International Journal of Emergency Medicine

REVIEW

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AI-assisted ophthalmic imaging for early detection of neurodegenerative diseases

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Abstract

Background Artificial intelligence (AI) plays a promising role in ophthalmic imaging by providing innovative, non-invasive tools for the early detection of neurodegenerative diseases such as Alzheimer's disease (AD) and Parkinson's disease (PD). Since early diagnosis is crucial for slowing disease progression and improving patient outcomes, leveraging AI-assisted ophthalmic imaging retinal imaging can enhance detection accuracy and clinical decision-making.

Methods This review examines clinical applications of AI in identifying retinal biomarkers associated with neurodegenerative diseases. Relevant data was gathered through a comprehensive literature review using PubMed, ScienceDirect, and Google Scholar to evaluate studies utilizing AI algorithms for retinal imaging analysis, focusing on diagnostic performance, sensitivity, specificity, and clinical relevance.

Results AI-assisted ophthalmic imaging retinal imaging enhances the early identification of neurodegenerative diseases by detecting microscopic structural and vascular changes in the retina. Studies have demonstrated that AI models analyzing Optical Coherence Tomography (OCT) and fundus images achieve high diagnostic accuracy. Studies have reported an area under the curve (AUC) of up to 0.918 in PD detection, with sensitivity ranging from 80 to 100% and specificity up to 85%. Similarly, AI-assisted OCT angiography (OCT-A) analysis has successfully identified retinal vascular alterations in AD patients, correlating with cognitive decline and an AUC of 0.73–0.91. These findings highlight AI's potential to detect preclinical disease stages before significant neurological symptoms manifest.

Discussion The integration of AI technologies into ophthalmic imaging holds the potential to improve early diagnosis and transform patient outcomes. However, challenges such as model interpretability, dataset biases, and ethical considerations must be addressed to ensure the responsible integration of AI into clinical practice. Future research should focus on refining AI algorithms, integrating multimodal imaging techniques, and developing predictive biomarkers to optimize early intervention strategies for neurodegenerative diseases.

Clinical trial number Not applicable.

Keywords Artificial intelligence, AI, Retinal biomarkers, Neurodegeneration, Optical coherence tomography, OCT, Alzheimer's, Parkinson's, Early diagnosis, Ophthalmic imaging

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Introduction

Neurodegenerative diseases are marked by the progressive loss of specific neuronal populations. These disorders can be classified by the regions of the brain they affect, their characteristic clinical symptoms, or their underlying molecular mechanisms [1]. The most prevalent neurodegenerative diseases are Alzheimer's disease (AD) and Parkinson's disease (PD). AD manifests as cognitive decline and memory impairment, whereas PD predominantly causes motor dysfunction due to the degeneration of dopaminergic neurons in the brain's substantia nigra [2]. Together, these conditions impose substantial societal and economic burdens. Currently, around 50 million people live with AD, while 10 million are affected by PD worldwide. By 2050, the number of AD cases is projected to triple to 150 million, and PD cases are expected to rise to 12 million [3]. Despite extensive research and investment, no treatments have been developed that can halt the progression of these diseases. Existing therapies remain focused solely on managing symptoms.

Early diagnosis and intervention to slow disease progression are crucial, as medications administered in the early stages can delay the onset of more severe symptoms [4]. However, detecting these diseases in their early phases is challenging due to a lack of accessible, non-invasive biomarkers. In recent years, the retina has emerged as a valuable window into the brain, offering potential biomarkers that reflect neurodegenerative processes. Retinal nerve fiber layer (RNFL) thinning has been observed in AD, correlating with cortical atrophy and cognitive decline [5]. Similarly, reduced contrast sensitivity due to the loss of dopaminergic retinal cells has been linked to neurodegeneration in PD [6]. These examples highlight the potential for retinal changes as early indicators of neurodegenerative diseases.

Artificial intelligence (AI) is rapidly emerging as a transformative technology in ophthalmology, particularly in retinal and optic nerve imaging. Advanced machine learning algorithms can effectively analyze large datasets and detect subtle retinal changes undetectable to the human eye [7]. AI-assisted ophthalmic imaging holds the potential to revolutionize the early detection of neurodegenerative diseases, providing medical professionals with a convenient, non-invasive screening method.

Methods

This narrative review examines the application of AI in ophthalmic imaging for the early detection of neurodegenerative diseases. Literature search principles were adapted from systematic approaches to minimize selection bias. Searches were conducted in PubMed/MEDLINE, ScienceDirect, and Google Scholar, using keywords such as "artificial intelligence", "ophthalmic imaging," "retinal biomarkers", "deep learning", "radiomics", "Alzheimer's disease", "Parkinson's disease", and "neurodegenerative diseases". MeSH terms were used to refine keyword selection.

