MAJOR REVIEW

Laser Trabeculoplasty

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Abstract. Over a decade, laser trabeculoplasty has evolved from being a novel new treatment to one that is a commonly accepted intervention in the management of open-angle glaucoma. Despite its widespread use, however, there are still many unanswered questions about laser trabeculoplasty, including its mechanism of action and the ideal treatment parameters. In this review, we will discuss the history of the technique, the clinical experience, and some of the experimental studies that have been conducted to answer the questions regarding its mechanism of action. (**Surv Ophthalmol 35:**407–428, 1991)

Key words. argon laser • glaucoma • intraocular pressure • laser trabeculoplasty

Argon laser treatment of the trabecular meshwork was described in the United States by Worthen and Wickham[172] in 1973. The modified technique later described by Wise and Witter[171] in 1979 gained acceptance and popularity within a short time and now plays an important role in the treatment of advanced open-angle glaucoma. Yet, despite widespread use, many basic questions concerning the treatment parameters, mechanism of action, and efficacy of the treatment remain unanswered. This will review the large body of literature concerning argon laser trabeculoplasty and will also attempt to offer a reasonable treatment approach to the patient who may benefit from argon laser trabeculoplasty (ALT).

I. Historical Perspective

Laser technology first became available in the early 1960s. Its application to the anterior chamber angle structures solely for the purpose of reducing intraocular pressure (IOP) was not reported in the American literature until 1973.[172] In that year, Krasnov described a "micropuncture" technique utilizing a Q-switched ruby laser in ten chronic open-angle glaucoma patients in Russia.[61] A temporary reduction of IOP in all subjects, accompanied by improved outflow facilities was noted in this early report.[62] This technique, termed laser trabeculotomy, attempted to provide a direct aqueous pathway into Schlemm's canal.

Worthen and Wickham described the cellular and histopathological changes associated with argon laser applications of varying intensity in monkeys.[172] The following year, their human clinical studies, which were the first conducted and published in the United States, drew attention to the potential use of laser treatment in open-angle glaucoma. Although the power levels and duration settings were significantly higher than those employed in present-day techniques,[173] an average IOP reduction of 9.6 ± 8.9 mm Hg in 20 patients three weeks after the treatment was noted. Four patients, who were followed up for one year, demonstrated an average decrease in IOP of 11.3 mm Hg. Extended follow-up of Worthen and Wickham's patients suggested that conventional surgery could be delayed for three months to three years following laser, which was a desirable treatment outcome in

itself. The results prompted these investigators to propose that "argon laser trabeculotomy" should be tried before resorting to conventional glaucoma surgery.[159] Ticho and Zauberman,[139] using the argon laser, noted improvement in the outflow facilities of glaucomatous eyes after laser treatment. Other investigators[44,133] reported success with argon laser treatment. However, enthusiasm for these techniques was dampened by the adverse effects (most significantly, increased IOP) of laser treatment to the trabecular meshwork reported in animals.[33,172]

Interest in argon laser treatment in glaucoma management increased after a report by Wise and Witter in 1979.[171] These investigators used less energy and reported moderate pressure reduction and few complications. One-hundred laser burns at a power level ranging from 1000 to 1500 mW were placed over 360° of trabecular meshwork. The burns, which were 50 μ in size and 0.1 sec in duration, produced an average pressure reduction of 10.29 mm Hg at three months in 41 patients with primary open angle glaucoma. They postulated that localized burns in the trabecular meshwork caused shrinkage of collagen in the tissue, resulting in a pulling or tightening of the adjacent tissues. This was thought to result in widening of the trabecular pores and a reduction in outflow resistance. Published reports in 1981 of this technique, now known as ALT, by Schwartz et al,[118] Wilensky and Jampol,[163] Sutton et al,[132] and Pohjanpelto[86] confirmed the initial success reported by Wise.[171]

II. Theories Regarding the Mechanism of Action of Argon Laser Trabeculoplasty

The effects of ALT on aqueous outflow as well as inflow have been studied. Many of the earliest investigators demonstrated that improvement of tonographic outflow facility occurred following laser treatment to the angle structures.[61,139] Clinical studies that utilized the Wise technique (ALT) also revealed increased outflow facility.[22,86,118,136,163,174] Utilizing fluorophotometry, Brubaker and Liesegang found that aqueous flow, corneal permeability to fluorescein, and the blood-aqueous exchange coefficient did not differ significantly in 17 treated eyes when compared to controls.[13] Other investigators noted a temporary breakdown in the blood-aqueous barrier following laser trabeculoplasty; however, this finding is unlikely to have any longterm significance.[27] Thus, it was established that an increase in the facility of aqueous outflow was the most significant determinant which modified intraocular pressure following ALT.

The question remains – by what mechanism is aqueous outflow improved? Some of the various

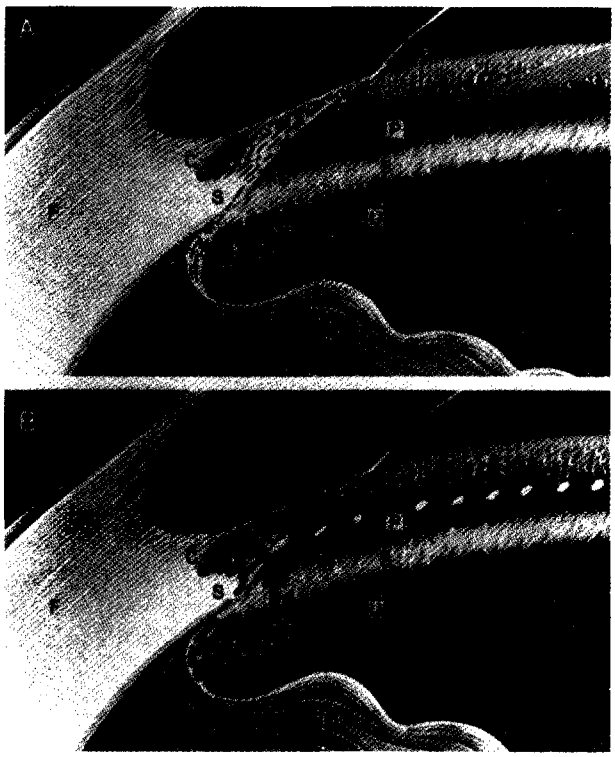

Fig. 1. Gonioscopic cross-sectional view of angle structure. *A.* Collapsed trabecular meshwork in a glaucomatous eye that has received laser treatment. Note the partially closed trabecular spaces (T1). [Cornea (E), Schwalbe's line (G), Schlemm's canal (C), Scleral spur (S), Sclera (F), Uveal meshwork (U), Iris (I). *B.* Laser burns (L), which were applied along the anterior edge of the pigmented band (P), have resulted in tissue shrinkage and contraction. This causes the trabecular spaces (T2) to open. (Reprinted from Wise JB[169]: *Highlights of Ophthalmology*, 30th Anniversary Edition, Volume I, courtesy of JB Wise, B.F. Boyd, and S. Gordon.)

theories proposed have been discussed in detail by Van Buskirk.[148] Initially, Wise and Witter[171] proposed that ALT worked by reversing a pathological laxity of the trabecular tissues, which resulted in a collapse of the meshwork, subsequently diminishing aqueous outflow facility. One could envision microscars causing tissue retraction around the entire trabecular circumference, which would literally pull the meshwork open between the scars (Fig. 1). This "mechanical" theory, perhaps the most popular explanation of ALT's mechanism of action, has been both mathematically (geometrically) and intuitively discussed in detail (Fig. 2).[167,169] Histopathological examination of laser-treated meshwork samples obtained from human subjects revealed early necrosis of cells and disruption of trabecular beams. There was no evidence of penetrating holes into Schlemm's canal.[101,166] However, there was shrinkage of certain collagenous elements seen in some

specimens.

Since there is no animal model for primary open-angle glaucoma or ALT, it is difficult to confirm the mechanical theory in the laboratory. However, it is interesting to note the studies of laser-treated monkey trabecular meshwork by Melamed et al.[74] These investigators noted widened intertrabecular spaces with juxtacanalicular tissue herniated into Schlemm's canal when the specimens were examined histologically. In a later study by this group, cationized ferritin was infused into the eyes of previously laser-treated cynomolgus monkeys. Light microscopy revealed that this compound, which may have acted as a tracer, had selectively shifted around the lasered areas and was noted in large quantities in the juxtacanalicular tissues, in vacuoles, and within Schlemm's canal.[72] These results must be interpreted with caution, because the distribution of cationized ferritin may be charge-dependent and not simply flow-dependent. Furthermore, this study was performed on a nonhuman, nonglaucomatous model and cannot be directly extrapolated to a proposed mechanism of action in humans.

Another theory of the mechanism by which ALT lowers IOP centers on the possibility of laser-induced physiologic changes in the trabecular cells. Van Buskirk et al first reported differences in glycosaminoglycan turnover, cell density, and cellular biosynthesis measured by ^{35}S-sulfate incorporation in laser-treated autopsy eyes.[149] Melamed et al also reported that laser-treated meshwork cells appeared to be more actively phagocytic and suggested that a cellular change had been promoted in the meshwork.[73] Recently, increased trabecular cell division following ALT has been demonstrated using tritiated thymidine uptake in a human organ culture system.[14,15] Cell division at sites distant to the laser burns and migration of cells into the burn areas were documented histopathologically. Other researchers have found an increase in fibronectin, an important component of extracellular matrix, following laser treatment of feline meshwork.[16]

In summary, despite questions regarding whether the exact cellular mechanism of action is purely mechanical, cellular, or a combination of both, virtually all investigators are convinced that ALT causes an enhancement of egress of fluid via the trabecular outflow system resulting in lowered IOP.

