Nanosecond laser (Ellex 2RT) in early AMD

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

Robyn Guymer
In 2RT
3ns = 1m

Then 0.1sec = CIRCUMFERENCE OF THE EARTH

2RT laser pulse has no time to create thermal damage

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

If 2RT laser treatment energy = your height

standard photocoagulator energy = 4 x height of Empire State building
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
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

- 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


• 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.
• **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

baseline

12 months post laser
RE treated

baseline 9 months post laser
RE: treated

baseline

12 months post laser
RE: treated 12 months ago

Baseline

12 months
LE treated over 12 months

Baseline

12 months post treatment
Non treated R eye over 12 months

Baseline

12 months

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<th>Central Subfield Thickness (μm)</th>
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Conclusions to date

- Treatment was painless with no clinically visible lesions.
- Greatest functional improvement occurred in the treated eyes between 3 & 6 months.
- 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 is not yet known but being explored.
- The nanosecond 2RT laser warrants ongoing evaluation as an early intervention.
LEAD
(Laser intervention in Early Age-related Macular Degeneration)

- 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
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:
Clinical Findings

   - 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

(a) 

(b) 

6 months Post-Treatment with 2RT

(c) 

(d)
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)