Inclusion criteria focused on original research articles, clinical trials, and observational studies discussing AI-assisted diagnostic approaches, imaging modalities, and their effectiveness in detecting neurodegenerative diseases. Exclusion criteria included studies unrelated to ophthalmic imaging, those lacking AI applications, and non-English articles. Preference was given to studies published within the last 15 years, with the oldest being 2013 and the most recent to 2025.

The selection process was iterative, including relevant references from chosen studies, and continued until thematic saturation was reached.

AI technologies in ophthalmic imaging

With ongoing technological development, the healthcare field is evolving. Since ophthalmology relies heavily on image-based data, AI has become a valuable tool in assisting clinicians [8, 9]. Ophthalmic imaging is crucial to diagnosing eye disease and monitoring patients' health improvements. Key clinical ocular imaging modalities include Optical Coherence Tomography (OCT), OCT-Angiography (OCT-A), fluorescein angiography, fundus imaging, and gonioscopic photography [9, 10]. The retina's unique characteristics allow for noninvasive blood vessel examination, making it a vital diagnostic tool for detecting systemic diseases.

Cheung et al. developed a diagnostic model for AD using fundus images from 11 studies involving both healthy individuals and AD patients. The AI model performed well in patients with eye disorders and successfully differentiated between those with beta-amyloid and those without. With an AUC (under the curve) of 0.73–0.91 [9]. OCT generates high-resolution cross-sectional images of internal structures using backscattered light, providing better resolution than ultrasonography [3]. OCT measures light amplitude and echo time delay, providing detailed imaging of retinal layers useful for assessing the causes of visual loss, treatment efficacy, and pharmacological outcomes [10]. To enable machine learning algorithms to detect and classify conditions affecting specific retinal layers, these must first be delineated. Biomarkers associated with various neurodegenerative diseases can then be identified and analyzed [10].

One important biomarker measurable through OCT is retinal thickness, which has been linked to AD and utilized in building AI models. For instance, OCT thickness mapping of the ganglion cell inner plexiform layer has helped researchers detect alteration linked to AD [9]. Recent studies also suggest that the retina may provide insights into the progression of PD due to structural changes in the retinal nerve fiber layer [11]. A

prospective study conducted at a single tertiary-care hospital applied a deep-learning algorithm to analyze fundus photographs from PD and non-PD participants. The algorithm contributed to identifying clinical features crucial for diagnosing PD, particularly in correlating motor symptoms with retinal abnormalities in PD patients [11]. Additionally, according to Salehi et al.'s systematic review and meta-analysis, OCT-A could potentially identify decreased vascular density in Parkinson's disease patients' foveal SCP (superficial retinal capillary plexus) [12].

Cross-sectional studies using OCT and OCT-A imaging have shown reductions in retinal perfusion density, vessel density, and choroidal vasculature index in PD patients compared to cognitively normal controls [13]. These findings highlight the potential of retinal imaging as a non-invasive tool for detecting microvascular changes associated with neurodegenerative diseases. To enhance the diagnostic accuracy of such imaging techniques, convolutional neural networks (CNNs) have been employed for image analysis. CNNs are particularly well-suited deep learning models for complex medical imaging applications, where identifying subtle patterns and anomalies is critical. Furthermore, these networks can automatically learn and extract key features from raw data, significantly improving diagnosed precision [14]. Richardson et al. applied CNNs to train, validate, and test OCT retinal images from both PD patients and healthy controls. With an AUC of 0.918, 100% sensitivity, and approximately 85% specificity, the best-performing model demonstrated how well CNNs detect retinal changes associated with Parkinson's disease [13].

Beyond CNNs, recent advances in AI methodologies have introduced radiomics and other deep learning techniques into ophthalmic imaging. Radiomics enables the extraction of high-dimensional imaging features from retinal scans, allowing for quantitative analysis of disease-related patterns that may be imperceptible to the human eye. Studies have shown that radiomics-based models achieve AUC values between 0.7 and 1.0, demonstrating strong diagnostic accuracy in ophthalmic disease detection [15]. Additionally, trilateral ensemble deep-learning models using OCT imaging have performed significantly in comparison traditional statistical models in detecting AD and mild cognitive impairment (MCI), achieving an AUC of 0.91 in Asian populations and 0.84 in White populations, compared to 0.71–0.75 for non-deep learning models [16]. Recent innovations in explainable AI frameworks aim to improve model transparency by identifying neuron-level retinal changes associated with AD, showing high effectiveness in classifying disease progression using vascular features from fundus imaging [17]. Moreover, multimodal AI approaches integrating fundus imaging, OCT, and magnetic resonance imaging (MRI) are being explored to refine neurodegenerative disease classification, with machine learning techniques increasingly focusing on image segmentation and deep learning post-processing [18]. These advancements underscore the evolving role of AI in ophthalmology and the potential for multimodal, data-driven approaches to improve early detection and personalized disease monitoring.

