Chapter 7
Laser for Retinal Vascular Occlusions

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Retinal Vein Occlusions

Introduction

Retinal vein occlusion (RVO) is, after diabetic retinopathy, the most common cause retinal vascular cause of visual loss. The incidence of RVO increases with age, peaking in the 7th decade. Li et al., [20] Predispositions, in addition to age, include diabetes mellitus, hypertension, smoking, open angle glaucoma, hypercholesterolemia and cardiovascular disease. In younger patients, systemic inflammatory disease, hyperviscosity syndromes, and hyper coagulopathies should be investigated. Except in younger patients, medical and laboratory workups are seldom indicated or fruitful. Studies differ on whether or not male sex is an independent risk factor for RVO [34, 35].

For RVO, the predominant cause of VO is thought to be thrombus formation impeding venous outflow. Because retinal circulation has one entry (the central retinal artery) and one exit (the central retinal vein), impediment of venous outflow similarly reduces arterial inflow, and thus retinal vascular blood transit. By reducing retinal blood flow to the affected area, whether it be the entire retina (central RVO, or CRVO) or part of the retina (hemi-or branch RVO, HRVO or BRVO), retinal oxygenation is reduced causing partial to complete retinal ischemia and concomitant degrees of retinal dysfunction [1].

The cause of intravenous thrombus development in most cases of RVO is thought to be physical compression of the retinal vein by the adjacent retinal artery. Retinal veins can be thought of like fire hoses or "floppy" low pressure vessels that tend to collapse when nonperfused. In contrast, retinal arterioles carry blood under high

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pressure. Thus, their structure is more robust, akin to typical garden hose or conduit, more firm and rigid.

With age, and further predisposed by systemic hypertension and cardiovascular disease, there is an increase in the retinal arterial wall-to-lumen ratio. This makes the retina arteries "harder" and more inflexible. Under the influence of systemic hypertension, myogenic hypertrophy may also occur, increasing the wall diameter [1].

The CRV and CRA lie side-by-side with the optic nerve, entering the eye through the highly inelastic lamina cribosa. Once entering the retina, the paths of the veins and arteries tend to diverge but remain roughly parallel, crossing paths at regular intervals. At these crossing points, the RVs and RAs are tightly bound together by a glial adventitial sheath which is also highly inelastic. Where the RV and RA are bound tightly together by inelastic sheaths, if there is thickening and increased density of the RA the only place the RA can expand is into the space occupied by the RV. This compression reduces the lumen of the retinal vein, leading to turbulent and variably reduced blood flow. If this reduction in flow is sufficient, patients may experience mild to moderate symptoms of visual disturbance, often intermittent and fluctuating, as well as clinical findings of retinal venous dilation and slowed retinal vascular transit by fundus fluorescein angiography in the affected area of the retina. More severe compression increases the chances of thrombus formation due to a combination of slowed and turbulent blood flow. Most often, thrombus formation results in incomplete obstruction of RV outflow. If the RV obstruction is complete, either due to severe arterial compression or complete thrombus formation, ischemia of the affected retina may be severe and permanent, and with it, the loss of visual function. Retinal, macular, and optic nerve edema, along with diffuse inner retinal hemorrhages, generally flame-shaped, are the typical clinical manifestations reflecting severe inner retinal ischemia due to RVO (the outer retina being served by the choroidal circulation). The superior hemi-retinal vein and superior branch retinal veins are most commonly affected, reflecting common anatomic variations in the posterior retinal distributions of retinal arteries and veins [27]. If it occurs or extends into the macula, retinal ischemia, indicated by capillary non-perfusion, will be visually significant. Elsewhere, areas of ischemia will result in scotomata of varying density that may or may not be symptomatic. However, the most important cause of visual loss in RVO is macular edema (ME) resulting from ischemic damage to perfused macular capillaries causing them to become incontinent and leak serum into the extracellular space of the macula, distorting anatomic relationships and reducing visual function. This tissue damage and dysfunction, along with the ischemia itself, lead to chronic inflammation which exacerbates and amplifies these changes, acting as an additional driving force maintaining the macular edema, and eventually leading to tissue degeneration [16] .