III. Technique

Over the years, investigators have modified their laser parameters in the hope of further maximizing therapeutic effects while minimizing adverse results. The importance of careful technique was shown by Khan et al, who noted definite differences between a group of patients treated with ALT by resident physicians and a group treated by more experienced attending physicians.[56] A more successful outcome was found in patients treated by the more experienced attending staff, suggesting that the application of identical laser parameters alone was not a guarantee of similar outcomes.

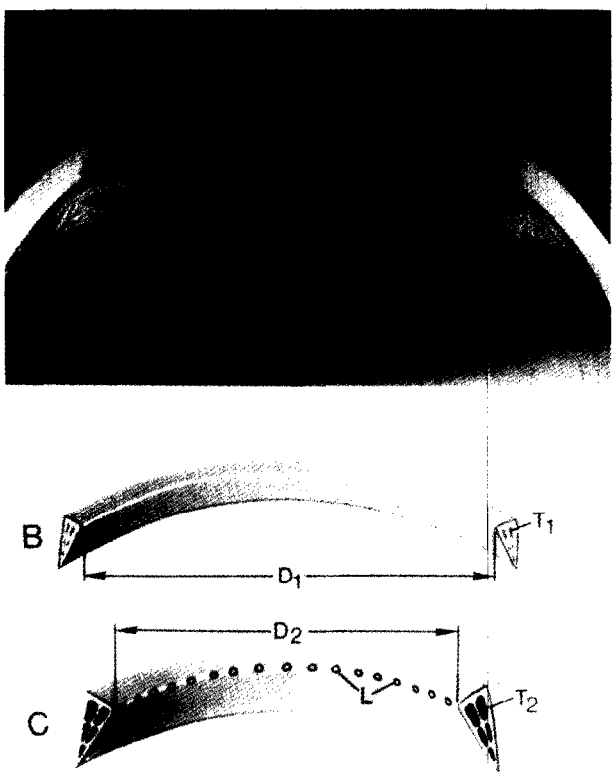

Fig. 2. A geometric model of laser trabeculoplasty. *A.* Saggital section through the anterior globe, which highlights the trabecular meshwork band. *B.* For illustrative purposes, half of the untreated trabecular meshwork ring is shown with a diameter D. *C.* Following treatment, tissue contraction causes the entire ring to become smaller with the diameter reduced to D2. Notice that the trabecular spaces (T2) have become more open, which allows for improved outflow facility. (Reprinted from Wise JB[169]: *Highlights of Ophthalmology*, 30th Anniversary Edition, Volume I, courtesy of JB Wise, B.F. Boyd, and S. Gordon.)

A. PROPORTION OF THE ANGLE TREATED

The minimum amount of angle treatment required in a given patient to obtain adequate pressure response remains uncertain. Treating only 90° of the angle, Wilensky and Weinreb reported a mean decrease in IOP of 6.85 mm Hg one month following treatment in 21 eyes.[164] In 16 eyes that underwent consecutive 90° of laser treatment, IOP dropped an additional 3.56 mm Hg on average. Schwartz et al, in disagreement with these results, found that treatment limited to 90° of the angle

resulted in only a 10% pressure drop on average compared to a 28% decrease in patients receiving 180° or more of treatment.[119]

In a prospective study, Weinreb et al demonstrated that treatment of half of the angle (180°) with 50 burns resulted in pressure reduction comparable to that achieved with treatment of the full angle (360°) with 100 burns, while causing much less acute post-treatment IOP elevation.[155] In another study of various types of glaucoma patients, 62% of patients treated over only 180° of angle were adequately controlled without requiring the second 180° to be treated.[53] Other reports also reported no significant differences between groups receiving full circumference and half-circumference treatment in a prospective study.[45,69] Of interest in this one report, however, was the observation that eyes with the largest pressure decreases (greater than 12 mm Hg) were most numerous in the 360° treatment group. Elsas, in contrast, in a nonconcurrent comparative study reported a higher degree of successful IOP control with 100 spots than with 50 spots.[74] Other investigators who have also corroborated the clinical efficacy of 180° treatment include Fazio et al[26] and Eguchi et al.[22] Wilensky and Weinreb have suggested, however, that full treatment was more likely to result in persistent pressure reductions.[157]

B. LOCATION OF BURNS

The optimal location for placement of the laser burns has been addressed in several studies. Popular sites of burn placement include just along the anterior border of the pigmented meshwork and more posteriorly, directly on the pigmented meshwork, but some have treated as far posteriorly as the scleral spur.[17] Schwartz et al studied several groups of patients having laser treatment to either posterior or anterior meshwork. They reported adequate pressure reduction regardless of treatment site.[119] Higgins similarly found the best response when either the posterior or anterior aspects of the meshwork were treated, although a good response was noted in all locations.[49] In contradistinction, Eguchi et al noted much less success with treatment over the anterior part of the trabecular band.[22] Most recently, Rouhiainen et al, reported that burn location did not affect outcome to any significant extent.[107]

An associated question is whether a laser surgeon can accurately place burns on specific angle structures. Starita et al[131] correlated clinical impression at the time of ALT with histopathological analysis of tissue specimens obtained at surgery. They reported that accurate placement of the laser spots was attained in 11 of 13 patients.[131] (The relationship of burn placement to particular complications will be discussed in Section VII.)

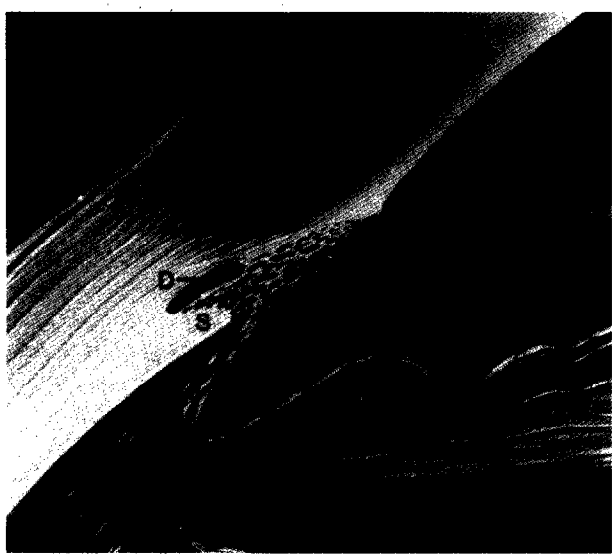

Fig. 3. Reason for proper laser focus. This magnified section of trabeculum shows the "aerial point of focus" [the 50μ size circle at (A)] of the laser beam (L) and the viewer's eyepiece focal point [solid lines (B)] both converging on the same point on the trabeculum. This results in a proper 50 μ burn size on the trabeculum with a simultaneous clear, focused view of the trabeculum through the eyepieces. [Cornea (E), Schlemm's canal (D), Scleral spur (S).] (Reprinted from Wise JB[169]: *Highlights of Ophthalmology,* 30th Anniversary Edition, Volume I, courtesy of JB Wise, B.F. Boyd, and S. Gordon.)

C. ENERGY DENSITY

Energy is determined by a combination of duration, power, and spot size. Blondeau et al studied the possibility that increasing duration of the laser burn, while individually adjusting the power setting, might favorably affect response.[7] Their result revealed no statistically significant difference in the pressure drop following burns of either 0.1 or 0.2 sec duration. Most clinicians presently utilize the 0.1 sec. spot duration, as initially described by Wise.[171]

As previously noted, histopathological work by Starita et al suggested direct correlations among the amount of power administered, degree of pigmentation present, and the histological changes obtained.[131] Since power level was shown to be a relevant and controllable variable, there was a question as to what power setting was required to obtain an optimal IOP response from ALT. Rouhiainen and Terasvirta were able to demonstrate a relationship between laser power, total energy delivered, and response obtained. Those eyes receiving laser power equal to or above 500mW responded with an IOP reduction; thus the minimum power level re-

quired was delineated.[104] In a later study, Rouhiainen et al found that varying the power levels (500–800mW) or the visible laser effect did not affect IOP response.[107] Others, however, do recommend a visible tissue response as the endpoint for successful treatment.[134] Wilensky reported using a uniform power level irrespective of visible response, and has obtained results comparable to those who vary their setting according to tissue response.[161]

Spot size is a frequently overlooked variable that can adversely affect the outcome of the treatment. One of the most vocal proponents of controlling spot size is Wise. He reported a wide range in the size of the burns created by several different lasers that had been set to deliver the same spot size.[168] On a theoretical basis he has proposed that larger spots affect the angle in less than an ideal way, causing undesirable scarring and adverse architectural modification (Figs. 3 and 4). To avoid this, Wise recommended adjustment of the objective settings of the delivery system so that the focused point of the aiming beam, as well as that of the slit-lamp, were identical. This would prevent defocused laser energy from creating too large a spot, which could cause diffuse damage to the meshwork. Also, it is worth noting that a doubling of spot size reduces power density by 75%, which may have its own deleterious effect on outcome. We would encourage careful attention to aiming beam focus to avoid astigmatic or unfocused spots which could increase the chance of failure.

