

# REFRACTIVE EYECARE™

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SPECTACLES, CONTACT LENSES, AND CORNEAL AND LENTICULAR REFRACTIVE SURGERY FOR PRACTICE GROWTH

## Donald Tan, MD, on NeuroVision™, a Non-optical Approach to Correcting the Effects of Refractive Error

### EXPERT OPINION

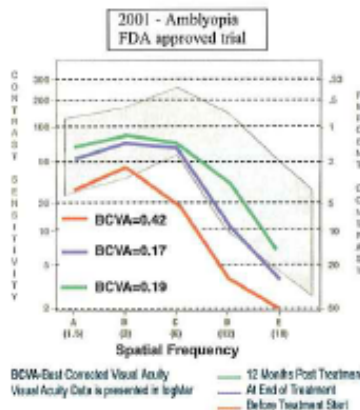
NeuroVision, a technology designed to reduce the effects of refractive error through a neural training process referred to as “perceptual learning,” has been developed in Singapore and is in the very early stages of commercialization in Asia, Europe, and North America. Based on sound neurophysiologic investigation and clinical studies in amblyopic eyes, for patients with low refractive errors, the technology promises good vision without glasses, contact lenses, or surgery. Donald Tan, MD, is professor of ophthalmology and director of the Singapore Eye Research Institute, Singapore. He is a scientific advisor to NeuroVision and is a principal investigator for the company’s clinical trials in Singapore. He has no other personal or financial connection to the company.

**Dr. Tan, can you describe the NeuroVision process as a patient would experience it?**

The NeuroVision treatment is a series of computer-

ized training sessions that are designed to improve the way the brain processes vision. The process starts with a baseline visual assessment per-

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**FIGURE 1** Contrast sensitivity results in amblyopic patients. Note the continuing improvement after the NeuroVision treatment ended.

### EXPERT OPINION *continued from page 1*

formed at one of the NeuroVision-certified eye centers. The primary objective of this examination is to determine whether the patient is a suitable candidate for NeuroVision. Once suitability is confirmed, the patient will undergo a short orientation session to become familiar with the NeuroVision interactive visual tasks the patient will undergo in the course of the treatment.

#### Can you describe the NeuroVision treatment process?

The patient is seated in front of a computer, 5 feet from the screen, where he or she is exposed to a series of images based on various combinations of Gabor patches. (The Gabor patch is a sine wave grating that has high contrast in the center but low contrast at its edges. [Editor's note: Illustrations and considerable information on Gabor patches can be found by means of a Google search.]) The patient is required to indicate whether he/she sees a target arrangement using the computer mouse. Audio feedback lets the viewer know if a mistake has been made.

Based on the patient's response, the system adjusts the task's level of difficulty to match the patient's visual abilities. The treatment is applied in successive 30-minute sessions, administered 2-3 times a week, for a total of approximately 30 sessions. The treatment sessions can be conducted either in an eye center or at home on a personal computer. Every five sessions, the subject's visual acuity and contrast sensitivity are tested in order to continuously monitor progress.

#### What is the session like for the patient?

The treatment is not stressful, but neither is it relaxing. Unlike using lenses or refractive surgery to correct vision, success with NeuroVision treatment depends heavily on the patient's performance. Concentration during the session and making a concerted effort to achieve the best performance throughout the entire treatment session, are key success factors. No doubt, the highly motivated patients are the most likely to achieve the biggest visual improvement. Please note that NeuroVision treatment bears no relationship whatever to unsubstantiated and unscientific "eye relaxation" exercises that appear to relax accommodation and reduce pseudomyopia. NeuroVision works at the level of the brain not the ciliary muscle.

The improvement in vision is gradual; patients start noticing an improvement after approximately 10 treatment sessions.

#### The NeuroVision literature states that the procedure is based on 20 years of research. Can you describe that research? Are there peer-reviewed clinical studies of the current NeuroVision process?

The NeuroVision technology has been developed through research focused solely on optimizing performance of the neural or "back end" of the visual system and is based on two decades of visual neuroscience research in renowned institutes, including the Weizmann Institute in Israel, and Smith-Kettlewell Eye Research Institute in San Francisco.

