

# THE FUTURE OF RETINA: EMERGING TECHNOLOGIES AND UNMET NEEDS

Meant to be a forum for new ideas and surgical innovations, the 2016 Vail Vitrectomy meeting did not disappoint. Experts from around the globe shared their expertise and, more so, their thoughts on the future of retina and where it still needs to improve.

*In the spirit of the Vail meeting, we sat down with Drs. Dean Elliott, Allen Ho, and Carl Regillo to gather their insights regarding the future of our field.*

—M. Ali Khan, MD

## 1. What emerging surgical technologies (eg, imaging, instrumentation, etc.) do you believe will make a major impact in the coming years?

**Allen C. Ho, MD:** I believe our next significant improvements in vitreoretinal surgery will be based on real-time intraoperative digital imaging. The optical operating microscope is 350 years old and has been refined for anterior segment surgery but does not address many imaging and visualization needs in the posterior segment. From 3-D heads-up surgical viewing, free from looking through microscope oculars, to a truly digital microscope and endoscope, we will be improving our ability to visualize surgical tissue. Ultimately we can incorporate a variety of technologies—simultaneous picture-in-picture “satellite view” and “street view” perspectives, collision avoidance, navigated laser therapy, robotic microsurgery, etc.

**Carl D. Regillo, MD:** I agree with Allen—the heads-up 3-D digital microscopic viewing system appears to be promising for both general ophthalmic and vitreoretinal surgery. I think it is possible that there will be relatively widespread adoption of this type of operative technology over the next 5 to 10 years. At the very least, it is excellent for use in teaching environments because it allows everyone in the room to have the same view as the surgeon.

**Dean Elliott, MD:** Intraoperative optical coherence tomography will continue to improve, and its use will expand. Other technologies, such as lighted vitrectomy probes (prototypes available; not commercially available), are also likely to gain widespread use, particularly for surgeons who operate without a skilled assistant.

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– Carl D. Regillo, MD

## 2. What emerging medical treatment strategies (eg, gene therapy, long-term drug delivery) do you believe will make a major impact in the coming years?

**Dr. Regillo:** Long-acting drug-delivery platforms are being tested, and, although it has been a long time coming, I think we will see a useful platform in the not-too-distant future. This should help ease the burden of intravitreal injection-based treatment paradigms and also minimize the potential for undertreatment when compliance with frequent follow-up is not strictly adhered to.

Also, gene- and cell-based therapies have the potential to be the biggest developments in retinal therapeutics in the coming years. There are many untreatable retinal disorders that could potentially benefit from gene therapy, namely the various hereditary retinal degenerations. Cell therapies may help patients with various advanced macular degenerative processes such as geographic atrophy (GA) in age-related macular degeneration (AMD) and Stargardt disease.

**Dr. Ho:** There are many variables (surgical technique, cell viability and transfection efficiency, dosing, etc.) to refine for gene- and cell-based therapies. Combining genetically modified human retinal pigment epithelial cells to make a therapeutic protein in a surgical implant (as with the Neurotech encapsulated cell technology) may eliminate some of these variables by combining them in a surgically implanted drug delivery platform. Simpler is better, and, despite some current challenges in their wet AMD program, I believe the Neurotech platform still has significant potential.

**Dr. Elliott:** I agree with Carl and Allen. Cell-based therapy, gene therapy, and long-term drug delivery options are of special interest.

### 3. Are there treatment modalities or strategies now in use that you believe may be phased out?

**Dr. Elliott:** Monthly anti-VEGF injections will be phased out once we have the option of sustained drug delivery.

**Dr. Ho:** I agree with Dean—monthly intravitreal injections will be phased out, but probably not in the next 5 years. We will likely do less destructive thermal laser therapy in the macula, particularly as we learn more

regarding nondestructive micropulse laser therapy for macular edema and macular exudation.

**Dr. Regillo:** I believe that there will be less and less pan-retinal photocoagulation (PRP) performed in the years to come, much like how focal laser use for macular edema and choroidal neovascularization has declined in the recent past. I think drug-based therapies early in the course of diabetic retinopathy (DR) to curb the development of proliferative diabetic retinopathy (PDR) will reduce the need for PRP.

### 4. Are there any retina conditions for which you believe current treatment strategies will significantly change?

**Dr. Regillo:** In addition to using drug therapies (anti-VEGF, etc.) to curb the progression of DR to the proliferative stage, early vitrectomy may also allow the prevention of PDR in eyes at imminent risk for conversion from nonproliferative DR to PDR. With the increased safety profile of vitrectomy, it now makes sense to put that approach to the test.

Also, combination treatment protocols in DR and AMD will be here in the near future and will represent a significant change in how we approach these conditions. It is possible

that combining drugs that work by very different mechanisms of action may not only enhance visual outcomes but also afford greater treatment durability. However, such combination therapies come with potentially complicated treatment algorithms, especially when there is an attempt to individualize therapy.

### 5. Is there a particular area of unmet need that you believe is especially deserving of further study?

**Dr. Elliott:** Proliferative vitreoretinopathy (PVR) stands out as an unmet need.

**Dr. Ho:** Dry AMD, before it gets to the advanced forms of disease. We need to look into neuroprotection for AMD and across many different disease states including retinal detachment. We already discussed surgical visualization; this remains an unmet surgical need.

**Dr. Regillo:** I agree with Dean and Allen: Common vision-threatening problems that are in desperate need of better interventions include dry AMD and PVR. To this day, we do not have effective ways to prevent or reverse development of GA, conversion of dry to wet AMD, or occurrence of PVR. The unmet need remains high for these common conditions.

### 6. Are there any perceived clinical controversies that you believe will receive special attention in the coming years?

**Dr. Ho:** Cost pressures and the freedom to choose treatments and drugs for patients will be major themes in our field in the years ahead. Thankfully, patients value vision highly—we need to pay attention to demonstrate the value of our services and treatments.

**Dr. Regillo:** I agree with Allen, particularly as we are on the verge of combination therapies. Costs will become an even greater issue in terms of how we manage our most common conditions that require frequent, expensive therapeutics as we move from monotherapies to combination therapies. The development of anti-VEGF biosimilars is just around the corner, and this will likely have a significant effect on the agents we use in practice. It will also be interesting to see how biosimilars influence the use of bevacizumab (Avastin, Genentech) in the field.

### 7. Are there any clinical trials that you believe will be particularly influential?

**Dr. Ho:** Clinical trials combining anti-VEGF and anti-PDGF agents, and of non-VEGF-mediated mechanisms of action in diabetic macular edema and wet AMD

will all have the potential to change treatment paradigms. Certainly, the current atrophic AMD trials will be important, but even if therapies are approved there will be challenges because patients will not be regaining vision; rather, these therapies will simply be slowing vision loss.

**Dr. Regillo:** For wet AMD, the combination protocols with anti-VEGF agents and new drugs that block PDGF and ANG2 are of special interest. We are hoping for better visual outcomes compared with anti-VEGF treatments alone. For dry AMD, complement inhibition, with agents such as anti-factor D, have the potential to slow the growth of GA. It is possible that visual cycle modulation is not far behind for dry AMD. I am also involved in phase 2 stem cell-based protocols that I find exciting, with the potential to make a significant favorable impact on advanced macular disease.

**Dr. Elliott:** I agree with Carl and Allen: Studies regarding anti-PDGF agents for wet AMD, complement inhibition for dry AMD, gene therapy for a variety of monogenic diseases, and stem cell therapy for dry AMD and retinal degenerations are of special interest. ■

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