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Advances in Optical Coherence Tomography for the Early Detection and Management of Diabetic Retinopathy

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Abstract- ***Diabetic retinopathy is now recognized as a neurovascular disorder characterized by neuronal dysfunction, capillary injury, inflammation, and barrier failure that precede the detection of sight-threatening disease by conventional ophthalmoscopy. Optical coherence tomography (OCT) has progressed beyond central retinal thickness measurement to serve as a multimodal platform for structural, angiographic, and computational phenotyping. This review thoroughly examines advances from 2020 to 2025 in spectral-domain OCT, swept-source OCT, OCT angiography (OCTA), wide-field acquisition, quantitative biomarker extraction, and artificial intelligence to enable early detection and longitudinal management of diabetic retinopathy. A structured narrative search of PubMed-indexed literature was carried out using combinations of diabetic retinopathy, diabetic macular edema, optical coherence tomography, OCT angiography, swept-source, biomarkers, nonperfusion, and deep learning. Human studies, systematic reviews, and clinically relevant validation studies were prioritized. Current evidence demonstrates that deep capillary plexus vessel loss, geometric perfusion deficits, foveal avascular zone remodeling, retinal thinning, disorganization of retinal inner layers, hyperreflective foci, ellipsoid-zone disruption, and vitreomacular interface abnormalities provide complementary diagnostic information. Wide-field swept-source OCTA enhances visualization of peripheral nonperfusion and neovascular complexes, while three-dimensional analysis and artificial intelligence lessen reliance on manually selected en face slabs. However, device-specific algorithms, segmentation errors, motion and projection artifacts, media opacity, and inconsistent outcome definitions limit cross-platform interchangeability. The most robust clinical approach is an integrated OCT framework that synthesizes structural wholeness, fluid phenotype, perfusion distribution, and temporal change. Standardized acquisition protocols, transparent algorithms, external validation, and prospectively defined outcome-linked thresholds are necessary before OCT-derived metrics can independently guide screening intervals or treatment decisions.***

Keywords: Diabetic Retinopathy, Optical Coherence Tomography, OCT Angiography, Swept-Source OCT, Diabetic Macular Edema, Biomarkers, Artificial Intelligence

I. INTRODUCTION

Diabetic retinopathy (DR) is still a major cause of preventable visual impairment, but the clinical problem has changed. Screening programs can identify visible retinopathy, and anti-vascular endothelial growth factor therapy can control many cases of diabetic macular edema (DME) and proliferative disease. The unresolved challenge is to identify biologically important injury before irreversible neural loss, distinguish eyes likely to progress, and customize treatment according to more than central thickness. Modern OCT tackles this challenge by resolving retinal layers, fluid compartments, microvascular plexuses, the choriocapillaris, and vitreoretinal relationships in a single visit. Recent imaging reviews emphasize that OCT and OCTA now support diagnosis, prognosis, treatment selection, and documentation across the DR spectrum (Nanegrungsunk et al., 2022; Parravano et al., 2024).

A previously published model review provided an important framework through categorizing OCTA evidence according to morphology, quantitative vascular measures, diabetic macular ischemia, edema, and technical limitations. That review characterized OCTA as a rapid, non-invasive adjunct offering depth-resolved visualization, while recognizing challenges related to segmentation and artifacts. The present review maintains a clinically oriented structure but pursues a distinct objective: to synthesize advances from 2020 to 2025 that integrate structural OCT, OCTA, wide-field swept-source imaging, and computational analysis for both initial detection and management. This expanded perspective is essential because a single vessel-

density metric cannot capture the multifaceted interplay among neural, vascular, inflammatory, and mechanical factors in diabetic retinal disease.

This review addresses four primary objectives. First, it evaluates which OCT-derived findings can detect subclinical damage in diabetes prior to the appearance of visible diabetic retinopathy. Second, it examines biomarkers that improve staging and prognosis following the onset of clinical retinopathy. Third, it assesses the role of OCT in guiding the management of diabetic macular edema and proliferative diabetic retinopathy, including observing treatment response and recurrence. Fourth, it identifies methodological issues that must be addressed to achieve high-level evidence and facilitate routine clinical translation. The primary assertion is that the value of OCT does not lie in supplanting clinical examination or fluorescein angiography, but in providing repeatable, layer-specific, longitudinal data that can be synthesized into an interpretable risk profile.

