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Interpretation and Misinterpretation of Results from the Tube Versus Trabeculectomy (TVT) Study

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INTRODUCTION

Glaucoma drainage devices, commonly referred to as tube shunts, are increasingly being utilized in the surgical management of glaucoma as an alternative to trabeculectomy in the United States. Medicare claims data show a 43% decrease in the number of trabeculectomies performed between 1995 and 2004 and a concurrent 184% increase in tube shunt surgery.¹ Surveys of the American Glaucoma Society membership reveal a lack of consensus regarding the best glaucoma surgical approach in patients who have undergone prior ocular surgery.^{2,3} In particular, some glaucoma surgeons favor placement of a tube shunt while others prefer trabeculectomy with an adjunctive antifibrotic agent for patients who require a glaucoma surgical procedure and have previously undergone either cataract extraction or failed filtering surgery. These two groups of patients, historically deemed to be at increased risk for trabeculectomy failure, were evaluated in the Tube Versus Trabeculectomy (TVT) Study to provide additional information in an effort to guide surgical decision making.

The TVT Study is a multicenter randomized clinical trial comparing the safety and efficacy of tube shunt surgery to trabeculectomy with mitomycin C (MMC) in patients with previous cataract and/or glaucoma surgery. Results of the TVT Study have been published through the first 3 years of follow-up.^{4–8} This review highlights major conclusions derived from study data, as well as misinterpretations of study results.

STUDY DESIGN

The design and methods of the TVT Study have been previously described in detail.⁴ The study is registered with <http://www.clinicaltrials.gov> (NCT00306852). A synopsis of the TVT Study design features is provided in Table 1. Enrolled patients were randomly assigned to treatment with a tube shunt or trabeculectomy with MMC. Patients in the tube group

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underwent placement of a 350-mm² Baerveldt glaucoma implant (Abbott Medical Optics, Abbott Park, Illinois, USA) in the superotemporal quadrant with a complete restriction of flow at the time of implantation. Patients in the trabeculectomy group had a superior trabeculectomy with a standard dosage of MMC of 0.4 mg/ml for 4 minutes. Follow-up visits were scheduled 1 day, 1 week, 1 month, 3 months, 6 months, 1 year, 18 months, 2 years, 3 years, 4 years, and 5 years postoperatively. Each examination included measurement of Snellen visual acuity (VA), intraocular pressure (IOP), slit lamp biomicroscopy, Seidel testing, and ophthalmoscopy. Standard automated perimetry, Early Treatment Diabetic Retinopathy Study (ETDRS) VA, and quality of life assessment made with the National Eye Institute Questionnaire (NEI VFQ-25) were performed at baseline and at the annual follow-up visits. A formal motility evaluation was performed in all patients at baseline and at the 1-year and 5-year follow-up visits, and at any visit after 3 months if the patient reported diplopia. The examining clinician provided a reason for loss of two or more lines of Snellen VA at follow-up visits after 3 months.

Failure was prospectively defined as IOP > 21 mm Hg or not reduced by 20% below baseline on two consecutive follow-up visits after 3 months, IOP ≥ 5 mm Hg on two consecutive follow-up visits after 3 months, reoperation for glaucoma, or loss of light perception vision. Reoperation for glaucoma or a complication was defined as additional intervention that required a return to the operating room. Cyclodestruction, whether performed in the clinic or operating room setting, was deemed to be a reoperation for glaucoma while vitreous biopsy with intravitreal antibiotic injection was classified as a reoperation for a complication. Serious complications included those that were associated with loss of two or more lines of Snellen VA, as well those requiring reoperation to manage the complication.

