Nanosecond laser (Ellex 2RT) in early AMD

Towards a randomized trial of 2RT laser for early AMD.

Robyn Guymer

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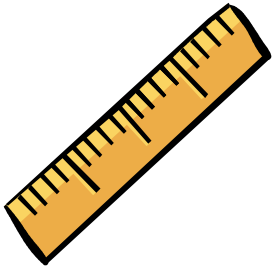
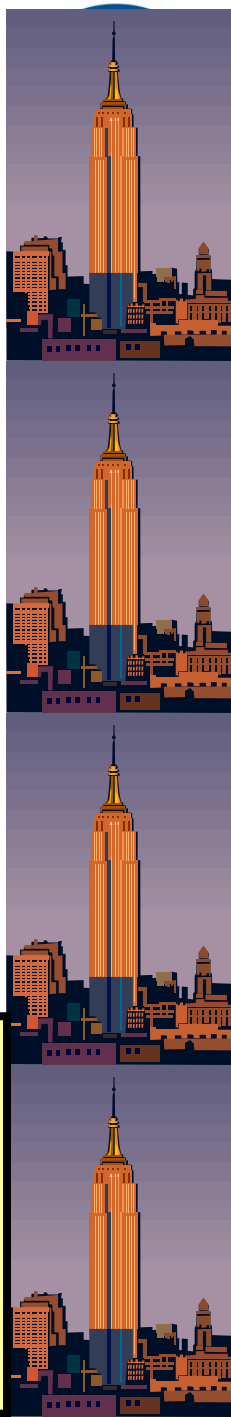
Ellex 2RT

In 2RT

3ns = 1m



If 2RT laser treatment energy = your height



2RT laser pulse has no time to create thermal damage

2RT laser produces completely different, non-thermal effects in the RPE

Then 0.1sec =

CIRCUMFERENCE OF THE EARTH

standard photocoagulator energy =

4 x height of Empire State building

2RT:Retinal rejuvenation therapy -AMD pilot study

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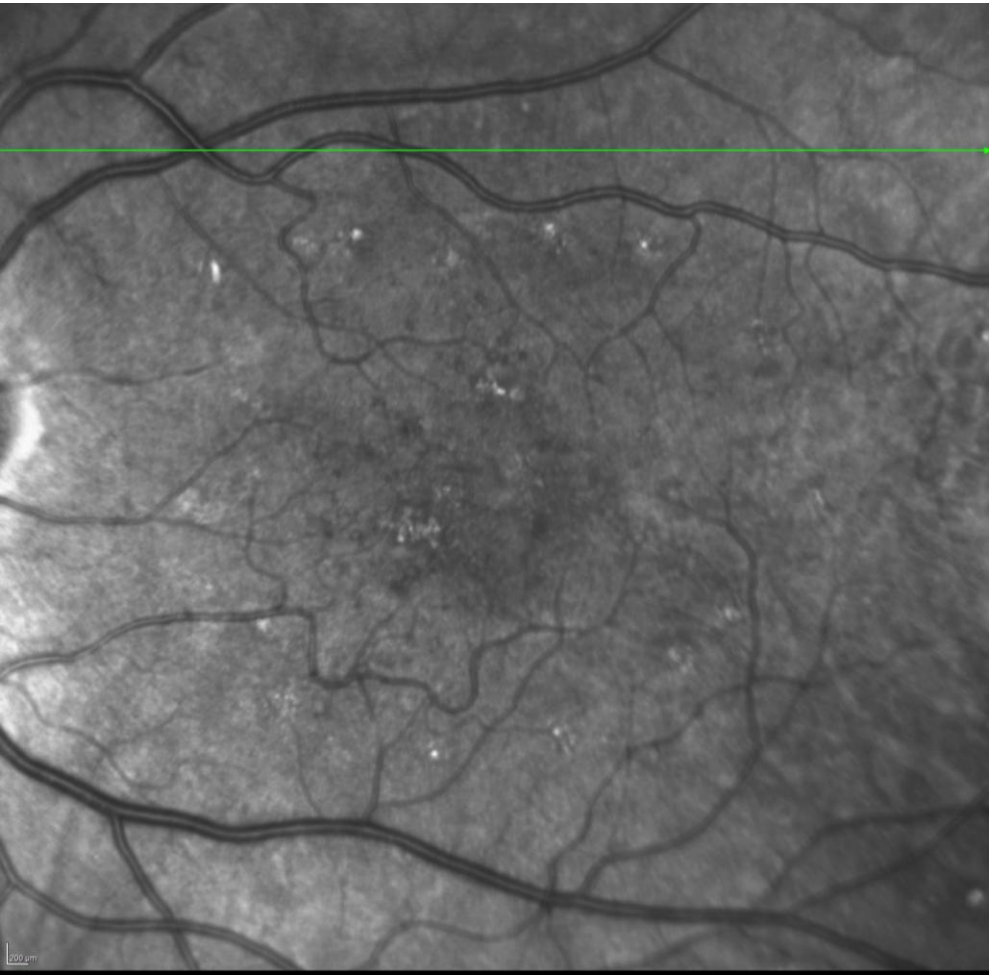
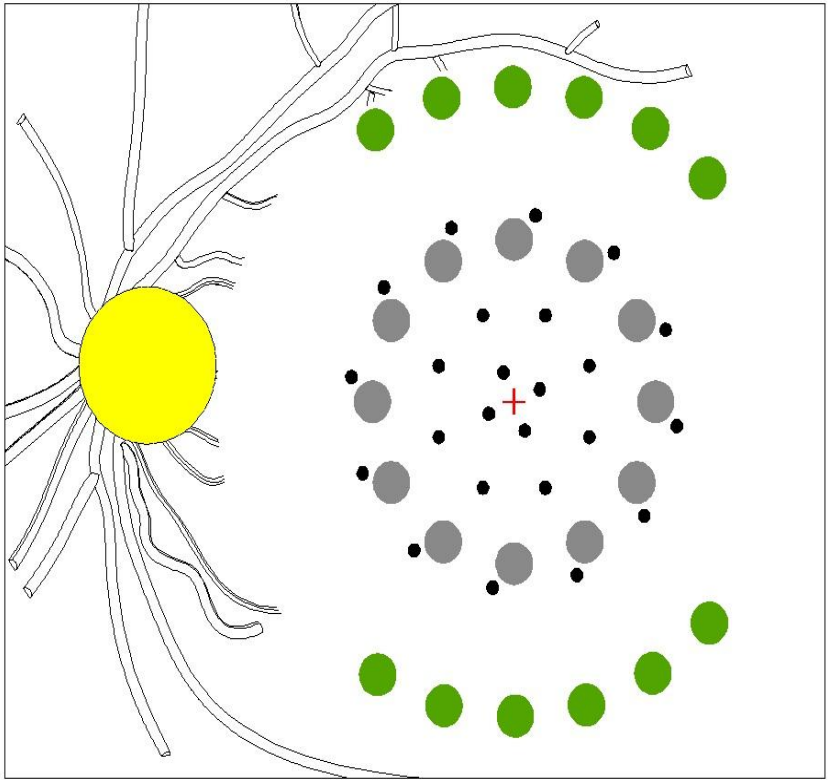
- **Design:** Proof of concept, non-randomized clinical trial of macular nanosecond laser for early AMD.

- **Participants:** 50 participants with bilateral high risk (ARED 4) early AMD.

