

# AN INSIDE LOOK AT INNOVATIONS IN OPHTHALMOLOGY

*Innovation Journal Club* explores recently published and presented data around innovations in eye care with a focus on how they might shape real-world practice.



The *Innovation Journal Club* series on Eyetube.net takes an in-depth look at podium data, peer-reviewed literature, and global experiences related to innovations and technologies that offer to change the way ophthalmology is practiced in the real world. Hosted by I. Paul Singh, MD, of the Eye Centers of Racine & Kenosha in Wisconsin, the series is editorially independent and supported with advertising from multiple companies, thus giving viewers an unvarnished and unbiased look at emerging trends in ophthalmology. Each episode features interviews with leading experts from across eye care subspecialties, which simultaneously broadens the scope of topics and sharpens the focus of the content of each discussion.

The following is a summary of three episodes in which Dr. Singh sat down with Mark J. Gallardo, MD, of El Paso Eye Surgeons in El Paso, Texas, to talk about innovations in glaucoma; with Steve Charles, MD, FACS, FICS, FASRS, of the Charles Retina Institute, in Germantown, Tennessee, to discuss two recent innovations in retina surgery; and with William F. Wiley, MD, of Cleveland Eye Clinic, to learn about the ever-expanding category of presbyopia-correcting IOLs.

## INNOVATIONS IN GLAUCOMA

### FEATURING MARK J. GALLARDO, MD



The MIGS category has undoubtedly changed the management of glaucoma. After more than a decade of use in clinical practice, the longer-term benefits associated with the procedural management of glaucoma are starting to emerge—and they appear to be substantial. In episode 7 of *Innovation Journal Club*, host I. Paul Singh, MD, sat down with Mark J. Gallardo, MD, to discuss long-term outcomes with canaloplasty and future trends in MIGS.

### LONG-TERM OUTCOMES WITH CANALOPLASTY

A study by Dr. Gallardo and colleagues reporting the 3-year follow-up of patients who received canaloplasty and viscodilation (iTrack; Nova Eye Medical), with or without cataract surgery, for the treatment of primary open-angle glaucoma, demonstrated sustainable reductions in postoperative IOP and medication usage.<sup>1</sup> The drop in medication requirement was slightly greater after combination procedures, but the difference was not statistically significant.

The mean IOP in both groups of patients was consistently in the range of 13 to 14 mm Hg at 12, 24, and 36 months postoperatively (Figure 1). A number of patients were able to stop all antiglaucoma medication use, again with a slight benefit for combination procedures: 42.9% in the overall population, 26.1% among those in the iTrack-only group, and 34.1% in the iTrack + cataract surgery group.

“In the past, when we thought about the definition of success, our complete success was meeting the target IOP with no medications. With a lot of the patients who we’re dealing with now going into cataract

surgery and implanting a major device, the goal really is to eliminate the medication burden on a number of those patients,” Dr. Gallardo said.

According to Dr. Gallardo, the mechanism of iTrack—mechanical dilation and forceful viscodilation—likely explains the long-term effectiveness he observed. The canaloplasty portion of the procedure functions to mechanically break any herniations that might impede aqueous outflow in the Schlemm canal; viscodilation complements this mechanism by flushing the canal while also opening blockages in the juxtacanalicular tissue, trabecular meshwork, and within collector channels. In all, the procedure has an impact on all the relevant anatomy in the complex aqueous drainage system.

“What you want to be able to do is create enough force within the canal that the viscoelastic not only causes changes to the proximal system, but also dilates things downstream,” Dr. Gallardo said. “I really do think that the force of the viscoelastic that’s introduced has a significant role in the expansion and the microscopic changes to the tissue that occur.”

### TRENDS IN MIGS, 2013-2018

It is perhaps unsurprising that a study reviewing MIGS usage trends between 2013 and 2018 found a substantial increase in the number of procedures performed, with a corresponding decrease in the number of traditional incisional glaucoma surgeries during the same period (Figure 2).<sup>2</sup>

The shift may be explained by a number of factors. For instance, the availability of

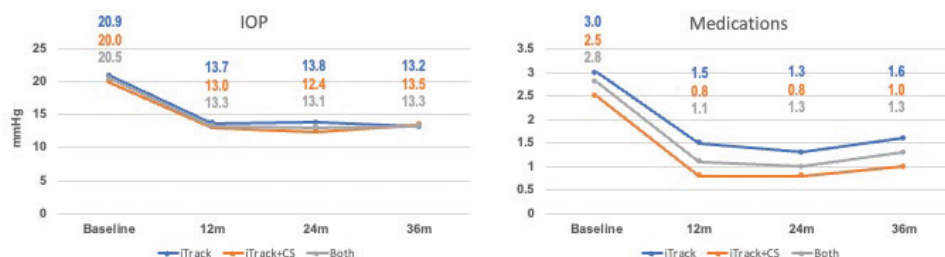


Figure 1. IOP and medication outcomes through 3 years of follow-up in a study led by Dr. Gallardo.

