Clinical Research

Optical coherence tomography enhanced depth imaging of chorioretinal folds in patients with orbital tumors

Zhi-Yu Peng^{1,2}, Lu Gan^{1,2}, Kang Xue^{1,2}, Akrit Sodhi³, Xiao-Feng Ye^{1,2}, Hui Ren^{1,2}, Jiang Qian^{1,2}

¹Department of Ophthalmology, Eye and ENT Hospital of Fudan University, Shanghai 200031, China

²Shanghai Key Laboratory of Visual Impairment and Restoration, Shanghai 200031, China

³Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, MD 21287, USA

Co-first authors: Zhi-Yu Peng and Lu Gan

Correspondence to: Hui Ren. Jiang Qian. Department of Ophthalmology, Eye and ENT Hospital of Fudan University, Shanghai 200031, China. rhui@sina.com; qianjiang58@ hotmail.com

Received: 2022-08-11 Accepted: 2022-11-29

Abstract

• **AIM**: To characterize spectral-domain optical coherence tomography (SD-OCT) features of chorioretinal folds in orbital mass imaged using enhanced depth imaging (EDI).

• **METHODS:** Prospective observational case-control study was conducted in 20 eyes of 20 patients, the uninvolved eye served as a control. All the patients underwent clinical fundus photography, computed tomography, EDI SD-OCT imaging before and after surgery. Two patients with cavernous hemangiomas underwent intratumoral injection of bleomycin A5; the remaining patients underwent tumor excision. Patients were followed 1 to 14mo following surgery (average follow up, 5.8mo).

• **RESULTS:** Visual acuity prior to surgery ranged from 20/20 to 20/200. Following surgery, 5 patients' visual acuity remained unchanged while the remaining 15 patients had a mean letter improvement of 10 (range 4 to 26 letters). Photoreceptor inner/outer segment defects were found in 10 of 15 patients prior to surgery. Following surgical excision, photoreceptor inner/outer segment defects fully resolved in 8 of these 10 patients.

• **CONCLUSION:** Persistence of photoreceptor inner/ outer segment defects caused by compression of the globe by an orbital mass can be associated with reduced visual prognosis. Our findings suggest that photoreceptor inner/ outer segment defects on EDI SD-OCT could be an indicator for immediate surgical excision of an orbital mass causing choroidal compression. • **KEYWORDS:** chorioretinal folds; orbital mass; enhanced depth imaging optical coherence tomography; choroidal thickness; inner/outer segment defects

DOI:10.18240/ijo.2023.02.09

Citation: Peng ZY, Gan L, Xue K, Sodhi A, Ye XF, Ren H, Qian J. Optical coherence tomography enhanced depth imaging of chorioretinal folds in patients with orbital tumors. *Int J Ophthalmol* 2023;16(2):233-237

INTRODUCTION

O rbital mass of all kinds would cause symptoms by mass effect mostly presenting as asymptomatic axial proptosis. And it would also influence visual acuity by optic nerve compression, retinal striae, hyperopia, increased intraocular pressure $etc^{[1]}$. The timing of surgery for most benign tumors remains unclear. Take cavernomas, the most common benign orbital tumor as an example, surgery is performed to prevent putative visual damage by increasing the pressure of the cavernoma on visually vital structures, to debulk a cosmetically unsightly orbit and to obtain a histologic diagnosis, especially in cases where imaging cannot predict the kind of tumour^[2-4].

Choroidal folds are produced by deformation of the globe where the expanding retrobulbar mass indents the sclera^[5]. Their relationship to visual acuity, visual prognosis and timing of surgery is not clear.

Enhanced depth imaging (EDI) optical coherence tomography (OCT) has been widely used for imaging the full-thickness of the choroid^[6-8]. Herein, we conduct a prospective observational case series study to find the features of chorioretinal folds in orbital mass imaged using EDI OCT, in order to explore the role of chorioretinal folds in the mass effect and determine whether EDI spectral-domain optical coherence tomography (SD-OCT) could be a more sensitive measure of damage to the outer retina and could be a useful prognostic and/or diagnostic tool for patients with orbital masses.

