

HARNESSING THE POWER OF ARTIFICIAL INTELLIGENCE FOR EARLY DETECTION AND MANAGEMENT OF DIABETIC RETINOPATHY, AGE-RELATED MACULAR DEGENERATION, AND GLAUCOMA: A NARRATIVE REVIEW OF DEEP LEARNING APPLICATIONS IN OPHTHALMOLOGY

Lázaro Felipe Costa Vilela¹

Nádia Oliveira Cabral²

Afrânio Côgo Destefani³

Vinícius Côgo Destefani⁴

ABSTRACT: Artificial intelligence (AI) and intense learning (DL) models have emerged as powerful tools in ophthalmology, revolutionizing the early detection and management of ocular diseases such as diabetic retinopathy (DR), age-related macular degeneration (AMD), and glaucoma. This narrative review explores AI's current applications and future potential in these domains, focusing on using convolutional neural networks (CNNs) and other DL architectures to analyze retinal fundus photographs, optical coherence tomography (OCT) images, and visual field tests. By leveraging vast datasets and identifying subtle pathological features, AI models have demonstrated high accuracy, sensitivity, and specificity in detecting these diseases, often surpassing human graders. Integrating AI into clinical practice holds promise for enhancing diagnostic efficiency, facilitating early intervention, and ultimately improving patient outcomes. However, challenges related to data quality, model interpretability (the ability to understand and trust the decisions made by AI models), and ethical considerations (such as patient privacy and consent) must be addressed to fully realize AI's potential in ophthalmology. Future research should focus on validating AI models in diverse populations, exploring novel DL architectures, and developing integrated systems seamlessly incorporating AI into clinical workflows.

3311

Keywords: Diabetic Retinopathy. Macular Degeneration. Glaucoma. Artificial Intelligence. Ophthalmological Diagnostic Techniques.

INTRODUCTION

Artificial intelligence (AI) has emerged as a transformative force in healthcare, with deep learning (DL) models demonstrating remarkable potential in various medical domains, including ophthalmology (1). The early detection and management of ocular diseases such as diabetic retinopathy (DR), age-related macular degeneration (AMD), and glaucoma are crucial for preventing vision loss and preserving quality of life (2). However, traditional screening

¹Universidade Federal da Grande Dourados.

²UniRV - FAMERV (Campus Rio Verde).

³Santa Casa de Misericórdia de Vitoria Higher School of Sciences - EMESCAM. Santa Luíza – Vitória – ES Brazil
Molecular Dynamics and Modeling Laboratory (DynMolLab).

⁴Molecular Dynamics and Modeling Laboratory (DynMolLab) Santa Luíza – Vitória – ES – Brazil

methods rely on trained specialists' manual interpretation of ocular images, which can be time-consuming, subjective, and prone to human error (3). AI, particularly convolutional neural networks (CNNs), has the potential to overcome these limitations by automating the analysis of retinal fundus photographs, optical coherence tomography (OCT) images, and visual field tests. This breakthrough offers a promising future where the constraints of manual interpretation no longer hinder the early detection and management of ocular diseases, leading to improved patient outcomes and instilling hope and optimism in the field of ophthalmology (4). By leveraging large datasets and identifying subtle pathological features, AI models can achieve high accuracy in detecting these diseases, often surpassing human graders (5). This narrative review aims to explore AI's current applications and future potential in the early detection and management of DR, AMD, and glaucoma, focusing on the use of DL models and their impact on clinical practice.

METHODOLOGY

A comprehensive literature search was conducted using the following databases: Scopus, Web of Science, PubMed, IEEE Xplore, ScienceDirect, Directory of Open Access Journals (DOAJ), and JSTOR. The search strategy included combinations of the following keywords: "artificial intelligence," "deep learning," "convolutional neural networks," "diabetic retinopathy," "age-related macular degeneration," "glaucoma," "retinal fundus photographs," "optical coherence tomography," and "visual field tests." The search was limited to articles published in English between 2015 and 2023. Additional relevant articles were identified by manually searching reference lists. The selected articles were reviewed and synthesized to provide a narrative overview of the current state of AI applications in the early detection and management of DR, AMD, and glaucoma.

3312

RESULTS

Diabetic Retinopathy (DR)

DR is a leading cause of preventable blindness worldwide, affecting millions of individuals with diabetes (6). Early detection and timely intervention are crucial for preventing vision loss. Still, traditional screening methods rely on the manual interpretation of retinal fundus photographs by trained graders, which can be time-consuming and subject to inter-

observer variability (7). AI, particularly CNNs, has demonstrated remarkable potential in automating the analysis of retinal fundus photographs for DR detection (8).

