MEETING NOTES FROM THE 45TH ANNUAL ARDS MEETING

The rate of change in technology for ophthalmic surgery is unprecedented. One of the benefits of the annual Aspen Retinal Detachment Society (ARDS) meeting is that it consistently shines a light on new techniques and breakthroughs. During the 2017 meeting, the presentations of both Allen C. Ho, MD, and Pravin U. Dugel, MD, served as a demonstration of how the field continues to move forward. Although the two speakers addressed notably different topics, with Dr. Ho discussing 3-D technology in the OR and Dr. Dugel taking on the role of anti-VEGF monotherapy for patients with diabetic macular edema, their presentations shared a common factor: progress.

As Dr. Ho noted, the current surgical microscopes based on 350-year-old Galilean technology were first introduced into the OR in 1950. Since then, the technology has improved, but it has not really deviated. So the introduction of a 3-D visual platform not only improved on the current technology in terms of reduced light toxicity, peripheral acuity, better ergonomics, and an improved ability to teach, but it also essentially reinvented the wheel, so to speak.

Dr. Dugel analyzed data from years of research to shed new light on an established issue. With the increasing presence of anti-VEGF monotherapy-resistant DME patients, leading to bimodal distribution, Dr. Dugel introduced the idea that a transition occurs in which inflammation becomes a greater factor in cell permeability. In this issue, Drs. Learned and Stringham provide overviews, respectively, of the presentations by Drs. Ho and Dugel.

—Timothy G. Murray, MD, MBA

3-D Viewing and the Future of Vitreoretinal Surgery

A new technology changes the OR.
By Daniel Learned, MD

"Visualization is an unmet need in retinal surgery"
—Allen C. Ho, MD

Allen C. Ho, MD, gave an overview of the evolution of the ophthalmic surgical microscope. He highlighted the fact that, whereas clinical viewing modalities have undergone significant improvements over the past several decades, surgical viewing systems have seen little change since early operating microscopes. Until recently, he said, vitreoretinal surgeons have been operating with the optical microscope, which is better suited for the anterior segment. Dr. Ho said that, in his opinion, a 3-D viewing platform such as the Ngenuity 3D Visualization System (Alcon) might provide better visualization for vitreoretinal surgeons and increased safety for patients.

HISTORY

Dr. Ho pointed out that operating microscopes are based on Galilean telescope technology that is more than 350 years old. The first OR microscope was introduced in 1950, and it was designed for the front of the eye. According to Dr. Ho, one of the requests of Robert Machemer, MD, to Zeiss in 1970 was for x-y movement, because current microscopes were not meeting the needs of posterior segment surgeons at the time. Since then, many advances have been made to surgical equipment, but the basis of the microscope has stayed the same.

A NEW FRONTIER

The Ngenuity system includes a 3-D, high-dynamic-range digital camera that attaches to the oculars of a standard operating microscope. The camera provides two feeds, one through each ocular and the other to a large ultrahigh-definition 4K OLED monitor. The lag time from when a movement is made to when it is displayed on the screen is almost undetectable, according to Dr. Ho.

Dr. Ho and Timothy G. Murray, MD, MBA, agreed that improvement in lag time has been the biggest change between an earlier version and the current system. Everyone in the OR can see the same image as the surgeon with the use of 3-D viewing glasses. The surgeon can sit in a more ergonomic position, rather than being tied to the oculars of the operating microscope.

BENEFITS OF 3-D SURGERY

Dr. Ho described many benefits of operating with a digitally enhanced surgical platform.

Reduction of light toxicity. The computer can enhance images without increasing light exposure in the eye. The viewing system can manipulate the lighting by making the aperture of the camera larger or smaller, giving the system the ability to take in more light through a larger opening. Enhancements can then be made digitally to the image on the screen.

Enhanced peripheral acuity. The system permits better viewing of the midperiphery, just outside the arcade, when the surgeon is working on the posterior pole. This is beneficial because improved visualization of these structures allows the surgeon to limit traction on them.

Enhanced ability to teach. Now, everyone in the room can see what the surgeon is doing. The surgery team can be better

WATCH IT NOW

3-D Surgery and the Digital OR

Allen C. Ho, MD, sits down with Timothy G. Murray, MD, MBA, and assesses how 3-D visualization for posterior segment surgery may offer retina surgeons opportunities to digitize their ORs. He notes the technology's benefits, including the ability to keep everyone on the same page while teaching, to import digital information, and to allow physicians to bring the same improvements seen in digital imaging in the office to the OR. The learning curve is not as steep as one might assume, he says, and he recommends starting off with vitreous hemorrhage cases.

WATCH IT NOW

Predicting Response to Anti-VEGF Monotherapy

Pravin U. Dugel, MD, joins Timothy G. Murray, MD, MBA, to discuss how best to identify patients with diabetic macular edema who may not respond to anti-VEGF monotherapy. Relying on a post-hoc analysis of the DRCR.net's Protocol I study, Dr. Dugel argues that data collected during the first three anti-VEGF treatments may reliably indicate how a patient will respond to anti-VEGF monotherapy in the coming years. He theorizes that, at a certain point, some patients with DME transition from a permeability-driven to an inflammatory-driven disease.

prepared, and residents and fellows can see the same things as the surgeon, making teaching easier. Dr. Ho shared a story about George A. Williams, MD, whose scrub tech said, "After 35 years, I finally get what you're doing inside the eye."

According to Dr. Ho, 85% of retina surgeons have neck and back pain. Sitting upright in a more ergonomic position may prevent surgeons from developing this pain over a lifetime of operating, he suggested.

