· Clinical Research ·

Retinal vascular diameter changes assessed with a computer-assisted software after strabismus surgery

Jin–Qiong Zhou, Jing Fu, Ji–Peng Li, Xiao–Zhen Wang, Wen–Ying Wang, Bo–Wen Zhao, Meng Qi

Beijing Tongren Eye Center, Beijing Tongren Hospital, Capital Medical University; Beijing Ophthalmology & Visual Sciences Key Laboratory, Beijing 100730, China

Correspondence to: Jing Fu. Beijing Tongren Eye Center, Beijing Tongren Hospital, Capital Medical University; Beijing Ophthalmology & Visual Sciences Key Laboratory, Beijing 100730, China. fu_jing@126.com

Received: 2019-05-10 Accepted: 2019-12-11

Abstract

● **AIM:** To quantitatively investigate the retinal vascular diameter changes, analyzing the early and long-term effects on the retinal circulation, with 6-month follow-up.

● **METHODS:** Patients underwent horizontal strabismus surgery were enrolled prospectively. Retinal vessel diameters on color fundus photographs were assessed before and 1, 7d, 6mo after surgery, using a computer-assisted quantitative assessment software. To evaluate the retinal vascular caliber changes, retinal vascular diameters were calculated by means of the Parr–Hubbard formula as the central retinal arteriolar equivalent (CRAE) and central retinal venular equivalent (CRVE). The arteriovenous ratio (AVR) was calculated as CRAE divided by CRVE.

● **RESULTS:** A total of 154 eyes of 104 consecutive patients were included. Compared with the data before surgery (121.55±24.67), the mean CRAE (131.18±28.29) significantly increased 1d after surgery (P=0.003), but went back to baseline level at 7d (118.89±30.35, P=0.15), and 6mo (123.22±15.32, P=0.60), so did the AVR (P<0.001, P=0.08, P=0.07). As for the mean CRVE, there was no significant difference between those four time points (172.43±33.25, 175.57±36.98, 174.03±40.18, 174.86±20.46, P=1.00).

● **CONCLUSION:** Strabismus surgery on both lateral and media rectus muscles, or single media rectus muscle may increase retinal blood flow during the early postoperative period, but would return to normal later. The number of transected anterior ciliary arteries rather might be the main cause of retinal hemodynamic changes early after strabismus surgery.

● **KEYWORDS:** retinal blood flow; retinal vascular diameter; strabismus; strabismus surgery

DOI:10.18240/ijo.2020.04.14

Citation: Zhou JQ, Fu J, Li JP, Wang XZ, Wang WY, Zhao BW, Qi M. Retinal vascular diameter changes assessed with a computer-assisted software after strabismus surgery. *Int J Ophthalmol* 2020;13(4):620-624

INTRODUCTION

The potential alteration of retinal blood flow after strabismus surgery has been an interest for ophthalmologists. Since the anterior ciliary arteries, which come from the rectus muscles, are the major source of blood supply (70%-80%) for the ocular anterior segment, and are transected during strabismus surgery, there might be some hemodynamic changes on the anterior segment[1-2].

Retinal arteries and anterior ciliary arteries are originated from the same ophthalmic artery. Some hemodynamic alteration may occur in retinal circulation due to the hemodynamic changes of the anterior segment after strabismus surgery[3-6]. Therefore, it is necessary to pay attention to the possibility of anterior segment ischemia and retinal ischemia, especially for those eyes with risk factors of ocular ischemia, such as ocular ischemic syndrome, retinal arterial occlusion, retinal vein occlusion, and so on.

Color Doppler imaging was used to investigate the orbital blood flow changes after strabismus surgery in several studies, showed conflicting results in terms of whether or not the blood flow of ophthalmic artery changes[7-10]. However, orbital Doppler ultrasonography is a user-dependent and time-consuming imaging method, with poor sensitivity and accuracy in vascular measurements.

Not long before, we performed a study using a computer-assisted quantitative assessment software, evaluated the retinal vascular diameter changes before and 1d after strabismus surgery[3]. It showed that strabismus surgery on horizontal rectus muscles might change retinal hemodynamics by increasing the central retinal arteriolar diameter one day after surgery. This study reported a large number of patients with short-term observation after surgery. However, the long-term trend of the retinal hemodynamic changes and the impact on the retina later after surgery is still unknown.