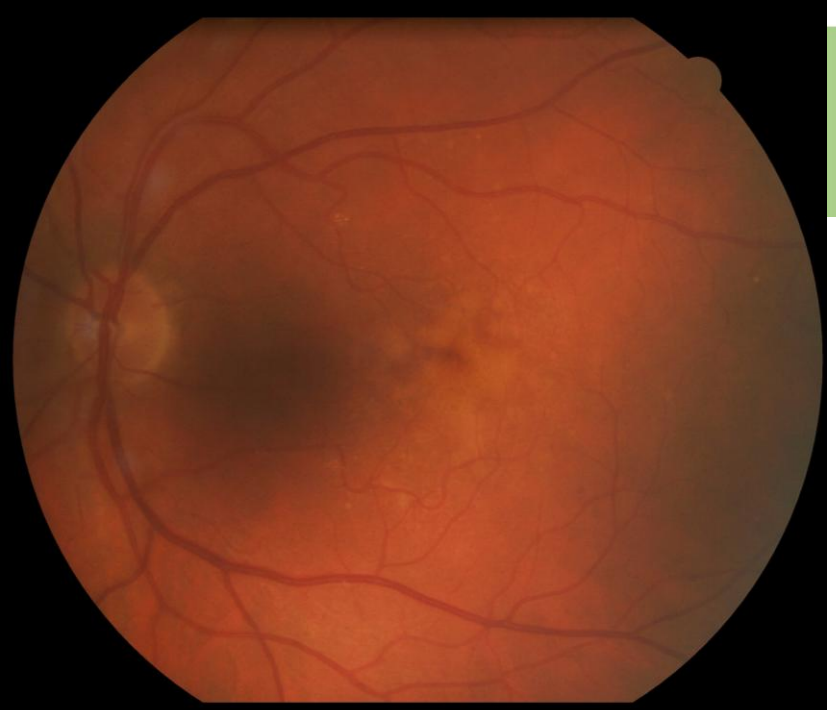
- **Method:** Ultra-low energy laser pulses (2RT laser) applied in 12 spots around the macula of one eye (0.15mJ to 0.45mJ), using 400um diameter spot, 3 nanosecond pulse length, 532nm wavelength and energy titrated to each patient (faint blanch then reduce).

2RT laser- 12 spots out at the arcades



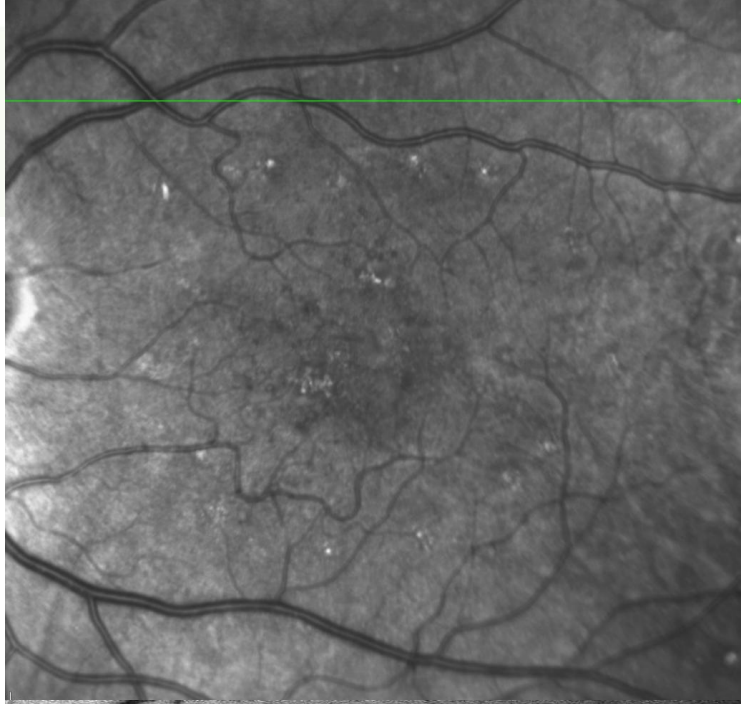


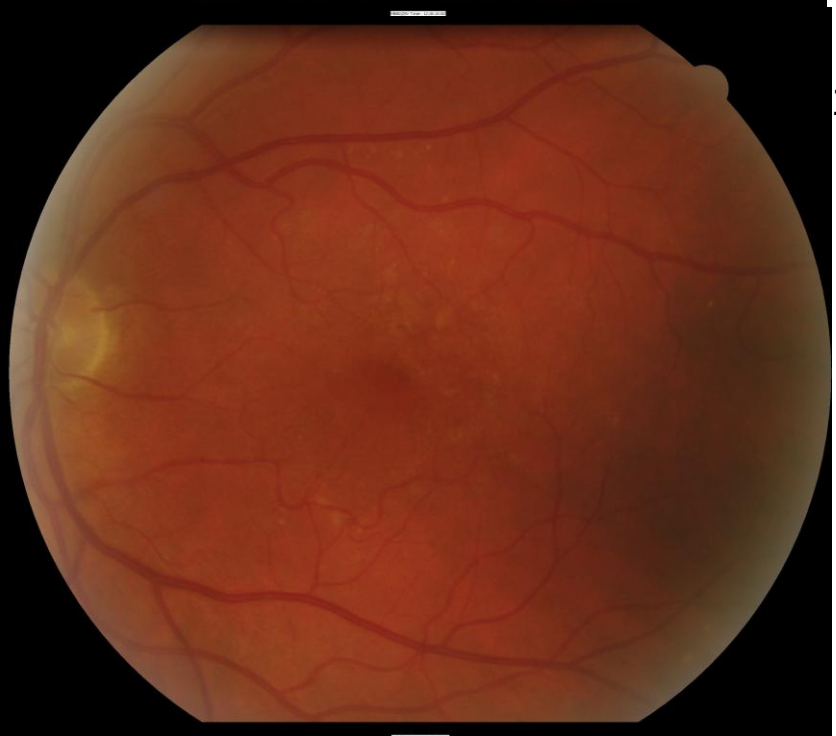
IR image at 12 months showing speckled appearance of lasered spots in second protocol pattern



Pre laser

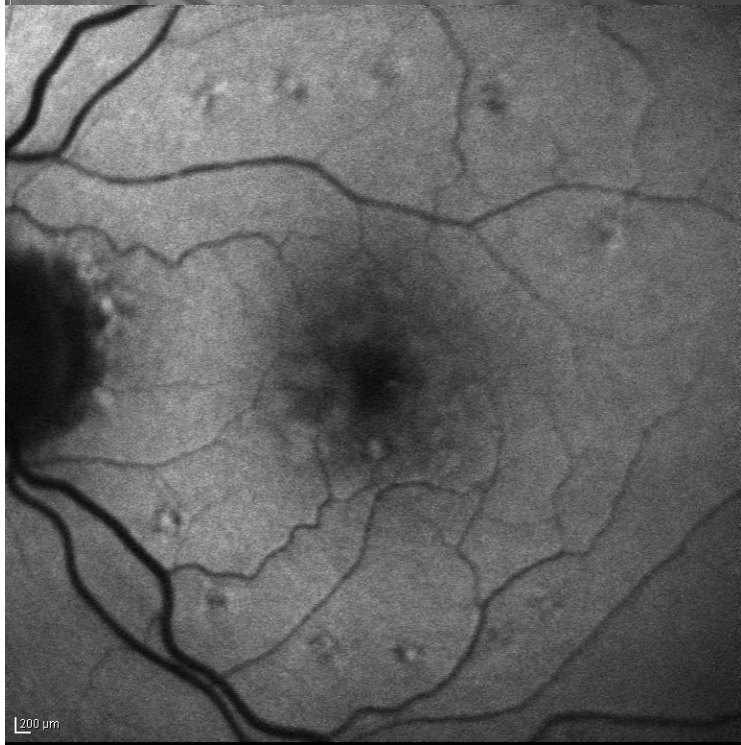
IR





12 months post laser

FAF



2RT:Retinal rejuvenation therapy -AMD pilot study (2010-2012)

- **Needed an outcome measure**
  - Major problem in early AMD research is the lack of an outcome measure
  - Need to be able to monitor progression, evaluate efficacy of interventions aimed at slowing progression
  - Can’t use BCVA
  - We know that there are functional deficits in early AMD.
  - Currently tested in a laboratory setting rather than in clinical trial setting

