# The impact of intraocular pressure on optical coherence tomography angiography: A review of current evidence

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## Abstract:

A scoping review of 45 peer-reviewed manuscripts involving intraocular pressure (IOP) change and concurrent optical coherence tomography angiography (OCTA) assessments was performed to aggregate knowledge, summarize major findings, and identify gaps in literature and methodology relating to the effect of IOP change on OCTA. Articles were identified through PubMed/Medline, Google Scholar, Cochrane, Web of Science, and article reference lists. A total of 838 results were identified, and 45 articles met the inclusion and exclusion criteria for detailed analysis. OCTA metrics including vessel density (VD), perfusion density, and flow density of the superficial capillary plexus and the radial peripapillary capillaries were analyzed in relation to relative temporal IOP changes. Overall, IOP changes were found to affect superficial vascular plexus (VD) measurements on OCTA, especially when IOP elevated above the physiologic normal range (10-21 mmHg). No significant association was found between diurnal IOP variation and OCTA metrics. Cataract surgery improved the whole-image signal strength and VD regardless of changes in IOP. Beta-blockers were associated with paradoxically reduced vessel density in normal tension glaucoma patients in two studies. Although glaucoma surgical intervention studies were inconsistent and limited by scan quality and low sample sizes, patients requiring glaucoma surgery exhibited attenuated postoperative superficial VD recovery despite significant IOP reductions with surgical intervention. In addition to ensuring near-perfect signal strength with minimal media opacities and controlling for high myopia, central corneal thickness, and the presence of retinopathy, clinicians should consider the statistically significant impact of IOP on OCTA metrics when interpreting results.

**Keywords:**

Angiography, blood flow, intraocular pressure, macula, optical coherence tomography microangiography complex, optical coherence tomography angiography ratio analysis, perfusion density, peripapillary, split-spectrum amplitude-decorrelation angiography, vessel density

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## Introduction

Split-spectrum amplitude-decorrelation angiography for optical coherence tomography was first introduced in 2012, which paved the way for commercialization of noninvasive axial and enface ocular angiography.[1] This technology allowed for optical tracking of red blood cells to determine angiographic flow. The first commercially available optical coherence tomography angiography (OCTA) was introduced outside of the United States in 2014.[2] Since that time, technology has improved dramatically allowing for faster scans and higher resolution imaging, with multiple versions available from multiple manufacturers. OCTA is currently utilized as a diagnostic tool for retinal disease and glaucoma and as a noninvasive alternative to fluorescein angiography, but further research and development may present new clinically significant applications. A major difference between OCTA and fluorescein angiography is the capillary quantifiability of OCTA data. However, the quantification of OCTA data may be limited by factors such as intraocular pressure (IOP) variability between scans. Herein and to the best of our knowledge, we present the first comprehensive review of current evidence relating to the effect of IOP on OCTA metrics to aggregate information and guide future studies.



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## Methods

The study was approved by our University Institutional Review Board. The research adhered to the tenets of the Declaration of Helsinki, and the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines were followed for this scoping review [Figure 1]. A comprehensive literature search for indexing terms and keywords was conducted from January 1, 2015 to August 27, 2022 using PubMed/MEDLINE, Web of Science, Cochrane, and Google Scholar databases. Search criteria for Google Scholar included "glaucoma" ("pressure change" OR "pressure elevation" OR "pressure normalization" OR "pressure restoration" OR "pressure spike" OR "IOP change" OR "IOP elevation" OR "IOP normalization") AND "optical coherence tomography angiography". Search criteria for PubMed/MEDLINE included ("optical coherence tomography angiography") AND (glaucoma) AND (ocular pressure). Search criteria for Web of Science included ((ALL= ("optical coherence tomography angiography")) AND ALL= (glaucoma)) AND ALL= (intraocular pressure). No reviews were identified by Cochrane when searching for optical coherence tomography angiography or OCTA. The search yielded a total of 838 articles including duplicates (572, 107, 0, and 159 articles from Google Scholar, PubMed/MEDLINE, Cochrane, and Web of Science, respectively) [Figure 1]. Two reviewers independently screened articles across the four databases.