II. REVIEW METHODOLOGY

A structured narrative review was designed to reflect the organization of a high-quality clinical imaging review while allowing synthesis across heterogeneous technologies and outcomes. PubMed and publisher-indexed records were searched for English-language human research published between January 2020 and December 2025. Search strings combined “diabetic retinopathy” or “diabetic macular edema” with “optical coherence tomography,” “OCT angiography,” “swept-source,” “wide-field,” “vessel density,” “nonperfusion,” “biomarker,” “treatment response,” “artificial intelligence,” or “deep learning.” References were supplemented through backward citation checking of recent reviews. The 2019 Springer/BMC model paper was used for conceptual structure rather than as evidence within the restricted citation window.

Eligible publications included systematic or narrative reviews, cross-sectional diagnostic studies, longitudinal cohorts, clinical-trial secondary analyses, reproducibility studies, and algorithm-validation studies. Priority was given to studies reporting clinically interpretable outcomes: DR presence or severity, visual function, progression, treatment response, recurrence, or detection of neovascularization. Studies confined to non-diabetic retinal disease, technical simulations without patient data, isolated case reports, and publications outside 2020-2025 were excluded from the reference set. Because acquisition protocols, devices, segmentation boundaries, and statistical definitions varied substantially, quantitative meta-analysis was not appropriate. Findings were therefore grouped into five domains: technology, preclinical detection, vascular biomarkers, structural biomarkers, and management applications.

Quality was considered through study design, sample size, independent validation, clarity of reference standards, artifact handling, and adjustment regarding systemic or ocular confounders. Particular caution was applied to metrics generated by proprietary software and to artificial intelligence studies without external testing. The review does not assign a single evidence grade because the purpose is translational synthesis rather than a therapeutic recommendation. Instead, each proposed biomarker is interpreted according to biological plausibility, repeatability, association with clinically meaningful outcomes, as well as readiness for use outside the originating device or dataset.

III. TECHNOLOGICAL ADVANCES RESHAPING OCT ASSESSMENT

Spectral-domain OCT remains the primary clinical modality due to its rapid, high-resolution cross-sectional imaging and established thickness mapping. Recent advances go beyond faster acquisition to include more sophisticated interpretation of 3D data. Automated layer segmentation enables assessment of the ganglion cell-inner plexiform complex, inner nuclear layer, outer retina, and choroid, while en face reconstruction reveals the horizontal distribution of lesions. These developments shift the focus from average central subfield thickness to regional tissue condition. Nevertheless, automated outputs call for careful inspection, as edema, hard exudates, traction, poor fixation, and shadowing can displace segmentation boundaries.

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Swept-source OCT uses a longer wavelength and higher scanning speed, improving penetration through media and enabling wider, deeper volumes. In DR, the practical benefit is simultaneous analysis of macular and more peripheral vascular territories. Wide-field swept-source OCTA can quantify nonperfusion area and detect neovascularization over fields that approach clinically meaningful retinal regions. Garg et al. (2022) demonstrated the importance of nonperfusion area as a wide-field metric, while Wang et al. (2022) showed that 12 × 12 mm imaging can characterize perfusion across standardized retinal sectors. Expanded-field studies additionally suggest that baseline ischemic burden and unstable intraretinal microvascular abnormalities may identify eyes at higher risk of significant outcomes (Ding et al., 2025). These developments narrow, but do not eliminate, the field-of-view advantage of ultra-widefield fluorescein angiography. OCTA derives flow contrast from repeated scans and therefore avoids intravenous dye. It separates superficial and deep capillary complexes, supports three-dimensional localization, and can be repeated frequently. Contemporary reviews describe growing clinical use in DR, especially for quantitative evaluation of capillary closure and neovascular morphology (Waheed et al., 2023; Crincoli et al., 2024; Nouri et al., 2024). Yet OCTA does not show leakage, and its signal is bounded by flow-detection thresholds. Slow flow may appear absent; projection may create false vessels in deeper slabs; movement can duplicate or erase structures; and edema can distort segmentation. Suspended scattering particles in motion may also mimic flow within cystic spaces and overestimate deep plexus density (Maltsev et al., 2021).