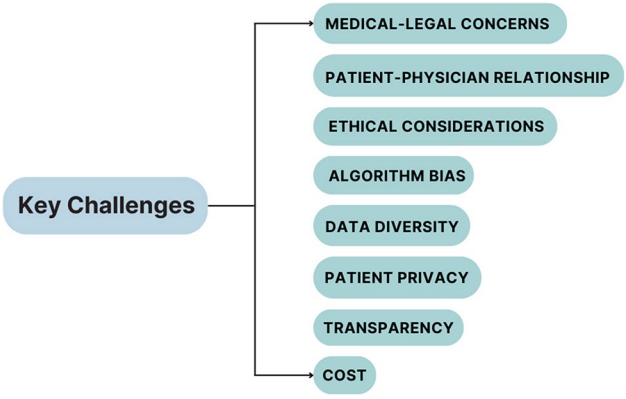

Fig. 1 Process by which AI analyzes and interprets fundus imaging and OCT data for better diagnosis accuracy

Figure 1 illustrates how OCT and fundus imaging are analyzed and interpreted by AI [10, 19]. By detecting patterns and details in medical images that may go unnoticed by the human eye, AI-assisted ophthalmic imaging offers the potential for earlier and more accurate detection of neurodegenerative diseases, such as PD and AD [18].

Neurodegenerative disease biomarkers in ophthalmic imaging

The retina and the brain share key characteristics linked to the pathogenesis of AD, PD, and other neurological and neurodegenerative conditions [11]. Recent advancements in ophthalmic imaging and AI have clarified the retina's role as a potential window into the brain, revealing retinal biomarkers associated with various neurodegenerative diseases. Considered an extension of the central nervous system (CNS), due to its anatomical and embryological origins, the retina provides a unique opportunity for non-invasive assessment [5]. AI algorithms utilizing techniques such as OCT can detect subtle structural and functional changes in the retina that correlate with neurodegenerative conditions.

This section discusses AI-detected retinal biomarkers for various neurodegenerative diseases, including AD, PD, multiple sclerosis (MS), and amyotrophic lateral sclerosis (ALS), which are summarized in Table 1.

As research in the field of neurology has advanced, biomarkers used for AD have expanded beyond traditional imaging modalities such as MRI and positron emission tomography (PET) scans to include ophthalmic imaging,

Table 1 Neurodegenerative diseases and their specific retinal biomarkers detectable by AI-assisted imaging

Neurodegenerative Disease	Retinal Biomarkers	AI Detection Method	References
Alzheimer's Disease (AD)	RNFL thinning, macular degeneration, retinal amyloid deposits	OCT, AI-assisted retinal image analysis	[20, 22]
Parkinson's Disease (PD)	Thinning of the GCL-IPL, reduced vessel, density, and increased tortuosity	OCT, AI-assisted vascular analysis	[23, 24]
Multiple Sclerosis (MS)	Thinning of the peripapillary RNFL and the GCL-IPL in MS patients	OCT, AI-assisted retinal thickness measurement	[25]
Amyotrophic Lateral Sclerosis (ALS)	Retinal thinning in ALS patients, particularly in the RNFL and GCL	OCT, AI-assisted retinal layer segmentation	[26]

particularly retinal biomarkers. Recent studies indicate a significant correlation between retinal nerve fiber layer (RNFL) thinning, as detected by OCT, and cognitive decline in individuals with AD [20]. AI algorithms have been effective in detecting RNFL thinning and macular degeneration, biomarkers linked to Alzheimer's disease, with some studies reporting higher diagnostic accuracy than traditional ophthalmic assessments [21]. Additionally, the presence of retinal amyloid deposits in AD patients suggests that ophthalmic imaging could play a crucial role in non-invasive, early-stage diagnosis [22].

PD, characterized by motor dysfunction including tremors, rigidity, and bradykinesia, also affects visual pathways, leading to changes in the retina. AI-assisted analysis of retinal images has shown that loss of contrast sensitivity and abnormalities in retinal vascular structure such as reduced vessel density and increased tortuosity, can help detect PD. Moreover, OCT imaging of the retina in PD patients reveals significant thinning of the retinal ganglion cell layer (GCL), and inner plexiform layer (IPL) [23]. The analysis of ophthalmic images through AI techniques can enhance the detection of critical retinal vascular and neural abnormalities, thereby aiding in the prediction of disease severity and progression [24].

MS, a chronic autoimmune disorder of the central nervous system, leads to widespread demyelination and neurodegeneration. These neurological changes also extend to the retina, reflecting the broader systemic impact of the disease. Studies have shown thinning of the peripapillary RNFL and the GCL-IPL in MS patients [25]. These changes have been associated with overall brain atrophy and cognitive decline which makes retinal imaging a valuable tool for tracking MS progression.

