Indonesian Journal of Global Health Research
Volume 6 Number 6, December 2024
e-ISSN 2715-1972; p-ISSN 2714-9749
http://jurnal.globalhealthsciencegroup.com/index.php/IJGHR

ROLE OF OPTICAL COHERENCE TOMOGRAPHY (OCT) IN MACULAR OEDEMA AND DIABETIC RETINOPATHY (DR) UPDATE; SYSTEMATIC LITERATURE REVIEW

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ABSTRACT
Diabetic retinopathy (DR) and diabetic macular oedema (DME) are significant causes of blindness globally, resulting from diabetes-induced retinal damage. Early detection and timely intervention are critical to prevent irreversible vision loss in diabetic patients. Recent advances in imaging technology, particularly Optical Coherence Tomography (OCT), have provided a powerful tool for detailed visualisation of retinal structures, enabling the early identification of microvascular changes associated with DR and DME. This systematic review synthesises insights from 20 studies to explore the effectiveness of OCT in diagnosing, monitoring, and guiding treatment for these conditions. A comprehensive literature search was conducted across databases including Scopus, Scholar, and PubMed, using Boolean operators to combine keywords such as “OCT,” “OCTA,” “diabetic retinopathy,” and “deep learning.” Studies were selected based on criteria that included the use of OCT or OCTA in assessing DR or DME, providing statistical data on diagnostic accuracy and treatment response. The results indicate that OCT, particularly when paired with OCT Angiography (OCTA) and AI-driven analysis, significantly enhances the accuracy of detecting early microvascular changes in diabetic eyes. For instance, Zhang et al. (2021) found that OCTA could identify early retinal vascular alterations in diabetic patients with a sensitivity and specificity exceeding 90%. Additional findings reveal that OCT plays a crucial role in tracking disease progression and evaluating treatment efficacy, with improved visual outcomes observed in patients receiving anti-VEGF therapy monitored via OCTA. In conclusion, OCT has established itself as an invaluable tool in the management of DR and DME, enabling early diagnosis, precise monitoring, and tailored therapeutic interventions. Integrating artificial intelligence further augments OCT’s diagnostic capabilities, enhancing its potential to revolutionise diabetic eye care. However, accessibility and cost barriers remain challenges, emphasising the need for future research to focus on optimising AI models and expanding OCT accessibility in routine clinical settings.

Keywords: diabetic retinopathy; macular oedema; optical coherence tomography

How to cite (in APA style)
Taufiq, I., Muhith, A., Zahro, C., & Hasina, S. N. (2024). Role of Optical Coherence Tomography (OCT) in Macular Oedema and Diabetic Retinopathy (DR) Update; Systematic Literature Review. *Indonesian Journal of Global Health Research*, *6*(6), 4227-4236. https://doi.org/10.37287/ijghr.v6i6.4761.

