CHOROID & GLAUCOMA

By
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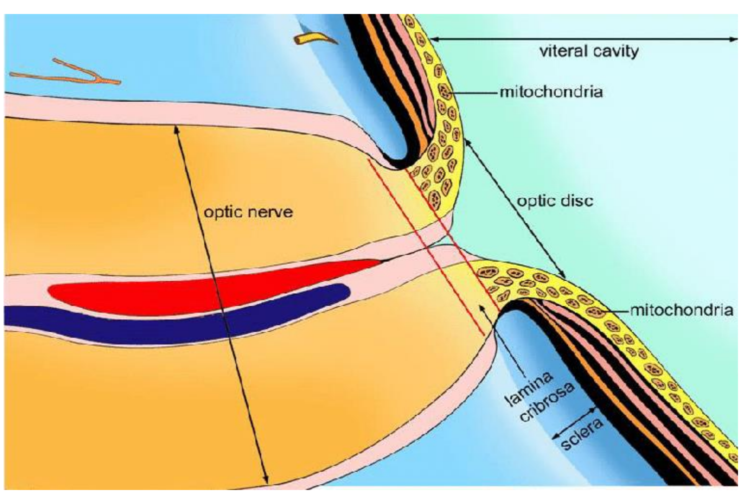
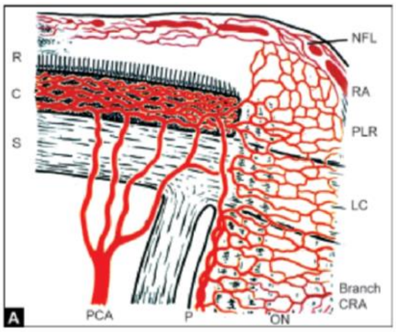
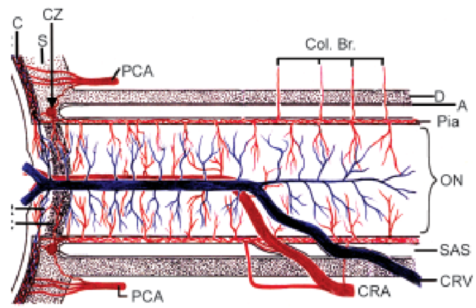
Two principal theories for the pathogenesis of optic nerve damage in OAG.
The mechanical theory: RGCs death due to high IOP, at least in POAG. When the IOP increases above the physiological levels, the pressure gradient through the lamina cribrosa also increases, blocking axonal protein transport in RGCs, causing cell death due to trophic insufficiency. Cannot fully explain NTG.



Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: a review. Jama. 2014;311(18):1901±11.

The vascular theory: intraneural ischemia due to decreased blood supply to the optic nerve at the level of lamina cribrosa. Since, the mechanical theory cannot fully explain NTG, the vascular theory attracts much more attention. Since the blood supply of the papillary sieve plate comes from the peripapillary choroid branches, increasing studies are being conducted to investigate the relationship between the choroidal circulation and glaucoma.

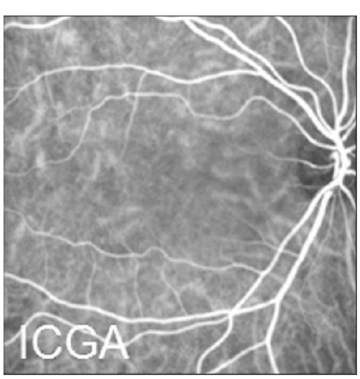


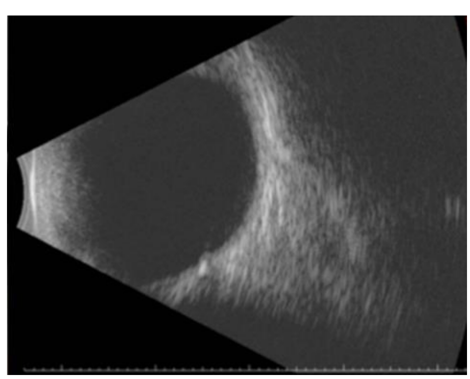


Xu S, Huang S, Lin Z, Liu W, Zhong Y. Color doppler imaging analysis of ocular blood flow velocities in normal tension glaucoma patients: a meta-analysis. J Ophthalmol. 2015.