In our study, we investigate the effects on retinal arteriolar diameter with 6-month follow-up after strabismus surgery for further research.

SUBJECTS AND METHODS

Ethical Approval The Ethics Committee of Beijing Tongren Hospital approved the study protocol, following the tenets of the Declaration of Helsinki. All of the participants gave written informed consent.

Patients Enrollment Consecutive patients underwent strabismus surgery between January 2016 and April 2018 at the Eye Center of Beijing Tongren Hospital were enrolled. The diagnosis of strabismus was made by an experienced surgeon (Fu J). Patients were excluded if: 1) patients had undergone previous ocular surgery, including previous extraocular muscle surgery; 2) patients had systematic diseases which may cause hemodynamic changes in the retina such as diabetes mellitus, hypertension, any other known vascular diseases; 3) patients who underwent or needed to undergo vertical rectus or oblique muscle surgery; 4) patients didn't finish the 6-month follow-up postoperatively.

Slit-lamp examination and color fundus photographs were evaluated pre- and postoperatively (1, 7d and 6mo after surgery). Signs of anterior segment ischemia were evaluated by slit-lamp examination, characterized by pupillary dilation and distortion, iris atrophy, lens opacities, and hypotonia. Color fundus photographs (45°) of each eye, centered on the optic disk (Diabetic Retinopathy Study standard field 1) and macula (Diabetic Retinopathy Study standard field 2), was taken using the CR6-45NM fundus camera (Canon Inc, Tokyo, Japan) before and 1, 7d, and 6mo after strabismus surgery, as described in the previous study[3].

Strabismus Surgery Horizontal rectus recession (range: 3-8 mm) or resection (range: 4-10 mm) were performed using the standard method and involved transecting the anterior ciliary arteries.

Retinal Vascular Caliber Measurement Computer-assisted quantitative assessment software (IVAN; University of Wisconsin, Madison, WI, USA) was applied to assess the retinal vascular diameters, as described in previous studies[3,11-12]. Average retinal vascular diameters were calculated by means of the revised Parr-Hubbard formula as the central retinal arteriolar equivalent (CRAE) or central retinal venular equivalent (CRVE). The arteriovenous ratio (AVR) was calculated as CRAE divided by CRVE[12-13]. Two trained graders, masked to participant characteristics, performed the vessel measurements on the optic disc-centered images. The largest six arterioles and venules coursing through a zone between 0.5- and 1-disc diameter from the optic disc margin were measured (Figure 1). Images were considered ungradable if the largest six arterioles and venules could not be able to be measured[14] (Figure 2).

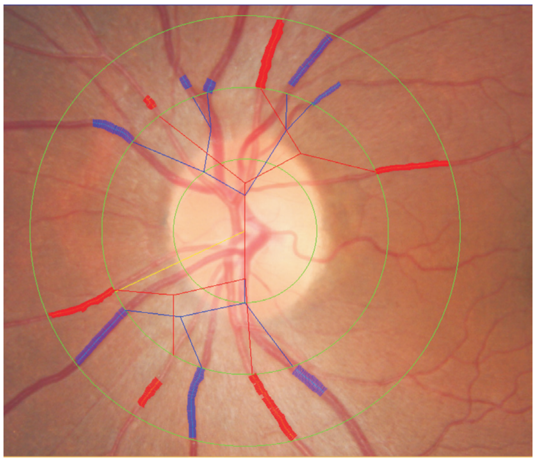

Figure 1 Computer-assisted quantitative assessment software.

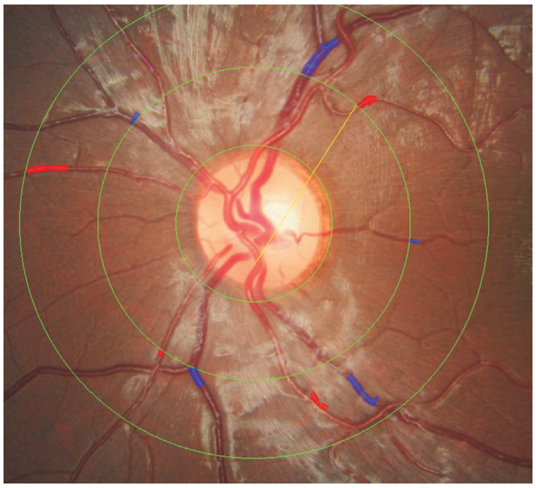

Figure 2 Ungradable image Because of reflection on retina, only four arterioles and five venules could be measured, it should be excluded.

