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Application of Artificial Intelligence in Glaucoma Diagnosis – a Literature Review

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Summary: Glaucoma is a serious, chronic, and progressive eye disease that can lead to irreversible blindness. The early phase of the condition is particularly critical, as it often remains unnoticed by the patient. Glaucoma is a leading cause of vision loss worldwide, which underscores the importance of screening and continuous monitoring of disease progression. Traditional diagnostic methods include intraocular pressure measurement, gonioscopy, fundus examination, optical coherence tomography, and visual field testing. However, the subjective nature of result interpretation and the time-intensive character of procedures have prompted growing interest in artificial intelligence. In recent years, substantial advances in artificial intelligence applications have significantly improved workflow and efficiency across various medical domains. The implementation of artificial intelligence in glaucoma diagnostics may lead to considerable improvements in ophthalmology by enabling earlier detection of individuals at risk, reducing the number of patients who lose their vision, and decreasing the burden on physicians while improving the overall quality of patient care. This paper presents a review of literature published over the past decade, examining the foundations of operation of artificial intelligence, the effectiveness of algorithms in identifying glaucomatous changes, and their capacity to assess disease risk. The review includes an in-depth evaluation of the diagnostic potential and possible limitations of artificial intelligence in diagnosing glaucoma.

Key words: artificial intelligence (AI), glaucoma, machine learning, deep learning, diagnosis.

1. Introduction

Glaucoma is a heterogeneous group of diseases characterized by progressive optic neuropathy. Based on gonioscopic examination, glaucoma can be divided into open-angle and angle-closure types. Ophthalmic examination makes it possible to determine whether glaucoma is primary or secondary to another condition, and depending on the time of onset, it can be classified as congenital or acquired. In glaucoma, aqueous humor usually drains too slowly through the trabecular meshwork due to increased outflow resistance or closure of the drainage angle. Primary open-angle glaucoma accounts for the majority of glaucoma cases among the adult population, and its risk factors include elevated intraocular pressure, age, sex, myopia, black race, and a positive family history [1].

Angle-closure glaucoma develops as a result of iridocorneal apposition and/ or apposition of the iris to the trabecular meshwork, which leads to closure of the drainage angle, an increase in intraocular pressure, and ultimately the development of glaucomatous neuropathy. Angle closure may be primary, occurring in individuals with an anatomical predisposition, or secondary, developing in the course of other ocular diseases. Secondary glaucoma arises in association with conditions such as diabetes, cataract, inflammatory disorders, neoplasms, or trauma. In its early stages, open-angle glaucoma is usually asymptomatic. The disease leads to the gradual loss of retinal nerve fibers, which may result in irreversible optic nerve damage.

Glaucoma is the main cause of irreversible blindness worldwide, and its prevalence is estimated to increase to approximately 111.8 million cases by 2040 [2]. For this reason, early detection of the disease is crucial, and the use of artificial intelligence (AI) in glaucoma diagnosis and early-stage detection offers the potential for substantial advances in the care of those affected by this condition.

2. Diagnostic tests used in glaucoma

Glaucoma diagnosis involves a range of examinations, including tonometry, i.e. measurement of intraocular pressure, which is considered the primary factor in glaucoma development and the only modifiable risk factor for the onset and progression of the disease. In applanation tonometry, pachymetry should also be performed to assess central corneal thickness, which helps determine whether the measurements are overestimated or underestimated. Gonioscopic evaluation of the drainage angle at the time of diagnosis can provide valuable insights into the disease's pathogenesis. An important part of diagnostic work-up in glaucoma is the evaluation of the fundus of the eye and the retinal nerve fiber layer. Indirect ophthalmoscopy allows for the evaluation of the optic disc and its parameters, enabling estimation of disease severity and monitoring of progression over time [3]. It is a key diagnostic method that facilitates the detection of structural changes in the optic disc, which may occur before visual field defects become apparent [4]. One approach to examining the fundus involves capturing color images using specialized devices known as fundus cameras. Another method is spectral optical coherence tomography (SOCT), which enables the assessment of optic disc morphology, the thickness of the retinal nerve fiber layer (RNFL), as well as the thickness of retinal ganglion cells (GCL) and the entire ganglion cell complex (GCC). While both techniques evaluate optic disc morphology, they operate through distinct mechanisms. SOCT provides precise numerical values and charts that allow for the assessment of optic disc morphology and the thickness of the RNFL in the peripapillary region. Based on these results, the device generates a report (depending on the SOCT model), which helps physicians identify changes associated with glaucoma. As a result, SOCT is easier to interpret than color fundus photographs, which require greater expertise and clinical experience [5]. In addition, perimetry (visual field testing) should be performed to evaluate the extent of functional impairment caused by the loss of optic nerve fibers. It is important to obtain reliable test results, which largely depends on patient cooperation. In this case, the learning effect plays a role, and sometimes only the second or even third examination is suitable for interpretation. Glaucoma diagnosis can be time-consuming and costly, and it relies heavily on the physician's knowledge and skills, which makes it susceptible to error. The introduction of AI into glaucoma diagnostics could eliminate the element of subjectivity and help relieve the burden on physicians, potentially improving the overall quality of patient care [6].

