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Review Article

Emerging Role of optical coherence tomography in the Diagnosis of diabetic retinopathy

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Abstract

Background: Diabetic retinopathy remains a leading cause of preventable vision loss, and optical coherence tomography (OCT) has become central to detecting its structural and vascular changes earlier and more objectively than clinical examination alone [2,3].

Objective: This review synthesizes the published evidence on structural OCT and OCT angiography (OCTA) in the diagnosis, staging, and monitoring of diabetic retinopathy and diabetic macular edema.

Methods: We synthesized landmark OCT validation studies, randomized treatment trials using OCT-based endpoints, quantitative OCTA cohort studies, and papers on automated and deep-learning-assisted OCT/OCTA interpretation.

Findings: Structural OCT reliably detects and quantifies diabetic macular edema and underpins the primary endpoints of major treatment trials [6,8,9], while OCTA reveals microvascular non-perfusion and foveal avascular zone changes that precede clinically apparent retinopathy and predict disease progression [23,25]; deep-learning systems applied to OCT and OCTA are increasingly able to detect referable disease at accuracy approaching human graders [28,32].

Conclusions: OCT and OCTA have moved from adjunct imaging tools toward central components of diabetic retinopathy diagnosis and screening, though cross-device standardization and prospective outcome validation remain needed before algorithm-assisted interpretation sees uniform clinical adoption [13,30].

Keywords: optical coherence tomography; OCT angiography; diabetic retinopathy; diabetic macular edema; deep learning

1. Introduction

Diabetic retinopathy remains the leading cause of preventable vision loss among working-age adults worldwide, and its burden continues to climb with the global prevalence of diabetes. Population surveys estimate that roughly one in three people with diabetes carries some degree of retinopathy, with vision-threatening disease affecting a substantial minority [1]. Wong and colleagues emphasized that microvascular injury begins years before it is detectable by ophthalmoscopy, placing a premium on imaging that resolves structural change earlier and more objectively than fundus examination [2]. Cheung and colleagues reached a similar conclusion, noting that screening built solely on fundus photography and clinical grading, however well standardized by frameworks such as the Early Treatment Diabetic Retinopathy Study severity scale, still misses subtle change that precedes overt lesions [3,4].

Optical coherence tomography, first described by Huang and colleagues as a technique for cross-sectional imaging of biological tissue using low-coherence interferometry, has become the single most transformative diagnostic tool in retinal medicine since its introduction [5]. Unlike fundus photography, which records a projection of the retinal surface, OCT resolves the retina's layers in cross-section at micrometer resolution, and its angiographic extension, OCT angiography (OCTA), visualizes retinal and choroidal blood flow without injected dye. Together these capabilities have reshaped how clinicians detect, stage, and monitor diabetic retinopathy and its principal complication, diabetic macular edema. This review synthesizes the evidence on structural OCT and OCTA in diagnosing diabetic retinopathy, covering their performance against clinical examination and fluorescein angiography, their role in staging and edema detection, and the growing literature on automated, AI-assisted interpretation.

2. Methods

We conducted a narrative synthesis of the peer-reviewed literature on OCT and OCTA in diabetic retinopathy and macular edema, drawing on landmark validation studies, randomized trials with OCT-based endpoints, multicenter OCTA cohorts, systematic reviews, and automated/deep-learning interpretation papers, prioritizing direct clinical relevance to diagnosis, staging, and monitoring. No formal risk-of-bias scoring or meta-analytic pooling was performed, consistent with the narrative-review format.

3. Structural OCT and the detection of diabetic macular edema

The earliest and still most direct clinical application of OCT in diabetic eye disease is objective detection and quantification of macular thickening. Hee and colleagues, applying time-domain OCT to eyes with diabetic macular edema, described patterns of retinal thickening, cystoid change, and subretinal fluid correlating with visual acuity more tightly than biomicroscopy alone, establishing OCT-measured thickness as a quantitative surrogate for edema severity, and characterizing diffuse thickening, cystoid change, and serous detachment as morphologically distinct patterns still useful for anticipating treatment response [6].