Recently, Ritch described a new lens, which is designed to improve the view of the superior angle, while also reducing the spot size to approximately 70% of its original.[95] The use of this lens may be helpful in minimizing spot size regardless of which laser is used. Unlike defocused larger spots, burns smaller than 50μ have been associated with satisfactory results by some investigators.[119]

Fig. 4. Principal cause of improper laser burn size. The surgeon sees the trabeculum clearly in focus [depicted by solid lines (B), which come to a focused point on the trabeculum], but the point of focus of the laser beam (L) is in front of the trabeculum. Adjusted as such, the laser beam diverges beyond this "aerial point of focus" (A) to create an improper, larger than 50μ size [larger circle at (C) on the trabeclum]. The goal is to adjust the viewing pieces so that they focus at the same location (on the trabeculum) as the laser beam 50μ focal point, as shown in Fig. 3. Then, as the surgeon focuses the eyepieces on the trabeculum, the 50μ laser spot will fall on the trabeculum. [Cornea (E), Schelmm's canal (D), Scleral spur (S). (Reprinted from Wise JB[169]: *Highlights of Ophthalmology*, 30th Anniversary Edition, Volume I, courtesy of JB Wise, B.F. Boyd, and S. Gordon.)

D. LASER WAVELENGTH

Most studies of ALT have used argon lasers emitting blue-green light; however, other wavelengths have been evaulated. Smith compared the effect of argon blue-green and green lasers in 100 patients with POAG. He found no difference in pressure response, post-operative course, or complication rate following blue-green or green laser treatment.[126] This finding was corroborated by Makabe.[70]

Utilizing the krypton red and yellow laser in 15 patients, Spurny and Lederer noted adequate pressure reduction following laser trabeculoplasty.[129] In direct contradistinction, however, Makabe found that krypton red laser had no sustained effect on pressure.[70]

Experience with the Q-switched laser has also been described. Bonney et al[17] and Gaasterland and Bonney[32] demonstrated the ability of the Q-switched ruby laser to create holds in the meshwork of monkeys. As discussed earlier, this was previously reported by Krasnov in 1973 to be somewhat successful in humans with glaucoma.[62] More recently, Robin and Pollack also proposed using a Q-switch ruby laser to avoid excessive thermal tissue destruction from argon blue-green light.[98] (The Q-switched laser has the feature of delivering high energy levels in short pulses, leading to mechanical instead of thermal effects.) In four eyes with secondary glaucoma that were poor candidates for ALT, Robin and Pollack reported an average IOP drop of 15 (±9) mm Hg with a follow-up of 2–15 months. Although extrapolation of results to typical POAG patients was discouraged, their pilot study suggested the possibility of an alternative to argon laser with some theoretical advantages.

Neodymium:YAG (Nd:YAG) lasers also have been used to treat the trabecular meshwork. Two different types of laser energy have been studied. In 1985, Melamed et al reported limited success following attempted trabecular puncture with the Q-switched Nd:YAG laser.[75] Robin et al and Epstein et al, each using a different technique, later applied Q-switched Nd:YAG laser energy to the trabecular meshwork of humans. Robin and coworkers applied 10 spots of 10mJ, approximately 4° apart and reported a pressure drop of 9 (±7) mm Hg at an average follow-up of five months.[99] Tonographic values improved from 0.07 ± 0.04 mm Hg to 0.17 ± 0.2 ml/min/mm Hg. Pressure spikes were seen in eight eyes, transient bleeding in six, and posterior displacement of the iris root in four. The authors proposed formation of minicyclodialyses and/or increased uveoscleral outflow as mechanisms of action. One-year follow-up of these patients found that 46% maintained an IOP of less than 22 mm Hg.[18] Of particular note was a successful outcome in five of six aphakic eyes. A more recent study of 18 eyes treated in a similar manner reported minimal success,[90] however. These authors found less pressure response and more complications, including pressure elevation that necessitated emergency filtration surgery in one eye.

Epstein et al utilized a technique in which 3–6 superimposed spots of 2–6 mJ of energy were applied at 4–6 sites in ten eyes with open angle glaucoma (exfoliation, POAG, or juvenile).[25] They reported a small pressure reduction of diminishing magnitude in four of six POAG eyes over a follow-up of 2–11 months. In this group, one eye suffered a severe pressure rise that necessitated urgent surgery. This led the authors to suggest avoiding the technique altogether in POAG. Treatment of the eyes with "juvenile" glaucoma produced more satisfactory results, and a possible future role for the technique in juvenile or congenital-type angles may exist.

The other group of studies with Nd:YAG lasers attempted to perform conventional laser trabeculoplasty using 10 msec pulses of neodymium laser energy.[111,112] Treatment results were reported to be comparable to those achieved with argon energy.

IV. Results

In discussing treatment results, the success rate can be defined in many ways – e.g., 1) a pressure drop of greater than a certain percent; 2) final pressure of less than a certain level with or without medications; or 3) absence of glaucomatous disc and field progression. In general, an acceptable result for most clinicians is a level of intraocular pressure that abates the progression of the disease and thus necessitates no further surgical intervention.

Because success is often defined differently in each paper, those readers requiring specifics should consult each reference for details. A more detailed discussion of the outcomes in specific glaucoma entities is covered in section VI of this review.

A. INTRAOCULAR PRESSURE

The degree of IOP reduction is largely dependent upon a multitude of patient factors. Therefore, a more detailed discussion of IOP reduction will follow later. At this point, the comments will concentrate on diurnal curves, postoperative antiglaucoma medication reduction, and duration of the IOP reduction.

1. Effect on Diurnal Curves

Several investigators have previously reported the presence of large diurnal pressure swings and high peak pressures in glaucoma patients compared to controls.[19,21,57] Greenidge et al[41] specifically looked at the effect of ALT on the diurnal curves of glaucoma subjects before and eight weeks after treatment. Although pressure spikes were not totally eliminated, a beneficial effect on the diurnal curve was found. Mean peak pressure, presumed to be of pathophysiologic importance in causing disc damage, was found to decrease by 25%. Improvement in both peak pressures and pressure ranges was reported in five patients who did not demonstrate any apparent laser response on a single office reading ("the index pressure"). This suggests that ALT can also offer a positive therapeutic effect to some patients who do not demonstrate an obvious pressure response on routine office visits.

2. Reduction in Antiglaucoma Medications

Perhaps another measure of success is the ability of the physician to remove some or all medications from a therapeutic regimen. In general, ALT has not allowed discontinuation of all antiglaucomatous medications, although some reduction in the number of medications has been reported.[30,53,120] Thomas et al, for example, were able to taper medications in 26.1% of eyes with primary open angle glaucoma (POAG) and in 41.2% of eyes with exfoliative glaucoma.[128] Similarly, Horns et al reported that medications could be reduced in 28.7% of eyes with open angle glaucoma.[53] Although Pollack and Robin noted that 82% of patients with POAG required some medications, 64.2% of patients who previously had required carbonic anhydrase inhibitors and 57% of those who had required miotics were satisfactorily controlled without these medications after ALT.[89] Follow-up of at least 18 months was obtained in this group. Previous work by these authors had re-

vealed similar results.[88] Therefore, ALT appears to be "curative" in only a minority of patients in that some or most of the previously used medication(s) are usually still necessary.

3. Duration of Effect

The duration of IOP reduction following ALT has been examined by several authors utilizing longterm follow-up studies. In interpreting any of these data, the reader must ask several questions. 1) Do the results include those patients who have failed ALT and gone on to conventional surgery or cyclodestructive therapy? If these patients have been removed from the data but are not statistically accounted for, as with Kaplan-Meier life table analysis, the success rate of the technique will appear better than it really is. 2) How is success defined? As previously discussed, the definition of success may be too lenient or too demanding. This could distort the conclusions, either exaggerating success or emphasizing failure. 3) What types of patients are being reported? Do they represent referral patients with more severe disease who are, thus, more likely to fail ALT, or are they representative of the average mix seen in clinical practice? 4) What type of glaucoma is being treated? The term "open-angle" can be loosely used to include several variants, such as exfoliation and pigmentary, which have different success rates and outcomes. With these questions in mind, the reader should be able to carefully analyze any data and reach his or her own conclusions as to how ALT might provide longterm impact in clinical practice.

In 1981, Wise published the results of longterm follow-up after ALT in 150 eyes.[166] All were followed for at least six months after treatment, and some had been followed for up to four years. The mean IOP reduction in 150 eyes was 12.26 mm Hg at six months. This remained fairly constant through 30 months, when 37 eyes had a mean IOP drop of 10.49 mm Hg. At 48 months, 11 eyes were found to have a mean pressure drop of 13.29 mm Hg. Of the 150 eyes, only 9% needed subsequent filtering surgery. Overall, the number and type of medications did not change greatly. The results of a smaller number of eyes suggested that the success rate was also quite high and long-lasting among blacks and native American Indians. On the basis of this study, Wise reiterated his previous conclusions that ALT was an efficacious and safe therapeutic technique that avoided the morbidity of conventional filtration surgery. Pohjanpelto also reported fairly stable pressure reductions at follow-up periods of 18 to 42 months.[87]

Schwartz and coworkers, however, were much less optimistic in interpreting results from their longterm study in 1985.[116] The average reduction in IOP fell from 9.7 mm Hg at two months to 4.9 mm Hg at five years. Kaplan-Meier analysis of the data suggested that black patients failed at a shorter interval than did white patients, a conclusion far different from that reached by Wise. In another study, Grinich et al reported the effect of ALT on intraocular pressure in 58 eyes over a three-year follow-up.[42] Success was defined as an IOP of less than 22 mm Hg with no further surgical or laser intervention. Using life-table analysis, cumulative success rates fell from 79% (112 eyes) at one year to 69% (85 eyes) at two years and finally 59% (58 eyes) at three years.

