HISTOPATHOLOGIC FEATURES OF TRABECULECTOMY SURGERY

BY *Anthony C. Castelbuono MD** AND ***W. Richard Green MD***

ABSTRACT

Purpose: Trabeculectomy surgery is the most common operative procedure for the treatment of medically uncontrolled glaucoma. Variability exists in both the design and the position of the limbal wound as well as in outcomes, even in cases with similarly designed wounds. The purpose of this study is to describe the histologic features of the surgical site of human eyes received at a pathology laboratory that had undergone trabeculectomy surgery and then attempt to explore possible associations of these features with success or failure of surgery.

Methods: We examined 64 autopsy and enucleated eyes of 53 patients obtained at the Eye Pathology Laboratory, Wilmer Eye Institute, Baltimore, Md, between January 16, 1974, and November 15, 1999. Examined aspects included the position, dimensions, and depths of the trabeculectomy site; features at the internal opening; and the inclusion of trabecular meshwork in the internal resection. An attempt was also made to judge the success of the trabeculectomy by a comparison of preoperative and postoperative intraocular pressures.

Results: Of all the histopathologic features examined, there was a statistical difference between the success and failure groups in only the presence of a cleft and the location of the posterior incision.

Conclusions: The main finding of this study is that there is a large degree of variability in the size, position, and pathologic features of trabeculectomy sites. Features that can be avoided with the initial surgical approach, particularly a posterior resection posterior to the scleral spur, may increase the chance of surgical failure.

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INTRODUCTION

Trabeculectomy surgery is the most common operative procedure for the treatment of medically uncontrolled glaucoma. While the premise behind the lowering of pressure by allowing aqueous to be directed out from the anterior chamber is intuitive, achieving that goal is sometimes elusive. There is variability in both the design and the position of the limbal wound as well as in the ultimate outcomes, even in cases with similarly designed wounds. Understanding of the variables associated with the design of a trabeculectomy wound and with healing after trabeculectomy surgery may lead to higher success rates. Histologic characteristics of conjunctival filtering blebs[1] and surgical trabeculectomy biopsy specimens[2,3] have been described, yet no large series of the histologic findings of the trabeculectomy site has been reported. In addition, a description of the histologic features that may be associated with success or failure may be helpful, and case reports of such features have been previously described.[4] The purpose of this study is to describe the histologic features of the surgical site of human eyes that have undergone trabeculectomy surgery and then attempt to explore possible associations of these features with success or failure of surgery.

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METHODS

We examined 64 autopsy and enucleated eyes of 53 patients obtained at the Eye Pathology Laboratory, Wilmer Eye Institute, Baltimore, Md, between January 16, 1974, and November 15, 1999. All eyes had a history of trabeculectomy, and the trabeculectomy site was located in each specimen. Forty-two eyes were obtained at autopsy, and 22 were surgical enucleations. Specimens were excluded from the study only if no trabeculectomy site was located in the histological sections. Clinical data for all cases were sought and collected when possible.

Eyes were processed for light microscopy with specific attention given to the identification of the trabeculectomy site. Specimens were fixed and processed in the routine fashion. Unstained sections were moni-

tored during sectioning to make certain that the operative site was included. Stepped serial sectioning and serial sectioning were often performed. Sections were stained with the periodic acid–Schiff, hematoxylin-eosin, and van de Grif stains.

Features evaluated included the anteroposterior dimension of the trabeculectomy site, the thickness of the scleral flap, the location of the posterior incision, the presence of a tract between the flap and the deep sclera, endothelialization and descemetization, cyclodialysis, iris melanocytization, iridocorneal adhesions, iris incarceration, foreign bodies at the site of surgery, epithelial ingrowth, the presence of a bleb, fibrous encapsulization of the bleb, ciliary body detachment, and the inclusion of trabecular meshwork in the internal resection.

Clinical data collected included age and sex of the patient, preoperative diagnosis, and reason for enucleation. An attempt was also made to judge the success of the trabeculectomy by a comparison of preoperative and postoperative intraocular pressures (IOPs). Cases were judged to be successful if there was a satisfactory lowering of the IOP as determined by the clinician or a decrease in the number of preoperative IOP medications with adequate postoperative IOP control, as was determined by the clinical records. By these methods, the cases were categorized into three groups. Of these 64 cases, 15 were determined to represent successful trabeculectomies and 23 were unsuccessful. In 26 cases, success or failure of the trabeculectomy could not be determined.

