The New World of **Virtual Reality**

Virtual reality technology is showing promise in augmenting traditional assessment and interventional strategies. A look at some lines of investigation.

By Linda Roach, Contributing Writer

VIRTUAL REALITY ISN'T JUST FOR video game buffs anymore. The same technology that fools gamers into believing they are flying an airplane or fighting a medieval battle is moving into multiple areas of medicine.

In ophthalmology, with the exception of education simulators, most of the research into virtual reality (VR) is in the early stages, and these applications have not yet been subjected to rigorous clinical testing. But the work to design and validate them is being carried forward enthusiastically.

Projects in the works include efforts to objectively assess glaucoma; the use of targeted light stimulation to try to rejuvenate failing retinal glanglion cells, and gamelike environments for patients with binocular vision disorders.

Detecting VF Deficits

In the Duke Visual Performance Laboratory directed by glaucoma specialist Felipe A. Medeiros, MD, PhD, researchers hope that their headset—the nGoggle (Ngoggle Diagnostics)—will be the VR tool that establishes a new era in glaucoma management. The goal: a wearable VR system that can detect and quantify visual field (VF) deficits without the subjectivity and inherent imprecision of standard automated perimetry (SAP).

"The idea behind our system was to be able to collect the information about the visual field in an objective way, without relying on subjective patient responses—like having the patient press a button or indicating in some other way that they saw a flash of light," said Dr. Medeiros, at Duke University in Durham, North Carolina.

How it works. The nGoggle integrates wireless electroencephalogram (EEG) and electrooculogram (EOG) sensors, a smartphone-based VR headset, and proprietary software to analyze the information collected. It transmits the data wirelessly to the test administrators. While wearing the headset, the patient passively views patterns of flickering lights on the phone's screen, as the 10 EEG/EOG sensors measure the resulting steady-state visual evoked potentials emanating from the occipital cortex.

Detecting disease progression. Last year, Dr. Medeiros and several colleagues at the University of California, San Diego, reported that the relative levels of these electrical signals could be used to distinguish glaucomatous from normal eyes in a clinic-based setting.[1] Dr. Medeiros has since begun a pilot longitudinal study to investigate whether nGoggle can detect disease progression. If the results are promising, the team hopes to expand the study into a large multicenter clinical trial, he said.

For use at home. "Our main goal is to bring glaucoma patients an evidence-based, portable device that could be used at home to monitor their visual fields," Dr. Medeiros said. "They could do a lot more tests and do them more often than can be acquired nowadays with the standard visual field testing devices, leading to earlier diagnosis and detection of change. Right now, in the office, the tests are subjective and time-consuming and we can only do them a couple of times per year."

For use in clinical trials? If the pilot trial on disease progression produces positive results, nGoggle also might be a boon to drug companies testing new glaucoma drugs and gene-based treatments for retinal diseases, for example. "There is a clear need for better endpoints that can help expedite clinical trials, allowing quicker, more precise, and more accurate evaluation of the effectiveness of newly proposed therapies," Dr. Medeiros said.

"For some forms of treatment, the FDA is now requiring companies to show that those therapies actually lead to an improvement in an outcome that has real importance to the patient," including quality-of-life outcomes. "[The FDA] is not happy only looking at visual acuity anymore. They want the trials to show, for example, that the new treatment leads to the patient being able to walk better in some type of obstacle course," Dr. Medeiros said. Thus, a VR headset would enable researchers to put subjects through such an obstacle course without exposing them to the risk of falling, he said.

Assessing quality of life. Another goal of Dr. Medeiros's work is to use a variety of virtual reality techniques, including other VR systems and 3-D simulators, to develop a better understanding of how losing vision to an eye disease affects patients' day-to-day lives.

