·Clinical Research·

Association between choroidal thickness and anterior chamber segment in eyes with narrow or open-angle

Song-Feng Li [1], Ge-Wei Wu [2], Chang-Xi Chen [1], Ling Shen [3], Zhi-Bao Zhang [1], Fei Gao [1], Ning-Li Wang [1]

[1]Beijing Ophthalmology and Visual Science Key Laboratory, Beijing Tongren Eye Center, Beijing Institute of Ophthalmology, Beijing Tongren Hospital, Capital Medical University, Beijing 100730, China
[2]Department of Ophthalmology, Beijing Shi Jing Shan Hospital, Beijing 100000, China
[3]Department of Ophthalmology, The 2nd Affiliated Hospital of Harbin Medical University, Harbin 150001, Heilongjiang Province, China
Correspondence to: Ning-Li Wang. Beijing Ophthalmology and Visual Science Key Laboratory, Beijing Tongren Eye Center, Beijing Institute of Ophthalmology, Beijing Tongren Hospital, Capital Medical University, No. 1 Dongjiao Min Xiang, Beijing 100730, China. ningl_w@163.com
Received: 2015-11-27 Accepted: 2016-07-06

Abstract

• AIM: To investigate the relationship between choroidal thickness and anterior chamber segment in subjects with eyes with narrow or open-angle.

• METHODS: The subfoveal choroidal thickness was measured with enhanced depth -imaging optical coherence tomography and anterior chamber parameters were measured with ultrasound biomicroscopy in one eye of 23 subjects with open-angle eyes and 38 subjects with narrow-angle eyes. The mean age was 59.52±7.04y for narrow-angle subjects and 60.76±7.23y for open-angle subjects (P=0.514). Multivariate linear regression analysis was performed to assess the association between choroidal thickness and narrow -angle parameters.

• RESULTS: There were no differences in subfoveal choroidal thickness between open- and narrow-angle subjects (P=0.231). Anterior chamber parameters, including central anterior chamber depth, trabecular iris angle, iris thickness 500 μm from the scleral spur (IT500), and ciliary body thickness at 1 mm and 2 mm from the scleral spur (CBT1, CBT2) showed significant differences between the two groups (P<0.05). Subfoveal choroidal thickness showed negative correlation (β=-0.496, P=0.016) only with anterior chamber depth in the open-angle group and with age (β=-0.442, P=0.003) and IT500 (β=-0.399, P=0.008) in the narrow-angle group. However, subfoveal choroidal thickness was not correlated with trabecular iris angle, anterior chamber depth, ciliary body thickness, or central corneal thickness in the narrow-angle group.

• CONCLUSION: Choroidal thickness does not differ in the two groups and has not correlated with anterior chamber parameters in narrow -angle subjects, suggesting a lack of relationship between choroidal thickness and primary angle-closure glaucoma.

• KEYWORDS: choroidal thickness; narrow-angle eye; optical coherence tomography; primary angle-closure glaucoma

DOI:10.18240/ijo.2016.08.10

Li SF, Wu GW, Chen CX, Shen L, Zhang ZB, Gao F, Wang NL. Association between choroidal thickness and anterior chamber segment in eyes with narrow or open-angle. *Int J Ophthalmol* 2016;9 (8):1143-1147

INTRODUCTION

Primary angle-closure glaucoma is a major blinding form of glaucoma in Asia. About 87% of Chinese people affected, two million Chinese residents, are blind in at least one eye due to primary angle-closure glaucoma [1-3]. Acute primary angle-closure glaucoma is a potential blinding form of the disease. The incidence of acute primary angle-closure glaucoma is particularly high in Asian people[4-5].

It is well known that ocular risk factors in acute primary angle-closure glaucoma include some differential biometric characteristics that distinguish affected eyes from healthy eyes, such as shallower central anterior chamber, thicker lens, anterior lens position, smaller corneal diameter, smaller radius of curvature, shorter axial length, and an anterior lens-iris diaphragm[6-7]. It has been reported that abnormalities in the choroid, an important structure of the eye, might be involved in the pathogenesis of acute primary angle-closure glaucoma[8].