Currently, the indices used to diagnose and evaluate optic neuropathy include optic nerve head, visual field tests, RNFL, ganglion cell layer with inner plexiform layer (GCIPL) and ganglion cell complex (GCC).

Despite the evidence that choroidal circulation is critically related to glaucoma, the morphological characteristics of the choroid are not appropriate to use in clinical practice, because the choroid could not be reliably visualized with previous instruments, such as indocyanine green angiography (ICGA), laser Doppler flowmetry and B-scan ultrasonography.



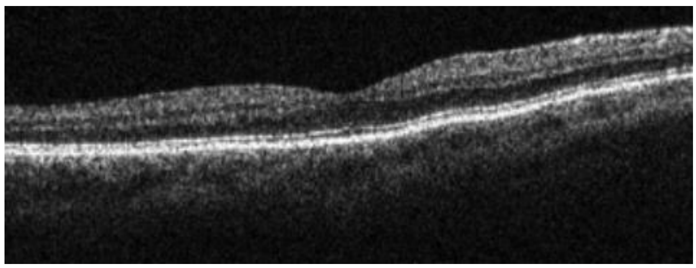


Riva CE, Geiser M, Petrig BL, Beijing 100193, PR China Ocular Blood Flow Research Association. Ocular blood flow assessment using continuous laser Doppler flowmetry. Acta Ophthalmol. 2010; 88 (6):622±9.

Landmark study by Spaide and colleagues on enhanced depth imaging EDI by OCT.

Typical OCT instruments use near infrared light that can image the retina and subretinal space well, but deeper penetration is limited because of scattering induced by the retinal pigment epithelium and the vascular nature of the choroid.

Clinical OCT devices use relatively low numerical aperture systems, which produce a beam of light that cones down not to a point, but to a disk, and then the beam of light expands outward, and consequently supply less lateral resolution. If the OCT is primarily imaging the retina, the expanding cone of light falls onto the choroid.



Spaide RF, Koizumi H, Pozonni MC. Enhanced depth imaging spectral-domain optical coherence tomography. Am J Ophthalmol. 2008; 146(4):496±500.

By displacing the instrument to image deeper layers purposefully, the most tightly focused portion of the illumination is delivered at the level of the choroid or inner sclera.
The choroidal thickness is segmented manually from the outer border of the retinal pigment epithelium (RPE) to the inner side of the choroidal-scleral interface

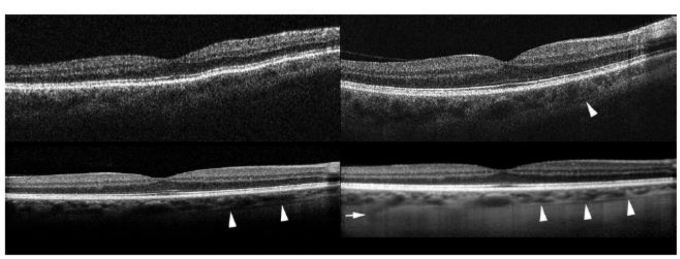
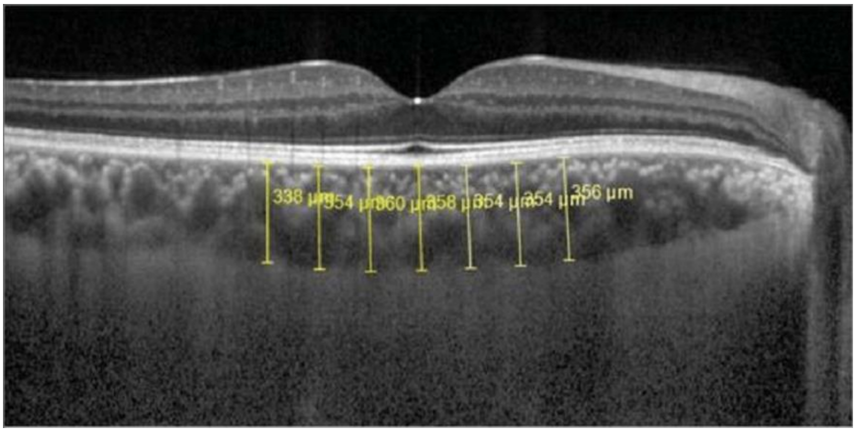


