Exploring Uveoscleral Outflow

A new treatment system seeks to take the bleb out of glaucoma surgery.

By Julia T. Lewandowski, Senior Associate Editor

Glaucoma Today's *"Innovators" column will profile promising technological developments in glaucoma and the companies bringing them to fruition.*

Throughout the past decade, the completion of several landmark studies and the development of new imaging technologies have given ophthalmologists unprecedented insight into the structural changes that accompany glaucomatous progression. Unfortunately, a revolution in the surgical treatment of the disease has not yet occurred. Despite the development of less invasive procedures such as selective laser trabeculoplasty (SLT) and argon laser trabeculoplasty, bleb-based filtration surgery is still the primary treatment option for glaucoma refractory to medical therapy.

In the search for alternative surgical therapies, glaucoma specialists are increasingly interested in the drainage potential of the suprachoroidal space. The Solx Glaucoma Treatment System (not available in the US; Occulogix, Inc., Mississauga, Ontario, Canada) represents one such surgical approach.

The Power of Observation

In 2000, entrepreneur Doug Adams surveyed hundreds of glaucoma specialists, many of whom expressed dissatisfaction with the scope of surgical options currently available. His solution was to establish Solx, Inc., a Boston-based research and development company. (Solx is now a division of Occulogix, Inc.)

The first technology acquired by Solx, Inc., was the titanium-sapphire laser. Originally developed in the early 1990s by Joseph Lowery, MSBE; Shlomo Melamed, MD; and Jim Hsia, PhD, for ab interno sclerostomy, this laser produced disappointing results when it was used in conjunction with an energy-absorbing chromophore dye. When the laser was applied to the eye's trabecular meshwork without the dye, however, the investigators observed a rapid reduction in the IOP,[1,2] sometimes within 10 minutes after treatment. With the help of the laser's inventors, Solx, Inc., developed a trabeculoplasty procedure that took advantage of the laser's near-infrared, 790-nm wavelength (Figure 1).

Figure 1. Applying the Solx 790 laser to the trabecular meshwork (black arrow) removes debris from this structure without damaging the surrounding tissue.

The Solx 790 laser's mechanism of action is similar to that of the blue-green argon (wavelength = 488 to 514 nm) and the green Nd:YAG (wavelength = 532 nm) lasers used for argon laser trabeculoplasty and SLT, respectively. All three lasers selectively remove debris from the trabecular meshwork, but the Solx 790 penetrates the structure more deeply (to approximately 200 µm), thus opening more drainage channels and improving aqueous outflow. In addition, histological examination of donor eyes exposed to SLT and the titanium-sapphire laser suggests that the former is more likely to cause thermal damage to the trabecular meshwork than the latter.[3]

Although Mr. Adams and his colleagues were encouraged by the IOP-lowering capabilities of the Solx 790 laser, they realized that this technique only partially satisfied the company's mission to eliminate glaucoma physicians' dependence on the bleb. Thus, they decided to investigate a new surgical approach for improving uveoscleral outflow.

Goodbye to the Bleb

When Solx, Inc., began recruiting scientists and engineers to develop a new drainage device, the company deliberately hired individuals whom they felt would not favor bleb-based procedures. The company's developmental strategy also included a comprehensive survey of more than 20 years' worth of ophthalmic literature, an approach that uncovered a description of a jeweler who had a piece of gold removed from his eye after 10 years.[4] A laboratory analysis had shown that the metal was completely free of proteins and cells, which suggested that this metal could work well inside the eye.

A second discovery came from an investigation of uveoscleral outflow in monkeys that showed that the IOP in the suprachoroidal space was always negative compared with the IOP in the anterior chamber.[5] The researchers at Solx, Inc., realized that a device connecting these two areas might be able take advantage of this negative gradient to lower IOP.

Using these data as a starting point, the development team at Solx, Inc., designed the Gold Micro-Shunt (GMS). Unlike traditional glaucoma drainage devices, which lower IOP by redirecting aqueous fluid through a tube from the anterior chamber to a filtering bleb, the GMS is a flat device that sits completely within the eye's suprachoroidal space. According to the company, the negative pressure there draws aqueous fluid from the anterior chamber through the 24-karat gold implant's 40-µm internal microtubules (Figure 2).