The choroid provides the vascular supply for the outer retina and the retinal pigment epithelium, which helps to regulate ocular volume and temperature. Some investigators have observed a common clinical feature in many patients with acute secondary angle-closure glaucoma. In these patients, the anterior chamber and choroid become thicker [9]. This phenomenon can be partially explained by Quigley *et al*'s[10] hypothesis. According to this hypothesis, choroidal expansion might be present in acute primary angle-closure glaucoma patients; this choroidal expansion is thought to contribute to the increase in choroidal thickness and to lead directly to an increase in vitreous cavity pressure, and hence an increased intraocular pressure. Simultaneously, it causes a forward movement of the lens and a greater iris convexity, which finally result in the closure of the anterior chamber angle and a steep elevation in intraocular pressure.

A recent study [10] showed that, in comparison with control eyes, acute primary angle-closure glaucoma eyes have a higher level of macular choroidal thickness when the intraocular pressure is reduced. Similarly, another study [11] found that eyes in primary angle-closure glaucoma subjects also have a thicker macular choroid. However, it is still unclear whether the increased choroidal thickness is related to the development of primary angle-closure glaucoma.

It has been reported that narrow drainage angle is another risk factor for the onset of acute primary angle-closure glaucoma[12]. Whether the thickness of the choroid in patients with narrow-angle is also a potential risk factor in the pathogenesis of acute primary angle-closure glaucoma, like ciliary body position and lens suspensory ligament laxity, has not yet, to our knowledge, been reported.

Therefore, we have studied the anatomical relationship between choroidal thickness and anterior segment in subjects with narrow angles to further understand the role of choroid in the pathogenesis of primary angle-closure glaucoma.

SUBJECTS AND METHODS

This is a prospective, comparative study conducted in Beijing Tongren Hospital. The study was conducted in accordance with the ethical standards stated in the 1964 Declaration of Helsinki and approved by the Ethical Review Committee of Beijing Tongren Ophthalmic Center. Informed consent was obtained from all subjects.

Subjects A total of 61 Chinese participants who visited our outpatient services between December 2012 and December 2013 were recruited. An initial diagnosis of a shallow anterior chamber was made based on peripheral anterior chamber depth [13], as measured using traditional techniques; detailed evaluations were then made using ultrasound biomicroscopy.

All participants underwent a full ophthalmic examination that included a best-corrected visual acuity of 20/40 or better, a spherical refractive error within the range of -3.00 to +3.00 diopters (D), clear ocular media, and no macular diseases. Only one eye per subject was selected. Individuals with a history of glaucoma, previous intraocular surgery or retinal laser treatment, penetrating eye injury, diabetes mellitus, optic nerve abnormalities, or corneal disorders preventing anterior chamber assessment were excluded.

Because ultrasound biomicroscopy and gonioscopy results are in good agreement [14], the anterior chamber angle of all eyes was evaluated using only ultrasound biomicroscopy in this study. According to the angle classification method of Schaffer [15], trabecular iris angles <20°, averaged for the four quadrants, were categorized as narrow and angles of ≥20° or more were regarded as open. Optic disks with narrow angles were observed by stereoscopic biomicroscopy for eyes with a cup-to-disk ratio <0.5, no retinal nerve fiber layer defect, and an intraocular pressure <21 mm Hg.

Methods

Ultrasound biomicroscopy The anterior segments of all subjects were imaged using a UBM P45 (Paradigm Medical, Salt Lake City, UT, USA). All ultrasound biomicroscopy examinations were performed by the same experienced examiner; eyes were imaged in the undilated state under room light illumination conditions. After surface anesthesia with 0.5% proparacaine, physiologic saline was applied to the eyeball between the eyelids. The probe was placed perpendicular to the ocular surface. Scanning was performed at the limbus and ciliary body region and got images of all four quadrants. Only images that showed a clear anterior segment were accepted.

The following parameters were determined: 1) central corneal thickness; 2) central anterior chamber depth measured on a line extending from the corneal endothelium perpendicularly to the anterior lens surface; 3) trabecular iris angle, defined as an angle formed with the apex at the iris recess and the arms passing through the point on the meshwork 500 μm from the scleral spur and the point on the iris perpendicularly opposite; 4) iris thickness, the distance at 500 μm (IT500) from the scleral spur; and 5) ciliary body thicknesses measured 1 mm and 2 mm from the scleral spur (CBT1, CBT2).

Spectral-domain optical coherence tomography Choroid imaging was performed by the same experienced doctors on all subjects by spectral-domain optical coherence tomography (Heidelberg Engineering, Heidelberg, Germany). To measure the thickness of the macula choroid, we used horizontal and vertical sections going directly through the center of the fovea. The automatic real-time (100 frames) averaging mode was applied, to maximize the signal-to-noise ratio and ensure good quality images. The resultant images were viewed and measured using Heidelberg Eye Explorer software (version 1.5.12.0; Heidelberg Engineering).

