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From Trials to Treatment: Real World Applications in Medical and Surgical Retina

Part 1 of 3

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From Trials to Treatment: Real World Applications in Medical and Surgical Retina

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CONTENT SOURCE

This continuing medical education (CME) activity captures content from a roundtable discussion held in May 2017.

ACTIVITY DESCRIPTION

It is clear that retina specialists will continue to see an increasing number of patients in the future, as both society

ages and as more people develop sight-threatening retina diseases. The need to be fully educated on the various treatment options remains crucial to delivering the best patient care. This need should be expanded beyond exposure to multiple clinical trial data and into real-world outcomes. In order for retina physicians to continue to deliver superior patient care, they will need to increase their awareness about the more sophisticated imaging devices being used in clinics to confirm retina disease diagnoses, along with newer surgical devices. Retina physicians will also need to increase their interest in developing pharmacologic treatments with longer duration of action or novel mechanisms of action.

With all the current and ongoing interest in treatments for retina disorders, it is imperative retina specialists remain educated on the latest developments.

TARGET AUDIENCE

This certified CME activity is designed for retina specialists and general ophthalmologists involved in the management of patients with retinal disorders.

LEARNING OBJECTIVES

Upon completion of this activity, the participant should be able to:

- Recognize the importance of early diagnosis and treatment of age-related macular degeneration and diabetic macular edema.
- Assess the response of anti-vascular endothelial growth factor intravitreal injections and define “suboptimal responders.”
- Understand the most recent monotherapy and combination therapy clinical study evidence using available therapies for AMD, DME, and RVO.
- Discuss the outcomes of pivotal studies in AMD, DME, and RVO and how study results may differ from real-world dosing methods.
- Develop individualized treatment plans for patients with retina disorders that use a combination of imaging, treat and extend, or treat and observe.
- Discuss the ocular and systemic effects of anti-VEGF therapies and how to educate patients on appropriate expectations.

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From Trials to Treatment: Real World Applications in Medical and Surgical Retina

PART 1 OF 3

Vitreoretinal surgical techniques continue to evolve. Small-gauge surgery, higher speed cutters, and novel cutter designs make vitreoretinal surgery safer and more effective than ever before, bringing benefits to both patients and surgeons. The following roundtable and accompanying videos demonstrate cutting-edge approaches to vitreoretinal surgery, including improvements in visualization, intraoperative optical coherence tomography, and novel surgical approaches for the delivery of cell-based therapies. Through a unique set of challenging cases, Evolve Medical Education LLC tasked each expert to work through the best possible management options in a detailed discussion. — *Jonathan L. Prenner, MD, Moderator*

CASE 1: ADVANCES IN VISUALIZATION

Jonathan L. Prenner, MD: The Ngenuity 3D Visualization System (Alcon) utilizes a heads-up digital video design that allows for improved ergonomics, enhanced depth of field, and reduction in light levels needed for surgery.¹⁻³ What has your experience been with Ngenuity?

Eric Nudleman, MD, PhD: The Ngenuity system allows retinal surgeons to operate looking at a high-definition 3D screen, rather than bending their necks to look through the eyepiece of a microscope, which really does help to minimize physician discomfort.² The system is also designed to optimize collaboration and teaching in the operating room (OR).

We have had the Ngenuity system for a couple months now, and I am comfortable using it for a variety of cases. The visualization of membranes is fantastic.

I think this system is a real advantage for training centers, because it allows the attending surgeon to see exactly what the trainee is doing. If you have a scope that has just one assistant set of oculars, you can still have other people in the room, such as medical students or residents.

Dr. Prenner: Dr. Nudleman, please describe your retinal detachment case and how the Ngenuity system was used.

Dr. Nudleman: This is a case of an inferior retinal detachment with a small atrophic hole in the periphery (Figure 1). The patient was still recovering from a Descemet membrane endothelial

keratoplasty 2 months earlier, which made the view foggy in the office. But as you can see here, there were issues with the view in the OR. This case was repaired with a scleral buckle and vitrectomy, so this video begins after the buckle was already placed. Some physicians have said that the view in the peripheral retina with the Ngenuity is not good as it is with the microscope and a noncontact viewing assistant, but I have not had that experience. As you can see, there was no issue with depressing and shaving in the periphery.

Dr. Prenner: Dr. Ho, you have had significant experience with this system. How much of a learning curve should new users plan for? What are your thoughts on your ability to view the peripheral retina? Is there more of a learning curve when viewing the anterior segment compared to the peripheral retina?

Allen C. Ho, MD: I have heard that from some of the physicians at Wills Eye. It may not be as intuitive or as natural as the macular work. I do think the macular view is superior, however, with the sense of depth and the resolution detail on the Ngenuity, it is probably



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Figure 1.

Case 1: ADVANCES IN VISUALIZATION

A case of an inferior retinal detachment with a small atrophic hole in the periphery.



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better than optical. When digitally assisted imaging debuted in ophthalmology back in 2008, the technology was not ready. But technology evolved, and now it is ready for surgeons to try.

Dr. Prenner: What do you consider to be the preferred surgical management in this case? Should one consider posterior retinotomy, drainage of subretinal fluid through the retinal break, perfluoro-N-octane (PFO),⁴⁻⁷ or something else?

Charles Wykoff, MD, PhD: I think it is reasonable to do any of the above. For inferior retinal detachments with far peripheral breaks, I like to leave the eye completely dry, so I often make a draining retinotomy. I typically make a nasal retinotomy as far in the periphery as I can if I cannot easily drain subretinal fluid through the break. I drain through breaks that are larger or more posterior and typically use PFO in more complex cases, as well as fovea-splitting or fovea-threatening cases to prevent subretinal fluid from migrating through the fovea.

