Multiple Laser Treatments for Macular Edema Attributable to Branch Retinal Vein Occlusion

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• PURPOSE: To report the visual outcome of multiple laser treatments for macular edema attributable to branch retinal vein occlusions (BRVO) and to determine if any prognostic factors exist for improvement.

• DESIGN: Retrospective chart review.

• METHODS: A private practice with four vitreoretinal surgeons performed laser treatments on 88 eyes of 88 patients with macular edema secondary to BRVO from 1984 to 2003. Mean preoperative and postoperative visual acuities were collected after each laser treatment. Final visual acuities were also documented.

• RESULTS: All 88 patients received at least one laser treatment, and 46 patients of the initial 88 underwent multiple treatments. Overall, forty-one (46.6%) of the total 88 patients improved by 2 or more lines, whereas 33 patients (37.5%) were within 1 line of the preoperative vision, and 14 patients (15.9%) worsened by 2 or more lines. The mean final visual improvement was 0.92 lines for all 88 patients. The group of patients that responded favorably to the first laser treatment (n = 37) showed an overall improvement of 3.5 lines. However, patients who responded poorly to the first laser treatment resulted in an overall worsening of vision by 0.96 lines.

• CONCLUSIONS: Our study found that multiple laser treatments can improve visual acuity and resolve macular edema and that each additional laser treatment gives a patient a modest chance of visual improvement. A positive or stable visual response to first laser treatment portends a favorable prognosis with subsequent laser treatments. (Am J Ophthalmol 2005; 139:653-657. © 2005 by Elsevier Inc. All rights reserved.)

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THE BRANCH VEIN OCCLUSION STUDY (BVOS) ESTABlished the paradigm for treating macular edema as a result of a branch retinal vein occlusion (BRVO).[1] In that landmark study, it was shown that laser photocoagulation can improve visual acuity in eyes with worse than 20/40 vision secondary to macular edema. The BVOS described a heterogeneous population with visual acuities ranging from 20/40 to 15/200 or worse, and their patients had from one to five lasers. The BVOS outcome data are reported as the net effect in all patients after all laser treatments and did not stratify visual outcomes based on the number of laser treatments. In clinical practice, however, vitreoretinal surgeons frequently advise patients of the risks and benefits of treatment every time a focal laser treatment (or re-treatment) is recommended. Patients commonly want to know the probability of seeing better or worse each time they have a laser treatment. Vitreoretinal surgeons also want to know the likelihood of improvement so that the patient's expectations can be appropriately managed. The goal of this article is to stratify the visual outcomes of single and multiple laser treatments to advise patients of their chances for improvement, stabilization, and worsening with each treatment and to determine if any prognostic factors exist.

METHODS

THIS RETROSPECTIVE STUDY WAS CONDUCTED IN A PRIvate practice involving four retina specialists (M.G.M., T.M.T., J.S.H., A.R.F.). Charts were retrieved from all patients first seen between 1984 and 2003 with both a diagnosis code for branch retinal vein occlusion and a treatment code for focal photocoagulation, yielding 164 eyes belonging to 157 patients. Of these 164 eyes, 76 eyes were excluded because of the following exclusion criteria: incorrect diagnosis coding, co-existing ocular disease (age-related macular degeneration, glaucoma), or treatments that may otherwise affect or alter data on final visual outcome (cataract surgery, neodymium/yttrium aluminum garnet capsulotomy). Patients with neovascularization or

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vitreous hemorrhage or any history of panretinal photocoagulation associated with BRVO were excluded as well. Patients with less than six months of follow-up were also excluded.

For this retrospective analysis, basic information was obtained from each patient's chart, including gender, age, and presence or absence of diabetes, smoking, hypertension, and vascular disease. The information about comorbidities was obtained from medical history forms filled out by the patients. Resolution or persistence of macular edema at the culmination of treatment was also noted.