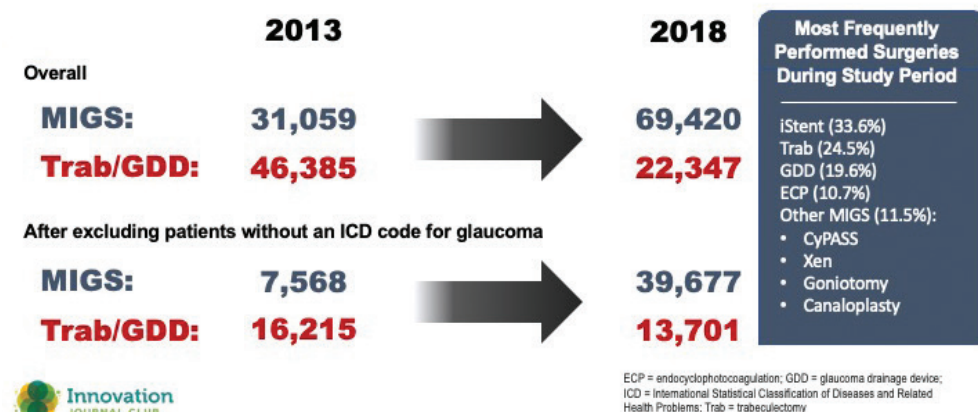


Figure 2. The volume of MIGS procedures increased 3-fold between 2013 and 2018, with a corresponding decrease in traditional incisional glaucoma procedures.

alternative options for surgically managing glaucoma, especially ones with a more favorable safety profile, should have organically reduced the number of trabeculectomy and tube surgeries performed year over year. Furthermore, that favorable safety profile has facilitated adoption by comprehensive ophthalmologists; the increase in provider base for procedural management, and expansion of this service beyond the sole purview of fellowship-trained glaucoma surgeons, also affects usage rates in the community.

And yet, there may be a much simpler explanation: MIGS procedures work.

"When I started practicing, I was doing about eight trabeculectomies a week, and now we probably do about 25 or 30 a year, and that's because MIGS procedures have worked very well," Dr. Gallardo said. "If there's a question of longevity of MIGS procedures, I can tell not only anecdotally, but just by what I see day in and day out in the patients in my practice, that MIGS procedures have prevented patients from requiring filtration surgeries."

Another trend revealed in the study of MIGS usage patterns was a growth in using combinations of MIGS procedures. Whether or not that is truly surprising may depend on one's mindset in thinking about offering options to patients. Dr. Singh offered that using two or more devices or procedures, aimed at different anatomy within the drainage pathways, appears to have synergistic effects.

"We're finding that combining procedures not only provides additional pressure reduction by maybe a point or two, but also provides greater medication burden reduction ... and results in fewer nonresponders," Dr. Singh said.

1. Gallardo MJ. 36-month effectiveness of ab-interno canaloplasty standalone versus combined with cataract surgery for the treatment of open-angle glaucoma. *Ophthalmol Glaucoma*. Published online February 17, 2022.
2. Yang SA, Mitchell W, Hall N, et al; IRIS<sup>®</sup> Registry Data Analytics Consortium. Trends and usage patterns of minimally invasive glaucoma surgery in the united states: IRIS<sup>®</sup> Registry Analysis 2013-2018. *Ophthalmol Glaucoma*. 2021;4(6):558-568.

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- Financial disclosures: AbbVie/Allergan, Aerie Pharmaceuticals, Alcon, Bausch + Lomb, Glaukos, Ivantis, Sight Sciences, Nova Eye Medical

## INNOVATIONS IN RETINA

### WITH STEVE CHARLES, MD, FACS, FICS, FASRS



The pace of innovation in the retina space over the past decade has been remarkable, bringing forth new drugs, novel treatment concepts, improved diagnostics, and even evolutions in how delicate operations in the posterior segment are viewed, illuminated, and performed. In episode 8 of *Innovation Journal Club*, renowned retinal surgeon Steve Charles, MD, FACS, FICS, FASRS, joined Dr. Singh to provide an update on two recent innovations.