Interobserver variability and intraobserver variability in the assessment of the retinal vascular diameter were analyzed in a masked manner. One-hundred fundus images were selected randomly and reviewed by two ophthalmologists (Zhou JQ, Li JP) independently. One observer (Zhou JQ) re-examined the same 100 photographs again 1mo later.

The details of participants, surgical protocols, examinations and the techniques of retinal vessels evaluation has been described in the previous study[3].

Statistical Analysis SPSS for Windows (IBM-SPSS, Chicago, IL, version 22.0, USA) was applied for statistical analysis. Repeated measures ANOVA was used to analyze the changes of the CRAE, CRVE and AVR before and 1, 7d, 6mo after surgery respectively. For those patients with two eyes included, statistical correction was done to deduce the statistical bias. A P-value of <0.05 was considered significant.

RESULTS

Of all the 118 consecutive patients, 6 patients who didn't finish the 6-month follow-up were excluded. Other 8 patients were excluded because of ungradable fundus images. Ungradable fundus images were due to reflection on retina (6 patients) or

Table 1 Comparison of retinal vessels caliber preoperative and postoperative of 154 eyes

Parameters	CRAE	*P*	CRVE	*P*	AVR	*P*
Pre-operation	121.55±24.67		172.43±33.25		0.70±0.07	
1-day post-operation	131.18±28.29	0.003	175.57±36.98	1.00	0.75±0.09	<0.001
7-day post-operation	118.89±30.35	0.15	174.03±40.18	1.00	0.69±0.09	0.08
6-month post-operation	123.22±15.32	0.60	174.86±20.46	1.00	0.71±0.07	0.07

CRAE: Central retinal artery equivalent; CRVE: Central retinal vein equivalent; AVR: Arteriovenous ratio.

Table 2 Comparison of retinal vessels caliber preoperative and postoperative for eyes undergoing one rectus muscle recession

Surgical methods	CRAE	*P*	CRVE	*P*	AVR	*P*
One rectus muscle recession, *n*=84						
Preoperative	119.45±21.75		169.03±31.20		0.71±0.08	
1d postoperative	128.58±26.86	0.003	169.80±35.11	0.198	0.76±0.08	0.02
7d postoperative	115.25±24.67	0.08	167.63±34.29	0.258	0.69±0.09	0.12
6mo postoperative	114.97±15.93	0.34	175.4±22.12	0.006	0.72±0.07	0.06
Medial rectus recession, *n*=23						
Preoperative	121.27±23.99		170.10±33.12		0.72±0.07	
1d postoperative	134.14±34.78	0.001	179.33±44.35	0.55	0.75±0.09	<0.001
7d postoperative	119.97±29.40	0.21	171.54±40.63	0.97	0.71±0.09	0.23
6mo postoperative	126.32±10.37	0.33	180.55±15.89	0.21	0.70±0.08	0.45
Lateral rectus recession, *n*=61						
Preoperative	118.77±21.01		168.63±30.71		0.71±0.08	
1d postoperative	126.48±23.21	0.09	166.21±30.59	0.20	0.76±0.08	0.73
7d postoperative	113.37±22.54	0.18	166.06±31.69	0.25	0.69±0.10	0.37
6mo postoperative	114.43±17.70	0.32	173.41±23.97	0.36	0.72±0.07	0.27

persistent ointment on corneal after surgery (2 patients). At the last follow up, a total of 154 eyes of 104 patients (88.14%) were analyzed, with 56 males (53.8%). The mean age was 10.45±2.34y (range: 3-14y). Seventy-five patients (72.1%) were diagnosed with exotropia and 29 patients with (27.9%) esotropia.

In all 154 eyes, no sign of anterior segment ischemia or retinal abnormality was found pre- and postoperatively. As for the assessment of variability, the interobserver correlation coefficient was 0.95 (95%CI 0.94-0.99) for CRAE and 0.96 (0.94-0.97) for CRVE. The intraobserver correlation coefficient was 0.97 (95%CI 0.95-0.99) for CRAE and 0.97 (0.96-0.98) for CRVE.