The initial diagnosis of BRVO and macular edema were made by fundoscopic examination and confirmed by fluorescein angiography. According to the recommendations developed in the BVOS, laser treatment was suggested for all patients with persistent macular edema with intact perifoveal capillaries and only after resolution of intraretinal hemorrhage. In general, the BVOS recommendations regarding patient selection and laser technique were used in our study, but each surgeon used his or her best judgment to determine when to treat or stop further treatments. Each patient was evaluated three months after the initial laser treatment. If at that point or later in follow-up the patient was found to have persistent macular edema and vision loss, he or she was offered an additional laser treatment. An ophthalmic examination was performed at each subsequent visit, including visual acuity measurement, fundoscopic examination by slit-lamp biomicroscopy to determine the presence, absence, or resolution of macular edema, and repeat fluorescein angiography if necessary. Optical coherence tomography was not performed on most of the subjects because the technology was not available to the practitioners at the time.

Visual acuities were recorded when the BRVO was first diagnosed, before each laser treatment, three months after each laser treatment, and at subsequent follow-up visits. The final vision at the most recent office visit was also recorded. The number and timing of laser treatments for macular edema were documented. Only focal or grid laser treatments conducted to treat macular edema were included in this study.

All visual acuities were measured on a standard Snellen chart, counting fingers (CF), and hand motions (HM). Outcomes of laser treatments were measured by counting lines of improvement. A change in acuity of 2 lines or more was considered either significantly improved or worsened. A change of 1 line better or worse than the preoperative vision was stable. The best-corrected or pinhole VA at each visit was recorded. Average visual acuities were determined by converting Snellen acuity fractions to logarithm of the minimal angle of resolution equivalents.[2] Lines of improvement among groups of patients were measured by subtracting the preoperative and postoperative logMar values. *T*-tests were used for statistical analysis to compare lines of improvement in patients with single vs multiple laser treatments. The effect of multiple laser therapy on clinical and visual outcome was determined using χ^2 analysis. The number of patients receiving three or more laser treatments (n = 15) was considered too small to make separate groups from which to infer statistical outcomes. Thus, data from patients who received three or more laser treatments were reported in the entire group of patients regarding outcomes (i.e., "all lasers" in Table 2).

TABLE 1. Number of Patients Who Underwent Single and Multiple Laser Treatments for Macular Edema After Branch Vein Occlusions

Number of Lasers	Number of Patients n (%)
One laser	88 (100%)
Two lasers	46 (52.3%)
Three lasers	15 (17.0%)
Four lasers	4 (4.5%)
Five lasers	1 (1.1%)

TABLE 2. Visual Response to Single vs Multiple Laser Treatments for Macular Edema After Branch Vein Occlusions

	Improved by 2 or More Lines	Plus or Minus 1 Line	Worsened by 2 or More Lines
Laser 0 → Laser 1 (n = 88)	37 (42.0%)	39 (44.3%)	12 (13.6%)
Laser 2 → Laser 5 (n = 46)	23 (50.0%)	16 (35.0%)	7 (15.0%)
All Lasers (n = 88)*	41 (46.6%)	33 (37.5%)	14 (15.9%)

*Includes all patients after undergoing all laser treatments.

RESULTS

EIGHTY-EIGHT EYES OF 88 PATIENTS WERE INCLUDED IN this study. The mean age at the time of diagnosis was 72.5, with 48 female and 40 male patients. All patients (n = 88) underwent at least one laser treatment. Forty-six patients underwent two laser treatments, 15 patients underwent three laser treatments, four patients underwent four laser treatments, and one patient underwent five laser treatments (Table 1). The average time to first laser was 5.8 months, and the average time to the final visual measurement after final laser was 17.5 months.

• **VISUAL OUTCOMES:** Visual acuity at the initial presentation of BRVO diagnosis was 20/91 for all 88 patients. The average time interval between diagnosis of the BRVO and any laser treatment was 5.8 months, allowing for clearance of intraretinal hemorrhage and any spontaneous resolution of macular edema.