STUDY POPULATION

A total of 212 eyes of 212 patients were enrolled at 17 Clinical Centers, including 107 in the tube group and 105 in the trabeculectomy group.⁴ The mean age of the study population was 71.0 years, and 53% were women. The baseline IOP was 25.3 ± 5.3 mm Hg (mean $\pm$ SD) on 3.1 ± 1.2 glaucoma medications (mean $\pm$ SD), and 81% of patients had primary open-angle glaucoma. Among enrolled patients, 44% had prior cataract surgery, 35% trabeculectomy, and 20% combined cataract and glaucoma surgery as the qualifying previous ocular surgery for the study. The demographic and ocular characteristics were not significantly different between the tube group and the trabeculectomy group, suggesting that randomization was very effective in generating two balanced treatment groups.

INTERPRETATION OF RESULTS

1. Tube shunt surgery had a higher success rate than trabeculectomy with MMC during the first 3 years of follow-up

The cumulative probability of failure was 15.1% in the tube group and 30.7% in the trabeculectomy group at 3 years, a difference that was statistically significant ($p = 0.010$, log rank test adjusted for stratum).⁸ Kaplan-Meier plots of the probability of failure are shown in Figure 1. The most common reason for failure during the first 3 years was inadequate IOP

control (i.e. reoperation for glaucoma or IOP above the failure criteria) in both the tube group (87% of failures) and the trabeculectomy group (68% of failures). Persistent hypotony was a less frequent reason for treatment failure in the tube group (13% of failures) and the trabeculectomy group (29% of failures), and only 1 patient in the trabeculectomy group lost light perception vision. No significant difference in the distribution of reasons for treatment failure was observed between treatment groups ($p = 0.71$, exact permutation chi-square test).

2. Both surgical procedures were associated with similar IOP reduction and use of supplemental medical therapy at 3 years

Data on IOP and glaucoma medical therapy at baseline and at the annual follow-up visits during the first 3 years of the study are presented in Table 2. Intraocular pressure measurements for patients who underwent additional glaucoma surgery were included in the analysis only until the point of reoperation. The trabeculectomy group achieved significantly lower mean IOPs than the tube group at all follow-up visits during the first three months, but no significant difference in the degree of IOP reduction persisted between treatment groups after 3 months.^{5,8} Supplemental medical therapy use was significantly greater in the tube group compared with the trabeculectomy group at all follow-up visits during the first 2 postoperative years. However, there was increasing utilization of medications in the trabeculectomy but not in the tube group in the 1 to 3 year follow-up period such that the mean number of medications did not differ between treatment groups at 3 years.⁸

3. Early postoperative complications occurred more frequently after trabeculectomy with MMC compared with tube shunt surgery, but both procedures had similar rates of late postoperative complications and serious complications

Early postoperative complications, defined as complications that developed during the first month after surgery, were more common in the trabeculectomy group (35%) than the tube group (21%) ($p = 0.026$, chi-square test).⁸ The rate of late postoperative complications occurring after 1 month was similar in the tube group (28%) and the trabeculectomy group (31%) through 3 years of follow-up ($p = 0.70$, chi-square test). All complications are not equal in severity, and serious complications requiring reoperation and/or loss of two or more Snellen lines of vision occurred with similar frequency in the trabeculectomy group (27%) and tube group (22%) at 3 years ($p = 0.58$, chi-square test). Wound leaks ($p = 0.004$, chi-square test), dysesthesia ($p = 0.018$, Fischer's exact test), and bleb leaks ($p = 0.028$, Fisher's exact test) were significantly more common in the trabeculectomy group compared with the tube group. New postoperative motility disturbances developed more frequently in the tube group (9.9%) than the trabeculectomy group (0%) during the first year of follow-up ($p = 0.005$, Fisher's exact test),⁷ and there was a tendency for diplopia to occur more commonly in the tube group (5%) compared with the trabeculectomy group (0%) ($p = 0.06$, Fisher's exact test).^{7,8}

Multivariate risk factor analysis at the 1 year postoperative time point revealed that persistent corneal edema ($p < 0.001$, exact permutation logistic regression) and choroidal effusion ($p = 0.001$, exact permutation logistic regression) were significant independent predictors of vision loss.⁶ Wound leaks ($p = 0.026$, exact permutation logistic regression) and hypotony maculopathy ($p = 0.049$, exact permutation logistic regression) were

significantly associated with treatment failure. Shallowing of the anterior chamber significantly increased the risk of cataract progression ($p = 0.008$, exact permutation logistic regression).