Amyotrophic Lateral Sclerosis (ALS) primarily affects motor neurons, but recent research suggests that the disease may also impact the retina. AI-assisted imaging studies have shown retinal thinning in ALS patients, particularly in the RNFL and GCL [26]. Although these findings are preliminary, they suggest that retinal imaging could offer insights into the systemic effects of ALS beyond motor symptoms.

AI in early diagnosis: accuracy and clinical application

AI-assisted ophthalmic imaging models have demonstrated improved diagnostic accuracy in detecting early neurodegenerative changes compared to traditional diagnostic methods as discussed so far. Advanced machine learning algorithms can analyze and detect subtle changes in the retina and optic nerve that may precede the development of clinical symptoms, offering a significant opportunity in preclinical diagnosis.

A 2022 study by Wang et al. evaluated macular vessel density using OCT-A in the superficial capillary plexus and foveal avascular zone area [27]. The findings revealed that macular vessel density was significantly decreased in AD patients compared with healthy controls, showing a significant correlation with cognitive function, medial temporal lobe atrophy, and the presence of the APOE ε4 genotype. The study demonstrated that machine learning algorithms analyzing OCT-A measurements provided the best diagnostic performance for AD [27]. Furthermore, a 2023 study by Ahn et al. employed a deep learning system to assess neurological dysfunction in PD patients using fundus images. The algorithm achieved a sensitivity of 80% and specificity of 67% in predicting the Hoehn and Yahr score and the Unified Parkinson's Disease Rating Scale Part III score, which are critical for staging functional disability and monitoring PD progression. Ahn et al. also reported an AUC of 0.67 indicating a moderate performance and a 70.48% accuracy [11, 28]. This underlines the potential role of the retina in the assessment of PD patients and the utility of AI in the detection of neurodegenerative diseases.

AI offers significant advantages in the early detection of neurodegenerative diseases. These systems can quickly analyze thousands of fundus images, significantly reducing the time required for manual review by ophthalmologists [29]. This reduces the workload of ophthalmologists, allowing them to focus more on interpreting results and making informed treatment decisions, ultimately enhancing diagnostic accuracy and treatment outcomes. Moreover, AI proves valuable in diagnosing neurodegenerative disorders at the preclinical stage by detecting subtle changes in retinal morphology or identifying biomarkers that may be missed during traditional examinations [30]. This technological advance holds

great promise for screening large at-risk populations for AD and PD.

AI enhances personalized medicine by customizing diagnostic and monitoring approaches according to individual patient profiles. For instance, AI algorithms can monitor retinal changes in patients over time, enabling healthcare professionals to adjust treatment strategies based on specific patterns of neurodegeneration [31]. This creates a predictive model of disease progression.

As AI systems evolve by analyzing large-scale datasets, their predictive capabilities and clinical value are likely to enhance the early diagnosis of neurodegenerative diseases, positioning AI as a tool that can impact patient care and outcomes by providing a non-invasive and efficient screening method. The following flowchart (Fig. 2) illustrates how AI integrates into the diagnostic pathway for neurodegenerative diseases, highlighting key points where AI can assist clinicians in decision-making.

Challenges and ethical considerations in AI-assisted ophthalmic imaging

AI carries the potential to improve diagnostic accuracy and enhance patient care in clinical practice. However, concerns related to data biases, patient privacy, regulatory oversight, and physician accountability must be carefully addressed before widespread adoption [8]. Figure 3 outlines some of the most common challenges.

One of the major challenges in the implementation of AI in healthcare is the "black box phenomenon". This term refers to AI systems whose underlying mechanics are so opaque, understanding their operability is either impossible or highly complex. This lack of transparency raises concerns in medical diagnosis, as physicians need to comprehend how and why a model reaches a specific conclusion to ensure clinical reliability and patient safety. Without explainability, AI recommendations may be difficult to validate, reducing trust in AI- assisted ophthalmic imaging diagnostics. Recent efforts in explainable AI (XAI) aim to enhance model interpretability, making AI outputs more transparent and justifiable in clinical settings [8, 10, 18, 32].

Another significant issue is the quality and reliability of the data used to train the model. The effectiveness of AI algorithms directly depends on the quality of the training data. If training datasets contain biases, errors, or poor-quality images, AI models may produce inaccurate or misleading results. In ophthalmic imaging, factors such as variability in image resolution, incorrect labeling, and inconsistencies in dataset composition can lead to diagnostic errors—such as misidentifying veins as arteries or failing to detect subtle retinal changes [10, 32]. Additionally, uncontrolled data cleaning and input elimination, influenced by the "garbage in, garbage out" principle may inadvertently exclude important, albeit poor-quality data. This could result in inaccurate outcomes, which may ultimately impact physician accountability [8]. To mitigate these risks, standardized data curation, rigorous quality control, and diverse dataset inclusion are essential.

