Centre for Eye Health

ATLAS LITERATURE REVIEW

Issue 1 • Aug 2021

Welcome to the inaugural issue of Centre for Eye Health's ATLAS Literature Review. Each quarter we'll be bringing you reviews from our pick of the latest literature as part of your ATLAS subscription.

This issue we'll be reviewing literature for vascular disease, glaucoma, and macular disease. These reviews have been prepared by Centre for Eye Health clinicians Gonzalo Jacome and Elizabeth Wong, and PhD candidate Sharon Ho.

We'd love your feedback on your experience with ATLAS so far, and your suggestions on what we should add next. Email us with your feedback.

Your purchase of ATLAS and our other educational materials helps to support Centre for Eye Health, and Guide Dogs NSW/ACT, and for that we are incredibly grateful.

Severity of Diabetic Retinopathy and the Risk of Future Cerebrovascular Disease, Cardiovascular Disease, and All-Cause Mortality

Authors: Modjtahedi BS et al.

Summary: This study showed the presence of diabetic retinopathy in patients with type 2 diabetes mellitus have a strong associated future risk for stroke, myocardial infarction, congestive heart failure and death, once all other related risk factors were controlled for at 5 years.

Higher diabetic retinopathy levels showed an even greater risk for each systemic disease aforementioned.

Clinical applications: This study reinforces the importance of accurate detection and grading of retinopathy. It demonstrates that patients with diabetic retinopathy, especially higher levels of disease may benefit from earlier intervention, more intense management & closer monitoring for systemic complications of DM. It also highlights the importance of a holistic, personalised multidisciplinary management of current & future morbidity and mortality.

Reference: *Ophthalmology. 2021 Aug;128(8):1169-1179*

Abstract

In this issue:

Validation of a Head-mounted Virtual Reality Visual Field Screening Device

Authors: Mees L et al.

Summary: The Humphrey Field Analyzer is a commonly used perimeter in clinical practice for assessing the visual field field. However, it is not without its limitations. Two such limitations are the size (clinic space and portability) and cost of the machine. Portable visual field screening tools using consumer friendly technology such as tablets have been developed to address these limitations however the seated testing position may be an obstacle for immobile patients. The use of virtual reality as a method for visual field testing has recently been investigated to overcome some limitations of other devices.

Key findings: In this study, Mees et al evaluated the C3 field analyser (CFA), a head mounted virtual reality visual field screening device as a subjective test for glaucoma screening. Previously diagnosed glaucoma and normal patients underwent OCT, fundus photography, and HFA 24-2 SITA standard testing, before being classified by two masked practitioners as glaucoma or normal. The patients then performed the HVFA and the CFA in a random order with a satisfaction survey completed following.

The CFA was able to identify moderate and advanced glaucoma better than mild disease. 38% of ≤18dB deficits detected on the HFA were picked up by the CFA with the inferior visual field being the least consistent.

Clinical applications: While screening for early glaucoma may be an issue, the monitoring of known cases of glaucoma has previously been shown to be effective. Using virtual reality technology for visual field assessment is becoming more widely accessible and accepted as an alternative to current clinical standards such as the HFA.

Reference: *J Glaucoma. 2020 Feb;29(2):86-91*

Abstract

Home Self-tonometry Trials Compared with Clinic Tonometry in Patients with Glaucoma

Authors: McGlumphy EJ et al.

Summary: Diurnal variations in IOP are of interest to practitioners when deciding on treatment initiation and treatment type for glaucoma. One such method of IOP profiling over a 24 hour period is the iCare Home.

Key findings: McGlumphy compared characteristics of intraocular pressure (IOP) measured during home tonometry over a 7 day period with in-clinic tonometry (5 previous clinic visits) in glaucoma patients. In a total of 107 eyes (61 patients, mean age 63.2 years), home tonometry was found to identify higher maximum IOP, lower minimum IOP and a greater IOP range than clinic tonometry. A key finding of this paper is that 74% of eyes (55 eyes) showed at least one home IOP measurement that exceeded the target IOP, and that of these 55 eyes, 38% did not show any clinic IOP measured above target. Furthermore, the highest peaks in home IOP occurred outside clinic hours. It should be noted however, that the majority of clinic tonometry measurements were performed with Goldmann applanation tonometry.