Three-dimensional vascular analysis is emerging as a corrective to the limitations of two-dimensional en face metrics. Borrelli et al. (2021) reported stronger intrasession repeatability for selected 3D OCTA measurements than for conventional 2D outputs. Three-dimensional maps preserve depth and may reduce dependence on arbitrary slab boundaries, especially around distorted retina. Likewise, geometric perfusion deficit analysis estimates tissue lying beyond a biologically relevant diffusion distance from capillaries and may better represent metabolic vulnerability than simple percentage vessel area (Nesper et al., 2022). Figure 1 summarizes the resulting workflow: acquisition, structural analysis, vascular analysis, and integrated decision support.

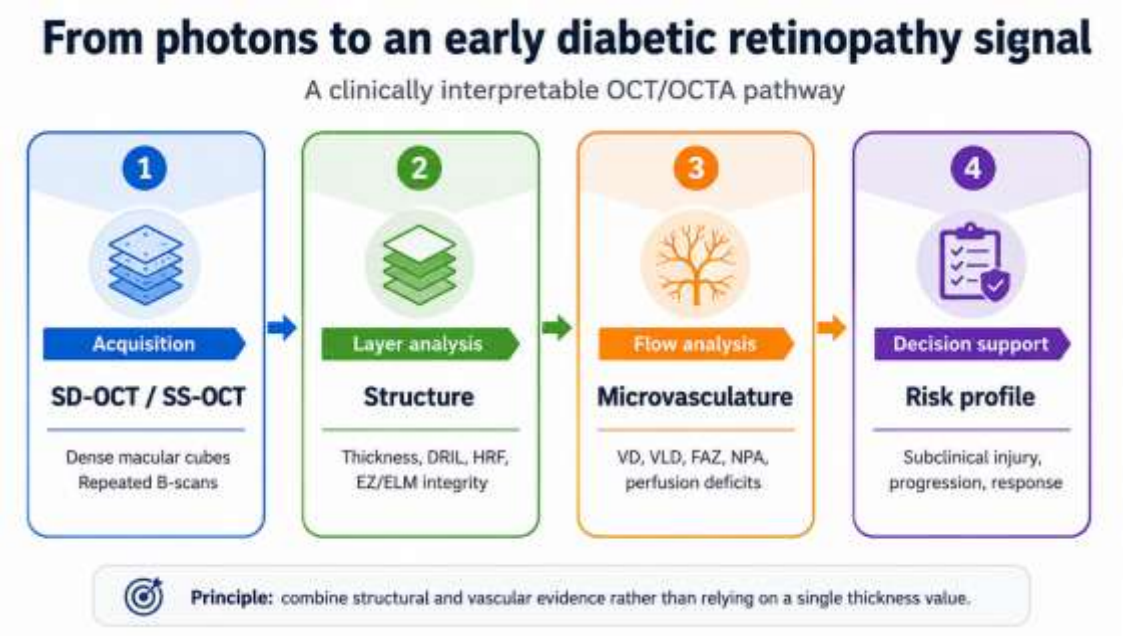

Figure 1. Integrated structural and vascular OCT workflow for early diabetic retinal risk assessment. Original conceptual illustration created for this review.

IV. EARLY DETECTION BEFORE VISIBLE RETINOPATHY

The earliest clinically useful OCT signal should identify damage in an eye that appears normal on color photography without producing excessive false-positive referrals. Studies from 2020 onward consistently report reduced macular perfusion in diabetes without visible DR, although the magnitude and most sensitive plexus vary. Xie et al. (2020) found altered macular vessel density using swept-source OCTA, and Altinisik et al. (2022) documented significant deep capillary plexus reduction in patients without clinical retinopathy. Yang et al. (2024) similarly concluded that OCTA can detect early intraocular microvascular changes. The results support the biological concept that capillary dysfunction precedes recognizable microaneurysms, but they do not yet establish a universal diagnostic cutoff.

The deep capillary plexus is frequently emphasized because it supplies metabolically active middle retinal layers and may be particularly sensitive to hypoxia. Reduced deep vessel density, increased intercapillary spacing, or geometric perfusion deficits may coexist with normal visual acuity. Functional work suggests that microvascular changes may correspond more closely with contrast sensitivity than with high-contrast acuity, which is affected later (Vingopoulos et al., 2024). This is important for early disease: a patient may read a standard chart normally while reporting subtle difficulty in low light or low contrast.