4. No difference in the incidence of vision loss was observed following trabeculectomy with MMC and tube shunt surgery after 3 years of follow-up

Reduction in VA occurred in both the tube and trabeculectomy groups during the first 3 years of follow-up, but Snellen and ETDRS VA were similar between treatment groups at baseline and at 3 years.⁸ The rate of loss of two or more lines of Snellen VA was not significantly different between the tube group (31%) and the trabeculectomy group (34%) after 3 years ($p = 0.65$, log rank test). Many causes of vision loss were not directly attributable to the surgical procedures under study, but rather to other ocular diseases such as macular degeneration and diabetic retinopathy. Not surprisingly, the proportion of patients who lost two or more Snellen lines was significantly higher for patients who developed postoperative complications (45%) than those without complications (20%) after 1 year of follow-up ($p < 0.001$, chi-square test).⁶

MISINTERPRETATION OF RESULTS

1. The rate of postoperative complications in the TVT study was higher than expected, particularly in eyes that underwent trabeculectomy:^{9,10}

Half of the patients in the TVT Study experienced complications during the first 3 years of follow-up, including 39% in the tube group and 60% in the trabeculectomy group.⁸ It is noteworthy that the rate of perioperative complications in the first month after trabeculectomy was 50% in the Collaborative Initial Glaucoma Treatment Study (CIGTS),¹¹ and 35% in the TVT Study. Most complications in both of these trials, such as shallowing of the anterior chamber and choroidal effusions, were transient without residual sequelae. The rigor in assessment and documentation of clinical findings substantially impacts the validity of prospective clinical trials such as the CIGTS and TVT Study, and thus it is common for such studies to report higher complication rates than retrospective case series and anecdotal self evaluations of surgical results. It is possible, and perhaps likely, that in routine clinical practice, most surgeons do not assess, much less document, findings such as mild changes in anterior chamber depth, shallow peripheral choroidal detachment or wound leakage via Seidel testing on every single postoperative visit. Such minor, transient complications are rightly not cause for concern in most clinical circumstances, but the inclusion of such information in large prospective clinical trials should enhance rather than diminish the credibility of such studies.

The TVT Study was not powered to determine the rates and differences between treatment groups in complications with low frequency of occurrence. Shallowing of the anterior chamber and wound leakage are two postoperative complications that have been cited as having “a remarkably high incidence” in the TVT Study.^{9,10} The rates of perioperative shallowing of the anterior chamber after trabeculectomy were similar in the TVT Study (10%),⁸ CIGTS (13%),¹¹ and Advanced Glaucoma Intervention Study (AGIS) (15.5%).¹² The frequency of wound leaks with trabeculectomy was slightly higher in the TVT Study

(11%)⁸ compared with CIGTS (5%)¹¹ and AGIS (6.5%).¹² However, there are fundamental differences in the study populations, use of antifibrotic agents, and methods for assessing for wound leaks between these studies. CIGTS and AGIS enrolled patients without prior ocular surgery, and MMC was not used adjunctively for any initial trabeculectomies in AGIS¹² and in only 5% of cases in CIGTS.¹¹ Patients in the TVT Study had previous cataract and/or glaucoma surgery, and all trabeculectomies were performed with adjunctive MMC. The TVT Study protocol required Seidel testing at every follow-up visit, and this method for meticulously detecting wound leaks was not used in AGIS and CIGTS. The Fluorouracil Filtering Surgery Study (FFSS) may be a more appropriate study to compare the rate of wound leaks with the TVT Study, because both studies enrolled similar patient groups (i.e. prior cataract extraction or failed filtering surgery) and employed the same protocol of compulsory Seidel testing at each visit. The rate of early postoperative wound leaks was 20% in the standard treatment group and 32% in the 5-FU group in FFSS,¹³ which is substantially higher than the 11% rate observed in the trabeculectomy group in the TVT Study.

