Effect of subthreshold nanosecond laser on retinal structure and function in intermediate age-related macular degeneration

Josephine R. Gunawan MD,1 Sarah H. Thiele MD,2 Ben Isselmann BSc,2 Emily Caruso BOrth,1 Robyn H. Guymer FRANZCO, PhD1,3 and Chi D. Luu PhD1,3

1Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, Melbourne, Australia.
2Department of Ophthalmology, University of Bonn, Bonn, Germany.
3Ophthalmology, Department of Surgery, The University of Melbourne, Melbourne, Australia.

Correspondence: Chi D Luu, Centre for Eye Research Australia, Level 8 SFW, 32 Gisborne Street, East Melbourne. VIC 3002, Australia.
Email: cluu@unimelb.edu.au

Short running title: Effect of nanosecond laser on the retina

Received 24 June 2021; accepted 6 October 2021

Funding sources / Financial disclosure: This study was supported by National Health & Medical Research Council of Australia (project grant no.: GNT1027624 [RHG and CDL], and fellowship grant no.: GNT1103013 [RHG]). The Centre for Eye Research Australia (CERA) receives operational infrastructure support from the Victorian Government. Ellex R&D Pty Ltd (Adelaide, Australia) provided the in-kind provision of Ellex 2RT® laser systems. The web-based Research Electronic Data Capture (REDCap) application and open-source platform OpenClinica allowed secure electronic data capture.

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi:10.1111/ceo.14018

This article is protected by copyright. All rights reserved.
Conflict of interest: None

ABSTRACT

Background: Subthreshold nanosecond laser (SNL) treatment has been studied as a potential intervention in intermediate age-related macular degeneration (iAMD). This study investigated the effect of 100 SNL treatment spots on retinal structure and function.

Methods: A single-arm interventional pilot study. SNL treatment was delivered as 100 spots around the retinal vascular arcades of the study eye (worst visual acuity) in a single session in subjects with iAMD. Multimodal retinal imaging and dark-adapted chromatic perimetry were performed at baseline and at 0.5, 3, 6 and 12 months post treatment. Post treatment changes in best corrected visual acuity (BCVA), retinal thickness, relative ellipsoid zone reflectivity (rEZR), rod-mediated functional parameters were compared to baseline.

Results: Twenty-one subjects with iAMD were recruited. SNL treatment was associated with an increase in retinal thickness (p = 0.008) and decrease in rEZR (p < 0.001) at 2 weeks post laser. Recovery of retinal thickness and rEZR was observed at the 3-month post laser visit. A gradual improvement in BCVA was observed after laser treatment. The mean change in BCVA between baseline and 12-month visit was +1.9 ± 3.3 letters for the SNL treated eyes, compared to -0.4 ± 3.0 letters for the fellow eyes (p = 0.027). Rod-mediated function improved at 3 months post laser (p < 0.001) and returned to the baseline levels at 12 months post treatment.

Conclusions: A single treatment with 100 SNL spots causes a short-term change in retinal structure and improvement in retinal function that are apparent at 3 months post treatment.

Key Words: Age-related macular degeneration, subthreshold nanosecond laser treatment, retinal thickness, relative ellipsoid zone reflectivity (rEZR), rod-mediated function.
1. INTRODUCTION

The retinal regeneration therapy (2RT®) laser selectively targets the retinal pigment epithelium (RPE), and when delivered at sub-threshold energy levels, it results in a non-thermal lesion. Preclinical and clinical studies have shown that this sub-threshold nanosecond laser (SNL) treatment results in alterations in extracellular matrix regulating factors produced by the RPE without causing collateral damage to the overlying neural retina, suggesting that it may be beneficial in altering the disease course in AMD where a lack of active matrix metalloproteinases have been implicated as a significant contributing factor in disease pathogenesis. A recent multicentre, randomised clinical trial - the Laser in Early stages of Age related macular degeneration (LEAD) study conducted in a cohort of participants with intermediate age-related macular degeneration (iAMD) - has suggested that SNL treatment may have a role in reducing the rate of progression in eyes with conventional drusen. Post-hoc analysis in LEAD suggests a slowing of progression in AMD eyes with conventional drusen but no reticular pseudodrusen (RPD), whilst those with RPD did not respond positively. However further validation studies are required to determine if this type of intervention will open potential treatments to slow progression to vision threatening late AMD.

