DR. LISA NIVISON-SMITH (Orcid ID : 0000-0001-6677-1949)

PROF. MICHAEL KALLONIATIS (Orcid ID : 0000-0002-5264-4639)

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Full title: Peripheral retinal findings in populations with macular disease are similar to healthy eyes

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Authors' names and institutional affiliations: Lisa Nivison-Smith^{1,2}; Rebecca Milston¹; Jaclyn Chiang¹; Angelica Ly^{1,2}; Nagi Assaad^{1,3}; Michael Kalloniatis^{1,2}

¹ Centre for Eye Health, University of New South Wales, Sydney, Australia

² School of Optometry and Vision Science, University of New South Wales, Sydney, Australia

³ Prince of Wales Hospital Ophthalmology Department, Randwick, New South Wales, Australia.

Corresponding author:

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Michael Kalloniatis

E-mail: m.kalloniatis@unsw.edu.au

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Abstract

Purpose: Recent evidence suggests several macular diseases are associated with peripheral retinal changes. This study investigated the number, type and management consequences of peripheral retinal findings detected in patients attending a referral only, eye-care clinic, the Centre for Eye Health (CFEH) with macular disease.

Methods: Records of 537 patients attending CFEH for a macular assessment were included in the study. Subjects were classified as having age-related macular degeneration (AMD), epiretinal membrane (ERM), central serous chorioretinopathy (CSCR), inherited macular dystrophy or no macular disease. Data extracted included reason for referral, macular findings, peripheral findings (based on examination by ultra-widefield scanning laser ophthalmoscopy), diagnosis and management.

Results: After age-matching, the number of peripheral findings in subjects with AMD, ERM or CSCR was not significantly different to normal subjects. The most common finding for all cohorts were non-specific, degenerative changes such as drusen or pigmentation (61 - 72%) except inherited macular dystrophy subjects who had mostly vascular findings (30%; $p < 0.05$). Subjects with AMD and ERM with peripheral findings were significantly more likely to

be reviewed or referred to an ophthalmologist than discharged back to their community eye care provider compared to subjects without findings. However only 8% of subjects had altered management based specifically on peripheral findings suggesting the macular findings in most subjects dictated their management. For those with a change, it was significant (upgrade to referral to an ophthalmologist). Peripheral findings also flagged 5% of subjects with vascular findings for referral to their general practitioner (GP).

Conclusions: Overall, the percentage and distribution of peripheral retinal findings in some macular diseases was similar to normal subjects. However, subjects with peripheral findings appeared to have significant differences in management. Considering some common findings, such as peripheral drusen may be relevant to AMD pathogenesis and therefore affect management of this disease, assessment of the peripheral retina should not be overlooked when the clinical focus is on the posterior pole.

Introduction

Findings in the peripheral retina such as retinal tears, holes and detachments can have severe, vision threatening consequences and warrant urgent referral for ophthalmological care.¹ Other peripheral retinal changes, such as vascular abnormalities, may not directly cause vision loss but require detection and monitoring as they can indicate significant ocular conditions such as diabetic retinopathy.¹⁻³ Recently, several macular-based pathologies have been associated with peripheral retinal changes.⁴⁻⁹ In central serous chorioretinopathy, greater prevalence of lattice degeneration, rhegmatogenous retinal detachment and abnormal peripheral fundus autofluorescence has been reported.^{4, 10-12} In age-related macular degeneration (AMD), up to 97% of eyes with at least one large drusen also had drusen in the periphery and 48% of AMD eyes had non-AMD specific peripheral changes such as Cobblestone degeneration.¹³ Abnormal peripheral fundus autofluorescence has been noted in AMD¹⁴ and post-mortem analysis suggests advanced AMD lesions such as neovascularisation also extend to the periphery.¹⁵ These changes may be associated with the AMD disease process, as peripheral drusen has been linked to known AMD genotypes.¹⁶⁻¹⁸

Diseases that have central and peripheral retina involvement such as diabetic retinopathy, have also shown links in severity between the two retinal locations. Specifically, alterations detected in the peripheral retina of eyes with diabetic retinopathy, result in a 3.75 fold increase in development of diabetic macular oedema.^{9, 19} A high percentage of peripheral retinal pigment epithelium (RPE) alterations have also been reported for patients with uveitis with central retinal involvement.⁸ Thus the health of the peripheral retina may have increasing importance in the detection and management of macular pathologies.