2. A lesser need for glaucoma medical therapy is a long-term advantage of trabeculectomy over tube shunt surgery:¹⁴

The Tube Versus Trabeculectomy (TVT) Study did find greater use of supplemental medical therapy in the tube group compared with the trabeculectomy group after 1 year of follow-up, and the trabeculectomy group had a higher rate of complete success (i.e. no adjunctive medical therapy) at 1 year.⁵ However, over the 1 to 3 three year follow-up time frame, a progressive increase in the use of medical therapy was observed in the trabeculectomy group, while the number of medications remained stable in the tube group.⁸ The mean number of medications was similar between the tube group and the trabeculectomy group at 3 years, and the rate of complete success was not statistically different between treatment groups after 3 years of follow-up. Although a lesser requirement for medical therapy may be a short-term advantage of trabeculectomy over tube shunt surgery, this benefit does not appear to persist with longer follow-up. One year is generally a short time frame in the life of a glaucoma patient and if the differences in medication use within the two groups over the 1 and 3 year postoperative time frame represents a trend, one would expect that this parameter may be more favorable to the tube group in the years to come.

3. A bias against reoperating for glaucoma existed in the tube group, and this explains the higher success rate in the tube group relative to the trabeculectomy group in the TVT Study:¹⁵

Patients who fail trabeculectomy and require additional glaucoma surgery will generally undergo repeat trabeculectomy or placement of a tube shunt. In contrast, additional glaucoma surgery in eyes that fail tube shunt surgery is more complex and usually involves placement of a second tube shunt or cyclodestruction. Because investigators were not masked to the treatment assignment and the decision to reoperate was left to the surgeon's discretion, a potential bias existed in the decision to reoperate for glaucoma. We explored for this reoperation bias by comparing the IOPs and use of adjunctive medical therapy between the two treatment groups among patients who failed because of inadequate IOP control.⁸ No significant difference in mean IOP and mean number of glaucoma medications was observed

between the tube group and the trabeculectomy group at the time of reoperation for glaucoma.^{5,8} Additionally, mean IOP and the use of glaucoma medications were similar between treatment groups at the time of failure in patients with inadequate IOP reduction (i.e. IOP > 21 mm Hg or not reduced by 20% from baseline) who did not undergo a glaucoma reoperation.^{5,8} These observations strongly suggest that there was not a bias against reoperating for glaucoma. One hypothesized explanation for this lack of bias may be that the placement of a second glaucoma drainage device in the inferonasal quadrant has become an increasingly frequent option in recent years, and thus the decision to place a second tube shunt inferiorly may not have been associated with significantly greater trepidation than the placement of a first shunt superiorly in the tube and trabeculectomy groups respectively. The issue of standardization of when a reoperation must be performed in any surgical study is highly complex, and the possibility that there will be greater dropouts if surgeons are forced to follow a particular reoperation protocol rather than being allowed to use their best judgment should not be underestimated. It is reassuring that the benefit of surgeon discretion did not lead to any untoward compromise with regard to the necessity for reoperation in the TVT study.

A greater proportion of patients in the trabeculectomy group (11%) underwent additional glaucoma surgery compared with the tube group (6%), but this difference did not reach the level of statistical significance ($p = 0.091$, log rank test adjusted for stratum).⁸ While there were a greater proportion of failures in the trabeculectomy group relative to the tube group for each of the criteria for failure and not just reoperations for glaucoma, the difference in failure between the two groups was statistically significant only when all reasons for treatment failure were taken into consideration.