RESULTS

The average age of the patients in this series was 69 years, and 26 (49%) of the 53 patients were female. Forty-two (66%) of the 64 eyes were obtained at autopsy, and 22 (34%) were obtained by surgical enucleation.

Clinical diagnoses included chronic open-angle glaucoma (15 eyes), chronic angle-closure glaucoma (12), uveitic glaucoma (4), neovascular glaucoma (4), congenital glaucoma (3), pseudoexfoliation glaucoma (2), and steroid-induced (1), traumatic (1), pigmentary (1), and acute angle-closure (1) glaucoma. Twenty eyes had no specific diagnosis.

The average anteroposterior length (Figure 1) of the internal resection was 760 µm. The average thickness of the resection was 310 µm, and the average outer lamellar thickness was 360 µm. Forty-two (66%) of the surgical sites involved resection of any part of the trabecular meshwork. The posterior incision was located in the trabecular meshwork (Figures 2 and 3) in 24 cases (38%), anterior to the trabecular meshwork (Figure 1) in 22 (34%), and posterior to the trabecular meshwork (Figure 4) in 18 (28%). Eight cases (12%) contained a full-thickness resection (Figure 5). A patent scleral cleft (Figure 6) was present in 20 cases (31%).

Although most surgical cases did not contain enough overlying conjunctiva to determine the features of a filtering conjunctival bleb, a bleb was present (Figure 7) in 28 eyes (44%). The number of eyes with filtering blebs in vivo may have been higher, since conjunctiva was not included in many surgical cases. In 3 cases (5%) there was an encapsulated bleb (Figure 8).

Particular attention was given to the internal aspect of the wound in all eyes. Some degree of endothelialization and descemetization (Figures 9 and 10) was present in 24 eyes (38%), and total endothelialization and descemetization were present in 4 (6%). Iridocorneal adhesions in the operative site (Figure 11) were present in 9 eyes (14%) and iris incarceration (Figure 12) in 14 (22%). Iris melanocytization of the operative site (Figures 13 and 14) was present in 4 eyes (6%). Cyclodialysis (Figure 5) was observed in two cases and epithelial ingrowth in one case that followed an extracapsular cataract extraction with insertion of an intraocular lens complicated by vitreous loss.

Foreign bodies were present at the surgical site in 15 cases (22%). Other than one intraocular lens haptic and one unidentified object, these consisted of suture material.

Fourteen eyes obtained at autopsy were determined to represent successful trabeculectomies based on the most recent available clinical history. One surgical eye also represented a successful trabeculectomy: the eye was enucleated as part of an exenteration for a melanoma in the lacrimal sac area. Twenty-three of the eyes were determined to represent failed trabeculectomies; the majority of these (19) were surgical enucleations.

Of all the features examined, there was a statistical difference between the successful and unsuccessful groups in only the presence of a cleft and the location of the posterior incision. A cleft between the scleral lamellae was present in 8 of 15 successful cases (53%) and only 4 of 23 unsuccessful cases (17%) ($P<.02$). The posterior margin of the internal lamellar resection was located posterior to the scleral spur in 10 unsuccessful cases (43%) and only one successful case (7%). Location of the posterior margin of the resection in or anterior to the trabecular meshwork was more frequent in successful cases (14 eyes, 93%) than in unsuccessful cases (13 eyes, 57%) ($P<.04$). Other features that were not statistically significant are shown in the Table.

DISCUSSION

The main finding of this study is that there is a large degree of variability in the size, position, and pathologic features of trabeculectomy sites. This variability, particularly in the position of the surgical internal resection, is

