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# Localized Administration of Tissue Plasminogen Activator through the Ophthalmic Artery in the Setting of Central Retinal Artery Occlusion

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## Abstract

Treatment of central retinal artery occlusion (CRAO) has been an ambiguous entity in the medical community. Many interventions have been explored; however, a standard of care has yet to be defined. Recent studies have suggested localized intra-arterial fibrinolysis as a promising method; however, a timeframe for optimal treatment initiation continues to be investigated. This case demonstrates an instance of CRAO treated with local fibrinolysis, however, what could be due to delayed time-to-treat, final visual outcomes were unfavorable. In conjunction with supporting literature, we believe optimization of thrombolytic protocols should be sought after to facilitate successful treatment outcomes. In addition, we encourage community awareness of the signs and symptoms of CRAO in hopes that earlier patient presentations will lead to swifter interventions and overall preservation of ocular function.

## Keywords

Central Retinal Artery Occlusion, Ophthalmology, Neuroendovascular, Localized Intra-Arterial Fibrinolysis

## 1. Introduction

Central retinal artery occlusion (CRAO) is a condition in which the blood flow to the retina is disrupted leading to acute ischemic retinal tissue dysfunction. The mechanism of a CRAO mirrors that of an ischemic stroke of brain tissue and can be due to large vessel atherosclerosis, embolic events, hypercoagulability, or inflammatory vasculitis. The visual prognosis following a CRAO is grim, with 17% of patients regaining some functional visual capacity [1]. In addition,

50% of CRAO patients are left with only a small island of peripheral vision in the affected eye [2]. There have been several postulated interventions for CRAO including ocular massage, anterior chamber paracentesis, intraocular pressure (IOP) lowering medications, hyperbaric oxygen therapy, and thrombolytic therapy; none of which have demonstrated superior efficacy and therefore no single recommendation has been made for preferred practice patterns [3] [4] [5]. To this end, the optimal treatment of acute CRAO is controversial and may differ amongst specialists and their respective healthcare systems.

Our case describes a 58-year-old male presenting to the emergency department after acute vision loss in his left eye manifesting as a CRAO. He received local intra-arterial fibrinolysis (LIF) with tissue plasminogen activator (tPA) through the left ophthalmic artery nearly 16 hours after symptom onset. Despite this intervention, the patient's VA did not rebound immediately after tPA, nor after a 1-month follow-up. This case sheds light on the variation in treatment response for LIF in CRAO and supports the need for established guidelines in order to achieve improved outcomes.

## 2. Case

A 58-year-old white male presented to the emergency department approximately 16 hours after experiencing painless vision loss in the left eye. The patient described his symptoms as a small portion of graying in the left eye, and upon awakening the next morning, it was discovered that most of his left field of view had darkened. He denied curtain-darkening sensations, flashes of light and floaters. He also denied jaw claudication, headache, scalp tenderness, joint or muscle pain, fever or chills. He has a history of hypertension and hyperlipidemia and is admittedly non-compliant with his medications.

Upon admission, the patient was found to be hypertensive (194/134 mmHg), and tachycardic (117 beats per minute). Aside from the above, remaining vitals and physical examination findings were found to be within normal limits—no extremity weakness, sensory deficits or facial droop was noted. His National Institute of Health stroke scale (NIHSS) was found to be 2, attributed to left nasal hemianopia.

The patient was immediately taken for computed tomography (CT) of the head without contrast which showed no signs of acute intracranial process. A CT angiogram (CTA) of the head and neck demonstrated a near 70% stenosis of the left internal carotid artery, as well as an ulcerated plaque situated at the left carotid bifurcation.

Ophthalmology was consulted and evaluated the patient within 30 minutes of arrival at the emergency department. Aside from the medical history previously disclosed, he denied any ocular conditions, surgeries, or ophthalmologic family history. Visual acuity (VA), assessed with a Rosenbaum near card and +2.00 correction, was found to be 20/20 oculus dexter (OD) and 20/200 oculus sinister (OS). The right pupil was found to be both round and reactive, however, the left

