NEW LASER MODALITIES FOR PREVENTING WET AMD

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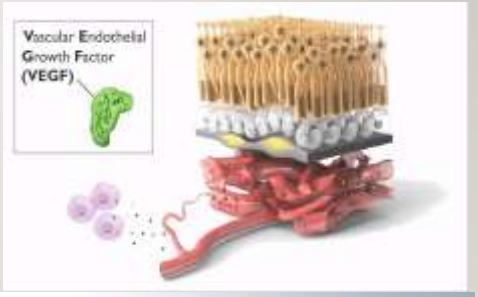
AMD

- Age-related macular degeneration (AMD) is the leading cause of irreversible severe vision loss and permanent impairment of fine or close-up vision in the elderly [> 65y] populations

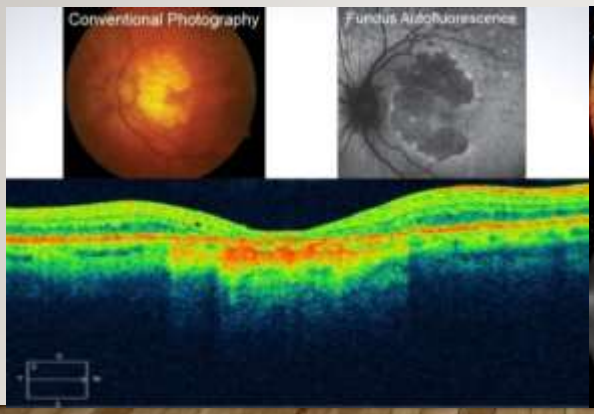
AMD

- In the early stages of disease, there are drusen between the RPE and Bruch's membrane → visual impairment.

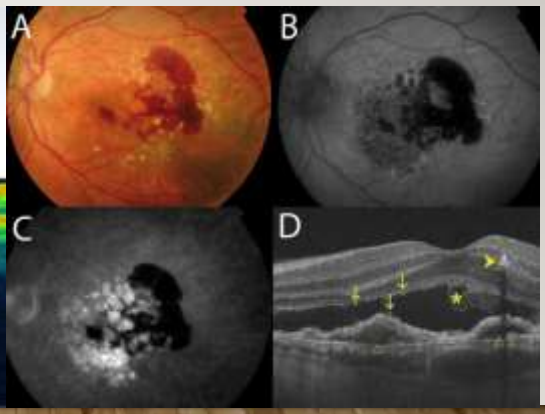


ADVANCED AMD

Geographical atrophy

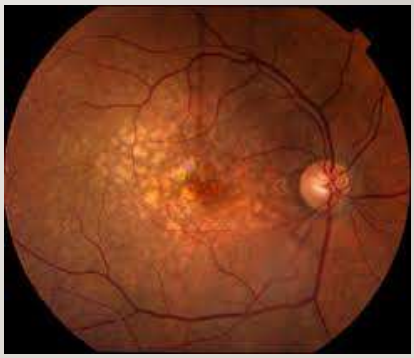


CNV



RISK FACTORS FOR WET AMD

- Large drusen >125um
- Multiple large drusen > 5
- Reticular pseudodrusen
- Wet AMD in other eye



AMD

- In the last decade, there was advances in the treatment of wet type-AMD by antiVEGF
- Pros: Reduce visual loss
- Cons:
  - Financial burden on patient or health systems worldwide
  - Long-term visual benefits are not always maintained despite treatment, with vision loss continuing to occur through atrophy or scar formation.