Clinical applications: Provided that the patient is willing and able to perform the iCare Home technique competently, iCare Home IOP measurements are an excellent way to acquire additional data in patients which show progressive glaucoma despite consistently low IOP measurements within clinic. In this particular paper, home tonometry trials led to an increase in the glaucoma therapy (additional medication, laser trabeculoplasty, or surgery) in 55 of the eyes. In addition, where therapy has been changed, iCare Home tonometry can monitor IOPs under changing treatment for glaucoma cases and provide a safe and effective telemedicine alternative to in-clinic measurements, particularly relevant to the current health climate.

Reference: *Ophthalmol Glaucoma. 2021 Apr 9:S2589-4196(21)00090-9*

Abstract

Cardiovascular Disease Predicts Structural and Functional Progression in Early Glaucoma

Authors: Marshall H et al.

Summary: In the vascular theory of glaucoma, optic neuropathy is thought to be a result of blood supply insufficiency due to elevated intraocular pressure (IOP) or other risk factors in reducing ocular blood flow. This theory has been proposed to explain why some patients with low pressures may still develop glaucoma. In a previous paper, Marshall et al found macular ganglion cell-inner plexiform layer (mGCIPL) loss to precede peripapillary retinal nerve fibre layer (pRNFL) loss in patients with glaucoma with lower average IOP (2). They then hypothesised that vascular dysfunction may also be present in these patients showing structural mGCIPL damage.

Key findings: In this study, Marshall et al investigated the association between cardiovascular disease and baseline structural defects and disease progression in glaucoma. Patients were classified according to the pattern of thinning present: predominantly mGCIPL, predominantly pRNFL, or both, then evaluated for disease progression on longitudinal optical coherence tomography (OCT) scans and/or progression on static automated perimetry. Those that showed no structural or functional change over the study period were classified as the 'reference' group.

Glaucoma patients with predominantly mGCIPL defects had a higher prevalence of hypertension and previous myocardial infarction when compared with those in the reference group. However, glaucoma patients with predominantly pRNFL structural change were not associated with a higher prevalence of any cardiovascular disease or medication compared to reference patients.

Clinical applications: As practitioners become increasingly holistic in their approach to patient management, knowledge of the patient's general health, and collaboration with their primary care physician is critical. Eye care providers should be aware of and consider systemic cardiovascular disease for several key reasons:

1. As an alternative cause of glaucomatous or glaucoma-like structural loss,
2. When determining the optimal treatment plan for glaucoma patients, and
3. If the patient presents with retinal vascular (not necessarily glaucoma) findings.

Reference: *Ophthalmology. 2021 Jan;128(1):58-69*

Abstract

Subthreshold Nanosecond Laser in Age-Related Macular Degeneration: Observational Extension Study of the LEAD Clinical Trial

Authors: Guymer RH et al.

Summary: Laser Intervention in the Early Stages of AMD (LEAD) aims to develop an effective treatment for those with earlier stages of AMD to prevent or slow progression. Subthreshold nanosecond laser (SNL) is a novel short-pulse, nanosecond laser shown to reduce drusen load without damaging overlying photoreceptors, though its exact mechanism is unknown. The 2019 LEAD randomised-controlled trial found no overall difference in the development of late AMD between SNL and sham treatment for intermediate AMD over 36 months. However, SNL treatment demonstrated a potential role in slowing progression for those without coexistent reticular pseudodrusen. This guided the current study to examine the longer-term impact of SNL treatment on development of late AMD.

Key findings: This 24-month observational study enrolled a subset of participants from the 2019 LEAD trial. Results continued to show no overall difference in the rate of progression to late AMD between SNL and sham treatment groups over the total 60-month period. However, progression significantly slowed by approximately 3-fold with SNL treatment for those without coexistent reticular pseudodrusen, though it was not significantly different for those with reticular pseudodrusen. The study also confirmed SNL treatment did not increase the risk of neovascular AMD over a longer follow-up period, addressing perceptions formed regarding laser safety.

Clinical applications: Current management strategies for non-neovascular AMD are limited, and there is no specific intervention that prevents or slows progression from earlier, asymptomatic stages of AMD to the visually devastating complications of late AMD. Findings from this study show potential benefit of SNL treatment for patients with intermediate AMD without coexistent reticular pseudodrusen.