To date, the ideal number of SNL treatment spots to be delivered to maximise the possible therapeutic effect, without compromising the RPE and the neuroretina, remains unknown. In our pilot study and in the LEAD study, SNL treatment involved delivery of 12 laser spots around the vascular arcades which was repeated every 6 months, for six treatments. Twelve spots was chosen as this was also used in the Drusen Laser Study, where thermal laser was applied to a similar cohort, for the same purpose of slowing progression of AMD and was found to be safe. In an attempt to discover a dose response in the LEAD trial, our group used a multivariant analysis to analyse the response from the number of visible laser lesions as seen on fundus autofluorescence imaging. We were unable to find a dose response effect with no significant associations between time to develop late AMD and number of visible laser...
spots at 6 months post SNL treatment nor laser energy used at baseline. It is possible that applying 12 treatment spots at each 6 monthly visit is not the optimal treatment protocol and that efficacy levels could be improved by increasing the number of treatment spots. However, it remains unclear about the impact of a greater number of SNL treatment spots applied in one session on retinal health. Hence, in this pilot study, we investigated the effect of delivering 100 SNL treatment spots on retinal structure and function. The findings from this study will guide decision making on SNL treatment regime and the design of future clinical trials.

2. METHODS

This prospective single-arm interventional study was conducted at the Centre for Eye Research Australia. Ethical approval was granted by the Human Research and Ethics committee of the Royal Victorian Eye and Ear Hospital. The study was registered at the Australian and New Zealand Clinical Trial Registry (ACTRN12609001056280) and undertaken in adherence with the tenets of the Declaration of Helsinki. Written informed consent was obtained from each participant.

2.1 Participants

Eligible participants were at least 50 years of age or older who met clinical criteria of bilateral large drusen ($\geq 125 \, \mu m$), thereby being a subset of the Beckman classification of iAMD group. Subjects were also required to have a best-corrected visual acuity (BCVA) of 6/12 or better in both eyes.

Exclusion criteria were subjects with any multimodal imaging (MMI) defined late AMD, including choroidal neovascularisation, geographic atrophy, nascent geographic atrophy or greater signs of atrophy on optical coherence tomography (OCT). Individuals with other ocular diseases including glaucoma, diabetic retinopathy, cataract grade $\geq 2$ (WHO grading system) and other systemic or neurological diseases were excluded.

2.2 Procedures
Clinical eye examinations, multimodal retinal imaging and functional assessments were performed at the baseline visit before the laser treatment, and at time 2 weeks and 3, 6, 12 months after the treatment. The eye with worse BCVA was chosen as the study eye and received the SNL treatment. If both eyes had the same BCVA, then the left eye was selected as the study eye. The fellow eyes were used as controls.

2.2.1 Visual acuity measurements
A standardised refraction protocol was performed monocularly using an Early Treatment Diabetic Retinopathy Study refraction chart at 4 m, and BCVA was measured. Participants had to guess all the letters in each line, and visual acuity measurements were recorded as number of letters read.

2.2.2 Rod-mediated function measurements
Dark-adapted chromatic perimeter (DACP; Medmont International Pty Ltd, Nunawading, Victoria, Australia) was used to examine static and dynamic rod-mediated function. In this study, we evaluated rod-mediated function at 16 retinal loci at 4°, 5.7°, 8° and 11.3° from the fovea (Figure 1A). Test was performed monocularly on the study eye, with the fellow eye patched. To avoid the patient's fatigue with long test duration, this test was performed only on the study eye and the data were compared to the baseline values. Pupils were dilated to at least 6 mm diameter with tropicamide 0.5% (Midiacryl; Alcon Laboratories Pty Ltd, French Forest, New South Wales, Australia). Participants were instructed to fixate at a small dim red fixation light at the center of the test grid, and fixation was monitored throughout testing using an infrared camera.