The gold standard for examination of the peripheral retina is a dilated fundus examination.²⁰⁻²² More recently, ultra-widefield (UWF) scanning laser ophthalmoscopy has gained popularity for peripheral retinal assessment and imaging as it can be conducted as a non-contact and non-mydriatic technique.^{3, 23} Several studies have demonstrated that UWF imaging aids visualisation of peripheral choroidal lesions and melanomas,²⁴ paediatric retinal diseases,²⁵ retinal detachments,²⁶ and hereditary retinal dystrophies²⁷ and these findings can lead to alterations in patient management.²⁸⁻³² UWF imaging has also been shown to have agreement to dilated fundus examination³³ or 7-field fundus photography³⁴ for diabetic retinopathy. This combination of clinical agreement, ease of use and non-invasiveness has led to the suggestion of UWF imaging as an effective screening tool for peripheral retinal health.²³

Considering the mounting evidence of the significance of peripheral retinal changes in macular disease and the availability of UWF imaging, this study investigated the frequency of peripheral retinal findings in patients with or without macular disease using UWF imaging. Specifically, we explored the number, type and management consequences of peripheral findings detected in subjects attending a referral-only eye-care clinic for a macular assessment.

Materials and Methods

Study Population

Subject data was obtained through retrospective analysis of medical records of patients attending the Centre for Eye Health (CFEH) in Sydney, Australia, for a macular assessment.

CFEH is a referral-only eye-care clinic that provides advanced diagnostic testing services and consultations by highly trained optometrists and ophthalmologists to patients referred by primary or community eye-care professionals.³⁵ A macular assessment consisted of patient history; pupil reactions; visual acuity; Amsler grid testing; colour fundus photography (central, 45 degrees) using a Kowa Non-Mydriatic WX3D retinal camera / analysis system (www.kowa.co.jp); UWF imaging (on -axis, red-green image) using an Optomap Panoramic 200Tx retinal imaging system (www.optos.com); fundus autofluorescence imaging and optical coherence tomography (OCT); posterior pole scans using Heidelberg Spectralis spectral domain OCT (www.heidelbergengineering.com); and Cirrus HD OCT macular 512 x 128 cube scan (www.zeiss.com). All images including UWF imaging were obtained through a dilated pupil.

Subject selection was performed as described in *Figure 1*. Records of all patients attending CFEH consecutively from January 2014 to July 2018 for a macular assessment were examined. Patients had provided written consent for research participation in accordance with the Declaration of Helsinki and research protocols were approved by a Biomedical Human Research Ethics Advisory Panel of the University of New South Wales. A total of 1813 independent records were obtained (for subjects who had attended the centre during this period as a follow-up appointment, only records from their initial appointment date were extracted). Records were then screened against the following inclusion criteria: subjects were referred for a complete macular imaging assessment with a CFEH referral form (available from www.centreforeyehealth.com.au); subjects had a central, 45-degree fundus photograph and standard, central (on-axis) red-green UWF image of both eyes. Although UWF images taken at CFEH are conducted under conditions specified by the manufacturer (alignment of patient's eye so pupil is centred, 3 and 9 o'clock sides of the limbus ring cover the patient's limbus and correct distancing of patient's eye signalled by instrument), we performed an additional quality control check, confirming UWF images covered at least the central 120° with or without the aid of changing contrast, brightness, and zooming in the Optos viewing software and image was not obscured by media opacities or lid/eyelash or face pad artefacts. Less than 2% of subjects were excluded for such artefacts.