Macular function as a marker of disease

visual functions laboratory

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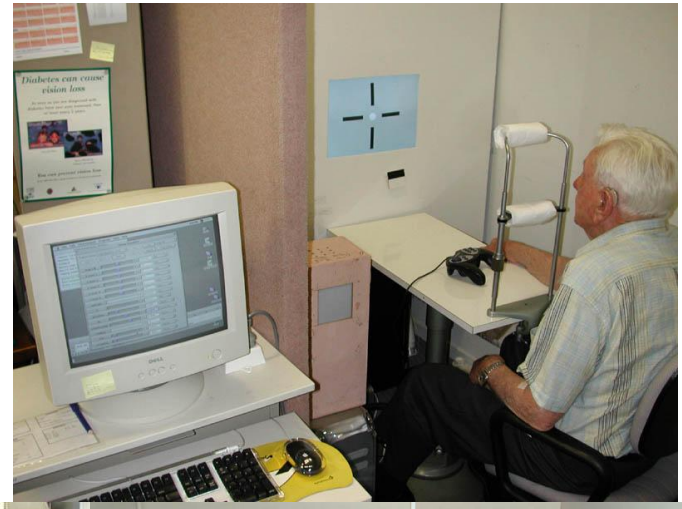
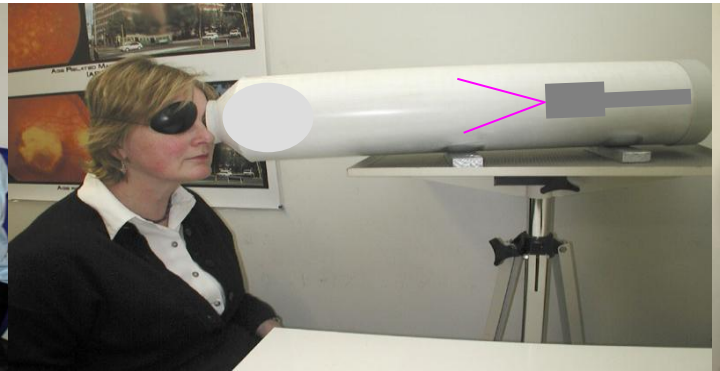
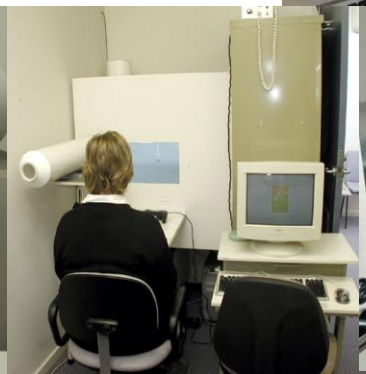
Algis Vingrys

Peter Dimitrov

- Looked at 13 parameters of function covering rods cones dynamic and static tests
- Tests on over 200 AMD and 100 controls
- 6 monthly for 3 years







Retinal function- a marker of disease

- Phipps JA, Guymer, R.H., Vingrys AJ. Temporal sensitivity deficits in patients with high risk drusen. Aust NZ J Ophthalmol. 1999; 27:265-267.
- Phipps JA, Guymer R.H., Vingrys AJ. Cone Loss in Age-related maculopathy. Invest Ophthalmol Vis Sci. 2003; 44: 2277-2283.
- Phipps JA, Dang TM, Vingrys AJ, Guymer RH. Flicker perimetry losses in age-related macular degeneration. Invest Ophthalmol Vis Sci. 2004; 45(9):3355-60.
- Peter N. Dimitrov, Robyn H. Guymer, Andrew J. Zele, Andrew J. Anderson, Algis J. Vingrys, Measuring Rod and Cone Kinetics in Age-related Macular Degeneration. Invest Ophthalmol Vis Sci. 2008;49:55-665.
- Gin T, Luu C, Guymer RH. Central retinal function as measured by the multifocal electroretinogram and flicker perimetry in early age-related macular degeneration. Invest Ophthal Vis Sci. 2011 52: 4639-44.

- Dimitrov PN. Robman L, Varsamidis M, Aung KZ, Makeyeva GA, Guymer RH, Vingrys AJ. Visual function tests as potential biomarkers in Age-related macular degeneration. Inv Ophthal Vis Sci. 2011: 52(13):9457-69

- Dimitrov PN. Robman L, Varsamidis M, Aung KZ, Makeyeva GA, Lucy Busija, Vingrys AJ, Guymer RH. Relationship between Clinical Macular Changes and Retinal Function in Age-related Macular Degeneration Invest Ophthalmol Vis Sci. 2012;53:5213–5220

- Luu C, Dimitrov P, Robman L, Varsamidis M, Makeyeva G, Aung KZ, Vingrys AJ, Guymer RH. The role of flicker perimetry in predicting onset of late stage age-related macular degeneration. Arch Ophthal 2012; 130: 690-9

Conclusion

- Eyes that went on to develop GA or CNV had a significantly reduced mean (SD) flicker sensitivity in the months before clinical detection of GA (15.8[5.6] dB) or CNV (19.1 [3.8] dB) compared with control eyes 22.9[3.0] dB) ($p<.001$) and eyes that did not progress to GA or CNV (21.4[3.4] dB) ($p<.001$).

- Macular flicker sensitivity testing could be used to monitor early AMD and predict which eyes, and which areas of the macula within these eyes, will develop GA.

- Flicker sensitivity measurements may prove to be a useful tool in monitoring progression of early AMD and in evaluating the efficacy of new treatments aimed at stopping progression.

- HYPOTHESIS: A region with reduced sensitivity is an area likely to go onto advanced AMD. If we can reverse this reduced function maybe we have “saved” the eye from that progression to vision loss.

2RT:Retinal rejuvenation therapy -AMD pilot study (2010-2012)

- **Methods:** Fundus images, best corrected visual acuity (BCVA), and macular flicker perimetry were recorded at baseline, 3, 6, and 12 months post-laser.

- **Main Outcome Measures:** macular flicker sensitivities and drusen area.