was noted to be round, slightly mydriatic (~5 mm), and sluggish in pupillary response with a 1+ afferent pupillary defect (APD). Confrontation to visual fields (CVF) using the count fingers method were full in all quadrants OD and demonstrated a full infranasal deficit with a partial supranasal deficit OS. Color plates and Amsler grid assessments were conducted and found to be unremarkable OD; evaluation OS was incomplete due to poor visual acuity. He was orthophoric at a distance without any restriction or nystagmus in extraocular motility testing. Intraocular pressure (IOP) was within normal limits oculus uterque (OU). Aside from 1+ nuclear sclerotic cataract, the anterior examination was unremarkable OU. He was then dilated for posterior examination where the right eye was found to be unremarkable aside from peripheral vascular tortuosity, likely secondary to his uncontrolled hypertension. Posterior examination of the left eye showed an optic nerve with blurred margins and significant retinal whitening was noted at the posterior pole extending along the distribution of the central retinal artery with a small area of apparent temporal peripapillary circulation, likely attributed to cilioretinal artery sparing (Figure 1). The macula appeared pale with an associated cherry-red fovea. Vasculature OS appeared tortuous as noted in the contralateral eye.

Due to ischemic changes noted during dilated fundus exam, the neuroendovascular team treated the left ophthalmic artery with cerebral angiogram guided LIF with tPA. The patient was admitted to the hospital for a complete stroke work-up, left carotid artery stenting, and started on aspirin/clopidogrel dual antiplatelet therapy.

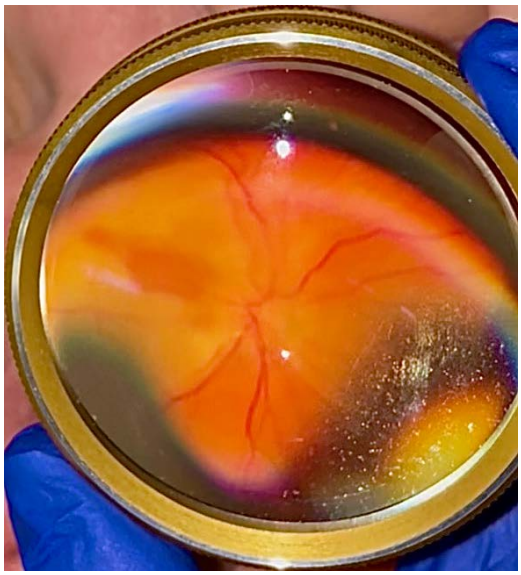

**Figure 1.** Color photo of the left posterior pole as seen with indirect ophthalmoscopy through a 20 diopter lens. The disc margins appear blurred and edematous. A cherry red fovea is surrounded by an area of retinal whitening which demonstrates ischemia secondary to CRAO –a red fovea is indicative of the inner macula's preserved blood flow by choroidal vessels. The temporal patch of coloration between the nerve and fovea is attributed to preserved perfusion of the area, likely by the cilioretinal artery.

One day after neuroendovascular intervention, ophthalmology reevaluated the patient's left eye. Anterior examination, VA, IOP and CVF remained unchanged from the previous examination apart from a now 3+ APD in the similarly mydriatic pupil. Posterior examination demonstrated findings seen in the prior examination, in addition to macular edema.

One month after the initial evaluation, the patient was re-evaluated in the clinic where he received a complete assessment including dilated fundus examination, optical coherence tomography (OCT), and formal visual field testing. Since discharge, he explained there was no apparent improvement in his vision OS. He denied any other ocular or systemic symptoms. He remained on dual antiplatelet therapy and anticipated follow-up with neuroendovascular the following week.

Near vision was found to be 20/400 OS. The left pupil remained fixed with a 2+ APD. CVF OS showed deficits in three of four quadrants, with some hand-motion vision in the supratemporal quadrant, and full preservation of the infratemporal quadrant. Anterior slit lamp examination OS remained unchanged from one month prior. Posterior examination OS demonstrated a mildly pale optic nerve with sharp margins and a cup-to-disc ratio of 0.1. The macula showed retinal whitening with evidence of cilioretinal artery sparing. Aside from the previously observed vascular tortuosity, there was also evidence of sclerotic vessels and two peripheral vascular plaques which were thought to be embolic in nature (**Figure 2**).

Humphrey Visual Fields (HVF) 24-2 baseline testing using Swedish Interactive Threshold Algorithms (SITA)-fast strategy was performed demonstrating general left eye depression with infratemporal quadrant sparing (**Figure 3**), similarly demonstrated in CVF testing. An OCT macula depicted diffuse thinning OS.