In mild and early non-ischemic, perfused cases of RVO (in which imaging of the retinal capillaries shows them to be present and intact), the macular capillaries are generally responsive to treatment. The response to treatment is to demonstrate reduced leakage and swelling of the macula and often improved visual acuity, which persists while effective treatment is present. Like any other disease process, milder

cases are generally more responsive to treatment, improving more, more quickly, and for longer periods than more severe cases. When the RVO is more severe and/or the ME more chronic, long-term ischemic damage to the macular capillaries, along with the effects of degenerative chronic inflammation, lead to permanent and irreversible damage to the microvasculature often rendering it unresponsive to any type of treatment, making visual loss permanent. Prior studies suggest the likelihood of developing degenerative, unresponsive ME is highest in cases 2 years or more in duration [11].

Severe ischemia resulting from total or near-total RVO results in loss of vascular perfusion and structure of both capillaries and larger vessels in the distribution of the watershed area served by the obstructed retinal vein. If this occurs in the macula irreversible visual loss occurs. Outside the macula, the main risk to visual function is the development of disc or retinal neovascularization (NV) and the resultant risks of vitreous hemorrhage, much less so, traction retinal detachment. The risk of NV is directly related to the degree and area of capillary non- perfusion, the more complete the capillary closure and larger the area involved, the greater the likelihood of developing disc or retinal NV. When such NV develops, it is typically at the junctions of perfused and non-perfused retina [16, 27].

As implied above, the clinical significance of RVO is largely due to a combination of severity and location. Unless completely non-perfused, and thus at risk for developing NV, extramacular RVO is generally inconsequential and requires no treatment. ME is the most common indication for treatment in RVO, thus RVO involving the macula is of primary importance. ME also may result from obstruction of the entire retinal outflow due to CRVO. In other cases, visually significant ME may result from obstruction of a small macular tributary retinal vein, sometimes described as a "twig" BRVO. Either may be difficult to treat, but generally the greater the area of impaired retinal circulation and greater the flow compromise, the more severe the ME and more difficult to treat [18].

Although the presumed thrombus at the heart of the VO primarily responsible for the impairment of blood flow will generally eventually resolve with re-cannalization of the vessel and restored or improved retinal vascular transit, damage to the retinal vasculature by this time in all but the very mildest cases is generally permanent. Thus, absent effective treatment, the ME associated with RVO will generally persist for many years, if not permanently. Because most effective treatments for RVO ME are short-lived, the clinical course of ME due to RVO is generally waxing and waning over many years [12].

Thus, the practical goal of treatment is to minimize both the severity of the ME, and the length of time the macula is swollen in order to prevent degenerative changes and preserve responsiveness to treatment with the hope that someday the ME will finally resolve and useful visual function will remain. Treatment of ME due to RVO is generally a long and difficult ordeal, with often modest rewards, for the patient and doctor alike [16, 20].

Subtypes of Retinal Vein Occlusion

Venous occlusive disease may affect either a branch retinal vein (BRVO), central retinal vein (CRVO), or in eyes in which the superior or inferior venous outflow of the retina has been occluded, the term hemiretinal vein occlusion (HRVO) is assigned.

Branch Retinal Vein Occlusion

BRVO occurs when a branch of the central vein is occluded. The site of obstruction usually occurs at a retinal venous artery intersection or crossover. BRVO usually occurs in the seventh decade of life [18]. An increased risk BRVO was seen in those with a history of cardiac disease, hypertension, an increased body mass index, history of elevated serum levels of alpha-2-globulin, and a history of glaucoma. Diabetes was not a strong independent risk factor for BRVO in one study. Elevated HDL cholesterol showed a decreased risk for BRVO [34]. Clinical findings for an acute BRVO, defined as one present for less than 6 months, consists of superficial and deep retinal hemorrhages, venous tortuosity and dilation, and retinal or macular edema [14].

Typically, the affected area is segmental in distribution corresponding to the region drained by the occluded branch retinal vein. Acutely, disc swelling and cotton wool spots may be present. The most affected branch is the superotemporal venous branch, seen 63% of the time. In almost all other cases, it is the inferotemporal branch [13]. Typically, visual acuity is worsened by ischemia of the macula, hemorrhage and or edema. Vision may not be affected if the blockage is outside the branches draining the macula or in the nasal retina. Generally, the peak of the distribution of the hemorrhages is the region where the obstruction occurred at an arteriovenous crossing. After 6 months, a BRVO may be defined as chronic. Collateral vessel formation may be seen along with a resolution of hemorrhage. A determination of perfusion status may be revealed with the use of fluorescein angiography. Existence of macular edema can be quantified with the use of OCT imaging. In about 40% of nonperfused or ischemic BRVO, retinal or disc neovascularization (NV) may develop. This may be further complicated by vitreous hemorrhage in about 60% of cases with NV. Neovascular tissue should not be confused with collateral vessel formation, which are venule to venule channels and can appear tortuous, dilated, intraretinal, and bypass the obstruction. Fluorescein angiography can be used to help differentiate. Neovascular glaucoma and neovascularization of the iris are not common in BRVO [14].