Analyzing risk—and fear—of falling. Dr. Medeiros' group used an Oculus Rift headset (Oculus VR) and a balance platform to demonstrate for the first time that, as glaucoma patients moved through a virtual tunnel, changes in their postural reactivity were indicative of their risk of falling in real life.[2] They also found that patients' postural reactivity to the visual stimulation presented in the VR environment was more closely related to their fear of falling than it was to SAP-measured visual field loss.[3]

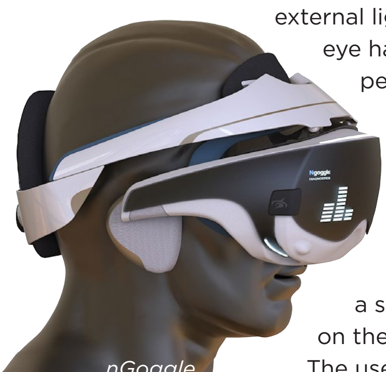
REAL-LIFE RISKS. *Dr. Medeiros (shown here with a patient) and his team have used VR to assess glaucoma patients' postural reactivity and fear of falling.*

Ken A. Huth Photography

Evaluating ability to navigate. The researchers

Basics of VR Headsets

Headsets for virtual reality fit like goggles, sealing out external light, and each eye has its own independent view of a display screen. The software controlling the images can reside on a nearby computer, on a smartphone, or on the headset itself. The user rotates the view within the virtual world through head movements and holds a pointer/clicker to move and take actions.



nGoggle

What differentiates one system from another? Some basics to consider:

Tethered. These higher-end headsets must be connected to a gaming system or a desktop computer. Sensors in the headset and an external camera tracker give "6 degrees of freedom" motion tracking (360-degree viewability) within the VR environment. The user holds a game controller, which is also tethered. Popular models include the Oculus Rift and HTC Vive, which sell for roughly $400 and $500, respectively.

Smartphone-based. For this low-cost VR option, a smartphone inserted into the headset frame provides both the viewing screen and the app software to run the VR simulations. One early version was Google Cardboard, which was literally made of cardboard and cost $20 or less; it even could be printed and built at home with online instructions. (Google has since released Daydream View, which sells for under $100.)

Fully mobile. The latest-generation versions require neither a tethered computer nor a smartphone to work. The viewing screen and controlling software are incorporated into the unit, and apps can be downloaded from the Internet. Entry-level models, such as the Pico Goblin and the Oculus Go, sell for under $300.

also used VR visualization screens and 3-D glasses to show that, compared with healthy subjects, people with visual field defects took longer to find their way through a virtual room in which previously visible wayfinding cues had been removed.[4]

"We want to go beyond basic assessment of visual function to more complex visual reality–based tasks that simulate real-world tasks, so that we can better gauge the impact of the disease in patients' lives. The hope is that this will help us determine management strategies to prevent disability, as well as develop new assistive technologies to help those in need," Dr. Medeiros said.

Augmenting VF Testing

Like Dr. Medeiros, vision scientist Benjamin T. Backus, PhD, is excited about what he sees as the potential for virtual reality to revolutionize and democratize VF testing.

"Visual field testing is to me probably the most exciting application of VR technology in terms of global impact. The Humphrey Visual Field is a fine gold standard, but you can't get a precise enough measurement in a single test to monitor progression and to know whether the person is getting significantly worse within a year," said Dr. Backus, at Vivid Vision, a VR company based in San Francisco.

For use at home. By buying an all-in-one VR headset and loading it with Vivid Vision's software, patients could do multiple VF tests at home and then upload the data to their ophthalmologist and schedule an office visit for conventional testing if the doctor deemed it necessary.

Alternatively, clinicians could invest in a few headsets to loan to patients. "You could send the device home for 2 weeks with every glaucoma patient you have, and they would do the test 10 times over 2 weeks, and the data would be collected over the internet for you to analyze," Dr. Backus said.

Pro: Doesn't require fixation. The Vivid Vision VR software is unique in that it does not require the patient to consciously maintain fixation, he said. "Currently for visual field testing, you have to stare at the same spot for 5 or 10 minutes, and it's difficult for people to do. That's not how the visual system is built," Dr. Backus said. "So [with our VR system], we intentionally have people move their eyes from one moment to the next.

"And we know where they're looking because in the virtual reality environment we built, they have to do a task at fixation, and people naturally

CAPTURING BUBBLES. In the "Bubbles" game, the player controls a virtual hand to pop the closest bubbles, one after the other. The depth interval between bubbles is controlled by an adaptive staircase procedure. In the default configuration, the 3-D bubble sizes are controlled so that all bubbles have the same image size, which isolates binocular disparity as a cue to depth.

Vivid Vision

put their fovea on that visual target in order to do the task. Then when you flash a stimulus relative to that location you know exactly where it is on the retina," he said.

