

Point/Counterpoint:

Will Surgery Become the First Line of Glaucoma Treatment in the United States?

It is highly unlikely.

BY SHAN C. LIN, MD



Incisional surgery is very unlikely to become the preferred first line of treatment for glaucoma in the near or distant future in the United States. The relative effectiveness of glaucoma medications and the downside of surgery have combined to create a treatment protocol in which medications are used first and surgery is deferred until maximal medical treatment is inadequate to prevent progression of the disease.

SURGERY TODAY

Trabeculectomy remains the standard incisional glaucoma surgery. In some parts of the world, including England, surgery has been considered the optimal initial therapy to prevent visual field loss. Furthermore, there is evidence that the long-term use of medications increases the likelihood of scarring after trabeculectomy,¹ which suggests that surgery should be the first line. Sponsored by the National Institutes of Health, the Collaborative Initial Glaucoma Treatment Study (CIGTS) was designed to determine whether trabeculectomy or medication is the best initial treatment.^{2,3} At 5 years, there was no clinically significant difference in visual field progression between the two groups. In terms of quality of life and ocular symptoms, however, the surgical group had more local eye symptoms and reported more problems with activities related to visual acuity.

Many surgeons have considered tube shunts to be a safer alternative than trabeculectomy. In the prospective Tube Versus Trabeculectomy (TVT) study, however, the mean IOP and number of medications used by patients 3 years after surgery were similar between the patients that received a Baerveldt glaucoma implant (Abbott Medical Optics Inc., Santa Ana, CA) and those who underwent a trabeculectomy.⁴ The rates of serious complications and reoperations also were not substantially different. Are tubes a plausible alternative for the first-line treatment of glaucoma? Hardly.

SURGERY TOMORROW

Efficacy

What about the current crop of new glaucoma surgeries that purportedly possess an improved safety profile and are associated with fewer complications? In a recent ophthalmic technology assessment, the American Academy of Ophthalmology reviewed many novel surgeries for glaucoma.⁵ They included the Fugo blade (Medisurg Ltd., Norristown, PA), the Ex-Press Glaucoma Filtration Device (Alcon Laboratories, Inc., Fort Worth, TX), the Solx Gold Shunt (Solx, Inc., Boston, MA; not available in the United States), excimer laser trabeculectomy (AIDA excimer laser system; TuiLaser AG, Gerning, Germany; not available in the United States), canaloplasty (iScience Interventional, Menlo Park, CA), trabeculotomy by an internal approach (Trabectome; NeoMedix Corporation, Tustin, CA), and a trabecular microbypass stent (iStent; Glaukos Corporation, Laguna Hills, CA; not available in the United States). Thus far, no prospective, randomized trials have compared these new techniques to the reference standard for glaucoma surgery—trabeculectomy. Quite likely, none of them will have greater efficacy than trabeculectomy with adjunctive antimetabolite therapy. Based on limited peer-reviewed data, most of these procedures would have poorer efficacy than trabeculectomy in terms of reducing patients' IOP and their need for medication.

Consequently, the potential benefits of these new procedures are fewer complications such as a shallow/flat anterior chamber, hypotony, blebitis/endophthalmitis, and ocular dysesthesia. In these situations where the efficacy is mild but the complications are relatively low, the clinician needs to decide if the cost-benefit ratio is in the patient's best interest. Given the efficacy and safety of current drugs such as the prostaglandin analogues, the scale tips toward medication as the best first-line treatment.

(Continued on page 40)

Safer, more efficacious procedures will mean earlier surgery.

BY GARRY P. CONDON, MD



Why shouldn't we ophthalmologists consider the possibility that incisional surgery will eventually replace medications as first-line therapy for established primary open-angle glaucoma here in the United States? The answer has come down to safety. None of us doubts the historic efficacy of trabeculectomies and tube shunts when it comes to dramatically lowering IOP, but we cannot shake our concerns about safety and predictability. For that reason, to this day, we continue to relegate our questionably compliant patients to the often expensive, frequently ineffective realm of medical therapy despite the potential for adverse reactions. For many patients, medication is neither the answer nor the best first-line approach. We need to do better.

IMPROVEMENTS ALREADY

For many of us, compared with argon laser trabeculectomy, selective laser trabeculectomy represents a more refined and less traumatic nonincisional surgical modality that we are willing to use as first-line therapy for early glaucoma. Can we move toward creating a disconnection between the increased risks inherent in traditional incisional surgery while achieving its historical efficacy? That is a work in progress.

Although aimed at patients with advanced disease, the Tube Versus Trabeculectomy (TVT) Study validated the safety and efficacy of tubes to the extent that a new study is underway to compare these two approaches as primary surgery.¹ Three-year data on canaloplasty (iScience Interventional, Menlo Park, CA) as primary surgery or in combination with cataract surgery point to a 30% reduction in IOP with a low rate of complications.² Other recent work suggests that modifying trabeculectomy by incorporating the Ex-Press Glaucoma Filtration Device (Alcon Laboratories, Inc., Fort Worth, TX) can lead to faster visual recovery while being as effective as

standard trabeculectomy.³ Clearly, we are improving on traditional surgical approaches.

