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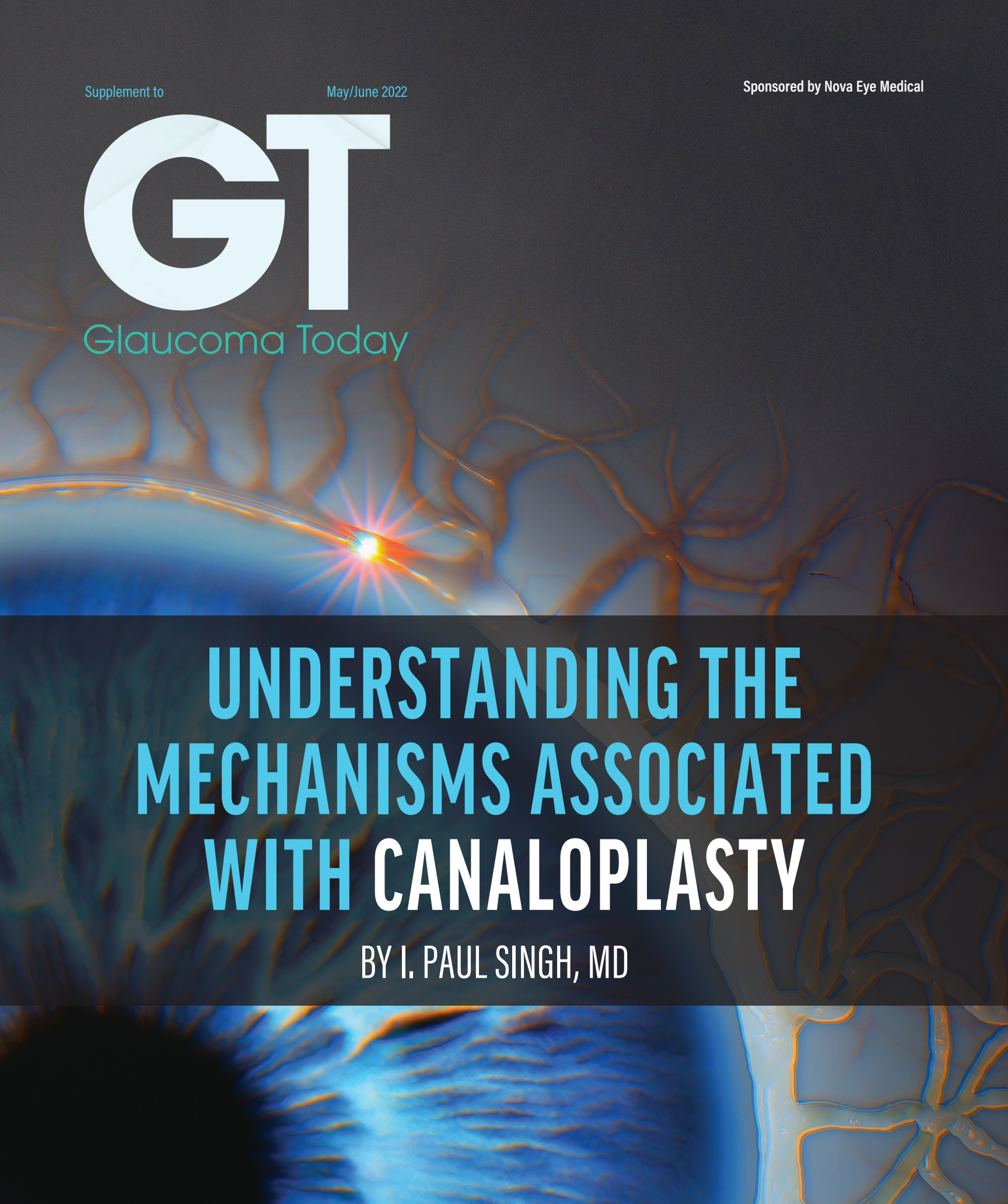

UNDERSTANDING THE MECHANISMS ASSOCIATED WITH CANALOPLASTY

BY I. PAUL SINGH, MD

UNDERSTANDING THE MECHANISMS ASSOCIATED WITH CANALOPLASTY

Live, intraoperative anterior-segment OCT imaging shows evidence of effect on the trabecular meshwork, Schlemm canal, and collector channels.