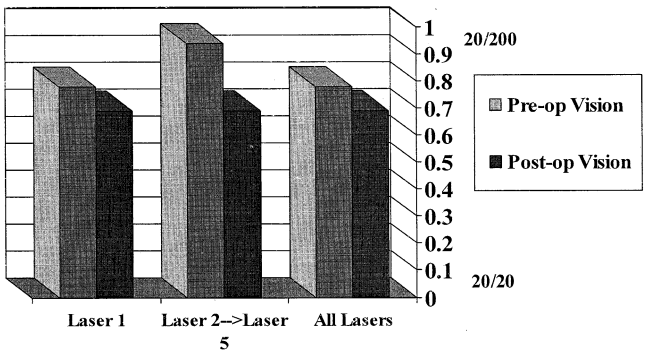

FIGURE 1. Preoperative and postoperative visual acuities in patients with macular edema after a branch vein occlusion, comparing visual outcomes in single and multiple lasers. Data are expressed in logMar units, where zero is equivalent to 20/20 and one is equivalent to 20/200.

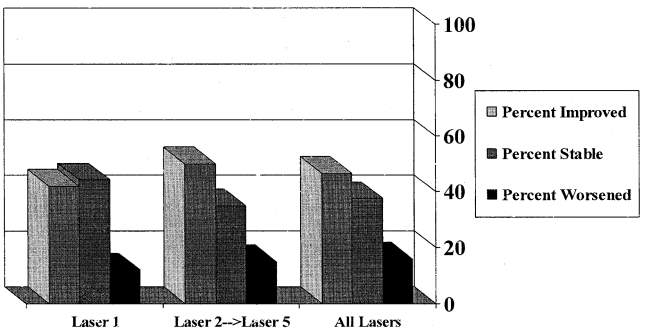

FIGURE 2. Percentage of eyes whose vision improved, stabilized, or worsened after laser treatment for macular edema from branch retinal vein occlusions. Percentages are used to compare single and multiple lasers.

Mean preoperative visual acuity for all 88 patients was 20/121 (± 4.7 lines). Among the 88 treated eyes, 37 patients (42.0%) gained 2 or more lines from baseline preoperative vision after one laser treatment. Thirty-nine patients (44.3%) remained within 1 line of the preoperative vision, and 12 patients (13.6%) lost 2 or more lines of vision ($P \leq .0001$, Table 2). After the first laser treatment, the mean preoperative vision of 20/121 improved to a vision of 20/99, a mean improvement of 0.88 lines.

Forty-six of the initial 88 patients went on to get anywhere from two to five laser treatments because of persistent macular edema as determined by clinical and fluorescein angiogram findings. Of these patients, 23 (50.0%) eventually gained 2 or more lines of vision, 16 (35%) remained stable, and seven (15.0%) worsened by 2 or more lines (Table 2, Figure 2). The mean visual acuity before the second laser was 20/174, which improved to an average vision of 20/98 after treatment, leading to a 1.28 line improvement. When comparing the visual outcome between single laser treatments to multiple laser treatments, this was not statistically significant ($P = .60$, Table 4).

Patients with three, four, or five laser treatments were not separately categorized for analysis because of such a small number of patients. These fifteen patients were grouped with the 46 patients who underwent multiple lasers.

When combining the data for all 88 patients (46 of whom underwent multiple laser treatments) 41 patients (46.6%) improved by 2 or more lines, 33 (37.5%) remained within 1 line of the preoperative vision, and 14 (15.9%) worsened by 2 or more lines (Table 2, Figure 2). Mean preoperative vision was 20/121, and the final postoperative vision resulted in 20/98, and average of 0.92 lines of improvement (±4.5 lines) over an average follow-up of 17.5 months (Figure 1).

