### Radial Optic Neurotomy for Central Retinal Vein Occlusion

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#### INTRODUCTION

When several and very different treatment modalities exist for one ailment, it usually means that none of them is generally effective or superior to others. Central retinal vein occlusion (CRVO) is a condition for which various types of management have been proposed. However, the only standard care suggested by the Central Vein Occlusion Study Group (CVOSG) is panretinal photocoagulation when the condition is complicated by iris neovascularization.<sup>1</sup>

In 2001, radial optic neurotomy (RON) was suggested by Opremcak<sup>2</sup> for treatment of CRVO. This therapeutic modality has raised much debate among authorities. Herein, we present the opposing views of two vitreoretinal specialists regarding this issue.

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In 1978, a neurologist proposed the theory of neurovascular compression at the optic nerve head in the pathogenesis of anterior ischemic optic neuropathy and suggested an external approach for relaxation of the optic nerve head for treatment of this condition. This approach was technically difficult and therefore abandoned very soon. In 2001, Opremcak<sup>1</sup> reconsidered the same theory and suggested that the anatomy of the optic nerve head plays an important role in the pathogenesis of CRVO which may be also considered a "scleral outlet compartment syndrome".

In addition to containing the optic nerve, the scleral outlet is the space through which the central retinal artery (CRA) and central retinal vein (CRV) pass into and out of the eye (Fig. 1). Furthermore, it contains the lamina cribrosa and is encompassed by the scleral ring. As the optic nerve approaches the eye, it consists of myelinated nerve fibers, CRA, and CRV and has a diameter of 3 mm; however, the internal diameter of the optic disc and scleral outlet is 1.5 mm (Fig. 2).

The pathophysiology of certain conditions such as CRVO and nonarteritic anterior ischemic optic neuropathy is thought to be related to the confined space of the scleral outlet resulting in neurovascular compression of the CRA, CRV and optic nerve. Many factors such as changes in the scleral ring, increase in arterial diameter, and presence of anatomical anomalies as well as systemic factors may act in concert to decrease venous lumen, increase intravenous turbulence leading to endothelial damage and thrombus formation.

Optic neurotomy has been the focus of attention by many vitreoretinal surgeons. Relieving the presumed "compartment syndrome" at the scleral outlet may improve venous outflow in an eye with CRVO thereby decreasing congestive macular edema and improving visual acuity. Since the first report of promising results of RON, its opponents have raised several concerns about this procedure.<sup>2-4</sup> Herein, I provide evidence-based answers for all these concerns.

# What is the mechanism behind RON in the treatment of CRVO?

This treatment is based on a pathophysiologic mechanism called the "scleral outlet compartment syndrome". In eyes with susceptible anatomy, the confined space of the optic nerve head might play a role in the pathogenesis of CRVO. This region is surrounded by the firm surrounding scleral ring. This unique tissue architecture at the scleral outlet results in an anatomical "bottle neck-like" configuration. Certain factors might increase pressure on elements within this ring and compress the lumen of the non-muscular vein, resulting in vein occlusion. Therefore, an incision on the margin of the disk could theoretically relieve this compression in eyes with CRVO, and improve blood flow and visual acuity.1

### Is the scleral ring a relaxable tissue?

In a histopathologic study on cadaver eyes, we demonstrated that optic neurotomy using a microvitreoretinal (MVR) blade seems effective for scleral outlet relaxation (Figures 3, 4). This study also demonstrated that the excimer laser can make non-mechanical cuts with relative ease and reliability.<sup>5</sup>

### Can an MVR blade perforate the sclera or lacerate vessels?

The findings of the above-mentioned study revealed that no eye sustained macroscopic or microscopic scleral perforation and there was no injury to the central retinal vein or artery<sup>5</sup> (Fig. 5).

# Can RON damage nerve fibers leading to or exacerbating optic atrophy?

Yes, it definitely can. However, this damage involves nasal nerve fibers which are not related to central vision. In other words, in this procedure macular fibers are saved at the expense of some nasal fibers (Fig. 6).

# Do all cases with CRVO demonstrate the same response?

Depending on the underlying pathophysiologic mechanism, the response to RON varies among different patients. Some cases respond dramatically and some do not benefit at all. We had a patient who had received 8 intravitreal bevacizumab injections with no effect, but demonstrated improvement in vision from counting fingers to 20/200 only 10 days after RON (Figures 7, 8).