Additionally, different filters allow better visualization of anatomic structures, including internal limiting membrane and epiretinal membrane, during macula surgery. Surgeons also notice an enhanced depth of field during macula surgery, possibly due to the viewing system changing its pupillary distance and creating better stereopsis.

POTENTIAL FOR THE FUTURE

Dr. Ho described aspects of surgery that could potentially be digitally manipulated, monitored, or studied with a digital system. Future surgical enhancements might include live feeds of surgery, sent across the world in real time, or computer-guided application of laser to selected areas of retina. It may also be possible to incorporate other technologies such as optical coherence tomography (OCT) or OCT angiography onto the same viewing screen.

Permeability or Inflammation?

Perspective from Pravin U. Dugel, MD, on the role of anti–VEGF-A therapy in diabetic retinopathy.

By Jack Stringham, MD

At the ARDS meeting in March, Pravin U. Dugel, MD, delivered a lecture on how to identify patients with diabetic macular edema (DME) who do not respond to anti–VEGF-A monotherapy and discussed alternative treatment strategies for this "resistant" DME population.

"It is clear from the RISE and RIDE data that anti–VEGF-A therapy works extremely well," said Dr. Dugel. "So what's the problem?"

He then described a study in which he had participated, which mined data from the Centers for Medicare and Medicaid Services database to look for patterns.[1] The investigators examined codes for a large volume of patients with DME to see how often anti–VEGF-A monotherapy was effective. According to Dr. Dugel, they found a bimodal distribution. That is, one group of patients responded remarkably well, but another group did not and required ongoing treatment.

Dr. Dugel then described a post-hoc analysis of the Diabetic Retinopathy Clinical Research Network's (DRCR.net's) Protocol I study in which he also participated. He cited this post-hoc analysis as further evidence of the bimodal distribution, showing that 50% of patients responded well, with at least 20% reduction in central retinal thickness after three injections, but the other 50% did not.[1] At first glance, it might appear that this response must be related to the number of injections, Dr. Dugel said, but, as shown in Protocol I, this was not the case. Those who responded worse received more injections.

BIMODAL DISTRIBUTION

Dr. Dugel posed the question of whether or not the disease process itself leads to this bimodal distribution. In the RISE and RIDE studies, when patients receiving sham treatment were switched to ranibizumab (Lucentis, Genentech) at month 24, these patients never "caught up" in terms of visual acuity gains to those in the treatment groups.[2] By contrast, he pointed out that patients in the sham group in the RESTORE trial did catch up to treated patients; one difference was that they were switched to ranibizumab after 1 year instead of 2.[3]

Is it the timing of treatment, then? Is there an inflection point at which some factor other than VEGF-A comes into play? Dr. Dugel pointed out that previous studies have shown a relationship between the expression of inflammatory cytokines and the severity of retinopathy and amount leakage seen on fluorescein angiography.[4,5]

Dr. Dugel suggested that, among patients who are nonresponders to anti–VEGF-A treatment, there may be an underlying multifocal switch that occurs, at which point the disease changes from being driven by VEGF-A permeability to being driven by inflammation. The difficulty, he said, is that there is no way to tell the difference between patients whose disease is VEGF-A–driven and those with inflammatory disease because they look the same phenotypically.

A TRANSITION IN DME

Dr. Dugel suggested that perhaps this is why different patients respond so differently to anti–VEGF-A monotherapy. He said he believes that the data support the idea that a transition occurs in DME, and that this is not a hardwired transition point but a continuum that may be different in each patient. Additionally, he said he believes that clinical trial data suggest that this transition occurs at around 2 years after DME is diagnosed.

How does one recognize anti–VEGF-A nonresponders? To address this question, Dr. Dugel returned to the post-hoc analysis of 340 patients in Protocol I.[1] For this analysis, the investigators classified patients into three groups based on how much visual improvement they experienced after three injections: 5 letters or less, between 5 and 9 letters, and 10 letters or more.

RESULTS

After three injections, 40% of patients had less than 5 letters improvement, a mean of 0.3 letters lost. The investigators then looked at 1-year outcomes for patients in all three groups. They found that patients who responded well after three injections with 10 letters or more improvement gained on average 16.5 letters at 1 year. Patients who gained less than 5 letters after three injections, despite receiving injections every 4 weeks for a year, gained only a mean 2.8 letters of vision. The intermediate responders, with between 5 and 9 letters gained after three injections, had a mean visual improvement of 6.9 letters at 12 weeks, and after a year of injections every 4 weeks they gained only 8.2 letters.

This post-hoc analysis also looked at OCT results in the same dataset.[1,6] They determined which patients were responsive to anti–VEGF-A therapy based on reduction in central retinal thickness. The 335 eyes that qualified for this study were classified as follows: limited response, if the response was a less than 20% reduction in central retinal thickness; and strong response, if there was a greater than 20% reduction in central retinal thickness after three injections. The researchers found that 35% of patients had a limited early anatomic response after three injections and 65% had a strong early response. Eyes with a limited early anatomic response were less likely to obtain a 20% reduction in central retinal thickness over the 3-year duration of the study.

SUMMARY

Dr. Dugel said he believes that a transition may occur in patients with DME who are nonresponders to anti–VEGF-A therapy, in which inflammation begins to play a greater role in vascular permeability. Further, it may be possible to identify these patients based on their visual acuity and anatomic response after three consecutive injections of anti–VEGF-A therapy. ■

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