Before the test commenced, the study eye was bleached approximately 20% using a customised Ganzfeld flash, as previously described. Retinal sensitivity was assessed regularly for 30 minutes after photobleaching using the 505nm wavelength stimulus. Once retinal sensitivity measurements for the 505nm stimulus were completed, a single perimetric examination using the 625nm stimulus was performed as part of the two-color perimetry (2CP) procedure. The changes in retinal sensitivity obtained with the 505nm stimulus over 30 minutes of dark adaptation (DA) were used to generate
the dark-adaptation curve and determine the rod intercept time (RIT) and rod recovery rate (RRR). Rod function was also assessed with the 2CP technique, by calculating the sensitivity difference between the 505 and 625 nm stimuli at 30 minutes after DA. The test protocol has been shown to have a good reproducibility.15

**Figure 1:** (A) DACP test grid with test spot located at 4°, 5.7°, 8°, 11.3° from the fovea. (B) EDTRS grid for retinal thickness measurements at the inner, outer and all rings. (C) A representative region of interest (ROI) on SD-OCT and the corresponding line profile showing the intensity (in grey scale) of various structures in the retina. The relative ellipsoid zone reflectivity (rEZr) was determined as the ratio between the intensities of the ellipsoid zone (EZ) and the external limiting membrane (ELM). (D) A fundus autofluorescence image showing the distribution of SNL laser spots. Many of the spots superior and inferior to the arcades can be seen as an alteration in the autofluorescence.

### 2.3 Multimodal imaging
Multimodal imaging was performed after all functional testing. All subjects underwent infrared reflectance (NIR), short-wavelength fundus autofluorescence (SW-FAF), SD-OCT (Spectralis HRA+OCT; Heidelberg Engineering, Heidelberg, Germany), and high-resolution digital colour fundus photographs (CFP; Canon CR6-45NM; Canon, Saitama, Japan). The SD-OCT volume scans were acquired from 49 B-scans within the central 20° x 20° and averaged 25 frames for a single B-scan.

### 2.4 Clinical Grading
The stage of AMD was graded according to Beckman classification.12 Reticular pseudo drusen (RPD) were graded as being definitely present when at least 5 round or cone-shape subretinal deposit above the RPE on SD-OCT, in more than one B-scan were seen as well as their presence on at least one *en-face* modality (NIR, SW-FAF, CFP). In addition RPD were considered present in an eye when they were definitely present in two *en-face* modalities when they were not seen on the SD-OCT.16

### 2.5 Retinal thickness measurements
Measurement of retinal thickness was performed for each subfield of the EDTRS grid using the Heidelberg Eye Explorer software (HEYEX, Heidelberg Engineering, Germany). The average retinal thickness at the inner and outer ring, as well as the entire central 20° macula was obtained after careful review, and if indicated manual correction, of the segmentation lines on each B-scan (Figure 1B). In this study, the retinal thickness was defined as the distance between the junction of the RPE/Bruch’s complex and the internal limiting membrane.

2.6 Relative ellipsoid zone reflectivity
Automated quantitative analysis of the rEZR was performed using MatLab (The MathWorks, Version 9.5 Natrick, MA, USA) on OCT raw images (exported via HEYEX, software version 1.10.4.0, Heidelberg Engineering, Germany), which provide linearly displayed reflectivity information allowing quantitative assessment of the actual and “native” image reflectivity as previously described. In brief, segmentation coordinates of the RPE (see above) were exported via XML-files, superimposed to the OCT raw images and used for straightening each OCT B-scan. Within each B-scan of the OCT volume raster scan, 51 regions of interest (ROI) were created. The width of each ROI was set at 20 pixels (~120 µm in high-resolution Spectralis OCT imaging) along the image x-axis. Within each ROI, the peak intensities of the EZ and the external limiting membrane (ELM) were determined from the reflectivity profile plot (Figure 1C). The rEZR at each region of interests (ROI) was determined by calculating the ratio of the EZ to ELM peak intensity (dynamic range of grey values: 0-1 arbitrary units [AU], Figure 1C).