RE: treated

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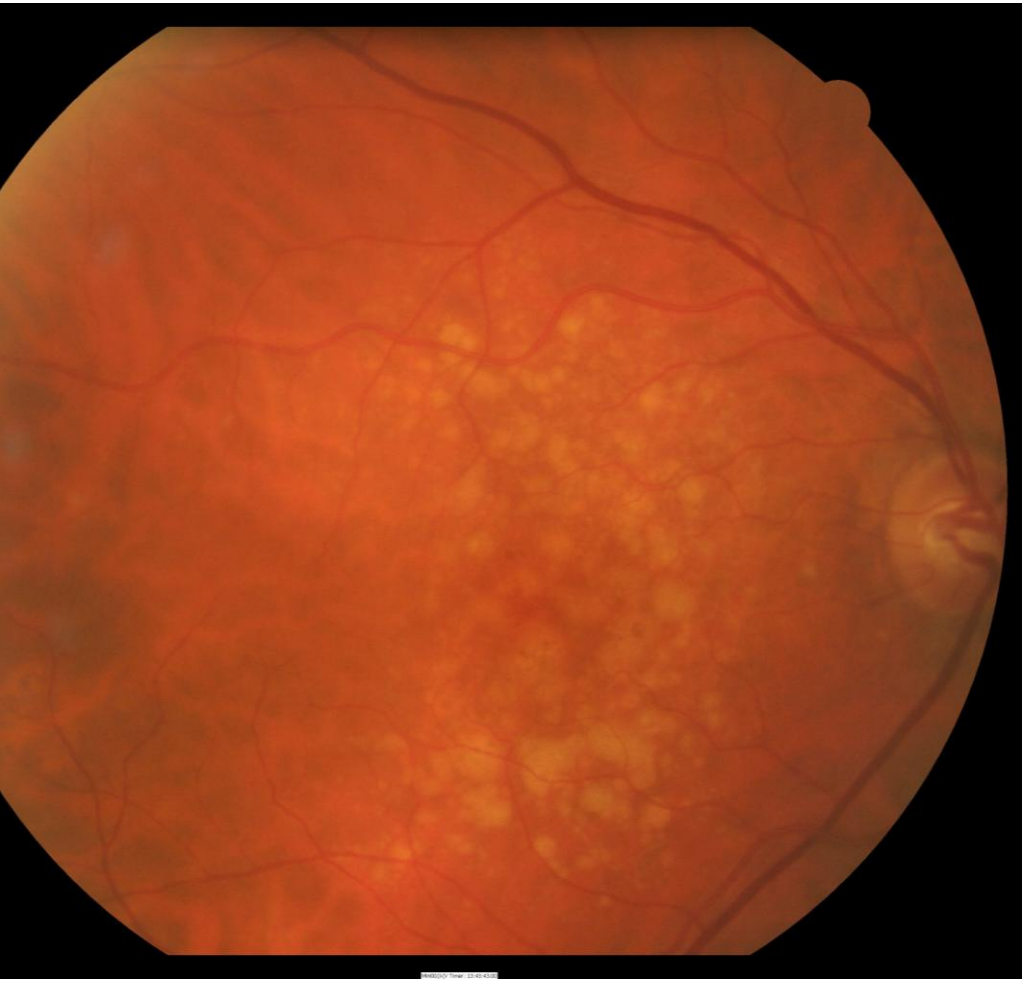
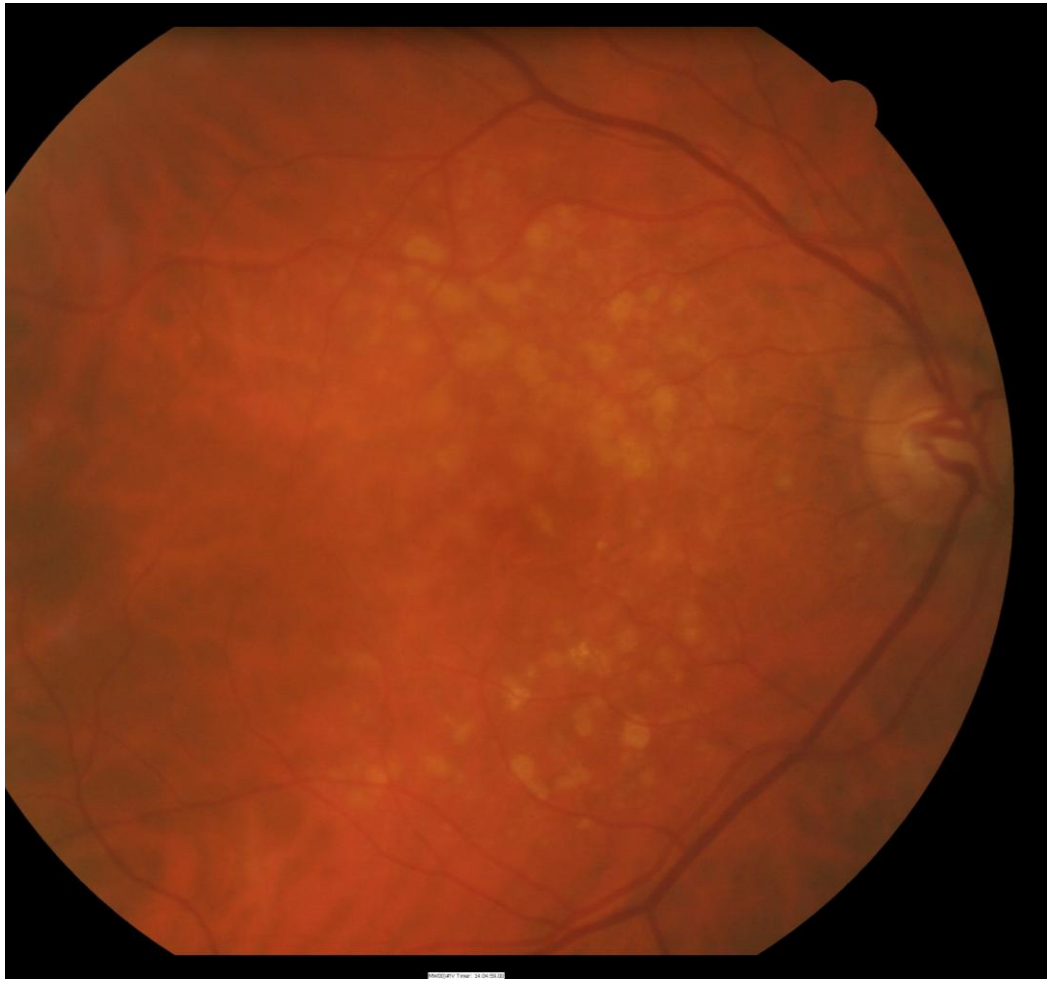
baseline

12 months post laser





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RE treated

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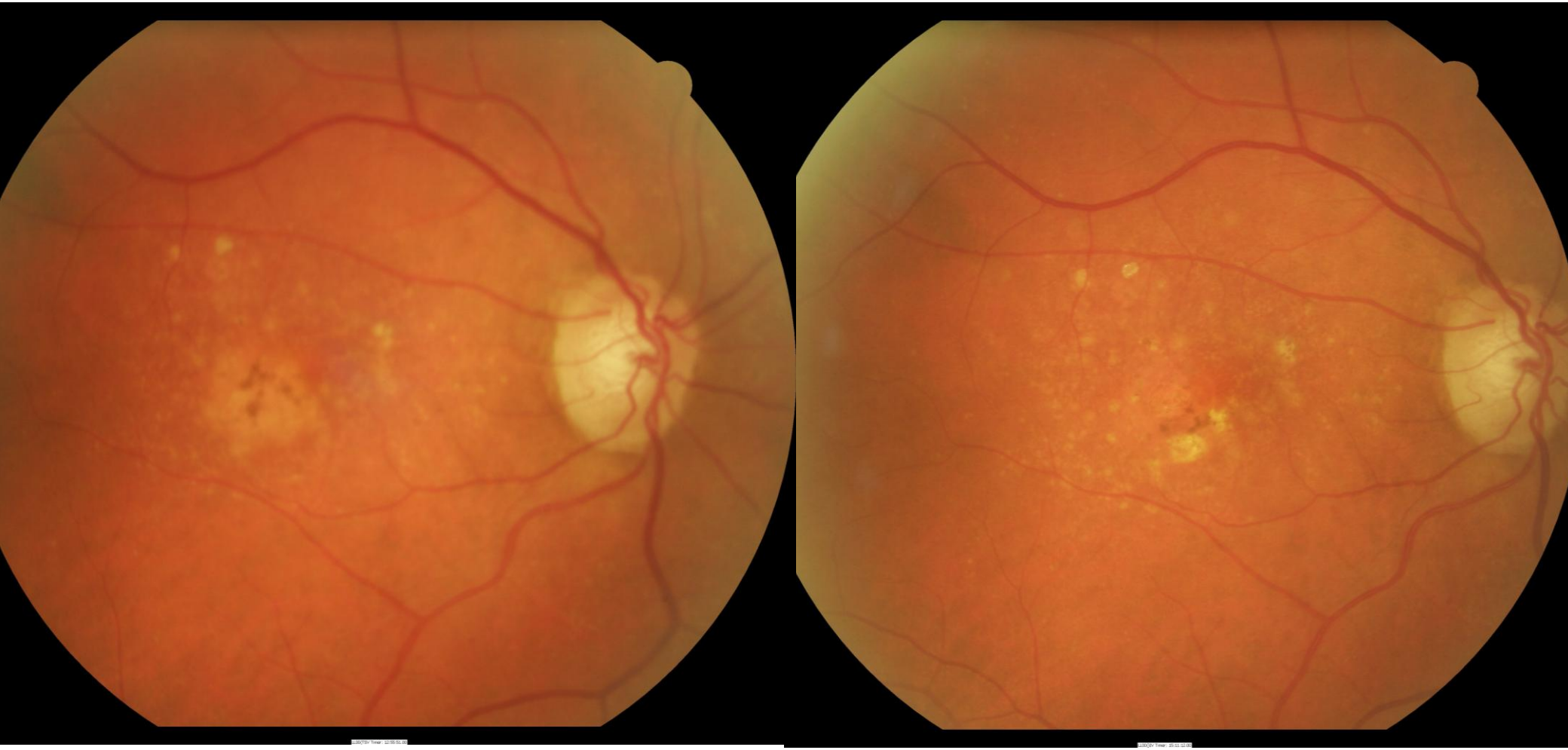
baseline