SUBJECTS AND METHODS

Ethical Approval Our study protocol was approved by the Institutional Review Board of the Eye & ENT Hospital of

Table 1 Profile of patients included in the study

| Patient No. | Gender | Age (y) | Time of follow up (mo) | Choroidal thickness of the diseased eye at the first time (µm) | Choroidal thickness of the diseased eye at the last follow up (µm) | IS/OS defect at the first time (µm) | IS/OS defect at the last follow up (µm) | Choroidal thickness of contralateral eye as normal control (μm) | VA at the first time | VA at the last time | Diagnosis |
|-------------|----------------|------------|---------------------------|--|--|-------------------------------------|---|---|----------------------|------------------------|---|
| 1 | М | 48 | 14 | 95 | 250 | 375 | 120 | 200 | 20/125 | 20/63 | PA |
| 2 | Fª | 40 | 13 | 251 | 250 | 8 | 0 | 375 | 20/63 | 20/32 | СН |
| 3 | F ^a | 47 | 1 | 200 | 205 | 0 | 0 | 175 | 20/40 | 20/32 | СН |
| 4 | F | 38 | 2 | 240 | 325 | 0 | 0 | 250 | 20/25 | 20/20 | Nerve sheath tumor |
| 5 | F | 28 | 3 | 325 | 275 | 175 | 0 | 300 | 20/50 | 20/25 | PA |
| 6 | Fª | 25 | 9 | 250 | 287.5 | 0 | 0 | 250 | 20/32 | 20/25 | СН |
| 7 | F | 53 | 1 | 80 | 182.5 | 50 | 0 | 125 | 20/100 | 20/32 | СН |
| 8 | F | 26 | 6 | 250 | 250 | 50 | 0 | 300 | 20/25 | 20/20 | СН |
| 9 | М | 40 | 4 | 266 | 250 | 0 | 0 | 266 | 20/25 | 20/20 | SFT |
| 10 | M^{a} | 60 | 12 | 270 | 285 | 100 | 0 | 280 | 20/400 | 20/100 | SFT |
| 11 | М | 27 | 10 | 138 | 228 | 0 | 0 | 195 | 20/20 | 20/20 | СН |
| 12 | M^{a} | 52 | 1 | 242 | 329 | 95 | 45 | 360 | 20/125 | 20/125 | СН |
| 13 | М | 40 | 1 | 325 | 330 | 0 | 0 | 337 | 20/20 | 20/20 | СН |
| 14 | F ^a | 34 | 3 | 300 | 320 | 0 | 0 | 340 | 4/20 | 20/20 | Dermoidcyst |
| 15 | F | 40 | 1 | 275 | 293 | 0 | 0 | 293 | 20/25 | 20/20 | СН |
| 16 | М | 43 | 6 | 136 | 300 | 80 | 0 | 373 | 20/32 | 20/20 | SFT |
| 17 | F | 29 | 2.5 | 227 | 240 | 0 | 0 | 267 | 20/20 | 20/20 | СН |
| 18 | М | 41 | 16 | 240 | 260 | 13 | 0 | 280 | 20/25 | 20/20 | PA |
| 19 | М | 40 | 4 | 213 | 320 | 80 | 0 | 360 | 20/25 | 20/20 | SFT |
| 20 | F | 48 | 6 | 186 | 320 | 0 | 0 | 362 | 20/20 | 20/20 | Squamous cell carcinoma of lacrimal cyst |

PA: Polymorphous adenomas; CH: Cavernous hemangioma; SFT: Solitary fibrous tumor. ^aPatients with papilledema. IS/OS: Inner segment/outer segment; VA: Visual acuity.

Fudan University. Informed consent was obtained from all individual participants included in the study.