Con: Limited data. The company intends for its VR-based visual field test to augment, not replace, SAP—and like SAP, the product will not require full FDA approval, Dr. Backus said. Although there is no published research on the testing algorithm, Dr. Backus has presented some of the research at scientific meetings. Last spring, he reported to the Imaging and Perimetry Society meeting in Japan that the VR technique successfully detected angioscotomata.

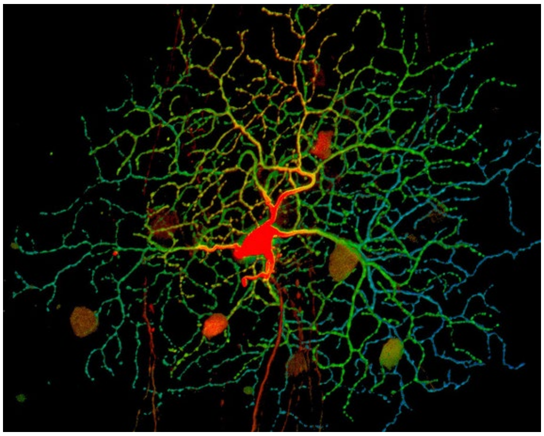
Other studies are in the works, including a small clinical trial to assess the practicality of the VR system and compare its results to SAP. That study is being conducted at the University of California, San Francisco.

Targeting Axon Regrowth

After demonstrating that visual stimulation could help coax the crushed axons of mouse retinal ganglion cells (RGCs) to regrow and reconnect to the brain,[5] neuroscientist Andrew D. Huberman, PhD, began trying to apply this newfound knowledge to humans—and VR headsets are his tool of choice.

Dr. Huberman, at Stanford University in Palo Alto, California, is in the early stages of testing whether specific forms of pattern visual stimulation, delivered daily with a VR headset, might protect and perhaps regrow RGCs in people with glaucoma. He hopes to report on outcomes at the spring 2019 ARVO meeting.

Since May, the first 2 trial subjects in his pilot



RECONNECTION. *One line of research is following the possibility that visual stimulation, delivered by VR, might help protect—and possibly even regrow—retinal ganglion cells (shown here) in people with glaucoma.*

study, ages 17 and 76, have spent 30 minutes a day, 5 days a week, inside a virtual world where customized patterns of white spots are flashed at or adjacent to areas that either are at risk for RGC damage or are already damaged, respectively. The locations are programmed into the wireless headset based on the results of visual field testing and structural measures of retinal health (e.g., optical coherence tomography scans), Dr. Huberman said.

"Some people just need to hold on to the vision they've got. Then, for other people, who have scotomas that are complete and extensive, you would want to deliver the stimulation [in the periscotoma area]." That's because some evidence suggests that, for visual improvement to take place at the level of the cortex, "stimulating central plasticity for the periscotomal region" needs to occur, Dr. Huberman said. In theory, he added, "the recovery in vision could occur through neural regeneration of ganglion cells, or through the filling in of scotomas at the level of the cortex deep in the brain, or both. We really don't know."

Advantages of VR. Dr. Huberman cited the following advantages of VR to his research:

Targeted. The VR headset "allows us to deliver visual stimulation to any location in the eye that we want," he said. Without it, "when you look at something and you move your eyes, the stimulation might not land in the correct place. With VR, we can adjust for that in real time."

Portable. "Patients come in, get their eyes examined and retinas and vision mapped, and then we equip them with wireless headsets that they take home. They can effectively bring the eye clinic home," he said.

Encourages attention. "Another advantage is the ability to vary the stimulation so the patient remains engaged for the 30 minutes per day that we think are required to get ganglion cells to survive better and regenerate," Dr. Huberman said.

Engagement and active attention also are key to the process of neural plasticity, which might factor into trial outcomes, he said. To keep the user's attention, the VR environment in the trial is a virtual art gallery with empty picture frames; after each pattern stimulation is completed successfully, the user is "rewarded" with a picture in the frame.

Improving Binocular Vision

Vivid Vision also is creating content for VR headsets that is aimed at addressing binocular visual function, including stereopsis, oculomotor control, and—perhaps—amblyopia.

The company already is marketing a VR therapy program for binocular vision in both children and adults, which patients can access either in the office of an ophthalmologist or optometrist or at home, after receiving a prescription for home use.