Browning and colleagues directly compared clinical biomicroscopic diagnosis of macular edema with OCT-based diagnosis in the same eyes and found meaningful discordance: slit-lamp examination both missed edema that OCT detected and, less often, flagged edema OCT did not confirm, and in a related analysis found that OCT macular thickness correlated with overall retinopathy severity even without clinically apparent edema (Table 1) [7]. The Diabetic Retinopathy Clinical Research Network incorporated OCT central subfield thickness as a primary endpoint in its randomized comparison of triamcinolone against laser, cementing OCT thickness as the standard quantitative outcome for edema trials [8]. That precedent shaped later anti-VEGF

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trials: RISE and RIDE reported OCT thickness reduction alongside acuity gain [9], Protocol I used OCT thickness to define retreatment criteria [10], and Protocol T reported two-year OCT outcomes across aflibercept, bevacizumab, and ranibizumab [11].

Table 1: Selected studies comparing OCT-based and clinical detection of diabetic macular edema, and OCT-based endpoints in major diabetic macular edema treatment trials [7,8,9,10,11].

Study	Comparison	Design	Key finding
[7]	Clinical biomicroscopy vs OCT	Cross-sectional	Clinical exam both misses and over-diagnoses edema relative to OCT
[8]	Triamcinolone vs focal/grid laser	Randomized trial	OCT central subfield thickness used as primary structural endpoint
[9]	Ranibizumab vs sham (RISE/RIDE)	Randomized trial	OCT thickness reduction accompanies visual acuity gain
[10]	Ranibizumab + laser vs triamcinolone + laser	Randomized trial (Protocol I)	OCT thickness defines retreatment criteria
[11]	Aflibercept vs bevacizumab vs ranibizumab	Randomized trial (Protocol T)	Two-year OCT thickness outcomes stratified by baseline acuity

Structural OCT is not without technical caveats. Sadda and colleagues catalogued systematic segmentation errors in automated thickness measurement, particularly in eyes with severe edema or epiretinal traction, where boundary-detection algorithms could misplace the retinal boundary and produce a spuriously high or low value [12]. A 2015 Cochrane review by Virgili and colleagues, pooling diagnostic accuracy studies of OCT against clinical examination, concluded that OCT has good but imperfect sensitivity and specificity relative to biomicroscopy, and recommended it as an adjunct rather than a wholesale replacement for clinical examination [13].

4. Diabetic retinopathy staging and disease classification

Diabetic retinopathy severity is traditionally graded using the modified Airlie House classification formalized in the Early Treatment Diabetic Retinopathy Study, later simplified into an international clinical severity scale for everyday use [4]. Both schemes rely on identifying microaneurysms, hemorrhages, venous beading, and intraretinal microvascular abnormalities on fundus photographs. OCT does not replace this lesion-based staging but increasingly supplements it, providing quantitative correlates of severity, macular thickness and, with OCTA, capillary non-perfusion and foveal avascular zone measures that track with stage even without macular edema.

Gross and colleagues, in a randomized comparison of panretinal photocoagulation against intravitreal ranibizumab for proliferative retinopathy, used OCT central subfield thickness alongside visual acuity as a structural outcome, illustrating how structural OCT is embedded even in trials targeting neovascularization rather than an OCT-defined lesion [14].

5. Optical coherence tomography angiography: principles and early validation

OCT angiography extracts motion contrast from sequential B-scans to reconstruct depth-resolved maps of retinal and choroidal blood flow without dye injection. Spaide and colleagues, in an influential review, catalogued the artifacts, motion, projection, and segmentation errors that clinicians must recognize when interpreting OCTA images, a caution echoed throughout the subsequent literature and closely tied to the need for standardized acquisition and quantification protocols across commercial platforms [15,16].

Applying OCTA to diabetic retinopathy for the first time, early prospective pilot studies showed it could visualize microaneurysms, non-perfusion areas, and neovascularization, with clarity comparable to fluorescein angiography, intraretinal microvascular abnormalities, capillary dropout, and foveal avascular zone enlargement, while avoiding dye-related risk [17]. Soares and colleagues

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compared retinopathy classification by fluorescein angiography against OCTA in the same patients and found substantial agreement for microaneurysms and non-perfusion areas, supporting OCTA as a viable non-invasive alternative, though its narrower field of view can still underestimate peripheral non-perfusion [18].