The choroid was measured from the outer portion of the hyper-reflective line corresponding to the retinal pigment epithelium to the inner surface of the sclera (Figure 1). The subfoveal choroidal thickness was measured manually from a vertical and a horizontal section under the center of the fovea, using optical coherence tomography data, by two independent experienced doctors in a blind manner, and then averaged for analysis.

Table 1 Comparison of clinical characteristics and anterior chamber parameters in subjects with open- and narrow-angle $\bar{x}\pm s$

Parameters	Narrow-angle (*n*=38)	Open-angle (*n*=23)	*P*
Spherical equivalent (D)	-0.27±0.65	-0.87±0.49	0.704
Intraocular pressure (mm Hg)	15.11±3.01	15.15±3.09	0.954
Subfoveal choroidal thickness (μm)	279.25±96.95	252.65±52.40	0.231
Central corneal thickness (mm)	0.53±0.03	0.54±0.03	0.709
Central anterior chamber depth (mm)	1.98±0.34	2.58±0.35	0.000[a]
Trabecular iris angle (°)	10.13±5.15	29.31±7.94	0.000[a]
CBT1 (mm)	0.54±0.70	0.65±0.09	0.000[a]
CBT2 (mm)	0.24±0.04	0.37±0.40	0.033[a]
IT500 (mm)	0.35±0.04	0.38±0.05	0.008[a]

CBT1, CBT2: Ciliary body thicknesses measured 1 mm and 2 mm from the scleral spur, respectively; IT500: Iris thickness, measured 500 μm from the scleral spur. [a]$P<0.05$.

Table 2 Multivariate linear regression analysis of subfoveal choroidal thickness in subjects with open- and narrow-angle $\bar{x}\pm s$

Parameters	Open-angle		Narrow-angle	
	β	*P*	*β*	*P*
Age (a)	0.123	0.529	-0.442	0.003
Spherical equivalent (D)	0.059	0.765	-0.089	0.532
Intraocular pressure (mm Hg)	0.181	0.353	-0.083	0.570
Central corneal thickness (mm)	-0.221	0.379	-0.039	0.786
Central anterior chamber depth (mm)	-0.496	0.016[a]	0.108	0.503
Trabecular iris angle (°)	-0.042	0.860	0.254	0.086
CBT1 (mm)	0.0000	1	-0.172	0.265
CBT2 (mm)	-0.066	0.736	0.081	0.598
IT500 (mm)	-0.024	0.909	-0.399	0.008[a]

CBT1, CBT2: Ciliary body thicknesses measured 1 mm and 2 mm from the scleral spur, respectively; IT500: Iris thickness, measured 500 μm from the scleral spur. [a]$P<0.05$.

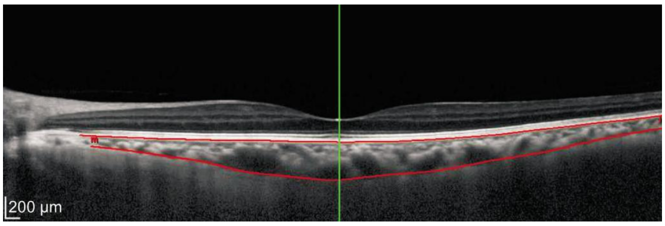

Figure 1 Subfoveal choroidal thickness The outer margin of the retinal pigment epithelium was considered the anterior margin of the choroid (upper line) and the choroidal-scleral interface was the posterior margin of the choroid (lower line).

Statistical Analysis All data were analyzed using SPSS analysis software (version18; SPSS Inc., Chicago, IL, USA). An independent-sample *t*-test was used to evaluate differences between the two different groups. Multivariate linear regression analysis was performed to assess the relationships between subfoveal choroidal thickness and age, spherical equivalent, intraocular pressure, central corneal thickness, anterior chamber depth, trabecular iris angle, IT500, CBT1, and CBT2. Statistical significance was considered for $P<0.05$.

RESULTS

A total of 61 subjects were enrolled in this study, and 38 were diagnosed as having narrow-angle. There were 4 men and 19 women in the open-angle group and 4 men and 34 women in the narrow-angle group. There was no difference in age distribution (P=0.514) between the narrow-angle group (59.52±7.04) and the open-angle group (60.76±7.23). There was no difference in spherical equivalent (P=0.704) or intraocular pressure (P=0.954) between the open- and narrow-angle groups. Anterior chamber parameters, including the anterior chamber depth, trabecular iris angle, IT500, CBT1, and CBT2 showed significant differences ($P<0.05$) between the two groups. However, we did not find any obvious differences in subfoveal choroidal thickness (P=0.231) and central corneal thickness (P=0.709) between the two groups (Table 1).