#### A SURGICAL OPTION FOR NEOVASCULAR AMD

Although intravitreal anti-VEGF injections have undoubtedly improved outcomes in the treatment of neovascular age-related macular degeneration (AMD), their use comes at a cost to patients and their families, as they must be re-injected on a frequent and recurring basis. Patients are monitored with

serial imaging to detect changes to the retina structure secondary to AMD, which proves additive in the overall treatment burden.

The real-world impact on patients' lives associated with anti-VEGF therapy is a motivating factor in ongoing research into options for improving the durability of treatment options. One potential solution, Susvimo ranibizumab injection for ocular implant (formerly Port Delivery System [PDS]; Genentech), a surgically implanted drug reservoir that can be refilled with a special formulation of the anti-VEGF agent ranibizumab (100 mg/mL, Genentech), recently gained FDA approval and is starting to become more widely used in retina practice. In the interest of updating ophthalmologists about an emerging trend in retina, Dr. Charles joined Dr. Singh in this episode to review the data from the Susvimo phase 3 clinical trial.<sup>1</sup>

- In terms of efficacy, Susvimo, which was refilled at week 24 per protocol, was noninferior and equivalent to monthly ranibizumab injections. As well, 98.4% of patients in the device group required no supplemental treatment (ie, rescue therapy) in the first 24-week interval.
- The safety analysis revealed some novel signals in the Susvimo arm, including necrotizing retinitis (secondary to endophthalmitis) and implant dislocation.

According to Dr. Charles, some of the safety issues have already been addressed by the device's sponsor; beyond that, how meticulously the surgeon attends to some of the details of the surgery, such as closure of the Tenon layer and conjunctiva, may affect the device's safety and performance postoperatively. Indeed, Dr. Charles said he prefers to refer consultations for Susvimo to his surgical associate, despite having been trained on the device. The safety issues are not overly concerning relative to the benefits, but it may be that surgeons willing to dedicate themselves to using the device correctly are more likely to achieve the intended result.

"My associate did the clinical trials work on the PDS," Dr. Charles said. "I trained him, and I said, 'You're great at this. You should do it. Let's keep at the highest level. I'll send my cases to you.' I'm not afraid to do the case. I just want to see his expertise built."

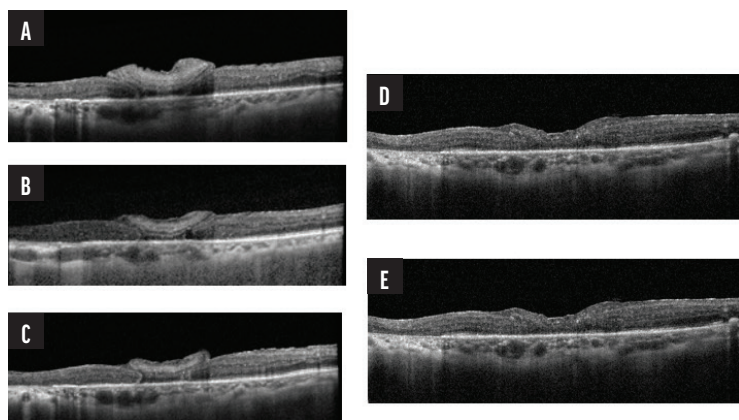


Figure 1. Although the exact mechanism of graph assimilation is unclear, Dr. Charles proposes that the graph tissue and retina demonstrate plasticity—retinal function returns as the intentionally oversized graph (seen most clearly in A) contracts to the space over time, connects with existing nerve signaling in the surrounding retina, and eventually becomes indiscernible from the rest of the retina (E).

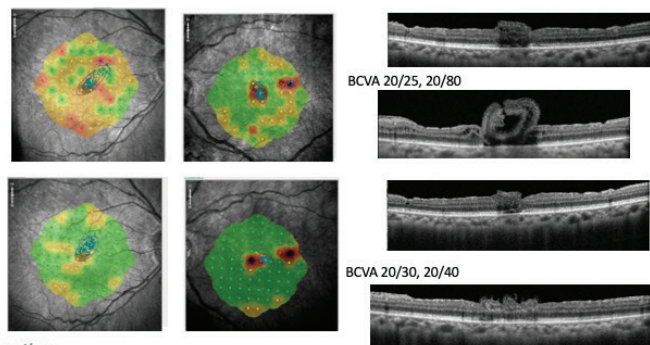


Figure 2. Microperimetry studies, performed 1 year apart, demonstrate improvement in macular function postoperatively. This finding also supports Dr. Charles' hypothesis about retinal plasticity.