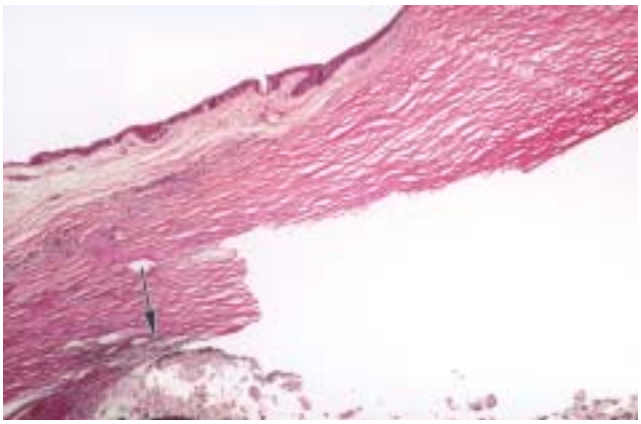

FIGURE 1
Trabeculectomy site showing clear distinction of the internal and external lamellae. Anteroposterior length of the beveled resection is 1,300 µm, and posterior incision is anterior to trabecular meshwork (arrow) (periodic acid–Schiff, ×34).

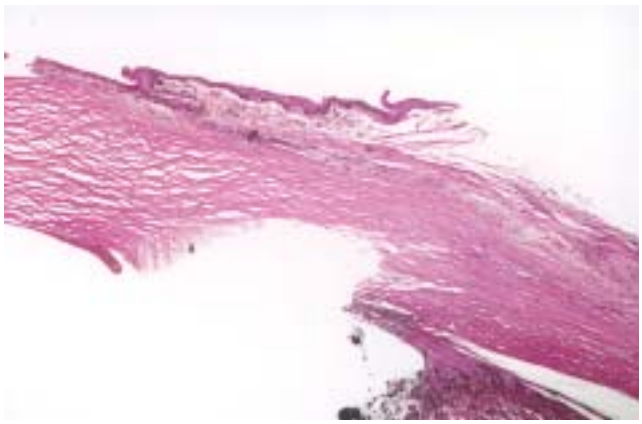

FIGURE 2
Internal limbal resection of 1,000-µm anteroposterior length and posterior incision located in anterior portion of trabecular network (periodic acid–Schiff, ×34).

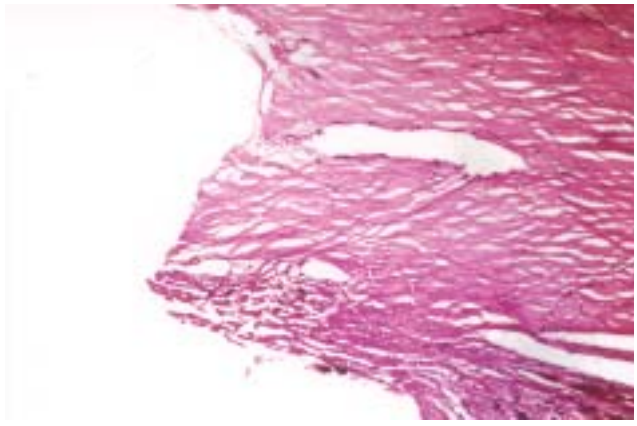

FIGURE 3
Higher magnification of Figure 2 showing location of posterior incision in anterior aspect of trabecular network (periodic acid–Schiff, ×136).

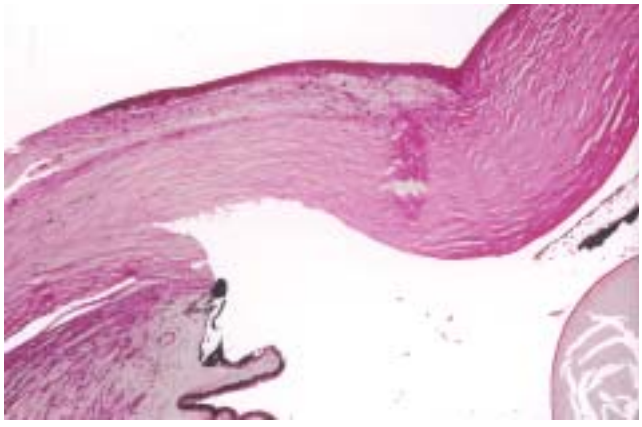

FIGURE 4
Surgical site with 700-µm anteroposterior length and posterior incision located posterior to trabecular network (periodic acid–Schiff, ×34).