Structural OCT adds a second dimension. Diabetes can be associated with thinning of inner retinal layers, altered ganglion cell-inner plexiform measurements, and relationships between neuronal function and reduced macular perfusion. Srinivasan et al. (2021) linked lower vessel density and perfusion with retinal neuronal dysfunction in diabetes without DR. Li et al. (2021) reported concurrent vascular reduction and changes in retinal thickness, supporting the view that diabetic retinal neurodegeneration and microangiopathy overlap rather than occur as isolated sequences. Choroidal and choriocapillaris alterations are also under investigation, but variability in scan size, signal compensation, and systemic determinants limits consensus. A recent review concluded that OCTA is promising for diabetic choroidopathy but requires standardized assessment (Nowroozzadeh et al., 2025).

Early-detection studies must be interpreted carefully. Age, sex, axial length, blood pressure, renal function, glycemic control, signal strength, scan size, and device software can alter quantitative values. Repeatability is generally acceptable under controlled conditions, yet interchangeability between instruments is poor. Levine et al. (2020) demonstrated that vessel area and skeleton density can be repeatable and reproducible, but this does not mean that a threshold derived on one platform can be transferred to another. The most realistic near-term role is risk enrichment: OCT can identify a subgroup with convergent neural and vascular abnormalities who may benefit from closer observation, systemic risk optimization, or enrollment in preventive trials.

Table 1. OCT and OCTA biomarkers for initial detection and staging

Biomarker	Biological meaning	Potential use	Key caution
Deep plexus vessel density / VLD	Capillary rarefaction in metabolically vulnerable middle retina	Subclinical detection and severity tracking	Device, scan size, and segmentation dependent
FAZ area and acircularity	Central capillary remodeling and ischemia	Early DR characterization and visual-risk context	Large normal inter-individual variation
Nonperfusion area / geometric deficit	Tissue beyond effective capillary supply	Progression and peripheral ischemic burden	Flow threshold and field-of-view effects

GCIPL and inner retinal integrity	Neurodegenerative component of diabetes	Detect convergent neural injury	Affected by age, glaucoma, and axial length
DRIL, EZ/ELM integrity	Inner retinal disorganization and photoreceptor injury	Visual prognosis in DME	Requires careful B-scan grading

V. QUANTITATIVE OCTA BIOMARKERS FOR STAGING AND PROGRESSION

Vessel density is the most familiar OCTA metric and usually represents the proportion of a region occupied by flow-positive vessels. It declines with increasing DR severity, but the result depends on whether larger vessels are included, whether images are binarized or skeletonized, and which plexus and scan size are analyzed. Alam et al. (2020) reported strong classification performance for quantitative OCTA features, and Kushner-Lenhoff et al. (2022) validated vessel skeleton density and vessel diameter index as predictors of DR severity across clinical cohorts. Marques et al. (2021) showed that vessel-density maps can quantify vessel closure and demonstrate greater loss with worsening retinopathy. These studies support clinical relevance yet also reveal that no single definition dominates.

Vessel length density emphasizes capillary length after skeletonization and is less influenced by vessel caliber. Vessel diameter index can reflect dilation or remodeling. Their joint interpretation may distinguish rarefaction from compensatory caliber change. Capillary density and caliber have provided strong discrimination between control, mild, and referable DR, suggesting that vascular geometry contains more staging information than vessel area alone (Kushner-Lenhoff et al., 2022). Three-dimensional density mapping may further identify layer-specific and regional patterns missed by two-dimensional averages (Sarabi et al., 2020).

Foveal avascular zone area, perimeter, acircularity, and surrounding density describe central capillary remodeling. Ragkousis et al. (2020) identified vessel density around the FAZ as a candidate severity marker. However, normal FAZ anatomy varies considerably, so shape and pericentral perfusion may be more informative than area alone. Metrics should also be interpreted with structural context: displacement by edema, segmentation error, or previous treatment can change apparent boundaries.

Nonperfusion area is particularly relevant because DR progression is driven by capillary closure and ischemia. Wide-field swept-source OCTA permits direct quantification over larger fields, and Garg et al. (2022) found that nonperfusion can be measured more readily than with dye angiography in selected settings. Peripheral lesions alter the relationship between central vessel density and overall severity; Ashraf et al. (2020) showed that central density associations differ when predominantly peripheral lesions are present. Consequently, a normal-looking macular metric cannot exclude substantial peripheral disease.