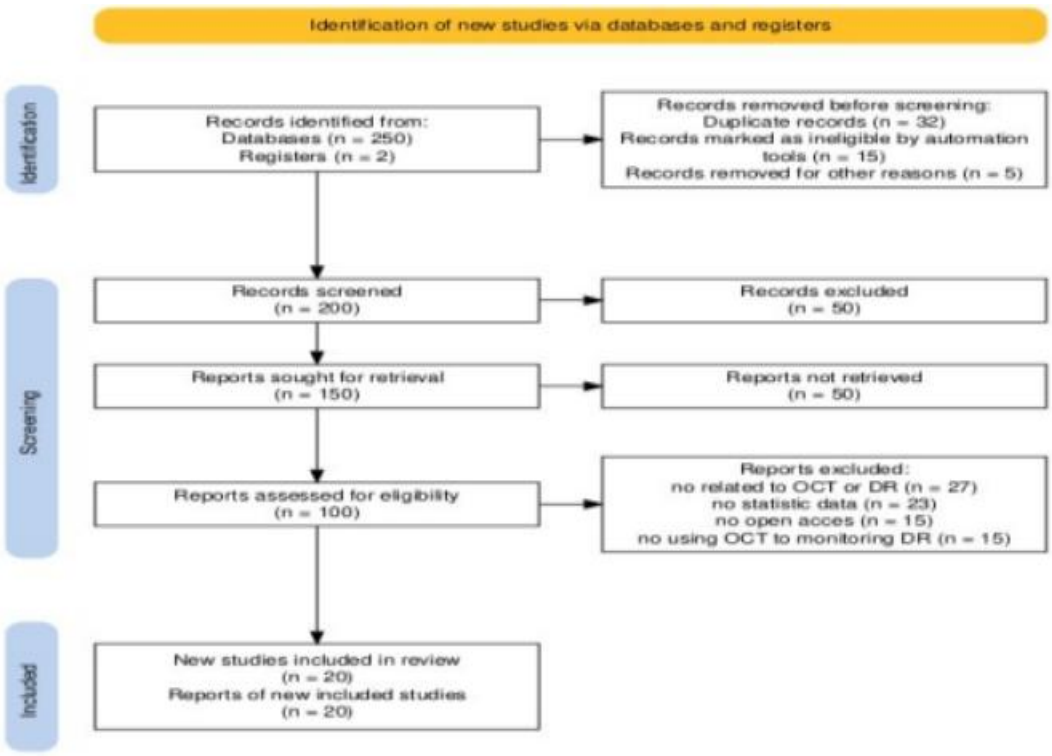
INTRODUCTION
Diabetic retinopathy (DR) and diabetic macular oedema (DME) are leading causes of blindness in diabetes, posing a significant global health problem. DR originates from diabetes-related damage to retinal blood vessels, beginning with non-proliferative changes like increased capillary permeability and mild retinal swelling. Without intervention, it can progress to proliferative retinopathy, marked by neovascularisation that risks severe haemorrhage and vision loss (Gao et al., 2024; Hamada et al., 2024). DME, a common complication of DR, involves fluid accumulation in the macula, leading to central vision impairment. Both conditions worsen with hyperglycaemia, which exacerbates vascular damage and fluid leakage (Velaga et al., 2024). Optical Coherence Tomography (OCT)

advancements have revolutionised DR and DME diagnosis and monitoring by enabling non-invasive microstructural retinal imaging. OCT aids in early disease detection and treatment evaluation, providing a reliable tool for assessing disease progression and response to therapy. The integration of deep learning and automated OCT analysis further enhances diagnostic speed and accuracy, potentially improving retinopathy screening. This review evaluates OCT's impact on managing DR and DME, with a focus on the role of emerging technologies like artificial intelligence (AI) and Optical Coherence Tomography Angiography (OCTA) in improving clinical outcomes (Ahmed et al., 2024; Sandhu et al., 2020). This systematic literature review aims to evaluate the role of OCT in detecting, monitoring and predicting the prognosis of patients with DR and DME. Through advances in retinal imaging and the utilization of AI, this review will also examine the latest trends in research related to the use of OCT as a biomarker in the management of DR and DME, and highlight the role of OCT Angiography (OCTA) in improving clinical outcomes in the future.

METHOD

A comprehensive literature search was conducted in Scopus, Scholar, and PubMed using Boolean operators ("AND," "OR," and "AND NOT") with keywords such as "OCT," "OCTA," "Optical Coherence Tomography," "diabetic retinopathy," "deep learning," and "automated diagnosis." Only studies published in reputable journals from 2020 to 2024 were included. In the identification phase, 252 records were retrieved (250 from databases and 2 from registers). After removing 32 duplicates, 15 records excluded by automated tools, and 5 others for various reasons, 200 records proceeded to screening. Of these, 50 were removed based on relevance, leaving 150 records for retrieval. Despite efforts, 50 reports were unavailable, narrowing the pool to 100 for detailed eligibility assessment. Among these, 27 studies unrelated to OCT or DR, 23 lacking statistical data, 15 without open access, and 15 not using OCT for DR monitoring were excluded. This rigorous process resulted in a final selection of 20 studies, providing a focused basis for in-depth analysis of OCT's role in DR monitoring.

Inclusion Criteria: 1) Studies involving patients with diabetic retinopathy, both with and without macular edema. 2)Studies that use OCT or OCTA for the purpose of diagnosis, monitoring disease progression, or assessing response to treatment. 3)Studies that provide quantitative data regarding changes in the retina or choroid, accuracy of diagnosis, or response to therapy. **Exclusion Criteria: 1)**Studies that did not directly use OCT or OCTA for diabetic retinopathy. 2)Publications in the form of reviews, opinions, or studies that do not present quantitative results. 3)Studies that focus more on other retinal conditions or imaging techniques that are not relevant to the research objectives. From each study, data regarding the study design, sample size, OCT methodology, main findings, and statistical significance were extracted. The results of the studies were organized in structured tables that summarized the findings based on the categories of diagnostic accuracy, disease monitoring, and therapeutic effectiveness.



