



by Howard Larkin

# Ellex looks to laser Retina Regeneration Therapy as future for treating maculopathy and AMD

*Early study suggests non-thermal treatment may prevent vision loss by rejuvenating Bruch's membrane*

With more than 14,000 systems installed worldwide, Ellex knows a thing or two about developing advanced ophthalmic lasers. The Australian-based firm's product line includes a wide range of photocoagulators for retinal work and YAG photodisruptors for glaucoma. And, of course, there's a complete line of selective laser trabeculoplasty (SLT) systems for non-thermal glaucoma treatment that lowers intraocular pressure without damaging the trabecular meshwork. Now Ellex is banking on a similar non-thermal, tissue-preserving laser procedure it calls Retina Regeneration Therapy, or Ellex 2RT™, as the next big thing for treating diabetic maculopathy and macular edema, and age-related macular degeneration.

An early clinical study shows promise, says John Marshall PhD FRCPATH, FRCOphth, Frost Professor of Ophthalmology, the Rayne Institute, St Thomas' Hospital, London, UK. In a study conducted there, most of 28 eyes in 17 newly diagnosed maculopathy patients showed stable to improved retinal condition and improved visual acuity six months after Ellex 2RT treatment. Central macular thickness decreased by five per cent or more in 47 per cent of eyes, was stable in 39 per cent of eyes, but increased by more than five per cent in 15 per cent of eyes. Visual acuity improved by two or more LogMar lines in 43 per cent of eyes and by one to two lines in 28 per cent. Visual acuity remained stable in 15 per cent of eyes and declined in 14 per cent.

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Follow-up with these patients is ongoing, and large-scale clinical tests for treating maculopathy are getting under way in Australia and the UK, says Prof Marshall, who heads Ellex's Scientific Advisory Board and sits on the firm's Board of Directors. He also hopes to

launch a trial for early-stage AMD, focusing on delaying or preventing development of the disease in the fellow eyes of those with AMD in one eye.

### Revolution in retinal treatment?

Prof Marshall believes that Ellex 2RT could ultimately revolutionise treatment of retinal edema and neovascular retinal maladies across the board. It might even prevent them in many patients. He believes this because, much as SLT appears to increase fluid outflow through the trabecular meshwork, Ellex 2RT treatment appears to increase the permeability of Bruch's membrane. In doing so, it addresses what Prof Marshall and other researchers believe is the root cause of many retinal pathologies – the reduction in both inflow of metabolites and outflow of fluids across Bruch's membrane, which separates the photoreceptor cells and retinal pigment epithelium from the rich blood vessels of the choroid on which they rely for support.



Prof Marshall notes that reduced fluid flow across Bruch's membrane is a normal part of ageing. By age 40, flow is down to about half of what it is in infants. By age 80, it is reduced to a small fraction. One result is that photoreceptor cells are progressively starved. This leads to declining sensitivity and visual acuity even among patients who show no signs of retinal pathology.

However, this reduction in flow also appears to play a central role in the development of retinal pathologies, Prof Marshall explains. Reduced fluid outflow contributes to retinal edema and may also account for accumulation of debris resulting in the formation of drusen. At the same time, reduced nutrition and oxygen may promote neovascularisation

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.

In the past, photocoagulation was used to control the progress of neovascularisation by destroying ischemic retina, Prof Marshall said. The trade-off was destruction of photoreceptor cells. As a result, treatment could not begin too early, and could not proceed too far without risking eyesight, he points out.

The Ellex 2RT laser treatment instead targets the retinal pigment epithelium and Bruch's membrane, stimulating what Prof Marshall describes as "photoregeneration". Energy from three-nanosecond pulses of 532 nm light produced by a Q-switched ND:YAG green laser causes the retinal pigment epithelium cells to release matrix metalloproteinase. These enzymes are believed to help "clean-up" Bruch's membrane. The result is an increase in fluid and metabolite flow that has been observed in the laboratory.

Because the treatment is non-thermal, it spares both the photoreceptor and retinal pigment epithelium cells. Indeed, it actually appears to restore the integrity of the damaged retinal pigment epithelium. By restoring metabolite flow to retinal cells, it may also cut down on cell production of endothelial growth factors and other precursors of neovascularisation, eliminating the need for anti-VEGF or related drug therapies. "With this treatment you get the benefit of photocoagulation without the downside of killing off the photoreceptor cells," Prof Marshall says. "You simultaneously clear the drain of Bruch's membrane and turn off the leaky tap."

The goal of the planned large-scale clinical trials is to demonstrate the viability of the Ellex 2RT concept in treating retinal pathology, Prof Marshall says. The idea is to slow or reverse diabetic maculopathy and edema, and delay the onset of AMD in the fellow eye of AMD patients from the current average of about three years to perhaps seven to 10 years. Ultimately, though, he sees a much broader application for Ellex 2RT as prophylaxis. By routinely treating patients at age 40 or so, it may be possible to slow the reduction in fluid flow across Bruch's membrane. This, in turn, not only may prevent many cases of AMD and diabetic retinal diseases, it might also slow the "normal" deterioration of eyesight in old age.



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### Future market

The Ellex 2RT laser was developed by the Ellex Advanced Research Team in Adelaide, and is supported in part by a grant from the Australian government. Prof Marshall emphasises that the laser is specifically designed for retinal treatment, and is capable of operating at speeds and power levels far more precise than existing laser systems. Under no circumstances should clinicians attempt to use an SLT laser for retinal treatment, he warns.

Pending the outcome of further clinical trials, Prof Marshall believes that Ellex 2RT could indeed revolutionise retinal therapy. If so, it would also solidify Ellex's position as a leading global innovator in ophthalmic laser therapy.