The appeal of minimally invasive glaucoma surgery (MIGS) is its proven safety relative to the old standby surgical procedures. The goal is reducing complications. George Spaeth, MD, once said to me, "An operation that works half the time, with few complications, can be a great operation for glaucoma." That thought underscores the growing interest in MIGS. New surgical approaches aim to access the indigenous outflow system or the supra-choroidal space. Examples of the former include the Trabectome, iStent, and Hydrus (respectively, NeoMedix Corporation, Tustin, CA; Glaukos Corporation, Laguna Hills, CA; and Ivantis Inc., Irvine, CA; iStent and Hydrus not available in the United States).^{4,5} The latter include the Transcend CyPass System and Solx Gold Shunt (respectively, Transcend Medical, Menlo Park, CA, and Solx Inc., Waltham, MA; neither available in the United States). Effective nontransscleral approaches with low complications would be attractive, especially considering how easily they could be combined with standard cataract surgery.

In addition to their safety profiles, what makes MIGS procedures attractive as a means of intervening early in a patient's disease is that they do not prevent us from performing more traditional surgery at a later date, if needed.

COMPLIANCE

I believe that patients experience less long-term IOP fluctuation when their pressure is lowered surgically rather than medically. That is because we cannot expect our patients to adhere to prescribed topical therapy as ideally as do subjects in a clinical trial. I ask my patients to estimate how closely they are following their drug regimen, because I want an idea of their real-life experience. Patients who tell me they miss their drops more often than they take them may benefit from surgical intervention.

(Continued on page 56)

(Continued from page 38)

A Combined Approach

There is a trend toward conducting studies that compare a new glaucoma procedure in conjunction with cataract surgery using phacoemulsification to cataract surgery alone.^{6,7} The combined procedure often provides a marginal added benefit in terms of reducing IOP and the need for medication. Can surgery truly be considered the first line in this situation, however, when the overriding reason to perform surgery in many of these cases was to remove the cataract to improve visual acuity? Also, the cataract surgery by itself often lowers the IOP and can reduce the patient's need for glaucoma medications postoperatively. Perhaps phacoemulsification, then, can be considered a reasonable and safe first-line treatment for mild glaucoma.

The Ideal

Certainly, the possibility exists that future developments in incisional surgery will yield a technique that is nearly as efficacious as trabeculectomy but is much safer and more predictable. Ideally, surgery would also be long lasting, have a fast recovery time, and allow for repeatability and other potential surgeries such as trabeculectomy. Given such requirements, the likelihood of such a procedure's being developed in the next 5 years is low.

THE DRAWBACKS OF TOPICAL THERAPY

A clear downside of topical medication is noncompliance. Eye drops are difficult to administer, and the elderly often forget to use them. An obvious advantage of surgery is that the ophthalmologist performs the treatment rather than the patient, but the continued development of newer and more potent medications will help to reduce the problem of noncompliance. The availability of prostaglandin analogues is an example of this progression in drug development. This class of medication is very potent, enduring (once-a-day dosing), and systemically safe. Several new classes of medications are already in clinical trials, including rho kinase inhibitors, serotonin receptor antagonists, and EP receptor agonists. Their approval might help physicians prevent progressive visual field loss.

Also on the horizon are better methods of delivering medication. Slow-release depots of prostaglandins and other drugs are already being tested. Potential areas for these depots include the punctal, subconjunctival, sub-Tenon, anterior chamber, and vitreous spaces. Successful developments in this arena, rather than in the surgical field, are more likely to result in future advances in the initial treatment of glaucoma.

ECONOMICS

Are there particular situations or social/economic circumstances in which incisional surgery is a reasonable first-line option? Certainly. In a recent case of neovascular glaucoma at my county hospital, the patient's IOP was 80 mm Hg and did not respond to maximal medical therapy over the course of 6 hours. Because the patient's visual acuity was in the usable range, he was taken to the OR for the urgent placement of a tube. The patient's IOP decreased to the teens, and his visual acuity was stabilized.

Additionally, in some parts of the world, medications are not readily available and/or are too expensive. Although not an incisional surgery, transscleral cyclophotocoagulation was used with some success in Ghana as a first-line treatment.⁸

CONCLUSION

Medications will probably remain the predominant first-line therapy for the treatment of glaucoma in the developed world. Current surgical techniques have not reached a level of safety and efficacy that justifies their use as initial treatment in the vast majority of cases. Future advances in medical treatment and delivery are likely to outpace surgical development, so drug therapy will remain the mainstay of first-line treatment. □

Shan C. Lin, MD, is a professor of clinical ophthalmology, Department of Ophthalmology, University of California, San Francisco. He is a consultant to Alcon Laboratories, Inc., and Allergan, Inc. Dr. Lin may be reached at (415) 514-0952; lins@vision.ucsf.edu.