The evolving nature of patient-physician interactions also poses a challenge in AI implementation. Patients value qualities such as empathy, contextual understanding, individualized patient communication and compassion in doctors, which AI systems cannot fully replicate [8]. Studies suggest that patients often prefer human-mediated AI interpretations, as direct AI-assisted diagnoses can raise concerns about reliability and transparency [8]. Furthermore, the integration of AI into clinical workflows should not compromise the importance of human judgment, particularly in cases where patient history, symptoms, and lifestyle factors play a crucial role in diagnosis and treatment decisions. AI models may overlook nuanced details that emerge during in-depth consultations, highlighting the need for a hybrid approach where AI assists rather than replaces physicians [32].

Ensuring data diversity and accessibility is fundamental for the equitable performance of AI in clinical practice. Limited access to extensive, representative datasets can result in AI models that are not generalizable across different populations, reinforcing existing racial and socioeconomic healthcare disparities. Studies have shown that retinal biomarkers may exhibit variations based on ethnicity, age, and environmental factors, meaning that AI systems trained on homogenous datasets may fail to detect disease patterns in underrepresented groups. To overcome this, researchers must prioritize inclusive data collection, bias audits, and fairness-driven AI model development. The high costs of AI infrastructure and diagnostic tools may create barriers to implementation, particularly in low-resource healthcare settings, further exacerbating disparities in early disease detection [18, 32]. Accessibility and cost of AI devices present further challenges, as developing, validating, and implementing these models require substantial financial investment [32]. There is also a lack of established medico-legal regulations governing AI model integration in patient diagnosis [8].

The implementation of AI in healthcare raises important legal and ethical concerns [18]. As AI technologies become more embedded in clinical practice, issues such as data security, informed consent, and the potential exacerbation of healthcare inequities must be carefully addressed [18].

One major issue is data privacy. AI systems rely on vast amounts of patient data to train and validate algorithms, which increases the risk of data breaches and unauthorized access. It is essential to comply with data protection regulations, such as the General Data Protection Regulation (GDPR) in Europe and the Health Insurance