The inclusion criteria required OCTA scans of either the optic disc or macula and a change in IOP with corresponding OCTA scans before and after the IOP change. All languages were included and translated appropriately. Studies involving animals or known retinal disease were excluded. After the removal of duplicates and exclusions, a total of 45 articles were included in the review. Statistical analysis was deferred due to data collection and reporting inconsistencies.

## Results

Forty-five manuscripts met the inclusion and exclusion criteria and were divided into six groups[3-47] based on the primary intervention category [Table 1]. Thirteen studies involved IOP reduction and glaucoma surgery.[25-37] Nine studies involved

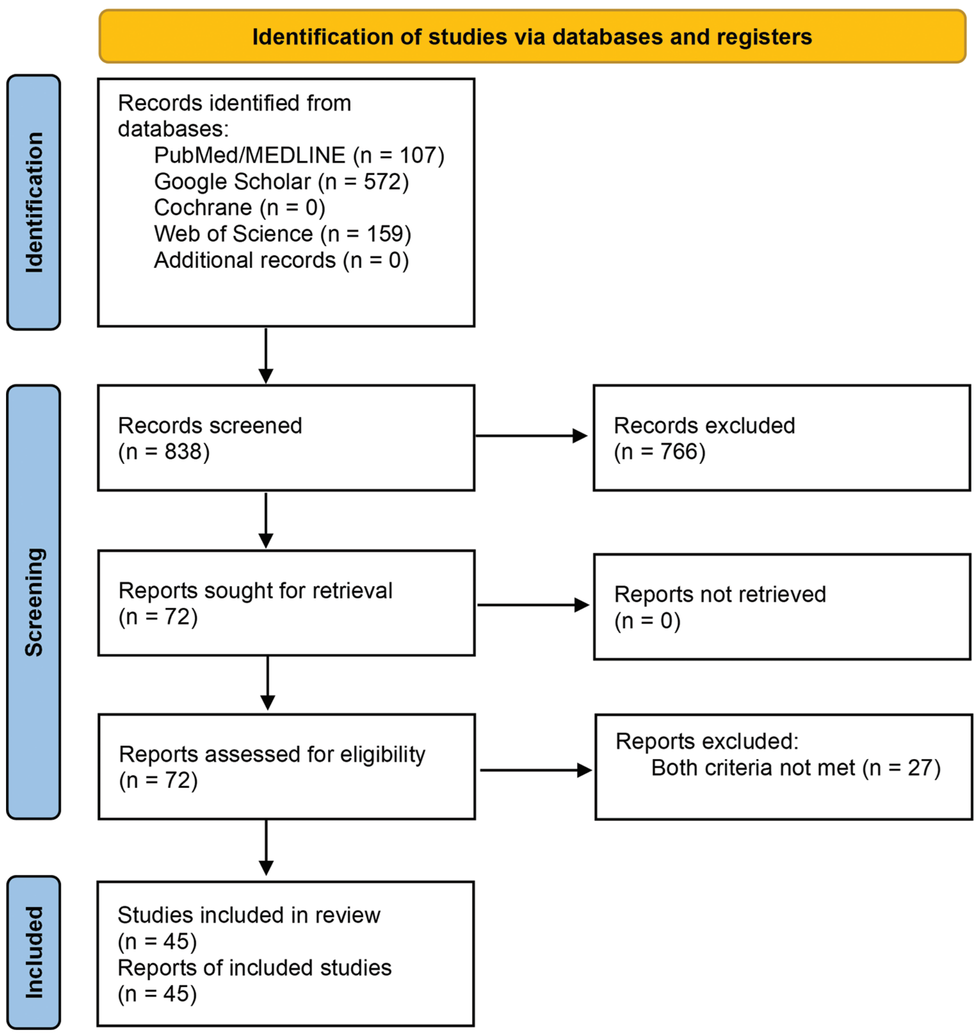


**Figure 1:** The Preferred Reporting Items for Systematic Reviews and Meta-analyses Flow Diagram of the Systematic Review. Diagram illustrating the procedure that led to the inclusion of 45 studies

IOP reduction and specific ophthalmic drops.[12-20] Nine studies examined the impact of diurnal IOP variability on OCTA.[3-11] Four involved IOP changes related to glaucoma lasers[21-24] and three studies examined the effect of cataract surgery on IOP and OCTA.[38-40] Another seven studies investigated distinct topics that could not be grouped meaningfully.[41-47]

Data collected included primary intervention, sample size (number of eyes), author-reported statistical significance of the IOP change and vessel density (VD) measurements with $P < 0.05$, temporal relationships between measurements, OCTA device maker, scan dimensions (millimeters), and reporting of signal strength (SS) cutoffs values [Table 2].

