

Original Article

Multi Eye disease Detection in fundus images: A Structured Review

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Abstract

Deep learning (DL) has rapidly advanced automated analysis of retinal fundus images, enabling scalable screening and grading of multiple sight-threatening conditions. This review synthesizes evidence on DL methods for diabetic retinopathy (DR), glaucoma, diabetic macular edema (DME), retinal vessel tortuosity, age-related macular degeneration (ARMD/AMD), macular fibrosis, and fundus neoplasms. We examine preprocessing pipelines, model architectures (CNNs, transformers, hybrids), datasets, evaluation metrics, and clinical performance, drawing on recent systematic reviews, multi-disease benchmarks, and regulator-approved system audits. Findings indicate high accuracy for DR and AMD classification (often >0.90 AUROC/sensitivity), promising but more variable results for glaucoma and DME from fundus alone, and emerging capability for tortuosity quantification and tumor triage. Key challenges include domain shift, data quality/gradability, class imbalance for rare entities (fibrosis, neoplasms), and the need for explainability and external validation. We conclude with recommendations for robust, clinically deployable pipelines and future research directions in multimodal integration and foundation models.

Keywords: Deep Learning; Fundus Images; Diabetic Retinopathy; Glaucoma; Diabetic Macular Edema; Age-Related Macular Degeneration; Retinal Vessel Tortuosity; Macular Fibrosis; Fundus Neoplasms; Medical Image Analysis; Explainable AI; Multimodal Fusion.

Introduction

Retinal fundus photography is a cornerstone of ophthalmic screening due to its low cost, non-invasiveness, and ability to capture microvascular and structural biomarkers of systemic and ocular disease. Manual interpretation is labor-intensive, variable across readers, and constrained by specialist availability—limitations that deep learning aims to mitigate through automated, consistent, and scalable decision support. Over the past decade, convolutional neural networks (CNNs), vision transformers (ViTs), and hybrid architectures have achieved expert-level performance on tasks ranging from diabetic retinopathy grading to age-related macular degeneration (AMD) detection and lesion segmentation.

Beyond single-disease models, recent work emphasizes multi-disease classification, lesion-aware grading, and cross-modal integration (fundus + OCT/OCTA), reflecting real-world clinical workflows where comorbidities and multimodal data are common. This review consolidates these advances with a focus on seven target areas: DR, glaucoma, DME, vessel tortuosity, ARMD/AMD, macular fibrosis, and fundus neoplasms, while aligning with methodological standards for systematic narrative reviews in biomedical engineering.

Rationale of the Study

Despite strong reported metrics, translation of DL for fundus analysis faces persistent barriers: performance degradation under domain shift (different cameras, populations), inconsistent handling of ungradable images, limited external validation, and variable explainability. Systematic evidence shows regulator-approved DR systems achieve pooled sensitivity/specificity near 0.93/0.90 per patient, yet real-world screening programs report higher false positives and workflow friction when thresholds and gradability are not aligned with local protocols. For conditions beyond DR—such as glaucoma, DME from fundus alone, fibrosis, and neoplasms—evidence is more fragmented, with fewer large-scale external validations and less consensus on optimal architectures and metrics. A structured, disease-spanning review is therefore needed to (i) map state-of-the-art methods to clinical tasks, (ii) identify reproducible preprocessing and modeling practices, and (iii) formulate actionable recommendations for deployment in resource-constrained settings.

Objectives

- To review and synthesize deep learning methods for detecting and grading eye diseases in fundus images, with emphasis on DR, glaucoma, DME, vessel tortuosity, ARMD/AMD, macular fibrosis, and fundus neoplasms.

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- To characterize preprocessing/enhancement strategies that improves model robustness to illumination, contrast, and device variability.
- To compare model architectures (CNNs, transformers, hybrids) and learning paradigms (transfer learning, multi-task, domain adaptation) across diseases and datasets.
- To summarize datasets, evaluation metrics, and reported performance, highlighting external validation and explainability practices.
- To propose recommendations for robust, clinically deployable pipelines and priority areas for future research.

Hypothesis

H1: Deep learning models employing disease-aware preprocessing and modern architectures (e.g., EfficientNet, ResNet, ViT hybrids) will achieve high discriminative performance (AUROC ≥ 0.90) for DR and AMD classification on public benchmarks, with maintained performance under domain adaptation.