## ART

Complex macular hole (MH) has historically been a challenging clinical problem. Although vitrectomy, with or without peeling of the internal limiting membrane, is effective for most cases of MH in terms of achieving anatomical closure, surgical options have remained limited for myopic MHs, refractory MHs, large to giant primary MHs, and combined MH-rhegmatogenous retinal detachments.

Autologous retinal transfer (ART), which involves harvesting a donor graft from one area of the retina and using it to close the MH, was introduced by Tamer Mahmoud, MD, PhD, from Associated Retinal Consultants in Royal Oak, Michigan, in 2016 and has since been performed by multiple surgeons around the world. Dr. Charles has worked closely with Dr. Mahmoud in developing the surgical technique. Despite initial pushback on the concept, ART has proven successful in achieving meaningful results in cases in which there was no other viable option. Data from a recent review of real-world global outcomes confirm that notion (Table).<sup>2</sup>

To date, Dr. Charles has performed more than 80 cases and says he achieves closure in around 80% of cases, with about three quarters also achieving what he called “reasonable vision outcomes.” In talking with Dr. Singh, he discussed some of the finer points of ART, including his

	Primary MH (n=35)	Refractory MH (n=76)	MH+RRD (n=19)
MH diameter, $\mu$ m: min-max	882-1480	796-1440	932-1630
Closure rate	85.7%	88%	95%
Preop BCVA, logMAR (Snellen)	1.090 (20/246)	1.258 (20/362)	2.36 (HM)
Postop BCVA, logMAR (Snellen)	0.838 (20/138)	1.063 (20/231)	1.403 (20/500)
% 3-line gain	37%	37%	74%
% 5-line gain	17%	25%	68%

Table. Outcomes with ART from a global consortium of real-world cases.

criteria for patient selection, why perfluorocarbon may be preferable as a tamponade, the procedure's suggested mechanism of action (Figure 1), and the evidence supporting functional outcomes after ART (Figure 2).

Throughout the interview, Dr. Charles highlighted the fascinating history of how ART was developed, and he suggested that it may impart some lessons about the nature of innovation itself. Despite significant skepticism and doubt from prominent members of the retina community when he first presented the concept, Dr. Mahmoud persisted because of his faith in its scientific principles. Over time, what was initially seen as unconventional has come to be accepted as a viable surgical option where none previously existed.

“The notion that the tissue is dead gone, and you can't fix it, is simply wrong,” Dr. Charles said. “But Tamer was attacked with people saying that, and the lesson is, listen to people and let the science work and give these people a chance. That's how things are advanced.”

“That's how innovation occurs,” Dr. Singh added, “because they don't give up on those ideas.”

1. Holekamp NM, Campochiaro PA, Chang MA, et al; all Archway Investigators. Archway randomized phase 3 trial of the Port Delivery System with ranibizumab for neovascular age-related macular degeneration. *Ophthalmology*. 2022;129(3):295-307.

2. Moysidis SN, Koulisis N, Adrean SD, et al. Autologous retinal transplantation for primary and refractory macular holes and macular hole retinal detachments: the global consortium. *Ophthalmology*. 2021;128(5):672-685.

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## INNOVATIONS IN PRESBYOPIA-CORRECTING IOLS

WITH WILLIAM F. WILEY, MD



Can having too many options be bad? When it comes to lens-based options for addressing presbyopia, the answer is “no,” as the array of choices increases the chances of individualizing the selection. Having myriad presbyopia-correcting IOLs available does, however, create some complexity for the clinician when making a recommendation. In episode 9 of *Innovation Journal Club*, William F. Wiley, MD, offered his take on a recent study of an IOL with extended depth of focus (EDOF) features, and described how he sorts through all the clinically available lens options.



## A NOVEL EDOF STYLE LENS

A recent study of the xact Mono-EDOF ME4 (Santen Pharmaceuticals)—an IOL with a CE Mark designation as a monofocal that features a biconvex, aspheric design with four diffractive rings—suggested a promising ability to restore far and intermediate vision with low potential for photic phenomena in a small, uncontrolled study.<sup>1</sup>

In the study, the visual acuity and refractive outcomes at 3 and 6 months were promising (Figure). In reviewing the data, though, Dr. Wiley said what stood out to him was how the investigators focused prominently on the balance between extending depth of focus and minimizing the potential for visual side effects—which is something he sees reflected in the expanding array of IOL options on the market.

“It seems like there’s a range of different lenses that might give off a little bit more focus, but have a little higher side effect profile, or some that maybe don’t have quite the focus, but have a little lower side effect profile,” he said.