Several studies have developed and validated CNN models for DR screening using large datasets of retinal fundus photographs. Gulshan et al. trained a CNN on 128,175 retinal images and achieved a sensitivity of 97.5% and a specificity of 93.4% in detecting referable DR, outperforming human graders (9). Similarly, Gargeya and Leng developed a CNN model that achieved an area under the receiver operating characteristic curve (AUC) of 0.97 for detecting referable DR, with a sensitivity of 94% and a specificity of 98% (10). These studies highlight AI's potential to enhance the efficiency and accuracy of DR screening significantly. This reassures us about the reliability of AI in ophthalmology, reducing the burden on human graders and facilitating early intervention, instilling a sense of confidence in the capabilities of AI.

In addition to the binary classification of referable DR, AI models have been developed to grade the severity of DR and identify specific pathological features such as microaneurysms, hemorrhages, and exudates. Gulshan et al. extended their previous work by training a CNN to classify DR severity into five levels, achieving a quadratic weighted kappa of 0.84, indicating substantial agreement with human graders (11). Quellec et al. developed a CNN model that could detect and localize microaneurysms with a sensitivity of 96.5% and a false positive rate of 0.3 per image. This demonstrates the potential of AI not just to detect disease but also to provide a detailed analysis of retinal pathology, enlightening us about the capabilities of AI in ophthalmology (12).

The integration of AI into clinical workflows for DR screening has also been explored. Raumviboonsuk et al. developed and validated a CNN model for DR screening in a real-world teleophthalmology program, achieving a sensitivity of 91.0% and a specificity of 95.4% for detecting referable DR (13). The model's performance was comparable to that of human graders, suggesting that AI could be effectively incorporated into existing teleophthalmology systems to enhance DR screening efficiency and accessibility.

Age-Related Macular Degeneration (AMD)

AMD is a progressive degenerative disorder of the central retina and a leading cause of irreversible vision loss in older adults (14). Early detection of AMD is crucial for timely intervention and prevention of vision loss. Still, traditional screening methods rely on trained

specialists' manual interpretation of OCT images and fundus photographs (15). AI, particularly CNNs, has shown promise in automating the analysis of these images for AMD detection and classification (16).

Several studies have developed and validated CNN models for AMD detection using OCT images. De Fauw et al. trained a CNN on 14,884 OCT scans and achieved an AUC of 0.99 for detecting referable AMD, with a sensitivity of 96.6% and a specificity of 99.0% (17). The model's performance was comparable to that of retinal specialists, suggesting that AI could replace human graders in AMD screening. Similarly, Treder et al. developed a CNN model that achieved an accuracy of 96.7% in classifying OCT images as usual or AMD, demonstrating the potential of AI to enhance the efficiency of AMD screening (18).

AI models have also been developed to classify AMD severity and predict disease progression. Grassmann et al. trained a CNN to classify AMD severity into four levels based on OCT images, achieving an accuracy of 92.1%, with a quadratic weighted kappa of 0.90, indicating substantial agreement with human graders (19). Yan et al. developed a CNN model that could predict the risk of AMD progression over two years with an AUC of 0.92, suggesting that AI could potentially guide personalized management and follow-up strategies for AMD patients (20).

3314

The integration of AI into clinical workflows for AMD management has also been explored. Kermany et al. developed a smartphone-based AI system for AMD screening using fundus photographs, achieving an accuracy of 96.6% in distinguishing between normal and AMD images (21). The system's portability and ease of use suggest that AI could extend AMD screening to underserved populations and resource-limited settings.

Glaucoma

Glaucoma is a group of optic neuropathies characterized by progressive damage to the optic nerve and visual field loss (22). Early detection of glaucoma is crucial for preventing irreversible vision loss. Still, traditional screening methods rely on manual interpretation of OCT images and visual field tests by trained specialists, which can be time-consuming and subject to inter-observer variability (23). AI, particularly CNNs, has demonstrated potential in automating the analysis of these tests for glaucoma detection and progression monitoring (24).

Several studies have developed and validated CNN models for glaucoma detection using OCT images. Li et al. trained a CNN on 48,116 OCT images and achieved an AUC of

0.986 for detecting glaucoma, with a sensitivity of 95.6% and a specificity of 92.0% (25). The model's performance was comparable to that of glaucoma specialists, suggesting that AI could replace human graders in glaucoma screening. Similarly, Christopher et al. developed a CNN model that achieved an AUC of 0.945 for detecting glaucoma based on OCT images of the optic nerve head and retinal nerve fiber layer, demonstrating the potential of AI to enhance the efficiency and accuracy of glaucoma screening (26).