### Optical coherence tomography angiography equipment

OCTA machine choice was notably variable between studies [Table 1]. This review included 37 reports using Optovue machines, four reports using Zeiss machines, and four using Topcon machines. All of the Optovue machines and the commercial-use Zeiss machines utilized spectral domain OCTA (SD-OCTA), which has been shown to produce excellent image quality of superficial retinal vasculature.[2] The Topcon machines and the research-use Zeiss machines all utilized Swept-Source OCTA (SS-OCTA), which has been shown to have superior image quality of the deep retinal vasculature and choriocapillaris because of attenuation of projection artifact.[2] Between machines and reports, common proprietary metrics of image quality included SS, signal strength index (SSI), and signal quality index.[2] SSI was most commonly reported with theoretical values between 0 and 100 and SS was the second most commonly reported with reported values between 0 and 10; however, these quality metrics were not interchangeable and were reviewed independently.

### Diurnal impact

Diurnal variability did not alter superficial retinal capillary measurements of the disc or the macula in any studies reviewed.[3-11] Glaucomatous eyes were more likely to have greater IOP variability than normal eyes, but no diurnal association with OCTA was identified.[10] Another study concluded that although diurnal variability minimally influenced OCTA, SSI was found to greatly impact results.[6] It is possible that these studies were influenced by additional uncontrolled factors; however, the current data support an autoregulatory ability of the superficial vascular plexus in individuals with physiologically normal IOP (10–21 mmHg) that limit significant changes of VD.[3-11]

### Glaucoma surgical interventions

The glaucoma surgery group included incisional surgeries. Eight of the 13 studies analyzed trabeculectomy alone,[26-29,31,32,34,36] and the remaining five studies involved various procedure combinations.[25,30,33,35,37] All studies reported a statistically significant change in IOP with study durations ranging from 1 month to 1 year. Twelve of the papers reported OCTA of the peripapillary region[25-34,36,37] and nine reported OCTA of the macula.[25,26,28,31-33,35-37] SSI was the most common metric of image quality due to OCTA device selection; however, cutoff values were variable ranging from 40 to 50. The papers that utilized Topcon machines reported image quality of 30 or greater, and the one Zeiss study reported a SS cutoff of 8/10 or greater. In addition to many potentially low cutoff values seen in the majority of studies, six of the 13 studies reported sample sizes of 25 eyes or less. The study performed on the Zeiss machine, included 108 eyes and concluded improved foveal avascular zone reduction and microvasculature with glaucoma surgery, but only utilized a 3 × 3 macular scan. Statistically significant increases in superficial VD were seen in five studies of the disc[27,28,30,32,34] and one study of the macula.[35] Although poor scan quality and small sample sizes likely limited results due to loss of image resolution and limited statistical power respectively, patients who require glaucoma surgery may demonstrate a blunted superficial VD improvement compared to earlier stages of glaucoma. Future studies with larger sample sizes, higher image quality, and improved control of preoperative and postoperative image quality metrics are warranted.

### Topical eye drops

Studies involving eye drops for the treatment of glaucoma or ocular hypertension were frequently limited by small sample sizes, but the data suggest potential future considerations. Although beta blocker drops were shown to increase superficial peripapillary VD (ppVD) in new primary open-angle glaucoma patients,[20] two reports suggested that beta blocker drop use may be associated with attenuated superficial VD in normal tension glaucoma patients.[16,17] Although not entirely conclusive, this supports the findings of the Low-Pressure Glaucoma Treatment Study that favored brimonidine over timolol in normal tension glaucoma patients.[48] One report studied the effects of latanoprostene over 4 weeks and found that superficial macular VD improved greater than ppVD when compared to timolol.[14] Another study comparing brimonidine to ripasudil only found a statistically significant effect of increased ppVD in the ripasudil group which may indicate a direct vascular effect.[13]