BY I. PAUL SINGH, MD

There has been a lot of interest of late around canaloplasty. Published studies have helped to highlight the meaningful benefits patients can achieve: Around 30% IOP reduction from baseline and high probability of reducing medication burden.[1-3] Furthermore, both in the setting of standalone procedures, as well as in combination with phacoemulsification, patients have a very good chance of completely eliminating medication use.[1] Recently published outcomes at 36 months after canaloplasty with iTrack (Nova Eye Medical) confirm the durability of IOP-lowering and medication reduction.[3] As with all MIGS procedures, the procedure is associated with a very favorable safety profile.[1-4]

One of the very big questions about canaloplasty is whether the mechanism of action is purely mechanical or whether the procedure induces a physiologic effect. That is, does canaloplasty simply break the herniations present in the Schlemm canal (SC), or does the controlled release of viscoelastic have any potential to restore the function of the conventional outflow pathway? And if canaloplasty is having a physiologic effect, what part(s) of the outflow pathway are being remodeled?

With these questions in mind, I recently decided to perform intraoperative OCT on a patient undergoing canaloplasty with iTrack. Scan the *QR code* on this page to watch a video summary of the case.

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In this article, I will explain some interesting findings that suggest canaloplasty helps to dilate the SC, open the collector channels, and stretch the trabecular meshwork (TM) tissue. In short, this is evidence that iTrack addresses resistance at multiple parts of the conventional outflow pathway.

BACKGROUND

This is a case of 64-year-old woman who came to my clinic for further management of her moderate open-angle glaucoma. She was previously prescribed three classes of medications but was having difficulty taking them due to forgetfulness and tolerability issues. On examination,

> "As shown with live anterior-segment OCT, canaloplasty has a complementary effect on the TM structure: As the trabecular beams become stretched, they become more porous to improve outflow facility."

her IOP was 22 mm Hg with evidence of ocular surface disease. She was pseudophakic with open angles to CBB on gonioscopy OU. Her cup/disc was 0.65 in this eye with slight thinning of retina nerve fiber layer inferiorly on OCT. Humphrey Visual Field revealed a superior arcuate defect. Based on her ocular nerve head and visual field findings, I felt her target IOP should be in the middle teens. Adding more medications would likely fail since she was not compliant with her current therapy. She did undergo a previous selective laser trabeculoplasty (SLT) with modest results and therefore another SLT would likely not be enough to reduce her IOP and reduce the drop burden. iTrack (Nova Eye Medical) canaloplasty seemed to be the optimal next step to reduce IOP and drops burden by breaking herniations within the canal, stretching open the TM, and flushing the distal collector system (see *Canaloplasty, Mechanism of Action*).

During the iTrack procedure, live intraoperative OCT using ZEISS Rescan (ZEISS) was used. The 9-o'clock position over the area of the incision was observed. Three screenshots were captured from the video summary and are presented on the next page; in each, the "A" image depicts an overview (the surgical view is on the left; two OCT images in horizontal and longitudinal orientation at the right), and the "B" image is a zoom-in of the horizontal OCT image. Of note, the video summary starts in the middle of the procedure, after the iTrack microcatheter has been advanced the entire 360° of the canal (ie, following the catheterization portion of the procedure), and while the microcatheter is being retracted to perform viscodilation (Figures 1-3).

CANALOPLASTY, MECHANISM OF ACTION

The canaloplasty procedure (iTrack and *iTrack Advance, Nova Eye Medical), mechanistically re-establishes the conventional outflow pathway in a stent-free, trabecular meshwork (TM) tissue-sparing procedure. In turn, preserving the structure and function of the TM has implications for maintaining an important physiologic mechanism for responding to IOP fluctuations and elevations via regulation of hyaluronic acid (HA) levels within the outflow pathway.[1,2] HA has various roles in this regard, including promoting cell motility, adhesion, and proliferation,[3] and activating matrix metalloproteinases 2 and 9 to clear the deposition of extracellular matrix (ECM) in the TM.[4,5] Fundamentally, then, canaloplasty, because it targets all the structures in the conventional outflow pathway, and because it is performed for 360° of the Schlemm canal (SC), is akin to hitting the reset button, ensuring that the system functions as it should–while also keeping future options viable should they become necessary.