Central Retinal Vein Occlusion

CRVO is a common cause of visual loss in patients 50 years and older [14].

The Eye Disease Case−Control Study showed that systemic hypertension, diabetes mellitus, and open angle glaucoma are risk factors for the development of

CRVO [35]. In addition, hypercoaguable or hyperviscosity syndromes can increase risk. CRVO is distinguished by diffuse intraretinal hemorrhages are superficial and deep and spread from the optic nerve head out to the periphery in all four quadrants. Cotton wool spots may be seen, and optic nerve head and macular edema are usually present. During its clinical course, CRVO may resolve within a few months with minimal effect, or may persist for longer and sometimes worsen over this period of time. Neovascular glaucoma may develop in these cases. A CRVO may also be perfused or non-perfused. Angiography can help to differentiate. Perfused CRVO will generally have few hemorrhages and milder venous tortuosity and dilation. Minimal disc hyperemia may be seen with or without edema. Capillary nonperfusion tends to be minimal and cotton wool spots are generally rare. Perfused CRVO may become non-perfused [36]. Non-perfused or ischemic CRVO reveal significant retinal hemorrhages, cotton wool spots and disc, macular, and retinal edema. Macular edema is the primary cause of vision loss. There is notable venous dilation and tortuosity.

Hemiretinal Vein Occlusion

HRVO is seen in eyes with superior or inferior venous outflow of the retina has been blocked. Typically, one sees intraretinal hemorrhage and venous dilation and tortuosity involved either the superior or inferior half of the fundus. There is some debate whether HRVO represents a subtype of CRVO or BRVO. The course of HRVO is similar to that of BRVO. In some eyes, it is not possible to identify the occlusion site. Twenty percent of eyes show that the branch retinal veins draining the superior and inferior halves of the retina enter the lamina cribrosa separately before joining to form a single central retinal vein. The occlusion of one of these dual trunks of the central retinal vein within the nerve results in an HRVO. In some eyes, the nasal retina is not drained by a separate vein but by a branch of either the superior or inferior temporal vein. It is the obstruction of one of these veins draining both the nasal retina and the superior or inferior retina near the optic nerve that results in HRVO in the majority of eyes [30].

Conventional Photocoagulation

The Collaborative Branch Vein Occlusion Study (BVOS) was a multicenter, randomized clinical trial supported by the National Eye Institute designed to answer three questions regarding the management of BRVO related complications [4].

The questions the BVOS sought to answer were the following: Can grid argon laser photocoagulation improve visual acuity in eyes with visual acuity of 20/40 or worse caused by perfused macular edema? Can peripheral scatter argon laser

photocoagulation prevent the development of neovascularization? Can peripheral scatter argon laser photocoagulation prevent vitreous hemorrhage in eyes with neovascularization? [4].

In the BVOS, eyes that were randomized to treatment with grid laser photocoagulation who had a visual acuity of 20/40 or less were more likely to have visual acuity improvement and have a final vision of 20/40 or better than untreated eyes at 3 years. [5]. The treatment technique consisted of applying laser to the macula in a grid pattern, with the spots only in the area of vascular leakage evident on fluorescein angiogram. Spots were not to be placed closer to the fovea than the edge of the capillary free zone or farther into the periphery than the major vascular arcade. Thick intraretinal hemorrhage areas were to be avoided, as conventional laser uptake by blood within the retina can cause fibrosis. The recommend laser settings were typically 0.1 s duration, 50 to 100 micron spot size, and power sufficient to produce a light to medium white burn. Higher power was needed in thickened areas, and complications of overly heavy burns included subretinal hemorrhage and choroidal neovascularization, and areas of geographic atrophy that may eventually spread and risk involving the macula. The laser uptake occurs at the level of the retinal pigment epithelium (RPE) and slowly resulted in decreased retinal vascular leakage over a period of 2 to 3 months. The mechanism was unclear, although one theory was that the grid treatment resulted in retinal thinning which allowed the choroidal vasculature to support the inner retina and triggered autoregulatory constriction of the retinal vasculature and decreased leakage in the area [38].