## 3. Discussion

Acute CRAO remains a devastating ocular condition with a poor visual prognosis for which a treatment modality has not been agreed upon. CRAO can be defined into two general categories: arteritic vs. non-arteritic. Arteritic CRAO is most caused by giant cell arteritis and is medically managed with corticosteroid treatment [6]. Non-arteritic CRAOs are most commonly due to an embolus or thrombus and are the most common type of CRAO seen in clinical practice [7]. Thrombolytic therapy has been exclusively used in non-arteritic CRAOs. This treatment has been implemented in many institutions; however, a standardized time-to-treatment varies widely amongst institutions leaving it a controversial topic [1] [8] [9] [10] [11]. In a national survey of treatments offered, 53% of the academic medical centers in the United States offer thrombolytic therapy for CRAO [12]. Studies regarding the efficacy of thrombolytic therapy for CRAO vary in the time-to-treatment, as well as final visual outcomes. No clear consensus as to when, or in which patient populations to utilize thrombolytic therapy, has been established.

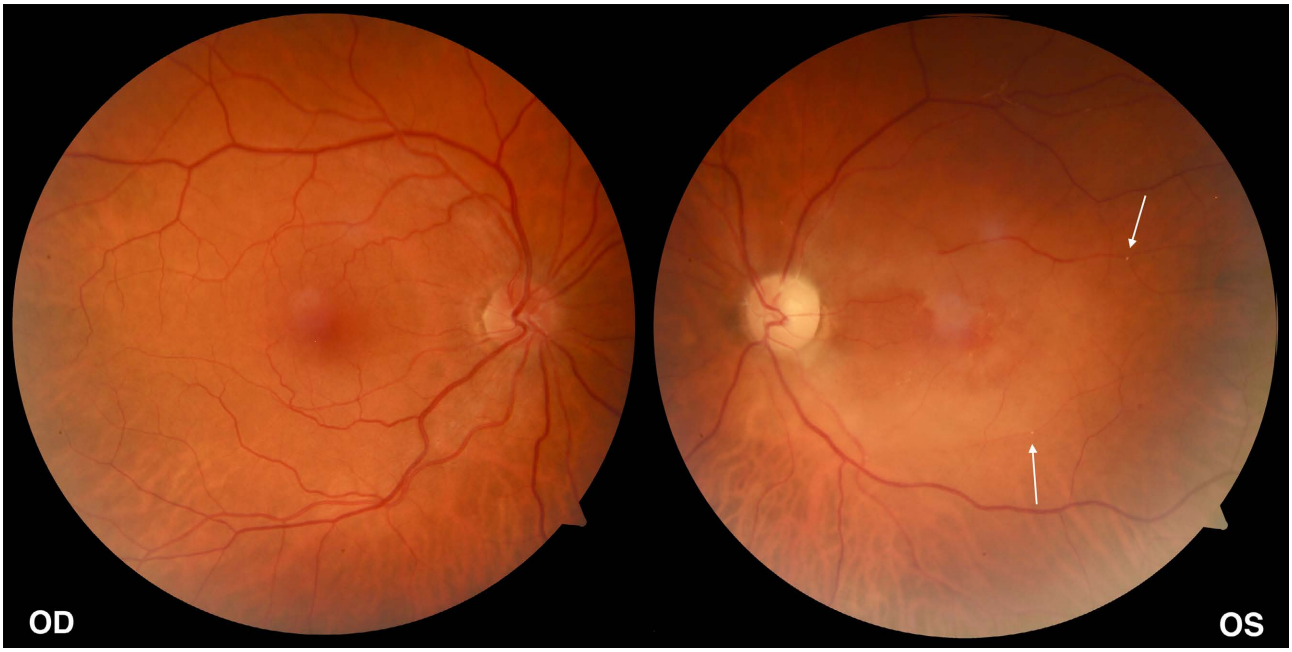


**Figure 2.** Color fundus photos taken one month following LIF to the left ophthalmic artery. OS shows a pale optic nerve, macular edema, central pallor with a small area of circulatory preservation likely secondary to CRAO with cilioretinal sparing, and mildly tortuous vessels. Two likely embolic plaques in distal vessels temporally visualized (arrows). OD shows mild vascular tortuosity, however is otherwise unremarkable and pictured for comparison.

