2RT: RETINAL REJUVENATION THERAPY

Clinical and scientific studies have demonstrated that 2RT®, a restorative non-thermal laser therapy, offers the potential to improve retinal function and to halt or delay the degenerative processes that cause some retinal diseases.[1,2,3,4]

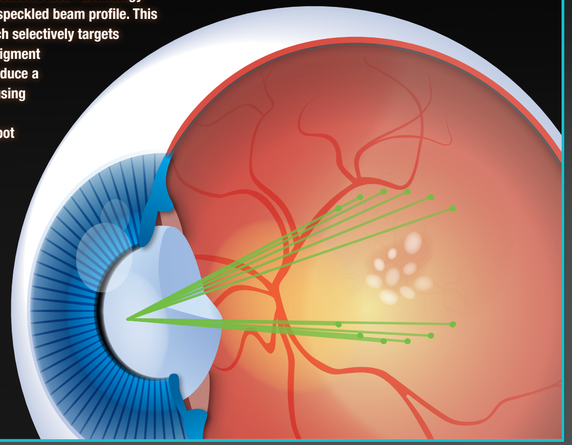
In a pilot study by Professor Robyn Guymer, MB, BS PhD, FRANZCO and colleagues, 2RT® was shown to reduce the area and volume of drusen from a baseline of 5% or more, and to deliver a functional improvement in some high-risk early AMD patients.[1]

In contrast to conventional retinal laser therapy, which can cause permanent collateral damage to the sensitive structures of the eye, 2RT® protects the retina from thermal damage. It also offers the potential to apply treatment earlier in the disease process with the aim of slowing retinal degeneration, thereby eliminating or delaying the risk of vision-threatening complications associated with the late-stage of retinal disease.

2RT® utilizes solid-state, nanosecond laser technology delivered through a patented speckled beam profile. This proprietary treatment approach selectively targets organelles within the retinal pigment epithelium (RPE) in order to induce a therapeutic effect without causing collateral damage. 2RT® also features a large 400 micron spot size, instead of a 50 micron spot size commonly used in conventional retinal laser therapy.

During the procedure, a series of laser spots are applied superiorly and inferiorly, inside the temporal retinal vascular arcades.

- 2RT® offers the potential to halt or delay the degenerative processes that cause retinal disease.
- 2RT® utilizes proprietary, solid-state nanosecond laser technology.
- All of the 2RT® laser energy is designed to stay within the targeted RPE cells.
- 2RT® uses approximately 500 times less energy than retinal photocoagulation.
- 2RT® induces a mononuclear cell response, including the stimulation of microglia.

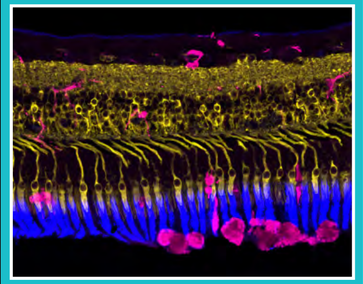


2RT: TAKING THE HEAT OUT OF PHOTOCOAGULATION

Ellex's proprietary, patented 2RT® technology features a speckled beam profile which exclusively targets selected organelles within the retinal pigment epithelium (RPE).

The application of 2RT® to the RPE results in the formation of microbubbles around melonasomes.[5] These microbubbles expand and then coalesce, causing intracellular damage. A key aspect of the 2RT® treatment approach is that cell damage is confined within the targeted RPE cells and does not extend to the neighboring cells. A process of extracellular signaling occurs in response to the selected death of the targeted RPE cells, which causes the neighboring RPE cells to migrate and proliferate into the cell space vacated by these dead RPE cells.

This stimulates a process of cell division and growth, which improves permeability of Bruch's membrane, and thereby restores the transport of fluid across Bruch's membrane.[2,6] As a result, the RPE is rejuvenated – and without damage to the overlying neurosensory retina.



Research conducted by Professor Erica L. Fletcher MScOptom, PhD and colleagues has shown that 2RT® induces a mononuclear cell response, including the stimulation of microglia. Microglia, the resident immune cell of the central nervous system, is known to remove cellular debris and facilitate healing.[2] In the above image, taken five days following the application of 2RT®, retinal microglia are shown extending their cell processes toward the laser treatment site.

Image courtesy of Professor Erica L. Fletcher MScOptom, PhD.

MECHANISM OF ACTION

1. 2RT selectively targets individual RPE cells.
2. Microbubbles around melanosomes expand, coalesce and cause intracellular damage.
3. Intracellular structure damaged, leading to individual RPE cell death.
4. Extracellular and Intracellular signalling occurs from neighboring RPE cells: neighboring cells migrate and proliferate into vacant cell space and RPE cells divide to produce a new RPE cell.
5. Microglial processes extending towards lasered site without any classical signs of stress (gliosis).
6. Permeability of Bruch's membrane improved and transport of fluid across Bruch's membrane restored.

2RT FOR EARLY AMD

As the eye ages, the permeability of Bruch's membrane is reduced, inhibiting its ability to remove and exchange fluid with the addition of accumulating waste deposits under the macula, known as drusen and pigmentary abnormalities.[7] Current estimates suggest that by age 40 the flow is reduced to approximately 50% of what it is in infants. By age 80, it is reduced to a small fraction.[8]

Reduced fluid outflow across Bruch's membrane has been shown to play a central role in the development of retinal pathologies. In addition, reduced nutrition and oxygen may promote neovascularization by stressing retinal cells to the point that they secrete endothelial growth factors and other enzymes that are part of the body's wound healing process.

Targeted at the RPE and Bruch's membrane, 2RT® stimulates a biological healing response in the eye which improves permeability of Bruch's membrane and thereby restores the transport of fluid across Bruch's membrane. By restoring metabolite flow to retinal cells, 2RT® may also reduce the cell production of vascular endothelial growth factors and other precursors of neovascularization.

To date, 2RT® is the first and only treatment that has demonstrated the potential to produce bilateral improvements in macular function and appearance and function in early AMD patients.

Conventional AMD treatments, such as ongoing intraocular injections of anti-vascular endothelial growth factor (anti-VEGF) medications, address late-stage complications associated with the disease. In contrast, 2RT® offers the potential to apply treatment earlier in the disease process and to intervene at the level of the underlying pathology, preventing progression to wet AMD.

> "With 2RT® the aim is to treat the causes of the disease before vision loss occurs."

2RT FOR CSME

Clinical studies have shown 2RT® to be as effective as retinal photocoagulation in reducing cystoid macular edema secondary to diabetic retinopathy. Unlike retinal photocoagulation, however, which results in localized destruction of photoreceptors, thereby leading to scotoma and architectural loss to overall tissue, 2RT® protects the photoreceptors, and therefore retinal function, from thermal damage. It also uses approximately 500 times less energy than retinal photocoagulation: the huge reduction in radiant exposure proportionately reduces the risk of damage to all aspects of retinal function.[3]

Historically, retinal photocoagulation has been used to reduce the rate of visual acuity loss from diabetic macular edema. The trade-off is destruction of photoreceptor cells. In contrast, 2RT® selectively targets the melanosome organelles of the RPE to stimulate a process of intra-cellular micro-bubble formation, which helps to increase fluid and metabolite flow across Bruch's membrane without causing damage to the retina.

> "2RT® uses approximately 500 times less energy than retinal photocoagulation."