Future directions: These findings provide justification for future randomised-controlled trials to examine the potential value of SNL treatment for slowing progression in intermediate AMD. It also raises questions regarding the required frequency and duration of SNL treatment needed to reduce the rate of progression.

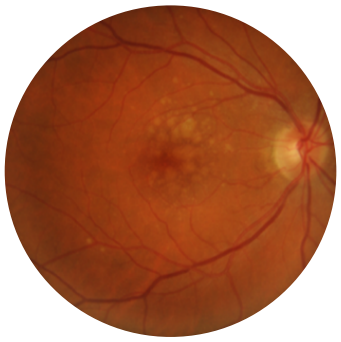
Reference: *Ophthalmol Retina. 2021 Mar 1:S2468-6530(21)00069-5*

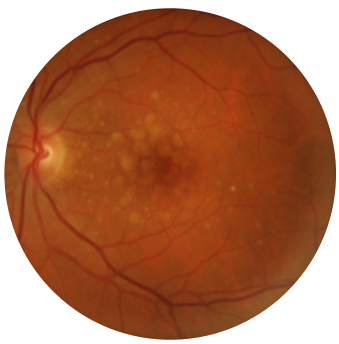
Abstract

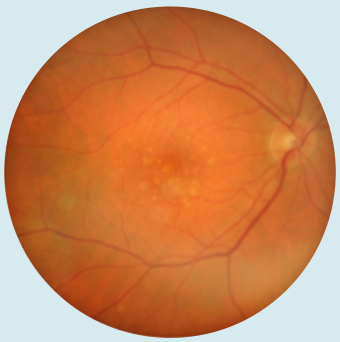
Centre for Eye Health case studies

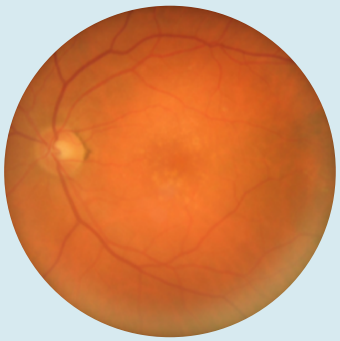
Intermediate AMD

Bilateral large confluent drusen with mild pigmentary changes, no reticular pseudodrusen





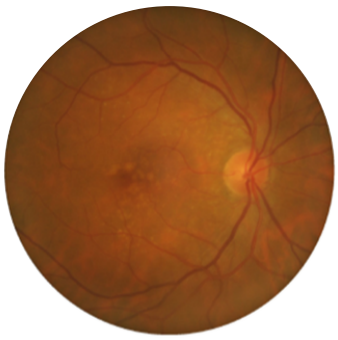


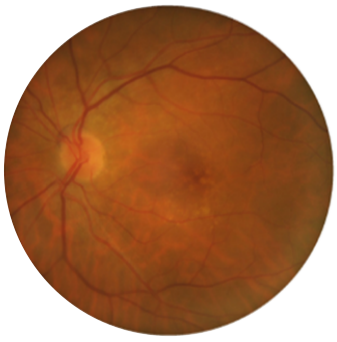


Intermediate AMD

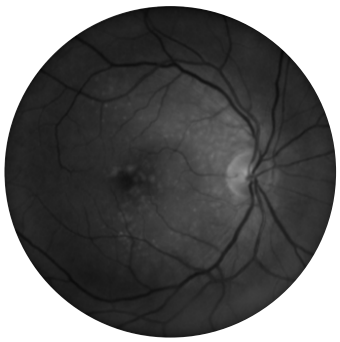
Bilateral large drusen, no reticular pseudodrusen

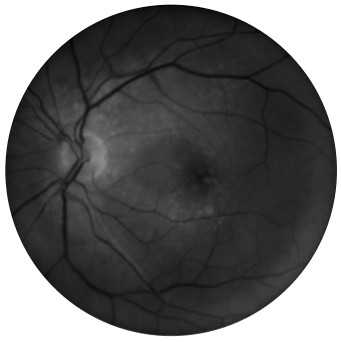
Intermediate AMD with reticular pseudodrusen





Reticular pseudodrusen more clearly seen on red-free imaging; mostly inferiorly and superiorly in right eye and superiorly in left eye





Pentosan Polysulfate Maculopathy versus Inherited Macular Dystrophies: Comparative Assessment with Multimodal Imaging

Authors: Barnes AC et al.