For the final subject cohort, extracted records included (1) a referral form from the primary eye-care professional; (2) results of the macular assessment; and (3) a clinical report written by the clinician at CFEH who performed the examination and reviewed independently by at least one other experienced clinician, including an ophthalmologist in 30% of cases where referral to ophthalmology was recommended or the diagnosis was uncertain.

Patient referral and diagnosis classifications

All subject classifications were based on previous work described by our group.³⁶ Briefly, subject's primary reason for referral was coded into one of five categories – signs of macular disease, symptoms of macular disease, case history relating to macular disease, further imaging/second opinion on macular findings or diagnosis confirmation. Subject's diagnosis was extracted from the CFEH clinical report and was coded into one of five categories – normal, age-related macular degeneration (AMD), epiretinal membrane (ERM), central serous chorioretinopathy (CSCR) or inherited macular dystrophy. Normal subjects were classified as those with no signs of macula disease or normal aging changes in the macula.³⁷ Diagnosis in CFEH clinical reports were based on all the medical and imaging information gathered at the visit including patient history, visual function testing, retinal photography, autofluorescence imaging, and OCT. Classification of AMD was based on the system reported by Ferris, *et al.*³⁷

Classification of peripheral findings

Individual peripheral findings from UWF imaging were extracted from CFEH clinical reports. Findings were classified as peripheral if they were found beyond the vascular arcades and not visible on the central 45-degree fundus photograph. For an additional level of quality control, 10% of subjects were randomly selected and re-evaluated by an ophthalmologist (NA) to confirm that reported peripheral findings were consistent with subject imaging records and patient clinical records. One hundred per cent agreement was observed with reported findings.

Findings were grouped into five categories: vascular findings (haemorrhages, microaneurysm, vessel abnormalities); tumours (choroidal naevus, congenital hypertrophy

of the retinal pigment epithelium or CHRPE); non-specific, degenerative findings (white-without-pressure, chorioretinal atrophy including pavingstone degeneration, drusen, non-specific hyper/hypopigmentation, microcystoid degeneration, reticular degeneration); findings predisposing to retinal detachment (lattice/snail-track degeneration, vitreoretinal tuft, retinoschisis); and urgent findings (retinal detachment, retinal tear, retinal hole). Examples of peripheral findings can be found in *Figure 2*. For lesions which occurred multiple times in a single eye (for example, multiple drusen lesions visible in *Figure 2A*), the finding was only counted once in that eye.

Findings were further separated based on the timing of discovery. For subjects with peripheral findings, their primary eye-care professionals were contacted and a finding was considered primary if the primary eye care professional confirmed the presence of the finding before the subject was assessed at the referral centre. Findings were considered secondary if it was first noted during the subject's assessment at the referral centre.

Secondary findings were further separated into incidental and non-incidental where non-incidental findings were those not specifically noted by the primary eye care professional but not unexpected during assessment at the referral clinic due to pertinent information on the referral which indicated the potential for peripheral retinal findings (i.e. subject had myopia, history of flashes and floaters, etc.). Incidental findings were those where there was no prior indication the findings would be present.

Patient management classifications

Subject's recommended management was determined from the CFEH clinical report and coded into three categories: discharged to routine review with the primary referring eye-care professional; review at the referral centre (patients at risk of disease progression that require monitoring); or referral to an ophthalmologist. To analyse the impact of peripheral findings on management, all subjects with peripheral retinal findings were re-examined by a trained clinician (RM) who was asked to determine a new management recommendation in the absence of the peripheral findings. This management was compared to that of the original report.

Statistical Analysis

Chi-squared analysis and Fisher's exact test were used to determine statistically significant differences between groups of subjects with and without macular disease in regards to sex, age, ethnicity, reasons for referral and distribution of findings or between groups with and without peripheral findings in regards to management. Student's t-test was used to compare average number of findings between normal and disease cohorts. Statistical analyses were performed with GraphPad Prism version 6 (www.graphpad.com). For all cases, $p < 0.05$ were considered significant.