Photocoagulation within the FAZ was always a concern. Staged approaches to treatment were typical, starting farther out and subsequently becoming closer toward the FAZ. Response to treatment was typically reassessed at 3 months. Retreatment was limited by photocoagulation scar development and decreasing space in which to add further laser spots.

In about 40% of untreated eyes with ischemic BRVO, NV develops [4]. The incidence of NV may be reduced to about 20% with the application of peripheral scatter laser photocoagulation. However, prophylactic laser was not recommended because if laser was added prior to NV as most eyes would have undergone laser treatment unnecessarily. Also, treatment of ischemic areas was effective for NV but not for macular edema. Vitreous hemorrhage developed in 60% of the 40% of untreated eyes with ischemic BRVO with NV. By adding peripheral scatter laser when NV first developed, one could decrease vitreous hemorrhage risk by 30%. The BVOS date showed that applying laser after the onset of NV was as effective in preventing vitreous hemorrhage as if it were applied before the development of NV. Sector PRP consisted of applying 200 to 500 micron spots of medium intensity laser spaced about one spot width apart to the entire area of ischemic retina and two disc diameters away from the fovea.

The Central Vein Occlusion Study (CVOS) was a multicenter, randomized, clinical trial designed to answer three questions about laser management of CRVO related complications including macular edema and anterior segment NV [36].

The questions the CVOS sought to answer were: Does macular grid pattern laser improve visual acuity in CRVO eyes with perfused macular edema? Does early PRP prevent iris NV in eyes with nonperfused CRVO? Is early PRP more effective than PRP at the first identification of iris NV in preventing neovascular glaucoma in eyes with perfused CRVO?

The CVOS found that eyes that were 20/50 or worse that received macular grid laser for macular edema did not have statistically significant improvement in visual acuity, although edema was decreased angiographically. Despite angiographic improvement, the visual outcome was comparable in eyes that were treated and that were not treated with laser. Therefore, the CVOS did not recommend the use of grid photocoagulation for CRVO macular edema.

The CVOS also did not support routinely performing prophylactic panretinal photocoagulation (PRP) for all ischemic CRVOs because in many of these eyes rubeosis never developed, and the treatment does not always prevent it from occurring [36]. Instead, it was recommended that the eyes be monitored closely and treated with PRP after iris or angle NV is first noted. This generally induced regression evident in 2 to 4 weeks post treatment. If any sign of NV progression was noted, supplemental PRP was recommended. Prophylactic treatment before NV of the iris developed could be considered in very ischemic CRVO. Rubeosis could still develop with prophylactic PRP, so close monthly examinations were still warranted. PRP could also be applied if disc or retinal NV was evident, as in diabetic retinopathy. With the advent of intravitreal injection of anti-VEGF agents, it became a superior option for early treatment of both and rapid reversal of edema and NV, superior to what conventional photocoagulation could offer. Certain sequelae of CRVO could also interfere with the delivery of PRP, in which case intravitreal injection was an alternative. If rubeosis and posterior synechiae prevented pupillary dilation, adequate PRP delivery may not be feasible. Also, corneal edema from elevated intraocular pressure may prevent PRP application. Vitreous hemorrhage could also limit laser application. Intravitreal anti-vascular endothelial growth factor (VEGF) drugs have become a mainstay in all these scenarios today. Also, since intravitreal anti-VEGF medications work rapidly and can be delivered at the onset of vascular occlusion, long term degenerative changes particularly to the macula secondary edema could be minimized when compared to laser photocoagulation protocols. In later studies, conventional PRP was studied to see if hoped for reduction in peripheral retinal ischemia by treating areas of peripheral capillary non-perfusion in CRVO might help reduce ME, but found not to be effective [9].

Intravitreal steroids such as dexamethasone and triamcinolone are also alternatives to anti-VEGF medications in retinal vein occlusion, especially in resistant cases. However, as monotherapy, steroids alone have not shown superiority to anti-VEGF medication.

Steroids also have more side effects after repeated dosing, including cataract formation and elevated intraocular pressure. Also, combination therapy of steroid and anti-VEGF has not shown superiority over anti-VEGF monotherapy [2]. However, intravitreal steroid implants such as Ozurdex has the advantage of controlling

edema in retinal vein occlusion for longer term, thus reducing the need for frequent injections.