This research has led to breakthrough discoveries in the field of visual neuroscience that have been published in prestigious scientific magazines, including publications in *Nature*, *Vision Research*, and *Proceedings of the National Academy of Sciences*.<sup>1,3</sup>

The technology has been clinically proven in the treatment of adult amblyopia, which until recently has been considered untreatable, with a very well conducted double-masked randomized clinical trial that led to FDA 510(k) approval. The adult amblyopia clinical trials were published in the *Proceedings of the National Academy of Sciences* in 2004 (Polar U, Ma-Naim T, Bellin M, Sagi D: Improving vision in adult amblyopia by perceptual learning. *Proc Natl Acad Sci USA* 2004; Apr 27; 101(17):6692-7.)

The NeuroVision technology was originally studied in amblyopia (Figure 1). In 2003 the Singapore Eye Research Institute, in collaboration with the Singapore Armed Forces, initiated a pilot study of NeuroVision for the treatment of low degrees of myopia. With the results of this study and clinical experience with several hundred commercially treated patients in Singapore, it certainly appears that NeuroVision treatment enhances both visual acuity and contrast sensitivity in the majority of individuals. In follow-up examinations, we have found that the visual improvement is maintained for more than 1 year after the end of the treatment (Figures 2-4). We are now in the advanced stages of a large double-masked,

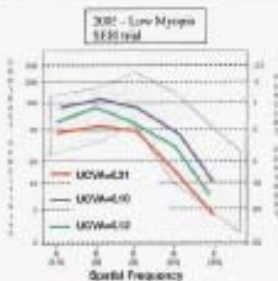


FIGURE 2 Contrast sensitivity results in the Singapore Eye Research Institute trial. Note the improvement was not lost 12 months after treatment.

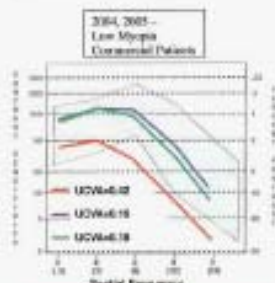


FIGURE 3 Contrast sensitivity results among commercial patients who paid for their treatment. Note the continued improvement.

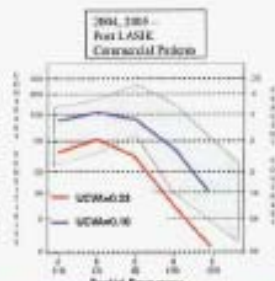


FIGURE 4 Contrast sensitivity results among post-LASIK commercial patients.



placebo-controlled randomized clinical trial in Singapore that will provide confirmatory scientific data about the efficacy of NeuroVision Myopia treatment.

### What kind of work has been done to support the theory and to understand the mechanism behind the improvement in vision?

The research looked into the neuronal responses in the primary visual cortex (V1) to different visual stimulations, connections (lateral interactions) between neuronal cells in V1, learning patterns to improve the lateral interactions, and normal/abnormal connections as a result of different vision related conditions.

It has been demonstrated that neuronal responses in the primary visual cortex can be modulated by stimulation of remote input parts, and neural plasticity in the primary visual cortex has been evidenced.

Those observations have been made using single-neuron recordings in cats and monkeys; visual evoked potential recordings in humans; and psychophysical tests in humans. Those studies were well documented and reported in scientific publications.<sup>1,2</sup>

### What is the maximum achievable correction? What are the median and average corrections? What is the dropout rate? Why do patients drop out?

The average improvement for the low myopia treatment is close to 3 LogMAR lines (2.7 lines) on ETDRS chart.

The maximum improvement achieved so far is 7 lines ETDRS, in a patient who went from 20/120 to 20/25. But this is clearly the exception—most treatment outcomes are less remarkable than this.

The drop-out rate is quite low, approximately 12%. About 7-8% dropout after 15 sessions because they show either no improvement or too little improvement to justify continuing. The rest of the dropouts occur for different reasons, but the chief reason seems to be the time commitment—for some people having a session 2-3 times a week is too much.