• **EFFECT OF MULTIPLE LASER TREATMENTS ON OVERALL OUTCOME:** Among the total 88 patients, 37 patients (42.0%) showed 2 or more lines of vision improvement after their first laser treatment. This group gained an average of 3.5 lines of vision over the entire treatment course. Because of persistent edema, 17 (45.9%) of these 37 patients required more laser treatments. Eight (47.1%) out of 17 achieved further improvement of 2 or more lines with more photocoagulation, and 7 (41.7%) remained stable within 1 line of their preoperative vision, whereas only 2 (11.8%) worsened ($P = .157$, Table 3).

Thirty-nine of the initial 88 patients remained stable, within 1 line of their preoperative vision, after their first laser treatment. Twenty of the patients in this group went on to receive additional laser, 12 (60%) of whom eventually improved by 2 or more lines, whereas seven (35%) remained stable, and only one (5%) worsened ($P = .007$, Table 3).

Patients who did not stabilize or improve but actually worsened (n = 12) after initial laser were the most likely candidates to receive additional laser. Nine patients (75%) who had worsened by 2 lines with initial laser received additional treatment, resulting in three that improved by 2 or more lines, two that remained stable, and four that continued to worsen ($P = .72$, Table 3).

• **RESOLUTION OF MACULAR EDEMA:** The presence or absence of macular edema was ascertained by clinical examination using slit-lamp biomicroscopy. For most of these patients, optical coherence tomography was not available at the time of their diagnosis and treatments. Seventy-nine of 88 eyes had documentation describing the presence or absence of macular edema after laser treatment, of which 82% showed complete resolution on clinical examination. Of the eyes that underwent single laser treatment, 36 (90%) of 40 eyes had resolution of macular edema. Among those that underwent multiple laser treatments, 29 (74%) of 39 eyes had resolution of macular edema.

TABLE 3. Effect of Further Laser Treatment Based on the Outcome of Initial Laser for Macular Edema After Branch Vein Occlusions (n = 46)

	Improved by 2 or More Lines n (%)	Plus or Minus 1 Line n (%)	Worsened by 2 or More Lines n (%)	*P* Value
Initially improved (37) n = 17	8 (47.1%)	7 (41.7%)	2 (11.7%)	.1578
Initially stable (39) n = 20	12 (60.0%)	7 (35.0%)	1 (5.0%)	.007853
Initially worsened (12) n = 9	3 (33.0%)	2 (22.2%)	4 (44.4%)	.716531

DISCUSSION

IN CLINICAL PRACTICE, VITREORETINAL SURGEONS ADVISE and recommend laser treatment for macular edema caused by a BRVO. Both patients and surgeons want to know the probability of improvement or worsening with each laser. Understanding the effect of multiple laser treatment allows us to communicate with patients more clearly and helps us to better manage patient expectations.

Many factors determine if a surgeon will recommend multiple laser treatments. Sometimes, edema resolves after one laser treatment obviating the need for further treatments. At other times, surgeons advise no further laser treatment because they feel it is of low value to the patient given the clinical context. In reviewing our data, we found several useful pieces of information that can help us understand a patient's prognosis.

First, multiple laser treatments lead to overall visual improvement. When looking at the data of all 88 patients who underwent one laser treatment, most showed either improvement or stabilization of vision. This outcome was already addressed and proven by the BVOS. Of these initial 88, a subset of them (n = 46) went on to receive multiple laser therapies, anywhere from two to five treatments. Twenty-three (50%) of these eyes improved further by 2 or more lines, whereas 16 (35%) remained stable. This is of particular interest because the BVOS did not look specifically at this subgroup of patients who received more than one laser. This data can be useful to both vitreoretinal surgeons and patients when counseling them on the risks and benefits of a second, third, or fourth laser treatment.