Dean Elliott, MD: I usually drain through the break. I make the break larger and drain everything by tilting the eye. I used to use PFO for most retinal detachment cases until one of my colleagues, Lucy Young, MD, PhD, showed me how to drain every detachment through the break. That became my preferred approach once I became more familiar with that technique.

Dr. Nudleman: With this patient, I opted to perform a retinotomy, and I made it in the same hemisphere as the primary tear with the intention of having the patient position on the opposite side. I try to make the retinotomy in a location away from any vessels and where it is comfortable to reach during the air exchange.

Dr. Wykoff: If a small hole is made, some patients do not need laser around the retinotomy site.⁸ If I see expansion of the hole when I am draining the fluid, then I will laser it. But, if it is small, I often will not. Ryan Isom, MD, showed me this technique, and in some cases, you cannot find the hole postoperatively.

Dr. Prenner: How do you feel at the end of the day of operating with the Ngenuity? Is your fatigue level lower than when you use a standard microscope?

Dr. Ho: It is a nice feeling not to be tethered to oculars. I will say, however, that the ergonomic optimization is not as balanced as it could be; because of the way the system is hooked up to the curve microscope, you have to turn your head a little bit off-angle to use it.

It is still a bit cumbersome because Ngenuity attaches to your regular microscope hardware that is either floor-based or hanging from the ceiling. You have to think of this as digital videography. Although phototoxicity is not a significant safety issue for vitreoretinal surgeons, the system allows you to reduce endoillumination.³ This could be beneficial, especially because a lot of our macular work is done with stains.

Dr. Wykoff: Is there any delay in the video output?

Dr. Ho: As the system was being designed, there were some glitches with that, but now it is almost imperceptible. As you pass the suture through the conjunctiva, I have noticed some delay. On the outside of the eye, there is a bit of a delay because the distances per unit time are greater.

Dr. Elliott: Some anterior segment surgeons do not like it because of that delay, but it is not as much of an issue for retina specialists.

Dr. Nudleman: Cataract surgeons may have a difference experience with the delay because they are performing faster and bigger (in terms of distance) maneuvers. Most maneuvers performed by retinal surgeons are slow in comparison.

There is another minor issue: there is no ideal spot for the 55" OLED high definition monitor. If the monitor is perfectly positioned for the surgeon, the assistant sometimes has to turn their head a lot; it is tricky to cut sutures with your head turned 90 degrees away and it takes some practice. I can imagine a benefit to having multiple monitors in the room.

That said, overall, the Ngenuity is a huge advantage to involve everyone in the room—anesthesiologist, trainees, scrub tech—and it allows each of them to see what you see.

Dr. Elliott: I agree that is a huge benefit. My staff could not believe how amazing the system was, and they were really appreciative that they were able to see things that they could not see before.

CASE 2: SMALL-GAUGE SURGERY

Dr. Prenner: In the next case (Figure 2), the patient presented with a visually significant vitreomacular traction and epiretinal membrane warranting surgical intervention. I am using a 27-gauge valved trochar system with a cut rate of 7,500 cuts per minute (cpm). When



Watch it Now

Figure 2.

CASE 2: SMALL-GAUGE SURGERY

Vitreomacular traction and epiretinal membrane repair with a 27-gauge valved trochar system with a cut rate of 7,500 cuts per minute.



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using 27-gauge, I do not bevel my incisions. Rather, I enter perpendicular to the sclera as the wounds are unlikely to leak. Importantly, the flexibility of 27-gauge instrumentation is magnified when you are fighting the orientation of a beveled trocar and minimized when you are going through the trocar in a parallel fashion. Because of this, I prefer direct entry rather than a beveled approach.

The high cut rate and port based, flow limiting nature of the 27-gauge cutter allows for a reduced sphere of influence, and you see very little motion during vitrectomy. A concern with smaller gauge surgery is whether you will have enough grip strength with smaller platform forceps during peeling and enough suction with the cutter to initiate a posterior vitreous detachment. In this patient with tight vitreomacular traction, I used steroid for enhanced visualization. I was able to use the cutter to develop a Weiss ring with little effort. I used end-grasping forceps to peel the pucker and the internal limiting membrane. The 27-gauge worked efficiently in this case.⁹⁻¹¹

Dr. Wykoff: Do you think the volume of vitreous you are moving is adequate and comparable to the 25-gauge?

Dr. Prenner: There was not a huge difference in the pace of vitrectomy or in my ability to manage the peeling efficiently. I think that using the 27-gauge in the anterior segment is a little bit cumbersome because of the flexibility of the instruments. For vitrectomy to treat a retinal detachment, I still use the 25-gauge platform. For puckers and holes, I use either a 27- or 25-gauge. I also am gaining experience and like the concept of mixed gauge vitrectomy, where one uses a 27-gauge cutter in combination with 25-gauge platform for difficult diabetic tractional retinal detachment cases. A 25/27-gauge approach in a complicated diabetic eye may not be the most cost-effective method, but it is not completely unreasonable when you balance the impact of the combined platform approach in terms of efficiency and outcomes.

Dr. Ho: I am a 23-gauge user for vitrectomy and the peripheral retina. I am more efficient with a 23-gauge cutter, I do not have wound problems, and there is not a bending issue. I do not care for 27-gauge because I want to get rid of the peripheral vitreous. I do not shave it closely, but I want to trim it. I do like 27-gauge for a diabetic tractional detachment because it allows me to get into the tissue planes.¹²

Dr. Elliott: For straightforward macular cases, such as puckers and holes, I may use 25-gauge. I still use, however, a 23-gauge for everything else.

Dr. Wykoff: I use 25-gauge for everything. I do notice a difference in efficiency from a 23- and 25- to 27-gauge. The 27-gauge hardware is more flexible than I like. It is also slower and less efficient in my hands at removing vitreous.