Chorioretinal Anastomosis for Central Retinal Vein Occlusion

One procedure, designed to address the core cause of CRVO, is Laser Chorioretinal Anastomosis. This involves the creation of a laser-induced chorioretinal anastomosis (LCRA) between the blocked high pressure retinal venous circulation and the unobstructed low pressure choroidal venous circulation. This would, in theory, lower central venous pressure and help relieve macular edema [9]. The technique involves choosing a site, nasal to the optic disc preferably, to minimize risk of submacular hemorrhage or choroidal neovascularization. The laser application is at the margin of the retinal vein and designed to rupture Bruch's membrane and the wall of the vein simultaneously. Typical settings with the Ellex laser are power of 2.5 to 3.5 W, 50 micron spot size, and 0.1 duration. Argon green laser has been used with a spot size of 50 micron, 100 ms duration, and power from 3.5 to 6.0 W. Argon blue-green laser combined with Nd-YAG laser and krypton red laser has also been used [21]. High power is generally needed, and indocyanine green sensitization may help increase absorption. Anastomosis may take anywhere from 2 to 6 weeks to form. Complications of the procedure include choroidal neovascularization, vitreous and subretinal hemorrhage, epiretinal membrane formation and traction retinal detachment [22]. It is important to confirm presence of posterior vitreous detachment prior to the procedure to help reduce risk of vitreoretinal complications.

Combination therapy of LCRA and intravitreal anti-VEGF has been shown to reduce injection frequency and duration along with improved vision and anatomical outcomes. The procedure has had limited adoption thus far, likely due to its inherent risks and the effectiveness intravitreal anti-VEGF medications.

Short Pulse CW Laser (SRT, 2RT, PASCAL)

Short pulse continuous wave lasers include Selective Retina Therapy (SRT), Nanosecond laser (2RT) and PASCAL or Pattern Scanning Laser. All are designed with the intention of reducing but still producing laser-induced retinal damage (LIRD), as well as reducing treatment related discomfort. The following is a review of these technologies and their application in the treatment of retinal vein occlusion. There are notably few published studies to date.

PASCAL

The PASCAL, or pattern scanning laser, was the first partially automated laser that allows the physician to choose various laser pattern presets to apply to the retina with one pedal depression. Destruction of retinal photoreceptors to reduce their oxygen consumption to decrease retinal oxidative stress was the goal of the PASCAL design. With regard to retinal vein occlusions, this suggests that it's most suitable application would be treatment of retinal neovascularization (NV). The laser was a short pulse (~10us) duration 532 continuous wave laser [8].

PASCAL PRP has been found to be less painful than conventional PRP because of less heat spread and the short duration of the laser spot. However, it has been reported to have less therapeutic benefit than conventional PRP [7]. In an attempt to improve the performance of the PASCAL for proliferative diabetic retinopathy (PDR), an analogue of NV complicating RVO, treatment density was increased. Despite this, PASCAL was still found to be less effective than conventional PRP or ranibizumab for PDR [3]. An algorithm was devised for PASCAL to be used as sublethal treatment and avoid LIRD, called end point management (EPM). This involved titrating the power using a test burn, and then reducing the power a proscribed amount. One report on PASCAL EPM treatment of CSR reported no LIRD [19]. Despite titration, the short pulse CW laser's narrow therapeutic range (0.010 W) makes it highly susceptible to surgeon misjudgment and eye-specific variations such as pigmentation, retinal thickness, and media opacity, making avoidance of LIRD, while theoretically possible, clinically unreliable [8]. At the same time, the short CW pulse limits heat spread from the spot of retinal ablation, resulting in little affected but surviving retina to produce a therapeutic effect, limiting its effectiveness [26]. It has not been shown to date that PASCAL effectively for treatment of branch or central RVO [8] .

Selective Retina Therapy (SRT)

SRT was designed using microsecond pulses to selectively target the RPE for damage while reducing injury to the photoreceptors and choroid. One theory of its mechanism of action is the development of a new RPE cell barrier, strengthening the RPE pump and barrier function. Another theory is that activation HSP 70, and tissue matrix metalloproteinases might play a role in healing of the RPE damage resulting from SRT [32]. SRT has not been reported for treatment of RVO or its complications.