In a study by Shingleton et al[122] of 118 eyes of 93 patients with POAG, exfoliation, or aphakia, Kaplan-Meier analysis predicted a 52% chance of satisfactory control at four years. Success was defined in terms of intraocular pressure, stability of visual field and optic nerve, and avoidance of surgery. Failure rate seemed highest (23%) within the first year following treatment, with failure occurring at a rate of 7–10% per year thereafter.

In what is probably the longest reported follow-up to date, Wise recently reported the first ten-year results in his series.[170] In this report, the proportion of eyes maintaining an IOP of less than 21 mm Hg was 79% at one year, 63% at four years, and only 45% (76 eyes) at seven years. Interestingly, this increased to 70% at ten years in a smaller group (10 eyes). Wise suggested that the lessened effect at year seven was due to patient selection factors that were as yet undefined. In the 37 treated eyes of 24 patients who later died, only one eye had required filtration surgery during the patient's lifetime. Thus, ALT did avoid the morbidity of conventional surgery in this group of individuals. The "surgical rate" as a whole was reported as 92% at one year and 63% at seven years. Of prognostic significance, Wise found that those eyes having the most severe disease (cup to disc ratio >0.9) had a 51% rate of undergoing surgery as opposed to those with less severe damage (cup to disc ratio <0.9) who had a 16% glaucoma surgery rate. Overall, 30% of 110 eyes followed to year six required surgery despite previous ALT.

Again, Wise found that a small number of eyes of non-white patients did not appear to fare any worse than the entire group of patients. Since a large number of patients were able to avoid glaucoma surgery throughout their lifetimes, Wise concluded that ALT did indeed do more than merely delay surgery. However, the results of this longterm study do suggest a loss of effect with time.

In the only longterm report following "low dose" ALT, Barnes and Wilensky reported that 11 of 16

eyes that had received 25 to 50 burns over 90° of the angle, demonstrated a significant and persistent IOP drop.[3] Follow-up ranged from 1 to 4.2 years and did not include two eyes that demonstrated an average pressure rise of 2 mm Hg. This report must be interpreted with the understanding that life-table analysis was not performed and that some patients did not return for follow-up. The results indicate, however, that low dose treatment can be a viable longterm option in some patients.

Another measure of the longterm efficacy of ALT has been described by Gilbert et al.[35] These authors examined the rate of filtration surgery in a residency program immediately following the introduction of ALT in the clinic and several years later. In the pre-laser period from 1978 through 1981, filtration surgeries were performed, compared to only one in 1982 and 18 in 1984, most of which were done in patients who had previous ALT.

In summary, it appears that ALT is not a cure or permanent success in all patients. ALT does, however, appear to control IOP for extended periods of time in many patients and in some may eliminate the need for filtering surgery, with its attendant risks and potential complications.

B. PERIMETRY

Several investigators have studied the effect of ALT on visual field test results. Holmin and Krakau reported that successful laser trabeculoplasty failed to halt progressive visual field loss over a one-year period in 15 patients.[51a] Heijl and Bengtsson could not demonstrate any correlation between pressure reduction and computerized field improvement in 42 eyes tested both before and one month after ALT.[46] Similarly, Holmin and Bauer studied 23 eyes and were unable to demonstrate any improvement in the visual field.[51] In a study of 19 patients, Schultz et al examined visual fields obtained at intervals of 1, 4, 8, and 12 months following ALT. They utilized one-way analysis of variance and trend analysis, finding that six patients showed visual field improvements, eight showed no change, and five showed progressive worsening (Octopus program 32).[113] Six of their original 25 patients were excluded because of glaucoma progression that necessitated surgery or changes in medication. Lieberman et al found a worsening of visual fields in 11% of eyes with chronic open angle glaucoma (6/53) despite IOP reduction following ALT. The authors attributed this finding to a continuation of the damage in these already diseased eyes.[65] In contrast, Spaeth, using intricate analyses of patients who had Octopus perimetry three months and one year following ALT, found a direct correlation between intraocular pressure reduction and visual field improvement.[127] Traverso et al also reported some improvement in Octopus fields following ALT-induced pressure reduction.[143]

V. Patient Factors

Ophthalmologists have observed that ALT may be more successful in some individuals than others. There are several patient factors that may be of importance in predicting a successful outcome in any particular laser candidate.

A. AGE

Over the years, a general impression has developed that younger patients have less of a response to ALT than their older counterparts. Safran et al conducted a retrospective study comparing patients younger than and older than 40 years who had POAG uncontrolled by maximally tolerated medical treatment (range, 14–37 years; 46–85 years).[109] Only 7% of eyes in the older group required surgical intervention after laser compared to 60% in the younger individuals. In addition, the older patients appeared to have a statistically greater decrease in pressure (12 ± 6 mm Hg) in response to ALT than those less than 40 years old (5 ± 6 mm Hg). The diagnosis of POAG in a younger population is complicated by the possibility that some or all of these individuals may actually represent a juvenile variant of POAG, having a prognosis and natural disease history different than the typical POAG seen in older patients. Regardless, the poorer response to ALT in younger patients has also been reported by others and should be borne in mind when counselling the younger laser candidate.[30,42,136]

B. RACE

There are a number of reasons why black patients would be ideal candidates for ALT. One of the most salient concerns is the significantly lower success rate following filtering surgery in this group than in white patients.[110] As such, avoidance of conventional surgery would be most desirable. Following ALT in a predominantly black group of patients, Schwartz et al reported a 97% success rate with an 18-month follow-up.[118] Krupin et al, retrospectively examined the results of ALT in 68 black and 42 white POAG patients over one- and two-year periods (only 13 patients had not returned for follow-up at two years), found no statistical difference in the response seen between black and white patients.[64] Similar results have also been reported in other studies,[30] and ALT in an Asian population has also provided equivalent responses and success rate.[125] With longer follow-up of previously studied individuals, however, Schwartz et al found that

ALT did fail to a greater degree in black patients than in whites.[116] In light of these conflicting findings, further studies are necessary to settle this controversy.

C. PIGMENTATION

Pigmentation of the trabecular meshwork has been proposed in numerous papers to be a possible factor in successful pressure responses. Degree of pigmentation may correlate with the post-laser pressure drop by one of several mechanisms: 1) ability to obtain good laser focus on a more pigmented trabecular meshwork; 2) absorption of laser energy by pigment, permitting more efficient conversion of laser energy to heat in the desired location; and 3) removal of pigment, which may play a pathogenic role in causing outflow compromise.[5] Although several authors have acknowledged some advantage to the presence of pigment,[8,44,107,143] agreement with this observation is not universal.[4,30] In pigmentary dispersion and exfoliation syndromes, assessment of the pigment factor is complicated by the fact that the ALT response may be affected by the disease itself, independent of the amount of pigment present (see Section VI).

D. PREOPERATIVE PRESSURE

Several papers have reported that the greatest absolute pressure reduction occurred in those patients with the highest initial pressures.[4,42,65,134,136,151,159,175] Although knowledge of this relationship may be helpful in predicting IOP response in some glaucoma patients, not all investigators accept this correlation.[30] Most investigators, however, do believe that the relationship is linear and that the average pressure drop obtained in primary open angle glaucoma is usually 30% or less. Although not absolute, this figure can serve as a guide in predicting the maximal response that could be reasonably expected in a given patient.[46,136]

E. RESULTS IN THE FELLOW EYE

Primary open-angle glaucoma is usually a bilateral disease, although there may be some asymmetry between the two eyes as to the time of presentation and the severity of the disease. Exfoliation and pigmentary glaucomas are bilateral in the majority of patients. Therefore, it is not unusual to have a patient who has already had ALT in one eye and presents with medically uncontrolled IOP in the second eye. Does the result in the first eye indicate what will happen in the second eye? In one of the early reports on ALT, the authors state that there was an asymmetric response between eyes in 9 of 19 patients, but did not provide details.[65] Two later larger studies in which statistical analysis was performed found a significant correlation between the response in the two eyes. In one of these studies the correlation was still present three years after treatment.[6,142]

These later studies are more in keeping with our own results. In general, if a good response has occurred in the first eye, the second eye will also do well. Conversely if we have not obtained much response in the first eye, it is uncommon for us to see a good response in the second eye.

F. STAGE OF GLAUCOMA

Some observers believe that ALT is more successful in early glaucoma than in more advanced disease. Wise states that 51% of eyes with a cup/disc ratio of 0.9 or more required surgery subsequent to ALT as compared to only 15% of eyes with smaller cup/disc ratios.[170] On the other hand he states that the prelaser average pressure and pressure drop from ALT were similar in the two groups. Thus, he is probably indicating that eyes with more advanced glaucomatous damage require a lower IOP to halt progression of disease, and not that ALT has a lesser IOP lowering effect in these eyes. Tuulonen et al studied factors influencing the outcome of laser trabeculoplasty. They reported that severity of the glaucoma alone would have been a significant predictor, but its importance was lost when the indication for treatment was included.[145a] They also found that previous use of pilocarpine was a negative predictive factor.

VI. Diagnosis-related Efficacy of Treatment

A. PRIMARY OPEN-ANGLE GLAUCOMA

The response to argon laser trabeculoplasty (ALT) seen in POAG could be designated as the standard against which the success rates in other types of glaucoma can be compared. (See Section IV for explanation of success.) In large studies of POAG patients with average follow-up of five months or more, success rate of 72.5% to 97% have been reported.[37,53,118,136]

In two of the larger reported series in the United States, Thomas et al found an average IOP reduction of 30.4% in 237 eyes, which is similar to the 29.8% decrease in 222 eyes reported by Horns et al.[53] Both of these studies had fairly short follow-up periods, ranging from one week to two years. In Germany, Lund[67] reported IOP control in 94% of eyes with chronic simple glaucoma after one year, which dropped to 82% after two years.