AMD

- Currently, no effective therapies for the atrophic form of AMD or preventative strategies for inhibiting the progression from early- to late-stage AMD

- In 1971, it was observed serendipitously that drusen regression occurred after thermal (continuous-wave) laser photocoagulation to the retina.
- These lasers result in:
  - Thermal damage to the photoreceptors and inner retinal neurons → loss of vision if applied on macula
  - CNV, subretinal fibrosis

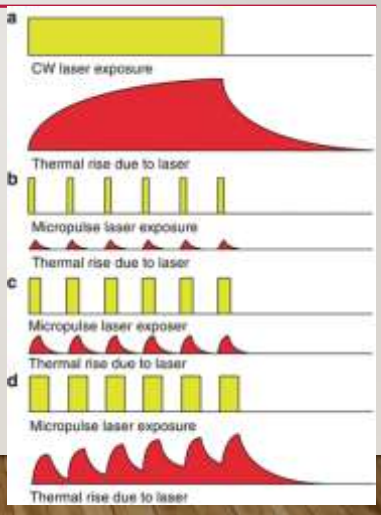
- Further use of thermal lasers for prophylactic treatment for early stages of AMD has not been continued

- Ongoing studies, however, have continued with the aim to develop lasers that could induce the positive effect of drusen reduction, but without the thermal damage seen with traditional lasers:
  - Divide single pulse into small pulses → micropulse
  - Shorten pulse duration → subtheroshold pulse

SUBTHRESHOLD MICROPULSE LASER

- In the traditional continuous-wave mode, a single laser pulse of 0.1–0.5 s delivers the preset laser energy.

- In the micropulse mode, a train of repetitive short laser pulses delivers the laser energy within an "envelope" whose width is typically 0.1–0.5s.



SUBTHRESHOLD MICROPULSE LASER

- Subthreshold micropulse laser (SML) use minimum laser irradiance [mild rise of temperature of RPE] → activation of the RPE cells without cellular damage of RPE.
- But the thermal wave will only reach the neural retina at temperatures beneath the protein denaturation threshold [minimum diffusion of heat to surrounding tissue]

SUBTHRESHOLD MICROPULSE LASER

- Subthreshold micropulse laser (SML) use minimum laser irradiance [mild rise of temperature of RPE] → activation of the RPE cells without cellular damage of RPE.
  - Repair of the inner blood retinal barrier
  - A modification of the gene expression initiated by the wound healing response after laser photo- coagulation
  - Sublethally injured RPE cells induce an up- and downregulation of various factors [pigment epithelium-derived factor (PEDF), vascular endothelial growth factor (VEGF) inhibitors,

SUBTHRESHOLD MICROPULSE LASER

Different lasers available with Micropulse mode:

- 810-nm Diode Laser [in the near-infrared range of the spectrum] → deep penetration into deep retinal layer & choroid sparing inner retina

- 577-nm Yellow Laser which is minimally absorbed by xanthophyll, [the pigment which is located in the inner and outer plexiform layers of the macula,] →so treatment near the fovea is relatively safe

SUBTHRESHOLD MICROPULSE LASER

- In 2016, Luttrull and his colleagues reported "functionally guided retina protective therapy" --> suggested that panmacular SDM may reduce the incidence of CNV in high risk dry AMD more than vitamin therapy alone.

- Prof Sergey, reported the efficacy of 577 nm (yellow) SML in reducing drusen over 12m.

SUBTHRESHOLD NANOSECOND LASER

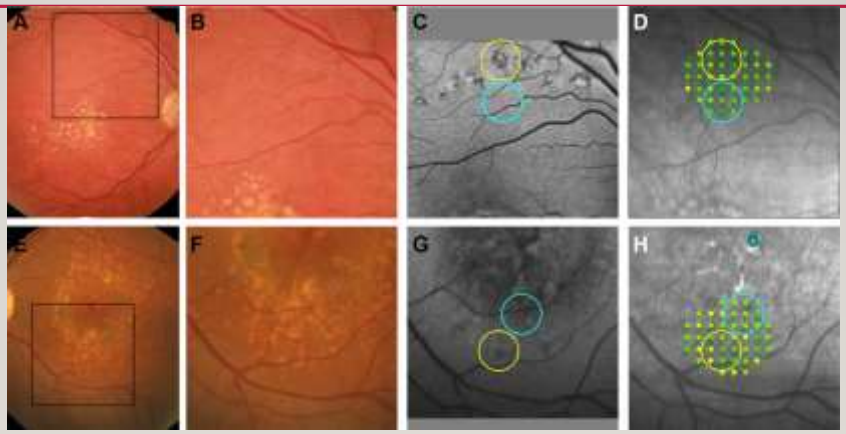
- Shorten the pulse of the laser and deliver a subvisible threshold laser spot--> 3-ns pulsed laser of Nd:YAG laser (532 nm)
- The SNL [laser device 2RT, Ellex Pty Ltd, Adelaide, Australia] uses the principle of selective photothermolysis :
  - Restrict injury to the RPE (sparing the overlying retina)
  - Induce beneficial RPE changes in eyes with the early stages of AMD