Dr. Prenner: Are cut rates a critical issue for you? Can you tell the difference between 5,000 cpm, 7,500 cpm, and 10,000 cpm? Is faster better?

Dr. Elliott: I can tell the difference, but the changes are slight.

Dr. Ho: The higher you go, the less obvious the advantages become. I like being able to go faster, but it may or may not make a difference. It depends on the case. Overall, I think the cut-rate focus has been beneficial over time. But I still prefer illuminated vitrectomy saws so I can do my own depression and shaving.

Dr. Wykoff: I think cut rate matters, certainly to a point. For me, the core issues are cut rate and the associated fluidics. I am using a cut rate of about 16,000 cpm. I noticed improved performance going from 5,000 cpm to 7,500 cpm. I am now used to a higher cut rate, and I notice a change when it is reduced to 7,500 cpm.

Dr. Prenner: What are your thoughts about angled cutters? If you are using them, do they give you a mechanical advantage for diabetic tractional retinal detachment cases?

Dr. Ho: The geometry makes sense. If the heel of your cutter is beveled, and you are getting very close to the retina, that can make a difference. What made the most difference was moving the aperture of the cutter toward the end of the probe itself. That was a manufacturing improvement that made a real difference.

Dr. Prenner: Does that allow you to use the cutter as a multipurpose tool?

Dr. Nudleman: I manage many exudative retinal detachments with the cutter using it as a cutter, but you can use it as a multifunctional instrument.¹³ I have not noticed a big difference between the beveled cutter and the standard 25-gauge cutter or between a 25-gauge and a 27-gauge cutter.

Dr. Elliott: Moving the port closer to the tip has revolutionized surgery for diabetic tractional retinal detachments.¹³ When the port was further from the tip, you had to use scissors, tissue manipulators, and all kinds of instruments for the surgery. It is very rare now that we have to use those instruments, because we can do almost anything with a cutter, with the exception of the extremely complicated cases.

Dr. Prenner: For the really complicated flat plaque diabetics, what is your go-to surgical approach? Is it still bimanual surgery with scissors?

Dr. Elliott: My approach to bimanual surgery is with scissors.

Dr. Ho: I use chandelier with forceps in one hand and the curved scissors in the other hand.

Dr. Wykoff: I like to use the 25-gauge vertical scissors with bimanual dissection for complex tractional retinal detachments. I typically use vertical scissor in one hand and either a lighted pick, forceps or simply the light pipe in the other. While I like using the cutter itself for tissue dissection in these cases, when needed, vertical scissors offer the thinnest possible dissector, often facilitating access between tightly adherent tissue planes.

Dr. Elliott: I agree that vertical scissors can accomplish quite a bit. I use the vertical scissors for most cases with flat plaques, but sometimes I will use the curved scissors. The technique Dr. Wykoff describes has its advantages in a tight plaque, where there is no space.

Dr. Prenner: What are your other secrets for performing small-gauge surgery?

Dr. Elliott: If you suture your sclerotomies, regardless of the size, you are less likely to have postoperative hypotony, and therefore less likely to have a postoperative hemorrhage.

Dr. Wykoff: I almost always suture my sclerotomies at the end of a tractional retinal detachment repair to minimize the chance of postoperative bleeding. I also suture sclerotomies when using silicone oil. Otherwise, I rarely suture sclerotomies.

Dr. Prenner: Prior to going to air, I always ensure that my infusion cannula is correctly oriented for fear of having suprachoroidal air infusion, which can be fatal. That is one of my automatic time outs now. Before we go to air, we make sure to check the infusion position. Also, before I remove the corneal epithelium, I double check that the patient has not had LASIK.

Dr. Elliott: We do up to three time outs during surgery: one before the case begins, one for the fluid air exchange, and one looking for prior LASIK if we have to scrape a cornea.

CASE 3: SUPRACHORODIAL DRUG DELIVERY

Dr. Prenner: We are continuing to push the boundaries of vitreo-retinal surgery, and there is significant potential of cell-based drug delivery and therapeutic delivery to the suprachoroidal space.¹⁴⁻¹⁶ Dr. Ho, how have you been refining suprachoroidal surgery over the last few years?

Dr. Ho: We have developed an ab externo technique using a flexible catheter that is about 1.5 mm in diameter and 0.5 mm in height. The Janssen Subretinal Access Kit is proprietary and being used only in an AMD trial at this point. The idea is that you can deliver a therapeutic into the subretinal space without creating a retinotomy. Using a wide-angle viewing system, we advanced a needle into the subretinal space and injected saline to detach the macula and create space. We then switched the hardware setup to create an air bubble and deliver the cells.

Once the cannula is in the right place, the injection device allows you to advance the needle under direct visualization from the OR microscope. You can push the needle in too far and create a retinal break if you are not careful. We have done 22 cases so far, and we have had no retinal tears, retinotomies, bridging vessels, or suprachoroidal hemorrhages. We have not performed the procedure on children, just patients in their 80s with geographic atrophy.

Dr. Nudleman: Do you always go for a temporal approach?

Dr. Ho: Yes, superotemporally. The catheter passes in parallel along the sclera very easily. It does not flex. It reduces the degrees of freedom of the internal catheter, so you do not get the catheter embedding into the retina. We did have a situation where the needle was not advanced far enough, and we were still in the suprachoroidal space. That is part of the learning curve.

Dr. Wykoff: And when that happened, you got the air in the right place, but the cells were not delivered to the correct location?

Dr. Ho: That is correct. We had air in the subretinal space, but there was a characteristic fluttering around the catheter that we think suggests suprachoroidal delivery instead of a subretinal delivery.

CASE 4: INTRAOPERATIVE OCT

Dr. Prenner: The promise of intraoperative optical coherence tomography (OCT) is now reaching the community surgeon.¹⁷ Many surgeons are using OCT in their OR with the evolving understanding of the benefit that it can provide. What are your thoughts?