Picture 1. Prism Flow Chart

RESULT

Table 1.
Data Distraction Method

No.	Researcher(s), Year, and Study Title	Design, Sample, Variables, Intervention, and Analysis	Final Result
1	(Ashrafkhorasani et al., 2024)- Spectral-domain OCT characteristics of intraretinal hyper-reflective foci associated with age-related macular degeneration and diabetic retinopathy	Design: Retrospective observational study Sample: 54 eyes on treatment (27 diabetic retinopathy (DR) and 27 age-related macular degeneration (AMD)) Variables: - Dependent: Intraretinal hyper-reflective foci (IHRF) characteristics - Independent: OCT technology Intervention: Segmentation of IHRF on B-scan OCT Analysis: There were 1149 IHRFs identified, with 39 ± 36 lesions in DR eyes compared to 4 ± 4 in AMD eyes ($p < 0.001$).	IHRF lesions in DR eyes tend to be larger and less hyper-reflective compared to AMD eyes.
2	(Tsuboi et al., 2024) - Early Sign of Retinal Neovascularization Evolution in Diabetic Retinopathy: A Longitudinal OCT Angiography Study	Design: Retrospective longitudinal study; Sample: 71 eyes with diabetic retinopathy (DR); Variables: Dependent: Retinal neovascularization (RNV); Independent: OCT and OCTA technology; Intervention: OCT and OCTA imaging; Analysis: Of 71 eyes, 20 eyes (28%) had RNV identified, with 38 sprout RNV and 26 frond RNV. 50% of eyes showed progression of RNV. Age was younger ($P = 0.014$) and less likely to be treated ($P = 0.07$) than eyes without progression.	The combination of OCT and OCTA can identify early forms of RNV before it can be recognized in en face OCTA, with 50% of eyes having RNV progression in follow-up.
3	(Velaga et al., 2024) - OCT outcomes as biomarkers for disease status, visual function, and prognosis in diabetic macular edema	Design: Longitudinal Prospective. Sample: 71 eyes of 71 patients with untreated DME. Independent Variables: OCT results (DRIL area, EZ integrity, SRF, IRF). DRIL area and extent were significantly reduced (-3.0 mm², $p < 0.001$ and -775.8 mm, $p < 0.001$), positively correlating with BCVA improvement ($r = -0.40$, $p = 0.003$ and $r = -0.30$, $p = 0.04$, respectively).	DRIL area and DRIL extent are shown to be novel biomarkers for assessing DME status, visual function, and prognosis. .