### Cataract surgery

Cataract surgery improved image quality in all three studies and significantly improved VD metrics throughout the retina despite limited and conflicting associations with IOP.[38-40] Although it could appear that cataract surgery improves vascularity, via increased VD, the apparent improvement in image quality suggests a direct result of improved translucency of the implanted IOL. In addition, all three papers employed sample sizes of 24 eyes which likely limited the assessment of statistical significance. It is known that VD accuracy depends on the highest quality of data to ensure that fine capillaries are not missed.[2] One report suggests that a SS of 9 or 10 out of 10 is acceptable for Zeiss machines; however, reports appear to be limited and warrant more attention.[49]

### Lasers and pathologic intraocular pressure changes

One robust study of 97 eyes found an average acute IOP increase of 6.5–14.3 mmHg after laser peripheral iridotomy to be associated with statistically significant reductions of superficial

**Table 1: Intraocular pressure and optical coherence tomography angiography study key demographic information**

| Publication | Intervention classification | Test interval | Pathology group sample size (eyes) | Total eyes | Quality metric | Quality reported | Device | Scan |
|---|---|---|---|---|---|---|---|---|
| Baek *et al*.,2019[3] | Diurnal | 3 h | 20 POAG, 19 healthy | 39 | "Signal Strength" | 45 or greater | Topcon | SS-OCT |
| Bochicchio *et al*., 2019[4] | Diurnal | 11 h | 46 glaucoma, 53 OHT, 62 healthy | 161 | Scan quality | >7 | Optovue | SD-OCT |
| Demirtaş *et al*., 2021[5] | Diurnal | 3 h | 34 POAG, 36 EXG, 35 healthy | 105 | SSI | 46 or greater | Optovue | SD-OCT |
| Mansouri *et al*., 2018[6] | Diurnal | 3 h | 74 OAG | 74 | SSI | 46 or greater | Optovue | SD-OCT |
| Milani *et al*., 2020[7] | Diurnal | 11 h | 40 OAG, 52 OHT, 73 healthy | 165 | Scan quality | >7 | Optovue | SD-OCT |
| Muller *et al*., 2019[8] | Diurnal | 4 h | 40 POAG | 40 | SSI | 47 or greater | Optovue | SD-OCT |
| Verticchio Vercellin *et al*., 2020[9] | Diurnal | 3 h | 32 OAG, 10 OHT, 25 healthy | 67 | SSI | >50 | Optovue | SD-OCT |
| Wang *et al*., 2020[10] | Diurnal | 2 h | 22 POAG, 15 healthy | 37 | SSI | 45 or greater | Optovue | SD-OCT |
| Wu *et al*., 2021[11] | Diurnal | 4 h | 29 healthy | 29 | Quality index | 4 of greater | Optovue | SD-OCT |
| Chen *et al*., 2021[12] | Drops | 4 weeks | 15 POAG, 3 OHT, 8 CACG | 34 | Scan quality | 6 or greater | Optovue | SD-OCT |
| Chihara *et al*., 2018[13] | Drops | 1–2 months (variable) | 36 POAG, 11 OHT | 47 | "Signal Strength" | 40 or greater | Optovue | SD-OCT |
| El-Nimri *et al*., 2022[14] | Drops | 4 weeks | 14 glaucoma, 10 OHT, 26 healthy | 50 | Scan quality and SSI | 4 or greater and 48 or greater | Optovue | SD-OCT |
| Kurysheva 2019[15] | Drops | 1 week | 36 POAG | 36 | SSI | >50 | Optovue | SD-OCT |
| Lin *et al*., 2021[16] | Drops | 6 months | 80 NTG | 80 | SSI | 40 or greater | Optovue | SD-OCT |
| Lin, Su *et al*., 2021[17] | Drops | 6 months (multiple) | 131 NTG | 131 | SSI | 40 or greater | Optovue | SD-OCT |
| Liu *et al*., 2021[18] | Drops | 3 weeks | 26 POAG, OHT, or CACG | 26 | "Signal Strength" | 40 or greater | Optovue | SD-OCT |