Results

Subject population

A total of 537 subjects were included in the study. Demographics of the cohort are shown in *Table 1*. As expected, the AMD and ERM cohorts were significantly older than the normal cohort (unpaired t-test; $t_{AMD} = 0.576$, $t_{ERM} = 0.461$, $p < 0.0001$). Reasons for referral were also significantly different with normal subjects most commonly referred for signs of macular disease (34%, 42/124), followed by symptoms of disease (24%, 30/124) compared to macular disease subjects where signs of disease was also the most common reason for referral (33-54%) but referral for symptoms was much less (4-13%). There was no difference in sex or ethnicity between normal and disease cohorts excluding CSCR for gender (Fisher's exact test; $p < 0.0001$) and AMD for ethnicity (Chi-square test; $df = 6$; $p = 0.011$).

Peripheral retinal findings

Overall, peripheral retinal findings were present in 31% (39/124) of normal subjects; 35% (67/194) of AMD subjects; 44% (51/115) of ERM subjects; 28% (22/80) of CSCR; and 21% (5/24) of inherited macular dystrophies subjects (*Figure 3A*). Fisher's exact test found a significant difference in number of peripheral retinal findings in ERM subjects compared to the normal cohort ($p = 0.045$) but not for other macular diseases (AMD, $p = 0.62$; CSCR, $p = 0.64$; inherited macular disease, $p = 0.34$). To account for the effect of age, each macular disease cohort was compared to a subset of age-matched, normal patients (*Figure 3B*). For AMD ($p = 0.51$), ERM ($p = 0.99$) and CSCR ($p = 0.64$), the number of peripheral findings was similar to an age-matched normal population suggesting age was a major contributor to the

difference in findings between groups in *Figure 3A*. Inherited macular dystrophy still showed a two-fold less percentage of peripheral findings compared to the normal cohort when accounting for age but this was not significant (Fisher's exact test, $p = 0.34$).

Each peripheral retinal finding was then counted individually and sorted into one of five categories (*Figures 3C-3F*). A total of 70 individual peripheral retinal findings were noted in 39 normal subjects resulting in an average 1.75 findings per subject. The ratio of findings for macular diseases was similar except for AMD, which was 2.30 (155 findings/67 AMD subjects). Age did not appear to play a role as the ratio of findings per subject was again only significantly different between normal and AMD subjects (*Figure 3D*; unpaired t-test, $t = 2.331$; $df = 55$, $p = 0.023$).

Types of peripheral retinal findings

The most common findings for normal subjects were non-specific, degenerative findings (67%, 47/70 findings) followed by tumours (13%, 9/70) and findings predisposing to retinal detachment (13%, 9/70; *Figure 4A*). No urgent vitreoretinal and retinal findings were observed in the normal cohort. Non-specific, degenerative findings were also the most common finding for most macular diseases except inherited macular disease (*Figure 4A*, Chi-square test, $t = 8.274$, $df = 3$, $p = 0.041$). ERM (9%, 9/105 findings), CSCR (15%, 6/39) and macular dystrophies (30%, 3/10) also had a higher proportion of findings predisposing to retinal detachment than AMD (5%, 8/155) although this was not significant. Again, age did not appear to play a role in distribution of findings, as there was no significant distribution in findings between normal and disease groups before or after age matching (*Figure 4B*).

The individual lesions contributing to the five categories of peripheral retina changes are listed in *Table 2*. For non-specific degenerative changes, the most common finding for normal subjects was drusen (43% or 20/47 of all non-specific findings) followed by hyper/hypopigmentary abnormalities (28% or 13/47 of all non-specific findings). For the AMD cohort, drusen was also the most common peripheral finding but contributed significantly more (70% or 111/155 of all non-specific findings) compared to normal or other macular pathologies (Chi square test; $t = 23.04$, $df = 4$, $p = 0.0001$). For vascular findings, the most common peripheral finding was haemorrhages for both normal and disease cohorts and for tumours, the most common finding was choroidal naevus. Findings predisposing to

detachment were most commonly vitreoretinal tufts or retinoschisis. Urgent findings consisted of retinal holes (43%) or tears (22%) across the macular disease cohort. Refractive error for eyes with urgent findings ranged from -3.25D to + 4.875D spherical equivalent with a median of -0.25D.