Since structural changes within the outer retina are known to impact the localized reflectivity profiles, the rEZR was not obtained at ROIs when conventional drusen were present. Only retinal areas without conventional drusen were included in the analysis. En-face plots were used to present the rEZR data within the central 20° x 20°.

2.7 SNL treatment
Laser intervention was performed using the 2RT® nanosecond laser (Ellex Medical Pty Ltd, South Australia, Australia) at subthreshold levels. This is a 532nm Q-switch Nd:YAG laser delivering a speckled beam profile of 3-nanosecond pulses with 400 µm laser spot size in diameter. All eligible participants received 100 SNL treatment spots in one eye at a single session (approximately equals to the cumulative number of SNL spots over 3 years in the LEAD study), with 50 SNL spots administered below the superior arcade and 50 spots above the inferior arcade of the retinal vasculature (Figure 1D). Treatment was kept outside the central macula and as much as possible the treating clinician aimed not to re-treat the lasered areas. For each subject the energy dose delivered was determined to be just below the energy needed to see a faint blanching of a test shot (threshold) delivered outside the arcades. All SNL treatments were performed by a single experienced medical retina specialist (RG).

2.8 Data Analysis
Data were analysed together as a group for all the parameters, and separately by RPD status for the rEZr and rod-mediated function parameters given that there is a difference in rEZr and rod-mediated function between iAMD eyes with and without RPD. Rod function was determined by three parameters: rod intercept time (RIT) and rod recovery rate (RRR) and the sensitivity difference of the 505nm and 625nm stimuli. We estimated the RIT and RRR through a dark adaptation curve that was fitted to the sensitivity value of 505 nm stimuli at various time points using exponential decay and Solver functions in Microsoft Excel. RIT was defined as the time required for sensitivity to reach a criterion level of -3.0 log units stimulus intensity after exposure to a photobleach. If the study did not reach the criterion threshold in 30 minutes after photobleaching, then the RIT was arbitrarily assigned to 30 minutes. RRR was defined as the slope that represents the second component of dark adaptation curve. Linear mixed-effect model or two-way ANOVA with Bonferroni’s correction for multiple comparisons were used to determine the structural and functional changes associated with laser treatment.

3. RESULTS
Twenty-one iAMD patients (21 eyes), with the mean age of 68.7 ± 7.2 years, were included in this study. Of the 21 study eyes, pigmentary abnormalities were detected in 14 (66.7%) and RPD was detected in 4 (19%) eyes. In the fellow untreated eyes, there were 11 eyes with pigmentary abnormalities and 4 with RPD. During the study period of 12 months none of the study patients developed signs of late AMD in either the study or fellow eyes, and none was lost to follow-up.

### 3.1 Visual acuity

The mean BCVA of the non-treated fellow eyes at baseline was (87.4 ± 4.8 letters, ~6/6 Snellen equivalent) and it remained relatively unchanged over the study period (p = 0.985, Figure 2). The mean BCVA of the SNL treated eyes at baseline (82.2 ± 5.3 letters, ~6/7.5 Snellen equivalent) was significantly lower than that of the fellow eyes (p = 0.002) due to the protocol requiring that the worst seeing eye be designated the study eye. There was a gradual improvement in the BCVA over time in the SNL treated eyes (Figure 2). Although the change in BCVA of the SNL treated eyes over 12 months was not statistically significant (p = 0.736), the difference in BCVA between the SNL treated and fellow eyes, which was significant at baseline (p = 0.002), became no longer significant 6 months post SNL treatment (p = 0.235, Figure 2). In addition, the mean change in BCVA between baseline and 12-month visit was +1.9 ± 3.3 letters for the SNL treated eyes, compared to -0.4 ± 3.0 letters for the fellow eyes (p = 0.027).

