

New technique delivers growth factor to eyes with retinitis pigmentosa

Nadja Geipert
in Fort Lauderdale

A NEW implant that delivers encapsulated growth factor-producing cells into the eyes of retinitis pigmentosa (RP) patients appears to be safe and has even produced minor improvements in vision, according to early results announced at the annual meeting of the Association for Research in Vision and Ophthalmology.

The device remained in ten eyes of ten patients for six months with no ill effects. Moreover, the patients, who were at an advanced stage of the disease, also showed a one-line improvement in their visual acuity scores from the treatment, reported Dean Bok PhD, Professor of ophthalmology at the Jules Stein Eye Institute at the University of Los Angeles.

"This is remarkable because they had very advanced RP," he stressed.

In a Phase I safety trial, vitreoretinal surgeons implanted the NT-501 device (Neurotech) in one eye of 10 legally blind patients with retinitis pigmentosa by making a 2.0 mm scleral incision, inserting it with a metal loop and suturing it in place. Every month after implantation, the researchers tested the patients' visual field, visual acuity and performed electroretinograms.

After six months, the surgeons extracted the device from the patients' eyes. One-month and one-year follow-up examinations did not find any serious complications from the procedure with the exception of one patient with ciliary detachment.

Moreover, even though the study was not an efficacy trial, the patients' eye examinations showed a moderate improvement of their visual acuity, said Rafael Caruso MD, a clinical researcher at the National Eye Institute (NEI) in Bethesda, USA and one of the investigators in the trial. Dr Caruso.

"This is an improvement usually not considered clinically significant, but provocative," he said, noting that the patients did not receive the treatment long enough to firmly establish if it could rescue photoreceptor cells from dying.

The safety trial's results clear the way for a Phase II efficacy trial that will test if the treatment can really prevent the progressive vision loss in RP patients.



Dean Bok

In development for over a decade

More than a decade of advances in basic science research, gene therapy and biotechnology created the foundation for this ingenious idea for treating retinitis pigmentosa, which affects at least 1.5 million people worldwide.

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In the early 1990s, researchers demonstrated that injecting ciliary neurotrophic factor (CNTF) into the eyes of patients with retinitis pigmentosa prevented photoreceptor cell death, a hallmark of the disease. Since then, additional research confirmed that CNTF slows photoreceptor cell degeneration in 12 different inherited retinal disorders in four different animal species.

However, simply injecting the protein into the eyes of human patients was deemed an unworthy, invasive treatment strategy because the patients would need to be injected repeatedly for the rest of their lives. In addition, the blood-retina

barrier limits the possibility of administering the protein orally. To solve this problem researchers and biotechnological companies searched for a safe and effective way to deliver CNTF into the eye.

Encapsulated cell technology

Enter the NT-501, a small device produced by the French biotechnology company Neurotech. The product uses Encapsulated Cell Technology (ECT) to overcome the drug delivery problems. In ECT, retinal pigment epithelial cells carrying a virus that has been genetically manipulated to overproduce CNTF are loaded into a semi-permeable plastic polymer basket that can be implanted into the eye.

"This little device is hung by a little hook inside the eye out of the path of vision and it constantly releases CNTF because these engineered cells are making it," explained Dr Bok.