4. The TVT Study is actually four studies in one comparing four different patient groups based upon type of previous ocular surgery:¹⁰

During the design of the TVT Study, there was concern that the type of previous ocular surgery might be an important risk factor affecting the rate of surgical failure. Therefore, patients were stratified at randomization into four groups based upon the type of qualifying surgery.⁴ This process was successful in balancing the treatment groups with respect to type of prior ocular surgery, and removed this as a potential confounder of the results. The study was never intended to be four studies in one, and it was not powered to try to discern treatment differences between individual strata. However, it is noteworthy that stratum was not a significant risk factor for failure,⁵ and the difference in failure rates was similar among strata (non-significant treatment by stratum interaction).^{5,8}

5. The surgical procedures investigated in the TVT Study were not standardized:^{9,10}

Both surgical procedures under investigation in the TVT Study were partially standardized, allowing the surgeon some latitude to perform the operations in a manner with which he or she felt comfortable. Patients randomized to the tube group all had placement of a 350-mm² Baerveldt glaucoma implant in the superotemporal quadrant with temporary tube occlusion at the time of implantation.⁴ The type of conjunctival flap, patch graft material, use of tube fenestration, and method of tube occlusion were at the discretion of the surgeon. Each patient randomized to the trabeculectomy group underwent a trabeculectomy superiorly with

a standard dosage of MMC of 0.4 mg/ml for four minutes. The type of conjunctival flap, dimensions of the scleral flap and internal ostium, and number of flap sutures were determined by the surgeon according to his or her usual practice. While one cannot scientifically argue against complete standardization being optimal in any clinical trial, such an approach is not always practical in surgical studies. There is great variability in how glaucoma specialists perform trabeculectomy and tube implantation, and it would be virtually impossible to get all to agree on one completely standardized technique for either operation. Even if such agreement could be reached via compromise, it would undoubtedly have an adverse impact on investigator comfort level when considering enrollment of prospective subjects. Another problem with complete standardization is that anyone who does not perform this standard operation can always deny that such a study has any relevance to their own practice in which they employ a different surgical technique. Thus while partial rather than complete standardization makes any study less robust from a scientific perspective, both the investigator comfort with enrollment and the generalizability of the study results is significantly enhanced by allowing individual surgeons some discretion on how the procedure should be performed to optimize, in their opinion, the likelihood of achieving an ideal result. It is noteworthy that the investigators in the TVT study represented a broad cross-section of North American glaucoma specialists, not only with regard to geography, but also prior training and clinical experience. The three investigators who enrolled the largest number of patients into the TVT Study were trained to performed trabeculectomy and tube implantation at different fellowship programs.

6. The TVT Study showed that tube shunt surgery is a superior glaucoma procedure to trabeculectomy with MMC

Patients who underwent tube shunt surgery had a lower rate of early postoperative complications and a higher rate of surgical success than those who had a trabeculectomy with MMC after 3 years of follow-up in the TVT Study.⁸ However, mean IOP and the rate of serious complications, including loss of vision, were similar with both surgical procedures at 3 years. The TVT Study does not demonstrate clear superiority of one glaucoma operation over the other. There are other factors that must be considered when selecting a surgical procedure in similar patients with medically uncontrolled glaucoma, such as the surgeon's skill and experience with both operations, the patient's willingness to undergo repeat glaucoma surgery, and the surgeon's planned surgical approach should failure occur. Additionally, the TVT Study enrolled patients who met specific eligibility criteria, and all patients randomized to the tube group underwent placement of a 350-mm² Baerveldt glaucoma implant. The results of the study cannot be generalized to other patient groups or implant types. The value of the TVT Study does not come from showing superiority of one operation over the other, but rather in providing comparative data on the outcomes of both surgical procedures that will help surgeons in selecting the most appropriate glaucoma operation for their individual patients. While the potential that investigators of any clinical trial have preconceived notions on what the study results should be and how these results should influence practice, such has not been the case with the TVT Study. Publications of the TVT Study group have not commented on standard of care issues and have not recommended, based upon the study results or otherwise, that patients with prior cataract surgery or failed trabeculectomy must undergo drainage device implantation. While we

expect that the results of this study may have impacted the practice patterns of many in our large community, it is widely acknowledged that both tube and trabeculectomy surgery will continue to be performed for the types of patients enrolled in this study and the decision regarding which procedure is optimal for an individual patient will remain complex, requiring expertise in the art and science of glaucoma care.