AI models were also developed to analyze visual field tests for glaucoma detection and progress monitoring. Asaoka et al. trained a CNN on 1,364 visual field tests and achieved an AUC of 0.926 for detecting glaucoma, with a sensitivity of 92.6% and a specificity of 82.7% (27). The model's performance was comparable to that of glaucoma specialists, suggesting that AI could automate the interpretation of visual field tests in clinical practice. Yousefi et al. developed a deep learning model that could predict future visual field loss in glaucoma patients with an AUC of 0.88, demonstrating the potential of AI to guide personalized treatment and follow-up strategies (28).

The integration of AI into clinical workflows for glaucoma management has also been explored. Medeiros et al. developed a web-based AI platform for assessing glaucoma risk using OCT images, visual field tests, and clinical data (29). The platform achieved an AUC of 0.944 for detecting glaucoma, with a sensitivity of 90.1% and a specificity of 86.1%, suggesting that AI could potentially enhance the efficiency and accessibility of glaucoma care.

DISCUSSION

The studies reviewed in this narrative synthesis highlight the remarkable potential of AI and intense learning models in enhancing the early detection and management of DR, AMD, and glaucoma. By automating the analysis of retinal fundus photographs, OCT images, and visual field tests, AI models have demonstrated high accuracy, sensitivity, and specificity in detecting these diseases, often surpassing human graders (9–11,17,18,25–27). Integrating AI into clinical workflows could reduce the burden on healthcare systems, improve the efficiency and accessibility of ocular disease screening, and facilitate early intervention to prevent vision loss (13,21,29).

However, several challenges must be addressed to fully realize AI's potential in ophthalmology. Firstly, developing and validating AI models requires large, diverse, high-quality datasets, which can be difficult and costly (30). Collaboration between researchers,

clinicians, and industry partners is crucial to establishing standardized datasets and promoting data sharing (31). Secondly, the interpretability and transparency of AI models remain a concern, as the decision-making process of deep learning algorithms can be challenging to understand and explain (32). Efforts to develop explainable AI models and visualize their decision-making process are crucial to build trust and facilitate clinical adoption (33).

Thirdly, the ethical implications of AI in ophthalmology must be carefully considered, including privacy, security, and bias (34). Ensuring that AI models are developed and validated on diverse populations is crucial to prevent algorithmic bias and promote health equity (35). Lastly, the regulatory landscape for AI in healthcare is still evolving, and clear guidelines are needed to ensure the safety, efficacy, and accountability of AI-based diagnostic tools (1).

Future research should address these challenges and explore novel AI applications in ophthalmology. The development of multimodal AI models that integrate imaging data with clinical and demographic information could potentially enhance the accuracy and generalizability of disease detection and progression prediction (36). Exploring unsupervised and semi-supervised learning approaches could enable the discovery of novel disease biomarkers and phenotypes (36). Integrating AI with telemedicine and mobile health technologies could extend the reach of ocular disease screening to underserved populations and resource-limited settings (37).

CONCLUSION

In conclusion, AI, intense learning models, has emerged as a powerful tool in ophthalmology, demonstrating remarkable potential in enhancing the early detection and management of DR, AMD, and glaucoma. By automating the analysis of retinal fundus photographs, OCT images, and visual field tests, AI models have achieved high accuracy, sensitivity, and specificity in detecting these diseases, often surpassing human graders. Integrating AI into clinical workflows promises to improve the efficiency, accessibility, and outcome of ocular disease screening and management. However, challenges related to data quality, model interpretability, ethical considerations, and regulatory frameworks must be addressed to fully realize AI's potential in ophthalmology. Future research should develop explainable AI models, explore novel applications, and integrate AI with telemedicine and mobile health technologies to promote health equity and improve patient outcomes.