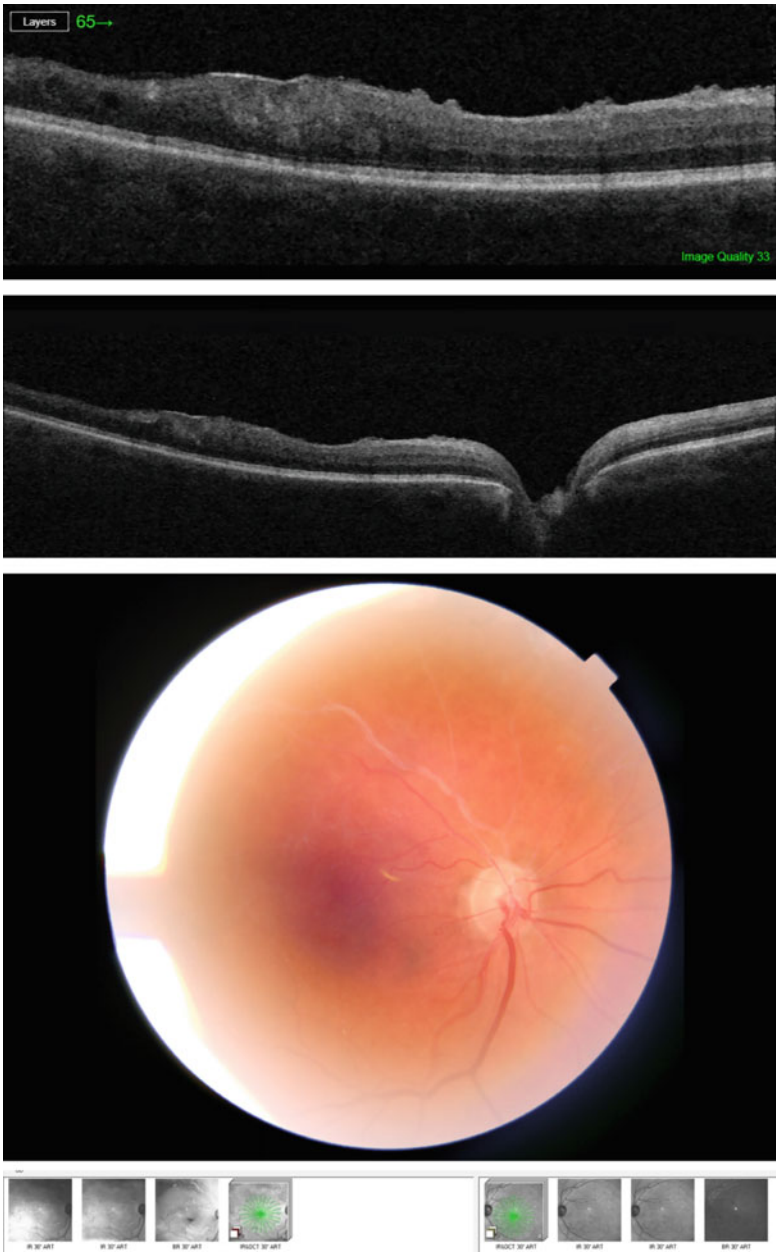
Nanosecond Laser (2RT)

Another laser with a goal of even more precisely selectively targeting the RPE are pulsed lasers in the nanosecond range (2RT). The 2RT laser (Ellex Pty Ltd, Adelaide Australia), is a 532 nm Q switched Yag laser. 2RT is designed to photodisrupt the RPE, hoping to avoid damage to Bruch's membrane and the neurosensory retina on either side [15] Nanosecond 2RT laser has been studied for the treatment of AMD and DME, but not thus far in RVO [15, 39] (Fig. 7.1).

Microsecond Pulsed Laser (MPL)

Before the arrival of intravitreal drugs, conventional laser photocoagulation was the only therapy for RVO. Although better than no treatment at all, photocoagulation had limited effectiveness, many adverse treatment effects, and little ability to retreat due to the threat to visual function with accumulating LIRD. With the advent of intravitreal injection, use of intravitreal medications rapidly replaced photocoagulation as it spared the retina while reducing macular edema. However, the results of drug therapy for RVO are still not always satisfactory, generally required frequently repeated treatment over many years [31]. Of all applications for MPL, MPL, like all other laser modes including photocoagulation, laser tends to have the least robust therapeutic effect in the treatment of retinal vein occlusions [8]. This is most likely due to the difference in disease process which is caused by dysfunction in inner retinal circulation and oxygenation rather than chronic progressive dysfunction of the RPE. MPL targets the retinal pigment epithelium which appears to have a limited role in retinal vein occlusion, which represents a catastrophic failure of retinal vascular perfusion, whether ischemic or non-ischemic. Either may cause permanent damage to the retinal vasculature and compromise perfusion, resulting in macular edema [12, 14]. In extreme injury or degeneration due to persistent chronic swelling, the edema may not respond to any therapy and atrophic and pigmentary damage may develop, worsening vision and limited any possibility of visual recovery [16].