FIGURE 2. Comparative optical coherence tomography (OCT) sections through the fovea obtained with various OCT instruments. (Top left) StratusOCT image showing that details from the level of the choroid are lost in noise. (Top right) Cirrus OCT image in which some choroidal details are visible, including a linear hyporeflective line (arrowhead). (Bottom left) With the Heidelberg Spectralis used in a normal fashion, more choroidal details are visible, including better visualization of the hyporeflective line (arrowheads). (Bottom right) Choroidal image obtained using the technique described in this article. Note the clarity and delineation of the hyporeflective line, which appears to be in the suprachoroidal space. The arrow points to a vessel coursing through the sclera.

Spaide RF, Koizumi H, Pozonni MC. Enhanced depth imaging spectral-domain optical coherence tomography. Am J Ophthalmol. 2008; 146(4):496±500.

- The mean choroidal thickness as measured in the present series was 318 µm
- Decreases with age by 4µm per year.
- Decreases by 15 µm per diopter of increasing myopia.



Spaide RF, Koizumi H, Pozonni MC. Enhanced depth imaging spectral-domain optical coherence tomography. Am J Ophthalmol. 2008; 146(4):496±500.

Comparison between choroidal thickness in normal and glaucomatous eyes using spectral domain optical coherence tomography

DELTA JOURNAL OF OPHTHALMOLOGY
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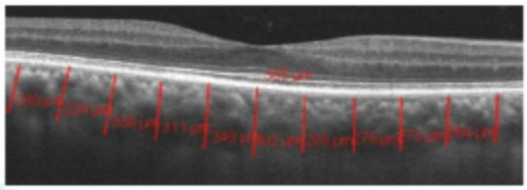
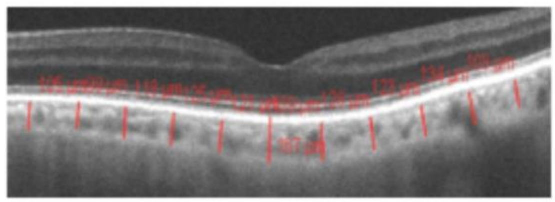
Two groups: group 1, 100 healthy eyes with normal intraocular pressure, and group 2, 100 juvenile and adult-onset POAG.

SD-OCT(Cirrus HD-OCT Model 4000) EDI technique. Choroidal thickness was measured in 11 points. The centre of the fovea (F0) plus five temporal points separated by 500 µm (T0.5, T1.0, T1.5, T2.0 and T2.5) and five nasal points separated by 500 µm (N0.5, N1.0, N1.5, N2.0 and N 2.5).





Mohsen AA, Karim MN. Comparison between choroidal thickness in normal and glaucomatous eyes using spectral domain optical coherence tomography. Delta Journal of Ophthalmology 2017; 18:104–107.