Second, the response to initial laser treatment is a helpful prognostic indicator of the patient's response to subsequent lasers. If patients showed visual improvement of 2 or more lines after the initial laser, they were more likely to show further improvement whether or not they underwent subsequent treatments. Of the patients that showed initial visual improvement (n = 37), 17 underwent further treatment, of whom 47.1% showed 2 or more lines of improvement, whereas another 41.7% stabilized (Table 3). Although these results were not statistically significant ($P = .157$), it shows a positive trend toward improvement with further laser therapy. Additionally, patients who stabilized after their first laser (within 1 line of their preoperative vision, n = 39) showed a statistically significant improvement with subsequent laser therapy ($P = .007$), with 60% improving by 2 or more lines and 35% stabilizing (Table 3) by the end of all treatments. The results of both of these groups support the statement that an improved or stable initial response to a single laser treatment predicts a positive response to subsequent laser treatments.

Conversely, if patients showed worsening of 2 or more lines after the first laser treatment, additional laser does not appear to improve overall outcome. All 12 patients worsened by an average of 0.96 lines by the end of treatment, with only 33% improving by 2 or more lines. Although these data are compelling, only a small number of patients fell into this category, which is not enough to draw any significant conclusions.

Third, the data show that each step of the laser treatment carries a modest chance of visual improvement (42% to 50%) over one to five treatments. It also shows a good chance that vision will remain stable (35.0% to 44.3%) and a low but constant (13.6%-15.9%) chance that the vision will drop by 2 lines. This observation is interesting since we expected a diminished return with each additional laser treatment.

Finally, patients who underwent single laser treatments were more likely to achieve resolution of macular edema than those who underwent multiple laser treatments. Intuitively, this makes sense, because patients with persistent macular edema were more likely to receive additional treatments.

There are methodologic differences between BVOS and our study. The BVOS was a randomized controlled clinical trial, whereas ours was a retrospective chart review. Lighted ETDRS charts were used in the BVOS, whereas our retrospective review looked at Snellen acuities.

In general, our data corroborate the BVOS. Both studies show that laser treatment is beneficial for patients with macular edema attributable to BRVO. The BVOS showed a better outcome in terms of mean lines of visual improvement (1.33) compared with our data (0.92). Overall, the percentage of patients gaining 2 or more lines of vision was 65% in the BVOS vs 46.6% in our study. These differences may have been as a result of many factors, such as worse average prelaser visual acuity seen in our patients and differences in stratification of visual acuities. A greater number of our patients also underwent more than one laser treatment in this study than in the BVOS. There may have

TABLE 4. Clinical Response to Single vs Multiple Laser Treatment for Macular Edema After Branch Vein Occlusions

	Pre-op Vision (logMar/Snellen)	Post-op Vision (logMar/Snellen)	Mean Lines Improved (Snellen Chart)
Single laser			
treatment	0.78	0.69	
(n = 88)	20/121	20/99	0.88
Multiple laser			
treatments	0.94	0.69	
(n = 46)	20/174	20/98	1.28
P-value	—	—	0.60

logMAR = logarithm of the minimal angle of resolution.

also been differences in patient population. Based on each physicians' clinical judgment, we treated six symptomatic patients with visual acuities better than 20/40 who would not have been eligible in the original BVOS, ultimately leading to a less impressive leap of visual improvement in these patients.

To our knowledge, we are unaware of previous reports in the literature that looked at the effects of multiple laser treatments for macular edema from a BRVO. Our study indicates that multiple laser treatments can be helpful for patients with persistent macular edema. Furthermore, each laser treatment results in a benefit measured by average acuity and chances for a 2-line improvement. Improved or stable vision after the first laser is a good prognostic sign. Conversely, failure to improve with initial laser is less likely to lead to a good visual outcome.

Newer approaches to the management of macular edema associated with branch vein occlusions, which include adventitial sheathotomy[3–7] or intravitreal triamcinolone acetonide,[8] are hopeful developments, particularly in patients with poor outcomes. Although these approaches are still in their early stages of development, multiple laser treatments should still be the initial treatment of choice.

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