1. Wilensky JT. The role of medical therapy in the rank order of glaucoma treatment. *Curr Opin Ophthalmol*. 1999;10(2):109-111.
2. Lichter PR, Musch DC, Gillespie BW, et al; CIGTS Study Group. Interim clinical outcomes in the Collaborative Initial Glaucoma Treatment Study comparing initial treatment randomized to medications or surgery. *Ophthalmology*. 2001;108(11):1943-1953.
3. Janz NK, Wren PA, Lichter PR, et al; CIGTS Study Group. The Collaborative Initial Glaucoma Treatment Study: interim quality of life findings after initial medical or surgical treatment of glaucoma. *Ophthalmology*. 2001;108(11):1954-1965.
4. Gedde SJ, Schiffman JC, Feuer WJ, et al; Tube Versus Trabeculectomy Study Group. Three-year follow-up of the Tube Versus Trabeculectomy Study [published online ahead of print August 11, 2009]. *Am J Ophthalmol*. 2009;148(5):670-684.
5. Francis BA, Singh K, Lin SC, et al. Novel glaucoma procedures. A report by the American Academy of Ophthalmology. *Ophthalmology*. In press.
6. Samuelson TW, Katz LJ, Wells JM, et al; US iStent Study Group. Randomized evaluation of the trabecular micro-bypass stent with phacoemulsification in patients with glaucoma and cataract [published online ahead of print September 15, 2010]. *Ophthalmology*. 2011;118(3):459-667.
7. Berke SJ, Sturm RT, Caronia RM, et al. Phacoemulsification combined with endoscopic cyclophotocoagulation (ECP) in the management of cataract and medically controlled glaucoma: a large, long term study. Paper presented at: American Glaucoma Society Annual Meeting; Charleston, SC; March 4, 2006.
8. Egbert PR, Fiadoyor S, Budenz DL, et al. Diode laser transscleral cyclophotocoagulation as a primary surgical treatment for primary open-angle glaucoma. *Arch Ophthalmol*. 2001;119(3):345-350.

(Continued from page 39)

A LITTLE NOW OR A LOT LATER?

The chief criticism of the new MIGS procedures is that they are less efficacious than trabeculectomy. Incrementally lowering a patient's IOP earlier in the course of the disease, however, can increase his or her chance of maintaining visual function longer. MIGS may delay this patient's need for riskier surgery. Moreover, many individuals with glaucoma do not need an IOP below the mid-teens. In fact, I see patients with pressures of 10 mm Hg who do not see well, because their IOP is too low.

LOOK FORWARD, NOT BACKWARD

In the long term, will our overall rate of surgical complications be lower? That is the subject of current study. Certainly, my level of confidence in surgical intervention is far higher than it was 15 years ago. I am more comfortable intervening earlier in the disease process than in the past. A current problem of glaucoma surgery, however, is that we are performing it on eyes with advanced disease. MIGS may allow us to intervene before the outflow system can no longer be revived.

Ophthalmologists who lack enthusiasm for MIGS bemoan the absence of well-structured studies—research that really has just begun. It does not benefit our field or our patients to trash the new procedures from the sidelines. What we need is more experience performing MIGS so that we can attempt to improve the procedures' efficacy without compromising safety. Ideally, the results will improve to the point that we need not justify performing these surgeries by combining them with other interventions such as cataract extraction. □

Garry P. Condon, MD, is an associate professor of ophthalmology at Drexel University College of Medicine, a clinical associate professor at the University of Pittsburgh, and the chairman of the Department of Ophthalmology at Allegheny General Hospital in Pittsburgh. He is a consultant to Alcon Laboratories, Inc., and Allergan, Inc. Dr. Condon may be reached at (412) 359-6298; garrycondon@gmail.com.

1. Gedde SJ, Schiffman JC, Feuer WJ, et al; Tube Versus Trabeculectomy Study Group. Three-year follow-up of the Tube Versus Trabeculectomy Study [published online ahead of print August 11, 2009]. *Am J Ophthalmol*. 2009;148(5):670-684.
2. Lewis RA, von Wolff K, Tetz M, et al. Canaloplasty: three-year results of circumferential viscodilation and tensioning of Schlemm canal using a microcatheter to treat open angle glaucoma. *J Cataract Refract Surg*. 2011;37:682-690.
3. Good TJ, Kahook MY. Assessment of bleb morphologic features and postoperative outcomes after Ex-Press drainage device implantation versus trabeculectomy. *Am J Ophthalmol*. 2011;151:507-513.
4. Samuelson TW, Katz LJ, Wells JM, et al; US iStent Study Group. Randomized evaluation of the trabecular micro-bypass stent with phacoemulsification in patients with glaucoma and cataract. *Ophthalmology*. 2011;118(3):459-467.
5. Francis BA, Winarko J. Combined Trabectome and cataract surgery versus combined trabeculectomy and cataract surgery in open-angle glaucoma. *Clinical and Surgical Ophthalmology*. 2011;29:2/3.