Progression of early AMD
Drusen laser studies of the 90s.

THE DRUSEN LASER STUDY
Dark adapted retinal thresholds improved after laser treatment

The improvement in function did not correlate with drusen resolution

The aim of this pilot study was to determine if a novel nanosecond laser (Ellex 2RT™) treatment could improve visual function and reduce drusen in high risk Early Age-related Macular Degeneration (AMD).

We hypothesize that in so doing, it would suggest that the treatment was reducing the risk of progression to late stage AMD.

Ultimate proof is a RCT with an endpoint of late stage AMD (CNVM or GA)
• large soft drusen or pigmentary changes in both eyes.

**Simplified AREDS severity scale**

• Left eye - Pigment changes = 1 risk factor
• Left eye – 1 or more large drusen >125 μm = 1 risk factor
• Right eye - Pigment changes = 1 risk factor
• Right eye – 1 or more large drusen >125 μm = 1 risk factor

• The 5yr risks of developing advanced AMD based on this scoring system are:

  • 0 risk factors = 0.5%
  • 1 risk factor = 3%
  • 2 risk factors = 12%
  • 3 risk factors = 25%
  • 4 risk factors = 50%
2RT-first in human pilot study

Enrolling 50 high risk bilateral cases

VA $\geq 6/12$
> 48 years old

The laser applied at one session
-twelve, 400um spots
-in a clock hour distribution,
-1000um from the fovea in one eye
-other eye would be control.

Worst performing eye chosen for treatment
First AMD patient in the world to receive nanosecond 2RT laser - Mar 2009
## Baseline characteristics

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Sex (M/F)</th>
<th>VA (OS) (ETDRS letters)</th>
<th>VA (OD) (ETDRS letters)</th>
<th>F-up period (Mths)</th>
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<td>F</td>
<td>88</td>
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</table>
2RT for early AMD

Before treatment to LE

3 months after laser to LE
2RT for early AMD

Before treatment to LE

3 months after laser to LE
Drusen reduction grading for patients at 12mth follow-up (n = 14)
The flicker perimetry was performed with an automated perimeter (model (M-700; Medmont Pty Ltd).

Flicker fields

- 1° rad from fovea, use worst result of 4 stimulus points
- 3° rad from fovea, use worst result of 8 stimulus points
- 6° rad from fovea, use worst result of 12 stimulus points
- 10° rad from fovea, use worst result of 24 stimulus points (not used for overall change assessment)
• Flicker Visual Field test points in relation to the foveal centre (red cross) and 12 laser treatment spots (○).

• Test points at 1° radius, 3° radius, at 6° radius and at 10° radius.

• Black test points represent an example of a cluster defect where spot 6 is the worst performing point, and points 1, 5, 7, & 15 have been added to allow a combined 5 spot cluster defect average to be calculated.

**Control population**
72 Visual field tests on normal participants were used to age correct all visual field results in this trial.
Flicker field testing - normal

Calculation of age related decline in flicker visual field perception thresholds at each visual angle.

Linear trend lines used to age correct all visual field results
Flicker visual fields

79 yo with pre-treatment flicker fields and 6 month post treatment fields
Graph showing the deviation in sensitivity from average age-matched normal for points of worst single point defect within rings at different visual angles of the same patient.
Bilateral visual function improvement in 55 year old patient with laser treatment to right eye. Sensitivity deviation for points of worst point defect within rings at different visual angles are shown compared to normal eyes.
Flicker threshold deviations

- Comparison graphs of individual patient pre and post treatment flicker visual field deviations @ 12months.

- The red line indicates stable function over time.

- The top graphs show the flicker visual field deviations of the worst single points identified pre-treatment and the same points followed at each follow-up test.

- The bottom graphs show the worst performing cluster defects separately identified at each follow-up.
Green = improvement, yellow = stable, pink = worsening.

VA:
- better was > 5 letters, worse was <5 letters, stable within +/-5 letters for either eye

Drusen:
- better = any reduction in either eye.

Function
- Better = >+2db, worse < -2db, stable = +/-2db flicker visual field following the worse performing point identified pre-treatment in either eye.

Patients listed in order of the level of pre-treatment visual function deviation, with patient 1 being the worst and patient 14 being the best.

<table>
<thead>
<tr>
<th>Patient</th>
<th>VA</th>
<th>Drusen</th>
<th>Function</th>
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<tbody>
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<td>Green</td>
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<tr>
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Conclusion

- To date there has been no proven intervention in early AMD that significantly halts or causes regression of the disease process. We believe the results presented here show that a single treatment of low intensity nanosecond laser is the first treatment to bring about changes in retinal function in early AMD that are likely to result in less risk of vision loss from this disease.
- We have found significant reductions in drusen as well as improved visual function, particularly in the highest risk regions, and often in both the treated and untreated eyes.
- This improvement in the highest risk regions provides circumstantial evidence that the bilateral risk of developing late stage disease has been reduced following an extremely low intensity laser treatment.
Conclusion

- These interim results provide circumstantial evidence that 2RT laser treatment can slow or reverse the progression of AMD towards late stage disease, however to show this conclusively there needs to be a randomized clinical trial (RCT) of the treatment and we will commence this trial now that we are aware of its safety profile and potential efficacy.

- The use of flicker perimetry has enabled small high risk regions to be identified and has proved to be a valuable test to monitor progression of disease and reversal of dysfunction with intervention.