B. PIGMENTARY AND EXFOLIATION GLAUCOMAS

As mentioned previously, some investigators

have correlated an increased success rate of ALT with the presence of trabecular pigmentation in open-angle glaucoma patients.[9,49,107,143] However, Lunde reported that ALT worsened pressure control in five of 13 treated eyes with pigmentary glaucoma.[68] This was particularly true in older patients with glaucoma of longer duration. Lieberman et al found that 7 of their 16 pigmentary glaucoma eyes (44%) had acceptable pressure reduction (an average of 7.3 mm Hg) though failure was also more common in slightly older individuals.[65] These results may suggest that chronic trabecular damage from pigment can make the meshwork more resistant to the ameliorating effects of ALT.

Contrary results were reported by Thomas et al, who obtained acceptable pressure levels in all of six pigmentary-type glaucomatous eyes treated with ALT.[128] The average pressure drop in these eyes was 40%, a response second only to exfoliative glaucoma, which suggested that pigmentary glaucoma was a reasonable indication for ALT. Success of ALT in pigmentary glaucoma has also been described elsewhere.[67,97,135] We have obtained good results in the majority of our pigmentary glaucoma patients and recommend ALT to those patients whose disease is not controlled medically.

Thomas et al reported a 97% success rate in a small number of individuals with exfoliative glaucoma.[136] Other authors have reported considerable success with ALT in these patients[96] and some have related this to the increased degree of pigmentation typically found in this type of glaucoma.[5] Of concern was the report from Higginbotham and Richardson,[48] which showed that, despite having a large immediate pressure response to ALT, these patients failed at a faster rate after both initial and second-stage treatments, as compared to POAG controls. Pohjanpelto also reported late failures in this group of patients.[87] However, Sherwood and Svedbergh[121] reported a 70% success rate in 55 eyes and late failure in only two patients. Because of the rather marked reduction in IOP that we have seen in our exfoliation syndrome patients, we have no hesitation about recommending ALT for our medically uncontrolled patients. We do, however, warn the patients that any reduction in IOP may be transient in nature.

C. LOW TENSION GLAUCOMA

A large study of patients with progressive low tension glaucoma (or, more correctly, normal tension glaucoma) was reported by Sharpe and Simmons,[120] who treated 85 eyes with this diagnosis. All subjects selected for inclusion into the study demonstrated progressive visual field loss or optic nerve damage despite maximal intraocular pressures of less than 19 mm Hg with medications. This group included classical low-tension eyes, but also included POAG eyes that progressed despite "acceptable" IOPs. Success was defined as a pressure drop of at least 20%, no need for increased medications, stable visual fields, and no subsequent glaucoma surgery (average follow-up, 30 months). Using these very rigid guidelines, treatment was found to be successful in 46.3% of the patients. Among "failures," however, visual field progression or requirement for surgery occurred in only 11 eyes, despite a pressure reduction of less than the desired 20%. Separation of patients into post ALT pressure groups of low (13–19 mm Hg), very low (10–12 mm Hg), subnormal (6–9 mm Hg) and hypotony (0–5 mm Hg) revealed the best success in patients achieving the lowest pressures. The authors' results support the widely held belief that reduction of pressures below the 12 mm Hg level can slow glaucomatous progression. They recommended consideration of ALT in all low tension glaucomatous patients, especially if surgical intervention is the only alternative. A sobering feature in this report was an early escape phenomenon, with many of the failures occurring by six months.

Schwartz et al[117] looked at a similar goup and defined success as a pressure reduction of as little as 2 mm Hg in addition to no further field progression. They reported a much more optimistic success rate of 73%, but also reported a discouraging loss of effect with time. The average pressure drop of 5.8 mm Hg at two months fell to 4.9 mm Hg at one year and 2.0 mm Hg at two years.[117] In another study, Watson et al found that ALT was unsuccessful in further reducing IOP in patients whose initial pressures were 21 mm Hg or less.[151]

D. APHAKIA/PSEUDOPHAKIA

ALT in aphakic glaucomatous eyes would seem an ideal treatment in light of the reported low filtering success rates and higher incidence of complications in these cases.[44] It is important to note that much of the literature deals with ALT following intracapsular cataract extraction (ICCE), a technique that has been replaced by extracapsular cataract extraction (ECCE). Success rates have varied from 64.7% of 22 eyes (Horns)[53] and 71.4% of seven eyes (Goldberg)[37] to 47% of 15 eyes (Spaeth).[128]

Other reports have conflicted as to the degree of pressure response obtained in aphakia,[65,97] which further complicates the issue. Horns et al, for example, achieved an average pressure drop of 27.5%, which is markedly better than the 12.5% found by Thomas et al.[136] We have found that the presence of vitreous in the anterior chamber of patients adversely affects the outcome of ALT. Although exten-

sive experience with ALT following ECCE and implantation of a posterior chamber intraocular lens is as yet unpublished, we believe, as does Thomas,[136] that a desirable pressure reduction can be obtained in many of these eyes. Actual success rates and magnitude of pressure reduction await further data. It would seem reasonable to attempt ALT in aphakic patients who are otherwise good candidates; however, results are unpredictable and the need for possible conventional surgery should be understood.

A related question concerns whether to perform ALT before cataract extraction in those glaucoma patients who have significant lens opacities. In a comparison between combined filtration surgery (with and without anterior chamber lens implantation) and ALT prior to the cataract extraction, the combined cataract extraction and filtering surgery appeared more successful in obtaining adequate pressure reductions.[34] Nonetheless, completion of full-circumference ALT in the months before ECCE is an option found useful by some clinicians. Brown et al, for example, reported that cataract extraction with or without posterior chamber lens implantation did not result in any loss of pressure control obtained by previous argon laser trabeculoplasty.[11] Cataract surgery was performed 2–26 weeks after the completed ALT (one or two sessions of 100 spots/360°) in 28 eyes. The average pressure decrease of 8 mm Hg was maintained following surgery, and this is certainly much more acceptable than the 2.1 mm Hg pressure reduction reported by Thomas et al, who performed ALT after ICCE.[136] In summary, although combined trabeculectomy/cataract procedures are useful in some individuals, full-circumference ALT in one or two sessions prior to cataract surgery does seem reasonable in selected cases.

E. UVEITIS

The success rate of ALT in uveitic open angle eyes has ranged from 0% to 75% in different studies.[37,38,53,65,97,128] Results must be cautiously interpreted, since these eyes consist of a very heterogeneous population in terms of etiology and degree of angle damage. Treatment is directed toward those aspects of the angle that remain open and accessible. Because ALT has been known to cause iritis in some patients (Section V), it would seem prudent to approach laser treatment very cautiously on an individual basis, employing careful follow-up and care.

Although ALT cannot be performed in angles with complete synechial closure, peripheral iridoplasty may open the angle sufficiently to allow for some treatment, but, again, the iridoplasty may cause exacerbation of the uveitis.

F. ANGLE RECESSION

Results of treatment in eyes with traumatic angle recession have been mixed, with success rates reported to be 0% to 63% in small numbers of patients.[30,37,65,128,136] As in uveitis, the lack of uniformity in severity of damage and the presence of other associated ocular pathology make interpretation of these numbers difficult. Some of our patients have benefited from treatment, although we cannot predict who will be most likely to do so, and we have experienced severe post-laser IOP elevations up to 70 mm Hg. More data are required before precise recommendations can be made, but, in general, we recommend extreme caution.

G. COMBINED MECHANISM

Hitchings described marked pressure reduction in 16 such eyes utilizing a two-stage procedure of peripheral iridotomy followed by ALT one to 12 weeks later.[40] When iridotomy does not suffice, some clinicians utilize an initial peripheral iridoplasty to obtain better visualization of the meshwork.[124]

H. STEROID-INDUCED GLAUCOMA

ALT in steroid-induced glaucoma has been attempted with varying success. Thomas et al first reported minimal post-laser response in two patients who underwent ALT to control unsatisfactory pressures associated with steroid use.[146] A more recent study involving a larger group of patients reported an average decrease in pressure of 35% in 12 individuals who were receiving oral prednisone. Unfortunately, the amount of follow-up time is not mentioned in this article. Although more data will help to settle the controversy, the use of ALT in this group of patients prior to conventional surgery seems reasonable.

I. JUVENILE GLAUCOMA

At present there is no consensus as to the precise definition of "juvenile glaucoma." Although it could be defined as the development of glaucomatous features before the age of 40, specific angle findings, such as a high insertion of the iris, have been described and may help identify this as a unique entity.[162] Horns et al reported that only 4 of their 10 "juvenile-type" patients were able to avoid conventional surgery after ALT.[53] In addition, a low success rate in younger individuals as a group has been reported by Safran et al.[109] Of particular concern, however, was Wilensky and Weinreb's report of failure in six patients following ALT, four of whom were made worse and required filtration surgery.[155]

J. PREVIOUS EYE SURGERY

As previously mentioned, ALT has been performed in eyes that had undergone prior intraocular surgery. On the basis of their experience with a small number of eyes, Lieberman et al,[65] as well as Forbes and Bansal[30,31] reported that eyes that had only one previous intraocular procedure had an ALT response similar to that obtained in eyes that had no previous surgery.