Longitudinal evidence is more valuable than cross-sectional discrimination. Wang et al. (2023) measured parafoveal vessel-density change during progression, while Srinivasan et al. (2023) found that OCT and OCTA measures may be more useful for predicting progression than for predicting the initial development of DR. This distinction is clinically plausible: once microvascular injury is established, its rate and spatial expansion may carry more information than a single baseline value. The ideal progression endpoint will likely combine change in perfusion, expansion of nonperfusion, new intraretinal microvascular abnormalities, and structural decline.

VI. STRUCTURAL OCT BIOMARKERS AND DIABETIC MACULAR EDEMA

DME management still is the setting in which structural OCT has the clearest immediate impact. Central subfield thickness objectively tracks anatomy, but thickness alone is an incomplete surrogate for vision and treatment need. Equal

thickness can arise from different distributions of intraretinal fluid, subretinal fluid, cyst size, exudation, traction, ischemia, and tissue loss. Recent reviews therefore advocate phenotype-based interpretation of OCT biomarkers rather than a binary "fluid present" approach (Szeto et al., 2024; Sen et al., 2025).

Disorganization of the retinal inner layers describes loss of recognizable boundaries within the inner retina and is associated with macular ischemia and impaired visual function. Ellipsoid-zone and external limiting membrane disruption indicate photoreceptor injury and often predict limited visual recovery still when edema resolves. Hyperreflective foci may represent activated microglia, lipid, or migrating retinal pigment epithelial material depending on size and location; their number and distribution can reflect inflammatory activity. Intraretinal cyst characteristics, subretinal fluid, hard exudates, and choroidal measurements contribute supplementary context. Shrivastava et al. (2024) linked systemic factors and DR stage with several imaging features, illustrating that OCT phenotypes reflect both ocular and systemic disease.

The vitreomacular interface is also clinically relevant. Epiretinal membrane, vitreomacular adhesion, and traction can sustain edema or alter response to pharmacologic therapy. Automated thickness maps may conceal focal traction, so clinicians must inspect B-scans. Likewise, large cysts and severe edema can disturb automated segmentation and attenuate OCTA signal, making apparent deep capillary loss partly artifactual. The presence of suspended scattering particles in motion can generate false flow within cysts (Maltsev et al., 2021). Structural and angiographic volumes should therefore be co-registered and reviewed together.

OCT biomarkers may help differentiate treatment pathways. Anti-VEGF therapy is first-line for many center-involving cases, whereas corticosteroid therapy may be considered in selected pseudophakic eyes, inflammatory phenotypes, or insufficient response. Persistent DME is not a single entity; it may reflect undertreatment, chronic barrier failure, ischemia, inflammation, traction, or irreversible tissue damage (Sorour et al., 2023). A biomarker panel can clarify why thickness remains elevated and prevent repeated treatment based solely on one numeric map.

Treatment monitoring requires both anatomical and functional interpretation. A reduction in fluid is favorable, but persistent DRIL or photoreceptor disruption may explain limited acuity gain. Conversely, stable small cysts in a chronically damaged retina may not justify indefinite escalation as vision and tissue condition are unchanged. Figure 2 presents a stage-specific model in which OCT objectives evolve from detecting subclinical injury to phenotyping edema and monitoring proliferative complications.

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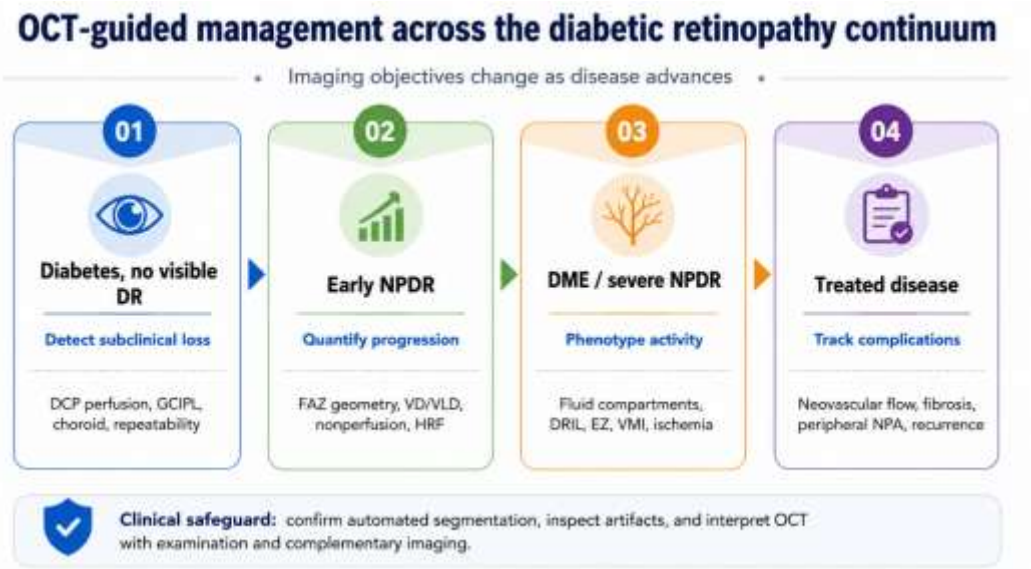