| Liu *et al*., 2022[19] | Drops | 1 week | 21 PSS | 21 | "SSI" | 8 or greater | Zeiss | SD-OCT |
| Nutterova *et al*., 2022[20] | Drops | 3 months | 98 glaucoma | 98 | ? | ? | Optovue | SD-OCT |
| Gillmann *et al*., 2022[21] | Laser | 6 months (multiple) | 37 POAG | 37 | SSI | 49.9 or greater | Optovue | SD-OCT |
| Ma *et al*., 2019[22] | Laser | 1 h | 58 CACG | 58 | SSI | >50 | Optovue | SD-OCT |
| Ma *et al*., 2020[23] | Laser | 1 h | 70 CACG | 70 | SSI | >55 | Optovue | SD-OCT |
| Wang *et al*., 2020[24] | Laser | 1 h | 97 CACG | 97 | SSI | >50 | Optovue | SD-OCT |
| Ch'ng *et al*., 2020[25] | Glaucoma surgery | 1 year (multiple) | 80 OAG | 80 | SSI | 47 or greater | Optovue | SD-OCT |
| Güngör *et al*., 2022[26] | Glaucoma surgery | 1 month (multiple) | 12 POAG, 8 EXG | 20 | "Signal Strength" | >6 | Optovue | SD-OCT |
| In *et al*., 2018[27] | Glaucoma surgery | 3 months | 25 POAG | 25 | SSI | 48 or greater | Optovue | SD-OCT |
| Kang *et al*., 2021[28] | Glaucoma surgery | 6 months | 20 glaucoma | 20 | ? | ? | Topcon | SS-OCT |
| Kim *et al*., 2018[29] | Glaucoma surgery | 3 months | 56 POAG | 56 | "Image Quality Score" | 30 or higher | Topcon | SS-OCT |
| Liu *et al*., 2021[30] | Glaucoma surgery | 6 months | 17 POAG | 17 | SSI | 50 or greater | Optovue | SD-OCT |
| Lommatzsch *et al*., 2019[31] | Glaucoma surgery | 6 months | 12 POAG, 7 EXG | 19 | SSI | >40 | Optovue | SD-OCT |
| Miraftabi *et al*., 2021[32] | Glaucoma surgery | 6 months (multiple) | 32 glaucoma | 32 | SSI | 40 or greater | Optovue | SD-OCT |
| Park *et al*., 2021[33] | Glaucoma surgery | Multiple | 88 POAG | 88 | "Quality Score" | >30 | Topcon | SS-OCT |
| Shin *et al*., 2017[34] | Glaucoma surgery | 3 months (multiple) | 31 POAG | 31 | SSI | 40 or greater | Optovue | SD-OCT |
| Shoji *et al*., 2022[35] | Glaucoma surgery | 3 months | 108 POAG | 108 | Signal strength | 8 or greater | Zeiss | SS-OCT |
| Yoon *et al*., 2021[36] | Glaucoma surgery | 1 year (multiple) | 65 POAG | 65 | SSI | 48 or greater | Optovue | SD-OCT |
| Zéboulon *et al*., 2017[37] | Glaucoma surgery | 1 month | 21 OAG | 21 | SSI | 40 or greater | Optovue | SD-OCT |
| Alnawaiseh *et al*., 2018[38] | Cataract surgery | Multiple | 48 OAG+cataract | 48 | SSI | ? | Optovue | SD-OCT |
| Karabulut *et al*., 2019[39] | Cataract surgery | 4 weeks (multiple) | 24 cataract | 24 | SSI | 60 or greater | Optovue | SD-OCT |
| Sung *et al*., 2020[40] | Cataract surgery | 6 months | 24 cataract | 24 | "Scan Quality Index" | 4 or greater | Optovue | SD-OCT |
| Dada *et al*., 2022[41] | Other | 6 weeks | 60 OHT | 60 | ? | ? | Optovue | SD-OCT |
| Gameiro *et al*., 2022[42] | Other | 1 h (multiple) | 20 healthy | 20 | ? | ? | Zeiss | SD-OCT |
| Guo *et al*., 2022[43] | Other | Unspecified (multiple) | 34 PSS | 34 | Signal strength | 7 or greater | Zeiss | SD-OCT |
| Holló 2017[44] | Other | 2–4 weeks | 4 OAG, 2 OHT | 6 | SSI | >50 | Optovue | SD-OCT |
| Ashraf Khorasani *et al*., 2022[45] | Other | Unspecified | 12 healthy | 12 | "scan quality" | 7 or greater | Optovue | SD-OCT |
| Zhang *et al*., 2018[46] | Other | 2 h | 40 healthy | 40 | SSI | 50 or greater | Optovue | SD-OCT |
| Zhang *et al*., 2020[47] | Other | 1 month (multiple) | 45 healthy | 45 | "Scan Quality" | 7 or greater | Optovue | SD-OCT |