Summary: Pentosan polysulfate sodium (PPS) maculopathy is a progressive vision-threatening pigmentary maculopathy recently implicated with long-term exposure to PPS; a drug commonly used to treat interstitial cystitis (bladder inflammation/irritation). It has often been misdiagnosed for macular dystrophies due to shared phenotypic characteristics, and the relatively small number of identified cases hence our understanding of it is still unclear. This study aimed to identify and compare key features of PPS maculopathy to those of hereditary maculopathies using multimodal fundus imaging, and evaluate whether the conditions may be reliably differentiated using fundus imaging alone. It also aimed to refine the case definition for PPS maculopathy.

Key findings: In this retrospective review of 1131 patient records diagnosed with macular dystrophy, graders masked to medication exposure and medical history identified cases of PPS maculopathy with 100% sensitivity and 99.6% specificity. Key distinguishing characteristics were: (1) Peripapillary fundus autofluorescence signal: hypo-autofluorescent peripapillary halo in PPS maculopathy, cf. peripapillary sparing in hereditary maculopathies, (2) Spacing of fundus autofluorescence abnormalities: densely packed in PPS maculopathy, cf. lesions may be scattered amid a fairly normal posterior pole in hereditary maculopathies , (3) Central macula: involved early in the disease course of PPS maculopathy, cf. other maculopathies tend to demonstrate foveal-sparing in early stages .

Clinical applications: Clinicians can reliably identify cases of PPS maculopathy with the aid of multimodal fundus imaging (particularly fundus autofluorescence and OCT) even in the absence of known exposure to the drug. Clinical implications for non-invasive imaging to obviate the need for costly, time-consuming testing (e.g. electroretinography, genetic testing).

Future directions: This study speaks to the importance of devising a systematic grading approach to differential diagnosis of PPS maculopathy.

Reference: *Ophthalmology Retina. 2020 Dec;4(12):1196-1201*

Abstract

Are you a member of our webinar program?

Coming up in September: "The Great AMD debate".

This special 90 minute interactive event will see CFEH clinicians Sophia Zhang and Meri Galoyan examine the evidence for and against a series of equivocal topics relating to AMD, with the ultimate winner selected by you - the audience. The power is in your hands!

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The Incidence of Neovascularisation in Central Serous Chorioretinopathy by Optical Coherence Tomography Angiography

Authors: Savastano MC et al.

Summary: The development of neovascularisation is an important complication of central serous chorioretinopathy (CSCR), being a major cause of reduced vision during long-term follow-up. Current dye-based angiography for visualisation of neovascularisation can be misleading due to masking by the dye leakage, and because features such as intraretinal or subretinal fluid, cystoid macular degeneration, retinal atrophy, and diffuse hyperfluorescence can be observed in eyes with or without neovascularisation. This limitation has been partially overcome by OCTA which offers a non-invasive means of assessing the retinal circulation. Therefore the purpose of this study was to evaluate the incidence of neovascularisation secondary to CSCR using OCTA.

Key findings: Of 175 eyes with acute or chronic CSCR, 20% had neovascularisation all of which were Type 1 and occurred in chronic cases only. Approximately 39.2% of patients with chronic CSCR developed neovascularisation, of these 20% were non-exudative. Neovascularisation occurred more in older patients (66.6 ± 10.2 years) possibly due to longer-standing CSCR.

Clinical applications: OCTA is more sensitive in detecting neovascularisation secondary to CSCR than structural OCT alone especially where signs of exudation are absent; these cases probably would have remained misdiagnosed. OCTA should be performed in chronic CSCR and particularly in older patients.