Implications relating to the detection time of peripheral findings

We further assessed peripheral retina findings based on the time they were first observed. Only 18% (7/39) of peripheral retina findings in normal subjects were first observed by the referring clinician (*Figure 5*). Similarly, less than 25% of findings in AMD, ERM and CSCR disease cohorts were primary findings. In contrast, 40% (2/5) of peripheral findings in inherited macular dystrophy subjects were first observed by the referring clinician but this was from a small sample size.

The remaining findings, considered secondary, were first observed at the referral clinic, the Centre for Eye Health (CFEH). The majority of these secondary findings were noted incidentally for all cohorts (56-75%) with no indication on the original referral form or the subject's history (i.e. history of myopia, flashes/floaters, etc.) to suggest the presence of peripheral findings before the secondary macular assessment.

Recommended management of subjects with peripheral findings

Finally, the recommended management plan of subjects with peripheral retinal findings were assessed (*Figure 5B*). The majority of normal subjects were discharged or recommended to return to CFEH in the future for review (93 -97%) with no significant difference in recommended management in the presence of peripheral retinal findings (Chi-square test, $\chi^2 = 1.401$, $df = 2$, $p = 0.50$). The remaining normal subjects (7/124 total normal subjects) were referred to an ophthalmologist due to continuation of symptoms (i.e. reduced visual acuity, blur) but not obvious signs of macular disease. For disease cohorts, there was a notable increase in recommendations for recall to CFEH in the future for review or referral to an ophthalmologist with significant differences in management for subjects

with peripheral findings versus no findings in AMD (Chi-square test, $t = 16.47$, $df = 2$, $p = 0.0003$) and ERM (Chi-square test, $t = 9.528$, $df = 2$, $p = 0.0085$; *Figure 5B*).

When all subjects with peripheral retinal findings (both normal and macular disease subjects) were re-evaluated in the absence of these findings, only 8.2% (15/184) of subjects would have had a different recommended management suggesting the macular findings in most subjects dictated their management. In cases with a management change, this change was usually a downgrade from ophthalmological referral to recall to the referral centre (80%, 12/15) or discharge back to the referring optometrist (20%, 3/15). As the majority of subjects with altered management had urgent peripheral findings, which could lead to sight-threatening consequences, the upgrade in management following discovery of the finding was a significant result. In the absence of peripheral findings, 10 out of 20 subjects who had peripheral vascular findings would have also missed out of the recommendation to have their findings communicated to their general practitioner.

Discussion

This study analysed the number and types of peripheral retinal findings detected in a population of normal and macular disease subjects using UWF imaging. We found 31% of subjects with no macular disease had peripheral findings. Although other studies have reported lower number of peripheral retinal abnormalities in asymptomatic populations using dilated fundus examination (4.8 - 7.7%),^{38, 39} and UWF imaging (16 - 18.5%),^{4, 11, 13} our normal population was older than these previous studies which may account for the higher number of peripheral retina findings. This is supported by our age-matched results where the number of peripheral findings in the normal population increased when matched to older cohorts such as AMD and ERM. Importantly, our normative cohort is considerable larger than comparative control populations for studies using ultra-widefield colour and FAF imaging and therefore may be more useful in future studies assessing older populations.^{4, 6,}