9 months post laser



RE: treated

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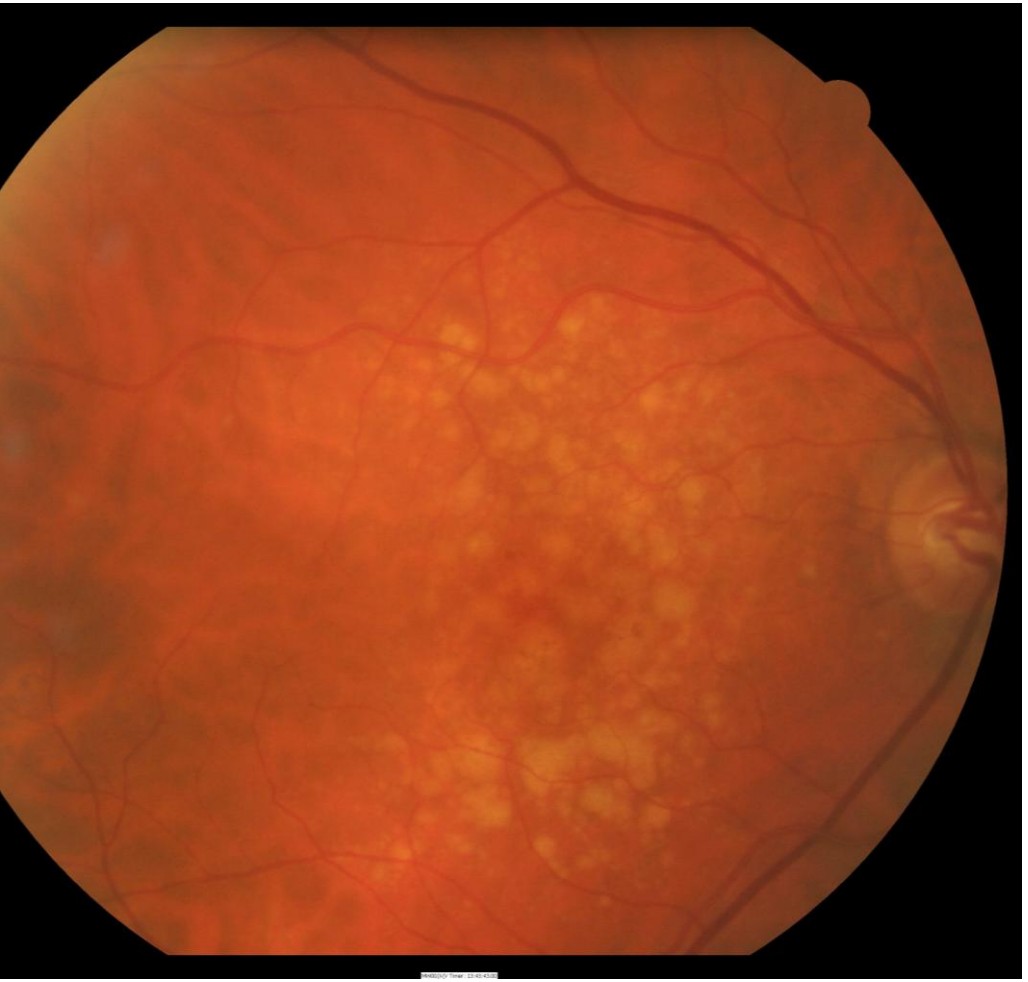
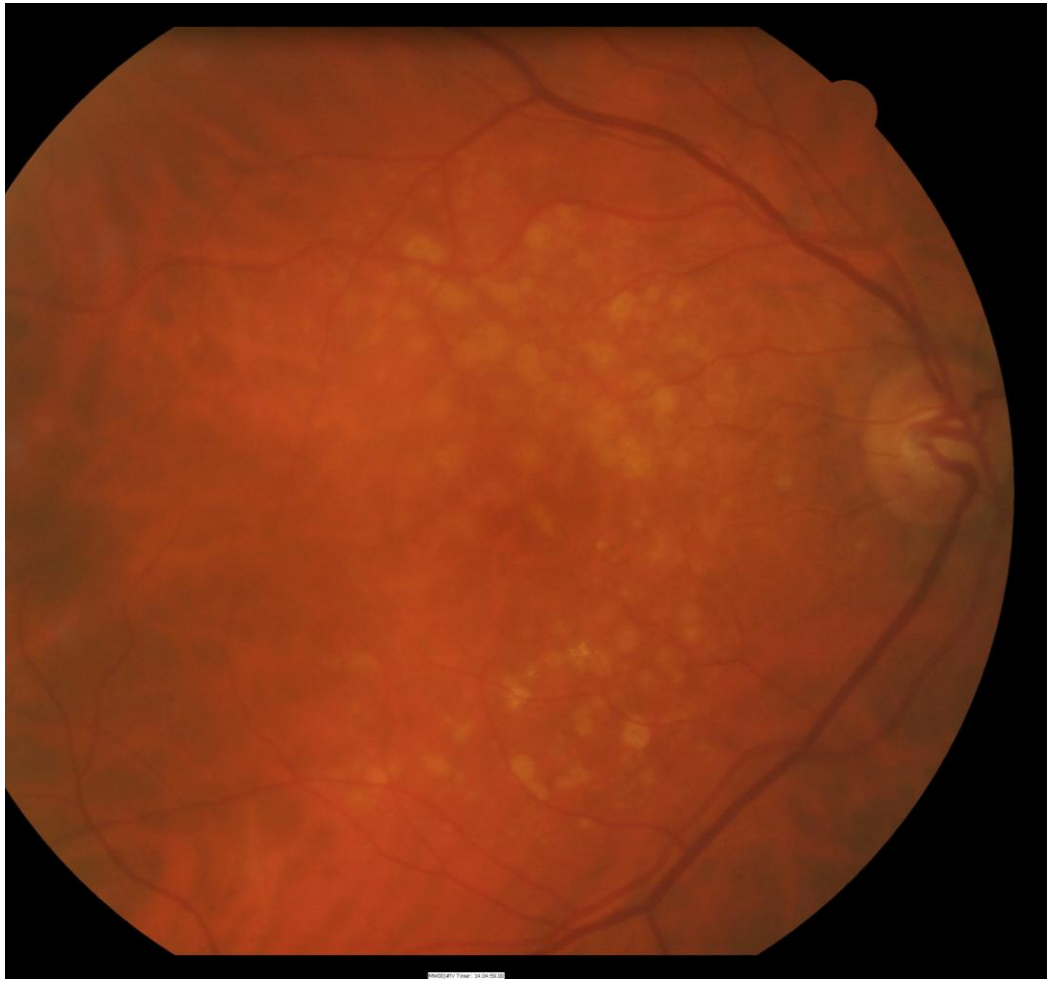
baseline