Current treatment for retinal vein occlusion relies predominantly on monthly injection of intravitreal medications. However, tissue sparing laser like MPL can still play a part in a treatment regimen for RVO. Combination therapy has been shown to be beneficial by reducing injection burden [11, 26, 33, 37]. Less severe RVO may respond MPL alone, precluding the need for injection. A study comparing the efficacy of threshold grid laser treatment to subthreshold grid laser treatment with an infrared MPL for macular edema from BRVO showed similar vision improvements and edema resolution when compared to conventional threshold photocoagulation, but without LIRD in the MPL eyes [29]. In another study, Parodi et al. showed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◀**Fig. 7.1** OCT macula fluorescein angiogram fundus photos 73 year old female with history of branch retinal vein occlusion and neovascularization who presented in 2015 with Hand Motion vision OD due to secondary vitreous hemorrhage. She required only Avastin × 3 and then was treated with SDM q 3 months. Her vision improved to 20/30 + 2 as of 2021 and has not required further Avastin injections

that vision results were superior with MPL combined with intravitreal triamcinolone compared to photocoagulation for RVO [28]. Luttrull et al. has also reported effective reversal of macular edema with subthreshold diode micropulse laser treatment absent LIRD by high-resolution macular imaging including spectral-domain OCT and autofluorescence fundus photography [26]. These studies suggest that MPL may help macular edema by stimulation of the RPE to normalize cytokines expression and response, increase the transretinal RPE fluid pump effectiveness, and reduce inflammation due to its anti-inflammatory effects [12]. It is useful to remember that anti-VEGF drugs are not anti-inflammatory and cannot address this critical part of the disease process. Laser-induced improvement in macular function and reduction of chronic inflammation may help preserve macular and visual function in the face of chronic recurrent swelling, the typical course of even effectively treated RVOs [14, 14] Even though MPL is generally insufficient as monotherapy for RVO macular edema, maximum MPL-induced preservation of macular function may afford the eye with RVO improved long-term prospects for retaining vision over the course of the disease.

NV development in ischemic retinal vein occlusion can be treated effectively with MPL, analogous to conventional laser photocoagulation in proliferative diabetic retinopathy. [24] MPL can be applied to the ischemic retina while sparing the retina and minimizing the need for intravitreal injections. Analogous to age-related geographic atrophy, MPL also can be used in hopes of reducing atrophic pigmentary damage that may develop due to chronic and recurrent macular edema in RVO, to limit scar expansion from previous photocoagulation, and augment drug treatment in eyes with scarring from prior conventional photocoagulation that cannot tolerate additional retinal damage [24, 25].

Gawecki [12] has shown that in terms of visual function, MPL may be more effective that conventional photocoagulation, likely due to avoidance of LIRD, with similar visual results to retina-sparing drug therapy in RVO [12]. MPL monotherapy has not been found to be as effective as intravitreal drug therapy, be it anti-VEGF medication or steroids [28]. Several studies of MPL with and without ranibizumab found that addition of MPL to ranibizumab for macular edema due to RVO did not improve macular thickening or VA, but did result in a reduced frequency of intravitreal injections [6, 11, 33]. Inagaki et al. showed that micropulse in patients with chronic edema in RVO and visual acuity better than 20/40 may benefit from MPL alone for long-term management [17] (Fig. 7.2).