**Figure 2**: BCVA in SNL treated and fellow untreated eyes at various follow up period. Asterisks indicate a significant difference in mean BCVA between SNL treated and fellow untreated eyes. Error bars represent 95% confidence intervals.

### 3.2 Retinal thickness

The average retinal thickness at baseline for the treated and fellow eyes was 328.9 ± 17.4 and 327.2 ± 16.7 µm, respectively. In the SNL treated eyes, there was an increase in retinal thickness at 2 weeks post treatment compared to the baseline. The increase in retinal thickness was mostly at the outer ring, which was closest to the site of SNL treatment (Figure 3). The average change in retinal thickness of the outer ring
between baseline and 2 weeks post treatment of the SNL treated eyes (3.79 ± 5.37 µm) was significantly greater than that of the fellow untreated eyes (0.21 ± 2.16 µm, p = 0.008). The retinal thickness of the fellow eyes remained relatively unchanged throughout the study period (p = 0.93).

**Figure 3:** Retinal thickness of the treated and fellow eyes at various follow up period. There was an increase in retinal thickness in the SNL treated eyes at the outer ring at 2 weeks post treatment (p = 0.008). There was no significant change in retinal thickness in the fellow untreated eyes (p = 0.93). Error bars represent 95% confidence intervals.

### 3.3 Photoreceptor ellipsoid zone reflectivity

The effect of SNL treatment on the rEZR are shown in Figure 4. At baseline, the average rEZR of the fellow eyes (44.4 ± 32.4 AU) was greater than that of the SNL treated eyes (39.9 ± 27.9 AU, p < 0.001). In addition, iAMD eyes without RPD had a greater rEZR than iAMD eyes with RPD (p <0.001). In the SNL treated eyes, there was a significant reduction in rEZR at 2 weeks post SNL treatment (32.98 ± 24.87 AU, p < 0.001), followed by a recovery of the rEZR at subsequent visits (Figure 4A). The rEZR reduction at 2 weeks post SNL treatment appeared to be similarly affected in iAMD eyes with and without RPD. A reduction in rEZR at the 2-week visit was also detected in the fellow eyes (40.5 ± 28.2 AU, p < 0.001), however, the magnitude of the rEZR reduction was much less than that of the treated eyes, especially in eyes without RPD (Figure 4A). A representative of the change in rEZR over time from an iAMD eye without RPD and an iAMD eye with RPD is shown in Figure 4B.

**Figure 4:** (A) Group data showing rEZR and the effect of SNL treatment on rEZR over time, presented as an average of all eyes and by RPD status. The rEZR was significantly reduced at 2 weeks after SNL treatment followed by a recovery of the rEZR at subsequent visits. (B) Representative rEZR en-face plots of an iAMD eye without RPD (RPD-) and an iAMD eye with RPD (RPD+) at each study visit. Error bars present 95% confidence intervals.
3.4 Rod-mediated function

The effect of SNL treatment on rod-mediated function is shown in Figure 5 and in Supplement Figures. Since rod-mediated function is influenced by the RPD status, the data were examined separately for eyes with and without RPD. At baseline, the average RIT of all test points was greater in iAMD eyes with RPD (27.0 ± 5.7 minutes) compared to that of iAMD eyes without RPD (12.4 ± 4.8 minutes, p < 0.001). There was an improvement in average RIT after SNL treatment, but this was only detected in iAMD eyes with RPD. The improvement was observed at the 8° ring (average improvement of -8.4 ± 5.3 minutes, p < 0.001) and 11.3° ring (-3.46 ± 9.2 minutes, p = 0.024) at 3 months post treatment (Figure 5). There was also a significant improvement in RIT at the 11.3° ring at 12 months post treatment (p = 0.04). There was no difference in average RIT between baseline and post-treatment in iAMD eyes without RPD at any ring eccentricities (p ≥ 0.834).