Multivariate linear regression analysis was performed to assess relationships between the subfoveal choroidal thickness, and age, spherical equivalent, intraocular pressure, central corneal thickness, anterior chamber depth, trabecular iris angle, IT500, CBT1, and CBT2. In the open-angle group, subfoveal choroidal thickness showed negative correlation (β=-0.496, P=0.016) only with anterior chamber depth (Table 2). In the narrow-angle group, subfoveal choroidal thickness correlated negatively with age (β=-0.442, P=0.003) and IT500 (β= -0.399, P=0.008), but not trabecular iris angle, anterior chamber depth, CBT1, CBT2, or central corneal thickness (Table 2; Figures 2, 3).

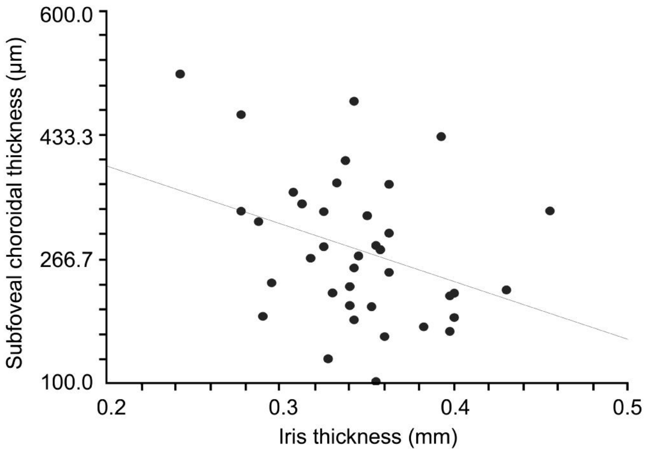

Figure 2 Scatter plot of simple linear regression analysis between subfoveal choroidal thickness and iris thickness in subjects with narrow angles.

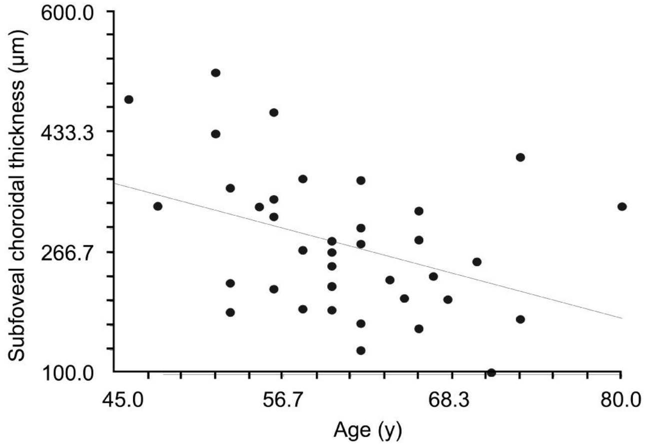

Figure 3 Scatter plot of simple linear regression analysis between subfoveal choroidal thickness and age in subjects with narrow angles.

DISCUSSION

We investigated the relationship between choroidal thickness and narrow- or open-angle. No significant association was observed between trabecular iris angle and subfoveal choroidal thickness in either the open-angle or the narrow-angle group. Age and IT500 were negatively associated with subfoveal choroidal thickness in narrow-angle subjects but not in open-angle subjects.

As is well known, eyes with primary angle-closure glaucoma have a particular characteristic shallow anterior chamber angle structure. Previous studies have shown that anatomical features of eyes with primary angle-closure glaucoma, such as central anterior chamber depth, iris thickness, central corneal thickness, and lens thickness, are different from those of open-angle eyes [16-19]. We found significant differences in anterior chamber depth, trabecular iris angle, iris thickness, CBT1, and CBT2 between the two groups. Quigley [20-21] hypothesized that choroidal expansion contributes to an increase in the posterior intraocular pressure. A differential posterior to anterior pressure would result in fluid outflowing from the anterior chamber, and the aqueous volume in the anterior chamber would be decreased. The lens would move forward and the angle would become narrow. The thicker choroid might be related to an increase in choroidal blood volume. The greater tendency to choroidal expansion may narrow the angle. In the predisposed eye with a narrow angle, expansion of the choroid would thus contribute to a greater chance of developing primary angle closure glaucoma.