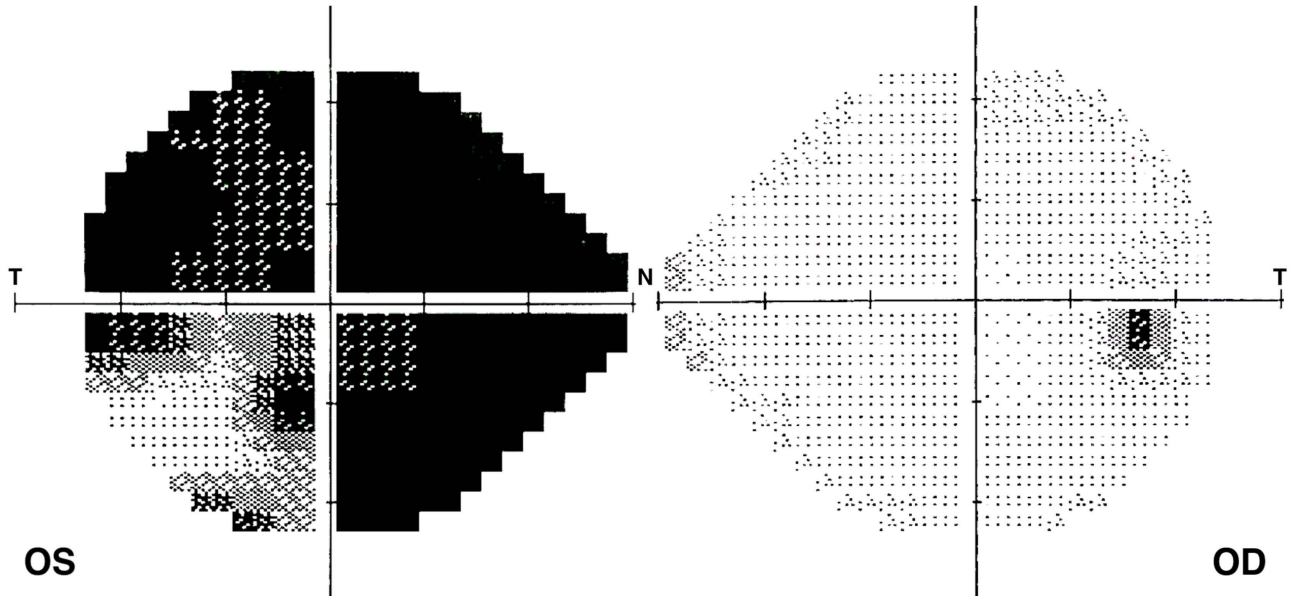


**Figure 3.** Humphrey Visual Field 24-2 conducted 4 weeks following LIF to the left ophthalmic artery. Testing OD shows an expected preservation of the VF. The physiological blind spot OD, correlating to the lack of photoreceptors in the retina where the optic nerve passes through the optic disc, is appreciated at the inferotemporal quadrant. Testing OS demonstrates a near total loss of VFs with the exception of the infratemporal quadrant. The results OS correspond appropriately with the CVF conducted during the same 1 month follow-up. Reliability of OD was good with 0/11 fixation losses, 0% false positives and 0% false negatives. The mean deviation was −2.72 with a few nonspecific defects. Reliability of OS was poor with 5/12 fixation losses, 0% false positives, and 20% false negatives. The mean deviation was −28.71 with severe generalized depression and partial sparing of infratemporal quadrant. For orientation purposes: T = temporal; N = nasal.

There are two ways in which thrombolytic therapy for CRAO can be administered; either systemically through IV, or via LIF by means of the internal carotid artery conduit to the ophthalmic artery as conducted in this patient's case. A study at Johns Hopkins Hospital found the use of LIF in CRAO led to a 66% VA improvement of 1 line, versus a 33% increase in VA of 1 line in the standard therapy group [13]. Furthermore, LIF has become an acceptable treatment when treating CRAO because localized administration of tPA versus systemic tPA administration may decrease the risk of adverse side effects. To date, however, LIF has yet to become a universally accepted treatment modality as a skilled interventionist is needed to perform the procedure and disparities in specialist availability may exist [14].