ALT has been found to be useful in some patients who have had unsuccessful filtering surgery. Fellman and associates,[28] for example, reported a 67% success rate of ALT in 30 previously filtered eyes that did not have satisfactory control of IOP. (Failure following ALT was defined as sustained unacceptable pressure levels, visual field progression and/or the need for further filtering surgery). Similarly, Robin and Pollack were able to avoid additional filtration surgery in six of seven previously filtered eyes that were treated with ALT.[97] In an unrelated report, a 71% success rate was attained in 34 previously filtered eyes.[38] In summary, the use of ALT would seem to be a reasonable therapeutic option in previously filtered eyes, especially when one considers the lower success rate encountered in repeated filtration surgery.

Finally, ALT has recently been described to be of benefit in post-keratoplasty patients by Van Meter et al.[150] They found a satisfactory response in small groups of aphakic and phakic post-corneal transplant patients during a mean follow-up period of 12 to 37 months.

K. MISCELLANEOUS

ALT has been performed in a wide variety of other glaucomas, such as congenital glaucoma, iridocorneal endothelial syndrome, and Sturge-Weber; however, not enough subjects with follow-up are available to determine whether ALT is a viable alternative in these and other secondary glaucomas.[65,97,128]

VII. Complications

As with all therapeutic interventions, benefits must be weighed against potential risks. ALT has been associated with several adverse effects, ranging from minor to catastrophic (Table 1). Together, physician and patient must be aware of these possible complications before proceeding with laser therapy.

TABLE 1

Complications Associated with ALT

Intraocular pressure rises (transient and chronic)
Loss of vision (central island)
Peripheral anterior synechiae
Uveitis
Hyphema
Corneal abrasion/punctate keratopathy
Corneal burns (epithelial/endothelial)
Syncope
Adverse effect on future filtering success

A. PRESSURE ELEVATION

Elevation of IOP following treatment has been reported by most investigators. Thomas et al reported a 25.3% incidence of pressure elevation in 300 treated eyes. This occurred in 20.9% of eyes considered successful, as compared to 47% of eyes that were later "failures."[136] In another study, Horns et al reported a 9.2% incidence of IOP elevation within the first 28 days after treatment.[53] When considering IOP elevation that occurred at any time following treatment (19.5% of patients), 11% of these eyes had between 1 and 4 mm Hg of elevation, 6.3% had a rise of 5–9 mm Hg, and 2.1% had a rise of greater than 8 mm Hg. Krupin et al reported a much higher (53%) incidence of pressure elevation, with a range of 1–22 mm Hg in 57 eyes.[63] Forbes and Bansal[30] found a 21% overall incidence of pressure elevation, with a range of 7–27 mm Hg. In agreement with the earlier report of Thomas et al, Forbes and Bansal noted a failure rate of 36%, twice that of the entire treated group, in those patients who experienced pressure elevation. Hoskins and coworkers reported a 22.5% incidence of IOP elevation within the first six hours following treatment.[54] Others have reported similar results.[175]

The Glaucoma Laser Trial Research Group[36] recently reported its findings regarding the acute effects of ALT on IOP in 271 eyes assigned to receive ALT as a first intervention (two sessions; four weeks apart). The incidence of an IOP rise 5 mm Hg or greater above baseline was noted in 34% of patients after one or both treatment sessions. Twelve percent of eyes demonstrated an increase of 10 mm Hg or more. Patients who had pressure elevation after the initial 180° treatment were more likely to demonstrate a rise in pressure after treatment two. Pigmentation of the trabecular meshwork proved to be the most significant risk factor for this acute pressure rise. In a separate study Keightley et al, using two-minute tonography performed with a pneumotonography unit, reported a correlation between a low coefficient of outflow and a greater risk of a post treatment rise in IOP.[55a] No statistical analysis was provided, however.

In terms of the onset of the elevation, Weinreb et al found that post-laser pressure elevation was most likely to occur within three to five hours in the 360°

treatment group and earlier in the 180° treatment group.[156] Krupin et al treated 360° of angle and found that 8 of 10 eyes that experienced a pressure elevation did so within the first post-treatment hour.[63] The remaining two eyes demonstrated pressure elevation at four hours and at seven hours, respectively. These results led the authors to recommend careful follow-up of patients, especially in the immediate postoperative period.

Over the long-term, Thomas et al reported that ALT made the pressure status worse in 3% of all eyes (primary and secondary glaucomas).[136] Similarly, Horns et al found that 7.4% of patients had a higher final post-treatment pressure reading[53] and Hoskins and coworkers reported this in 6% of their patients.[54] These reports indicate that ALT can sometimes permanently worsen the pressure status in some patients. This risk must be appreciated by the physician and understood by the laser candidate.

Since, in some cases, an acute rise in IOP following ALT has been associated with loss of central vision,[136,154] avoidance of post-laser pressure elevation has been a goal of laser therapists. Variations in laser burn location, number, power, and duration have all been tried to minimize this untoward result. Schwartz et al reported less IOP elevation with anterior placement of the laser burns.[119] Thomas et al also have correlated placement of the burns to pressure elevation.[137] They noted a higher incidence of pressure elevation in reports from investigators who treated the posterior meshwork (Kitazawa et al, *International Symposium on Laser Surgery for Glaucoma,* Saratoga Springs, NY, July 20–21, 1981) as compared to those who treated the anterior trabecular band (Beckman H, *International Symposium on Laser Surgery for Glaucoma,* Saratoga Springs, NY, July 20–21, 1981). Kitazawa and coworkers in a separate report, however, did not find any difference in those patients treated on the posterior versus the anterior aspects of the trabecular meshwork.[58]

Many investigators have reported significantly fewer and lower pressure elevations (frequency, magnitude, or duration) when they treated only 180° per session as opposed to the full circumference of the angle.[22,54,58,123,136,156] Weinreb et al, for example, randomized 40 patients with different types of glaucoma into groups of either 180° or 360° treatment.[156] They corrected pressure changes for diurnal variation by subtracting the pressure change in the untreated eye from that in the treated eye. They found that this mean corrected maximal pressure rise following trabeculoplasty was 1.3 ± 4.91 mm Hg in the 180° group, as compared to 7.35 ± 9.28 mm Hg in the 360° group. This difference was significant, and was found to be of even greater magnitude when eyes not experiencing pressure spikes were excluded.

Another proposed association of post-ALT IOP elevation is laser energy. In monkeys, Quigley and Hohman demonstrated an increased risk of pressure elevation when higher levels of laser energy were delivered to the primate trabecular meshwork.[91] On the basis of this work in animals, these investigators proposed not exceeding 0.1 sec duration to maintain a window of safety against inadvertent over-treatment, damage to the angle structures, and subsequent pressure elevation in clinical human studies. Investigators have, in fact, described more frequent postoperative pressure increases with higher laser energy levels.[102,105] For these reasons, clinicians generally limit treatment to power levels of 500 to 1000 mW.

The etiology of post-treatment pressure elevation has proved elusive. In light of the known effects of prostaglandins on IOP, these substances have been suspected to be possible causative factors in the post-ALT pressure spikes. Neither aqueous analysis[20] nor treatment with antiprostaglandin agents have corroborated a role for prostaglandins in acute post-laser pressure rise.[20,55,83,145,154] Greenidge and associates examined histological specimens from four patients with medically unresponsive pressure elevation following ALT with and without peripheral iridotomy.[40] These specimens revealed intertrabecular inflammatory debris not seen in eyes without pressure elevation, which suggested an inflammatory etiology. Koss and coworkers reported similar findings in cynomolgus monkeys.[60] Unfortunately, pretreatment with topical steroids for 36 hours before laser therapy has not been shown to prevent postoperative pressure rises or to affect final pressure outcomes.[108] Ofner et al reported that instillation of 4% pilocarpine in the immediate post-laser period reduced the frequency and magnitude of pressure elevations compared to controls.[52] They postulated that post-laser pressure spikes might be due to a mechanical blockage of outflow channels that could be somewhat alleviated by a cyclotonic agent, such as pilocarpine hydrochloride.

Various attempts have been made to control postoperative pressure spikes with pharmacologic agents and other means. Indomethacin, flurbiprofen, and corticosteroids, as mentioned previously, were not efficacious in preventing this complication.[55,108,145,154]

Recently, Robin and associates have reported on their experience with the use of apraclonidine hydrochloride, a member of a relatively new class of agents, the alpha-2 agonists.[100] In a prospective ran-

domized, double-masked study, these investigators compared 1% apraclonidine hydrochloride against placebo in 73 eyes undergoing 360° of ALT. No eyes in the apraclonidine hydrochloride group, compared to 18% of the placebo group, had pressure elevations of 10 mm Hg or greater. Only 21% of the treated group compared to 59% of the placebo group, had any elevation at all. These findings were confirmed by Brown et al.[10] Because it is a topical drug, apraclonidine hydrochloride should circumvent the side effects associated with osmotics or carbonic anhydrase inhibitor type agents that are often used to treat post-laser pressure elevation. In addition, since apraclonidine hydrochloride is not presently used in the longterm treatment of glaucoma, this agent could have the distinct advantage of preventing pressure spikes when used in patients receiving maximal medical therapy.