Patient Patients with intraorbital tumors indenting the sclera were included in the study (Figure 1). Those who had a history of previous vision-affecting eye disease or who required orbital exenteration or extensive tumor excision were excluded from the study.

Enhanced Depth Imaging SD-OCT Images were obtained in both eyes pre- and post-surgery. Considering axial length, myopia and to some extent age have a significant influence on choroidal thickness^[9-10], the contralateral eye served as a control. The images were obtained by positioning an OCT device close enough to the eye to acquire an inverted image. Twenty sections were obtained within a $5 \times 30^{\circ}$ rectangle encompassing the macula and optic nerve, with 100 scans averaged for each section, and the horizontal section passing directly through the center of the fovea selected^[11-12]. Postoperation EDI SD-OCT scans were performed using the follow-up mode. Inner segment/outer segment (IS/OS) defects were measured as the missing length of IS/OS layer. IS/ OS defects and subfoveal choroidal thickness was measured manually on EDI SD-OCT images using the Image J tool (National Institute of Health, Bethesda, MD, USA). Choroidal thickness is the distance from the outer edge of the hyperreflective retinal pigment epithelium (RPE) to the inner sclera. Statistical Analysis Statistical software was IBM SPSS

Statistics (version 26, USA). Descriptive statistics was performed to evaluate variations of choroidal thickness and Pearson correlation coefficient was applied to correlate choroidal thickness between both eyes. A P value less than 0.05 was considered significant.

RESULTS

Totally 20 patients were included in this study. Patients' profile was shown in Table 1. The mean age of the patients was 39.95 (range, 25 to 60)y, 11 (55%) were female and the rest 9 (45%) were male. Totally 10 of the 20 patients were cavernous hemangioma, 3 cases were polymorphous adenomas of lacrimal gland, 4 cases were solitary fibrous tumor (SFT), 1 nerve sheath tumor, dermoidcyst, and squamous cell carcinoma of lacrimal cyst respectively. Two patients with cavernous hemangioma underwent intratumoral injection of bleomycin A5^[13-14] and the rest patients received tumor excision. Patients were followed 1 to 14mo after surgery, 5.8mo on average. Visual acuity prior surgery ranged from 20/200 to 20/20 and 5 patients' visual acuity remained the same after the surgery and the other 15 patients' visual acuity was improved during follow-up. Among the 5 patients whose visual acuity was the same, 4 patients' visual acuity was 20/20 at the first time. While the rest one whose visual acuity was 20/125 at presentation followed 1mo only. Photoreceptor IS/OS defect was found in 10 of all the patients and 8 of them fully recovered after excision of orbital mass, 2 were better (Figure 2). Visual acuity



Figure 1 Contrast-enhanced magnetic resonance image demonstrating an orbital cavernous hemangioma indenting the posterior sclera.



Figure 2 EDI OCT of the left eye of a 53-year-old female with cavernous hemagioma A: Before the surgery; B: Both chorioretinal folds and IS/ OS defect improved a lot after 1mo post-surgery. EDI OCT: Enhanced depth imaging optical coherence tomography; IS/OS: Inner segment/ outer segment.

was improved in 9 of 10 patients with IS/OS defect after surgeries. And the rest one followed 1mo only and with papilloedema. Papilloedema was found in 6 patients whose visual acuity was lower than 20/32 at presentation and 3 of them did not present with IS/OS defect in EDI OCT. The subfoveal choroidal thickness prior surgeries was $225\pm15 \mu m$, and the thickness increased $50\pm14 \mu m$ after surgeries. IS/OS defect was $51\pm20 \mu m$ on average at beginning. Both choroidal thickness and IS/ OS defect are closely related to visual acuity (*P*<0.05).