SUBTHRESHOLD NANOSECOND LASER

Efficacy

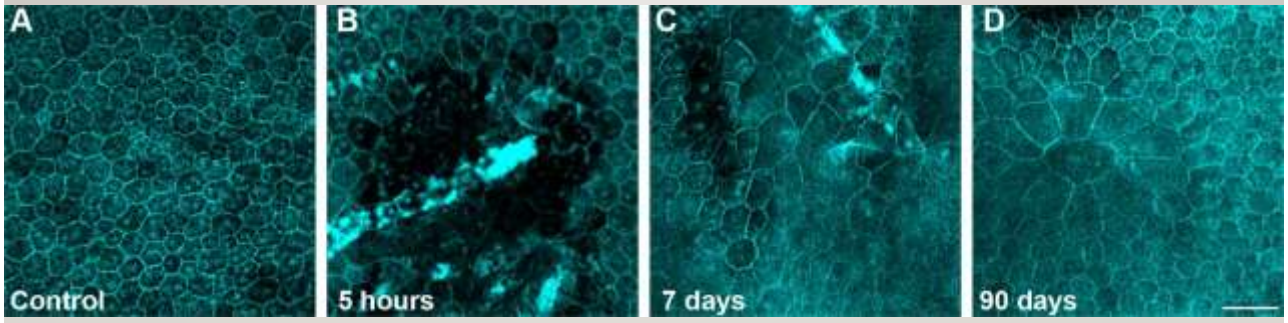
- Jobling et a, 2015 found SNL induce thinning of Bruch's membrane, which is thickened in early AMD, by modulating RPE gene expression, while producing no photoreceptor death.
- Lek et al, 2016 reported a useful for reducing drusen load in patients with AMD
- The Laser Intervention in Early Stages of Age-Related Macular Degeneration (LEAD) study [a world-first, 36- month, investigator-initiated, multicenter, double-masked, randomized, controlled, medical device clinical trial] reported its efficacy in slowing the progression of ARMD in cases without reticular pseudodrusen (RPD) [x4] and may be inappropriate in those with RPD,

SUBTHRESHOLD NANOSECOND LASER



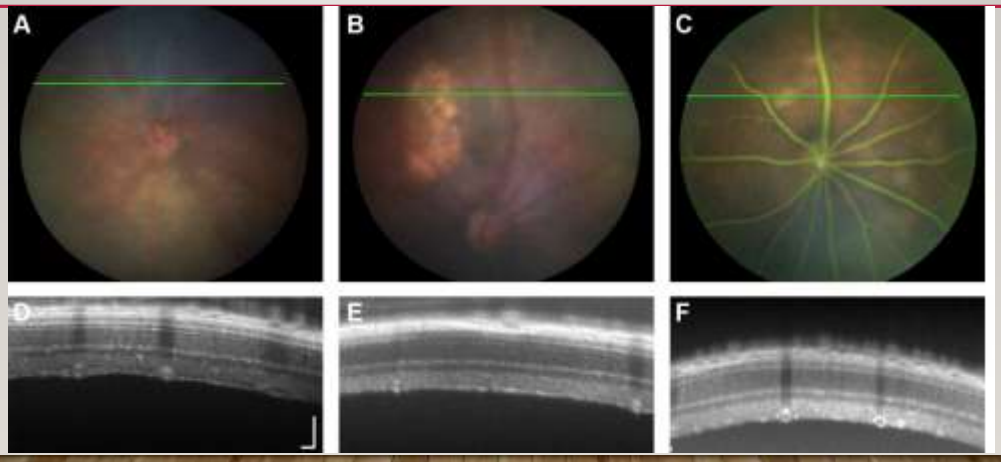
- Did not affect retinal sensitivity assessed by microperimetry, which was similar in laser and control regions