CONCLUSIONS

The TVT Study offers a wealth of data comparing two commonly performed glaucoma procedures. These data should be analyzed and interpreted critically. Appropriate conclusions may then be made to help surgeons in selecting the optimal glaucoma operation for their individual patients. Additional follow-up is needed to fully evaluate the relative merits of trabeculectomy with MMC and tube shunt surgery in patients who have undergone prior cataract extraction and/or failed filtering surgery.

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References

1. Ramulu PY, Corcoran KJ, Corcoran SL, Robin AL. Utilization of various glaucoma surgeries and procedures in Medicare beneficiaries from 1995 to 2004. *Ophthalmology*. 2007; 114:2265–2270. [PubMed: 17466376]
2. Chen PP, Yamamoto T, Sawada A, et al. Use of antifibrosis agents and glaucoma drainage devices in the American and Japanese Glaucoma Societies. *J Glaucoma*. 1997; 6:192–196. [PubMed: 9211144]
3. Joshi AB, Parrish RK, Feuer WF. 2002 Survey of the American Glaucoma Society. Practice preferences for glaucoma surgery and antifibrotic use. *J Glaucoma*. 2005; 14:172–174. [PubMed: 15741822]
4. Gedde SJ, Schiffman JC, Feuer WJ, et al. The Tube Versus Trabeculectomy Study: Design and baseline characteristics of study patients. *Am J Ophthalmol*. 2005; 140:275–287. [PubMed: 16086949]
5. Gedde SJ, Schiffman JC, Feuer WJ, et al. Treatment outcomes in the Tube Versus Trabeculectomy Study after one year of follow-up. *Am J Ophthalmol*. 2007; 143:9–22. [PubMed: 17083910]
6. Gedde SJ, Herndon LW, Brandt JD, et al. Surgical complications in the Tube Versus Trabeculectomy Study during the first year of follow-up. *Am J Ophthalmol*. 2007; 143:23–31. [PubMed: 17054896]
7. Rauscher FM, Gedde SJ, Schiffman JC, et al. Motility disturbances in the Tube Versus Trabeculectomy Study during the first year of follow-up. *Am J Ophthalmol*. 2009; 147:458–466. [PubMed: 19038375]
8. Gedde SJ, Schiffman JC, Feuer WJ, et al. Three-year follow-up of the Tube Versus Trabeculectomy Study. *Am J Ophthalmol*. 2009; 148:670–84. [PubMed: 19674729]
9. Spaeth GL. Comment on TVT findings. *Ocular Surgery News*. 2009; 27(21):5.
10. Ahmed I, Lewis R, Mahdavi KN, et al. Glaucoma dialogue: Comment on three-year follow-up of the Tube Versus Trabeculectomy Study. *Int Glaucoma Review*. 2009; 11(4):159–163.
11. Jampel HD, Musch DC, Gillespie BW, et al. Perioperative complications of trabeculectomy in the Collaborative Initial Glaucoma Treatment Study (CIGTS). *Am J Ophthalmol*. 2005; 140:15–22.
12. AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS): 11. Risk factors for failure of trabeculectomy and argon laser trabeculoplasty. *Am J Ophthalmol*. 2002; 134:481–498. [PubMed: 12383805]

13. Parrish RK, Schiffman JC, Feuer WJ, et al. Prognosis and risk factors for early postoperative wound leaks after trabeculectomy with and without 5-fluorouracil. *Am J Ophthalmol.* 2001; 132:633–640. [PubMed: 11704024]
14. Katz LJ, Myers JS, Fudenberg SJ. The perils of glaucoma surgical outcomes analysis. *Am J Ophthalmol.* 2009; 148:634–635. [PubMed: 19878755]
15. Garudadri CS, Rao HL, Senthil S. Three-year follow-up of the Tube Versus Trabeculectomy Study. *Am J Ophthalmol.* 2010; 149:686–687.