Figure 5: Effect of SNL treatment on the rod intercept time (RIT) over 12 months at each concentric ring of eccentricity. There was a significant improvement in RIT detected in iAMD eyes with RPD (RPD+) detected at 3 months after SNL treatment at the 8° and 11.3° rings and at 12 months after treatment at the 11.3° ring. There was no difference in average RIT between baseline and post-treatment visits in iAMD eyes without RPD (RPD-). Error bars represent 95% confidence intervals. *p<0.05, **p<0.001.

Similar findings were also observed with the rod recovery rate (Supplement figure S1) and sensitivity difference (Supplement figure S2) parameters. There was an increased in rod recovery rate at 8° ring compared to baseline at 3 months post-treatment (average improvement of 0.029 ± 0.03 log units/minute, p = 0.0025) in iAMD eyes with RPD (Figure S1). The average sensitivity difference of iAMD eyes with RPD was also significantly improved at 3 months post treatment and returned toward the baseline level at subsequent visits (Figure S2). In iAMD eyes with RPD, the average improvement in sensitivity difference between 3 months post SNL treatment and baseline was 5.25 ± 10.2 dB for the 4° ring (p < 0.001), 4.33 ± 9.0 dB for 5.7° ring (p
< 0.001), 4.12 ± 10.2 dB for 8° ring (p < 0.001) and 0.93 ± 9.2 dB for 11.3° ring (p = 0.103).

4. DISCUSSION

In this pilot study, we explored the effect of delivering SNL treatment on retinal structure and function. We found that delivery of 100 SNL spots to the retina in a single session was associated with a short-term increase in retinal thickness near the treatment site and reduction in rEZR in the treated as well as the untreated fellow eyes at two weeks after SNL treatment. There was also evidence of improvement in retinal function 3 months after SNL treatment as determined by BCVA and rod-mediate functional parameters in the study eye.

The temporary increase in retinal thickness at 2 weeks was likely related to a transient inflammatory response to the SNL treatment as the increase in retinal thickness was only observed in the SNL treated eyes and only at the region nearest the laser lesions. Changes in retinal thickness resolved 3 months after the laser treatment and remained stable thereafter over the 12-month follow-up. This short-term effect on retinal tissue is encouraging from a safety point of view.

Although the changes in retinal thickness coincided with the reduction in rEZR at 2 weeks post laser, it did not entirely explain the rEZR reduction because the reduction in rEZR was also occurred in the fellow untreated eyes in which there was no change in retinal thickness. A fellow eye effect following SNL treatment, as seen here with the rEZR, has been previously reported in both preclinical and clinical studies. In a preclinical study in which SNL treatment was applied to one eye, we reported that there was thinning in BM and increased genes expression in matrix metalloproteinases in the treated eye as well as in the fellow eye. Another recent clinical study of SNL has also reported a bilateral improvement in objective measures of retinal function by multifocal electroretinogram. It is therefore not surprising that there might be some detectable changes in the fellow eye, presumably as a result of a systemic alteration as a result of the inflammatory response.
In the current study, when comparing the change in rEZR between baseline and 12 months, the reduction in rEZR post SNL treatment in the treated eyes was less than that in the fellow untreated eyes. Given the rEZR is thought to be a marker of the integrity of photoreceptor mitochondria, the data seem to suggest that SNL treatment preserved the functioning of the photoreceptor. Along with improvement in the rEZR we also observed a gradual increased in BCVA in the treated eyes but not the untreated fellow eye. Although the improvement in BCVA over time in the SNL treated eyes was not significant, it significantly reduced the difference in BCVA between the SNL treated and fellow untreated eyes. Whilst this small change in BCVA is unlikely to be clinically significant it does raise the possibility that the treatment has, in some way, improved the BCVA in the eyes receiving treatment as the same change was not noted in the untreated fellow eyes. However, due to a small sample size and lack of a control group it was unclear whether this improvement was associated with a real improvement in retinal function following SNL treatment or was related to regression to the mean.