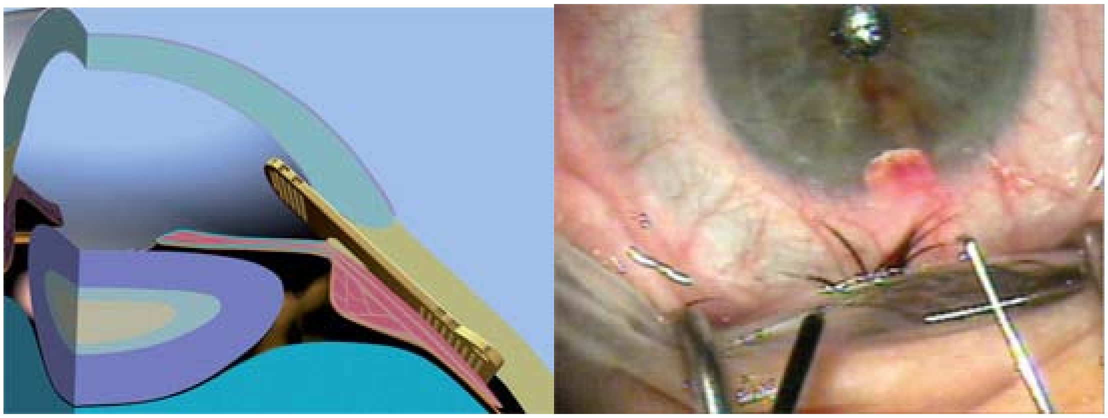

Figure 2. The GMS improves uveoscleral outflow by facilitating the flow of aqueous from the anterior chamber into the suprachoroidal space (left). The implant is visible in the anterior chamber after its insertion through a clear corneal incision (right).

An Interesting Experiment

The team at Solx, Inc., originally developed the Solx 790 laser and the GMS as stand-alone therapies for glaucoma. One day, however, Gabriel Simon, MD, PhD, the company's director of clinical research and the inventor of the drainage device, decided to see what would happen if he fired the laser into the gold shunt. When the laser created a perfect hole in the GMS, he realized that combining these technologies might allow surgeons to customize the rate at which aqueous flowed from the anterior chamber into the suprachoroidal space.

"We are currently focused on demonstrating the clinical safety and effectiveness of the laser and the GMS in clinical trials," Mr. Adams said in an interview with Glaucoma Today. The Solx 790 laser and the Solx GMS are approved only for experimental use in the US pending the results of phase 3 clinical trials.

Clinical Results

To date, surgeons have implanted more than 300 Solx GMS devices worldwide. Two-year follow-up data from a prospective study presented during the 17th Annual Meeting of the AGS in San Francisco showed that the GMS lowered IOP by an average of 30%.[6] The mean IOP in 18 of 76 eyes decreased from 27.7 ±7.9 to 19.7 ±3.3 mm Hg by 24 months postoperatively.

Iqbal Ike K. Ahmed, MD, a consultant for Solx, Inc., Assistant Professor at the University of Toronto, and Clinical Assistant Professor for the John A. Moran Eye Center at the University of Utah in Salt Lake City, has treated more than 20 patients with the GMS. He is also a principal investigator for the ongoing FDA trial comparing the device with the Ahmed Glaucoma Valve (New World Medical, Inc., Rancho Cucamonga, CA).

"Previous attempts to harness the suprachoroidal space's potential, such as cyclodialysis clefts and suprachoroidal silicone tubes, have not been very successful," Dr. Ahmed said in an interview with GToday. "In my experience, however, the GMS has significantly lowered IOP while reducing serious complications."

Except for some transient postoperative hypotony, the only complication Dr. Ahmed has observed with the GMS occurred when the implant came into contact with the cornea. "For the most part, proximity with the cornea has not been an issue, but I have observed cellular growth over the implant in some patients," he said. "This complication can be avoided by positioning the implant posteriorly within the anterior chamber, however."

Dr. Melamed, Director of the Sam Rothberg Glaucoma Center, Goldschleger Eye Institute, Sheba Medical Center, Tel-Hashomer, Israel, and a consultant for Solx, Inc., has implanted approximately 80 GMS devices. During the 2006 AAO Annual Meeting, he reported that the number of IOP-lowering medications used by patients who received the device decreased from 2.0 ±1.2 preoperatively to 1.2 ±0.8.[7]

Despite his early promising results, Dr. Melamed anticipates that additional design changes will improve the GMS' function. "I believe the shunt failed in some of my patients because the microtubules were obstructed by scar tissue," he told GToday. "This problem may be avoided in the future by enlarging the channels to 60 or 80 µm, or by applying an antimetabolite such as 5-fluorouracil to the suprachoroidal space. We plan to investigate these strategies in future studies." Dr. Melamed is currently investigating the IOP-lowering capability of the next-generation, 60-µm Solx GMS Plus.

Improving Uveoscleral Outflow

"We need to learn a lot more about the physiology of the suprachoroidal space before we fully understand its IOP-lowering potential," said Dr. Ahmed. Nevertheless, he believes that the Solx GMS may be an alternative to trabeculectomy for high-risk glaucoma patients whose IOPs cannot be controlled with medical therapy. First, however, he said that studies must determine not only if the implant works, but if it works well enough.

Iqbal Ike K. Ahmed, MD, may be reached at (905) 820-3937; ike.ahmed@utoronto.ca.
Shlomo Melamed, MD, may be reached at +1 972 522 866 736;
melamed_shlomo@hotmail.com.

Doug Adams is the president of the Glaucoma Division at Occulogix, Inc. He may be reached at (978) 808-6926; doug.adams@occulogix.com.

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