Demographic information and OCT equipment information were provided for 45 studies included in the review. POAG: Primary open-angle glaucoma, OHT: Ocular hypertension, EXG: Exfoliative glaucoma, OAG: Open-angle glaucoma, NTG: Normal-tension glaucoma, PSS: Posner-Schlossman Syndrome, CACG: Chronic angle-closure glaucoma, SSI: Signal strength index, OCT: Optical coherence tomography, SS-OCT: Swept-source OCT, SD-OCT: Spectral-domain OCT, ?: unknown data

**Table 2: Intraocular pressure and optical coherence tomography angiography study methodologies and findings**

| Publication | Intervention | IOP change | Macula scan dimensions (mm) | Superficial macular VD change | Other comments | Disc scan dimensions (mm) | RPC or ppVD change | Other comments |
|---|---|---|---|---|---|---|---|---|
| Baek *et al*., 2019[3] | Diurnal: 800, 1100, 1400, 1700, 2000 | No | 4.5×4.5 | No | None | 4.5×4.5 | No | None |
| Bochicchio *et al*., 2019[4] | Diurnal: 800, 1900 | No | N/A | | | 4.5×4.5 | No | None |
| Demirtaş *et al*., 2021[5] | Diurnal: 900, 1100, 1400, 1600 | No | 6×6 | No | None | 4.5×4.5 | No | None |
| Mansouri *et al*., 2018[6] | Diurnal: 800, 1100, 1400, 1600 | No | 6×6 | No | None | 4.5×4.5 | No | None |
| Milani *et al*., 2020[7] | Diurnal: 800, 1900 | No | 3×3 | No | None | N/A | | |
| Muller *et al*., 2019[8] | Diurnal: ~800, ~1100, ~1500, ~2000 | No | 3×3 | No | None | 4.5×4.5 | No | None |
| Verticchio Vercellin *et al*., 2020[10] | Diurnal: 900, 1100, 1400, 1600, 1800 | No | N/A | | | 4.5×4.5 | No | None |
| Wang *et al*., 2020[11] | Diurnal: 800, 1000, 1200, 1400, 1600, 1800, 2000 | No | 3×3 | No | None | N/A | | |
| Wu *et al*., 2021[12] | Diurnal: 800, 1200, 1600, 2000 | No | 3×3 | No | None | 4.5×4.5 | No | None |
| Chen *et al*., 2021[13] | Latanoprost | Yes | 3×3 | No | None | 4.5×4.5 | Yes | ppVD |
| Chihara *et al*., 2018[14] | Ripasudil versus brimonidine | Yes | N/A | | | 4.5×4.5 | Yes (ripasudil only) | ppVD/SS |
| El-Nimri *et al*., 2022[15] | Latanoprostene versus timolol | Yes | 6×6 | Yes (latanoprostene only) | Whole image and segments | 4.5×4.5 | No | Macula>ppVD |
| Kurysheva 2019[16] | Tafluprost versus timolol/tafluprost | Yes | 6×6 | No | None | 4.5×4.5 | No | Only VD inside disc |
| Lin *et al*., 2021[17] | Carteolol | No | 3×3 | Unspecified | None | 4.5×4.5 | Unspecified | Possibly inverse with carteolol |
| Lin, Su *et al*., 2021[18] | Carteolol versus brimonidine versus dorzolamide | Yes | 3×3 | No | None | Unspecified | Yes (dorzolamide) | Superior ppVD, inverse with carteolol |
| Liu *et al*., 2021[19] | Latanoprost | Yes | 4.5×4.5 | No | None | 4.5×4.5 | No | None |
| Liu *et al*., 2022[20] | Prednisolone, timolol, brimonidine | Yes | 6×6 | No | VLD, VPD | 4.5×4.5 | No | Assessed CP |
| Nutterova *et al*., 2022[21] | Carteolol versus latanoprost | Yes | N/A | | | Unspecified | Yes | ppVD |
| Gillmann *et al*., 2022[22] | SLT | Yes | 6×6 | Yes/no | Increase at 2 months only | 4.5×4.5 | Yes/no | Increases at 2 months only |
| Ma *et al*., 2019[23] | LPI | Yes | 6×6 | Yes | None | 4.5×4.5 | Yes | All |
| Ma *et al*., 2020[24] | LPI | Yes | 6×6 | Yes | None | N/A | | |
| Wang *et al*., 2020[25] | LPI | Yes | N/A | | | 4.5×4.5 | Yes | RPC and whole image |
| Ch'ng *et al*., 2020[26] | Glaucoma surgery | Yes | 3×3 and 6×6 | No | None | 4.5×4.5 | No | None |
| Güngör *et al*., 2022[27] | Trabeculectomy | Yes | 6×6 | No | Only deep circulation | 4.5×4.5 | No | None |
| In *et al*., 2018[28] | Trabeculectomy | Yes | N/A | | | 4.5×4.5 | Yes | Whole image, ppVD |
| Kang *et al*., 2021[29] | Trabeculectomy | Yes | 6×6 | Unspecified | Unspecified | 6×6 | Yes | Peripapillary |
| Kim *et al*., 2018[30] | Trabeculectomy | Yes | N/A | | | 4.5×4.5 | No | VD in disc increased |
| Liu *et al*., 2021[31] | Trabeculectomy, canaloplasty | Yes | N/A | | | 4.0×4.0 crop | Yes | ppVD |
| Lommatzsch *et al*., 2019[32] | Trabeculectomy + MMC | Yes | 6×6 | No | None | 4.5×4.5 | No | None |
| Miraftabi *et al*., 2021[33] | Trabeculectomy | Yes | 6×6 | N | None | 4.5×4.5 | Yes | Whole image and ppVD |
| Park *et al*., 2021[34] | Trabeculectomy, ExPRESS, Ahmed | Yes | 4.5×4.5 | N | FAZ smaller at 1 month | 4.5×4.5 | No | Intradisc increase at 1 month |
| Shin *et al*., 2017[35] | Trabeculectomy | Yes | N/A | | | 4.5×4.5 | Yes | Microvasculature whole image |