Stereopsis. Virtual reality is well-suited to address lack of binocularity because the content seen through each lens can be carefully controlled, Dr. Backus said. The image in the stronger eye can be displayed in lower contrast or blurred to try to force the 2 eyes to work binocularly (dichoptic stimuli). "Virtual reality lets you take control of the visual input. So you also have complete separation of the left and right eye images. They're generated independently in 2 different displays," he said.

"We did a study in which we had people playing off-the-shelf 3-D video games," said Dennis M. Levi, OD, PhD, who leads a VR testing laboratory at the University of California, Berkeley. Results of the study, conducted in 21 adults, showed improvment in stereo vision.[6]

Amblyopia. Results with amblyopia have been limited so far, Dr. Levi said. In randomized multicenter trials of patching versus a dichoptic game (using red-green glasses to present separate images to the 2 eyes), researchers found no advantage of the video game therapy over patching.[7,8] But those studies used an iPad "falling blocks" game, not an immersive VR game, and the children did not find the game itself compelling enough to play it regularly, Dr. Levi said. "I think we can do much better by using very tailored 3-D or virtual reality games."

Dr. Levi hypothesized that, when given a purposefully designed virtual reality game, children with amblyopia will play the game more often and perhaps will achieve more visual benefit from it than they did in the earlier trials. Vivid Vision is designing a VR game for him to use in this way in a clinical trial, which is set to begin this fall.

National Eye Institute

From Bench to Bedside

VR's availability makes it possible for very recent basic research to move into clinical testing quickly, and with minimal risk to participants, Dr. Huberman said. With regard to his own research on RGCs, he said, "Our study isn't only based on findings from 20 years ago. It is grounded in the latest findings from the neuroscience community, defining what types of stimuli the different kinds of ganglion cells like and how electrical activity of RGCs can influence their survival and regenerative capacity."

Dr. Huberman added, "We feel the patients deserve the best of what's been extracted from the animal studies, in terms of safe clinical trials. We should not be satisfied with continually promising patients that an advance is coming in 5 years, or in 10 years, unless we are also actively moving the research into clinical trials in the fastest way we safely can. I think we—researchers, clinicians, the NIH, and foundations—should all be pushing ourselves to try to shorten that timeline, as long as it can be done in a safe and effective way."

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8 Manh VM et al., on behalf of the Pediatric Eye Disease Investigator Group. *Am J Ophthalmol.* 2018;186:104-115.

LOOKING AHEAD. For an update on the use of VR in surgical simulation and resident training, watch for the January 2019 issue of *EyeNet*.

MEET THE EXPERTS

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Dennis M. Levi, OD, PhD Professor of optometry and vision science and immediate past dean of the School of Optometry at the University of California, Berkeley, and a researcher at the university's Helen Wills Neuroscience Institute. *Relevant financial disclosures: None.*

Felipe A. Medeiros, MD, PhD Professor of ophthalmology at Duke University, vice chair for technology and director of clinical research at the Duke Eye Center, and director of the Duke Visual Performance Laboratory, all in Durham, N.C. *Relevant financial disclosures: Carl Zeiss Meditec: C,S; Heidelberg Engineering: C,S; Ngoggle Diagnostics: P; Reichert: S; Topcon: S.*

See disclosure key, page 10. **For full disclosures,** see this article at aao.org/eyenet.

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ART + SCIENCE

MORE AT THE MEETING

Proficiency-Based VR Cataract Surgery for Residents (event code 413). ***When:*** *Monday, Oct. 29, 9-10 a.m.* ***Where:*** *Room S501.* ***Access:*** *Academy Plus course pass.*

Prototyping a 3-D Printed VR Visual Field Analyzer (Po400). ***When:*** *Monday, Oct. 29, 12:45-1:45 p.m.* ***Where:*** *South Hall A.* ***Access:*** *Free.*

Effect of Using a VR Device on Refractive Errors in Children (Po457). ***When:*** *Monday, Oct. 29, 12:45-1:45 p.m.* ***Where:*** *South Hall A.* ***Access:*** *Free.*

A 3-D Visualization Helmet for Vitreoretinal Surgery (Po549). ***When:*** *Monday, Oct. 29, 12:45-1:45 p.m.* ***Where:*** *South Hall A.* ***Access:*** *Free.*

VR Visual Fields and New Algorithms for Visual Field Computer Learning (LL33). ***When:*** *Monday, Oct. 29, 2:30-3:30 p.m.* ***Where:*** *Booth 126, South Hall A.* ***Access:*** *Free.*