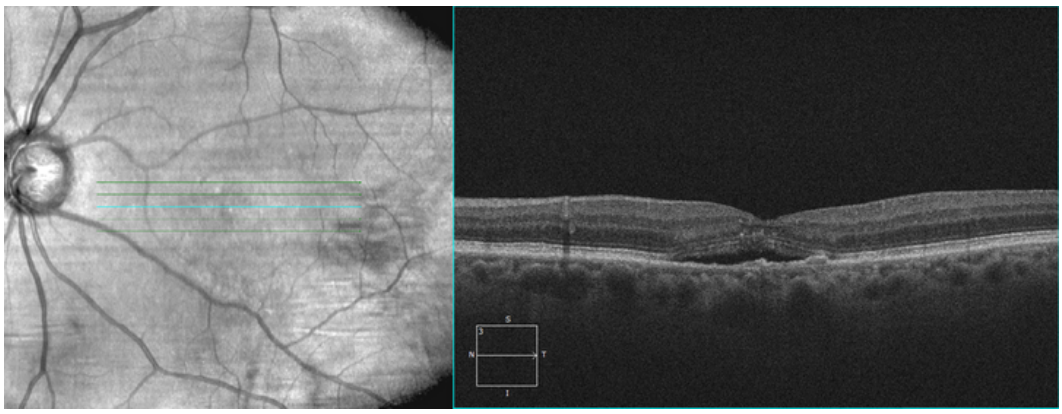
Future directions: Areas for future research include comparing the performance of OCTA to fluorescein angiography and/or indocyanine green angiography for the diagnosis of neovascularisation in CSCR, and evaluating the risk of exudation in non-exudative neovascularisation secondary to CSCR over time.

Reference: *Retina. 2021 Feb 1;41(2):302-308*

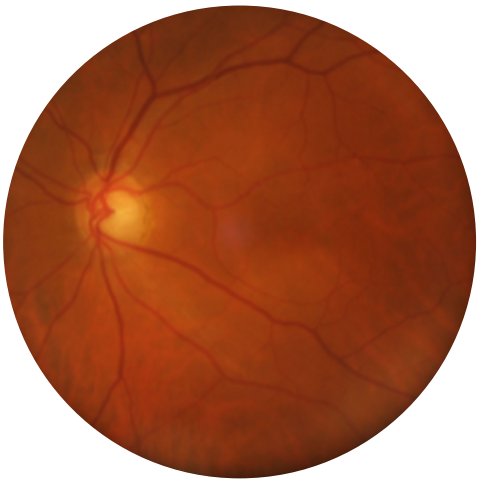
Abstract

Centre for Eye Health case studies

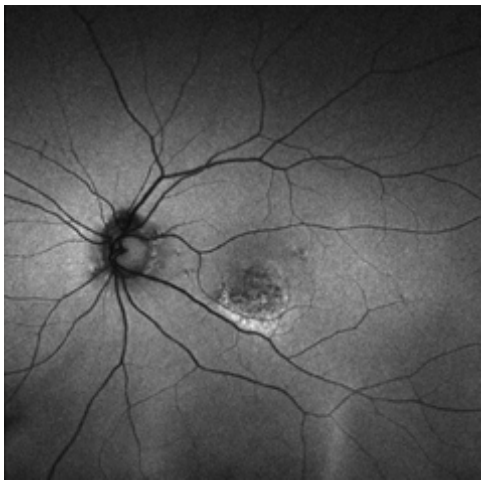
Chronic CSCR with associated Type 1 neovascularisation and persistent subretinal fluid