Dr. Nudleman: My case describes the first time I used the ZEISS Cirrus HD-OCT (Carl Zeiss Meditec) system. This is a macular pucker case (Figure 3), and I used indocyanine green for staining, which allows you to see the edge of epiretinal membrane (ERM). In this case, I positioned the OCT over border of the staining, and you can see the edge of the epiretinal membrane. I used that as a guide for where to start the peel. Here you can see me grabbing that edge, and you can see it lift up on the OCT. I would have been able to do that without an OCT, but it is a nice confirmation of the pathology.

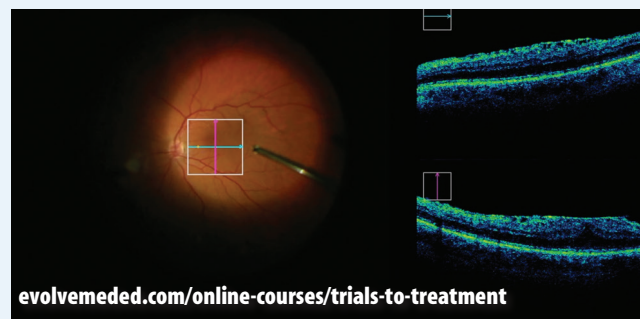
Dr. Prenner: When do you all use intraoperative OCT? Do you find it helpful in specific scenarios or in every scenario?

Dr. Wykoff: When it is eventually integrated seamlessly, it will be

Watch it Now

Figure 3. CASE 4: INTRAOPERATIVE OCT

A macular pucker repair using indocyanine green for staining, which allows visualization of the edge of epiretinal membrane.



fantastic to use routinely. Right now, I use it in specific cases, such as a chronic, large macular hole where I am trying to create a flap or in eyes with Staphyloma with irregular macular pigment making visualization challenging.

Dr. Eliott: We do not have the device, but we have evaluated it. The resolution is not where I would like it to be, so we are waiting for the next generation.

Dr. Nudleman: In a case like ERM peeling, OCT raises the possibility of performing these procedures without any staining and still confirms you have removed all of the pathology. It saves a step and could potentially be safer.

Dr. Ho: We have this device, and we use it on a ZEISS microscope. I agree that the resolution is not where I would like it to be, nor is it as integrated as I would like. But for those surgeons who are going to digitally assisted surgery, to have this as part of your surgical cockpit, to see your intraoperative OCT, is a huge advantage.

Consider what will happen when we can get a cube of information for a tractional retinal detachment. It might really improve the efficiency if you can look and see where the planes are in a diabetic tractional retinal detachment to help position the 27-gauge probe more accurately. I agree this is the way we need to go. It could be very useful once the resolution improves.

CASE 5: SILICONE OIL MANAGEMENT

Dr. Prenner: I have always had trouble reliably using silicone oil in small-gauge surgery. It can be a challenge to achieve the proper fill without overfilling. Does anyone have a technique for managing this?

Dr. Eliott: I have a technique for aphakic and pseudophakic eyes (Figure 4). I do not recommend it for phakic eyes because there is a needle in the eye that acts as a vent, and I do not want the needle to strike the crystalline lens. Before we begin, let us review the instruments. The nasal sclerotomy is open, and the cannula is removed. The superotemporal sclerotomy has the oil injector with the cannula still in place.

The inferotemporal sclerotomy is where the infusion line is. We put in the oil until about halfway or two-thirds of the way. We then remove the infusion line and its cannula and insert some more oil. As we get close to the pupil plane, we put a 25-gauge short needle on a tuberculin syringe (with the plunger removed) in through the inferotemporal sclerotomy. Keep in mind that in some aphakic patients, the pupil plane is moved a little bit forward because there is air pushing the iris forward. You want to put the tip of the 25-gauge needle, which acts as a vent, where the pupil plane should be. The accompanying two videos illustrate this technique. In a pseudophakic patient, you just place the tip of the needle right up to the back of the lens implant, and you will obtain a good oil fill.

Dr. Prenner: How do you tell that you are two-thirds of the way full — through the light reflex?

Dr. Eliott: Yes. When we are handed the oil syringe, we always

check to confirm the amount of oil in the syringe. And as we are infusing, we pay attention to what is roughly two-thirds the volume of a normal eye. You can tell as the oil surface rises, and when in doubt you just put the needle in and tilt the needle tip to where the reflex changes when you touch the oil surface. Once the oil level is sufficient and where you need it to be, pull both instruments out quickly.

As long as you infuse the oil slowly and remove the needle and the oil injector quickly when the oil reaches the pupil plane, you will never have an overfill or an under-fill. It is a great technique. I do this in both pseudophakic and aphakic patients.

Dr. Wykoff: How do you position your aphakic patients to keep silicone oil out of the anterior segment?

Dr. Eliott: We try to get these patients face down as quickly as possible, but that does not always occur. This technique is fairly straightforward, and I have found it unlikely to cause a problem. With a phakic eye, it is a little different because you should not use the needle. In some cases, we will insert the needle just to get a sense of how close the oil is to the crystalline lens. Once the oil gets close, we remove the needle. But it is important to hold the other sclerotomy open with 0.12-mm forceps so the air vents as we are infusing the oil to avoid an overfill. An overfill in a phakic eye is a disaster.

Dr. Nudleman: I do the same technique. I use a soft tip cannula that is not connected to anything as a vent, and at the same time, I can touch the top of the oil interface as it is coming up. That helps me to know exactly where it is. I always tilt the eye at the end to see the air-oil interface, and I leave a small bubble of air. That confirms there is some space and there will not be an overfill.

Dr. Ho: I do not have as much of a problem establishing where the oil level is. I will turn down the infusion pressure in the eye from



Watch it Now

Figure 4.