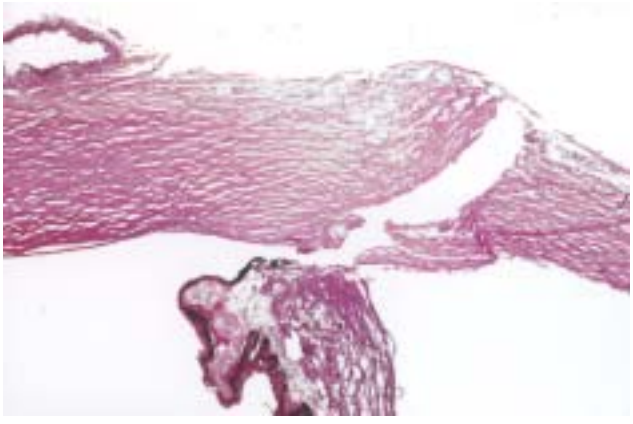

FIGURE 5
Surgical site demonstrating 200-µm full-thickness resection and cyclodialysis. Posterior wound margin is posterior to scleral spur (periodic acid–Schiff, ×34).

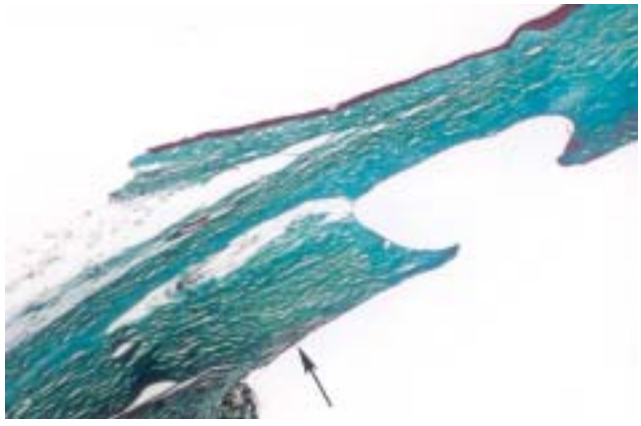

FIGURE 6
Patent cleft between scleral flap and deeper sclera with 1,200-µm anteroposterior inner lamellar defect and posterior incision located anterior to trabecular network (arrow) (van de Grif, ×34).

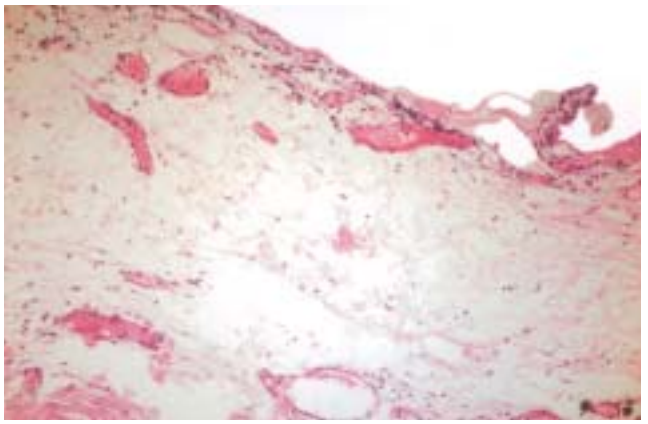

FIGURE 7
Example of filtering bleb present at a trabeculectomy site (hematoxylin-eosin, ×136).

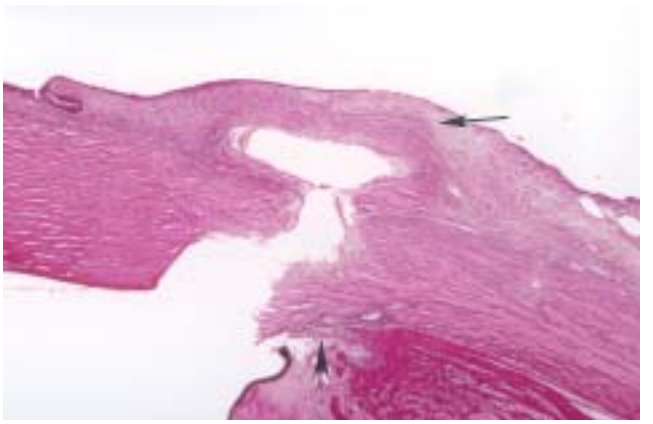

FIGURE 8
Encapsulated bleb (arrow) and a tract at surgical site with an inner lamellar resection of 400 µm (anteroposterior) and a posterior incision located anterior to trabecular network (arrowhead) (periodic acid–Schiff, ×34).