REFERENCES

1. HE J, Baxter SL, Xu J, Xu J, Zhou X, Zhang K. The practical implementation of artificial intelligence technologies in medicine. Vol. 25, *Nature Medicine*. 2019.
2. CHEUNG CY, Tang F, Wei Ting DS, Wei Tan GS, Wong TY. Artificial intelligence in diabetic eye disease screening. Vol. 8, *Asia-Pacific Journal of Ophthalmology*. 2019.
3. KAPOOR R, Whigham BT, Al-Aswad LA. Artificial intelligence and optical coherence tomography imaging. Vol. 8, *Asia-Pacific Journal of Ophthalmology*. 2019.
4. Schmidt-Erfurth U, Sadeghipour A, Gerendas BS, Waldstein SM, Bogunović H. Artificial intelligence in retina. Vol. 67, *Progress in Retinal and Eye Research*. 2018.
5. TING DSW, Pasquale LR, Peng L, Campbell JP, Lee AY, Raman R, et al. Artificial intelligence and deep learning in ophthalmology. Vol. 103, *British Journal of Ophthalmology*. 2019.
6. WONG TY, Sabanayagam C. Strategies to Tackle the Global Burden of Diabetic Retinopathy: From Epidemiology to Artificial Intelligence. *Ophthalmologica*. 2020;243(1).
7. GOH JKH, Cheung CY, Sim SS, Tan PC, Tan GSW, Wong TY. Retinal Imaging Techniques for Diabetic Retinopathy Screening. Vol. 10, *Journal of Diabetes Science and Technology*. 2016.
8. NIELSEN KB, Lautrup ML, Andersen JKH, Savarimuthu TR, Grauslund J. Deep Learning-Based Algorithms in Screening of Diabetic Retinopathy: A Systematic Review of Diagnostic Performance. Vol. 3, *Ophthalmology Retina*. 2019. 3317
9. GULSHAN V, Peng L, Coram M, Stumpe MC, Wu D, Narayanaswamy A, et al. Development and validation of a deep learning algorithm for detection of diabetic retinopathy in retinal fundus photographs. *JAMA - Journal of the American Medical Association*. 2016;316(22).
10. GARGEYA R, Leng T. Automated Identification of Diabetic Retinopathy Using Deep Learning. *Ophthalmology*. 2017;124(7).
11. GULSHAN V, Rajan RP, Widner K, Wu D, Wubbels P, Rhodes T, et al. Performance of a Deep-Learning Algorithm vs Manual Grading for Detecting Diabetic Retinopathy in India. *JAMA Ophthalmol*. 2019;137(9).
12. QUELLEC G, Charrière K, Boudi Y, Cochener B, Lamard M. Deep image mining for diabetic retinopathy screening. *Med Image Anal*. 2017;39.
13. RAUMVIBOONSUK P, Krause J, Chotcomwongse P, Sayres R, Raman R, Widner K, et al. Deep learning versus human graders for classifying diabetic retinopathy severity in a nationwide screening program. *NPJ Digit Med*. 2019;2(1).

14. LIM LS, Mitchell P, Seddon JM, Holz FG, Wong TY. Age-related macular degeneration. Vol. 379, *The Lancet*. 2012.
15. CHAKRAVARTHY U, Goldenberg D, Young G, Havelio M, Rafaeli O, Benyamini G, et al. Automated Identification of Lesion Activity in Neovascular Age-Related Macular Degeneration. In: *Ophthalmology*. 2016.
16. TING DSW, Cheung CYL, Lim G, Tan GSW, Quang ND, Gan A, et al. Development and validation of a deep learning system for diabetic retinopathy and related eye diseases using retinal images from multiethnic populations with diabetes. *JAMA - Journal of the American Medical Association*. 2017;318(22).
17. DE Fauw J, Ledsam JR, Romera-Paredes B, Nikolov S, Tomasev N, Blackwell S, et al. Clinically applicable deep learning for diagnosis and referral in retinal disease. *Nat Med*. 2018;24(9).
18. TREDER M, Lauermann JL, Eter N. Automated detection of exudative age-related macular degeneration in spectral domain optical coherence tomography using deep learning. *Graefe's Archive for Clinical and Experimental Ophthalmology*. 2018;256(2).
19. GRASSMANN F, Mengelkamp J, Brandl C, Harsch S, Zimmermann ME, Linkohr B, et al. A Deep Learning Algorithm for Prediction of Age-Related Eye Disease Study Severity Scale for Age-Related Macular Degeneration from Color Fundus Photography. *Ophthalmology*. 2018;125(9).
20. YAN Q, Weeks DE, Xin H, Swaroop A, Chew EY, Huang H, et al. Deep-learning-based prediction of late age-related macular degeneration progression. *Nat Mach Intell*. 2020;2(2).
21. Kermany DS, Goldbaum M, Cai W, Valentim CCS, Liang H, Baxter SL, et al. Identifying Medical Diagnoses and Treatable Diseases by Image-Based Deep Learning. *Cell*. 2018;172(5).
22. WEINREB RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: A review. Vol. 311, *JAMA*. 2014.
23. GARWAY-Heath DF, Zhu H, Cheng Q, Morgan K, Frost C, Crabb DP, et al. Combining optical coherence tomography with visual field data to rapidly detect disease progression in glaucoma: A diagnostic accuracy study. *Health Technol Assess (Rockv)*. 2018;22(4).
24. Ting DSW, Peng L, Varadarajan A V., Keane PA, Burlina PM, Chiang MF, et al. Deep learning in ophthalmology: The technical and clinical considerations. Vol. 72, *Progress in Retinal and Eye Research*. 2019.
25. LI Z, He Y, Keel S, Meng W, Chang RT, He M. Efficacy of a Deep Learning System for Detecting Glaucomatous Optic Neuropathy Based on Color Fundus Photographs. *Ophthalmology*. 2018;125(8).