DISCUSSION

Theoretically, orbital neoplasms of most kinds besides some kind of lymphomas like mucus associated lymphoid tissue lymphoma would ident the sclera resulting to the formation of chorioretinal folds if the tumor volume was big enough or it was growing right beside the eyeball. During the study, we encountered different kinds of orbital neoplasms including cavernous hemangioma, polymorphous adenoma, SFT, dermoidcyst, adenoid cystic carcinoma, embryonal rhabdomyoma, mesenchymal chondrosarcoma, nerve sheath tumor, squamous cell carcinoma. But some of them received orbital exenteration or extensive excision of the tumor which would influence the visual acuity and were excluded from the study. Cavernous hemangioma is the most commonly seen benign tumor in the orbit^[15] and it is soft. So, the chorioretinal folds causing by cavernous hemangioma do not accompany IS/OS defect that often. Four out of 10 patients diagnosed with cavernous hemangioma in this study were with IS/OS defect. To the contrary, all of the 3 patients with polymorphous adenoma of lacrimal gland in the study were found with IS/OS defect in EDI OCT. And 3 of 4 patients with SFT in this study had IS/OS defect. It implies that those firm tumors might be more easily to cause IS/OS defect and the superior temporal location of the tumors is more easily to affect the fovea and result visual loss.

The choroid is a highly vascular structure with blood flow and thickness varying in relation to the intraocular pressure, perfusion pressure^[16], endogenous nitric oxide production^[17], vasoactive secretory production of choroidal ganglion cells^[18-19], endogenous circulating catecholamines^[20-23], and its intrinsic vasomotricity^[24]. The choroidal layer is crucial for the metabolic function of the outer layers of the retina, including the RPE and photoreceptors^[25-26]. The microvascular loss may decrease the ability of the choroid to supply proper levels of oxygen and other metabolites to the RPE and outer retina^[11,27-30]. Zaben *et al*^[31] reported a study to estimate the association between choroidal thickness in the macular area and retinal sensitivity in eyes with high myopia. And they found that retinal sensitivity in highly myopic eyes is directly correlated with choroidal thickness and does not seem to be associated with retinal thickness^[10,31-32]. All these findings are consistent with current study. In this study, tumor indentations decreased the choroidal thickness and the choroidal thickness was slightly related to the visual acuity and IS/OS defect (Pearson correlation coefficient =-0.33).

On the other hand, patients included in this study do not have other eye diseases besides orbital tumor. After surgeries, when the compression was resolved most of IS/OS defect would recover except one patient with IS/OS defect as long as 375 μ m at presentation and did not fully recovered after a 14-month follow up (Figure 3). It implies that some extent of IS/OS defect can be recovered if there was no further damage to the retina.



Figure 3 EDI OCT of the left eye of a 48-year-old male with polymorphous adenoma of lacrimal gland A: IS/OS defect measured as 375 μm was found in this patients before the surgical removal of the tumor. B: IS/OS defect did not fully recovered after 14mo post-surgery. EDI OCT: Enhanced depth imaging optical coherence tomography; IS/OS: Inner segment/outer segment.

Papilloedema was found in 6 patients whose visual acuity was lower than 20/32 at presentation and 3 of them did not present with IS/OS defect in EDI OCT suggesting that papilloedema was one of the causes beside IS/OS defect for visual loss in these patients.

Totally 4 patients' visual acuity were 20/20 before surgery in this study even with the presentation of chorioretinal folds. And there were no obvious complains about their visual acuities at beginning. It might imply that even there are wrinkles of the retina the visual acuity might not be influenced dramatically without IS/OS defect.

In conclusion, decreased choroidal thickness as well as chorioretinal folds alone is not a necessity affecting visual acuity. Photoreceptor IS/OS defect caused by chronic compression of orbital mass is closely related to visual acuity, and it could recover in most of the patients but might not recover after surgery in a few patients. Besides, the presence of papilloedema, with or without IS/OS defect, suggests visual acuity damage. Identification of IS/OS defect in patients with chorioretinal folds using EDI-OCT might help to improve visual acuity to operate patients with orbital mass and choroidal compression as soon as possible.

ACKNOWLEDGEMENTS

Foundation: Supported by National Natural Science Foundation of China (No.81300805).