FIGURE 9
Endothelialization and descemetization of internal aspect of the trabeculectomy site with a 1,000-µm anteroposterior length and a posterior incision in the posterior aspect of trabecular network. A portion of a tract (asterisk) is present (periodic acid–Schiff, ×34).

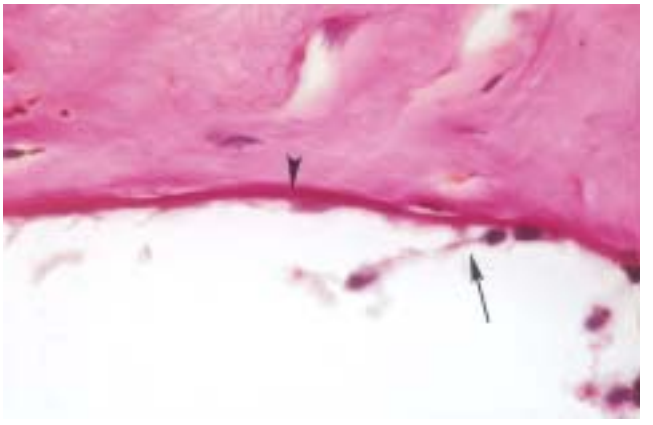

FIGURE 10
Higher-power view of endothelium (arrow) and a basement membrane (arrowhead) lining internal aspect of trabeculectomy site (same case as in Figure 9) (periodic acid–Schiff, ×544).

FIGURE 11
Iridocorneal adhesion at anterior margin of trabeculectomy site with anteroposterior length of 560 µm; posterior incision anterior to trabecular network (periodic acid–Schiff, ×34).

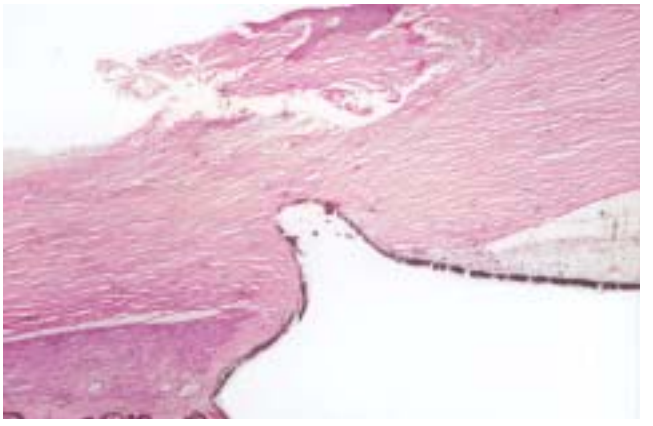

FIGURE 12
Iris incarceration in trabeculectomy site that has 300-µm anteroposterior length; posterior margin is located within trabecular network (periodic acid–Schiff, ×35).

FIGURE 13
Iris melanocytization of trabeculectomy site that has an anteroposterior length of 1,000 µm; posterior incision is posterior to trabecular network (periodic acid–Schiff, ×35).

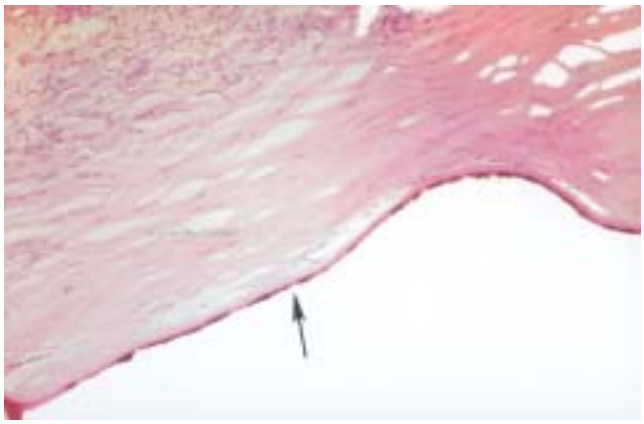

FIGURE 14
Higher-power view of a layer of pigmented cells with fine pigment granules lining inner aspect of trabeculectomy site (arrow) shown in Figure 13 (periodic acid–Schiff, ×544).