CASE 5: SILICONE OIL MANAGEMENT

These two videos feature a technique for using silicone oil in small-gauge surgery in aphakic and pseudophakic eyes.



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25 mm Hg to 10 mm Hg under air. I will look to see where the oil syringe is to measure where I think the fill will be. It usually fills up to about 7 mL from the oil. Then, I will start flowing oil in, and I will use the vent that is given with the valved cannula system. As I get close, I will make sure that I tilt the vent; let it port to the high point in the eye. The air will float up, and I will see the oil-air interface come across because as the eye is tilted, the air will go higher toward the vent. Then we are kind of tapping on the exterior of the globe to make sure the pressure is not too high.

Dr. Prenner: For most of these cases, under-filling is not a huge problem. Overfilling can cause problems.

Dr. Eliott: That is a really important statement. A slight under-fill in an eye with a retinectomy is irrelevant because there is no retina to tamponade inferiorly. But the last thing you want is an overfill; that is a disaster in any case.

Dr. Nudleman: Do you leave a little bit of an air bubble, or do you chase all of the air out?

Dr. Eliott: I like to get all the air out. At the end of the surgery, I take a cotton swab, push on the eye a little, and open the sclerotomy with a 0.12 forceps, and squeeze out a small amount of oil. If there is a small choroidal effusion postoperatively, which is rare, that is going to push your oil forward. So, I always like a little under-fill.

Dr. Prenner: I also recommend checking the pressure digitally at the end of these cases. Particularly in an aphakic patient with an air-filled eye, the pressure you measure with a device may not be accurate.

Dr. Eliott: Right. I like to leave the eye slightly soft because I do not want an overfill.

CASE 6: MANAGING INTRAOPERATIVE BLEEDING

Dr. Prenner: For the next case, we will discuss how to manage intraoperative bleeding.

Dr. Wykoff: This was a complex, diabetic tractional retinal detachment (Figure 5). There was a lot of firmly adherent fibrovascular tissue causing distortion of the macula over and adjacent to the optic nerve head. Removing that tissue caused profuse bleeding from a blood vessel just adjacent to the optic nerve head. Let us walk through the options for controlling bleeding. At this point, I have got a light pipe in my left hand and the 25-gauge cutter in my right. My first objective is to aspirate the blood. Then I switch out efficiently to the diathermy tip, which in many cases works well. In this case, the bleeding was too profuse and by the time the diathermy tip was in position the bleeding vessel was obscured.

Next, I raised the IOP, in this case initially to 40 mm Hg then 50 mm Hg and then 60 mm Hg. While this slowed the bleeding, it continued. The patient's blood pressure at this stage was noted to be exceptionally high and the anesthesia team was engaged to normalize the blood pressure. I then put in a chandelier so I could use bimanual

manipulation and try aspirating with one hand and diathermy with the other. This also fails and I then used direct tamponade with the cutter to the bleeding vessel until the bleeding subsided.

Dr. Nudleman: Was this the arcade artery?

Dr. Wykoff: There was pulsatile flow from it. Ultimately direct tamponade stopped the bleeding. As a side note, in cases of severe and extensive pre-retinal proliferative tissues, especially those with a rhegmatogenous component, I have moved away from using preoperative anti-VEGF agents because of the so-called "crunch phenomenon."¹⁸ I find the tissue planes easier to dissect in the absence of the contraction seen after anti-VEGF dosing. On the flip side, there is definitely more oozing and hemostasis to manage intraoperatively in the absence of a preoperative anti-VEGF injection.

Dr. Ho: What about using anti-VEGF therapy postoperatively?

Dr. Wykoff: There are multiple postoperative considerations here. I sutured all the sclerotomies, and I gave this patient an intravitreal injection of bevacizumab during the first postoperative week. I then treated this patient regularly with anti-VEGF therapy until the eye stabilized.

Dr. Prenner: What do you do when you see that blood vessel pumping?

Dr. Eliott: I increase the pressure to 40 mm Hg or 50 mm Hg. If it is a massive bleeder like Dr. Wykoff described, then I might apply direct compression and I do not remove the instruments until the bleeding stops or significantly slows. I will even raise the pressure to 60 mm Hg or higher if necessary.

Dr. Prenner: How do you feel about diathermizing those vessels? Is there any other way that you would manage this?



Watch it Now

Figure 5

CASE 6: MANAGING INTRAOPERATIVE BLEEDING

A complex, diabetic tractional retinal detachment.



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Dr. Ho: My sequence is a little different. I will go right to a pressure of 65 mm Hg to see if that will tamponade it. I am very wary of diathermizing around anything near the optic nerve because of optic neuropathy. You have to be pretty careful about that. I will use the cutter to do direct tamponade and just sit there. I do try to use bevacizumab preoperatively, but only within a couple of days of surgery. I think that averts some of the crunch. The crunches are dramatic and you remember them, but I think bevacizumab can be beneficial, generally.

Dr. Prenner: I always make sure that my patient is cleared for surgery prior to giving bevacizumab preoperatively. Even if you get a crunch scenario, I think, I prefer a combined tractional rhegmatogenous detachment compared to a highly vascular and bleeding tractional retinal detachment.

Dr. Ho: I find it very interesting the varied tamponade pressures from the group. Some of you go to 45 mm Hg, while I go to 65 mm Hg.

Dr. Elliott: Years ago, we used a tissue manipulator, which is a four-function device. It had irrigation, aspiration, diathermy, and illumination. You never had to come out of the eye and grab a diathermy. There were no valved cannulas. You came out of the eye, the pressure of the eye went to zero, and it massively bled. By the time you got back into the eye, you could not find what was bleeding because there was so much blood. But with the tissue manipulator, you moved the instrument closer to the bleeding vessel, and the tip of the instrument had diathermy. You touched it, and it stopped bleeding. But now, nobody uses that instrument. It was a 20-gauge instrument, so that is why it is not used anymore; small gauge tends to work better.