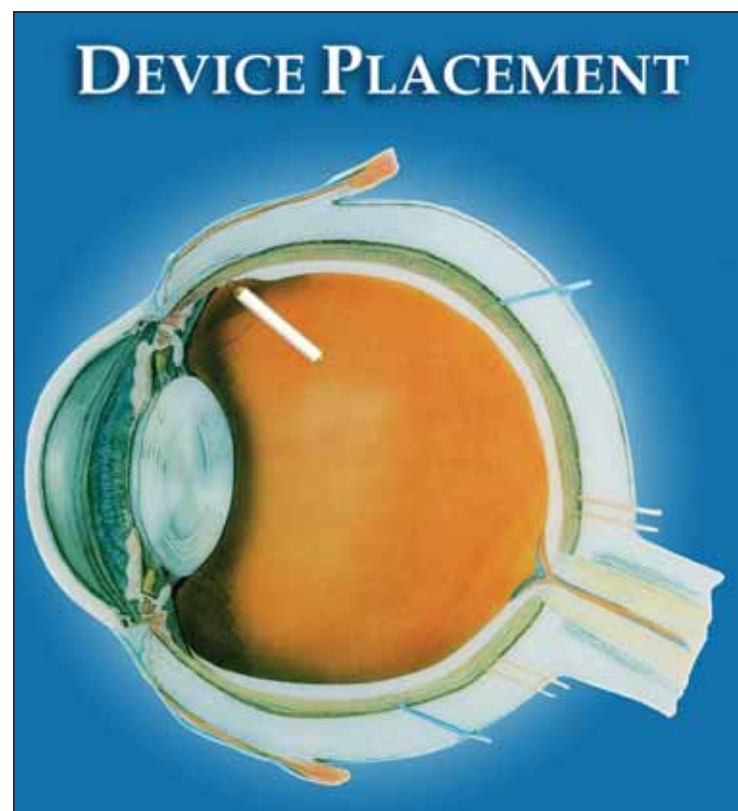
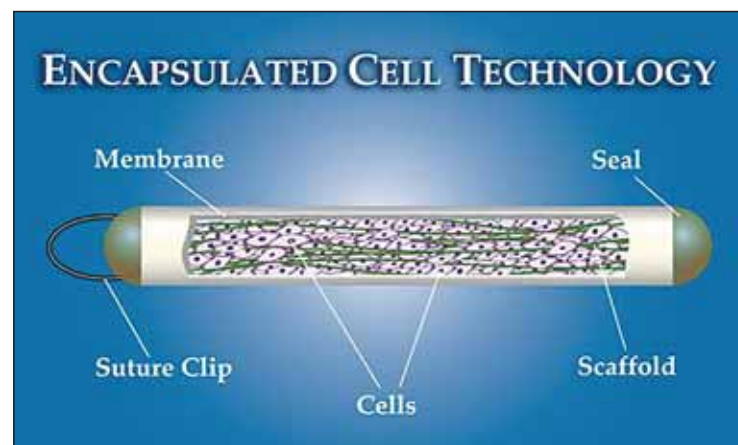
The plastic device protects the CNTF-releasing cells from immune attacks, yet its semi permeability allows the cells to release the CNTF into the eye tissue. In doing so, the CNTF enters the gel-filled cavity of the eye, percolates between the cells of the retina and bathes them in the CNTF, which keeps the photoreceptors alive, he explained.

Preparations underway for phase II trial

Bernard Davitian, President of Neurotech, told *EuroTimes* that the Phase I trial has validated the safe use of the Encapsulated Cell Technology to deliver CNTF to the vitreous. He added that the visual acuity outcomes observed in some patients are encouraging enough to follow on with clinical evaluation of NT-501 in Phase II trials.

"In addition to further studies with NT-501, we are evaluating other neurotrophic factors and agents that can be used with ECT for treating other retinal diseases."

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Courtesy of Neurotech

Currently, Dr Caruso and his colleagues are screening patients for the Phase II trial of NT-501 in retinitis pigmentosa. The researchers will select at least 100 patients who are in less advanced stages of the disease, so changes in vision can be detected faster. The patients will need to

other retinal degenerative diseases. While CNTF cannot cure retinal diseases, it seems to be a survival factor for receptor cells, and RP is not the only disease where photoreceptors are affected, according to Dr Caruso.

"This may be useful for other diseases of the retina in which the common thread is photoreceptor cell loss", he said.

Dr Bok shares Dr Caruso's preliminary optimism about possible other applications of the treatment.

"The reason I'm excited about this is because it could have generic applications, in other words, one could conceive of this not only for RP but also other degenerative disease like age-related macular degeneration," he said.

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retain the implant for at least two years to determine if it can interfere with apoptosis, Dr Caruso said.

If the Phase II yields positive results, NT-501 might also hold promise for the treatment of