Compared with preoperative value (121.55±24.67), the mean CRAE at postoperative 1-day (131.18±28.29) was significantly increased (P=0.003), but returned to preoperative level at postoperative 7-day (118.89±30.35, P=0.15), and 6-month (123.22±15.32, P=0.60). As for the mean CRVE, there were no significant differences between those four time points (preoperative value 172.43±33.25, 1-day 175.57±36.98, 7-day 174.03±40.18, 6-month 174.86±20.46, P=1.00). The AVR at postoperative 1-day was significantly larger than preoperative value (0.75±0.09 *vs* 0.70±0.07, P<0.001), but turned back to preoperative level on day 7 (0.69±0.09, P=0.08) and 6-month (0.71±0.07, P=0.07; Table 1).

Of those 154 eyes, 84 eyes (54.55%) underwent surgery on single rectus muscle, lateral or medial rectus muscle. The other 70 eyes underwent surgery on both horizontal rectus muscles. For both of the two groups, CRAE and AVR were significant increase at postoperative 1-day, and turned back to preoperative level at 7-day and 6-month (Tables 2 and 3).

For those 84 eyes, further subgroup was performed. Totally 23 eyes underwent surgery on medial rectus, and the same trend of CRAE and AVR in different time points was found. However, the other 61 eyes underwent surgery on lateral rectus didn't show any significant difference between four different time points, both CRAE and CRVE (Table 2).

We also conducted a comparison of retinal vessels caliber between eyes undergoing single-muscle and 2-muscle surgery. Except for the CRAE of 2-muscle surgery group was a little bit larger than the single muscle surgery group (P=0.02) at 1-day after surgery, there was no significant difference of CRAE, CRVE and AVR between two groups on other time points (Table 4).

Table 3 Comparison of retinal vessels caliber preoperative and postoperative for eyes undergoing 2-muscle surgery *n*=70

Parameters	CRAE	*P*	CRVE	*P*	AVR	*P*
Pre-operation	124.84±4.50		177.96±5.21		0.70±0.01	
1d post-operation	137.40±4.22	0.04	184.14±5.70	0.95	0.75±0.01	0.001
7d post-operation	123.12±5.88	0.06	184.79±7.38	0.69	0.66±0.01	0.03
6mo post-operation	121.82±2.20	0.43	175.95±2.84	0.05	0.69±0.01	1.00

Table 4 Comparison of retinal vessels caliber between eyes undergoing single muscle and 2-muscle surgery

Parameters	CRAE-1	CRAE-2	*P*	CRVE-1	CRVE-2	*P*	AVR-1	AVR-2	*P*
Pre-operation	119.45±21.75	124.84±4.50	0.25	169.03±31.20	177.96±5.21	0.37	0.71±0.08	0.70±0.01	0.09
1d post-operation	128.58±26.86	137.40±4.22	0.02	169.80±35.11	184.14±5.70	0.41	0.76±0.08	0.75±0.01	1.00
7d post-operation	115.25±24.67	123.12±5.88	0.20	167.63±34.29	184.79±7.38	0.62	0.69±0.09	0.66±0.01	0.24
6mo post-operation	114.97±15.93	121.82±2.20	0.34	175.4±22.12	175.95±2.84	1.00	0.72±0.07	0.69±0.01	0.07

Single muscle surgery group: CRAE-1, CRVE-1, AVR-1; 2-muscle surgery group: CRAE-2, CRVE-2, AVR-2.

DISCUSSION

IVAN as a computer-assisted quantitative assessment software, has been used to measure the retinal vascular diameter for evaluating the retinal hemodynamic alterations for about 15y, with great reliability and repeatability[15]. In our previous study, we used this noninvasive approach to evaluate the retinal vascular diameters, showed that CRAE and AVR significantly increased at 1-day after strabismus surgery[3]. And in current study, compared with preoperative values, CRAE and AVR was still significantly increased at 1-day after surgery, but returned to preoperative levels at 7-day and 6-month after surgery. We believed that the early postoperative alterations on the central retinal arteriolar diameter reflected the increase blood flow of retinal circulation.