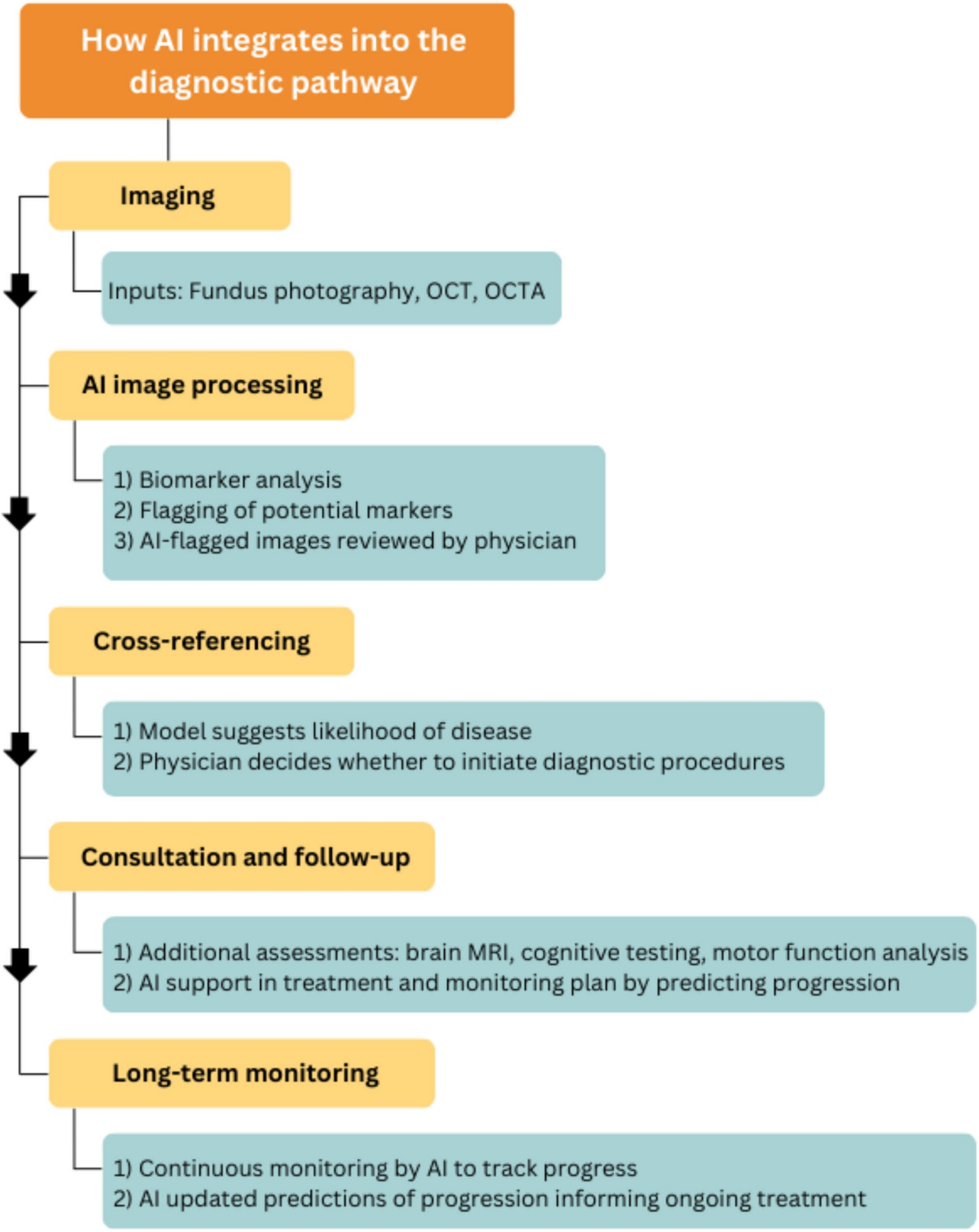

Fig. 2 AI-assisted medical imaging analysis pathway for neurodegenerative diseases

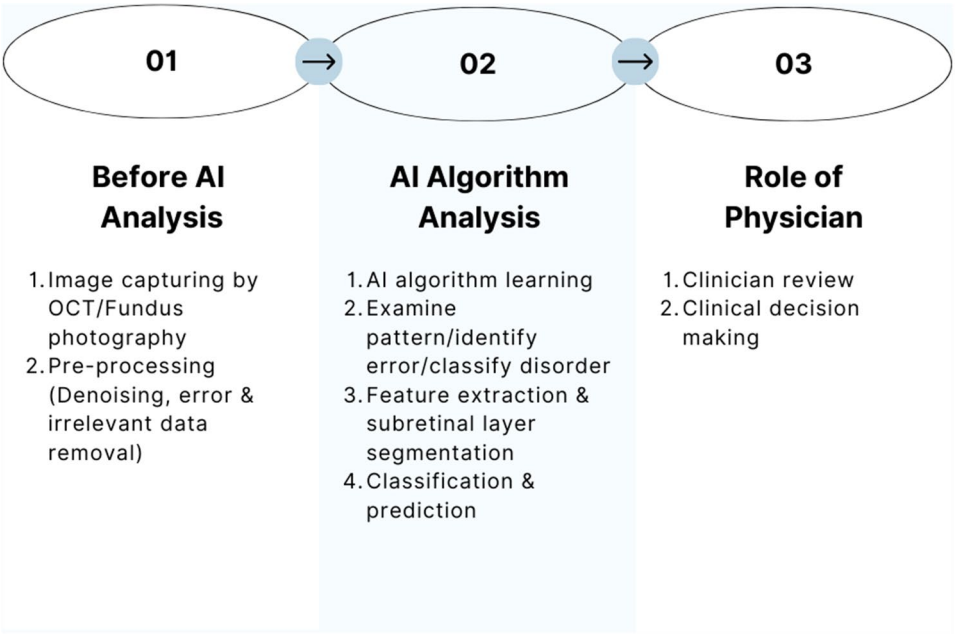

Fig. 3 Key challenges in the integration of AI-Assisted Ophthalmic Imaging

Portability and Accountability Act (HIPAA) in the United States, to ensure patient privacy is safeguarded. Informed consent is another crucial issue, requiring clear communication with patients about how their data will be used in AI-assisted diagnostics [8]. Another critical concern is algorithmic bias, as AI systems may reflect biases present in their training datasets. If these datasets are not diverse or representative, the AI models can produce skewed diagnostic outcomes, disproportionately affecting certain populations. This can exacerbate existing healthcare disparities. To mitigate this risk, it is important to train AI models on diverse datasets that better represent all demographic groups, ensuring that diagnostic accuracy is equitable across different patient populations [33].

The "black box" phenomenon, where AI systems provide results without offering transparency into the decision-making process, is another challenge. This lack of interpretability makes it difficult for healthcare professionals to fully trust AI-generated recommendations, raising concerns about accountability and the "do no harm" principle. Enhancing AI interpretability is critical to allow clinicians to understand how decisions are made and ensure that AI systems are used responsibly in patient care [8, 33].

Regulatory frameworks are necessary to address these ethical challenges. The U.S. Food and Drug Administration (FDA) and the European Union's AI Act (EU AI Act) are both working to establish guidelines for the use of AI in medical diagnostics. For instance, the EU AI Act classifies medical AI as "high-risk", requiring strict evaluation processes before approval. These frameworks aim to ensure that AI technologies meet rigorous safety, efficacy, and transparency standards before being implemented in clinical settings. By setting clear regulatory guidelines, these efforts seek to promote the ethical deployment of AI in healthcare while maintaining patient safety and trust [33].