Canaloplasty achieves these multiple mechanisms of action through both mechanical and physiological effects.

Mechanical Effect: Microcatheterization of 360° of the SC:
- Breaks adhesions in the SC;
- Breaks tethering of the juxtacanalicular tissue;
- Separates herniations of the inner wall of SC from the outer wall; and

Physiologic Effect: Delivery of viscoelastic into the SC via pressurized viscodilation:
- Dilates the SC and
- May also dilate the distal outflow system,[6-8] which is frequently blocked in eyes with primary open-angle glaucoma.[9,10]
- Creates focal disruptions within the TM.[6-8]

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*iTrack Advance is not available for use or sale in the USA.

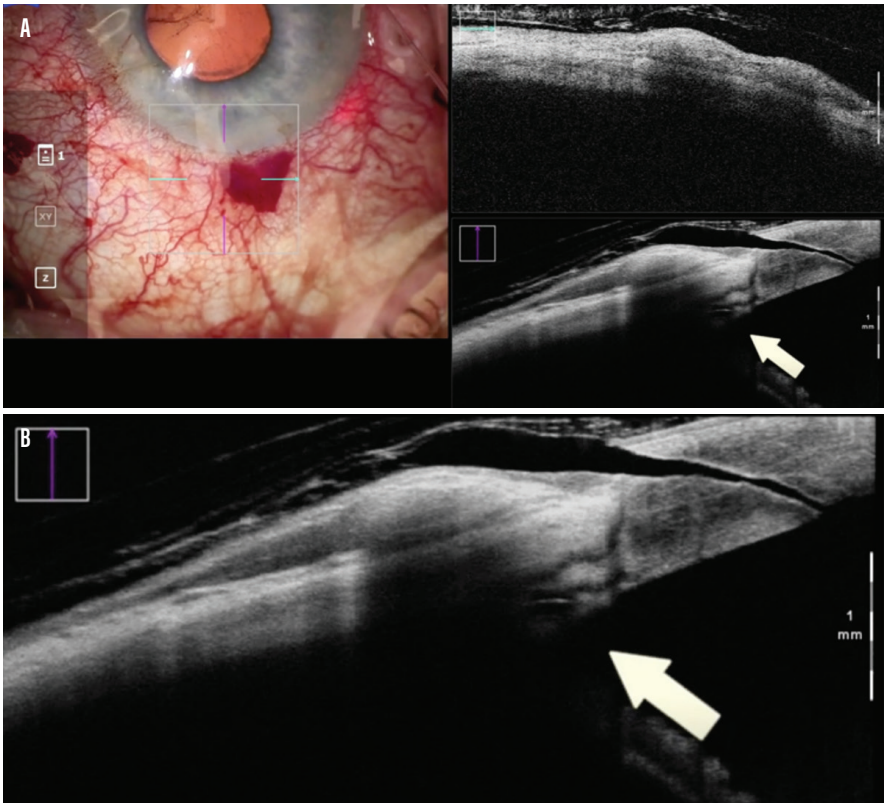

Figure 1. Narrow SC prior to viscodilation in the area under observation on intraoperative OCT. At this point in the procedure, with the iTrack microcatheter roughly in the 7-o'clock position (red blinking fiber optic beacon in the left image of figure A [top]), the SC at 9-o'clock appears flat (white arrow in lower right image of figure A, and more easily appreciated in a zoomed-in display of the same image in figure B).