No.	Researcher(s), Year, and Study Title	Design, Sample, Variables, Intervention, and Analysis	Final Result
4	(Remolí Sargues et al., 2024) - Optical coherence tomography angiography analysis of choroidal microvasculature in various forms of diabetic macular edema	Design: Retrospective Sample: 53 patients with diabetic macular edema (DME). Variables: Dependent: Choroidal microvasculature; Independent: OCTA technology Intervention: OCTA choroidal imaging Analysis: Vascular density (VD) in the choriocapillaris (CC) and superficial capillary plexus (SCP) was significantly higher in patients with early DME than patients with advanced DME (P value < 0.01).	CC ischemia plays an important role in the pathogenesis of DME. Studies have shown decreased CC VD in patients with severe DME, and deep retinal layer disorganization (DRIL).
5	(Wijesingha et al., 2024) - Optical Coherence Tomography Angiography as a Diagnostic Tool for Diabetic Retinopathy	Design: Literature Review Sample: 159 articles reviewed Variables: Dependent: Detection of diabetic retinopathy (DR); Independent: OCTA technology Intervention: Use of OCTA in the diagnosis and management of DR Analysis: OCTA demonstrated effectiveness in visualizing the retinal microvasculature and detecting early microvascular changes that precede clinical signs of DR.	OCTA is proven to be a rapid and non-invasive alternative to FFA in the diagnosis and management of DR, and shows great potential to improve clinical outcomes in the management of DR.
6	(Hamada et al., 2024) - Practical Utility of Widefield OCT Angiography to Detect Retinal Neovascularization in Eyes with Proliferative Diabetic Retinopathy	Design: Retrospective cross-sectional study; Sample: 114 eyes from 57 patients with suspected PDR; Variables: Dependent: RNV detection; Independent: WF-OCTA technology; Intervention: WF-OCTA imaging. Analysis: 95% sensitivity and 88% specificity for detecting eyes with RNV.	Widefield OCT angiography showed a high success rate, achieving 95% sensitivity for detecting eyes with RNV in real clinical practice.
7	(L. Wang et al., 2024) - Optical coherence tomography image recognition of diabetic retinopathy based on deep transfer learning	Design: Cross-sectional analysis Sample: 103 patients with Diabetic Retinopathy (DR). Variables: Dependent: Recognition of diabetic retinopathy; Independent: Deep transfer learning technology Intervention: OCT image recognition Analysis: VGG19 and DenseNet models showed better segmentation performance after transfer learning compared to models without transfer learning.	The neural network model utilizing deep transfer learning showed significant improvement in DR recognition ability based on OCT images in clinical practice.
8	(Gao et al., 2024) - Comparative study of the vascular structures of the retina and choroid in Chinese Han and Uygur Sample s with proliferative diabetic retinopathy: An OCTA study	Design: Comparative analysis Sample: 53 eyes of 40 proliferative diabetic retinopathy (PDR) patients (20 from Han and 20 from Uygur), 53 healthy volunteers (25 from Han and 28 from Uygur). Variables: Dependente: Choroidal thickness (CT) and retinal vascular density of Han and Uygur races ; Independent: swept-source OCTA (SS-OCTA). Intervention: Swept-source OCTA (SS-OCTA) analysis. for retinal and choroidal parameters Analysis: PDR showed significantly lower CT and reduced vessel density compared to controls, with more severe choroidal damage in Uygur PDR patients than Han.	PDR patients from Han and Uygur showed significantly lower CT and reduced vessel density compared to controls, but Uygur PDR patients had more severe choroidal damage than Han patients, which is likely associated with a worse visual prognosis.
9	(Massengill et al., 2024) - Response of Diabetic Macular Edema to Anti-VEGF Medications Correlates with Improvement in Macular Vessel	Design: Retrospective study Sample: 41 eyes from 30 patients with DME, mean age 58.83 ± 11.71 years Variables: Dependent: Blood vessel diameter, perfusion density, vessel length; Independent: Anti-VEGF injection Intervention: Intravitreal injection of anti-VEGF Analysis: 2-way ANOVA followed by linear trend test and	Intravitreal injection of anti-VEGF agents improved retinal vascular microstructure parameters evident on OCTA examination at 3 to 9 months, with the most

No.	Researcher(s), Year, and Study Title	Design, Sample, Variables, Intervention, and Analysis	Final Result
	Architecture Measured by OCT Angiography	Tukey's multiple comparison test were used to determine statistical significance, with P value <0.05 considered significant.	pronounced effects in eyes with increased BCVA and CST.
10	Akpinar, M. H., Sengur, A., Faust, O., Tong, L., Molinari, F., & Acharya, U. R. (2024). Artificial Intelligence in Retinal Screening Using OCT Images: A Review of the Last Decade (2013-2023). *Computer Methods and Programs in Biomedicine*, 108253.	Design: Systematic Review Sample: 76 articles from 1787 publications Variables: - Dependent: Eye disease detection - Independent: AI techniques (ML and DL) Intervention: Use of OCT images Analysis: AI techniques can accurately detect various eye diseases and structural changes.	This research shows that AI methods, particularly deep learning, can improve the quality and reliability of diagnostic processes for eye diseases
11	(Zhang et al., 2021) - Early detection of microvascular impairments with optical coherence tomography angiography in diabetic patients without clinical retinopathy: a meta-analysis	Design: Systematic review and meta-analysis Sample: 2241 diabetic eyes without diabetic retinopathy (NDR) and 1861 healthy eyes. Variables: Dependent: Retinal microvasculature; Independent: OCTA technology Intervention: OCTA imaging Analysis: Weighted mean differences and 95% confidence intervals were used to assess the strength of the association.	Our results suggest that retinal microvascular disorders may have occurred before clinically apparent diabetic retinopathy and can be detected early with OCTA.
12	(Elgafi et al., 2022) - Detection of diabetic retinopathy using OCT image	Design: Cross-sectional Study Sample :100 patients Variables: Dependent: Diabetic retinopathy indicators; Independent: OCT imaging Intervention: OCT image detection Analysis: Based on the gradient information, the retinal layers in the optical coherence tomography image are segmented automatically.	The high-resolution retinal OCT image provides the information about the retina which is useful in the diagnosis and deciding the treatment of diabetic retinopathy.
13	(Schwartz et al., 2020) - Objective evaluation of proliferative diabetic retinopathy using OCT	Design: Retrospective, observational case series; Sample: 47 eyes of 35 patients with proliferative diabetic retinopathy (PDR); Variables: Dependent: Disc neovascularization (NVD) and neovascularization elsewhere (NVE); Independent: OCT and OCT angiography technology (OCTA); Intervention: Standardized PDR protocol using OCT and OCTA; Analysis: Structural OCT had the highest detection rate (100%) for NVD and new NVE, while B-scan OCTA had the highest detection rate (100%) for regression or reactivation of neovascularization.	This study demonstrates the benefits of novel multimodal imaging in the management of PDR patients... the best detection rate for NV, and B-scan OCTA showed the greatest potential for objective monitoring of disease after treatment.
14	(Sandhu et al., 2020) - Automated diagnosis of diabetic retinopathy using clinical biomarkers, optical coherence tomography, and optical coherence	Design: Cross-sectional image analysis and machine learning study. Sample: 111 patients with diabetes mellitus II (DM II) (36 without DR, 53 with mild NPDR, and 22 with moderate NPDR). Variables: Dependent: NPDR diagnosis; Independent: Clinical data and OCT/OCTA images. Interventions: Use of machine learning techniques for data analysis. Analysis: Diagnostic accuracy using OCT	Combining general clinical data with OCT and OCTA data increases the power of computer-assisted diagnosis for NPDR.