SUBTHRESHOLD NANOSECOND LASER



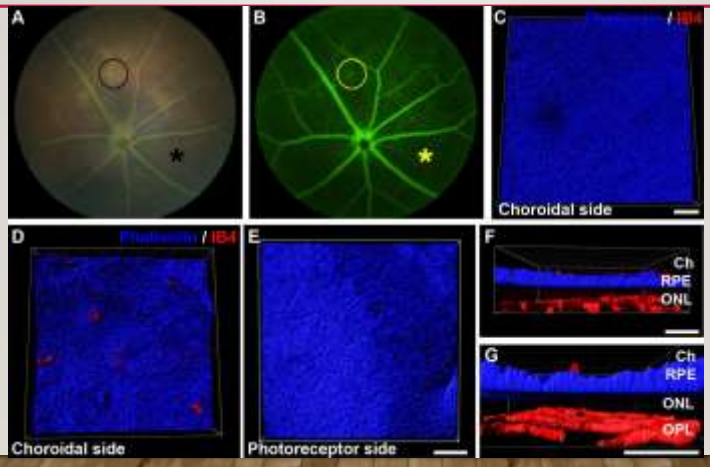
- In the mouse, SNL ablates RPE only

SUBTHRESHOLD NANOSECOND LASER



- In the mouse, retinal structure was preserved directly under the laser sites up to 3 months after treatment, reinforcing the safety

SUBTHRESHOLD NANOSECOND LASER

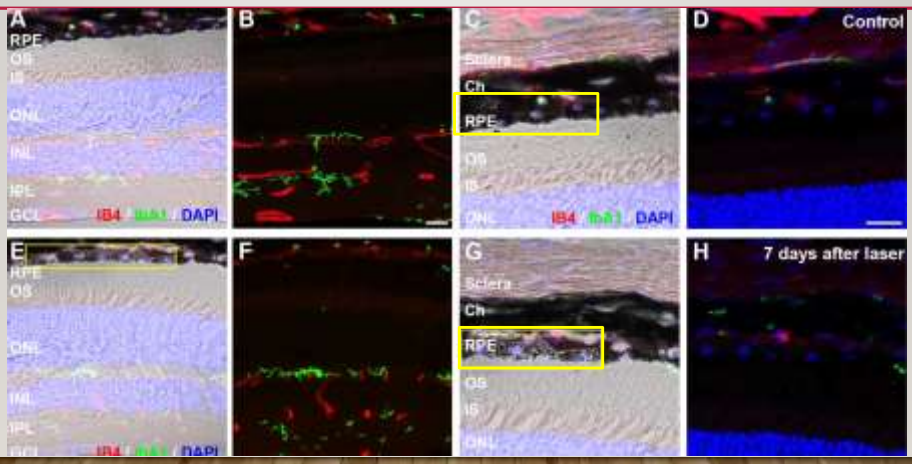


EM study showed Subthreshold Nanosecond Laser Treatment Does Not Disrupt the Choroidal/RPE/Photoreceptor Complex or Bruch's Membrane

SUBTHRESHOLD NANOSECOND LASER

- TEM images of RPE and Bruch's membrane (BM) structure showed subtle change in melanosomes of RPE at laser treated area with intact other retinal layers and BM

SUBTHRESHOLD NANOSECOND LASER



No evidence of vessels breaking through from the choroid was observed

CONCLUSIONS

- Micropulsed laser and Nanosecond laser selectively modulate RPE without destroying surrounding retinal layers
- Micropulsed laser and Nanosecond laser resolved drusen and improved BM [Bruch's membrane] structure,
- These treatment modalities has the potential to reduce AMD progression.

CONCLUSIONS

- SNL treatment has the potential to reduce the rate of progression to late AMD by 4 folds in eyes without RPD, but this intervention currently should be considered with caution in eyes with RPD because of the potential for this treatment to increase the rate of progression for such eyes.

THANKS FOR YOUR ATTENTION