*Contd...*

**Table 2: Contd...**

| Publication | Intervention | IOP change | Macula scan dimensions (mm) | Superficial macular VD change | Other comments | Disc scan dimensions (mm) | RPC or ppVD change | Other comments |
|---|---|---|---|---|---|---|---|---|
| Shoji *et al*., 2022[36] | Glaucoma surgery | Yes | 3×3 | Yes | FAZ decrease | N/A | | |
| Yoon *et al*., 2021[37] | Trabeculectomy | Yes | 6×6 | Unspecified | None | 4.5×4.5 | Unspecified | None |
| Zéboulon *et al*., 2017[38] | Filtering surgeries | Yes | 3×3 | No | None | 3×3 | No | None |
| Alnawaiseh *et al*., 2018[39] | CEIOL+iStent | Yes | 3×3 | Yes | All metrics | 4.5×4.5 | Yes | All metrics |
| Karabulut *et al*., 2019[40] | CEIOL | Yes | N/A | | | 4.5×4.5 | Yes | All metrics |
| Sung *et al*., 2020[41] | CEIOL | No | 6×6 | Yes | All metrics | 4.5×4.5 | No | None |
| Dada *et al*., 2022[42] | Mindfulness | Yes | N/A | | | 6×6 | Yes | Superficial and whole image |
| Gameiro *et al*., 2022[43] | Water drinking test | Yes | 3×3 | No | Deep vessels VD increased | N/A | | |
| Guo *et al*., 2022[44] | PSS attack | Yes | 6×6 | Yes | Whole image | N/A | | |
| Holló 2017[45] | Medical reduction case series of 6 patients | Yes | N/A | | | 4.5×4.5 | Yes | ppVD |
| Ashraf Khorasani *et al*., 2022[46] | Suction cup to eye | Yes | 3×3 | Yes | Whole image and segments | 4.5×4.5 | No | Only intradisc |
| Zhang *et al*., 2018[47] | Dark room prone provocation test | Yes | 3×3 | No | None | 4.5×4.5 | No | None |
| Zhang *et al*., 2020 | LASIK | Uncertain | 6×6 | No | None | 4.5×4.5 | No | None |

