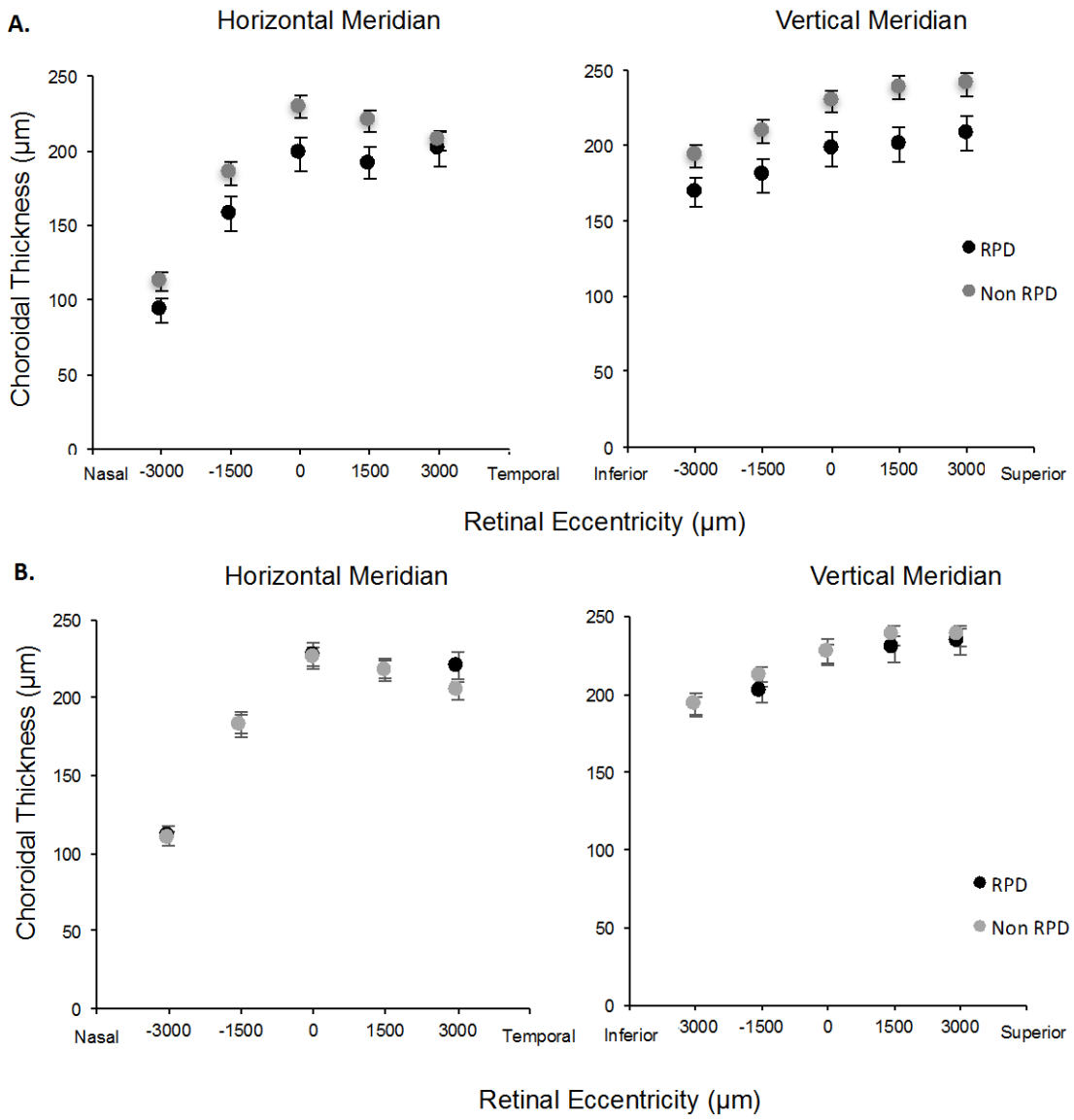

Figure 3: A. Unadjusted analysis of choroidal thickness along horizontal and vertical meridians compared between RPD and non-RPD group. Eyes with RPD had a thinner choroid compare to eyes without RPD at all retinal locations except 3000 µm

temporally. **B.** Adjusted analysis of choroidal thickness along horizontal and vertical meridians compared between RPD and non-RPD group. ChT was no longer significantly different between those with RPD as compared to the group without RPD at all locations.