B. LOSS OF CENTRAL ISLAND OF VISION

It should come as no surprise that even transient elevation in intraocular pressure has been associated with permanent visual loss. Laser trabecular treatment in animals that caused pressure elevation has resulted in subsequent optic nerve damage.[71,92] Clinical reports from Thomas et al[136] and Weinreb et al[156] describe patients with end-stage disease who lost remaining central islands of vision following a post-laser pressure rise. Although a cause-effect relationship was assumed, progressive loss of vision has also occurred in patients having had no apparent pressure elevation after ALT.[50] In counseling patients and weighing options, clinicians should remember that this catastrophic complication is not limited to ALT, considering that it has been reported following conventional filtration surgery.[157]

C. PERIPHERAL ANTERIOR SYNECHIAE

Schwartz et al[118] and Wilensky and Jampol[165] were among the first investigators to report peripheral anterior synechiae (PAS) formation following ALT. In their group of 35 eyes, Schwartz et al noted PAS in 29% of their patients. They were not able to correlate PAS occurrence to success or failure of the treatment and did not find any relationship to racial characteristics. Wilensky and Jampol reported PAS in two patients who had developed a significant postoperative uveitic reaction. Other studies have reported rates of PAS formation ranging from 12% to 47% following similar treatment protocols.[136,141] Unlike Schwartz et al, Pappas and associates[83] found a much higher incidence of PAS in black patients (91%) compared to whites (13%). They also reported that treatment with topical indomethacin did not prevent this complication. The Glaucoma Laser Trial Research Group[36] reported an incidence of

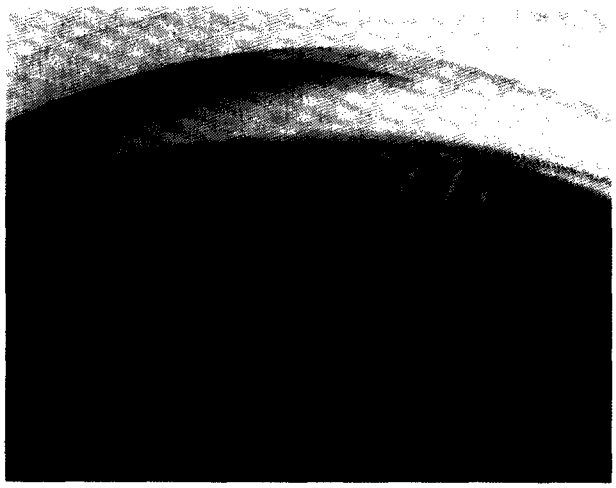

Fig. 5. Typical pattern of peripheral anterior synechiae (PAS) produced by ALT. (Reprinted from Schwartz AL et al[118] with permission of the authors and publisher of *Ophthalmology*.)

PAS formation in 46% of those eyes that received ALT as an initial intervention. In 33% of the eyes peripheral anterior synechiae involved the trabecular meshwork. Factors presumed to predispose to PAS formation include high power levels and posterior placement of the burns. Traverso et al reported that ALT was no less effective when burns were placed anteriorly, but that PAS developed in only 12% of anteriorly treated eyes, compared to 43% of those eyes treated posteriorly.[141] Rouhiainen and associates reported a similar relationship, and observed more PAS formation in those eyes receiving higher levels of laser power.[106]

Many investigators have suggested that PAS, which usually just extend to the scleral spur, are of no real clinical significance (Fig. 5).[36,115,136] In contradistinction, Rouhiainen et al reported that those eyes with PAS demonstrated smaller post-laser decreases in intraocular pressure.[106] Treatment of the anterior aspects of the trabecular meshwork is recommended to minimize PAS formation.

D. UVEITIS

Uveitis after ALT has generally been transient and of minor significance.[118] Wilensky and Jampol, however, described two patients who developed severe nongranulomatous iritis following ALT. In one patient, this condition lasted nine months and appeared recalcitrant to topical, sub-Tenons, and systemic corticosteroids.[163] Pappas and colleagues found that those eyes in which "significant" iritis developed were more prone to PAS formation.[83] Most clinicians now use frequent topical steroids in the immediate post-operative period, which is

thought to help minimize this undesirable complication.[54,134]

E. HYPHEMA

Transient microhyphemae were found in 2.3% of treated patients in the study by Thomas et al.[136] Earlier, Wise had reported a similar incidence of 5%.[166] These small hyphemae can usually be controlled by direct photocoagulation, as described by Wise[166,169] and Thomas et al,[134] and are of minor significance.

F. CORNEAL SEQUELAE

Corneal burns of both the epithelium and deeper layers have been seen and described by several authors, but these were in the early studies and have not been reported recently.[86,163,166] Hong et al reported significant increases in cell size following laser trabeculoplasty in 10 eyes at 6 and 12 months of follow-up.[52] In other prospective studies, however, no real effect on endothelial morphology, cell density,[138,140] or function[13] could be found. Although transient worsening of corneal edema in a patient with Fuchs' dystrophy[163] and late-onset bullous keratopathy in a traumatized eye[166] have been reported, we do not believe that permanent or significant corneal damage is a likely complication. Perhaps more significant is that corneal pathology may adversely affect the view of the angle structures, making treatment more difficult and at times impossible.

G. SYNCOPE

As with any procedure that involves pressure on the globe or ocular manipulation in anxious patients, syncope should be anticipated. Hoskins et al reported four such patients, three of whom were less than 40 years old.[54] It is unclear whether the laser aspects of the procedure might actually play a role in this adverse reaction.

H. EFFECT ON FUTURE FILTRATION SURGERY

In recent years, there have been thoughts expressed in the literature that ALT may lessen the chances of success of conventional filtration surgery.[43,85,94] In a series of 438 trabeculectomies on 435 eyes of 344 patients, Gross et al reported an overall 28% incidence of encapsulated blebs, increasing from 26% in 1983 to 33% in 1986. Patients with previous ALT demonstrated a doubling in the incidence of encapsulated blebs compared to those without it (33% versus 16%).[43] Perkins et al[85] and Richter et al[94] have also expressed the concern that ALT may in some way be related to the increased rate of encapsulated blebs seen in recent years. In the study by Richter and associates, encapsulation of the bleb was found to have occurred in 56 of 409 consecutive filtering procedures during a 40-month period. This complication occurred in 42 of 272 (15.4%) eyes that had received previous ALT compared to only 4 of 85 non-laser-treated eyes (4.7%). Neither the interval between laser and filtration surgery nor the number of spots were statistically linked to the risk of encapsulation in these subjects. The Advanced Glaucoma Intervention Study, which will be described in Section IX, may provide definitive information regarding this association. Until that time, however, we would discourage the routine use of ALT in every presurgical patient unless a reasonable chance of success exists.

It is worthwhile noting, however, that ALT avoids much of the acute morbidity usually associated with conventional filtration procedures. Post-treatment discomfort, medical care, and requirements for follow-up are usually less of a problem with this technique. Risks of expulsive choroidal detachments, endophthalmitis, and anesthetic reactions are avoided. ALT also has the distinct advantage of avoiding progressive cataract formation, which is often seen in the years following conventional filtration surgery.[152]

VIII. Retreatment

Unfortunately, most clinicians have seen a return to unacceptable intraocular pressure levels in some of their patients who initially had been controlled following ALT. Since filtration surgery is usually the next option, several investigators have been motivated to try retreatment with ALT in selected cases. Starita et al retreated 17 eyes that had been classified as failures after initial full ALT.[130] In 35% of eyes, a reduction in IOP of greater than 3 mm Hg along with stabilization of visual fields was obtained (average follow-up, 12 weeks). Three of the patients (18%) experienced an acute rise in IOP $\geq$10 mm Hg within four hours of treatment and one additional patient had a similar elevation at one week.

Brown and associates retreated 26 eyes with both primary and secondary glaucomas that had shown pressure reduction following previous initial ALT treatment (360° in one session or 180° in two sessions), on average, 16 months earlier.[12] Following the retreatment, which was divided into two sessions of 180° in most subjects, ten eyes (38.5%) had pressure elevation averaging 9.9 mm Hg and three of these had increased pressure ranging from 10 to 37 mm Hg. Eight of these retreatment failures demonstrated progressive visual field deterioration and required surgery within one month. Fourteen eyes (54%) did respond with a pressure reduction averaging 10.4 mm Hg. These eyes had stable visual

fields and were considered retreatment successes at an average follow-up of five months.

Richter and coworkers retreated 180° of angle in 40 eyes that had undergone previously successful ALT with 360° of treatment.[93] Retreatment success, described as an IOP decrease of 3 mm Hg or more, stable optic disc and visual fields, and avoidance of conventional surgery was achieved in only 32% of all eyes. Furthermore, Kaplan-Meier survival analysis predicted a progressively lower likelihood of maintained success, particularly after one year. Unlike in the study by Brown et al,[12] who treated the full circumference, no patients experienced IOP elevation greater than 6 mm Hg in the immediate post-laser period and none required urgent filtration surgery as a result of the technique.

Recently, Grayson et al reported on their experience with retreatment of 38 eyes, most of which were phakic and had POAG.[39] Retreatment was performed an average of two years following the initial treatment, which was at first successful. They reported a successful outcome in 73% of eyes at 12 months following retreatment. However, of those 15 eyes that underwent a second retreatment at 6 to 47 months after the first retreatment, eight (53%) required conventional filtration surgery. It is important to recognize that the initial ALT treatment consisted of fewer burns (mean = 65) than are usually applied by most clinicians. Similarly, Weber et al retreated 37 eyes classified as late treatment failure with an additional 50 laser spots scattered over 360°.[153] The IOP decreased by an average 6.4 mm Hg one month after the retreatment and all eyes were considered to have had a successful response at one month. The success rate had dropped to 70% by one year, and to 47% at 16 months. In a smaller series, Messner et al found retreatment successful in only a small percentage of their patients. They have raised the point that ALT retreatment may serve to delay necessary filtering surgery in the majority of cases.[76]

As can be seen, experience with retreatment has been variable and only a minority of patients have been able to avoid progression of disease for more than an additional year or two. All patients should be aware of the lower success rate, and the possibility of acute and chronic pressure elevation that have been described with retreatment. We tend to limit the use of retreatment to very elderly or infirm patients who experienced a good response to ALT that had been performed at least several years earlier.