Dr. Nudleman: Do you always remove the fibrosis from the nerve?

Dr. Wykoff: Yes, I remove the fibrosis if it is causing persistent distortion of the macula. I often leave areas of isolated proliferative tissue in the mid-periphery, but around the nerve I do try to remove any tissues causing significant traction through the macula.

CASE 7: MACULAR SURGERY PATIENT MOVEMENT

Dr. Ho: I am going to describe a patient with a macular hole, and my partner, Jason Hsu, MD, is performing the surgery using a 25-gauge system (Figure 6). Dr. Hsu starts the peel on the patient. The patient coughs, which leads to a bad bleed. The good news is that there was a positive outcome, we were able to close the hole and the patient recovered. But let us discuss some of the details that led to the bleed.

It is important to note that the patient's head was taped, which is standard procedure at Wills Eye. But you can never tape well enough to prevent a sudden movement like a cough. We teach our fellows to keep their hands on the forehead, so that if the patient moves, the surgeon's hands are moving with them.

We had many discussions about this case and how the bleeding could have been prevented. Most of us like to have the patient

awake, but is that the safest option? We spoke to our anesthesiologist on what kind of anesthesia could be helpful. Most surgeons do not like to use propofol right before surgery, or prefer no propofol because of the startle.

Dr. Prenner: You give them propofol for the block, and then after that, no propofol?

Dr. Ho: Many surgeons are avoiding propofol for macular peel, and some surgeons do not use propofol at all. You do not know how long it is going to last in a particular patient. The standard anesthesia is midazolam and fentanyl. Midazolam is a benzodiazepine, and it seems to blow off a little bit more. It does not cause as much wake up "startle" in fentanyl as a narcotic in a potentiator of the benzodiazepine does.

Dr. Prenner: Given our patient population, which tends to be older adults, we may be over sedating our patients.

Dr. Nudleman: I do all my cases under general anesthesia because of concern about them moving. When I talk to the patients about being asleep for the surgery, many give me a sigh of relief. They want to be asleep. There are risks with general anesthesia and risks with the patient moving. It is a balance.

Dr. Ho: If you are going to give local anesthetic around the eye, I think an ophthalmologist should do it. There have been reports of anesthesiologists doing this, which makes me uncomfortable.

Dr. Elliott: I prefer to have the patient awake because it offers me more control in communicating. For example, patients could potentially jerk their head or start snoring at an inopportune time. You have to be prepared for a sudden movement. If the patient is awake, I can let them know that we are doing a critical maneuver and that they need to lay still.



Watch it Now

Figure 6

CASE 7: MACULAR SURGERY PATIENT MOVEMENT

A macular hole repair using a 25-gauge system.



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Dr. Wykoff: I use local anesthesia for more than 95% of my cases and do something similar. In any case involving work on the macula, right before I move toward the macula, I pull my instruments out of the eye, put my hand on the patient's shoulder, and engage with them verbally. By that point in the case, any propofol used during the initial block will typically have worn off, and the patient may be just waking up or about to wake up. I tell them we are at a critical point in the surgery and not to move. If they do not respond, I do not wake them. But most of the time, they respond.

CASE 8: SICKLE CELL RETINOPATHY

Dr. Prenner: Let us move onto a sickle cell proliferative vitreoretinopathy (PVR) case.

Dr. Eliott: My colleague had already operated on the patient a couple of times. The patient presented with advanced proliferative sickle retinopathy with traction/rhegmatogenous retinal detachment (Figure 7). My colleague performed surgery, and the patient then developed recurrent detachment due to proliferative vitreoretinopathy (PVR). He then underwent another surgery that included a large retinectomy up to the temporal edge of the macula, and silicone oil was placed. He then re-detached due to PVR and was referred to me. The edge of the retinectomy had contracted, causing a fold through the macula, and there was a subretinal band. On the video, there is an obvious fold with tractional elevation. As we started the case, we noted some preretinal membranes, the retinectomy with its scarred edge, and the subretinal band under the macula.

Our plan was to peel the preretinal membranes, open the retinectomy, and remove the subretinal band. We then wanted to use perfluorocarbon, and iron out this big fold that was through the fovea. In the video, we see an epiretinal membrane, which we peeled from nasal to temporal. We see the band under the fovea. It was not very large, but we had to open the edge of the retinectomy to gain access

to the subretinal band. We lifted the edge of the retinectomy and removed the band.

Dr. Prenner: How are you getting into that tight space?

Dr. Eliott: We found a small plane using vertical scissors. We successfully removed the subretinal band and put in the perfluorocarbon. The retina flattened and we removed the blood. Here you can see the oil being injected. I held the nasal sclerotomy open, and eventually closed all the sclerotomies. After we removed the oil a few months later, the eye looked good. You can see where the old TRD and fold were, but you have some thinning on the OCT. The outcome was excellent; the retina remained attached, there was no recurrent proliferation, and the visual acuity was 20/250.

Dr. Prenner: I tend to use a lighted laser on continuous delivery rather than in a pulsatile fashion. It is great for retinectomy edges and for retinal tears. Does anyone else prefer using continuous laser or see a problem with it?

Dr. Eliott: I do use a lighted curved laser; it is one of my favorite instruments. Some of my colleagues use continuous lasers, though. Out of habit, I do individual spots in rapid succession. The most important thing about treating PVR sickle cell cases is to aggressively laser the other eye. You will want to thoroughly laser the area of nonperfusion out to the ora.

Dr. Wykoff: What if the patient is asymptomatic in the other eye?