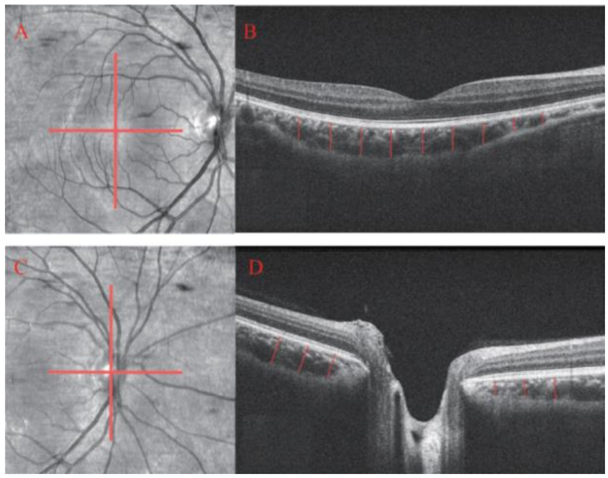
Choroidal thickness in group 2 was significantly less than that in group 1 in all studied points with the exception of T0.5 and subfoveal (F0) choroidal thickness.

	Group 1 (*n*=100) (mean±SD)	Group 2 (*n*=100) (mean±SD)	*P*
T2.5	263.58±50.24	207.95±53.39	<0.001*
T2	261.0±51.07	212.71±55.55	<0.001*
T1.5	259.27±52.5	223.81±54.65	0.006*
T1	253.27±45.34	227.81±55.28	0.026*
T0.5	239.40±44.62	235.57±63.19	0.741
F0	271.0±51.02	256.29±61.99	0.250
N0.5	276.63±54.34	225.33±59.13	<0.001*
N1	270.44±57.09	211.19±54.81	<0.001*
N1.5	264.93±55.8	198.95±55.02	<0.001*
N2	257.24±58.12	182.71±55.97	<0.001*
N2.5	252.79±51.88	171.76±55.55	<0.001*

*$P \leq 0.05$, statistically significant.

Mohsen AA, Karim MN. Comparison between choroidal thickness in normal and glaucomatous eyes using spectral domain optical coherence tomography. Delta Journal of Ophthalmology 2017; 18:104–107.

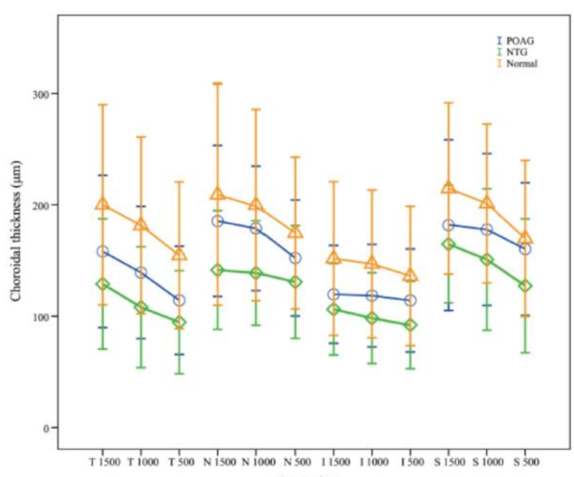
The diagnostic use of choroidal thickness analysis and its correlation with visual field indices in glaucoma using spectral domain optical coherence tomography



Lin Z, Huang S, Huang P, Guo L, Shen X, Zhong Y (2017) The diagnostic use of choroidal thickness analysis and its correlation with visual field indices in glaucoma using spectral domain optical coherence tomography. PLoS ONE 12(12): e0189376.

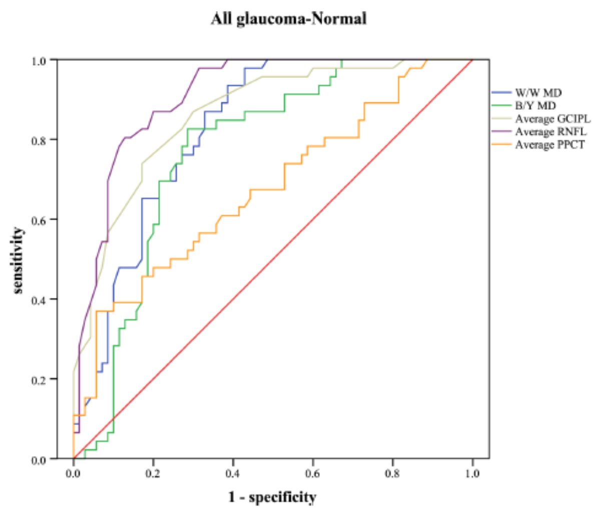
No significant differences for macular CT among the different groups.