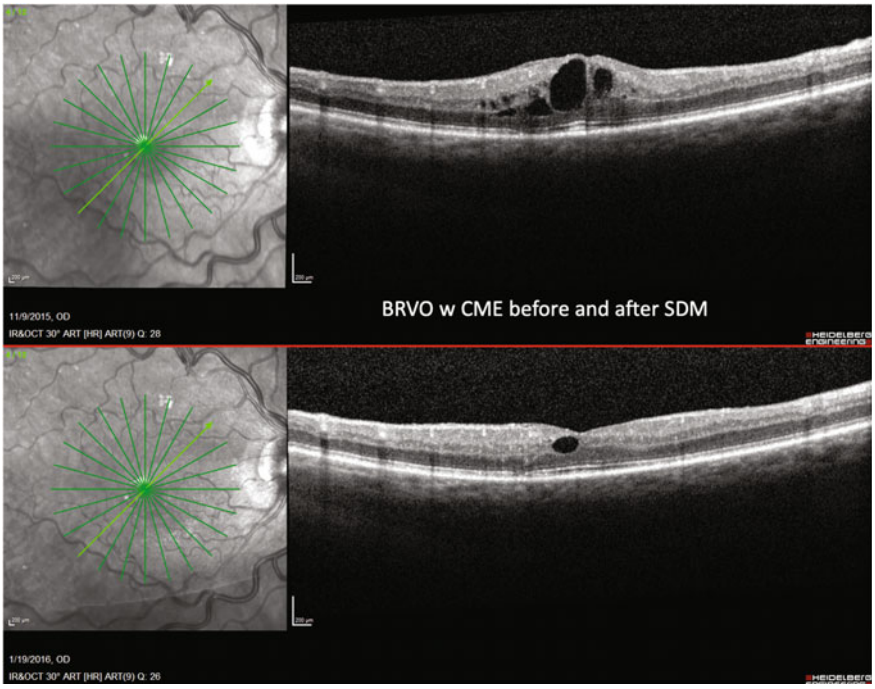

Fig. 7.2 OCTs of and eye with a branch retinal vein occlusion before and after MPL panmcular SDM monotherapy for CME. Not marked resolution of macular edema. While SDM is seldom effective monotherapy for RVO with ME, it may reduce the number of intravitreal injections required over time, and in some cases, such as mild ME or where injections are not possible or refused, SDM may be effective, as in the eye shown here

Retinal Artery Occlusion

Retinal arterial occlusion presents other potential roles for MPL. Fundus examination of CRAO reveals superficial whitening of the retina usually mostly in the macular region. A "cherry red spot" can sometimes be seen, because thinning of the opaque ischemic retina in the fovea allows visualization of the subretinal pigmentation. Segmentation of the blood column, or box-carring, may be seen in severe CRAO. In 20−40% of cases, emboli can be found. These are typically calcific or cholesterol, originating in the heart or internal carotid arteries. Ocular complications of CRAO, in addition to vision loss, include rubeosis and disc neovascularization. Rubeosis may occur in 18% of eyes at a mean time of 4−5 weeks after occlusion, with a range of 1−15 weeks [10].

Early in the course of the disease, conventional PRP in severe/complete CRAOs was to ablate the ischemic retina outside the major vascular arcades to decrease the ischemic drive and amount of VEGF released that might lead to new vessel formation, particularly in the anterior segment [10]. The typical visual adverse effects

of conventional PRP, such as permanent decrease in peripheral, color, and night vision, are less a concern in CRAO due to the already generally profound visual loss. Conventional panretinal photocoagulation can induce regression of iris vessels in about 65% of eyes. Disc neovascularization of the optic disc occurs in 2−3% of eyes [10]. There are no literature reports of the PASCAL, SRT, 2RT or MPL for the treatment of RAOs. However, experience with other causes of ischemic ocular neovascularization such as proliferative diabetic retinopathy suggest that MPL or PASCAL treatment may be helpful in CRAO should NV develop [7, 25].

Summary

Macular photocoagulation for macular edema from RVOs should be avoided, as it is ineffective in CRVO, and does not improve outcomes compared to retina sparing drug and/or MPL laser and may lead to late geographic atrophy in the macula due to laser scar expansion and coalescence. PRP for NV, particularly anterior segment NV from ischemic retinal vein occlusion or central retinal artery occlusion is effective, slightly slower acting than anti-VEGF therapy, but longer acting. The clinical setting should indicate if one, or both, is most appropriate to address anterior segment NV at any point in time. Retina-sparing sparing SDM MPL peripheral retinal treatment of ischemic eyes may also be effective, limiting peripheral vision loss and treatment associated inflammation that may aggravate macular edema.

Because the course of ME in BRVO waxes and wanes over many years, maximizing preservation of visual function while minimizing intravitreal injections is desirable. MPL maybe effective as monotherapy for eyes with better VA and lesser degrees of macular thickening. In eyes with worse VA and greater degrees of macular thickening, the addition of MPL has been shown to reduce the frequency of intravitreal injections. Finally, the development of anti-VEGF drug tolerance may occur over the long course of RVO treatment, rendering medication ineffective. MPL has been shown to reverse anti-VEGF drug tolerance in wet AMD [23]. MPL may thus also reduce the risk of drug tolerance in RVO, possibly accounting in part for reduced in anti-VEGF injection frequency in RVO management when combined with MPL. Because MPL is retina-sparing, MPL can be repeated as often as needed without adverse treatment effects, and important consideration as treatment of macular edema due to RVO may go on for years [31].

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