The European Assessment Group for Lysis in the Eye (EAGLE) prospective study conducted from 2002 to 2007 was the first of its kind to assess CRAO treatment with LIF versus conservative measures as seen within a 20-hour time-to-treat window [11]. Findings from this large multi-center study suggested that not only was the efficacy of results similar between LIF and standard treatment groups, but LIF was associated with rare, yet higher incidences of adverse reactions including headache, dizziness vasospasm, corneal complications and intraparenchymal hemorrhage. Since this time, recent analyses have further evaluated the efficacy and safety of LIF in the setting of CRAO with continued variation of corresponding results [1] [7] [8] [9] [10] [15]. This variation in the literature may serve as an indication of the need for broadened assessments in hopes to optimize treatment guidelines and more closely delineate benefits and risks of LIF treatment in CRAOs.

In addition to the strides in tangible care of patients with CRAOs, we feel as though it is equally as important to spread awareness about symptomatology and risks in hopes swift intervention can correlate to preferable outcomes. As in the brain, ischemic events of the retina can cause loss of tissue function which ultimately leads to substantial visual deficits. The retina can be considered an extension of neurological tissue, yet the bulk of current literature has evaluated LIF outcomes far after tPA's 4.5-hour time-to-treat window as seen in ischemic cerebrovascular accidents [1] [7] [8] [11] [16]. Animal studies have demonstrated that in a hypertensive and atherosclerotic population, CRAOs did not produce detectable optic nerve or retinal damage if the occlusion was present for <97 minutes. Contrastingly, it was noted after 240 minutes of occlusion, severe and irreversible retinal damage occurred [17] [18]. Schragg *et al.* portray how such timely intervention may play a role in treatment success, yet contrastingly, Page *et al.* suggest that time-to-treat may not be correlated with such outcomes [1] [16]. However, the time-to-treatment for the studies included by Page *et al.* ranged from 7.6 to 15.4 hours. This time-to-treatment range is substantially longer than the observed time in which irreversible damage is seen in CRAO animal models. Thus, the absence of correlation in this particular study may be attributed to the irreversible damage of the retinal tissue, as opposed to the opportunistic time-to-treat window itself.

## 4. Conclusion

This case demonstrates the clinical course of a non-arteritic CRAO treated with LIF within a 16-hour window. No improvement was noted neither immediately after intervention, nor during a 1-month post-intervention follow-up. With varying results in the literature, we advocate for further investigation in hopes to optimize LIF treatment and maximize desirable outcomes in such patient populations. To this end, public health measures regarding education for patients on the signs and symptoms of CRAO may also prove beneficial in producing more desirable outcomes. These measures would hopefully encourage patients to present for evaluation earlier in the disease course, allowing for the swift reperfusion and preservation of viable retinal tissue.

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## Consent

The patient orally consented to the publication of this case. This case does not present any information which could lead to the identification of the patient.

## Ethics Statement

The paper reflects the authors' own research and reporting was conducted in a truthful and complete manner.

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## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

## References

[1] Schrag, M., *et al.* (2015) Intravenous Fibrinolytic Therapy in Central Retinal Artery Occlusion. *JAMA Neurology*, **72**, 1148-1154. https://doi.org/10.1001/jamaneurol.2015.1578

[2] Hayreh, S.S., and Zimmerman, M.B. (2005) Central Retinal Artery Occlusion: Visual Outcome. *American Journal of Ophthalmology*, **140**, 376-391. https://doi.org/10.1016/j.ajo.2005.03.038

[3] Fieß, A., Cal, Ö., Kehrein, S., *et al.* (2014) Anterior Chamber Paracentesis after Central Retinal Artery Occlusion: A Tenable Therapy? *BMC Ophthalmology*, **14**, Article No. 28. https://doi.org/10.1186/1471-2415-14-28

[4] Cugati, S., Varma, D.D., Chen, C.S. and Lee, AW. (2013) Treatment Options for Central Retinal Artery Occlusion. *Current Treatment Options in Neurology*, **15**,

63-77. https://doi.org/10.1007/s11940-012-0202-9

[5] Olsen, T.W., *et al.* (2017) Retinal and Ophthalmic Artery Occlusions Preferred Practice Pattern®. *Ophthalmology*, **124**, 120-143. https://doi.org/10.1016/j.ophtha.2016.09.024