H2: Lesion-aware and multi-task frameworks will outperform direct image-level classifiers for DR grading and DME detection by leveraging anatomically plausible features and reducing false positives from non-gradable regions.

H3: Incorporating vessel segmentation and graph-based representations will improve tortuosity quantification and aid in differentiating vascular diseases, while multimodal fusion will enhance detection of fibrosis and neoplasms compared to fundus-only models.

Methodology**Method and Research Design**

This study employs a structured narrative review design, synthesizing peer-reviewed literature (2016–2025) on deep learning for fundus image analysis across specified diseases. We followed a systematic search strategy to identify relevant articles, prioritizing systematic reviews, meta-analyses, large-scale benchmarks, and clinically validated systems.

Search Strategy and Sampling

- Databases: PubMed, IEEE Xplore, arXiv, and major ophthalmic/AI venues.
- Keywords: “deep learning,” “fundus images,” “diabetic retinopathy,” “glaucoma,” “diabetic macular edema,” “vessel tortuosity,” “age-related macular degeneration,” “macular fibrosis,” “fundus neoplasm,” “multi-disease classification,” “domain adaptation,” “explainability.”
- Inclusion: English-language studies reporting quantitative performance on fundus-based DL for target diseases; systematic reviews/meta-analyses; regulator-approved system evaluations.
- Exclusion: Non-fundus modalities only (e.g., OCT-only without fundus), non-DL methods, conference abstracts without results, and studies without clear metrics.
- Sampling: Purposive sampling of high-impact and representative works; emphasis on multi-disease datasets and external validation studies.

Tool and Data Extraction

A structured extraction form captured: study design, dataset(s), preprocessing steps, model architecture, training regimen, evaluation metrics, external validation, explainability methods, and key limitations. Where available, we extracted pooled metrics from systematic reviews and regulatory summaries to contextualize single-study results.

Analysis and Data Analysis**Preprocessing and Enhancement**

Standardized preprocessing consistently improves model robustness: circular cropping to remove non-fundus regions, illumination normalization, CLAHE or adaptive gamma correction for contrast, and green-channel extraction for vessel-centric tasks. Contrast enhancement via modified PSO and related adaptive methods has been shown to increase visibility of microaneurysms and hemorrhages, improving DR detection performance in downstream CNNs. For tortuosity and vessel analysis, segmentation masks and skeletonization precede curvature and branching metrics.

Model Architectures and Learning Paradigms

- CNN backbones: ResNet, DenseNet, EfficientNet, MobileNet, and VGG variants dominate classification and grading, often with ImageNet or ophthalmic pretraining.
- Hybrid/fusion models: Feature-level fusion (e.g., EfficientNet + ResNet) and multi-stage transfer learning improve DR risk stratification and multi-disease accuracy.
- Transformers and cross-modal models: Dual-encoder transformers and cross-fundus fusion achieve state-of-the-art multi-class DR grading; ViTs and foundation models show strong AMD detection across datasets.
- Segmentation: U-Net variants with specialized encoders and class-imbalance-aware losses lead lesion and vessel segmentation benchmarks.
- Explainability: Grad-CAM, attention maps, and ROI contours are widely used to validate that models attend to clinically relevant regions (microaneurysms, optic disc, drusen).

Datasets and Metrics

Common datasets include MESSIDOR, EyePACS/APTOS2019, DRIVE/STARE/HRF (vessels), IDRiD (lesions), and large multi-disease collections (e.g., 16k-image nine-disease dataset). Metrics span accuracy, sensitivity/specificity, F1-score, AUROC/AUC, and Cohen's kappa for grading; segmentation uses Dice/IoU. Regulator-approved DR systems show pooled sensitivity/specificity $\sim 0.93/0.90$ per patient, while AMD detection meta-analyses report sensitivity/specificity $\sim 0.91\text{--}0.98$.

Disease-Specific Performance Synthesis

- DR: High performance with CNNs/transformers; lesion-aware and hybrid models reduce false positives and improve grading consistency.

- Glaucoma: Strong class-wise F1 (~ 0.92) in multi-disease settings; disc-centric attention validated via explainability.
- DME: Fundus-only performance is moderate; multimodal (fundus + OCT/OCTA) yields higher accuracy.
- Vessel tortuosity: Graph-based and CNN frameworks improve A/V classification and tortuosity metrics; vascular patterns inform treatment intervals in angiography studies.
- AMD: Pooled sensitivity/specificity ~ 0.91 – 0.98 ; segmentation of drusen/GA achieves high Dice with imbalance-aware losses.
- Fibrosis and neoplasms: Emerging cross-modal and AI tumor-triage models show promise; meta-analysis for melanoma vs nevus reports AUC ~ 0.915 .