Figure 2. Stage-specific OCT objectives across the diabetic retinopathy continuum. Original conceptual illustration created for this review.

VII. OCT IN PROLIFERATIVE DISEASE AND TREATMENT MONITORING

In proliferative diabetic retinopathy (PDR), OCTA can localize flow above the internal limiting membrane and display the branching architecture of neovascularization. This helps distinguish neovascular complexes from intraretinal microvascular abnormalities, especially when leakage on fluorescein angiography obscures fine morphology. Wide-field montages and swept-source systems extend assessment beyond the posterior pole, enabling serial documentation of neovascular area and adjacent nonperfusion.

The response of vascular metrics to treatment is complex. Panretinal photocoagulation reduces ischemic drive but may alter retinal perfusion through redistribution and remodeling. Abdelhalim et al. (2022) reported improvement in selected macular OCTA parameters after photocoagulation, but these outcomes should not be interpreted as regeneration of lost capillaries without corroboration. Anti-VEGF therapy can cause rapid involution of neovascular flow, while fibrous scaffolds or low-flow residual networks may persist. Macular vessel density may remain relatively stable despite anatomical improvement in DME; secondary analyses and early treatment studies have reported little short-term change after anti-VEGF therapy (Alagorie et al., 2020; Cheong et al., 2020).

OCT is indispensable for identifying tractional complications. Cross-sectional scans demonstrate posterior hyaloid attachment, fibrovascular proliferation, retinal distortion, schisis, and tractional detachment that may be missed on en face vascular maps. The clinician must therefore interpret declining neovascular flow alongside structural signs of contraction. An eye can show less perfused neovascular tissue but increasing traction, which changes urgency plus may require surgery.

Longitudinal OCTA may eventually support individualized retreatment by distinguishing active fine-caliber neovascular sprouts from mature, pruned, or fibrotic complexes. Current evidence is insufficient to define universally accepted flow thresholds for recurrence. Image registration, scan-area consistency, segmentation correction, and artifact review are essential because apparent change can result from acquisition rather than biology. Fluorescein angiography is valuable when leakage, peripheral extent, or uncertain activity will change management.

Table 2. Modality selection for common diabetic retinopathy questions

Clinical question	Preferred OCT contribution	Complementary test	Interpretive safeguard
Is there center-involving edema?	Structural OCT thickness and fluid compartments	Visual acuity and examination	Inspect segmentation and traction
Is macular ischemia contributing to poor vision?	OCTA plexus perfusion and FAZ geometry	FA when leakage/perfusion timing matters	Account for edema-related signal loss
Is PDR activity changing?	Wide-field OCTA neovascular flow and area	Ultra-widefield photography/FA	Use registration and identical scan fields
Why is treatment response limited?	DRIL, EZ/ELM, HRF, VMI, residual fluid	Systemic and treatment history	Avoid using thickness alone
Is peripheral ischemia underestimated?	Wide-field SS-OCTA nonperfusion maps	Ultra-widefield FA	Recognize resolution-field trade-off

VIII. ARTIFICIAL INTELLIGENCE AND AUTOMATED INTERPRETATION

Artificial intelligence addresses two practical barriers: the volume of OCT data and the complexity of multivariate interpretation. Conventional software measures thickness or vessel density, whereas deep learning can analyze entire structural and angiographic volumes, detect spatial patterns, and integrate information across layers. Ryu et al. (2021) developed an automated OCTA model for diagnosing and identifying referable DR, and subsequent work classified disease severity using combined structural and vascular inputs (Ryu et al., 2022). Zang et al. (2022) demonstrated a framework using three-dimensional OCT and OCTA with class-activation maps intended to improve interpretability.