Table 2: Generalised estimation equation for ChT adjusting for age, gender, smoking status and refractive error

Parameter	B Coefficient	95% CI		p-value
		Lower	Upper	
RPD (presence)	2.4	-10.0	14.7	0.708
Age (per year)	-3.4	-4.7	-2.1	**<0.001**
Gender (male)	9.7	-8.9	28.4	0.307
Smoking history (current or ex-smoker)	0.2	-17.8	18.2	0.985
Refractive error (per dioptre)	8.0	2.9	13.2	**0.002**
BCVA (per letter)	-0.5	-1.3	0.3	0.248

BCVA, best corrected visual acuity

When adjusted for variables that were significantly different between the RPD and non-RPD group (age and BCVA) as well as variables that have been considered to influence ChT, although not significantly different in our cohort, (refractive error, gender and smoking status), only age and refractive error remained significantly associated with ChT (Table 2). As from Table 2, a year increase in age is associated with a 3.4 μm decrease in ChT. Similarly, for every dioptre increase in refractive error is associated with an 8.0 μm increase in ChT (i.e. myopia is associated with a decrease in ChT). The unadjusted and adjusted ChT at all retinal eccentricities in RPD and non-RPD group are shown in Figure 3. This demonstrated that once adjusted for variables, ChT was no longer significantly different between the RPD and the non-RPD group at all locations. The relationships between ChT and age at

different retinal locations in eyes with and without RPD are also shown in Figure 4. The ChT appeared to be reduced linearly with increasing age in both RPD and non-RPD groups.