Regarding PPCT, significant differences were observed among the three groups. A significant difference in the NTG-normal comparison group. The inferior and temporal PPCT in POAG patients were significantly thinner than those in normal subjects.



Lin Z, Huang S, Huang P, Guo L, Shen X, Zhong Y (2017) The diagnostic use of choroidal thickness analysis and its correlation with visual field indices in glaucoma using spectral domain optical coherence tomography. PLoS ONE 12(12): e0189376.

PPCT was not significantly correlated with the W/W MD (all P > 0.05). Similar results were observed for W/W PSD. However, PPCT significantly correlated with the B/Y MD (all P < 0.05) and the B/Y PSD.



Lin Z, Huang S, Huang P, Guo L, Shen X, Zhong Y (2017) The diagnostic use of choroidal thickness analysis and its correlation with visual field indices in glaucoma using spectral domain optical coherence tomography. PLoS ONE 12(12): e0189376.

The Effect of Glaucoma Medication on Choroidal Thickness Measured with Enhanced Depth-Imaging Optical Coherence Tomography

Serife BAYRAKTAR [1], Zafer CEBECI [1], Belgin IZGI [1], Kamber KASALI [2]

The aim of glaucoma medication is to lower IOP, but future treatment methodologies may include vaso-protective drugs, which influence blood flow. Choroidal thickness, a marker of choroidal flow, can be affected by the type of glaucoma medication administered. Thus, this study evaluated the effect of glaucoma medication on CT, using SD-OCT, with the EDI technique.

Bayraktar S, Cebeci Z, Izgi B, Kasali K. The Effect of Glaucoma Medication on Choroidal Thickness Measured with Enhanced Depth-Imaging Optical Coherence Tomography. Med Hypothesis Discov Innov Ophthalmol. 2019 Spring; 8(1): 44-51.

The researchers aimed to study the impact of glaucoma medication on CT as a sign of choroidal flow and ocular perfusion. In POAG, the researchers found a significant difference in CT under anti-glaucomatous treatment.

	Before treatment	After treatment	P
Choroidal thicknesses(µm ± SD)			
Subfoveal	301 ± 91	319 ± 85	0.0017*
Nasal 1mm to fovea	264 ± 87	275 ± 88	0.162
Temporal 1 mm to fovea	271 ± 84	291 ± 80	0.007*

SD: standard deviation; µm: micrometer; mm:milimeter. Note: Wilcoxon test applied for analysis. *: P value less than 0.05.

Bayraktar S, Cebeci Z, Izgi B, Kasali K. The Effect of Glaucoma Medication on Choroidal Thickness Measured with Enhanced Depth-Imaging Optical Coherence Tomography. Med Hypothesis Discov Innov Ophthalmol. 2019 Spring; 8(1): 44-51.

With respect to choroidal thickness in angle closure glaucoma, choroidal thickness was significantly greater in ACG group than OAG group and normal subjects, with no significant difference between OAG and normal subjects.