### Are there any studies comparing RON with other recently suggested interventions for CRVO?

Yes. One study has compared the natural course of recent CRVO with four newly introduced treatment options including: (1) intravitreal triamcinolone acetonide, (2) RON, (3) combined RON and intraocular triamcinolone injection, and (4) combined internal limiting membrane peeling, RON and intraocular triamcinolone injection. This report demonstrated that among the four different approaches, RON combined with intraocular triamcinolone injection may lead to better visual outcomes.<sup>6</sup> However, no study has compared RON with anti-VEGF agents yet.

### Does this technique entail complications?

Like any other surgical procedure, this technique may entail adverse effects. In addition to complications inherent to vitrectomy in general, the surgeon may encounter vitreous hemorrhage, retinal detachment<sup>7</sup> and peripapillary choroidal neovascularization<sup>8</sup> following RON. The Pan-American Collaborative Retina Study Group has classified complications of RON for CRVO into three major categories: manageable, difficult to manage, and non-salvageable.<sup>7</sup> Most complications encountered after RON are considered manageable.

# Which eyes with CRVO may benefit most from optic neurotomy?

Eyes in which the underlying cause of CRVO is scleral outlet compartment syndrome with some viable tissue seem to benefit most from RON. Examination of the fellow eye often discloses signs such as a small crowded disc with absent or small physiologic cup which are suggestive of a compartment syndrome. In contrast, visual prognosis for ischemic CRVO with severe initial visual loss is poor in general; loss of vision is the rule and a cause of great disability irrespective of treatment.<sup>9</sup>

In conclusion in light of exisiting knowledge and available evidence, RON can be considered beneficial for some patients with CRVO. Our experience demonstrated that outcomes of RON are superior to the natural history of the condition. We have provided before and after photographs, (Figures 9, 10) fluorescein angiograms and visual fields to provide evidence supporting the role of RON in CRVO. Complications do occur but the great majorities are manageable. From another perspective, surgery for CRVO is analogous to vascular surgery therefore any attempt to restore retinal circulation has considerable merit. We need to extrapolate from the experience of colleagues in the fields of cardiovascular, neurosurgical and vascular surgery and to reemphasize the goal of vascular surgery and the mission of the vascular surgeon: to restore blood flow and allow reperfusion of salvageable tissue.



**Figure 1** A schematic figure showing elements passing through the scleral outlet.



**Figure 2** Histological section demonstrating internal and external structures of the scleral outlet at the optic nerve head.





**Figures 3, 4** The site of radial optic neurotomy in cadaver eyes with a mechanical cut using MVR blade (Fig. 3) and non-mechanical cut by an excimer laser (Fig. 4). Note that the incisions are well away from the central retinal artery and vein.



Figure 5 Histologic depth of optic neurotomy incision showing no scleral perforation

#### Controversy; Optic Neurotomy for CRVO



**Figure 6** Improvement of visual field (b) in comparison to the preoperative field (a) after RON in a patient with CRVO. Note that isopter I4e is represented after RON.





**Figure 7** Color fundus photograph (a) and optical coherence tomography (b) in a case of central retinal vein occlusion after 8 injections of intravitreal bevacizumab.





**Figure 8** Color fundus photograph (a) and optical coherence tomography (b) in the same patient 10 days after radial optic neurotomy demonstrating marked improvement of macular edema.



Figure 9 Color fundus photograph (a) and fluorescein angiogram (b) in a case of central retinal vein occlusion before radial optic neurotomy.





**Figure 10** Color fundus photograph (a) and fluorescein angiogram (b) in the same eye after radial optic neurotomy demonstrating restoration of laminar flow and a marked decrease in retinal edema and hemorrhages. Visual acuity improved from counting fingers to 20/200 one month after surgery.

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Radial optic neurotomy (RON), also called transvitreal optic neurotomy (TON), was first described by Opremcak<sup>1</sup> in 2001. In this procedure a radial incision is made at the edge of the optic nerve towards deeper tissues to make a split in the posterior scleral canal (scleral outlet), lamina cribrosa and adjacent sclera.

In the initial study, 11 eyes of 11 patients with severe hemorrhagic CRVO were operated; of whom, 8 (73%) had improvement of visual acuity and all eyes had clinical improvement.1 The same authors and coworkers later reported the results of this procedure on 117 consecutive cases of CRVO<sup>2</sup> as well as another series of 63 eyes in which RON was combined with intravitreal triamcinolone.3 In both studies, the authors achieved good results with minimal complications. This technique has been tried by other investigators with variable and sometimes disappointing results.4-7 In addition, there have been strong arguments against the rationale behind this technique and its results.8-14 In this brief discussion, I will review these criticisms and also present an overview of the results of this procedure reported by different investigators.