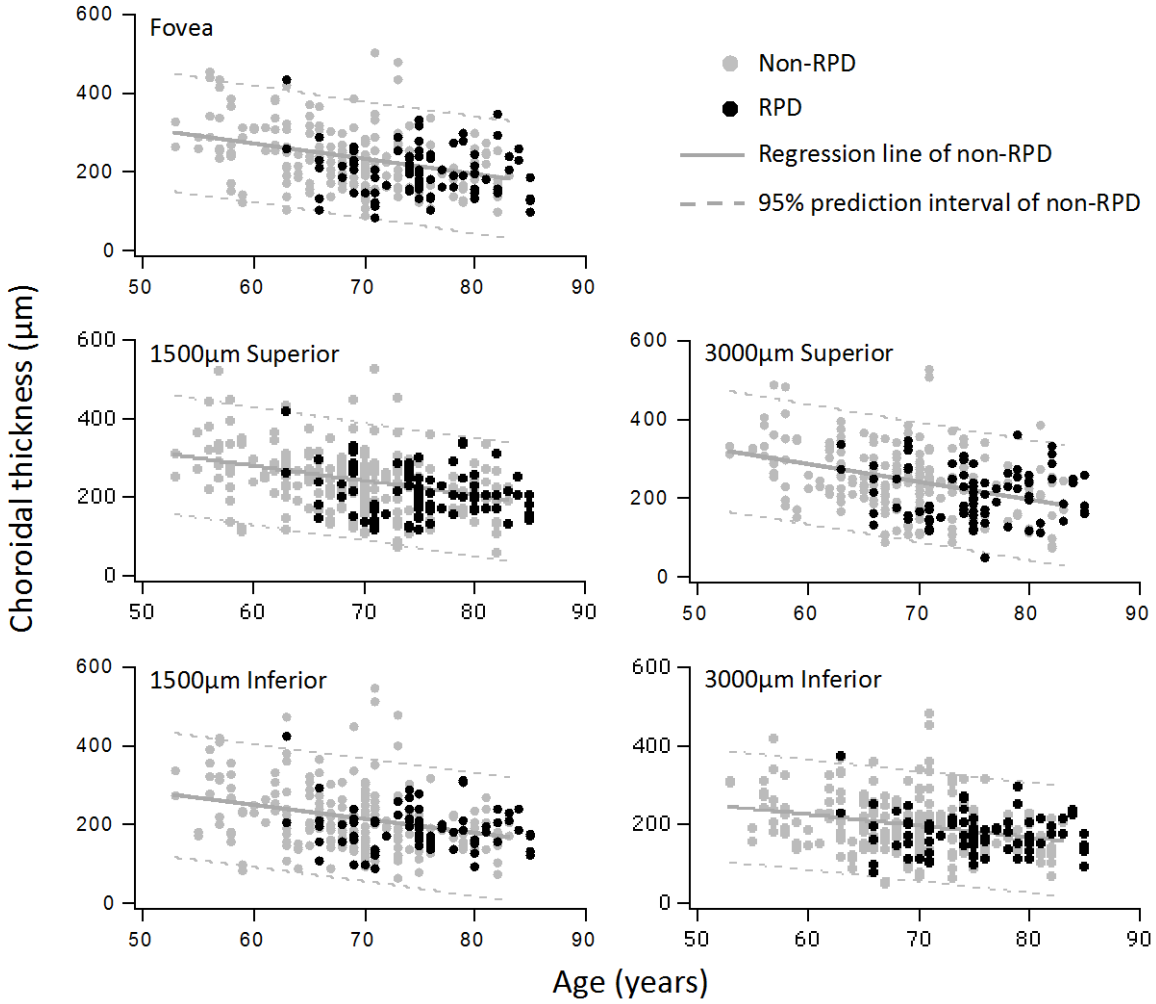

Figure 4: Scatter plots for choroidal thickness and age at various retinal locations. Most ChT measurements in the RPD group fell within the 95% prediction interval of non-RPD group, indicating that the changes in choroidal thickness with age are similar between RPD and non-RPD group.

When stratified all participants by the median age (70 years), we did not find any significant difference in ChT in the younger age group (≤70 years) in eyes with RPD

compared to eyes without RPD (p = 0.305) nor did we find any significant difference in ChT in the older age group (p = 0.160). We also stratified participants looking at those ≤82 years old and those >82 years old. We did not find any significant difference in ChT in either groups (p = 0.721; p = 0.112 respectively).

Comparison of Choroidal Thickness to Extent of RPD

To determine whether there may be an association with extent of RPD and ChT we repeated the analysis dividing extent of RPD into small, medium and large based upon the areas affected with RPD on FAF and NIR modalities. ChT was compared between the three groups. We found no significant difference in ChT between differing extent of RPD (p values ≥ 0.232) (Table 3 and 4).

Table 3: Choroidal thickness at varying extent of RPD as measured by NIR

Retinal Eccentricity	ChT in Small Area (μm)	ChT in Medium Area (μm)	ChT in Large Area (μm)	*P Value	**P Value
Subfovea	197.5 ± 72.1	207.4 ± 58.0	209.2 ± 54.6	0.482	0.724
1500μm nasal	161.8 ± 69.6	165.8 ± 58.4	170.5 ± 51.7	0.560	0.642
3000μm nasal	99.0 ± 53.0	97.4 ± 38.1	100.1 ± 39.9	0.631	0.602
1500μm temporal	202.5 ± 72.9	201.6 ± 46.9	207.8 ± 34.8	0.954	0.831
3000μm temporal	209.9 ± 77.1	196.8 ±57.1	221.8 ± 38.8	0.923	0.892
1500μm inferior	191.4 ± 62.1	187.1 ± 51.5	185.1 ± 38.7	0.741	0.704
3000μm inferior	177.4 ± 57.6	177.4 ± 48.0	169.3 ± 44.5	0.482	0.232
1500μm superior	213.1 ± 72.4	214.1 ± 55.3	202.1 ± 53.3	0.964	0.961
3000um superior	211.4 ± 75.9	214.6 ± 58.1	204.8 ± 59.5	0.681	0.684