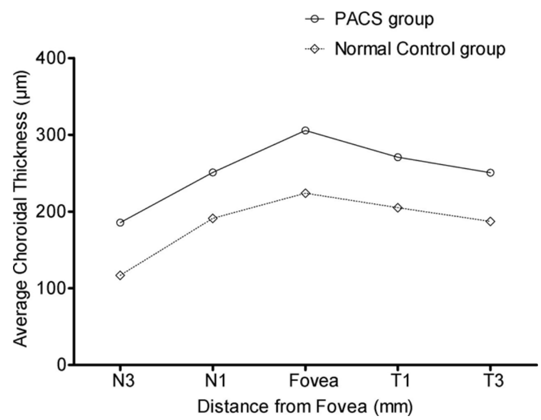
In another investigation, significant increase in choroidal thickness and a decrease in anterior chamber depth when water drinking test was performed in eyes with anterior chamber angle closure as compared to eyes with open anterior chamber angles.

Table 1. Characteristics of the Study Population Overall and Three Major Subgroups

	Overall		Normals		POAGS/POAG		PACS/PAC/PACG		
Characteristic	*N*	Value	*N*	Value	*N*	Value	*N*	Value	*P* Value*
CT, µm (mean [SD])	225	264 (102)	40	234 (75)	106	235 (78)	79	318 (120)	<0.0001

Arora KS, Jefferys JL, Maul EA, Quigley HA. The choroid is thicker in angle closure than in open angle and control eyes. Invest Ophthalmol Vis Sci 2012;53:7813-7818.
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;53:6393-6402.

In another recent study on fellow eyes of 44 patients with unilateral acute primary angle closure, the unaffected fellow eyes had thicker choroid than a group of control



Zhou M, Wang W, Ding X, Huang W, Chen S, Laties AM, et al. 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;54:1971-1978

Hosseini and Colleagues did not find any significant difference in SFCT or peripapillary CT (except for the temporal region) between patients with OAG and non-glaucomatous individuals.

Mwanza et al. studied one eye in 38 normal patients, 20 with NTG, and 56 with POAG and No relationship between glaucoma and average macular CT was detected.

Rhew et al. measured SFCT in 32 patients with NTG, whose results were compared with 35 healthy controls and they found no meaningful difference.

Jonas et al. measured CT in 71 patients with glaucoma and 228 normal individuals, and their findings revealed no significant differences.

Wang et al. examined the CT of patients with POAG using EDI-OCT and compared them with healthy subjects and reported no significant difference.

Hosseini H, Nilforushan N, Moghimi S, Bitrian E, Riddle J, Yoo Lee G, et al. Peripapillary and macular choroidal thickness in glaucoma. J Ophthalmic Vis Res 2014;9:154-161.

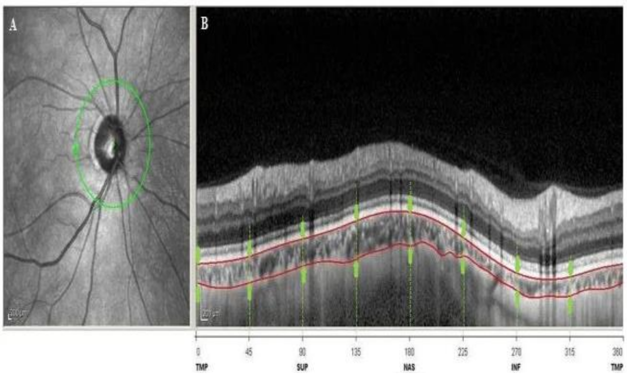
Mwanza JC, Hochberg JT, Banitt MR, Feuer WJ, Budenz DL. Lack of association between glaucoma and macular choroidal thickness measured with enhanced depth-imaging optical coherence tomography. Invest Ophthalmol Vis Sci 2011;52:3430-3435.

Rhew JY, Kim YT, Choi KR. Measurement of subfoveal choroidal thickness in normal-tension glaucoma in Korean patients. J Glaucoma. 2014;23(1):46-9.

Jonas JB, Steinmetz P, Forster TM, Schlichtenbrede FC, Harder BC. Choroidal Thickness in Open-angle Glaucoma. J Glaucoma. 2015;24(8):619-23.