Although the above thinking is an oversimplification of the breadth of options available for patients who want a bit more visual function than what a monofocal can offer, it may provide a framework for presenting options to patients. During consultations, one subtle point Dr. Wiley seeks to understand is the patient’s tolerance for side effects relative to what they want to accomplish with their vision postoperatively.

“Sometimes my decision process is a little bit more binary, where I have full trifocal or full monofocal,” Dr. Wiley said. “The EDOF lenses that sit in between are a little more nuanced to try to tease out ... The more we learn about what patients want between the extremes of optimized vision and side effects, we’ll start to find what patient criteria, patient expectations, and personality types fit with those lenses.”

## AN EVER-GROWING MARKET

Throughout their conversation, Drs. Wiley and Singh addressed a question many surgeons face on a daily basis: How, exactly, do you sort through the options so that patients are offered the best lens for their

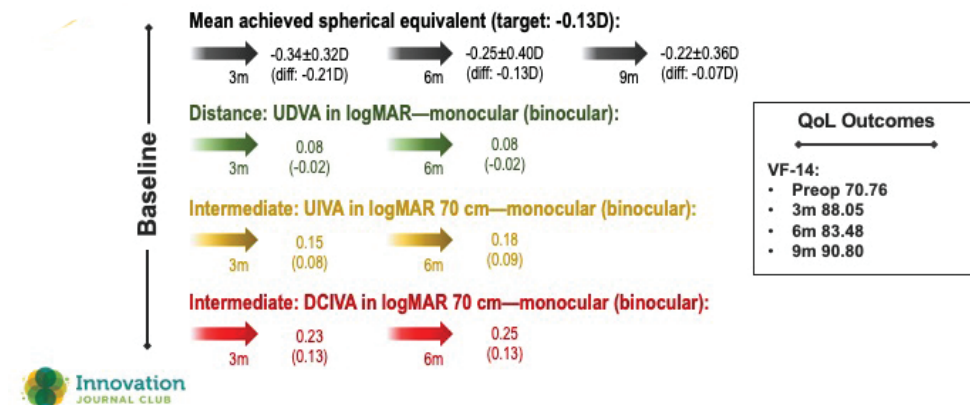


Figure. Three- and 6-month outcomes with a novel EDOF-style lens.

individual optical system—and what criteria or patient factors are most helpful in making that determination?

In his clinic, Dr. Wiley said he takes a decidedly conservative approach to IOL selection, looking for reasons on the physical exam and imaging that would exclude a patient from a multifocal. Sometimes the best use of surgical judgment is deciding when not to offer certain options.

“What might be ‘premium’ for a particular optical system may be excluding a complex optical system. Some eyes may not be able to handle a complex optical system, and if you try to add that in with a multifocal, you could be making the optical system more complicated,” Dr. Wiley said.

However, he added that he may have to revisit how he uses so-called “premium lenses” as options that are more suitable for complicated cases that come to the clinic. For example, early experiences with the IC-8 (AcuFocus), which features small-aperture optics, suggest it may be viable for aberrated corneas, eyes that are post-refractive surgery, and in eyes with mild retinal pathology—cases for which traditional multifocals are considered less than ideal.

“What we find is that aperture optics take great intermediate vision and extend the focus both ways, extending both distance and near vision,” Dr. Wiley said. “We’re so used to thinking about presbyopia correction as [an addition]—you take plano and add something to it just in one direction, but aperture optics extends focus on both sides of that curve.”

Aperture optics might also be an option for patients who are considering monovision. Although pseudophakic monovision can be successful in many cases, hitting the refractive target is crucial, as any refractive surprise tends to get magnified. The pinhole effect from the IC-8, which is more forgiving in this regard, may be a consideration, especially if the patient did not have success with monovision contact lenses.

In a similar fashion, the Light Adjustable Lens (RxSight) could be an answer for patients who are uncertain whether monovision is right for them. Because the surgeon can titrate the lens power postoperatively, patients can be targeted for monovision initially, for example, and then do a real-world trial to see if their new vision is suitable for their lifestyle.

“We’ve had a lot of success with the Light Adjustable Lens,” Dr. Wiley said. “It has some spherical aberration that’s built into the system, so we do see some depth of focus gains that rival other lenses as far as the range of vision. Plus, it’s very precise on hitting those targets—we know we can nail that distance vision and nail that monovision target if that’s what the patient wants.” ■

1. Baur ID, Khoramnia R, Weindler J, et al. Clinical outcomes of a new hybrid monofocal iol with extended depth of focus. *J Refract Surg.* 2021;37(9):601-608.

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