*Comparison between small and large area

Table 4: Choroidal thickness at varying extent of RPD as measured by FAF

**Comparison between medium and large area

Retinal Eccentricity	ChT in Small Area (μm)	ChT in Medium Area (μm)	ChT in Large Area (μm)	*P Value	**P Value
Subfovea	194.1 ± 58.0	208.6 ± 60.3	202.7 ± 55.7	0.611	0.693
1500μm nasal	158.5 ± 55.1	163.4 ± 62.3	167.7 ± 49.7	0.603	0.452
3000μm nasal	192.2 ± 56.9	210.0 ± 53.6	202.8 ± 28.4	0.561	0.732
1500μm temporal	181.7 ± 47.0	192.2 ± 50.8	177.6 ± 42.4	0.952	0.933
3000μm temporal	202.8 ± 57.9	221.7 ± 60.6	190.7 ± 46.2	0.822	0.631
1500μm inferior	91.7 ± 36.3	100.2 ± 46.1	97.8 ± 42.0	0.671	0.604
3000μm inferior	197.6 ± 60.9	207.0 ± 66.3	213.8 ± 34.5	0.431	0.404
1500μm superior	200.9 ± 69.9	223.4 ± 61.2	199.7 ± 47.6	0.873	0.824
3000μm superior	169.0 ± 46.3	180.5 ± 45.6	163.2 ± 50.2	0.532	0.361

*Comparison between small and large area

**Comparison between medium and large area

Comparison of Choroidal Thickness Within RPD Group

Z-scores were calculated to determine whether there were preferential changes in ChT within RPD eyes. We found no significant difference in Z-score along the vertical meridian (all Z-scores < 1) in eyes with RPD (n = 84). Further to this, we also analysed RPD eyes where RPD was purely located in the superior field (n = 19). We found no significant difference in Z-score between superior and inferior retina in eyes with localised superior RPD only (all Z-scores < 1).

DISCUSSION

Our study sought to further investigate the choroid in a large cohort of AMD cases, all at the same stage of disease with extensively imaged and well phenotyped iAMD given the current importance many place on the state of the choroid in the patho-etiology of RPD.

We found that in our large sample of consecutive participants that reduced selection bias of participants, those with RPD were found amongst an older cohort (mean 75.1 years RPD group; mean 68.7 years non-RPD group). This was similar to Cheng et al whom studied ChT in eyes with early AMD with and without RPD.[15] They found that those with RPD were older and composed of more females when compared to the non-RPD group.

When we initially investigated the ChT between RPD and non-RPD eyes, we found that ChT was thinner in RPD eyes (184.5 μm ± 58.1) across all tested locations compared to non-RPD eyes (209.4 μm ± 76.4, $p \leq 0.022$) except at the location 3000 μm temporal from fovea. However, when adjusted for age, refractive error, gender, smoking history and BCVA, the significant associations between ChT and RPD were lost ($p = 0.708$). In fact, in our study, age and refractive error was the only variable associated with both RPD and ChT that remained significant. We found that a year increase in age is associated with a 3.4 μm decrease in ChT. Similarly, for every dioptre increase in refractive error, there is an associated 8.0 μm increase in ChT (i.e. myopia is associated with a decrease in ChT). From these results, it appears that age is driving the association with choroidal thinning rather than the presence of RPD. Similar to and supporting our findings, Cheng et al found that mean ChT was significantly thinner in RPD eyes prior to adjustment but this result was no longer significant when adjusting for variables such as age and axial length.[15] Similarly, Thorell et al studied choroidal thickness in early AMD eyes adjusting for age and axial length and concluded the same findings however, this was based on only three participants with RPD.[25]

Cheng et al further dichotomized their group by median age of all subjects.[15] They found that among subjects ≤82 years old, eyes with RPD had significantly thinner

choroids than AMD eyes without RPD, suggesting that the effects of RPD on ChT occur earlier in the AMD process as there was no difference in ChT in the ≥ 82 year old group. Our study however, did not support this finding. Among participants in both analysis (≤70 or ≤ 82 years old) with adjustment for variables, we found no significant difference in ChT between RPD and non-RPD groups ($p = 0.302$; $p = 0.721$ respectively). Further to this, we found that in our large cohort, ChT of the RPD group remained within 95% confidence interval of the non-RPD group for all tested locations (Figure 4) suggesting that there was indeed no difference in ChT found. Illustration of regression lines for both RPD and non-RPD group were not appropriate due to the RPD group being significantly older than non-RPD group.