12 months post laser





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RE: treated 12 months ago

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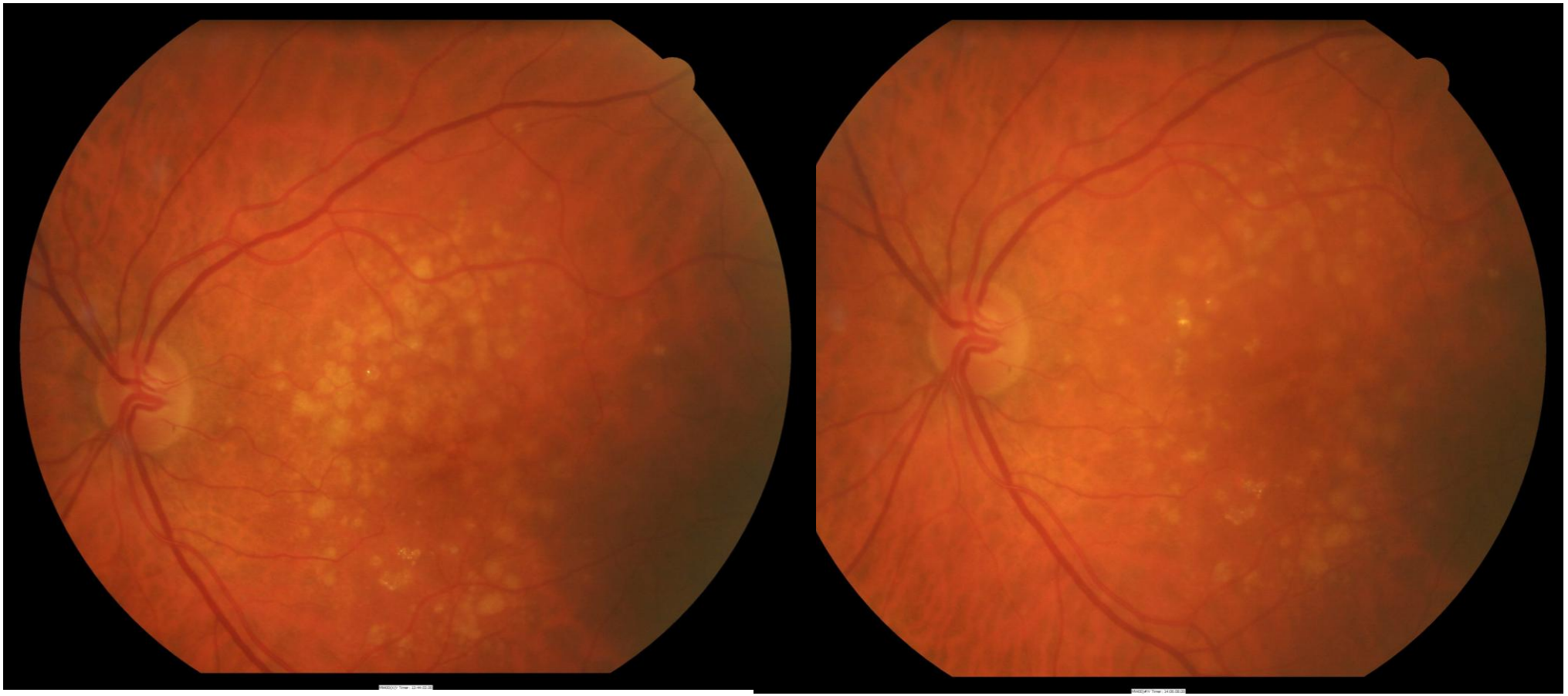
Baseline

12 months



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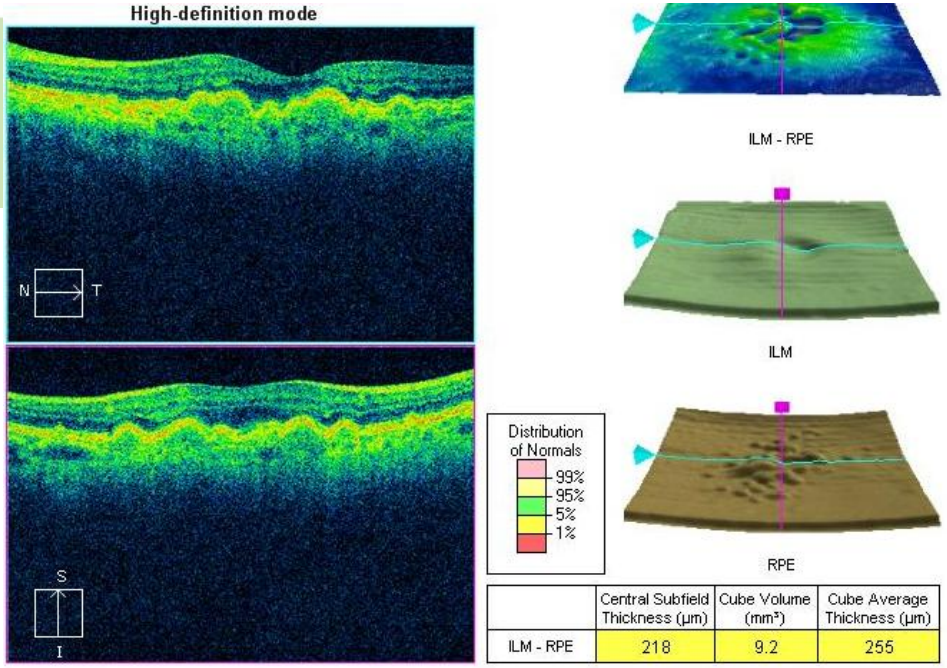
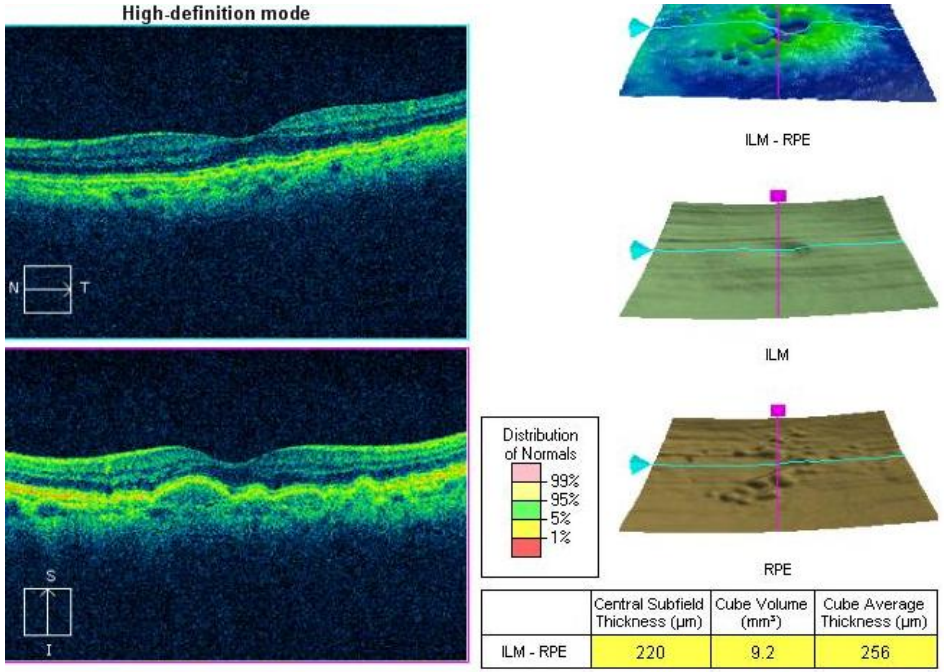
LE treated over 12 months

Baseline



	Central Subfield Thickness (µm)	Cube Volume (mm³)	Cube Average Thickness (µm)
ILM - RPE	218	9.2	255