Some associated articles reported similar changes in ophthalmic arteries or other potentially affected retrobulbar arteries[8-11], except Bayramlar *et al*[7]. Bayramlar *et al*[7] reported 19 patients who underwent surgery on horizontal rectus muscles, didn't find any significant change on ophthalmic arteries. However, they evaluate the ophthalmic arteries on postoperative first week rather than the first day. Pelit *et al*[8] reported that after horizontal rectus surgery, the ophthalmic artery flow on color Doppler imaging was significantly increased at postoperative 1-day but returned to baseline levels by day 7. They presumed that the blood flow increased at postoperative 1-day was partly contributed by inflammation after surgery, and the phenomenon of return to baseline levels at 7-day and later may signify a reduction of inflammation. As one of the branches originated from ophthalmic artery, the blood flow of retinal arteries might be affected. In our current study, retinal arteriolar diameters showed the similar trend. We presume that there might be a compensation process between anterior ciliary arteries, retinal arteries and ophthalmic artery.

In this study, there was no sign of anterior segment ischemia pre- or postoperatively. Anterior segment ischemia is a severe complication of strabismus surgery[16]. Some researchers presumed that hemodynamic changes of ophthalmic artery in the early postoperative period might be a compensate that prevent anterior segment ischemia[8,17]. As branches of ophthalmic artery, changes in retinal vessel diameter found in this study may be a contributor to the above compensation process. Hence, for patients with risk factors of ocular ischemia, it is necessary to observe not only the anterior segment ischemic syndrome, but also the retina hemodynamics early after surgery.

In anatomy, except for the lateral rectus, the other rectus muscles (the medial rectus and both vertical rectus muscles) typically carry two anterior ciliary arteries. And the lateral rectus muscle carries only one artery that originates from the lacrimal artery. Due to these characteristics, both of our previous study and current study found that significant increase of CRAE and AVR at 1-day postoperatively was only found in patients underwent single medial rectus surgery group but not on single lateral rectus group[3]. This result was not consistent with the study by Pelit *et al*[8]. In their study, patients in group 1 underwent surgery on single rectus muscle and group 2 underwent surgery on both horizontal rectus muscles. They found that the blood flow of ophthalmic artery was significantly increased in 2-muscle group but not in the single muscle group. And they supposed that eyes with 2 muscles surgery developed more inflammation than those who underwent only 1 muscle surgery. However, in our current study, we found out that for eyes underwent single rectus muscle surgery, retinal homodynamic changes could be detected on eyes underwent medial rectus muscle surgery but not on lateral rectus muscle. This result suggests that it's not the inflammation but the number of transected anterior ciliary arteries contributed to be the main cause of retinal hemodynamic changes[18-20]. At least two anterior ciliary arteries injury was needed to change the retinal blood flow.

Potential limitations of this study should be considered. First, this is a hospital-based study, selective bias could have accentuated some estimates and masked others. Second, the retinal vascular diameters were assessed on routinely taken fundus photographs, which may lead overlooking of the systolic or diastolic effect on retinal vascular diameter. Third, in our study, we supposed to interpret the retinal vessels diameter changes in eyes with anterior segment ischemia. However, there was no patient presented with anterior segment ischemia. Hence, we failed to prove the relation between the risk of development of anterior segment ischemia and retinal vascular diameter changes after strabismus surgery, but only assumptions.

In conclusion, this study showed that strabismus surgery on both horizontal rectus muscles or single media rectus muscle may increase retinal blood flow during the early postoperative period, but would return to normal later. It reminds us that for patients with risk factors of ocular ischemia, it is necessary to observe not only the anterior segment ischemic syndrome, but also the retina hemodynamics early after surgery. We also found that, surgery on lateral rectus muscle played a minor role on postoperative retinal blood flow, because it carries only one anterior ciliary artery, which stated that the number of transected anterior ciliary arteries might be the main cause of retinal hemodynamic changes early after strabismus surgery.

ACKNOWLEDGEMENTS

Foundation: Supported by the Project for Collaboration Between Basis and Clinic of Capital Medical University (No.14JL04).

Conflicts of Interest: Zhou JQ, None; **Fu J,** None; **Li JP,** None; **Wang XZ,** None; **Wang WY,** None; **Zhao BW,** None; **Qi M,** None.

REFERENCES

1 Güven DM, Ziraman IM, Tomaç SM, Sancak DM, Karademir AM, Hasiripi H. Hemodynamic changes after strabismus surgery. *Strabismus* 2000;8(1):21-27.