26

For macular disease subjects, there was a large variation in number of peripheral findings; only 21% of inherited macular dystrophy subjects had peripheral findings, while 44% of ERM

subjects had findings. Lengyel, *et al*⁷ found peripheral retinal findings in 57.4% of subjects with macular abnormalities and Heussen, *et al*⁴ who reported peripheral findings in 79.3% and 52.9% of AMD and CSCR subjects referred to a tertiary eye clinic, respectively. The majority of AMD subjects enrolled in the Age-Related Eye Disease Study 2 (AREDS2) were found to have peripheral abnormalities with 97% of subjects having mid-peripheral drusen.¹³ The lower frequency of peripheral retina findings in our study may relate to age, as our disease cohorts had a mean age approximately 15 years younger than the abovementioned studies. For AMD specifically, differences between our cohort and those enrolled in the AREDS2 trial also likely relates to inclusion criteria where eyes classified with early or intermediate AMD based on medium drusen and/or pigmentary changes were included in our AMD cohort, but not AREDS2. Differences may also stem from larger imaging area due to the use of steering. Lower incidence of peripheral findings may also be associated with limited definition of peripheral retinal lesions as one study only considered fundus autofluorescence abnormalities.⁴

We found drusen and pigmentary changes were the most common peripheral retinal findings in subjects with no pathology, which matches cross-sectional studies indicating that 10.1% of the general population aged over 62 years old have AMD-like abnormalities in the periphery.⁷ Vascular abnormalities were uncommon in subjects with no pathology although this may be an underestimate as Shah, *et al*⁴⁰ found a high prevalence of peripheral vascular variations in normal eyes when using UWF fluorescein angiography that allows for dynamic assessment of the retinal vasculature, rather than static imaging used in our study.

In subjects with a macular disease, peripheral retinal findings are often associated with known disease presentations and/or mechanisms. For example, drusen and pigmentary changes typical in the macula in AMD were also the most common peripheral finding of AMD subjects. Evidence on the role of specific peripheral lesions and macular disease pathogenesis is mostly limited to AMD, with peripheral drusen and pigmentary changes suggested to be associated with greater disease severity and known disease genotypes.^{14,}

¹⁶⁻¹⁸ However, histological studies indicate peripheral and macular drusen differ in their lipid

and protein composition therefore peripheral elements of AMD may not operate under the same disease mechanisms as their macular counterparts.⁴¹ Large, longitudinal studies are currently under way regarding the role of peripheral findings in AMD.⁴²

Over 50% of all peripheral findings were observed incidentally at the referral centre for both normal and macular disease cohorts. The high number of incidental, secondary findings suggests peripheral retinal assessment may not have been considered by the referring primary clinician for subjects with suspected macular pathology. The reasons for this are not known, but do not necessarily reflect poor clinical performance by referring clinicians, as previous studies indicate high levels of congruency between primary and secondary eye-care in regards to diagnosis of macular³⁶ and other eye diseases.³⁵ More likely, omission of peripheral retinal assessment may be due to lack of indication. Indeed, studies suggest peripheral retina screening of asymptomatic populations is costly and unnecessary, due to the low yield of clinically significant findings,^{39, 43} and that patient symptomatology is a better indicator for peripheral retinal findings.⁴⁴ Whilst our study found most peripheral retinal findings did not lead to a change in management, some findings could have significant future implications - for example, 54% of findings in AMD subjects were peripheral drusen or pigmentary changes that have been associated with AMD genetic polymorphisms and therefore could be important to patient's family members. Thus while general screening for peripheral retina findings may not be cost effective, routine examination of the periphery in the context of macular pathology may be appropriate.

There were some limitations to this study. Firstly, CFEH, the referral centre used in this study, has a general policy that only non-urgent cases be referred and, accordingly, patients with recent onset of symptoms may be directly referred to ophthalmology. This may account for the high proportion of clinically significant peripheral findings being discovered as incidental, secondary findings. In addition, findings were categorised based on current knowledge; however, some findings are part of evolving definitions. For example, white-without-pressure has been classically associated as a factor predisposing to retinal detachment; however, in this study we classified white-without-pressure as a 'non-specific, innocuous finding' based on Fawzi, *et al*⁴⁵ who showed white-without-pressure leads to a change in ellipsoid zone reflectivity on OCT rather than from vitreoretinal traction as previously thought. Secondly, peripheral retinal findings were based solely on those