TABLE: SUBSET MEASUREMENTS AND FEATURES*

CRITERION	SUCCESS (N=15)	FAILURE (N=23)
Mean AP length of inner resection	720±380	800±600
Mean thickness of resection	300±160	370±180
Mean outer lamellar thickness	400±190	310±210
Trabecular meshwork in resection		
None	6 (40%)	8 (35%)
Some	9 (60%)	15(65%)
Location of posterior incision		
Anterior to trabecular meshwork	7 (47%)	7 (30%)
Within trabecular meshwork	7 (47%)	6 (26%)
Full-thickness resection	1 (7%)	3 (13%)
Any endothelialization and descemetization	7 (47%)	7 (30%)
Total endothelialization and descemetization	1 (7%)	3 (13%)
Encapsulation of bleb	0 (0%)	1 (4%)
Iridocorneal adhesions	3 (20%)	4 (17%)
Iris incarceration	3 (20%)	8 (35%)
Iris melanocytization	1 (7%)	2 (9%)
Epithelial ingrowth	0 (0%)	1 (4%)
Foreign body	2 (13%)	3 (13%)

AP, Anteroposterior dimension.
*Differences are not significant (exact chi-square test).

consistent with that shown in other histologic series.[3]

Because of the number of cases where enough clinical information could be obtained to determine success or failure, and the criteria by which these classifications were made, generalizations from these cases are to be made with caution. Nonetheless, the findings are worthy of contemplation. Features that can be avoided with the initial surgical approach, particularly a posterior resection posterior to the scleral spur, may increase the chance of surgical failure. It was shown in this series that other features, specifically the surgical depth of the lamellae, had no bearing on success or failure; however, there was a trend toward a greater number of full-thickness resections in the failed group, though this was not statistically significant. Indeed, in one case, an enucleated eye deemed a failure after the eye experienced multiple episodes of endophthalmitis exhibited ciliary body incarceration in a full-thickness wound. Such rare features are presumably associated with the failure of this case.

In addition, selected features associated with the internal aspect of the trabeculectomy site may also be associated with surgical failure. Specifically, endothelialization and descemetization of the internal wound tended to be higher in the failed cases, but neither this nor any

other individual feature of the internal wound was statistically significant in this series. It could be that, individually, each of these features is rare but contributes to failure. If one grouped these processes of the internal wound opening, the presence of any one such feature might correlate with failure. Outcomes such as this may be avoidable, but surgical methods to avoid the late-forming features at the internal wound site, such as endothelialization or iris melanocytization, may remain elusive. The presence of a cleft between the scleral lamellae appears to be a desirable effect and was associated with success.

ACKNOWLEDGMENT

Clinical histories were provided by Dr Harry Quigley, Dr Henry Jampel, Dr Irvin Pollack, Dr Donald Abrams, and Dr John Payne. One case each was included in the study through the courtesy of Dr Andrew P. Ferry, Dr Robert Y. Foos, and Dr Elise Torczynski.

REFERENCES

1. Addicks EM, Quigley HA, Green WR, et al. Histologic characteristics of filtering blebs in glaucomatous eyes. *Arch Ophthalmol* 1983;101:795-798.
2. Rodrigues MM, Spaeth GL, Sivalingam E, et al. Histopathology of 150 trabeculectomy specimens in glaucoma. *Trans Ophthalmol Soc UK* 1976;96:245-255.
3. Taylor HR. Histologic survey of trabeculectomy. *Am J Ophthalmol* 1976;82:733-735.
4. Putnam D, Wilson DJ, Morrison JC. Epithelial ingrowth and apparent filtering bleb encapsulation. *Am J Ophthalmol* 1994;118:113-114.

DISCUSSION

Dr Alan H. Friedman. Ophthalmologists have for years been attempting to predict with some degree of accuracy why some eyes operated on for glaucoma do well while others do poorly. Unlike cataract surgery where the technique is more or less universal and the results are very predictable, trabeculectomy is plagued by many more pitfalls. Seemingly flawless trabeculectomies are often followed by dismal failures.

This paper seeks to answer some of the questions as to why many cases fail. Castelbuono and Green pointed out that there is great variability in the size, position and histopathological features of trabeculectomy sites. They concluded that a more posterior-placed resection posterior to the scleral spur was associated with surgical failure. Likewise, a full-thickness resection may also be associated with failure. Other noteworthy causes of failure were endothelialization and melanocytization. They also observed that the presence of a cleft was associated with success. Cyclodialysis redux.