In this study, rod-mediated function was assessed by three different parameters; rod intercept time, rod recovery rate and the sensitivity difference. We found a temporary improvement in rod-mediated function at 3 months after SNL treatment, with the function returning to the baseline level at 12 months post laser treatment. The improvement was more evidence in iAMD eyes with RPD, than those without, and at test points between 5.7° and 8° from the fovea. The improvement in rod-mediated function may be as a result of a general improvement in the health of the RPE and Bruch’s membrane following SNL treatment, which has been reported previously in preclinical study. Eyes without RPD, on average had a relatively normal rod-mediated function, therefore, it was not possible to detect any improvements in function due to a ceiling effect. We did not test the fellow un-treated eye, due to the arduous nature of testing dark adaptation, and as such did not have a comparison of the un-treated eyes.
In the LEAD trial, with 12 laser spots being delivered every 6 months, we did not see any benefit to the eyes with RPD at baseline. Post-hoc analysis indicated a worsening in the rate of progression to late AMD in the SNL treated RPD eyes compared to the sham treated RPD eyes. Possible more laser, in one setting, might induce a greater beneficial effect to the RPE, which appears to be more dysfunctional in the presence of RPD than when they are not present. Potentially repeat RPE injury every 6 months may have been more detrimental to the RPE in RPD eyes than the once off higher number of spots. Furthermore, treating with higher number of laser spots early on might have been the dose needed to prevent further RPE demise in RPD eyes. Three months also appeared to be the extent of the beneficial effect, whereas in LEAD the treatments were at 6 monthly intervals. The findings from this study and that of the LEAD seem to suggest that the retina responds differently to different SNL laser doses in AMD eyes with RPD. Further studies are warranted to identify safe and efficacious treatment parameters for eyes with RPD.

The strength of this study was that we only included participants with the same stage of AMD, which was people with bilateral large drusen, to minimise the variation in AMD severity. By using DACP, we were able to specifically examine the static and dynamic rod-mediated function at 16 different retinal loci and allowed us to follow the functional changes at various retinal eccentricities. Laser treatment was performed by a single experienced medical retina specialist to ensure the consistency of the SNL treatment. Limitations of the study included a small sample size, the treatment was not randomised and the lack of an independent age-matched control group. Another potential limitation of the study was that the long-term safety of treating with 100 SNL spots is unknown, especially if repeated treatments are required. Nevertheless, this pilot study provided important data which could guide the design of subsequent investigations.

Further work is needed on this potentially novel treatment that is aimed at slowing progression from the early stages of AMD to its late vision threatening complications. There is much to learn about the mechanisms of action, the dose required and protocols to optimize any beneficial effect and whether one protocol will be sufficient
for all types of AMD phenotypes. Clinical and pre-clinical studies are ongoing or planned to continue to explore a potential novel intervention, in a disease where there is still little to offer to slow progression from early to late stages of the disease.⁶

In conclusion, we examined the effect of delivering SNL treatment on retinal structure and function in eyes with iAMD. We found that SNL treatment was associated with a temporary increase in retinal thickness and reduced rEZR at two weeks after SNL treatment. These changes recovered and did not cause a long-term detrimental effect on retinal function. There was some evidence of short-term improvement in retinal function following SNL treatment.
REFERENCES


The figure shows the retinal thickness (µm) over time (months) following SNL treatment. There are three panels: All rings, Inner ring, and Outer ring. Each panel compares SNL treated eyes (red) and fellow eyes (blue) with error bars indicating standard deviation.
Minerva Access is the Institutional Repository of The University of Melbourne

Author/s:
Gunawan, JR;Thiele, SH;Isselmann, B;Caruso, E;Guymer, RH;Luu, CD

Title:
Effect of subthreshold nanosecond laser on retinal structure and function in intermediate age-related macular degeneration

Date:
2021-10-24

Citation:

Persistent Link:
http://hdl.handle.net/11343/299121