observed by UWF imaging without steering. UWF on axis imaging is limited to 200° field of view meaning eyelid and eyelash artefacts can mask changes in the far superior and inferior periphery leading to an underestimate in peripheral findings. To minimise this, subjects were only included if they had high quality UWF imaging of both eyes with no shadowing or artefacts. We acknowledge that this could introduce a selection bias towards younger eyes, as many issues that reduce image quality, such as cataract, are age-related. However, considering the median age of our study cohorts and the fact that CFEH is primarily an ocular imaging clinic (and thus the majority of patients referred do not have significant cataract), this bias is potentially limited in our cohort. Warping, stretching and changes of magnification in the most peripheral areas is also not uniform in UWF imaging and may have been an issue in this study due to the use of on-axis imaging alone.^{7, 46, 47} Future studies could consider using steering or new technology to overcome imaging quality issues with montaging and correcting for peripheral distortion.⁴⁸

Conclusion

This study found the number of peripheral retinal findings in some macular diseases is up to 44% when detected using UWF imaging. This was not significantly different to normal subjects for AMD, ERM and CSCR following age-matching. The majority of these findings were drusen or pigmentary changes for all macular diseases assessed. Although only 8% of subjects had a management change following peripheral findings discovery, some may have future implications as the role of peripheral lesions in certain disease such as AMD continues to evolve.

Figure Legends

Figure 1. Flowchart indicating the method of acquiring data for this retrospective study. All data was extracted from records of patients who attended the Centre for Eye Health (CFEH) in Sydney, Australia for a macular assessment following a referral from their eye care practitioner (usually an optometrist). Records included a referral form, results of the macular assessment which consists of patient history, pupil reactions, visual acuity, Amsler

grid testing, colour fundus photography, UWF imaging, fundus autofluorescence (FAF) imaging and optical coherence tomography (OCT) and a report summarising clinical findings. To ensure data quality in the study, two quality control checks were performed. All UWF images were assessed for image quality before inclusion of subject record in the study. A subset of included subjects were also reassessed by an independent ophthalmologist to validate findings provided in clinical report.

Figure 2. Examples of peripheral findings recorded in the study including (A) peripheral drusen, (B) chorioretinal atrophy, (C) pavingstone degeneration, (D) haemorrhage (haem), (E) CHRPE, (F) choroidal naevus, (G) white-without-pressure (WWOP), (H) lattice degeneration, (I) vitreoretinal tuft, (J) snail-track degeneration, (K) retinal detachment, (L) retinal hole. Arrows indicate location of finding and for smaller findings, a magnified image of the finding is provided in the insert.

Figure 3. (A – B). Percentage of subjects with peripheral findings and (C - D) the mean number of peripheral findings per subject for (A, C) the total population and (B, D) a subset of the disease (dark bars) and normal population (light bars) which has been age-matched. n indicates the number of total number of subjects in each cohort. Abbreviations: NAD, no apparent defect; AMD, age-related macular degeneration; ERM, epiretinal membrane; CSCR, central serous chorioretinopathy. * = $p < 0.05$

Figure 4. The types of peripheral retina findings for (A) the total population and (B) a subset of the disease and normal population which has been age-matched. Peripheral findings include degenerative findings (grey), vascular findings (light pink) tumours (dark pink), findings requiring monitoring (blue) and urgent findings (black). n indicates the number of total number of peripheral findings in each cohort. Abbreviations as in *Figure 2*. * = $p < 0.05$

Figure 5. (A) The number of primary (red) and secondary (non-incidental; blue and incidental; teal) peripheral retina findings and (B) the management recommendation for each disease type as a comparison between those with peripheral findings (PF) and those without (no PF). Recommendations include discharge to community (white); recall (grey) or referral to tertiary care (black). Abbreviations: PF, peripheral findings. All other abbreviations as in *Figure 2*.