Dr. Eliott: I bring them back multiple times. I believe in thorough laser for severe sickle cell patients or severe diabetics. Many of these patients have gone blind from not enough laser. There are not too many downsides to doing a near confluent pattern in a patient with massive ischemia. It is difficult to do that in one setting because the patient cannot tolerate so much laser at once. You have to bring them back for repeat laser until all areas of ischemia are treated.

CASE 9: GIANT RETINAL TEARS

Dr. Prenner: Our next case is a 17-year-old patient with a giant retinal tear (GRT).

Dr. Nudleman: This patient had trauma; he was hit in the eye with a 2x4 piece of lumber. This is a closed globe injury. The lens was a bit subluxed preoperatively, but it did not cause any problems during the surgery, which was about a month after the injury. He also presented with a low pressure and a choroidal, which I treated with oral prednisone for about a week preoperatively.

I am using a 25-gauge for the procedure (Figure 8). I start by placing an encircling scleral buckle and then start the vitrectomy. I remove as much of the anterior flap of the GRT as I can. The rip in this case went pretty far posteriorly.

After the vitrectomy, I went to PFO, and it unraveled nicely. But there was a small subretinal bleb of fluid that was trapped. At that point, I removed the PFO, re-detached the macula, and then put the PFO back in. This was to try to avoid a fold in the macula.



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Figure 7.

CASE 8: SICKLE CELL RETINOPATHY

A procedure to peel the preretinal membranes, open the retinectomy, and remove the subretinal band.



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Figure 8.

CASE 9: GIANT RETINAL TEARS

Repair of a giant retinal tear due to trauma.



Dr. Eliott: Were there subretinal bands? What was caused the fluid to stay under there?

Dr. Nudleman: There were not any subretinal bands. I think it just got trapped there as I was putting the PFO in. It did not completely iron out, but it went away after the second effort.

Dr. Eliott: What did you do with the subluxated crystalline lens?

Dr. Nudleman: I left it there because it did not cause any problems during the case. When I went to air at the end, there was some air in the anterior chamber, but the oil did not come forward during the first surgery.

Dr. Prenner: One thing to note is if you see air in the anterior chamber in a phakic or a pseudophakic patient, and you go to silicone oil, you are at high risk of getting oil in the anterior chamber. These eyes need a PI.

Dr. Wykoff: One point I would make is about going to air with PFO in the eye—I intentionally remove the fluid very slowly. Typically, there is enough PFO in the eye to cover the entire anterior lip of the GRT at this stage. I remove as much of the fluid anterior to the PFO that I can and then wait. Fluid will build up anterior to the PFO again. I repeat this multiple times before beginning to remove the PFO. This minimizes the risk of the GRT edge slipping posteriorly when the PFO is ultimately removed.

Dr. Nudleman: I agree. I was doing that, slowly removing all the fluid until the edge was completely dry. I put the oil in, and everything stayed down. The eye looked good postoperatively on day one. Six weeks later, however, he contracted inferiorly. You can see it here. There was quite a bit of PVR, and the traction pulled a full

thickness macular hole. His lens had not moved yet, so I took him back in the OR and peeled everything. I did have to do an inferior retinectomy.

Dr. Prenner: Would anyone take the lens at this point?

Dr. Eliott: I probably would have taken the lens the first time because the edge of the GRT seemed to be inferior. I am assuming the lens is going to move later if it is subluxated, or you are going to get oil in the anterior chamber. It is going to give you problems. In my personal experience, phakic eyes with GRTs do not do as well as pseudophakic or aphakic eyes with GRTs. Sometimes, we buckle the phakic ones; I also like to buckle when the edge is inferior.

Dr. Nudleman: The patient was buckled. I had placed a 41 band.

Dr. Prenner: For GRTs, do people prefer vitrectomy alone or vitrectomy in combination with a scleral buckle?

Dr. Wykoff: I am a buckle fan. I put on buckles on almost all of my GRT patients.

Dr. Prenner: I do as well. I am rarely upset that I placed a buckle, but the reverse is not always the case.

Dr. Wykoff: I have never regretted it.

Dr. Prenner: What are the keys to making these cases go as smoothly as possible?

Dr. Eliott: I usually do a buckle in phakic patients with inferior edges. In aphakic or pseudophakic patients, I may buckle them as well if the edges are inferiorly located. I use a small buckle, a 42 band. I keep the height relatively low. The key for going from perfluorocarbon to air is to do it slowly so that it dehydrates the vitreous base. It does not slip as much, and you can sweep the edge of the GRT as you are slowly removing the perfluorocarbon. You have to dry the edge as much as you can.

Dr. Prenner: What happens if you slip?

Dr. Eliott: You have a few options. You could sweep it with an instrument to get it back where it came from. If that does not work, then you can go back to fluid, and put more perfluorocarbon in and do it even slower. Or you can do the perfluorocarbon silicone oil exchange, which I used to do years ago, but I do not really do anymore since it is hard to see the interface. A radial retinectomy is another option. I think the key is speed; the slower the better.

Dr. Prenner: A radial retinectomy also helps to reduce slipping as you reduce the tangential force impacting the retina. These tend to work well as a response to persistent slippage.

Dr. Eliott: It is amazing how it opens. You make the line radially, and it opens several clock hours, indicating relief of traction.

Dr. Wykoff: I noticed you used silicone oil in this case. Why did you use oil the first time around and not gas?

Dr. Nudleman: I was worried about PVR, and I was hoping to keep the oil in for a long-term tamponade. I would have kept it in for 6 months. But the retina contracted under oil, requiring a second surgery, and then to your point, oil came to the anterior chamber. He had elevated pressure and pain about a week or two after his second surgery. I did not want to take the oil out at that point, so I took him back to the OR and removed the oil out of the anterior chamber and exchanged it for air. That worked, and his pressure went down. I kept the oil in for an additional 6 months and he stayed attached, and then I took it out. We removed the lens and put in an IOL at the time of the oil removal. Here you see his post op photos and his most recent OCT. He has remained attached, and his vision is stable at about 20/80.