Previous studies [10-11] reported that subfoveal choroidal thickness is significantly greater in the subjects with primary angle closure and in groups with acute primary angle closure than in groups with open angles. This may be related to the development of primary angle closure glaucoma. Researchers hypothesized that eyes with thicker choroids had a more anterior lens position and a shallower anterior chamber, contributing to an acute increase in intraocular pressure [22]. However, the current study did not find significant differences in subfoveal choroidal thickness between open-angle and narrow-angle subjects, although narrow-angle subjects tended to have thicker choroids (279.25±96.95 *vs* 252.65±52.40, P=0.231) than open-group subjects. Here, only subjects with narrow-angle who did not have glaucoma were recruited, while patients diagnosed with primary angle-closure glaucoma or pre-glaucoma had been enrolled in previous studies. This criterion may lead to the difference in findings.

Disorders of the anterior segment contributed greatly to the development of acute primary angle-closure glaucoma. We evaluated the relationship between choroidal thickness and anterior segment parameters for open-angle eyes and eyes with shallow anterior chambers. According to previous studies, there is a positive correlation between anterior chamber depth and axial length. Eyes with longer axial lengths had thinner choroids [23]; this supports our findings, since axial length is usually consistent with anterior chamber depth. We found a significant association between subfoveal choroidal thickness and anterior chamber depth in open-angle subjects, but we did not find, such an association in shallow anterior chamber eyes. These results suggest that there might be an additional effect of the lens or iris on narrowing the anterior chamber in those older than 45 years old. In addition, no significant association was found between subfoveal choroidal thickness and other anterior segment parameters, including iris thickness, central corneal thickness, and ciliary body thickness, in open subjects.

The previous finding that choroidal thickness decreases as age increases is in agreement with our results [24-25]. Our study showed a negative correlation between subfoveal choroidal thickness and age in eyes with shallow anterior chambers, which tended to have a thicker subfoveal choroid, but not in open-angle subjects 45 years or older. This suggests that age is more significantly associated with subfoveal choroidal thickness in eyes with shallow anterior chambers.

In this study, we found a negative correlation between subfoveal choroidal thickness and iris thickness in shallow anterior chamber eyes, but not with trabecular iris angle, ciliary body thickness, or central corneal thickness. To the best of our knowledge, there are still no studies assessing relationships between subfoveal choroidal thickness and these anterior chamber parameters. Further research is needed to clarify the relationships between these factors.

Although choroidal expansion may contribute to acute episodes of glaucoma, no correlation was found between central corneal thickness and trabecular iris angle or anterior chamber depth in shallow anterior chamber eyes. However, our study has a number of limitations. First, choroidal thicknesses were measured manually, which might have introduced some inaccuracy. Second, the sample size was limited and subjects were only drawn from a single center. In future, a multicenter study with larger samples of subjects might provide more accurate outcome predictions. Moreover, the subjects older than 45 years were selected in this study. Thus, future studies should be conducted to confirm whether the choroid plays an important role in the pathogenesis of primary angle closure glaucoma.

ACKNOWLEDGEMENTS

Conflicts of Interest: Li SF, None; **Wu GW,** None; **Chen CX,** None; **Shen L,** None; **Zhang ZB,** None; **Gao F,** None; **Wang NL,** None.

REFERENCES

1 Foster PJ, Johnson GJ. Glaucoma in China: how big is the problem? *Br J Ophthalmol* 2001;85(11): 1277-1282.

2 Liang Y, Friedman DS, Zhou Q, Yang XH, Sun LP, Guo L, Chang DS, Lian L, Wang NL; Handan Eye Study Group. Prevalence and characteristics of primary angle-closure diseases in a rural adult Chinese population: the Handan eye study. *Invest Ophthalmol Vis Sci* 2011;52(12): 8672-8679.

3 Lai JS, Liu DT, Tham CC, Li RT, Lam DS. Epidemiology of acute primary angle-closure glaucoma in the Hong Kong Chinese population: prospective study. *Hong Kong Med J* 2001;7(2):118-123.

4 Sng CC, Aquino MC, Liao J, Ang M, Zheng C, Loon SC, Chew PT. Pretreatment anterior segment imaging during acute primary angle closure: Insights into angle closure mechanisms in the acute phase. *Ophthalmology* 2014;121(1):119-125.