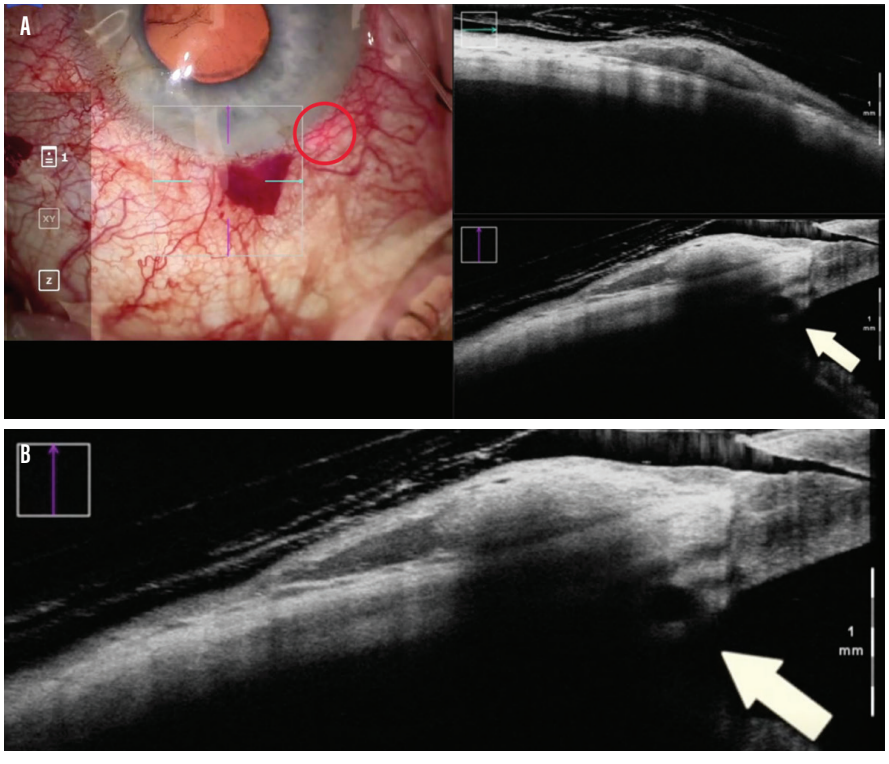

Figure 2. Dilation of the SC. The microcatheter is now within the area under observation (red blinking fiber optic beacon in the left image of figure A [top]). As viscoelastic is released, the SC has now expanded in diameter (white arrow in lower right image of figure A, and more easily appreciated in a zoomed-in display of the same image in figure B).