APPENDIX

Participating Centers and Committees in the Tube Versus Trabeculectomy Study

Clinical Centers:

Bascom Palmer Eye Institute, Miller School of Medicine, University of Miami (Miami, Florida): Principal Investigator: Steven Gedde, M.D.; Coinvestigators: Douglas Anderson, M.D., Donald Budenz, M.D., M.P.H., Madeline Del Calvo, Francisco Fantes, M.D., Fouad El Sayyad, M.D., David Greenfield, M.D., Jessica Hochberg, Elizabeth Hodapp, M.D., Richard Lee, M.D., Ph.D., Alexia Marcellino, Paul Palmberg, M.D. Ph.D., Richard Parrish II, M.D.

Duke University (Durham, North Carolina): Principal Investigator: Leon Herndon, M.D.; Coinvestigators: Pratap Challa, M.D., Cecile Santiago-Turla, M.D.

Indiana University (Indianapolis, Indiana): Principal Investigator: Darrell WuDunn, M.D., Ph.D.

Loyola University (Maywood, Illinois): Principal Investigator: Geoffrey Emerick, M.D.

Medical College of Wisconsin (Milwaukee, Wisconsin): Principal Investigator: Dale Heuer, M.D.

Medical University of South Carolina (Charleston, South Carolina): Principal Investigator: Alexander Kent, M.D.; Coinvestigators: Carol Bradham, Lisa Langdale.

Moorfields Eye Hospital (London, England): Principal Investigator: Keith Barton, M.D.; Coinvestigator: Francesca Amalfitano, Poornima Rai, M.D.

New York Eye and Ear Infirmary (New York, New York): Principal Investigator: Paul Sidoti, M.D.; Coinvestigators: Amy Gedal, James Luayon, Roma Ovase, Katy Tai

Scripps Clinic (La Jolla, California): Principal Investigator: Quang Nguyen, M.D.; Coinvestigator: Neva Miller

St. Louis University (St. Louis Missouri): Principal Investigator: Steven Shields, M.D.; Coinvestigators: Kevin Anderson, Frank Moya, M.D.

University of California, Davis (Sacramento, California): Principal Investigator: James Brandt, M.D.; Coinvestigator: Michele Lim, M.D., Marilyn Sponzo.

University of Florida (Gainesville, Florida): Principal Investigator: Mark Sherwood, M.D.; Coinvestigator: Revonda Burke

University of Oklahoma (Oklahoma City, Oklahoma): Principal Investigator: Gregory Skuta, M.D.; Coinvestigators: Jason Jobson, Lisa Ogilbee, Adam Reynolds, M.D., Steven Sarkisian, M.D.

University of Southern California (Los Angeles, California): Principal Investigator: Rohit Varma, M.D., M.P.H.; Coinvestigators: Brian Francis, M.D., Frances Walonker

University of Texas Houston (Houston, Texas): Principal Investigator: Robert Feldman, M.D.; Coinvestigators: Laura Baker, Nicholas Bell, JoLene Carranza, Athena Espinoza

University of Virginia (Charlottesville, Virginia): Principal Investigator: Bruce Prum, M.D.; Coinvestigator: Janis Beall

University of Wisconsin (Madison, Wisconsin): Principal Investigator: Todd Perkins, M.D.; Coinvestigators: Paul Kaufman, M.D., Tracy Perkins, Barbara Soderling.

Statistical Coordinating Center, Bascom Palmer Eye Institute, Miller School of Medicine, University of Miami (Miami, Florida): William Feuer, M.S., Luz Londono, Joyce Schiffman, M.S., Wei Shi, M.S.

Safety and Data Monitoring Committee: Philip Chen, M.D., William Feuer, M.S., Joyce Schiffman, M.S., Kuldev Singh, M.D., M.P.H., George Spaeth, M.D., Martha Wright, M.D.