### What is known about the duration of effect of NeuroVision's effect treatment?

Theoretically the learning process that happens in the Primary Visual Cortex is similar to a skill acquisition (like learning to walk, swim, or ride bicycles). This kind of learning, once achieved is never quite forgotten; therefore, the effect should be sustained.

The clinical data gathered so far supports this assumption. The NeuroVision amblyopia study shows that the effect is maintained at least 1 year with no significant regression. Similar results have been demonstrated in the Singapore Eye Research Institute Myopia Pilot Study, as well as at the Singapore National Eye Centre, which has provided NeuroVision treatments commercially since mid 2004. Ultimately, more work will have to be done in this area to establish long-term efficacy, but results are quite encouraging at this stage.

### Is your personal vision in the NeuroVision correction range? If so, have you tried it?

Unfortunately I have too much myopia for NeuroVision, and I also have significant astigmatism, which has not yet been investigated fully by the technology. I have tried a few sessions to get a better feeling for the treatment regimen, but, unfortunately, I don't expect it to be beneficial for me.

### Does NeuroVision have any effect on the eye itself?

No. NeuroVision does not alter the anatomy of the eye; therefore, it does not alter the refraction. NeuroVision improves the visual processing in the visual cortex. By doing that, it is able to compensate for some level of blur on the retina caused by a relatively mild optical defect.

So, a myope with a -5.00 D prescription might be able to use reduced power after NeuroVision treatment, if he finds this beneficial. However his vision will always be the best with -5.00 D spectacles, because then not only would the visual processing be optimized but also the optics of the eyes.

### Can other refractive errors be helped by NeuroVision?

As I mentioned before, NeuroVision is effective in sharpening vision and compensating for relatively low levels of refractive errors. It works best for low myopes with -1.50 D or less, and probably also astigmatism of 0.75 D or less. A recent study by NeuroVision shows that it also appears to be effective in early stages of presbyopia—ie, patients with near addition needs of up to 1.50 D will be able to put their reading glasses away for several years (Figure 5).

Theoretically it should work on low degrees of hyperopia as well; however, we have not tested this yet. Most of our clinical research is done in Singapore, and we simply don't have many hyperopes!

### Is there any potential for harm with NeuroVision?

So far, after treating more than 1,000 patients in Singapore and other Asian countries, in both clinical trials and commercial environments, we can confirm that there are no known risks or side effects associated with this technology.

The only complaint we hear from some patients is that they feel their eyes are tired immediately after the treatment. But this symptom disappears quickly as they leave the clinic.

### Are there any new studies currently contemplated?

We are now starting an exciting controlled study to

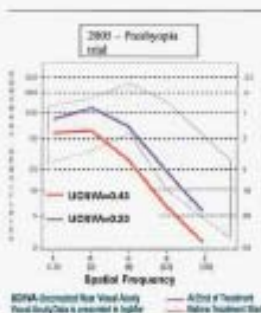


FIGURE 5 Contrast sensitivity results in the recent presbyopia trials.

evaluate whether we can slow the progression of myopia in children by using NeuroVision. The study—a collaborative effort of the Singapore Eye Research Institute, the Singapore Health Promotion Board, The Singapore Ministry of Education, and NeuroVision—will be conducted in several schools in Singapore. The study addresses one of the major concerns in Asian societies.

#### **Going forward, what do you know of the company's plans for commercializing NeuroVision?**

NeuroVision is based in Singapore. Therefore, the Singapore market is the first to be exposed to NeuroVision's products. Other countries with commercial treatment available include Malaysia, and most recently, Japan.

The treatments are provided to the patients through eyecare professionals: ophthalmologists, eye centers, optometrists, and optical stores with trained staff. Patients can choose to do the

treatment in the clinic/eye center or on their own schedule at home on their own personal computer. In both cases, the treatment is monitored by eyecare professionals, as the patient visits the clinic every 5 sessions for visual examination.

The presbyopia treatment has just been introduced in Singapore, and the company expects to introduce a new product for myopic children, with a game integrated in the software, very shortly. The game is intended to act as motivator to keep the children interested, concentrated, and alert.