The strongest conceptual advantage is multimodal fusion. A model can weigh deep plexus nonperfusion, FAZ distortion, inner retinal thinning, fluid, and photoreceptor integrity simultaneously, approximating expert synthesis rather than reproducing a single metric. Reviews published in 2024-2025 describe promising AI-assisted hemodynamic analysis and screening performance (Pradeep et al., 2024; Hayati et al., 2025). Automated segmentation of nonperfusion and FAZ area can also improve consistency and reduce manual workload; recent deep-learning systems have achieved high agreement for nonperfusion indices in validation datasets (Le Boité et al., 2025).

However, high internal accuracy does not guarantee clinical usefulness. Models can learn device signatures, scan-quality artifacts, prevalence patterns, or treatment history rather than transferable disease biology. Many datasets are small, retrospective, single-center, or enriched for clear disease. External validation over ethnicity, diabetes type, camera manufacturer, scan protocol, and care setting is essential. Explainability should identify image regions and features that drive decisions, but attention maps are not equivalent to causal explanations. Few-shot and explainable approaches are currently explored for OCTA staging, yet they still require prospective testing (Movassagh et al., 2025).

For safe implementation, AI should initially function as quality control and decision support. It can flag segmentation errors, identify scans needing review, calculate uniform metrics, and prioritize high-risk change. Final decisions should remain traceable to visible structural and vascular evidence. Regulatory evaluation must also address dataset shift, calibration, missing data, and performance in eyes with coexisting retinal disease.

IX. LIMITATIONS, STANDARDIZATION, AND RESEARCH PRIORITIES

The principal limitation of OCT research in DR is heterogeneity. Devices use different wavelengths, scanning speeds, motion-correction methods, segmentation boundaries, and flow algorithms. A

vessel-density value is therefore not a universal biological measurement. Scan size introduces another trade-off: small scans offer high sampling rate, whereas wide fields sacrifice resolution and may increase motion. Signal strength, defocus, cataract, vitreous opacity, blinking, and fixation instability can all lower apparent perfusion.

Segmentation error is especially consequential in DME, high myopia, traction, and advanced DR. Automated boundaries must be reviewed, corrected when possible, and reported. Studies should disclose whether projection-removal algorithms were used and how images with artifacts were excluded. Reproducibility work should include intervisit rather than only same-session measurements and should define the minimum detectable change. Comparisons across devices require either harmonized raw-data processing or validated conversion, not simple pooling of manufacturer outputs.

Future trials should predefine clinically meaningful endpoints. Cross-sectional separation between healthy and diseased eyes is insufficient. Biomarkers should predict incident referable DR, progression by at least two severity steps, development or recurrence of center-involving DME, neovascular complications, visual-function decline, or treatment burden. Models should be compared with practical baselines such as retinopathy grade, HbA1c, disease duration, renal status, and conventional OCT thickness. Added value should be shown by calibration, decision curves, and external validation.

A consensus reporting framework is needed for acquisition parameters, segmentation, artifact grading, systemic covariates, and metric definitions. Publicly accessible, diverse longitudinal datasets would accelerate robust AI and device-independent biomarkers. Emerging adaptive optics, visible-light OCT, and faster swept-source systems may reveal capillary and oxygenation changes at finer scales, but clinical adoption must be motivated by improved outcomes rather than image novelty.

Clinical interpretation should also preserve uncertainty A mildly abnormal metric may reflect normal biological variation acquisition noise or systemic status on the day of imaging Repeated measurements obtained with the same device scan pattern and quality threshold are more informative than isolated comparisons with a manufacturer database Reports should distinguish observed change from change exceeding test-retest variability and should document treatment timing glycemic status blood pressure and media clarity This discipline prevents overdiagnosis and supports meaningful communication between retina specialists diabetologists researchers and patients A staged implementation pathway can convert promising metrics into dependable clinical tools The first stage constitutes analytical validation Investigators should specify the exact retinal slab scan dimensions sampling rate signal-strength threshold image-processing version and rules for manual correction Raw and processed images should be retained so that errors can be traced Repeatability should be tested within a session between visits and across operators The minimum detectable change should be calculated for each metric rather than inferred from statistical significance Where automated segmentation is used studies should report the frequency direction and clinical consequence of boundary errors The second stage is biological validation A proposed biomarker should correspond to a plausible component of diabetic retinal injury and should show coherent relationships with other measures For example reduced deep plexus perfusion should be examined alongside middle retinal thickness contrast sensitivity ischemic findings and systemic microvascular burden A metric that changes with signal strength but not with independent evidence of disease is unlikely to be reliable Confounding by age axial length refractive status blood pressure renal disease anemia sleep apnea and medication should be evaluated because these variables can influence retinal circulation or tissue thickness The third stage is clinical validation in longitudinal cohorts Baseline abnormalities must predict a future event that matters to patients or clinicians Useful outcomes include development of referable DR progression to severe NPDR or PDR incident center-involving DME meaningful visual-function loss need for treatment recurrence after treatment reduction or surgical traction Models should be tested in populations that differ from the development cohort Reporting only an