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Disclosures

The authors report no proprietary interest in any of the materials mentioned in this article. All the authors certify that there is no conflict of interest regarding the material presented in this manuscript.

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Table 1: Characteristics of subject cohort.

Abbreviations: AMD, age-related macular degeneration; ERM, epiretinal membrane; CSCR, central serous chorioretinopathy. IQR, inter-quartile range, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

	No pathology	Macular pathology			
		AMD	ERM	CSCR	inherited
TOTAL	124	194	115	80	24
AGE		***	***		
Median (years)	52	69	66	48	55
Range (years)	23 – 80	50 – 90	26 – 86	29 – 76	42 – 90
IQR (years)	43 – 60	62 – 74	59 – 70	42 – 56	48 – 65
SEX				***	
Male	60 (48%)	79 (41%)	60 (52%)	69 (86%)	14 (58%)
Female	64 (52%)	115 (59%)	55 (48%)	11 (14%)	10 (42%)
ETHNICITY		*			
Caucasian	60 (49%)	104 (54%)	49 (43%)	35 (44%)	18 (75%)
Asian/Indian	34 (27%)	27 (14%)	37 (32%)	26 (33%)	1 (4%)
Arabic/Persian	8 (7%)	6 (3%)	3 (3%)	6 (8%)	0 (0%)
Hispanic/Sth American	2 (2%)	3 (2%)	0 (0%)	1 (1%)	0 (0%)
Mixed	2 (2%)	2 (1%)	2 (2%)	1 (2%)	0 (0%)
Aboriginal	0 (0%)	3 (2%)	2 (2%)	2 (3%)	0 (0%)
Unknown	17 (14%)	49 (25%)	21 (18%)	9 (11%)	5 (21%)
REASON FOR REFERRAL		***	***	**	
Signs	42 (34%)	87 (45%)	34 (30%)	28 (35%)	13 (54%)
Second opinion/imaging	30 (24%)	69 (36%)	32 (28%)	26 (33%)	5 (21%)
Symptoms	31 (25%)	8 (4%)	14 (12%)	6 (8%)	1 (4%)
Diagnosis	12 (10%)	26 (13%)	34 (30%)	17 (21%)	2 (8%)
Case History	9 (7%)	4 (2%)	1 (1%)	3 (4%)	3 (13%)

Table 2: Specific peripheral findings of each disease cohort.

Note each different finding was only counted once per eye regardless of the total number of lesions in a single eye; i.e. multiple drusen lesions in a single eye were counted as one peripheral finding of drusen.

Abbreviations: AMD, age-related macular degeneration; ERM, epiretinal membrane; CSCR, central serous chorioretinopathy. CHRPE, congenital hypertrophy of the retinal pigment epithelium

	Normal	AMD	ERM	CSCR	Inherited macular dystrophy
Total subjects with findings	40	67	51	23	5
Total no of findings	70	155	105	39	10
NON-SPECIFIC DEGENERATIVE FINDINGS					
Drusen	20	78	24	8	-
Hyper/hypopigmentation	13	5	13	9	2
White without pressure	8	9	12	2	-
Chorioretinal atrophy	3	5	9	4	1
Reticular degeneration	-	12	10	-	-
Cystoid degeneration	3	2	-	2	-
VASCULAR FINDINGS					
Haemorrhage	5	4	4	2	1
Microaneurysm	-	1	1	-	-
Vessel abnormalities	-	4	2	1	2
TUMOURS					
Choroidal naevus	9	19	8	2	-
CHRPE	-	1	2	2	1
FINDINGS PREDISPOSING TO DETACHMENT					
Vitreoretinal tuft	5	3	4	2	-
Retinoschisis	3	2	4	4	1
Lattice & snail-track degeneration	1	3	1	-	2
URGENT FINDINGS					
Retinal tear	-	2	3	-	-
Retinal hole	-	3	6	1	-

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Author/s:

Nivison-Smith, L;Milston, R;Chiang, J;Ly, A;Assaad, N;Kalloniatis, M

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