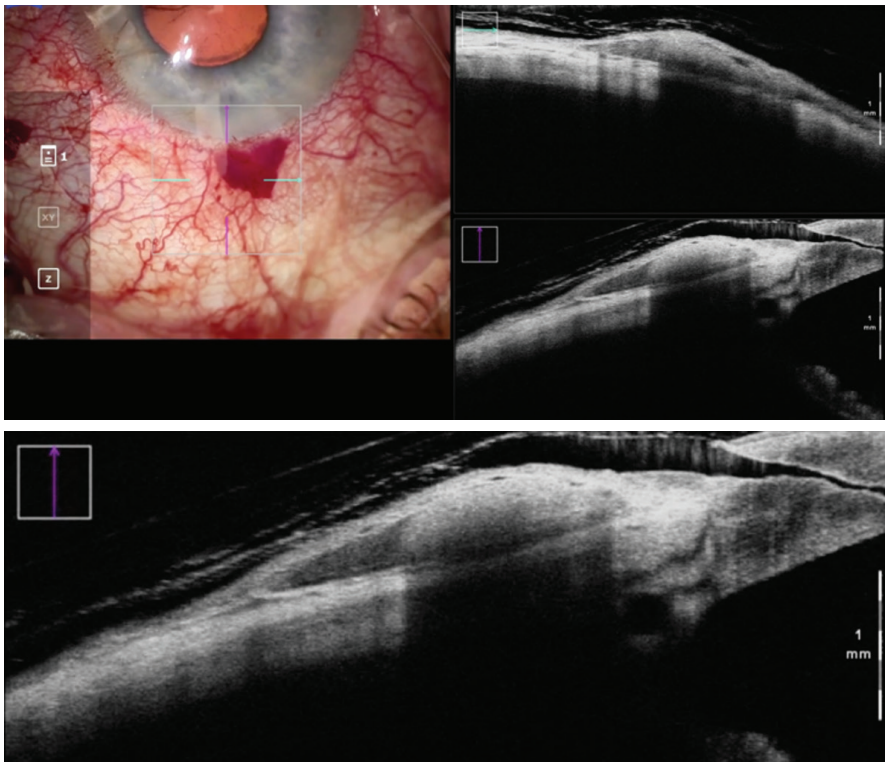

Figure 3. A fully dilated SC. The microcatheter has now moved past the area of observation, yet the SC remains fully dilated. With the iTrack, the surgeon can titrate the volume of viscoelastic delivered. In this eye, I used 36 clicks (at 2.8 µL/click) to release viscoelastic in a controlled manner. Notably, the iTrack features a patented, pressurized mechanism for viscoelastic release across the entire 360° of SC.

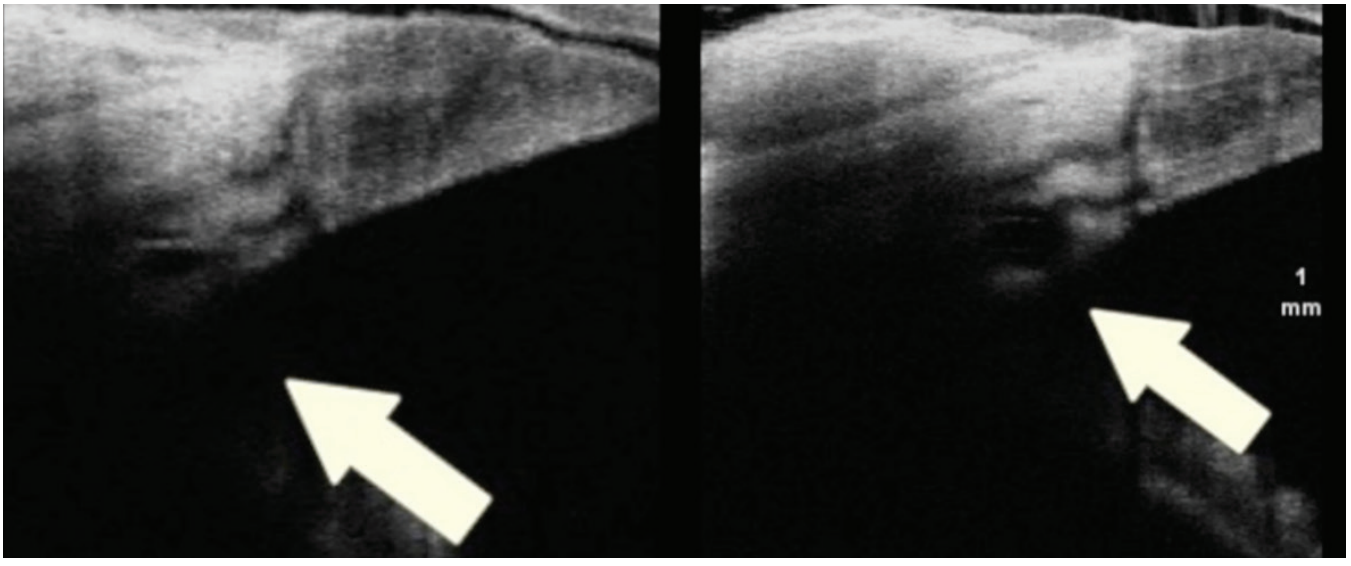

Figure 4. Side-by-side comparison of pre- and post-delivery of viscoelastic demonstrating three distinct mechanistic effects. (1) The SC. Expansion of the SC can be easily appreciated (white arrow). (2) Collector Channels. In the post image (right), there is also evidence of the impact of canaloplasty on the collector channels (black, wavy lines extending from the SC border), with the opening to the channel more evident and the channel as a whole appearing to be dilated, suggesting that fluid is now draining through these structures. (3) The TM. In this view, thinning of the TM tissue is also evident.

"During canaloplasty, pressurized viscodilation dilates the diameter of the canal by 2 to 3 times.[12] Video from the case... shows dilation of the canal after the microcatheter has been removed, thus confirming that it is not only the mechanical effect of intubation/catheterization that dilates the canal, but also viscodilation itself."