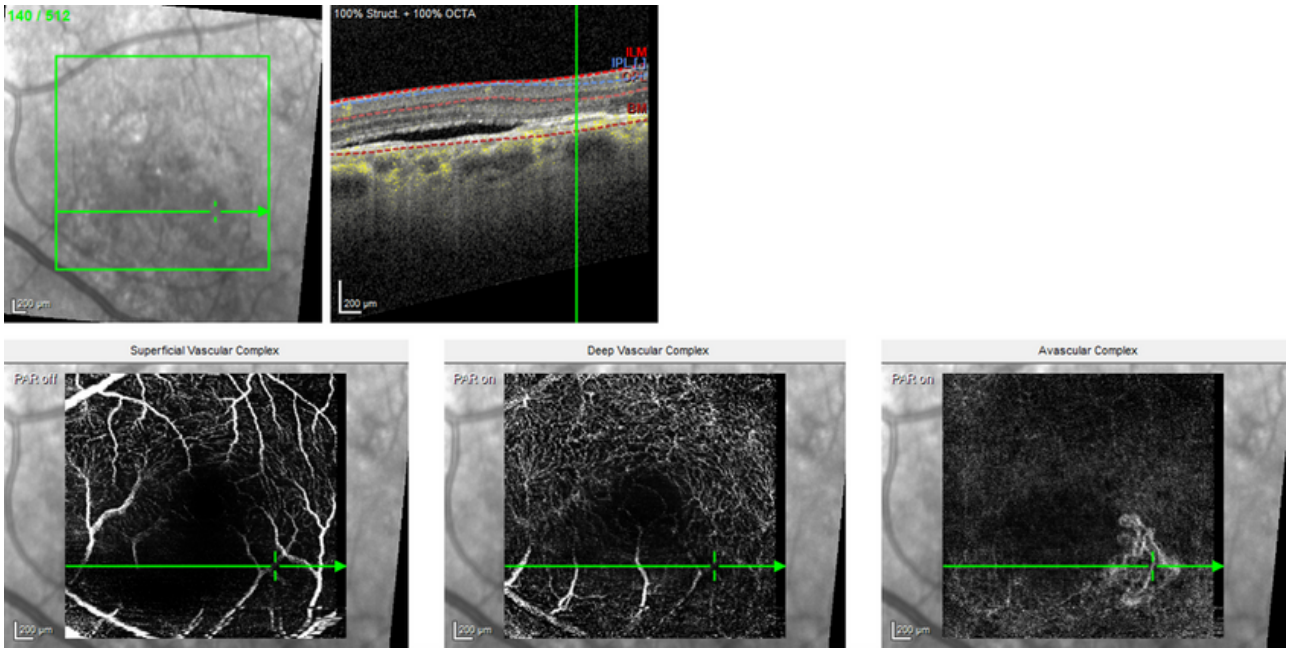
OCT



Colour fundus photography

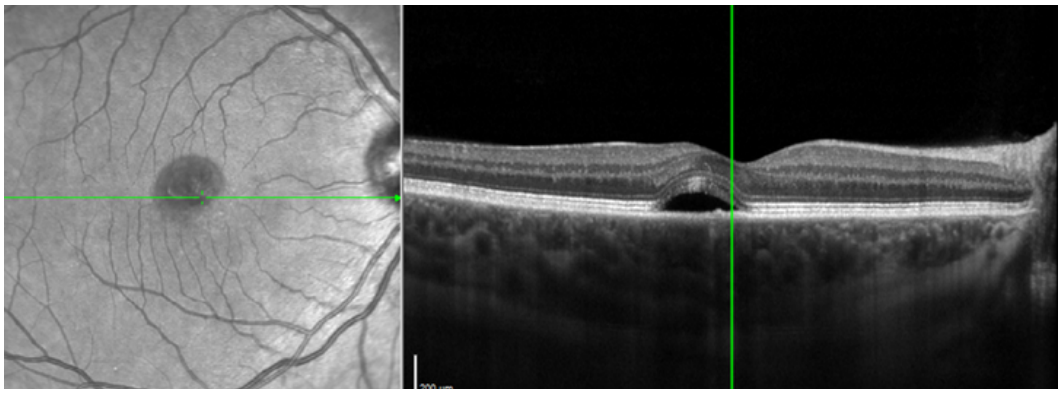


Fundus autofluorescence

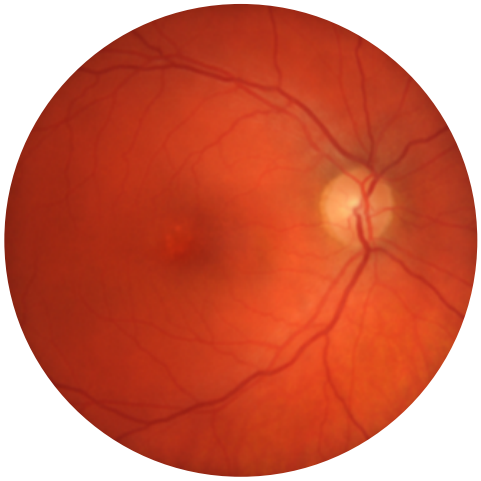


OCTA imaging (neovascularisation clearly seen)

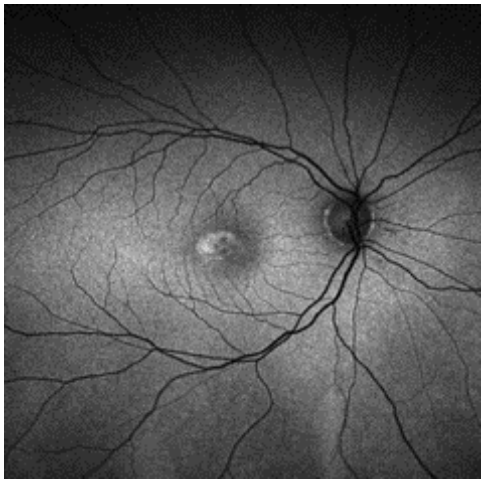
Chronic CSCR without secondary neovascularisation