CP: Capillary perfusion, IOP: Intraocular pressure, ppVD: Peripapillary VD, RPC: Radial peripapillary capillaries, SS: Signal strength, VLD: Vascular length density, VD: Vessel density, VPD: Vessel perfusion density, LASIK: Laser *in situ* keratomileusis, PSS: Posner-Schlossman Syndrome, NA: Not available, SLT: selective laser trabeculoplasty, LPI: laser peripheral iridotomy, MMC: Mitomycin C, CEIOL: cataract extraction with intraocular lens implantation

ppVD in patients with narrow angles.[24] This relationship was also observed to be dose-dependent between the IOP stratified groups, with greater increases in IOP being inversely correlated with superficial VD. This suggests that elevated IOP can affect superficial VD of the disc when the is pressure elevated above physiologic normal range (10–21 mmHg) and continues to have and increasing effect with increased pressure. Another study of 60 eyes with elevated baseline IOP and ocular hypertension found IOP reductions of only 4–5 mmHg to statistically significantly increase disc VD measurements with 6 weeks of mindfulness.[41] These two study results suggest that there is a threshold value of IOP that must be reached to overcome vascular autoregulation and impact superficial VD. Only one study evaluated selective laser trabeculoplasty, which observed reduced IOP and increased superficial VD at 2 months with a return to baseline superficial VD at 6 months.[21]

## Discussion

### Background and rationale

Despite significant advances in technology and research over the last decade, questions remain regarding the limitations and full implications of OCTA.[2] One variable that has yet to be fully understood is the impact of IOP fluctuation on OCTA outputs and the clinical relevance of the effects.

Retinal blood supply is derived from the central retinal artery that perfuses the inner two-thirds of the retina and the short posterior ciliary arteries that perfuse the outer one-third of the retina and retinal pigment epithelium.[50] Through the capabilities of OCTA imaging, the inner retinal vasculature and capillaries have been further divided into the superficial capillary plexus (SCP) that primarily perfuses the ganglion cells and retinal nerve fiber layer (RNFL) as well as the deep capillary plexus (DCP) made up of intermediate and deep capillary layers that straddle the inner nuclear layer.[51] As the SCP of the macular retina approaches the optic disc, the superficial capillaries travel in parallel with the RNFL which is referred to as the radial peripapillary capillaries (RPC).[51]

The SCP and the RPC have been targets of glaucoma and IOP research because of their close associations with the ganglion cell layer and the RNFL respectively, their superficial localization that is less affected by OCTA projection artifacts, and their presumed responsiveness to aberrant IOP fluctuation.[37,52] Conversely, studies focusing on the DCP and choriocapillaris, which may offer significant utility in the future, were uncommon and inconsistent.[52] For these reasons, a targeted analysis of the superficial retinal capillaries of the macula and the disc were the focus of this review.

### Limitations

This review was limited by gaps in literature and inconsistencies in data collection and reporting between studies, variability of imaging strategies, and small sample sizes. Although papers generally scanned 6 mm × 6 mm scans of the macula and 4.5 mm × 4.5 mm scans of the optic disc, scan sizes varied and only 58% of studies reported scans of both locations. In addition, OCTA metrics varied between machines and different papers reported different metrics, which prevented quantitative analysis. Image SS and quality were found to be significant in multiple papers;[37,43] however, SS cutoff values varied widely, and mean SS was irregularly reported. Given the importance of detecting small capillaries for accurate VD measurements, it is important to determine the true ideal cutoff value of SS to ensure correct evaluations, and it is imperative that scans with opacity-related shadowing defects are removed. It is likely that studies were limited by small sample sizes and may have demonstrated statistical significance with improved statistical power.

## Conclusion

IOP changes can affect superficial vascular plexus VD measurements on OCTA especially when IOP elevates above physiologic normal. Diurnal variation does not appear to significantly impact OCTA metrics in normal or glaucomatous populations. Cataract surgery for narrow angles and angle closure primarily improves OCTA indices via improved image quality secondary to improved SS. This study highlights the importance of standardization of image acquisition and reporting of OCTA data to enable data aggregation. In addition to ensuring near-perfect SS with minimal media opacities and controlling for high myopia, central corneal thickness, and the presence of retinopathy, clinicians must consider the statistically significant impact of IOP on OCTA metrics when interpreting results.

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### Conflicts of interest

There are no conflicts of interest.

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