DISCUSSION

One of the very big challenges inherent to treating glaucoma is that we cannot be certain where resistance is occurring. However, one of the greatest opportunities with a procedure like canaloplasty is that we can address resistance at multiple points of the outflow pathway. The positive outcomes data we have amassed to date,[1-3] indicating reliable and consistent IOP lowering, are proof that iTrack has a clinically meaningful benefit. The fact that we can typically reduce medication burden suggests that the procedure is having a physiologic effect. Imaging captured on intraoperative OCT adds proof of the intended mechanism of canaloplasty, showing us that, indeed, the SC is being dilated, that the collector channels are expanding, and that the trabecular tissues are being stretched (Figure 4).

The MIGS era has ushered in a new mindset for glaucoma intervention, one in which we have been challenged to think more about the mechanisms of treatment and the intended target for procedures. Clinical outcomes data are more or less a surrogate marker that an intervention is achieving its intended effect; advances in technology, such as intraoperative OCT, allow a greater facility to demonstrate the effects at the intended target. In this way, we can start to understand whether the anatomic effect of any given intervention has any clinically meaningful impact.

In eyes with primary open-angle glaucoma, we know that up to 75% of outflow resistance occurs at the TM, with the juxtacanalicular portion of the TM immediately adjacent to the SC accounting for the majority of reduced outflow facility.[5] Canaloplasty has two effects in this regard: Herniations are mechanically disrupted, and any pigment that is present is pushed back into the TM. Importantly, this is accomplished by leaving the trabecular tissue in place, rather than via removal. This preserves an important mechanism of regulating pressure dynamics.[6-10] Further, the preservation of TM tissue leaves future treatment options open—an important consideration in cases of mild to moderate glaucoma. As shown with live anterior-segment OCT, canaloplasty has a complementary effect on the TM structure: As the trabecular beams become stretched, they become more porous to improve outflow facility.

While the TM is an important aspect of aqueous outflow dynamics, other components of the complex aqueous pathway are also highly relevant. Up to 50% of decreased outflow resistance is due to blockages within the SC.[11] During canaloplasty, pressurized viscodilation dilates the diameter of the canal by 2 to 3 times.[12] Video from the case highlighted here shows dilation of the canal after the microcatheter has been removed, thus confirming that it is not only the mechanical effect of intubation/catheterization that dilates the canal, but also viscodilation itself.

Lastly, blockage of collector channels results in increased outflow resistance.[13] In live anterior-segment OCT, we can see dilation of the collector channels, not only at the junction with the canal, but along the full length of the collector channel. Taken together, there is proof of restoration of the conventional outflow pathway after iTrack, which in turn creates an

important physiologic linkage to distal drainage to the episcleral veins.

There are two important limitations of the exploratory investigation reported here that point to future areas of possible research. First, live, intraoperative anterior segment OCT was performed only during the viscodilation step. On the one hand, this allows us to delineate the effects of viscodilation on the anatomic structures under review. However, it would be interesting to review intraoperative OCT during the microcatherization phase of the canaloplasty procedure to understand how each part of the procedure targets resistance within the aqueous outflow pathway.

Second, live intraoperative OCT assesses only structural effect. It would be interesting to review a larger series of patients and follow them for clinical outcomes (ie, IOP and medication outcomes postoperatively), in addition to structural effect, thus providing insights on structure-function relationships associated with the iTrack procedure. While a clinically meaningful outcome was achieved in the patient in this report, we do not have follow-up OCT imaging to review the patency of the SC over time. It is likely that the canal will regress as the viscoelastic is removed by the eye; however, the relative patency after that occurs is unknown, nor do we have insight on how that reduction in patency might impact outflow dynamics. The recently published 36-month study from Gallardo provides confidence that the effect is durable; it would be interesting to be able to follow eyes after an iTrack procedure with advanced imaging to complete the picture.[3] ■

"In live anterior-segment OCT, we can see dilation of the collector channels, not only at the junction with the canal, but along the full length of the collector channel."