2 Takkar B, Sharma P, Singh AK, Sahay P. Anterior segment optical coherence tomography for identifying muscle status in strabismus surgery. *Int J Ophthalmol* 2016;9(6):933-934.

3 Zhou JQ, Fu J, Li JP, Wang XZ, Wang WY, Zhao BW, Qi M. Quantitative measurement of retinal vascular diameter changes in the early postoperative period after strabismus surgery. *J AAPOS* 2017;21(4):274-277.

4 Inal A, Yilmaz I, Ocak OB, Aygit ED, Celik S, Pasaoglu I, Yilmaz BS, Gokyigit B. Optical coherence tomography angiography: are there any changes in measurements after strabismus surgery? *J Pediatr Ophthalmol Strabismus* 2019;56(2):95-100.

5 Mintz HR, Waisbourd M, Kessner R, Stolovitch C, Dotan G, Neudorfer M. Macular thickness following strabismus surgery as determined by optical coherence tomography. *J Pediatr Ophthalmol Strabismus* 2016;53(1):11-15.

6 Nelson LB. Macular changes following strabismus surgery confirmed by the use of optical coherence tomography. *J Pediatr Ophthalmol Strabismus* 2016;53(1):10.

7 Bayramlar H, Totan Y, Cekiç O, Yazicioglu KM, Aydin E. Evaluation of hemodynamic changes in the ophthalmic artery with color Doppler ultrasonography after strabismus surgery. *J Pediatr Ophthalmol Strabismus* 2000;37(2):94-100.

8 Pelit A, Barutçu O, Oto S, Aydin P. Investigation of hemodynamic changes after strabismus surgery using color Doppler imaging. *J AAPOS* 2002;6(4):224-227.

9 Akyüz Unsal AI, Unsal A, Ozkan SB, Karaman CZ. The effect of strabismus surgery on retrobulbar hemodynamics. *J AAPOS* 2007;11(3):277-281.

10 Lee NH, Lee SN. Investigation of hemodynamic changes in the ophthalmic artery using color Doppler imaging after strabismus surgery. *Korean J Ophthalmol* 2005;19(3):208-212.

11 Kawasaki R, Cheung N, Wang JJ, *et al*. Retinal vessel diameters and risk of hypertension: the Multiethnic Study of Atherosclerosis. *J Hypertens* 2009;27(12):2386-2393.

12 Xu L, Zhou JQ, Wang S, *et al*. Localized retinal nerve fiber layer defects and arterial hypertension. *Am J Hypertens* 2013;26(4):511-517.

13 Knudtson MD, Lee KE, Hubbard LD, Wong TY, Klein R, Klein BE. Revised formulas for summarizing retinal vessel diameters. *Curr Eye Res* 2003;27(3):143-149.

14 Sun C, Liew G, Wang JJ, Mitchell P, Saw SM, Aung T, Tai ES, Wong TY. Retinal vascular caliber, blood pressure, and cardiovascular risk factors in an Asian population: the Singapore Malay Eye Study. *Invest Ophthalmol Vis Sci* 2008;49(5):1784-1790.

15 Wong TY, Knudtson MD, Klein R, Klein BE, Meuer SM, Hubbard LD. Computer-assisted measurement of retinal vessel diameters in the Beaver Dam Eye Study: methodology, correlation between eyes, and effect of refractive errors. *Ophthalmology* 2004;111(6):1183-1190.

16 Tibrewal S, Kekunnaya R. Risk of anterior segment ischemia following simultaneous three rectus muscle surgery: results from a single tertiary care centre. *Strabismus* 2018;26(2):77-83.

17 Velez FG, Davila JP, Diaz A, Corradetti G, Sarraf D, Pineles SL. Association of change in iris vessel density in optical coherence tomography angiography with anterior segment ischemia after strabismus surgery. *JAMA Ophthalmol* 2018;136(9):1041-1045.

18 Hayreh SS. Proceedings: anatomy and pathophysiology of ocular circulation. *Exp Eye Res* 1973;17(4):387-388.

19 Wilcox LM, Keough EM, Connolly RJ, Hotte CE. The contribution of blood flow by the anterior ciliary arteries to the anterior segment in the primate eye. *Exp Eye Res* 1980;30(2):167-174.

20 Morrison JC, van Buskirk EM. Anterior collateral circulation in the primate eye. *Ophthalmology* 1983;90(6):707-715.