Gaps and the future of AI in ophthalmology

A major challenge in integrating AI into ophthalmology is the absence of longitudinal studies that track the long-term predictive accuracy of AI-detected retinal biomarkers. While AI models have demonstrated efficacy in detecting retinal abnormalities correlated with diseases such as AD and PD, most studies are cross-sectional, limiting our understanding of how these biomarkers change over time [34].

Another significant gap is the insufficient large-scale validation of AI models across diverse populations. The majority of AI models in ophthalmology have been developed and validated using datasets from specific populations, often in developed countries. This presents a generalizability problem, as retinal structures and disease presentations can vary across ethnic groups and regions [35].

On another hand, the potential for AI-assisted ophthalmic imaging multimodal imaging to combine structural data from OCT with functional data such as electroretinograms and vascular flow analysis is considerable. By integrating different types of ophthalmic data, AI could provide a more comprehensive picture of retinal health and its relationship to systemic neurodegenerative processes [36]. This integration could enhance diagnostic accuracy, allowing clinicians to detect diseases at earlier

stages and differentiate between conditions presenting similar retinal changes.

Furthermore, machine learning algorithms can be trained on longitudinal retinal data and validated across different populations to identify patterns that correlate with faster or slower disease progression which can ultimately help specialize treatment strategies to individual patients, enabling earlier and more effective interventions of neurodegenerative diseases [37].

Management and integration into ophthalmic practice

The integration of AI-assisted ophthalmic imaging tools into ophthalmic practice offers significant promise for enhancing the early diagnosis of neurodegenerative diseases. These technologies can be incorporated by adopting AI-assisted retinal imaging systems that streamline diagnostic workflows and enhance the accuracy of identifying biomarkers indicative of neurodegenerative disease [38].

Collaboration between ophthalmologists and neurologists is crucial to maximize the benefits of AI-assisted ophthalmic imaging diagnostics. As these technologies advance, the significance of AI in interpreting retinal imaging becomes increasingly important for early interventions and potentially improve long-term patient outcomes. Both specialties must collaborate to analyze the implications of AI-generated findings, ensuring that the detected retinal changes are interpreted within the broader context of the patient's neurological health. In addition to this, neurologists are essential in contextualizing imaging findings through cognitive assessments and neuroimaging [39]. Such interdisciplinary collaboration helps to validate the AI-generated findings and facilitates timely interventions.

To integrate AI effectively, clinicians should [1] include an early adoption of AI-assisted retinal imaging systems into their practice as one of their priorities, and [2] engage in ongoing training to stay informed about advancements in AI, particularly XAI, to ensure transparency and trust in AI-assisted ophthalmic imaging diagnoses. It is understandable that not every ophthalmologist and expert can start integrating AI systems of diagnoses, the barrier to entry still needs improvement; however, the first step is reducing resistance and being open to learning the help these models can offer.

The cost-effectiveness of implementing AI in routine practice should not be overlooked. Although the initial investments in AI technologies may be substantial, these costs could be offset over time through earlier disease detection with increased diagnostic efficiency [40]. By reducing the need for manual imaging analysis, ophthalmologists can devote more time to patient care and follow-up evaluations, especially beneficial in high-volume clinics, where large datasets are collected.

Furthermore, the integration of AI reduces the diagnostic burden, enabling earlier interventions for patients with neurodegenerative disease. This proactive approach contributes to a more efficient healthcare system, where timely interventions can prevent the progression of neurodegenerative conditions and their associated complications. For example, PD was estimated to create an economic burden of 51.9 billion USD in the United States in 2017 [41]. This includes direct costs with healthcare expenditure as well as indirect costs incurred by psychological well-being practitioners and caregivers. Projections indicate that this economic burden could exceed $79 billion by 2037 [41]. Consequently, leveraging AI tools for diagnosis and treatment may significantly alleviate the economic impact of neurodegenerative disorders, allowing resources to be redirected toward the research and development of treatments that can effectively slow disease progression rather than merely managing symptoms.

Algorithm performance

The clinical application of AI in ophthalmic imaging presents several challenges related to reliability, false positives, and false negatives, which must be addressed before widespread adoption. Despite AI's high sensitivity in detecting neurodegenerative markers, it remains susceptible to errors, particularly when dealing with poor-quality images or heterogeneous patient populations. The accuracy of AI models heavily depends on the quality of retinal images, and factors such as low resolution, improper illumination, and media opacities (cataracts, vitreous haze, e.t.c) can significantly reduce AI performance, leading to misdiagnosis [10]. AI models may misclassify normal anatomical variations as pathological, increasing the likelihood of false positives, which can result in overdiagnosis and unnecessary clinical follow-ups [13]. In AD detection, for instance, AI models analyzing RNFL thinning may incorrectly attribute normal age-related changes to neurodegeneration [20]. Similarly, in Parkinson's disease, AI-assisted vascular analysis may flag minor microvascular changes as potential biomarkers, increasing false positive rates [24].