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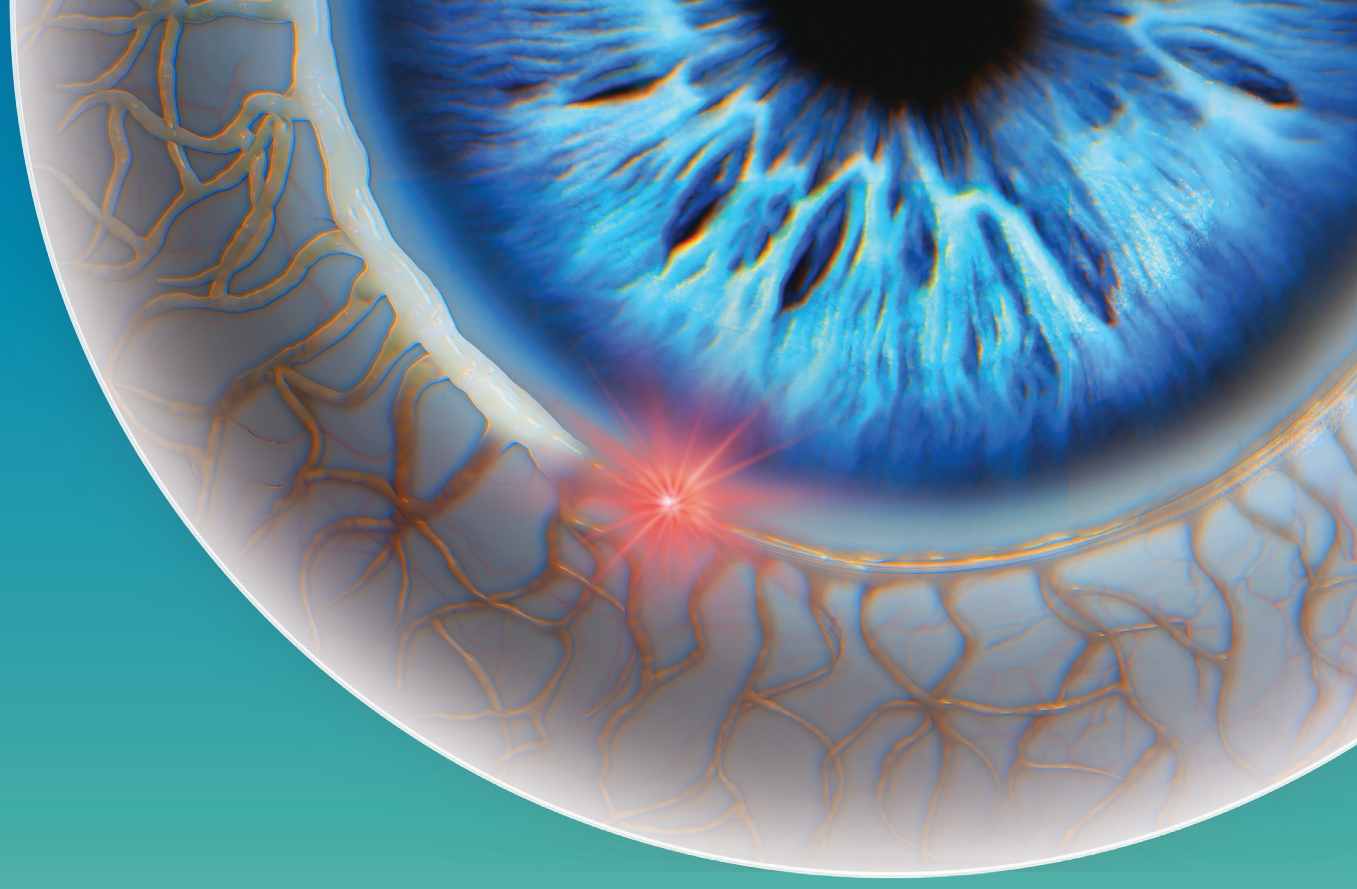

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For over a decade, Nova Eye's proprietary **iTrack™** canaloplasty device has been used across the globe, combining pressurized viscodilation with catheterization over the entire 360° of the conventional outflow pathway – with the added benefit of an illuminated microcatheter – to effectively treat more than 100,000 glaucoma patients.

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