IX. Ongoing Studies

A. ALT AS A PRIMARY TREATMENT

The use of ALT as a primary treatment has been described by several authors. In countries where access to medication and follow-up are limited, ALT appears to offer many advantages. Thomas et al reported their experience with 30 eyes of 20 Egyptian patients primarily treated with ALT for open angle glaucoma (average follow-up, 7½ months).[135] Success, which was defined as a pressure of less than 22 mm Hg without further optic disc or visual field progression, was achieved in 83% of subjects. In a similar study, but in an English population, Rosenthal et al reported that only 55% of patients obtained an IOP less than 22 mm Hg.[103]

In a retrospective study, patients who either were reluctant to use medical therapy or had other problems that precluded good medical compliance. Tuulonen reported an 81% success rate at 12 months (59 eyes) and 78% success (46 eyes) at 18 months after using ALT as the primary treatment.[144] In a prospective follow-up of 32 eyes that received ALT as their initial treatment, 50% had pressures less than 22 mm Hg at five years.[147] Tuulonen is now conducting a prospective randomized study comparing ALT and medical treatment. At the end of one year there was no statistically significant difference between the two groups.[146]

A second prospective study of ALT as initial therapy for open-angle glaucoma is being conducted in London. In this study, 168 patients with open-angle glaucoma were randomized into three groups. The first group was treated with trabeculectomy, the second with laser trabeculoplasty, and the third with medication. Interim analysis showed lowest mean IOP and least diurnal variation in the trabeculectomy group. Medical therapy was least effective in lowering IOP.[78]

A third multicenter prospective trial study is the Glaucoma Laser Trabeculoplasty Trial (GLT) sponsored by the National Eye Institute in the United States. Twenty-seven patients who have primary open-angle glaucoma are being evaluated over a minimum five-year time period. One eye was randomly selected to begin treatment with laser trabeculoplasty while the other eye is treated with medication. Medication was added to either eye as needed to obtain adequate IOP control and prevention of further visual field loss.

The two year follow-up results of the GLT Study have recently been published. In the eyes that were treated with ALT as the initial treatment, 44% remained under control after two years of follow-up with the laser treatment alone, and 70% remained under control with either the laser alone or a combination of the laser treatment and timolol. If another single topical antiglaucoma drop (pilocarpine or dipivefrin) was substituted for the timolol, then a total of 84% of eyes were controlled by laser alone or laser plus one antiglaucoma medication. Of eyes begun on medical treatment, 30% had the intraocu-

lar pressure controlled at the end of two years with timolol alone. If another single antiglaucoma topical medication (again, pilocarpine or dipivefrin) was substituted for the timolol, then an additional 21% were controlled, and, thus, a total of 51% of the medically treated eyes were controlled by a single agent. With any combination of one or two antiglaucoma drops, a total of 66% of eyes were under control at the end of two years.

Looking at the same data in the opposite way, 16% of the eyes were not controlled at the end of two years by laser alone or a combination of laser and one antiglaucoma medication, while 34% of the medically treated eyes were not controlled by one or any combination of two antiglaucoma medications at the end of two years. Also, the average intraocular pressure in the eyes that were treated first with ALT was approximately 2 mm Hg lower than the average intraocular pressure in the eyes that are treated with medicines alone. There was no significant difference at the end of two years in the visual field between the eyes treated first with the laser or with medication.

Among the arguments for beginning with laser treatment are that patients will be spared the exposure to the potential of serious side effects and complications of medical therapy and that patient compliance is eliminated as a factor in control of the glaucoma. Since more than half the patients in the GLT Studys56ended up on medical therapy by the end of two years of follow-up, then those potential advantages were of only transient benefit to those patients. On the other hand, there clearly may be a convenience factor for the patient to use only one drug rather than the two, and the average IOP in the eyes treated with the laser was lower than that of the eyes treated with medicine alone. Therefore, a reasonable case can be made to justify using ALT as the first avenue of treatment of primary open angle glaucoma. Whether these advantages are sufficient to justify this break with traditional practice and whether just two years of follow-up is adequate to make such a decision is something that each practitioner will have to decide individually.

B. ALT VERSUS FILTERING SURGERY

In 1984, Watson et al prospectively randomized medically uncontrolled glaucomatous eyes into surgical and laser treatment groups.[151] Although differences between the results prevented more detailed conclusions, the following statements were made by participating clinical centers: 1) ALT caused less of a pressure reduction than surgical trabeculectomy; and 2) 21% of patients in the ALT group required changes in their medical regimen or surgical intervention because of unsatisfactory pressures or progressive visual field loss as opposed to 10% of the trabeculectomy group.

A similar but much larger prospective study is the multicenter National Eye Institute sponsored Advanced Glaucoma Intervention Study (AGIS). Individuals will be randomized into one of two treatment pathways: 1) ALT followed by trabeculectomy if necessary, followed by repeated trabeculectomy as needed; or 2) trabeculectomy followed by ALT, if needed, followed by repeated trabeculectomy as needed. It is hoped that this study will not only provide indications for the use of ALT versus filtering surgery, but will also indicate whether ALT itself has any effect on the success of subsequent filtering surgery.

X. Recommendations for Treatment

A. TREATMENT PARAMETERS

Since many patients achieve a significant (and sometimes minimal) IOP reduction with treatment of only 180°, which reduces the risk of post-treatment elevated IOP, we recommend performing laser trabeculoplasty in two sessions. In rare instances when there is very advanced glaucomatous damage, we may deliver the treatment in 90° increments. Usually the second treatment will be performed one month after the initial one, but occasionally when the IOP reduction has exceeded our treatment objective, we may defer the second treatment session.

We recommend placing the treatment burns at the junction of the anterior border of the pigmented and nonpigmented trabecular meshwork. This seems to result in less pain during treatment, fewer peripheral anterior synechiae, and less postoperative inflammation. We use a 50μ spot for 0.1 seconds. We differ among ourselves as to laser power. One of us uses a standard power setting (800mW) for all treatments while the other two vary the power between 500 and 1000mW, depending on the tissue reaction. We all use blue-green argon laser energy for the treatment.

B. PATIENT MANAGEMENT AT THE TIME OF TREATMENT

Patients are instructed to continue their usual glaucoma medication. In eyes with very advanced visual field loss and for cupping of the optic nervehead, a drop of apraclonidine is instilled in the eye at the conclusion of the laser treatment. The patient's IOP is then monitored hourly for three hours. If a significant elevation of IOP is detected (generally defined as a rise of 10 mm Hg), apraclonidine, a carbonic anhydrase inhibitor and/or hyperosmotic agent, is administered.

When the patient is allowed to leave, he is instructed to begin using a topical corticosteroid drop in the eye every two hours until bedtime that day

and then four times a day for the next four days. The patient returns for a check-up in one week.

C. CASE SELECTION

We believe that ALT should be considered in most patients with primary open-angle glaucoma, exfoliation syndrome glaucoma, pigmentary glaucoma, and angle-closure glaucoma successfully treated with laser iridectomy but having residual elevated IOP. We frequently recommend it in low tension glaucoma and aphakic/pseudophakic glaucoma, but are much more selective about its use in eyes with uveitis, angle recession glaucoma and juvenile glaucoma. Other factors besides the glaucoma diagnosis must be taken into consideration in making the decision. What level of IOP is desired? In a patient with early POAG and IOP of 26 mm Hg, ALt may be appropriate since a 25% reduction will lower the IOP below 20 mm Hg. In a similar patient whose disease is advanced and the goal is to lower the IOP to below 15 mm Hg, filtration surgery may be more appropriate.

Another factor that must be considered is the age of the patient. As has been pointed out, younger patients do not tend to respond as well to ALT. Also, because of their longer life expectancy, younger patients need their IOP reduction to be sustained for a longer time. As has been demonstrated, the ALT-induced IOP reduction does not appear to be permanent in most cases. Therefore, in general, the younger the patient, the less likely we are to recommend ALT. Conversely, the older and more infirm the patient, the more likely we are to use it.

C. TIME OF TREATMENT

The place of ALT in glaucoma therapy is in flux. Initially, we used it only in eyes uncontrolled on maximum medical therapy. With time we have gradually used it earlier in the therapeutic regimen. We now often use it prior to carbonic anhydrase inhibitors, as a substitute for miotics in symptomatic patients or prior to cataract extraction in otherwise controlled eyes. With the growing reports of the successful use of ALT as an initial treatment for glaucoma, it is possible that before long we may begin to use it as our first line of therapy.

XI. Summary

In a relatively short time, ALT has become a standard in the treatment of various open angle glaucoma. Presently it serves as a logical step before conventional filtration surgery in selected medically uncontrolled patients, although there is a growing body of evidence that it may be appropriate as the initial form of therapy in open-angle glaucoma. Although the exact mechanism by which it lowers IOP is still uncertain, a measurable increase in tonographic outflow facility has been demonstrated and, as such, ALT is one of the few therapeutic modalities that actually reverses a pathologic factor found in most open angle glaucomas. Reported success rates and degree of pressure reduction vary with the exact type of glaucoma, particular features of the patient population, and technique employed. The duration of effect is variable and, although it usually is thought to diminish with time, it does avoid the need for filtration surgery in many patients. Studies are underway that should help to better determine the appropriate place for ALT in the treatment of the open angle glaucomas.

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