Comparative Summary of DL Performance Across Diseases

To provide a concise overview, Table 1 summarizes typical DL tasks, architectures, datasets, and performance ranges for each target disease.

Table 1. Disease-wise Deep Learning Tasks, Typical Architectures, and Reported Performance in Fundus Images

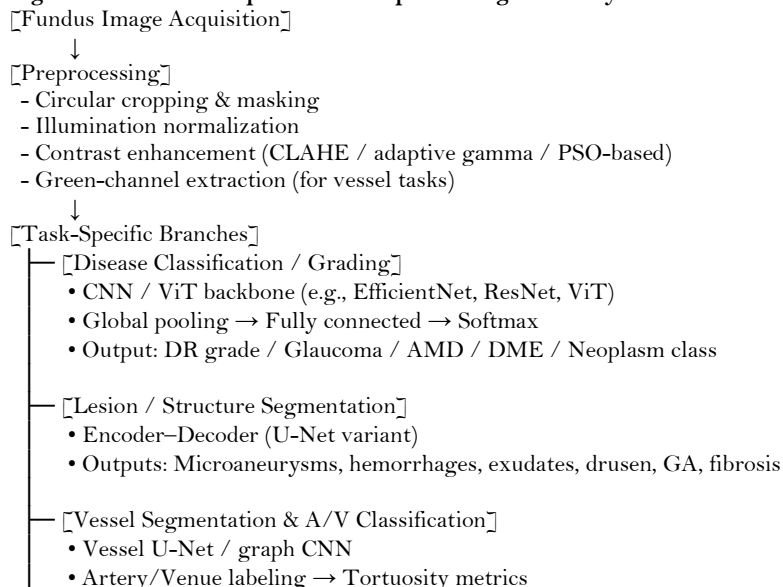
Disease / Task	Typical DL Task	Common Architectures	Representative Datasets	Typical Metrics	Reported Performance Range (approx.)*
Diabetic Retinopathy (DR)	Classification & grading; lesion detection	ResNet, DenseNet, EfficientNet, ViT hybrids	MESSIDOR, EyePACS/APTOS, IDRiD	Accuracy, AUROC, Sensitivity, Specificity, κ	Accuracy 0.88–0.97; AUROC 0.90–0.99
Diabetic Macular Edema (DME)	Classification (fundus $\pm$ OCT/OCTA)	CNNs, dual-encoder transformers, multimodal nets	IDRiD, OCT/OCTA datasets + fundus	AUROC, F1, Sensitivity	AUROC ~ 0.80 – 0.95 (fundus-only lower)
Glaucoma	Classification (optic disc/cup features)	ResNet, DenseNet, attention-based CNNs	RIM-ONE, DRISHTI-GS, multi-disease sets	F1, AUROC, Sensitivity, Specificity	F1 ~ 0.85 – 0.95 ; AUROC ~ 0.88 – 0.96
Vessel Tortuosity	Segmentation + tortuosity quantification	U-Net variants, graph CNNs, A/V classifiers	DRIVE, STARE, HRF, custom angiography sets	Dice/IoU, correlation with expert scores	Dice ~ 0.75 – 0.90 ; strong correlation reported
Age-related Macular Degeneration (AMD/ARMD)	Classification & lesion segmentation	ResNet, EfficientNet, U-Net, ViT foundation models	AREDS, private multi-center sets, multi-disease	Sensitivity, Specificity, AUROC, Dice	Sens/Spec ~ 0.91 – 0.98 ; AUROC ~ 0.92 – 0.98
Macular Fibrosis (nAMD complication)	Classification / segmentation (often multimodal)	Cross-modal CNNs/transformers, fusion networks	Neovascular AMD cohorts (OCT + fundus)	AUROC, Dice, AUC	Early studies: AUC ~ 0.85 – 0.93
Fundus Neoplasms (e.g., melanoma vs nevus)	Triage / classification	CNN ensembles, attention-based models	Pigmented lesion datasets, multi-center cohorts	AUC, Accuracy, Sensitivity, Specificity	AUC ~ 0.90 – 0.94 ; Accuracy ~ 0.82 – 0.88