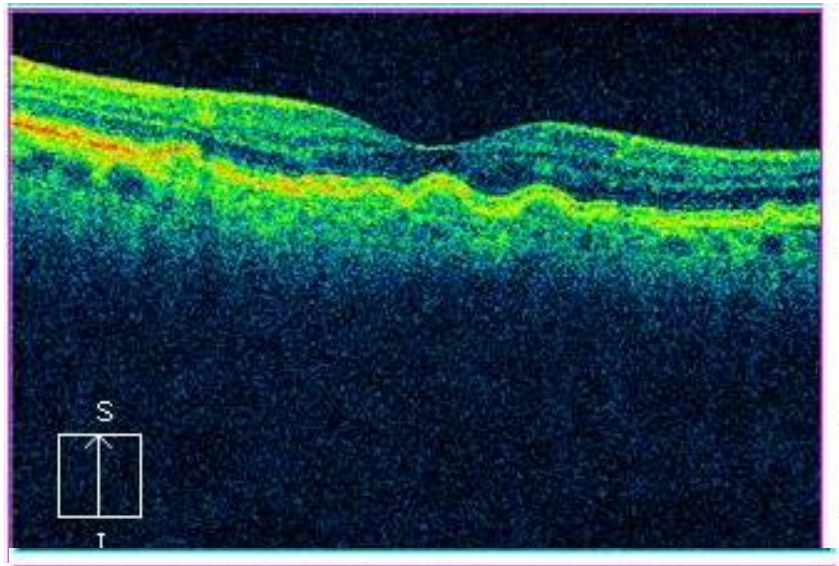
12 months post treatment

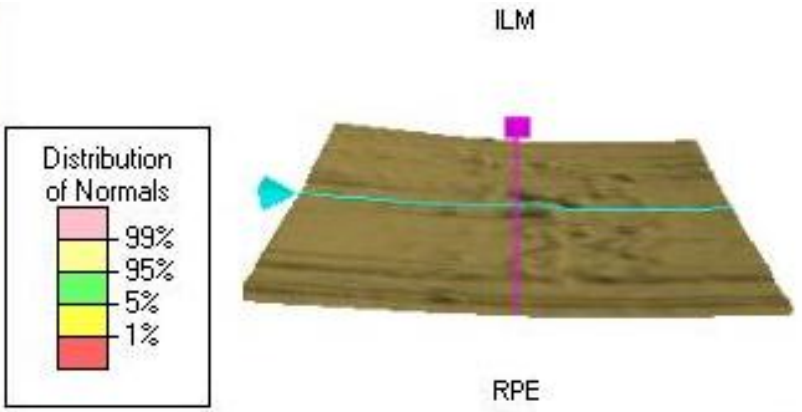


	Central Subfield Thickness (µm)	Cube Volume (mm³)	Cube Average Thickness (µm)
ILM - RPE	220	9.2	256

Non treated R eye over 12 months

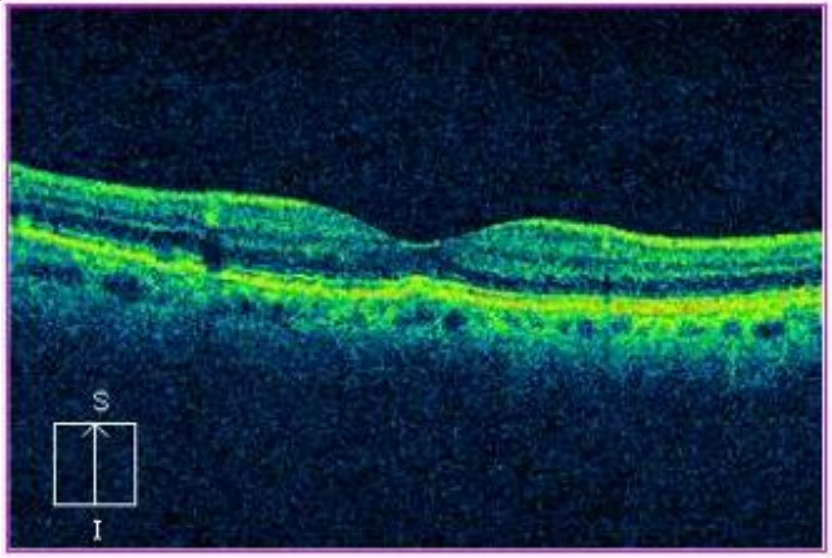
Baseline

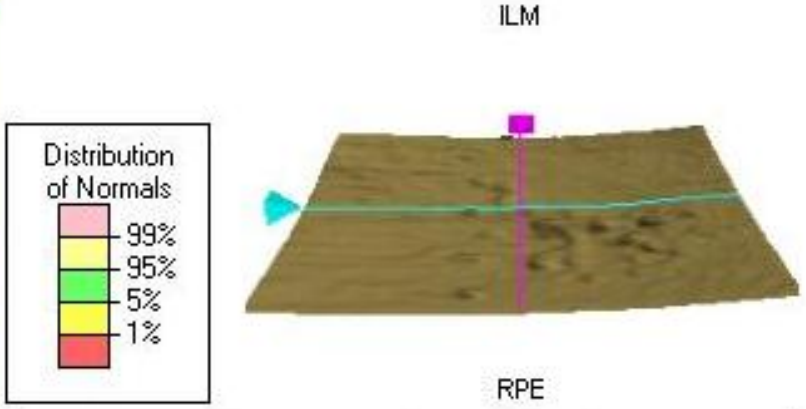




	Central Subfield Thickness (µm)	Cube Volume (mm³)	Cube Average Thickness (µm)
ILM - RPE	229	9.4	260

12 months





	Central Subfield Thickness (µm)	Cube Volume (mm³)	Cube Average Thickness (µm)
ILM - RPE	224	9.4	260

Conclusions to date

- Treatment was painless with no clinically visible lesions.
- Greatest functional improvement occurred in the treated eyes between 3 & 6months
- Resolution of drusen continued over a 12 month period
- Changes in drusen and function were not always co-incident
- Avoid large subfoveal PEDs, any sign of atrophy
- Is the improvement in worst point flicker sensitivity an indication that we are reversing the defect that leads to advanced AMD?
- The explanation for the bilateral effect in not yet known but being explored.
- The nanosecond 2RT laser warrants ongoing evaluation as an early intervention.

LEAD

(**L**aser intervention in **E**arly **A**ge-related Macular **D**egeneration)

- a multi-centred RCT, initially in Australia then the world
- 200 people, 3 years follow up
- Inclusion criteria
  - Bilateral AREDS simple severity score of 4 (drusen plus pigment)
  - Reduced flicker sensitivity on two occasions in same region
- Exclusion criteria
  - any hint of GA on any image,
  - thin on OCT
  - Large subfoveal PED
- Randomized to laser or sham 1:1
  - Retreated at 6 monthly intervals if not contraindicated
- Progression to advanced AMD is primary endpoint
  - Change in static sensitivity with MAIA perimetry is secondary endpoint

2RT for DME - Summary

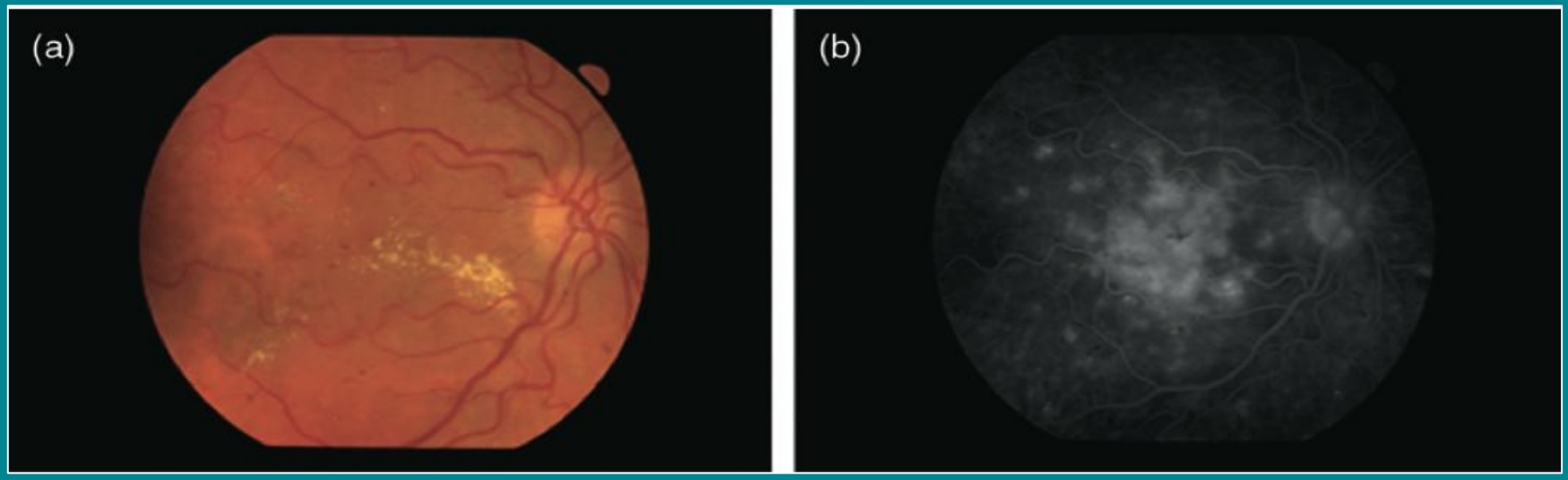
Clinical Research:

- COMPLETE:
  2008, St Thomas' Hospital, London, UK. Case series over 6 months.
- COMPLETE:
  2010, Royal Adelaide Hospital, Adelaide Australia. Prospective trial over 6 months.
- IN PROGRESS:
  2012. London, UK. Moorfields Eye Hospital. Pilot study over 6 months.