A paper such as this, which tries to correlate pathologic findings with clinical observations, is faced with many stumbling blocks. Several questions come to mind. What for instance was the duration of follow-up, mean age of the patients and Race. Were any of the eyes treated with intraoperative 5-Fluorouracil or Mitomycin or postoperative 5-Fluorouracil? Was ultrasonic biomicroscopy performed at any time? Was the presence of a bleb noted clinically prior to enucleation? Was the duration of glaucoma or the clinical diagnosis associated with more tendencies to failure? I would ask to authors why a posterior placed incision is "bad" while a cleft is "good!"

I wish to congratulate the authors on the quality of their work. They sent the paper in more than ample time. Anyone who has worked in an ocular pathology laboratory realizes the difficulty of obtaining really good histologic sections to evaluate as well as the effort required to get and evaluate serial and step sections. The quality of the photomicrographs is uniformly excellent.

I would like to acknowledge the assistance of Drs Janet Serle and Donna Gagliuso, who made helpful comments.

Dr George L. Spaeth. Could you expand on what you called a cleft? Do you think that was possibly artifactual? Were those real cyclodialysis clefts or were they just something that showed up in the specimen? Most of us performing trabeculectomies make a point to not take the trabecular meshwork at all. Taking it seems to increase complication rate, especially bleeding. Shouldn't they be called guarded filtration procedures, because we don't do trabeculectomies anymore?

Dr Richard P. Mills. Back in the days of the development of trabeculectomy Dr Cairns, whose operation we perform today, had a colleague Dr Peter Watson who described a trabeculectomy which approaches the resection from posterior to the scleral spur, detaching the insertion of the ciliary muscle and proceeding anteriorly to the trabecular meshwork, where the excision was completed. The initial intention was to create a cyclodialysis, which it virtually never did. The success rate of Cairns and Watson were very similar in those days but the Watson operation was discarded, mainly because of its higher surgical difficulty. However, the equal success of the very posterior approach seems to conflict with the findings of your paper.

Dr James C. Bobrow. A study was presented at the Washington University Eye Alumni meeting in1989 in which Dr Morton Smith examined a total of 57 or 58 excised specimens from trabeculectomies. Consistent with your observations, the ones that were removed by the

various surgeons involved were either just approaching the trabecular meshwork anteriorly or involved the meshwork; very few of them involved the posterior scleral spur. We made observations, concluding that removal of the meshwork was not essential to successful filtration surgery although clinical correlations and long-term follow up for those individuals was not available.

Dr David J. Wilson. All of your specimens were whole globes, so you may not have received a lot of conjunctiva, but I was wondering how many of them actually had the bleb present? What were your criteria for calling a bleb encapsulated? Was it based on histologic grounds or clinical grounds, and were you able to correlate that?

Dr Victor M. Elner. A major factor of failure is episcleral scarring after filtering surgery. Did you assess the episcleral scarring? Was scarring a factor in the posterior approach since it may have been more vascular than an anterior approach? Could this have contributed to failure?

Dr Anthony C. Castelbuono. Dr Friedman brings up several points about the clinical histories of the patients: what types of surgeries were performed and with which antimetabolites and whether ultrasound biomicroscopy was performed. A lot of this information was not available for a number of the eyes. He asked us to speculate on why a posterior incision may be not be ideal. Dr Spaeth pointed out some of the complications that can occur when bleeding is encountered. A posterior incision is not a suitable location for filtration from the anterior chamber.

The cleft that we saw associated with success is an actual tract between the superficial and deep lamellae at the site. It is not a cyclodialysis cleft. It is a contiguous cleft between the layers of the sclera. It is associated with success because it is a sign that there is filtration occurring. Surgeons today do not necessarily remove the trabecular meshwork, so changing the name of the surgery may be appropriate.

In a number of these cases there wasn't much of the episcleral tissue or blebs to be examined. There may have been an absence of the bleb in a number of these cases because of the way that the eyes were obtained. The encapsulation was seen, not as a clinical sign from the history, but as seen on histology and the same is true for episcleral scarring. A lot of that information was not available from the history and, in the cases that we had, we frequently did not have much of the episcleral scarring in that region to examine as compared to the internal aspects of the wounds.

I would like to thank Dr Friedman and the other discussants for their comments.