[6] Hayreh, S.S. (2018) Central Retinal Artery Occlusion. *Indian Journal of Ophthalmology*, **66**, 1684-1694. https://doi.org/10.4103/ijo.IJO_1446_18

[7] Varma, D.D., Cugati, S., Lee, A.W. and Chen, C.S. (2013) A Review of Central Retinal Artery Occlusion: Clinical Presentation and Management. *Eye* (*London*, *England*), **27**, 688-697. https://doi.org/10.1038/eye.2013.25

[8] Nedelmann, M., Graef, M., *et al.* (2015) Retrobulbar Spot Sign Predicts Thrombolytic Treatment Effects and Etiology in Central Retinal Artery Occlusion. *Stroke*, **46**, 2322-2324. https://doi.org/10.1161/strokeaha.115.009839

[9] Préterre, C., Godeneche, G., Vandamme, X., *et al.* (2017) Management of Acute Central Retinal Artery Occlusion: Intravenous Thrombolysis Is Feasible and Safe. *International Journal of Stroke*, **12**, 720-723. https://doi.org/10.1177/1747493016687578

[10] Schultheiss, M., Härtig, F., *et al.* (2018) Intravenous Thrombolysis in Acute Central Retinal Artery Occlusion—A Prospective Interventional Case Series. *PLoS ONE*, **13**, e0198114. https://doi.org/10.1371/journal.pone.0198114

[11] Schumacher, M., Schmidt, D., Jurklies, B., Gall, C., Wanke, I., Schmoor, C., Maier-Lenz, H., Solymosi, L., Brueckmann, H., Neubauer, A.S., Wolf, A., and Feltgen, N. (2010) Central Retinal Artery Occlusion: Local Intra-Arterial Fibrinolysis versus Conservative Treatment, a Multicenter Randomized Trial. *Ophthalmology*, **117**, 1367-1375. https://doi.org/10.1016/j.ophtha.2010.03.061

[12] Youn, T.S., Lavin, P., Patrylo, M., *et al.* (2018) Current Treatment of Central Retinal Artery Occlusion: A National Survey. *Journal of Neurology*, **265**, 330-335. https://doi.org/10.1007/s00415-017-8702-x

[13] Aldrich, E.M., Lee, A.W., Chen, C.S., Gottesman, R.F., Bahouth, M.N., Gailloud, P., Murphy, K., Wityk, R. and Miller, N.R. (2008 ) Local Intraarterial Fibrinolysis Administered in Aliquots for the Treatment of Central Retinal Artery Occlusion: The Johns Hopkins Hospital Experience. *Stroke*, **39**, 1746-1750. https://doi.org/10.1161/STROKEAHA.107.505404

[14] Biousse, V., Calvetti, O., Bruce, B. and Newman, N.J. (2007) Thrombolysis for Central Retinal Artery Occlusion. *Journal of Neuro-Ophthalmology*, **27**, 215-230. https://doi.org/10.1097/WNO.0b013e31814b1f66

[15] Mercier, J., Kastler, A., Jean, B., Souteyrand, G., Chabert, E., Claise, B., Pereira, B. and Gabrillargues, J. (2015) Interest of Local Intra-Arterial Fibrinolysis in Acute Central Retinal Artery Occlusion: Clinical Experience in 16 Patients. *Journal of Neuroradiology*, **42**, 229-235. https://doi.org/10.1016/j.neurad.2014.02.007

[16] Page, P.S., Cambon, A.C. and James, R.F. (2016) Visual Improvement after Intra-Arterial Thrombolysis for Central Retinal Artery Occlusion Does Not Correlate with Time to Treatment. *Interventional Neurology*, **5**, 131-139. https://doi.org/10.1159/000446853

[17] Hayreh, S.S. and Jost, B.J. (2000) Optic Disk and Retinal Nerve Fiber Layer Damage after Transient Central Retinal Artery Occlusion: An Experimental Study in Rhesus Monkeys. *American Journal of Ophthalmology*, **129**, 786-795. https://doi.org/10.1016/s0002-9394(00)00384-6.

[18] Hayreh, S.S., *et al.* (2004) Central Retinal Artery Occlusion. *Experimental Eye Research*, **78**, 723-736. https://doi.org/10.1016/s0014-4835(03)00214-8