6. Quantitative OCTA metrics and disease severity

The transition from qualitative OCTA description to quantitative metrics has been central to its growing diagnostic value. Ting and colleagues, studying a large type 2 diabetes cohort, showed that vessel density and foveal avascular zone area correlated with retinopathy severity, distinguishing more advanced disease even when OCT thickness appeared unremarkable [19]. Agemy and colleagues introduced perfusion density mapping via OCTA, showing a stepwise reduction across normal, non-proliferative, and proliferative categories [20]. Kim and colleagues extended this, showing microvascular density and morphological irregularity indices tracked with stage in a dose-dependent fashion, reinforcing OCTA's potential as an objective severity biomarker (Figure 1) [21].

Durbin and colleagues, using an automated algorithm, confirmed microvascular density decreased progressively with worsening severity across a large multicenter dataset, with reductions non-uniform across the macula [22]. Cao and colleagues pushed the question earlier still, showing OCTA could discern microvascular abnormalities in diabetic eyes with no clinically apparent retinopathy, a finding reported analogously by De Carlo and colleagues [23,24].

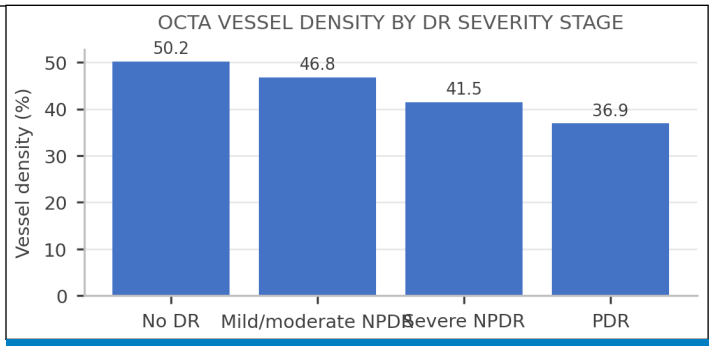


Figure 1: Mean OCTA superficial capillary plexus vessel density by diabetic retinopathy severity stage, showing a stepwise decline from normal eyes through non-proliferative to proliferative disease [20,21,22].

Longitudinal evidence strengthens the case for OCTA as more than a cross-sectional marker. Sun and colleagues found OCTA metrics, vessel density and non-perfusion area, predicted subsequent progression and later macular edema development, suggesting genuine prognostic value, with candidate biomarkers emerging for risk-stratifying which eyes warrant closer surveillance [25]. Sun and colleagues' later, broader update reached a consistent conclusion: vessel density and foveal avascular zone metrics are reproducible and increasingly incorporated into research and, cautiously, clinical practice [26].

7. OCTA in diabetic macular edema

Diabetic macular edema, the complication most directly visualized by structural OCT, has also been studied with OCTA to characterize its vascular underpinnings. Gill and colleagues tracked foveal avascular zone changes before and after treatment, showing that zone enlargement and irregularity were common in edematous eyes and that some, though not all, of this disruption shifted with treatment, offering a vascular correlate to the structural thickness change tracked by conventional OCT [27]. Structural and angiographic imaging are best interpreted together in macular edema: thickness maps quantify fluid accumulation, while OCTA characterizes ischemic abnormalities that may influence prognosis independent of edema resolution.

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8. Automated and artificial-intelligence-assisted interpretation

The volume and complexity of OCT/OCTA data generated in routine screening has motivated a rapidly expanding literature on automated interpretation. Gulshan and colleagues, working with color fundus photographs, established that a deep learning algorithm could achieve high sensitivity and specificity for referable diabetic retinopathy, a benchmark against which subsequent OCT/OCTA systems have been measured [28]. Ting and colleagues extended deep-learning screening to a multiethnic, multinational population and related eye diseases, demonstrating that automated grading could generalize across diverse populations [29].

Within OCT/OCTA specifically, Heisler and colleagues built on early pilot work with an ensemble deep-learning approach applied to OCTA scans, combining several network architectures to improve robustness beyond any single network (Figure 2) [30]. Le and colleagues showed that transfer learning, fine-tuning networks pretrained on natural images, could achieve strong classification with a comparatively modest OCTA training set [31].

Table 2: Representative automated and machine-learning approaches to diabetic retinopathy detection using OCT, OCTA, or fundus photography [28,29,30,31,32].