Wang W, Zhang X. Choroidal thickness and primary open-angle glaucoma: a cross-sectional study and meta-analysis. Invest Ophthalmol Vis Sci. 2014; 55(9):6007±14.

In contrast, Hirooka et al. suggested that CT was focally diminished in patients with glaucoma . The authors studied 62 normal eyes and 45 eyes with NTG and investigated the difference.



Location	Choroidal thickness (μm)		P value
	Normal	NTG	
Temporal	142.6 ± 69.1	129.3 ± 55.9	0.29
Superotemporal	149.6 ± 62.2	131.5 ± 51.1	0.11
Superior	163.0 ± 56.1	143.1 ± 51.5	0.07
Superonasal	169.8 ± 57.5	148.5 ± 53.5	0.06
Nasal	168.5 ± 59.4	146.4 ± 55.1	0.05
Inferonasal	148.2 ± 60.3	125.0 ± 49.3	0.04
Inferior	121.8 ± 55.5	100.8 ± 37.0	0.03
Inferotemporal	127.1 ± 60.7	100.0 ± 42.7	0.01
Average	148.8 ± 53.3	128.1 ± 44.6	0.04

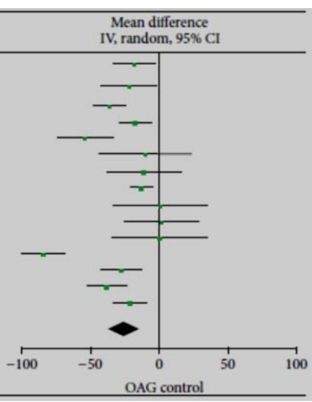
NTG, normal-tension glaucoma.

Hirooka K, Tenkumo K, Fujiwara A, Baba T, Sato S, Shiraga F. Evaluation of peripapillary choroidal thickness in patients with normal-tension glaucoma. BMC Ophthalmol. 2012;12(1):29.

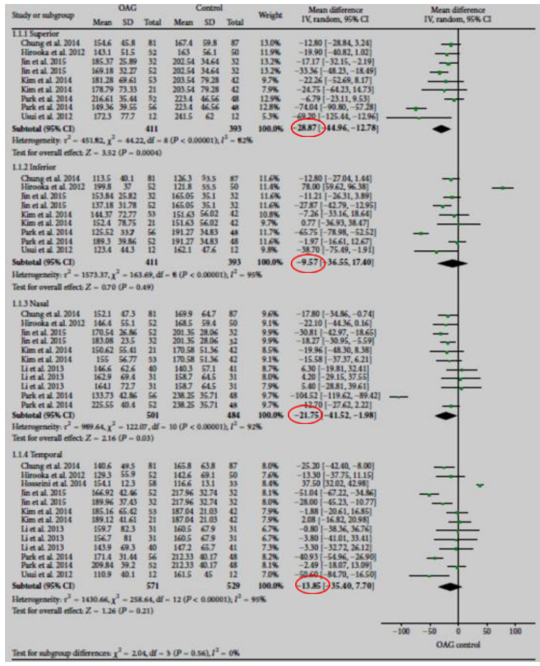
Meta-analysis suggests that OAG patients have significantly decreased PPCT compared to healthy individuals. PPCT measured by OCT may be an important parameter to consider in OAG.