No.	Researcher(s), Year, and Study Title	Design, Sample, Variables, Intervention, and Analysis	Final Result
	tomography angiography	images alone was 76%; when combining OCT and OCTA data, accuracy reached 92%.	
15	(Ghazal et al., 2020) - Early detection of diabetics using retinal OCT images	Design: Classification analysis based on computer-aided diagnosis (CAD). Sample: 5 patients (2 normal and 3 diabetic) Variables: Dependent: Diabetes detection Independent: Retinal thickness, reflectivity, and curvature. Intervention: Feature measurement of 12 segmented retinal layers using Random Forest (RF). Analysis: Evaluation of accuracy, sensitivity, specificity, and AUC of feature classification.	Results showed good classification performance with 80% accuracy, 100% sensitivity, and 50% specificity for all features potential to be used in early diabetes detection.
16	(Sharafeldeen et al., 2021) - Precise higher-order reflectivity and morphology models for early diagnosis of diabetic retinopathy using OCT images	Design: Cross-sectional Analysis Sample: 130 patients (260 OCT images) Variables: Dependent: Diabetic Retinopathy (DR); Independent: OCT morphology and reflectivity markers. Intervention: computer-aided diagnosis (CAD) Analysis: Using support vector machine (SVM) classifiers and backpropagation neural networks (BNN) for diagnosis,	The proposed CAD system shows better performance in diagnosing DR compared to other machine learning method incorporation approaches. The AUC of the system shows high accuracy for detecting DR
17	(Marina, Barraso et al., 2020) - Optical Coherence Tomography Angiography in Type 1 Diabetes Mellitus. Report 1: Diabetic Retinopathy	Design: Prospective analysis Sample: 478 patients with type 1 diabetes and 115 controls Variables: - Dependent: OCT and OCTA parameters - Independent: HbA1c level Intervention: OCT and OCTA measurements Analysis: DM-no DR patients with HbA1c > 7.5% showed lower vascular density (VD) than DM-DR patients and controls (20.16 vs. 20.22 vs. 20.71, $p < 0.05$).	Higher HbA1c levels were associated with changes in OCTA in DM-no DR patients, and with changes in OCT structure in DM-DR patients.
18	(Borrelli et al., 2021) - Optical Coherence Tomography Angiography in Diabetes	Design: Cross-sectional analysis Sample: 20 patients (20 eyes) with diabetic retinopathy. Variables: Dependent: Microaneurysms Independent: OCTA technology Intervention: 3D OCTA Imaging Analysis: showed that 70% of microaneurysms were connected with two vessels, and the majority of microaneurysms were located in the inner nucleus layer (INL).	OCTA has provided better characterization of vascular changes in diabetes, with 3D analysis displaying microaneurysms that resemble histopathological representations.
19	(Chua et al., 2020) - Optical Coherence Tomography Angiography in Diabetes and Diabetic Retinopathy	Design: Cross-sectional analysis; Sample: 196 DR-related articles; Variables: Dependent: Retinal microvasculature changes; Independent: OCTA technology; Intervention: Choroidal OCTA imaging; Analysis: OCTA effectively quantifies retinal microvasculature changes and can be used as an objective tool for DR classification.	OCTA technology holds promise for progression monitoring and early detection of diabetic retinopathy (DR)...
20	(Szeto et al., 2021) - OCT-based biomarkers for predicting treatment response in eyes with center-involved diabetic macular oedema treated with anti-VEGF injections	Design: Retrospective cohort study Sample: 196 eyes with diabetic macular oedema (DMO) that received anti-VEGF injection. Variables: - Dependent: Visual acuity (VA) - Independent: Spectrum-based OCT biomarkers Intervention: Evaluation of SD-OCT biomarkers before and after anti-vascular endothelial growth factors (VEGF) treatment.	in eyes with DMO treated with anti-VEGF injection. The proposed SD-OCT-based system can be used in real eye clinics to improve decision-making in DMO management.