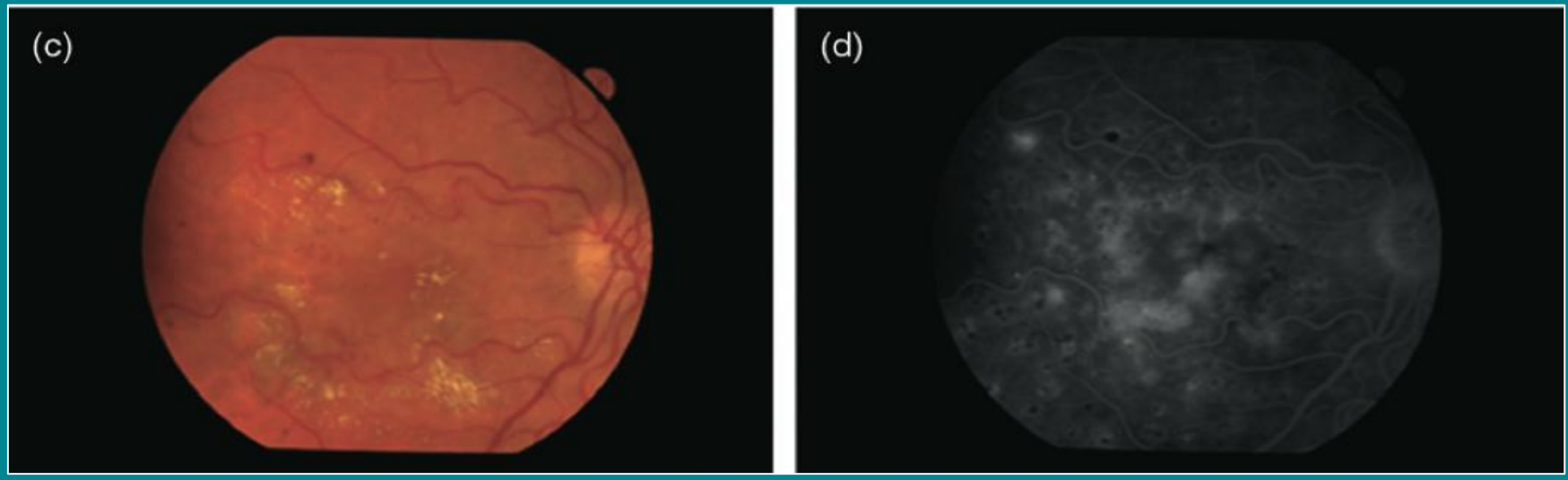
Clinical Findings

1. Pilot randomized trial of a nanopulse retinal laser versus conventional photocoagulation for the treatment of diabetic macular oedema. Casson et al, Royal Adelaide Hospital, Adelaide Australia.
    - Produces very similar reductions in macular edema as compared to conventional photocoagulation
    - Reduces macular thickness without causing collateral damage such as burns, lesions or visual deficit
    - Uses approximately 500 times less laser energy than photocoagulation

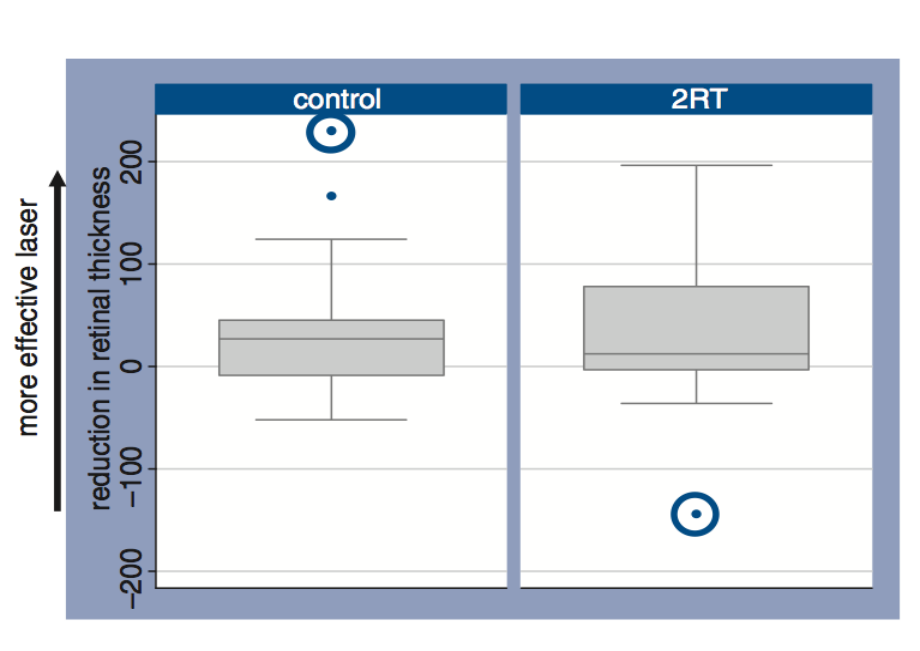
Pre-Treatment with 2RT



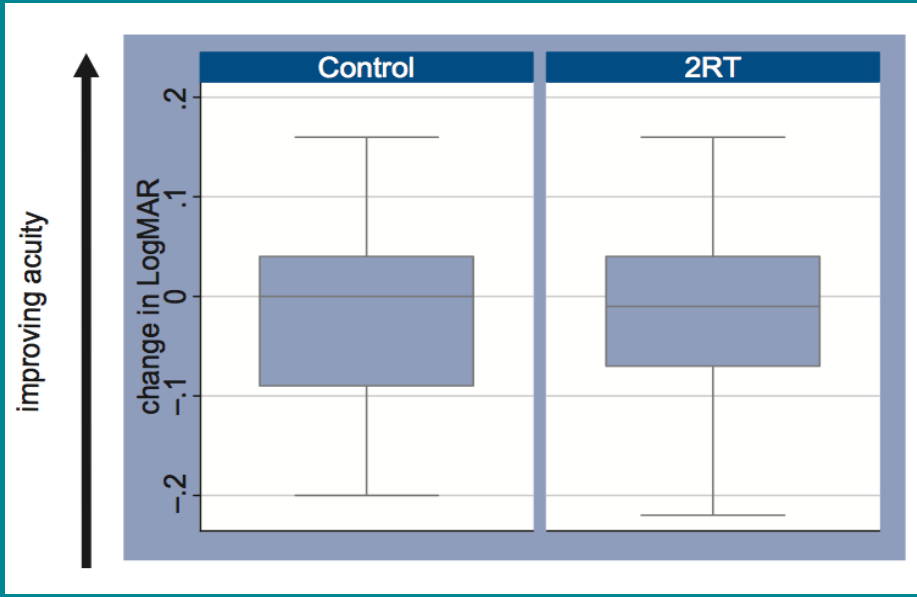
6 months Post-Treatment with 2RT



Reduction in Retinal Thickness (at 6 months)



Improvement in Visual Acuity (at 6 months)



Control = thermal laser

Trial Results of First London DME Trial (at 3 months and 6 months)