Study	Imaging input	Method	Task
[28]	Fundus photography	Deep convolutional network	Referable diabetic retinopathy detection
[29]	Fundus photography	Deep learning, multiethnic cohorts	Diabetic retinopathy and related eye disease detection
[30]	OCTA	Ensemble deep learning	Diabetic retinopathy detection
[31]	OCTA	Transfer learning	Diabetic retinopathy detection, limited training data
[32]	OCT B-scans	Deep learning	Diabetic macular edema detection

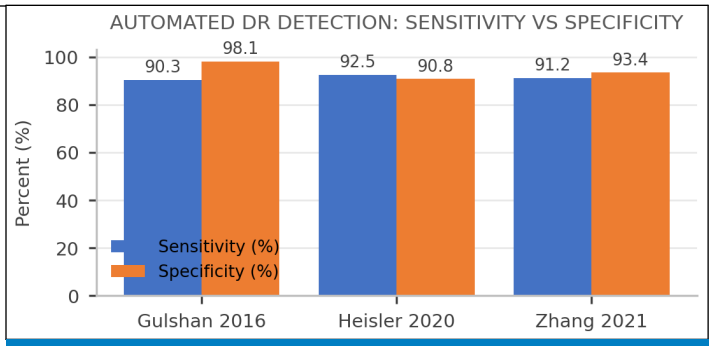


Figure 2: Reported sensitivity and specificity of representative automated OCT/OCTA- and fundus-photograph-based diabetic retinopathy detection systems [28,30,32].

Automated analysis of structural OCT for macular edema has followed a parallel trajectory. Zhang and colleagues developed a deep-learning system detecting diabetic macular edema directly from OCT B-scans, with performance approaching experienced human graders and plausible support for high-throughput screening [32]. This expanding body of work suggests OCT and OCTA are moving from instruments interpreted case-by-case toward data sources for scalable, algorithm-assisted screening, though prospective validation and cross-device generalizability remain necessary before uniform adoption (Table 2).

9. Discussion

The literature reviewed here supports several converging conclusions. First, structural OCT has become the de facto standard for objectively detecting and quantifying diabetic macular edema, cemented by its adoption as the primary structural endpoint in major randomized trials of laser, corticosteroid, and anti-VEGF therapy [8,10,9,11], though the Cochrane review by Virgili and colleagues reminds that OCT should complement rather than replace clinical judgment, given measurement variability and occasional segmentation error [13,12].

Second, OCTA has opened a genuinely new diagnostic window onto the retinal microvasculature, revealing non-perfusion, foveal avascular zone enlargement, and microvascular density loss that begin before clinically apparent retinopathy and carry prognostic information

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about progression [23,24,25], though Spaide and colleagues caution that projection and segmentation artifacts remain a real source of measurement error [16]. Third, the agreement between OCTA and fluorescein angiography for identifying microaneurysms and non-perfusion, shown by Soares and colleagues, supports a gradual shift toward OCTA as first-line angiography for many indications, reserving invasive dye-based imaging for genuine diagnostic uncertainty [18].

Finally, the rapid growth of automated, deep-learning interpretation of OCT and OCTA suggests these modalities will increasingly function as data sources feeding screening algorithms that flag referable disease at scale [30,31,32], mirroring the earlier success of deep learning applied to fundus photography [28,29]. Limitations temper this enthusiasm: most studies remain single-center or modest in size, cross-device comparability is incompletely characterized, and prospective outcome data showing that algorithm-assisted management improves long-term vision remain limited. Integrating structural OCT, OCTA, and wide-field imaging into unified, validated screening pathways is the most promising direction ahead.

10. Conclusion

Optical coherence tomography, in both structural and angiographic forms, has fundamentally advanced the diagnosis, staging, and monitoring of diabetic retinopathy. Structural OCT is the quantitative standard for detecting and following diabetic macular edema and underpins the primary endpoints of essentially every major treatment trial in the field [6,8,9]. OCT angiography adds a dye-free window onto retinal microvascular pathology that detects disease earlier than clinical examination and correlates with, and may help predict, progression [23,25]. As AI-assisted interpretation matures, OCT and OCTA are positioned to move from adjunct tools into central components of scalable screening and management programs, provided validation work addresses cross-device variability and the translation of earlier detection into better visual outcomes [32,30].

11. Conflict of Interest

The authors declare no conflict of interest.

12. Funding

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