area under the receiver-operating-characteristic curve is inadequate calibration sensitivity at a clinically acceptable specificity positive predictive value in the intended population and net benefit should also be presented The fourth stage is workflow validation Even an accurate biomarker may fail if acquisition takes too long correction is burdensome or reports are difficult to interpret Studies should measure imageability technician time reading time referral consequences and patient acceptability Automated systems should show why a case was flagged and display the relevant B-scans en face slabs and quality warnings A compact report could present current status change from the previous visit confidence intervals or repeatability limits and the specific features responsible for risk categorization Such transparency would make the result clinically auditable The fifth stage is outcome and economic evaluation Randomized or pragmatic studies should test whether OCT-guided pathways improve vision reduce avoidable treatment detect progression earlier or safely extend follow-up for low-risk patients Cost-effectiveness depends on disease prevalence equipment availability operator training and referral capacity and the consequences of false reassurance plus false alarm Resource-limited settings may benefit from portable or simplified OCT but algorithms trained in tertiary centres must not be assumed to generalize Equity analyses should examine performance among age sex ethnicity pigmentation diabetes type and coexisting ocular disease Research publications can improve comparability through a minimum dataset Authors should provide participant flow eye-selection rules diabetes duration HbA1c blood pressure renal status prior ocular treatment lens status visual acuity retinopathy grade and coexisting pathology Imaging details should include device software version scan protocol averaging motion correction segmentation boundaries artifact exclusion and whether graders were masked Outcome definitions and statistical plans should be registered when possible Sharing de-identified images code and metric definitions would permit independent replication and facilitate federated or multicenter learning without transferring identifiable clinical data Finally patient communication deserves attention OCT images are visually persuasive but apparent color-map changes can exaggerate small numerical differences Clinicians should explain that OCT identifies risk markers rather than certainties and that systemic diabetes control is fundamental Shared decisions should integrate symptoms visual function examination imaging treatment burden pregnancy status cardiovascular and renal health and patient preferences This considered approach keeps state-of-the-art imaging connected to the purpose of care preserving useful vision and quality of life Prospective registries should additionally record adverse consequences of imaging decisions including delayed treatment unnecessary angiography patient anxiety and inequitable access These outcomes will clarify whether technological sophistication produces measurable benefit across ordinary practice rather than only in carefully selected research cohorts in diverse populations.

X. CLINICAL INTEGRATION AND CONCLUSION

A practical OCT strategy begins with the clinical question. In diabetes without visible DR, the objective is to detect convergent subclinical neural and vascular injury, not to label disease from one abnormal number. In early NPDR, longitudinal change in vessel density, nonperfusion, FAZ geometry, and inner retinal integrity can refine risk. In DME, fluid distribution, DRIL, photoreceptor status, hyperreflective foci, ischemia, and vitreomacular interface features should be interpreted together. In PDR, OCTA documents neovascular flow while structural OCT evaluates traction and tissue composition.

The evidence from 2020-2025 supports OCT as a central platform for initial detection and management, but not as an autonomous replacement for examination, photography, or dye angiography. Its greatest strength is repeatable, depth-resolved follow-up. Its greatest risk is false precision from proprietary metrics and uncorrected artifacts. Clinicians and researchers should favor integrated patterns and change over time, verify segmentation, and use complementary imaging when leakage or peripheral activity matters.

The next advance will not be a single superior scan. It will be a standardized, interpretable framework that combines structure, perfusion, function, systemic risk, and longitudinal behavior. When validated against patient-centered outcomes, such a framework could allow personalized screening intervals, earlier intervention trials, more rational treatment switching, and safer reduction of unnecessary visits. Until then, OCT-derived biomarkers should strengthen clinical judgment rather than substitute for it.

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