The main point raised in support of RON is the concept of a "compartment syndrome". Considering the fact that the diameter of the optic nerve is 3 mm behind the globe decreasing to about 1.5 mm at the lamina cribrosa and anterior to it, it is assumed that the optic nerve is under neurovascular compression and is vulnerable to any additional pressure. When there is swelling due to CRVO or due to ischemia as in ischemic optic neuropathy, the confined space of the scleral outlet causes build-up of pressure inside it resulting in further occlusion of the vessels thereby aggravating the ischemia. RON is supposed to relax this rigid scleral ring, relieve the pressure and improve optic nerve circulation.

Several arguments have been raised against this concept. First, the reason for the decrease in optic nerve diameter at the level of the lamina cribrosa is loss of myelin sheath at this point and therefore this is no reason for "neurovascular compression". Second, if the scleral outlet is a rigid ring, then making an incision at one point of this ring does may not result in relaxation around its entire circumference, in other words the rest of the ring may still maintain its rigidity and tightness. Third, the scleral outlet is not a hollow space; it is composed of many small fenestrations each confined by a rigid wall. A cut in the wall of the ring does not relieve the pressure within individual spaces. Fourth, the central retinal vein has been shown to be occluded by thrombus and not merely by compression. Therefore, even if the presumed pressure is removed, the vein still remains occluded. Fifth, the thrombus may form at variable points anterior and posterior to the lamina cribrosa. Sixth, and probably the most important argument, is that CRVO has a variable course with spontaneous improvement is some cases. Therefore, properly-sized randomized controlled clinical trials are needed to verify the outcome of any therapeutic intervention including RON.

Friberg et al<sup>10</sup> by designing a computerized biomechanical model of the eye and taking into account the tensile strength of sclera, intraocular pressure, and other factors, investigated the effects of making a radial incision in the scleral outlet on the central retinal vein. They concluded that the increase in the surface area of central retinal vein lumen remains trivial after making such an incision, ranging from 1-5%.

Horio and Horiguchi<sup>9</sup> studied the effect of RON on retinal blood flow and macular edema

in seven eyes with CRVO from dye dilution curves of fluorescein angiograms. One week after surgery, they observed significantly reduced blood flow. Six months postoperatively, retinal blood flow was not significantly different from preoperative values although all seven eyes developed chorioretinal anastomoses. Foveal thickness was significantly reduced which was attributed to vitrectomy and removal of the posterior hyaloid face or may have been due to the natural course of the disease.

Vagel et al<sup>15</sup> reported the histopathologic findings of an eye enucleated 18 weeks after RON due to neovascular glaucoma. They observed a discrete scar at the site of the operation which reached the cribriform plate. The optic nerve showed advanced atrophy with a small temporal sector of viable nerve fibers. They concluded that the observed histopathologic findings do not support the postulated mechanism of effect from RON.

The results of RON for treatment of CRVO vary greatly. Most studies in this regard are plagued by retrospective nature, lack of a control group, and small sample size. These studies share the common fact that the superiority of their results over the natural course of the condition cannot be ascertained. Hasselbach and coworks<sup>4</sup> described the results of RON in 107 cases of CRVO. The median preoperative visual acuity was 5/100 which improved to 8/100 after a median follow-up of 6 months, obviously not a striking improvement. The important finding in their study, however, was that of 30 cases with one year follow-up, 18 eyes developed chorioretinal anastomosis detected by fluorescein angiography and these eyes had an average of 6 lines of visual improvement. Visual field defects developed in 86.8% of these eyes. Garcia Arumi et al6 performed RON on 13 eyes with hemicentral retinal vein occlusion. Nine eyes (69.2%) experienced 2 or more lines of visual improvement. Arevalo and colleagues7 reported the result of this procedure in 73 eyes with CRVO. They concluded that the procedure by itself does not seem to improve the outcome of CRVO when compared with its natural course and that complications are common.

Complications of RON include severe immediate vitreous hemorrhage, neovascularization at the RON site and in the anterior segment, visual field defects, and retinal detachment originating from the incision site.<sup>7,16-18</sup>

Based on available evidence, it may be stated that RON proposed for treatment of CRVO, lacks solid scientific basis and its rationale is difficult to understand. It has not been shown experimentally to increase blood flow and also available histopathologic evidence does not support its proposed mechanism of effect. Moreover, clinical experience 8 years following the advent of this procedure remains inconclusive. Probably the main problem is that the safety and efficacy of RON has not been evaluated in properly sized randomized clinical trials. Until then, it may be suggested not to perform RON for CRVO outside research settings.

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