#### **What do you want American ophthalmologists to know about NeuroVision?**

The NeuroVision technology takes a distinctly alternative approach, compared to treating eye disease by drugs, laser, or surgery in order to restore vision. Instead, the NeuroVision technology enhances existing vision through a logical treatment derived from recently discovered but

## **Bringing NeuroVision to the Market**

NeuroVision was recently an exhibitor at Vision Expo in New York, where *Refractive Eyecare* was able to speak with Alain Leveue, CEO, and Nir Ellenbogen, COO and CTO, of the company. The following report was taken from an interview with Leveue and Ellenbogen, who were in the USA to introduce their technology and to speak with potential strategic partners.

#### **Taking New Technology to Market**

Working from its base in Singapore, NeuroVision is bringing its technology to patients through the Singapore National Eye Center and an optical chain in that country as well as eye centers in Malaysia and Japan. A small company, NeuroVision is looking to partner with an established major eyecare company for commercialization in the large North American market. Leveue and Ellenbogen foresee the availability of NeuroVision treatment for refractive error in the USA within approximately 1-2 years.

The model for delivery of NeuroVision treatments has two arms: patients can treat themselves at home or work using their own computers or they can come to a center for treatment. Ellenbogen likens NeuroVision treatment to working out: you can buy a machine and exercise at home or you can go to a gym, where there are trainers to give you a hand. Both are effective, but if structure and motivation are issues, then going to the gym may help.

#### **Price and Publicity**

The NeuroVision executives note that marketing NeuroVision has been relatively easy in Singapore, where 60% of the children are myopic, making myopia a major public health issue and a very serious concern of

Singaporean parents. Hence, publicity for NeuroVision in Singapore typically brings an outpouring of interest, from which appropriate patients can be selected. These patients then form a nucleus for spreading information about NeuroVision by word of mouth. With just modest effort on the company's part, 30% of the Singaporean population is aware of the technology.

As a working model, NeuroVision treatment has been priced at 30-40% of the price of LASIK. Just as LASIK varies in cost from several hundred dollars in countries like India to an average over \$1,500 in the USA, Leveue and Ellenbogen expect that NeuroVision will be offered at different price points in different countries.

#### **A Proven Technology**

Leveue and Ellenbogen note that the efficacy of NeuroVision's technology has been repeatedly demonstrated, starting with proof of the concept in adult amblyopic eyes, which have been successfully trained to achieve enhanced acuity and contrast sensitivity (and some have actually gained stereovision). What this indicates is that the human brain retains considerable plasticity with respect to image quality improvement even into adult years.

Because NeuroVision technology improves acuity and contrast sensitivity, its value isn't limited to individuals with low refractive errors. Emmetropes who want to further sharpen their vision can potentially benefit, its backers claim. Although further studies are needed, it seems reasonable that NeuroVision may be helpful for pilots, athletes, artists, and others for whom optimum vision is critical. It may even offer a nonsurgical means of enhancing refractive surgery outcomes. ●

clearly sound principles of visual neuroscience. The NeuroVision technology represents a new strategy that can complement our conventional medical and surgical therapies to enhance vision.

NeuroVision's technology comes from a considerable background of scientific and clinical research in the field of visual neurophysiology. NeuroVision's technology is still largely unfamiliar to clinicians because these articles are not (yet) found in the scientific journals of greatest interest to practicing ophthalmologists.

What needs to be stressed is that NeuroVision technology appears to be a new platform for modulation of "neural adaptation" of the human visual system, which has been legitimately and scientifically assessed and is undergoing rigorous clinical trials. I would emphasize strongly that this form of visual cortex adaptation is also now called "perceptual learning" by vision scientists and is vastly different from the current unscientific "vision exercises" that can be found at various sources today.

The major advantage of the technology is the fact that it is completely noninvasive and, therefore, carries virtually no risk to the patient. To date, there is no other non-invasive, non-pharmacological, and non-surgical treatment for conditions like myopia or presbyopia.

NeuroVision seems to be one of the most promising technologies evaluated by the Singapore Eye Research Institute in recent years. I believe it has the potential to make a tremendous impact in the eyecare industry in Asia and worldwide. ●

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