Study or subgroup	OAG Mean	OAG SD	OAG Total	Control Mean	Control SD	Control Total	Weight	Mean difference IV, random, 95% CI
Chung et al. 2014	140.2	41.6	81	157.3	54.7	87	7.3%	−17.10 [−31.74, −2.46]
Hirooka et al. 2012	128.1	44.6	52	148.8	53.3	50	6.6%	−20.70 [−39.81, −1.59]
Jin et al. 2015	144.18	24.11	52	178.32	24.88	32	7.9%	−34.14 [−44.97, −23.31]
Jin et al. 2015	161.68	19.86	32	178.32	24.88	32	7.9%	−16.64 [−27.67, −5.61]
Keer et al. 2015	106.9	50.4	48	157.8	47	54	6.7%	−50.90 [−69.89, −31.91]
Kim et al. 2014	167.37	63.08	21	177.16	55.54	42	4.7%	−9.79 [−41.57, 21.99]
Kim et al. 2014	166.47	71.46	53	177.16	55.54	42	5.6%	−10.69 [−36.23, 14.85]
Lamparter et al. 2015	118.67	36.3	213	130.94	35.83	152	8.3%	−12.27 [−19.77, −4.77]
Li et al. 2013	154.7	68.9	31	154.2	60.9	31	4.6%	0.50 [−31.87, 32.87]
Li et al. 2013	139.6	60.3	40	138.2	56.7	41	5.6%	1.40 [−24.10, 26.90]
Li et al. 2013	154.3	69.7	31	154.2	60.9	31	4.6%	0.10 [−32.48, 32.68]
Park et al. 2014	147.01	35.31	56	226.35	39.52	48	7.4%	−79.34 [−93.85, −64.83]
Park et al. 2014	200.11	32.16	52	226.35	39.52	48	7.4%	−26.24 [−40.43, −12.05]
Roberts et al. 2012	118	48	89	154	40	76	7.5%	−36.00 [−49.43, −22.57]
Zhang et al. 2014	133.99	56.89	216	154.12	44.11	106	7.8%	−20.13 [−31.45, −8.81]
Total (95% CI)			**1067**			**872**	**100.0%**	**−24.07 [−34.29, −13.85]**

Heterogeneity: $\tau^2 = 314.04$, $\chi^2 = 92.49$, df = 14 ($P < 0.00001$); $I^2 = 85\%$
Test for overall effect: $Z = 4.62$ ($P < 0.00001$)



Lin Z, Huang S, Xie B, and Zhong Y. Peripapillary Choroidal Thickness and Open-Angle Glaucoma: A Meta-Analysis. Journal of Ophthalmology Volume 2016, Article ID 5484568



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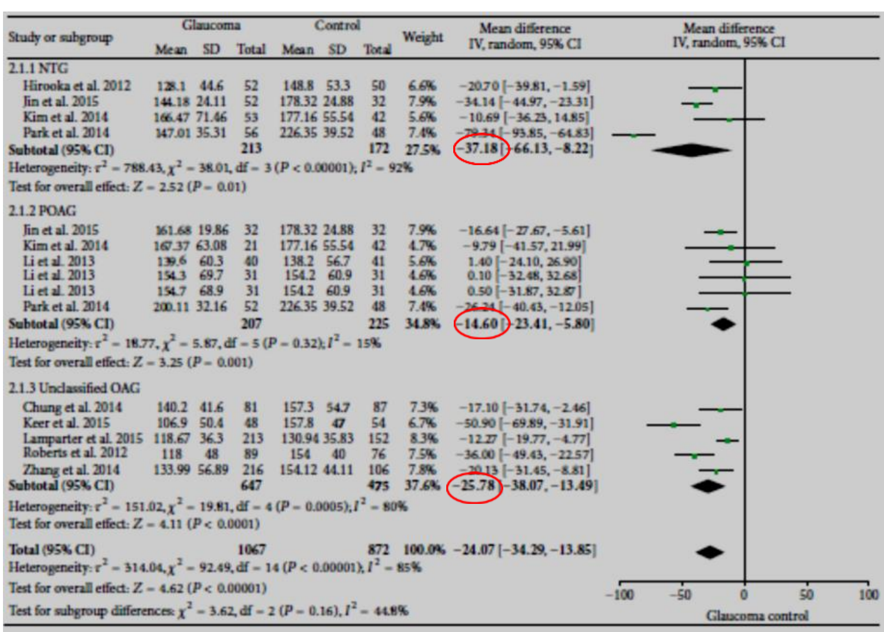

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Thank You