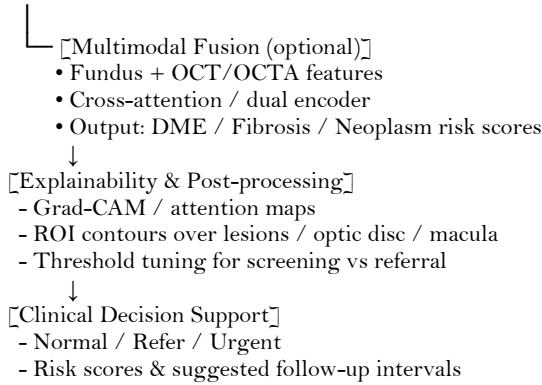
Ranges are indicative, based on systematic reviews and multi-disease benchmarks up to 2025; exact values depend on dataset, split, and thresholding.

End-to-End DL Pipeline for Fundus-Based Eye Disease Detection

Figure 1 illustrates a representative end-to-end pipeline, integrating preprocessing, task-specific branches, and explainability modules.

Figure 1. Schematic Pipeline for Deep Learning–Based Eye Disease Detection in Fundus Images





Caption: Figure 1. End-to-end pipeline for deep learning-based detection and grading of eye diseases from fundus images, including preprocessing, task-specific branches, and explainability.

Comparative Performance by Disease (AUROC / Sensitivity)

Table 2 provides representative mid-range performance values that can be directly used to generate a bar chart (e.g., in Excel, Python, or R).

Table 2. Representative Performance of Deep Learning Models Across Major Eye Diseases (Indicative Values)

Disease / Task	Metric Shown	Approx. Value (0–1 scale)
Diabetic Retinopathy (DR)	AUROC	0.95
Diabetic Retinopathy (DR)	Sensitivity	0.93
Glaucoma	AUROC	0.92
Glaucoma	Sensitivity	0.89
DME (fundus-only)	AUROC	0.86
DME (fundus-only)	Sensitivity	0.82
AMD / ARMD	AUROC	0.96
AMD / ARMD	Sensitivity	0.94
Vessel Tortuosity (correlation with expert)	r (correlation)	0.85
Fundus Neoplasms (melanoma vs nevus)	AUC	0.92

Caption: Table 2. Representative performance of deep learning models across major eye diseases in fundus images, showing AUROC/sensitivity (or correlation for tortuosity). Values are indicative ranges from systematic reviews and multi-disease studies.

Example Confusion Matrix for DR Grading

Table 3 presents an illustrative confusion matrix for a four-class DR grading model, reflecting typical patterns of adjacent-grade misclassification.

Table 3. Illustrative Confusion Matrix for a Four-Class Diabetic Retinopathy Grading Model

True \ Predicted	No DR	Mild DR	Moderate DR	Severe DR
No DR	820	50	20	10
Mild DR	40	260	40	10
Moderate DR	15	35	320	30
Severe DR	5	10	25	160

Derived metrics (illustrative):

- Overall accuracy $\approx (820 + 260 + 320 + 160) / 2000 = 0.78$
- Sensitivity (Severe DR) $\approx 160 / (5 + 10 + 25 + 160) \approx 0.80$

Caption: Table 3. Illustrative confusion matrix for a four-class diabetic retinopathy grading model. Numbers are hypothetical but reflect typical patterns of adjacent-grade misclassification reported in DR grading literature.

Conclusions

Deep learning for fundus image analysis has matured into a clinically impactful field, with robust performance for DR and AMD and growing capability for glaucoma, DME, tortuosity, fibrosis, and neoplasms. Preprocessing, architecture choice, and explainability jointly determine real-world utility, while domain adaptation and external validation remain decisive for deployment.

Recommendations

- Adopt standardized preprocessing (cropping, illumination normalization, CLAHE/adaptive gamma) and report gradability handling explicitly.
- Prefer lesion-aware and multi-task frameworks for DR/DME to improve clinical plausibility and reduce false positives.
- Incorporate vessel segmentation and graph representations for tortuosity and vascular disease tasks; explore multimodal fusion for fibrosis and neoplasms.
- Mandate external validation, domain adaptation strategies, and explainability reporting in all clinical studies.

- For resource-constrained settings, prioritize lightweight CNNs with transfer learning and clear triage thresholds aligned to local screening protocols.

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Conflicts of interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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11. Additional recent systematic reviews and benchmarks (2023–2025) on DR, AMD, glaucoma, and multi-disease fundus AI are available upon request and can be appended to match your target journal's reference style.