Conflicts of Interest: Peng ZY, None; Gan L, None; Xue K,

None; Sodhi A, None; Ye XF, None; Ren H, None; Qian J, None.

REFERENCES

- 1 Scheuerle AF, Steiner HH, Kolling G, Kunze S, Aschoff A. Treatment and long-term outcome of patients with orbital cavernomas. *Am J Ophthalmol* 2004;138(2):237-244.
- 2 Wiegand S, Zimmermann AP, Eivazi B, Sesterhenn AM, Sekundo W, Bien S, Werner JA, Barth PJ. Analysis of clinically suspected orbital cavernomas. *Br J Ophthalmol* 2010;94(12):1653-1656.
- 3 Rootman DB, Heran MKS, Rootman J, White VA, Luemsamran P, Yucel YH. Cavernous venous malformations of the orbit (socalled cavernous haemangioma): a comprehensive evaluation of their clinical, imaging and histologic nature. *Br J Ophthalmol* 2014;98(7): 880-888.
- 4 Yang P, Li Y, Liu HC, Qiu E, Zhang JL, Ren J, Jiang LB, Liu HG, Kang J. Prognosis analysis and clinical features of orbital cavernous venous malformations with refractory insidious onset. *Front Oncol* 2022;11:745479.
- 5 Hedges TR Jr, Leopold IH. Parallel retinal folds; their significance in orbital space-taking lesions. *Arch Ophthalmol* 1959;62:353-355.
- 6 Spaide RF, Koizumi H, Pozzoni MC. Enhanced depth imaging spectral-domain optical coherence tomography. *Am J Ophthalmol* 2008;146(4):496-500.
- 7 Yu ZY, Ye J, Lu F, Shen MX. Trends in research related to ophthalmic OCT imaging from 2011 to 2020: a bibliometric analysis. *Front Med* (*Lausanne*) 2022;9:820706.
- 8 Kessler LJ, Bagautdinov D, Łabuz G, Auffarth GU, Khoramnia R. Semi-automated quantification of retinal and choroidal biomarkers in retinal vascular diseases: agreement of spectral-domain optical coherence tomography with and without enhanced depth imaging mode. *Diagnostics (Basel)* 2022;12(2):333.
- 9 Xie JM, Ye LY, Chen QY, Shi Y, Hu GY, Yin Y, Zou HD, Zhu JF, Fan Y, He JN, Xu X. Choroidal thickness and its association with age, axial length, and refractive error in Chinese adults. *Invest Ophthalmol Vis Sci* 2022;63(2):34.
- 10 Duan F, Yuan ZH, Deng JY, Wong YL, Yeo AC, Chen X. Choroidal thickness and associated factors among adult myopia: a baseline report from a medical university student cohort. *Ophthalmic Epidemiol* 2019;26(4):244-250.
- 11 Margolis R, Spaide RF. A pilot study of enhanced depth imaging optical coherence tomography of the choroid in normal eyes. *Am J Ophthalmol* 2009;147(5):811-815.
- 12 Zheng F, He JL, Su ZT, Liu Y, Xu YF, Liu L, Ye PP. OCT biomarkers related to subthreshold micropulse laser treatment effect in central serous chorioretinopathy. *BMC Ophthalmol* 2022;22(1):252.
- 13 Yue H, Qian J, Elner VM, Guo J, Yuan YF, Zhang R, Ge Q. Treatment of orbital vascular malformations with intralesional injection of pingyangmycin. *Br J Ophthalmol* 2013;97(6):739-745.
- 14 Faiz K, Finitsis S, Linton J, Shankar JJS. Bleomycin for orbital and peri-orbital veno-lymphatic malformations a systematic review.

Interv Neuroradiol 2021;27(2):291-297.