No.	Researcher(s), Year, and Study Title	Design, Sample, Variables, Intervention, and Analysis	Final Result
		Analysis: Relationship between baseline biomarkers and changes with visual acuity after treatment.	

DISCUSSION

Studies demonstrate that OCT and OCTA are effective in detecting early microvascular changes in diabetic patients, even before clinical symptoms of retinopathy appear. Zhang et al., (2021) showed that OCTA can identify early vascular changes, allowing for preventive interventions, while Sandhu et al., (2020) used OCTA with biomarkers to improve automated diagnosis accuracy through deep learning models. OCT also facilitates monitoring disease progression, as Tsuboi et al., (2024) observed that OCTA could detect early retinal neovascularization, and Velaga et al., (2024) found correlations between OCT biomarkers and visual function in diabetic macular edema. OCT is instrumental in assessing treatment response, particularly for anti-VEGF therapies. Massengill et al., (2024) linked improvements in macular vessel architecture to positive responses to anti-VEGF, and Hamada et al.,(2024) highlighted widefield OCTA's utility in guiding treatment decisions for proliferative diabetic retinopathy. Advances in AI and deep learning are enhancing OCT's diagnostic and prognostic accuracy, as shown by Wang et al., (2022) and Akpinar et al. (2024), with AI models significantly improving early detection and monitoring capabilities.

Consequently, these results underscore the importance of OCT in various aspects of diabetic retinopathy management namely early detection, monitoring progression and response to therapy. OCT angiography (OCTA) is a non-invasive imaging technique that allows for visualization of the superficial and deep plexus vessels within retinal and choroidal vasculature, providing valuable information on early changes in diabetic retinopathy that may not be seen with traditional imaging (Ahmed Khalil et al., 2021; Ashrafkhorasani et al., 2024). Deep learning and automated OCT analysis have greatly enhanced diagnostic performance, which provides the possibility of efficient screening especially in settings with few specialists (Sandhu et al., 2020; David et al., 2020). Adapting treatment plans to specific retinal biomarkers may ultimately lead to better clinical outcomes from OCT predictive capabilities (Massengill et al., 2024; Velaga et al., 2024). However, there are still barriers such as the expensive and limited availability of OCT technology and the lack of validation of models using AI methods in diverse populations (Gao et al., 2024; Schwartz et al., 2020). These studies indicate that clinical AI model optimization and expanding global access to OCT technology are now natural next steps for future research (Hamada et al., 2024; Wijesingha et al., 2024).

CONCLUSION

Optical Coherence Tomography (OCT) has an important role in the management of diabetic retinopathy, including its use for early diagnosis. OCT technology, when operated by a clinician or allied staff working in tandem with the equipment and experts could improve diagnosis and access to care tremendously. The systematic literature summary highlights the influence of OCT on subscriber care as evidenced by the utility of this system in treatment tailoring. Artificial intelligence enhances diagnostic accuracy, and innovations such as widefield OCTA and longitudinal tracking facilitate more personalized management. These findings confirm the position of OCT as a key tool in the management of diabetic retinopathy, from early intervention to further monitoring and evaluation of therapy.

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