False negatives present a significant risk, as AI may fail to detect early neurodegenerative markers, delaying diagnosis and treatment [27]. AI algorithms trained on non-diverse datasets may not generalize well to underrepresented populations, potentially overlooking disease variations linked to ethnicity, age, or coexisting ocular conditions such as glaucoma or diabetic retinopathy [35]. This limitation highlights the need for AI training on large, diverse datasets to improve model robustness and ensure equitable diagnostic performance [37]. Additionally, image acquisition variability between different ophthalmic imaging systems can impact AI accuracy, making

standardization of imaging protocols critical for consistent performance across clinical settings [38].

Given these mentioned limitations, ophthalmologists, precisely experts, play a crucial step in validating and interpreting AI-generated findings acting as the ground truth. AI should function as an assistive tool rather than a replacement for clinical expertise, ensuring that physicians critically evaluate AI outputs, particularly in ambiguous or borderline cases [14]. A hybrid and multimodal diagnosis model, in which AI serves as an initial screening tool while final verification remains with human specialists, can help mitigate AI-related diagnostic errors and optimize patient care [8]. Furthermore, improving AI XAI is essential, as current black-box models provide little insight into their decision-making process, limiting clinician trust and adoption [32]. Future advancements should focus on refining AI decision thresholds to balance sensitivity and specificity, enhancing AI's ability to detect subtle retinal changes while minimizing misclassifications [11]. The development of real-time AI feedback systems that assess image quality before analysis could improve diagnostic accuracy and reduce error rates [36]. By addressing these challenges, AI-assisted ophthalmic imaging can become a reliable and effective tool for early neurodegeneration detection while maintaining physician oversight and ensuring patient safety.

Conclusion

AI-assisted ocular imaging holds considerable promise for the early detection of neurodegenerative diseases. AI algorithms can identify early signs of PD, AD, and other neurodegenerative disorders by detecting microscopic changes in the retina. Research has demonstrated that AI algorithms can identify minimal retinal alterations, including thinning of the retinal nerve fiber layer and microvascular changes associated with AD, PD, and other neurodegenerative diseases. This capability facilitates accurate and rapid diagnoses, which can aid in developing individualized treatment plans.

It is important to create AI algorithms based on data from patients representing a diverse range of backgrounds and ethnicities to enhance their sensitivity. The ethical and unbiased use of AI in clinical practice is as important as ensuring appropriate access to advanced diagnostic methods and mitigating algorithmic biases that can adversely affect patient outcomes. Ultimately, while the management of neurodegenerative disorders through AI could be transformative, its implementation should be monitored carefully to adhere to ethical and technological standards, and ensure that a diverse base of patients can benefit from the technological advancements.

Abbreviations

AI	Artificial intelligence
AD	Alzheimer's disease
PD	Parkinson's disease
OCT	Optical Coherence Tomography
AUC	Area under the curve
OCT-A	OCT-Angiography
RNFL	Retinal nerve fiber layer
SCP	Superficial retinal capillary plexus
CNNs	Convolutional neural networks
MCI	Mild cognitive impairment
MRI	Magnetic resonance imaging
CNS	Central nervous system
MS	Multiple sclerosis
ALS	Amyotrophic Lateral Sclerosis
PET	Positron emission tomography
GCL	Ganglion cell layer
IPL	Inner plexiform layer
GCL-IPL	Ganglion cell layer-inner plexiform layer
XAI	Explainable AI
GDPR	General Data Protection Regulation
HIPAA	Health Insurance Portability and Accountability Act
FDA	Food and Drug Administration
EU AI Act	European Union's AI Act

Acknowledgements

We would like to thank Oli Health Magazine Organization (OHMO) members for their contributions and support for this manuscript.

Author contributions

O.U: Conceptualization, Project Administration, Writing, and DesigningData collection and Assembly: H.N.T, O.U, H.A, D.S, I.F.S.CO.U: Reviewed and edited the first and final draft Manuscript writing: H.N.T, O.U, H.A, D.S, I.F.S.C I.F.S.C: Reviewed and edited the second draft H.N.T: Reviewed and edited the third draf tO.U: Reviewed and edited the final draftFinal approval of manuscript: H.N.T, O.U, H.A, D.S, I.F.S.C Figure (1) was drawn and analyzed by D.S Figure (2) was drawn and analyzed by H.N.T Figure (3) was drawn and analyzed by D.S Table 1. was created by H.A.

Funding

We have not received any financial support for this manuscript.

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethical approval

Not applicable

Consent for publication

Not applicable All co-authors approved the final manuscript. All co-authors have read and approved the submission.

Financial interests

None

Competing interests

The authors declare no competing interests.

Received: 17 January 2025 / Accepted: 15 March 2025
Published online: 06 May 2025

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