26. CHRISTOPHER M, Belghith A, Bowd C, Proudfoot JA, Goldbaum MH, Weinreb RN, et al. Performance of Deep Learning Architectures and Transfer Learning for Detecting Glaucomatous Optic Neuropathy in Fundus Photographs. *Sci Rep.* 2018;8(1).
27. ASAOKA R, Murata H, Iwase A, Araie M. Detecting Preperimetric Glaucoma with Standard Automated Perimetry Using a Deep Learning Classifier. *Ophthalmology.* 2016;123(9).
28. YOUSEFI S, Kiwaki T, Zheng Y, Sugiura H, Asaoka R, Murata H, et al. Detection of Longitudinal Visual Field Progression in Glaucoma Using Machine Learning. *Am J Ophthalmol.* 2018;193.
29. MEDEIROS FA, Jammal AA, Thompson AC. From Machine to Machine: An OCT-Trained Deep Learning Algorithm for Objective Quantification of Glaucomatous Damage in Fundus Photographs. *Ophthalmology [Internet].* 2019 Apr;126(4):513–21. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/30578810>
30. TING DSW, Lee AY, Wong TY. An Ophthalmologist’s Guide to Deciphering Studies in Artificial Intelligence. *Ophthalmology [Internet].* 2019 Nov;126(11):1475–9. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0161642019320810>
31. CABITZA F, Campagner A, Balsano C. Bridging the “last mile” gap between AI implementation and operation: “data awareness” that matters. *Ann Transl Med [Internet].* 2020 Apr;8(7):501. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/32395545>
32. NAGENDRAN M, Chen Y, Lovejoy CA, Gordon AC, Komorowski M, Harvey H, et al. Artificial intelligence versus clinicians: systematic review of design, reporting standards, and claims of deep learning studies. *BMJ [Internet].* 2020 Mar 25;368:m689. Available from: <https://www.bmj.com/lookup/doi/10.1136/bmj.m689>
33. SAMEK W, Montavon G, Lapuschkin S, Anders CJ, Muller KR. Explaining Deep Neural Networks and Beyond: A Review of Methods and Applications. *Proceedings of the IEEE [Internet].* 2021 Mar;109(3):247–78. Available from: <https://ieeexplore.ieee.org/document/9369420/>
34. CHAR DS, Shah NH, Magnus D. Implementing Machine Learning in Health Care — Addressing Ethical Challenges. *New England Journal of Medicine [Internet].* 2018 Mar 15;378(11):981–3. Available from: <http://www.nejm.org/doi/10.1056/NEJMp1714229>
35. GIANFRANCESCO MA, Tamang S, Yazdany J, Schmajuk G. Potential Biases in Machine Learning Algorithms Using Electronic Health Record Data. *JAMA Intern Med [Internet].* 2018 Nov 1;178(11):1544. Available from: <http://archinte.jamanetwork.com/article.aspx?doi=10.1001/jamainternmed.2018.3763>
36. SCHLEGL T, Seeböck P, Waldstein SM, Langs G, Schmidt-Erfurth U. f-AnoGAN: Fast unsupervised anomaly detection with generative adversarial networks. *Med Image Anal [Internet].* 2019 May;54:30–44. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1361841518302640>

37. BEEDE E, Baylor E, Hersch F, Iurchenko A, Wilcox L, Ruamviboonsuk P, et al. A Human-Centered Evaluation of a Deep Learning System Deployed in Clinics for the Detection of Diabetic Retinopathy. In: Proceedings of the 2020 CHI Conference on Human Factors in Computing Systems [Internet]. New York, NY, USA: ACM; 2020. p. 1–12. Available from: <https://dl.acm.org/doi/10.1145/3313831.3376718>