Dr. Elliott: Did you use 1,000 or 5,000 centistoke oil?

Dr. Nudleman: I used 1,000 centistoke, and there was a little emulsification when it was removed.

Dr. Prenner: Did you think about using systemic or local medication to try and reduce the risk of PVR?

Dr. Nudleman: That is partly why I want to discuss this case.

Dr. Elliott: This is off-label and not approved, but I have been using methotrexate in recurrent detachments due to PVR in patients who have had two or more operations. I have also been using it off-label in open globe-associated retinal detachments because they have such a high rate of PVR. I give 400 µg in 0.1 mL at the end of surgery, right into the oil. I am only using it in the highest risk cases trying to establish proof of concept. I then give additional injections once a week for 8 weeks. I follow up those injections with four injections, one given every other week, for a total of 13 injections.

The methotrexate bubble sits within the oil bubble because the methotrexate is hydrophilic and the oil is hydrophobic. They do not mix at all. Then the methotrexate bubble slowly sinks. Once the edge of the methotrexate bubble hits the bottom of the oil bubble, it immediately disperses and washes the inferior and posterior retina. It has to be preservative-free methotrexate. It is a teratogen, so the patient cannot be pregnant or cannot be planning on getting pregnant. But it is a safe drug that has been around for more than 50 years.

In the eye, the only toxicity is corneal. If a patient has pre-existing dry eye or is a diabetic patient, we have had to use aggressive lubrication. We have noticed corneal epithelial whirl in some patients, which can be an issue if you are not aggressive with lubrication. You may need to refer those patients to corneal specialists to maximize the health of the ocular surface. But if it is a typical nondiabetic patient without dry eye, then they do not need to see a specialist. I tell those patients to use frequent drops and ointment at least four times a day, especially before bedtime. You will need to examine the eye every week. If you see the cornea showing signs of compromise due to the toxicity, you have to really insist on the importance of lubrication.

I always tell my patients this is an off-label therapy and not approved. I have done this in about twenty patients so far. It is labor intensive and requires many office visits, but patients are compliant. These patients are highly motivated because they have had multiple surgeries. We have had excellent results, but that may be due to good luck or drug efficacy, and we will not know if it actually works until we conduct a clinical trial. ■

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FROM TRIALS TO TREATMENT: REAL WORLD APPLICATIONS IN MEDICAL AND SURGICAL RETINA

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FROM TRIALS TO TREATMENT: REAL WORLD APPLICATIONS IN MEDICAL AND SURGICAL RETINA CME QUESTIONS

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1. During surgical repair of a diabetic traction retinal detachment, a bleeding vessel is observed. An option to expedite cessation of unwanted bleeding is:

- a. Lower the intraocular pressure
- b. Direct tamponade of the bleeding vessel with a blunt instrument
- c. Increase the patient's blood pressure
- d. Perform an anterior chamber paracentesis

2. Please rate your confidence in your ability to use the 27G instrument while beveling trochar wounds during insertion. (Based on a scale of 1 to 5 with 1 being not at all confident and 5 being extremely confident).

- a. 1
- b. 2
- c. 3
- d. 4
- e. 5

3. All of the following may be helpful to prevent inadvertent macular trauma during patient movement, except to:

- a. Sedate the patients so they are sleeping
- b. Place hands on patient forehead to move with the patient
- c. Tape the patient head in preparation for surgery
- d. Speak to the patients so they are awake and aware to be stable

4. A patient presents with a simple inferior retinal detachment that has a small atrophic hole in the periphery. According to the panelists, what are potential techniques to consider:

- a. Posterior draining retinotomy
- b. Draining subretinal fluid through the retinal break
- c. Perfluoro-N-octane (PFO)
- d. All of the above
- e. None of the above

5. When using silicone oil:

- a. Use a needle in phakic eyes for the entire procedure
- b. Do not overfill the phakic eye
- c. Remove the instruments as quickly as possible to avoid hypotony
- d. Ignore infusing after removing your foot

6. What is an advantage to suture a sclerotomy?

- a. Minimize postoperative bleeding/hemorrhage
- b. Preventing exposure of the scleral tunnel
- c. Increasing patient comfort compared to tissue glue
- d. Avoids a scleral flap technique

7. A patient presents with visually significant vitreomacular traction and epiretinal membrane than necessitates surgical intervention. According to the panel, which instruments are preferred?

- a. Beveled trochar system
- b. 23-gauge valved trochar system
- c. 27-gauge valved trochar system
- d. All the above

8. For PVR with subretinal bands, all of the following are reasonable options except:

- a. Leave as is
- b. Laser the bands until they rupture
- c. Create access retinotomies to remove the bands
- d. Create a large peripheral retinectomy, fold the retina over to access the subretinal space, and remove the bands

ACTIVITY EVALUATION

Did the program meet the following educational objectives?

Agree

Neutral

Disagree

Recognize the importance of early diagnosis and treatment of age-related macular degeneration and diabetic macular edema.

Assess the response of anti-vascular endothelial growth factor intravitreal injections, and define "suboptimal responders."

Understand the most recent monotherapy and combination therapy clinical study evidence using available therapies for AMD, DME, and RVO.

Discuss the outcomes of pivotal studies in AMD, DME, and RVO and how study results may differ from "real-world" dosing methods.

Develop individualized treatment plans for patients with retina disorders that use a combination of imaging, treat and extend, or treat and observe.

Discuss the ocular and systemic effects of anti-VEGF therapies and how to educate patients on appropriate expectations.

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____ Create/revise protocols, policies, and/or procedures. Please specify:

Please identify any barriers to change.

____ Cost

____ Lack of time to assess/counsel patients

____ No barriers

____ Lack of consensus or professional guidelines

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