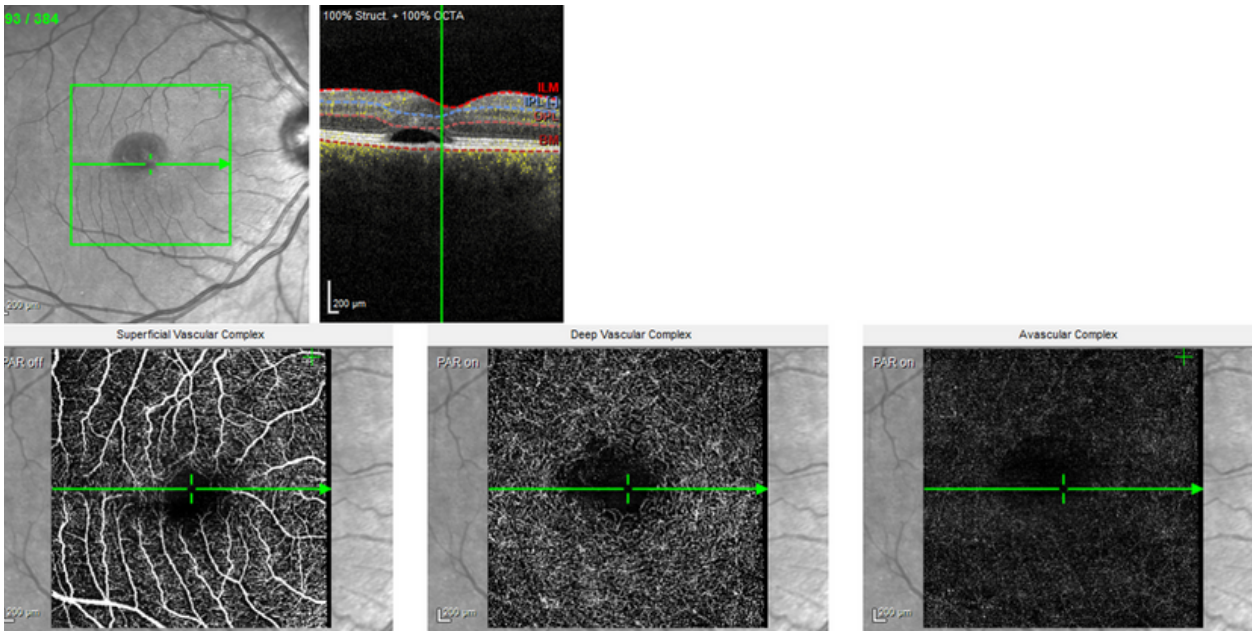
OCT



Colour fundus photography

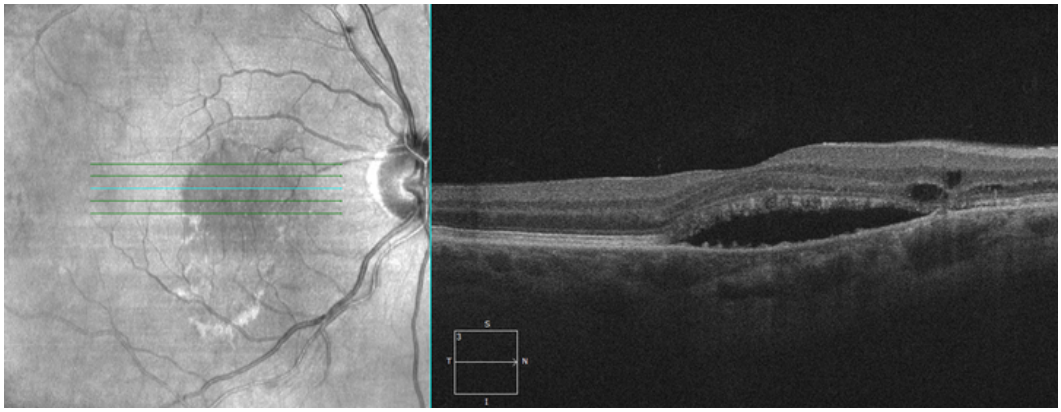


Fundus autofluorescence

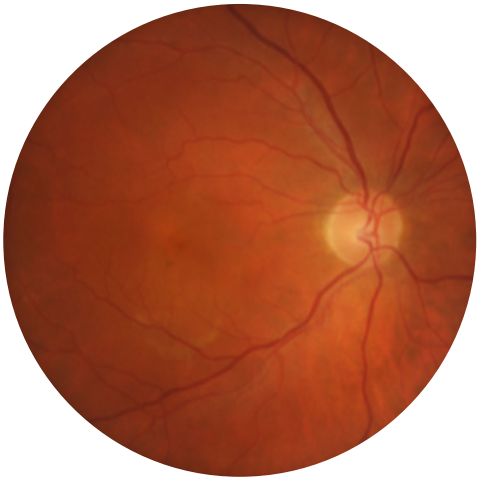


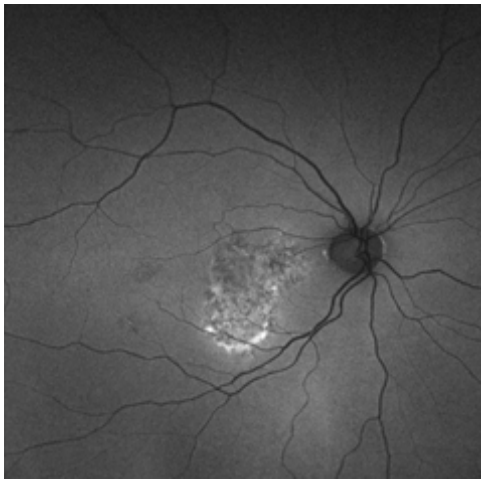