RPD is often seen preferentially distributed at the superior temporal arcades and some have reported that ChT being thicker in the superior than corresponding inferior sectors.[14, 25] Whilst, most reports suggest choroidal thinning is associated with RPD, others have suggested that, within a generalized thinning, there may be some focal increase in the choroidal thickness in the geographical distribution of RPD, perhaps as a result of local fibrosis.[11, 14] In our study, we found no significant difference in Z-scores along the vertical meridian in eyes with RPD and in eyes where RPD was purely located in the superior field. Given this finding, we do not believe there is an association between a reduced ChT within an RPD eye regionally as previously reported.

Additionally, we have recently published the results of a unique opportunity to histopathologically examine an eye with extensive RPD, exenterated and fixed within a minute of removal, making the issue of post mortem artefact irrelevant. In this eye, there was no evidence of sclerosed choroidal vessels in regions immediately beneath RPD, suggesting that choroidal vessels remain patent across the choroid despite the presence of extensive RPD, thus we were unable to find any evidence to

support an abnormal choroid. [26]

In our study, we evaluated not only the ChT between RPD and non-RPD group, but we also studied ChT based upon extent of area of RPD and between superior and inferior choroids within the RPD group. We did not find reduced ChT in eyes with RPD in any of these analysis both globally and regionally. We showed that in an unadjusted model, reduced ChT was indeed found in the RPD group, however, once factoring in variables, especially age and refractive error, this association was lost. It is thus important that variables known to influence ChT need to be accounted for in any future analysis involving ChT.

The strength of our study was that we had a large cohort all with the same AMD stage which allowed us to adjust for variables that might contribute to ChT in a single analytical model and our extensive grading and classification of the presence or not of RPD. Several studies have reported the association of RPD with a thin choroid, however, these studies were limited either by a small sample size, a cohort with various stages of AMD, had elements of selection bias with matching of their control and non-control groups or did not adequately adjust for variables known to influence ChT such as age and refractive error.[11-14, 25, 27-29] No other study to date has been large enough to allow all such variables to be adjusted for in their analysis. In addition, we used multimodal imaging to detect the presence of RPD with strict grading criteria for determining presence of RPD whereas in most if not all previous studies, the methodology used for grading their presence within an eye is unclear, and the extent of their presence not well described. This may account for difference between previous studies and our current findings.

As mentioned, our cohort, whilst large also has all AMD cases at the same AMD severity which we believe is important as RPD are thought to be dynamic structures

that can change over time and as such might be influenced by the stage and progression of disease severity.[30] Therefore whilst we are very confident that our cohort represents the situation in iAMD, we are unable to comment at all on RPD and ChT correlations in any other stage of AMD, in particular we cannot comment upon later stages of AMD or in situations of regressed RPD that have been associated with a thin retina and underlying choroid.[30]

Whilst our study did measure ChT at nine macular locations (subfovea, 1500um and 3000um along vertical and horizontal meridians) it is possible that we may have been unable to detect focal changes in thickness. A better method of understanding choroidal thickness associations might lie with the addition and use of choroidal thickness maps.[31]

Furthermore, we ensured as accurate as possible measurements of ChT by using EDI SD-OCT images that allowed well demarcated choroids to be viewed and we excluded eyes where choroidal/scleral interface could not be identified precisely. Further to this, our study found intra-observer variability of ±21 μm, which demonstrates a high level of reproducibility.[32]

In conclusion, our study is the largest study to date that examined the important relationship between ChT and RPD in a cohort of participants with iAMD. We found that increased age and more myopic refractive error, but not the presence of RPD, was associated with reduced choroidal thickness. This suggests that the choroidal insufficiency may be a less important variable in RPD etiology than had previously been considered.

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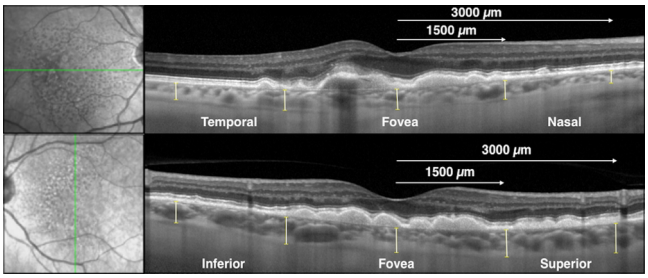

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Author/s:
Ho, CYD; Lek, JJ; Aung, KZ; McGuinness, MB; Luu, CD; Guymer, RH

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