- 15 Ohtsuka K, Hashimoto M, Suzuki Y. A review of 244 orbital tumors in Japanese patients during a 21-year period: origins and locations. *Jpn J Ophthalmol* 2005;49(1):49-55.
- 16 Kiel JW, van Heuven WA. Ocular perfusion pressure and choroidal blood flow in the rabbit. *Invest Ophthalmol Vis Sci* 1995;36(3):579-585.
- 17 Liu HH, Prokosch V. Energy metabolism in the inner retina in health and glaucoma. *Int J Mol Sci* 2021;22(7):3689.
- 18 Lütjen-Drecoll E. Choroidal innervation in primate eyes. *Exp Eye Res* 2006;82(3):357-361.
- 19 Spaide RF. CHOROIDAL BLOOD FLOW: review and potential explanation for the choroidal venous anatomy including the vortex vein system. *Retina* 2020;40(10):1851-1864.
- 20 Li CY, Fitzgerald MEC, Del Mar N, Haughey C, Reiner A. Defective choroidal blood flow baroregulation and retinal dysfunction and pathology following sympathetic denervation of choroid. *Invest Ophthalmol Vis Sci* 2018;59(12):5032-5044.
- 21 Chou PI, Lu DW, Chen JT. Adrenergic supersensitivity of rabbit choroidal blood vessels after sympathetic denervation. *Curr Eye Res* 2001;23(5):352-356.
- 22 Shimura M, Uchida S, Suzuki A, Nakajima K, Aikawa Y. Reflex choroidal blood flow responses of the eyeball following somatic sensory stimulation in rats. *Auton Neurosci* 2002;97(1):35-41.
- 23 Reiner A, Fitzgerald MEC, Del Mar N, Li CY. Neural control of choroidal blood flow. *Prog Retin Eye Res* 2018;64:96-130.
- 24 Delgado E, Marques-Neves C, Rocha I, Sales-Luís J, Silva-Carvalho L. Intrinsic vasomotricity and adrenergic effects in a model of isolated

rabbit eye. Acta Ophthalmol 2009;87(4):443-449.

- 25 Rewbury R, Want A, Varughese R, Chong V. Subfoveal choroidal thickness in patients with diabetic retinopathy and diabetic macular oedema. *Eye (Lond)* 2016;30(12):1568-1572.
- 26 Gupta C, Tan R, Mishra C, Khandelwal N, Raman R, Kim R, Agrawal R, Sen P. Choroidal structural analysis in eyes with diabetic retinopathy and diabetic macular edema-a novel OCT based imaging biomarker. *PLoS One* 2018;13(12):e0207435.
- 27 Nickla DL, Wallman J. The multifunctional choroid. Prog Retin Eye Res 2010;29(2):144-168.
- 28 Zhou H, Lu J, Chen K, Shi YY, Gregori G, Rosenfeld PJ, Wang RK. Mitigating the effects of choroidal hyper- and hypo-transmission defects on choroidal vascularity index assessments using optical coherence tomography. *Quant Imaging Med Surg* 2022;12(5):2932-2946.
- 29 Platzl C, Kaser-Eichberger A, Benavente-Perez A, Schroedl F. The choroid-sclera interface: an ultrastructural study. *Heliyon* 2022; 8(5):e09408.
- 30 Corvi F, Cozzi M, Corradetti G, Staurenghi G, Sarraf D, Sadda SR. Quantitative assessment of choriocapillaris flow deficits in eyes with macular neovascularization. *Graefes Arch Clin Exp Ophthalmol* 2021;259(7):1811-1819.
- 31 Zaben A, Zapata MÁ, Garcia-Arumi J. Retinal sensitivity and choroidal thickness in high myopia. *Retina* 2015;35(3):398-406.
- 32 Liu XT, Wang YL, Ying XX, Zhang F, Huang J, Yu H, Wang Q, Zheng MR, Hou F, Lesmes L, Lu ZL, Lu F, Mao XJ. Contrast sensitivity is associated with chorioretinal thickness and vascular density of eyes in simple early-stage high myopia. *Front Med (Lausanne)* 2022;9:847817.