OCTA imaging (neovascularisation clearly absent)

Chronic CSCR without secondary neovascularisation

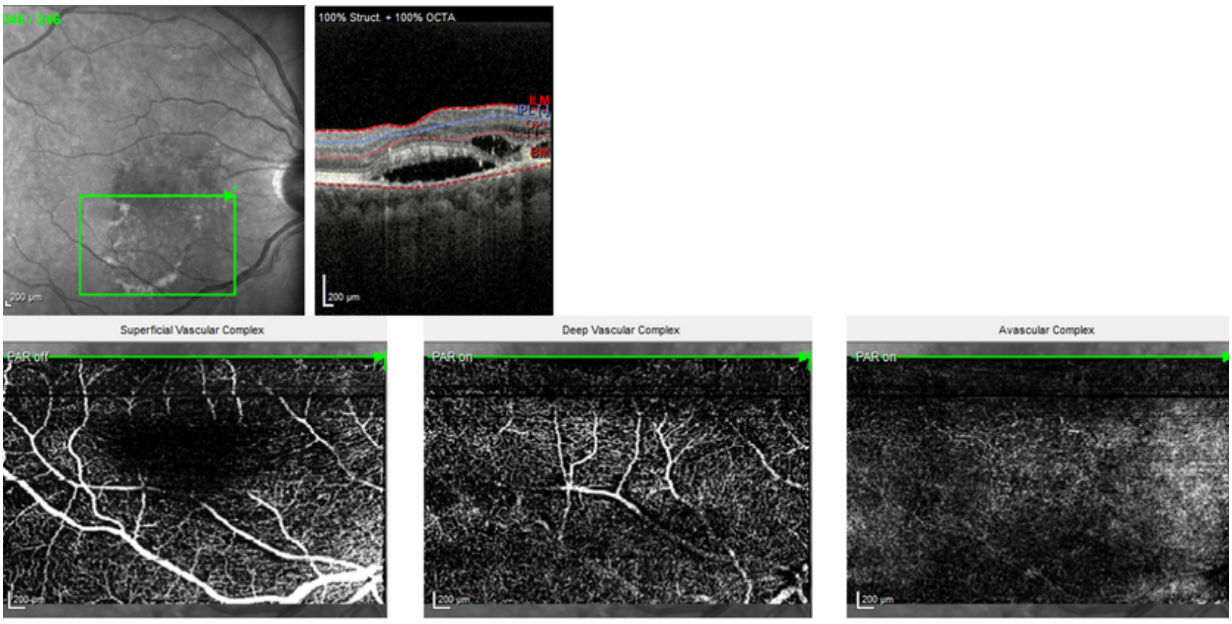


OCT





Colour fundus photography



OCTA imaging (neovascularisation clearly absent)