Steering Committee: Keith Barton, M.D., James Brandt, M.D., Geoffrey Emerick, M.D., Robert Feldman, M.D., Steven Gedde, M.D., Leon Herndon, M.D., Dale Heuer, M.D., Alexander Kent, M.D., Quang Nguyen, M.D., Richard Parrish II, M.D., Todd Perkins, M.D., Bruce Prum, M.D., Mark Sherwood, M.D., Steven Shields, M.D., Paul Sidoti, M.D., Gregory Skuta, M.D., Rohit Varma, M.D., M.P.H., Darrell WuDunn, M.D., Ph.D.

Study Chairmen: Steven Gedde, M.D., Dale Heuer M.D., Richard Parrish II, M.D.

Figure 1.
Kaplan-Meier plots of the probability of failure in the TVT Study.

Table 1

TVT Study Synopsis

Purpose	To compare the safety and efficacy of tube shunt surgery to trabeculectomy with MMC
Inclusion criteria	Age 18 to 85 years
	Inadequately controlled glaucoma with IOP ≥ 18 mm Hg and ≥ 40 mm Hg on maximum tolerated medical therapy
	Previous cataract extraction with intraocular lens implantation, trabeculectomy, or both
Exclusion criteria	Unwilling or unable to give consent, unwilling to accept randomization, or unable to return for scheduled protocol visits
	Pregnant or nursing women
	No light perception vision
	Active iris neovascularization or active proliferative retinopathy
	Iridocorneal endothelial syndrome
	Epithelial of fibrous downgrowth
	Aphakia
	Vitreous in the anterior chamber for which a vitrectomy is anticipated
	Chronic or recurrent uveitis
	Severe posterior blepharitis
	Unwilling to discontinue contact lens use after surgery
	Previous cyclodestructive procedure, scleral buckling procedure, or silicone oil present
	Conjunctival scarring precluding a trabeculectomy superiorly
	Need for glaucoma surgery combined with other ocular procedures (i.e. cataract surgery, penetrating keratoplasty, or retinal surgery) or anticipated need for additional ocular surgery
Enrollment	212 patients
Treatment groups	350-mm ² Baerveldt glaucoma implant
	Trabeculectomy with MMC (0.4 mg/ml for 4 minutes)
Treatment assignment	Random
	Stratified by clinic and type of previous intraocular surgery
Follow-up examinations	1 day, 1 week, 1 month, 3 months, 6 months, 12 months, 18 months, 2 years, 3 years, 4 years, 5 years
Outcome measures	IOP
	Supplemental medical therapy
	Complication rates
	Visual acuity
	Visual field
	Quality of life
	Reoperation for glaucoma
	Surgical success and failure rates
Failure criteria	IOP > 21 mm Hg or not reduced by 20% below baseline on two consecutive follow-up visits after 3 months
	IOP ≥ 5 mm Hg on two consecutive follow-up visits after 3 months
	Additional glaucoma surgery
	Loss of light perception vision

Study centers and committees	17 Clinical Centers
	Safety and Data Monitoring Committee
	Statistical Coordinating Center
	Steering Committee

IOP = intraocular pressure; MMC = mitomycin C

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Table 2

Intraocular Pressure and Medical Therapy in the TVT Study

	Tube Group (n = 107)	Trabeculectomy Group (n = 105)	P-value *
Baseline			
IOP (mm Hg)	25.1 ± 5.3	25.6 ± 5.3	0.56
Glaucoma medications	3.2 ± 1.1	3.0 ± 1.2	0.17
1 year			
IOP (mm Hg)	12.5 ± 3.9	12.7 ± 5.8	0.73
Glaucoma medications	1.3 ± 1.3	0.5 ± 0.9	< 0.001
2 years			
IOP (mm Hg)	13.4 ± 4.8	12.1 ± 5.0	0.101
Glaucoma medications	1.3 ± 1.3	0.8 ± 1.2	0.016
3 years			
IOP (mm Hg)	13.0 ± 4.9	13.3 ± 6.8	0.78
Glaucoma medications	1.3 ± 1.3	1.0 ± 1.5	0.30

Data are presented as mean ± standard deviation.

IOP = intraocular pressure

* Student t-test