5 Moghimi S, Vahedian Z, Fakhraie G, Ghaffari R, Eslami Y, Jabarvand M, Zarei R, Mohammadi M, Lin S. Ocular biometry in the subtypes of angle closure: an anterior segment optical coherence tomography study. *Am J Ophthalmol* 2013;155(4):664-673. 673.e1.

6 Huang W, Wang W, Gao X, Li X, Li Z, Zhou M, Chen S, Zhang X. Choroidal thickness in the subtypes of angle closure: an EDI-OCT study. *Invest Ophthalmol Vis Sci* 2013;54(13):7849-7853.

7 Marchini G, Chemello F, Berzaghi D, Zampieri A. New findings in the diagnosis and treatment of primary angle-closure glaucoma. *Prog Brain Res* 2015;221:191-212.

8 Banitt M. The choroid in glaucoma. *Curr Opin Ophthalmol* 2013;24(2): 125-129.

9 Thambt L, Kapcala LP, Chamber W, Nourjah P, Beitz J, Chen M, Lu S. Topirama-accociatated secondary angle-closure glaucoma: a case series. *Arch Ophthalmol* 2002;120(8):1108.

10 Quigley HA, Friedman DS, Congdon NG. Possible mechanisms of primary angle-closure and malignant glaucoma. *J Glaucoma* 2003;12(2):167-180.

11 Wang W, Zhou M, Huang W, Chen S, Ding X, Zhang X. Does acute primary angle-closure cause an increased choroidal thickness? *Invest Ophthalmol Vis Sci* 2013;54(5):3538-3545.

12 Zhou M, Wang W, Ding X, Huang W, Chen S, Laties A, Zhang L Choroidal thickness in fellow eyes of patients with acute primary angle-closure measured by enhanced depth imaging spectral-domain optical coherence tomography. *Invest Ophthalmol Vis Sci* 2013;54 (3): 1971-1978.

13 George R, Paul PG, Baskaran M, Ramesh SV, Raju P, Arvind H, McCarty C, Vijaya L. Ocular biometry in occludable angles and angle closure glaucoma: a population based survey. *Br J Ophthalmol* 2003;87(4): 399-402.

14 Van Herick W, Shaffer RN, Schwartz A. Estimation of the width of the angle of anterior chambers: incidence and significance of the narrow angle. *Am J Ophthalmol* 1969;68(4):626-629.

15 Kaushik S, Jain R, Pandav SS, Gupta A. Evaluation of the anterior chamber angle in Asian Indian eyes by ultrasound biomicroscopy and gonioscopy. *Indian J Ophthalmol* 2006;54(3):159-163.

16 Shaffer RN. Gonioscopy, ophthalmoscopy and perimetri. *Trans Am Acad Ophthalmol Otolaryngol* 1960;64:112-127.

17 Congdon NG, Youlin Q, Quigley HA, Hung PT, Wang TH, Ho TC, Tielsch JM. Biometry and primary angle-closure glaucoma among Chinese, white, and black populations. *Ophthalmology* 1997;104(9):1489-1495.

18 He M, Lu Y, Liu X, Ye T, Foster PJ. Histologic changes of the iris in the development of angle closure in Chinese eyes. *J Glaucoma* 2008;17 (5): 386-392.

19 Sihota R, Lakshmaiah NC, Agarwal HC, Pandey RM, Titiyal JS. Ocular parameters in the subgroups of angle closure glaucoma. *Clin Experiment Ophthalmol* 2000;28(4):253-258.

20 Quigley HA. Angle-closure glaucoma-simpler answers to complex mechanisms: LXVI Edward Jackson Memorial Lecture. *Am J Ophthalmol* 2009;148(5):657-669.e1.

21 Quigley HA. What's the choroid got to do with angle closure? *Arch Ophthalmol* 2009;127(5):693-694.

22 Arora KS, Jefferys JL, Maul EA, Quigley HA. Choroidal thickness change after water drinking is greater in angle closure than in open angle eyes. *Invest Ophthalmol Vis Sci* 2012;53(10):6393-6402.

23 Mwanza JC, Hochberg JT, Banitt MR, Feuer WJ, Budenz DL. Lack of association between glaucoma and macular choroidal thickness measured with enhanced depth-imaging optical coherence tomography. *Invest Ophthalmol Vis Sci* 2011;52(6):3430-3435.

24 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.

25 Fujiwara T, Imamura Y, Margolis R, Slakter JS, Spaide RF. Enhanced depth imaging optical coherence tomography of the choroid in highly myopic eyes. *Am J Ophthalmol* 2009;148(3):445-450.