3. Fundamentals of artificial intelligence

AI-based automated models can help reduce diagnostic subjectivity among doctors in glaucoma assessment. These systems are able to analyze and accurately compare images of the retina and optic nerve. By optimizing workflow organization in ophthalmology departments, AI enables doctors to devote more time to patient interaction, thereby enhancing the overall quality of care. Artificial intelligence is a term that encompasses various technologies and methods that enable machines to perform tasks typically requiring human intelligence. Examples of AI applications include image processing, which involves recognizing the content of images, and expert systems, i.e., programs based on specialist knowledge that operate according to predefined rules. Not all aspects of artificial intelligence require expert programming. One such area is machine learning, which allows computers to learn independently from collected data (Fig. 1). This enables systems to predict outcomes in new, unfamiliar situations. Machine learning is categorized into two main types: supervised and unsupervised learning. In the former, algorithms learn from data that has been appropriately labeled in advance. For example, images of eyes are tagged as either glaucomatous or healthy, allowing the system to learn which image features indicate the disease. In unsupervised learning, the computer receives data without any labels and then attempts to identify hidden patterns or groupings on its own. In medicine, so-called deep convolutional neural networks (CNNs) have also gained significant importance. These are advanced artificial intelligence algorithms that excel at analyzing images including X-rays, MRI scans, or photographs of the retina. Their operation resembles the way humans recognize visual information: first noticing simple shapes and colors, then integrating these elements to identify the overall image. CNNs function in a similar manner, initially detecting basic components such as lines, edges, or colors. It does this using so-called convolutional layers, which can be compared to small windows sliding across the image and capturing specific features. Then, in subsequent layers, the network analyzes increasingly complex structures until it is ultimately able to recognize, for example, signs of disease in a retinal image or a tumor in a CT scan. Additionally, the network uses the ReLU (Rectified Linear Unit) activation function, which accelerates learning and improves its efficiency, along with a pooling process that condenses input data while preserving key features. Thanks to these mechanisms, the operation of the network becomes more efficient, and the models themselves can recognize even very subtle changes in images – often with accuracy comparable to that of specialists [7, 8]. An important aspect of AI is the phenomenon known as the "black box". This term refers to a situation where a neural network can provide an accurate answer, such as detecting the presence of glaucoma, yet it is difficult to explain exactly how the decision was reached. The decision-making process is based on millions of calculations and interactions between an enormous number of parameters, which are far too complex for a human to trace step by step. In practice, this means that even the creators of an algorithm often do not know exactly how the model arrived at its decision. For example, a network may detect a tumor in an image, but it remains unclear what specific features it identified to reach that conclusion. This raises important questions about safety and trust, especially in the field of medicine [9].

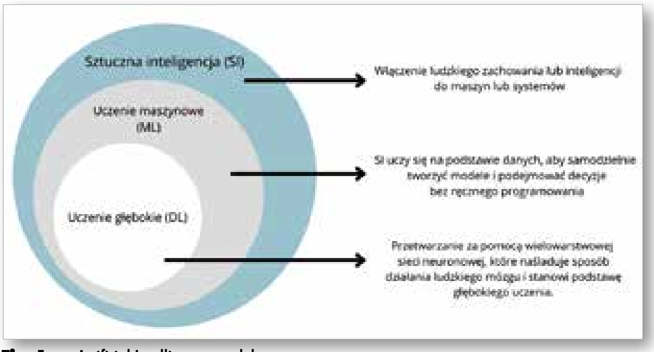

Fig. 1. Artificial Intelligence models.

4. Artificial intelligence in glaucoma diagnostics

4.1 Intraocular pressure

Intraocular pressure (IOP) is the most important modifiable risk factor for glaucoma. It can fluctuate significantly in patients over both short and long periods of time. Elevated IOP, typically defined as exceeding 21 mmHg, warrants further diagnostic evaluation for ocular hypertension or glaucoma [10]. To date, AI has been applied to the analysis of data generated by Sensimed Triggerfish (Sensimed AG, Lausanne, Switzerland) (Fig. 2). It is a contact lens–based device that enables continuous monitoring of IOP by measuring corneal deformation. Built-in strain gauges continuously record changes in corneal shape, transmitting the data to an antenna attached to the patient's orbit, which then relays it to a recorder. Analysis of these data enables relative measurements of IOP fluctuations, which may indicate the development of open-angle glaucoma associated with chronically elevated IOP. Martin et al. used data from 24 prospective studies utilizing Triggerfish and applied machine learning to assess the usefulness of this tool in monitoring diurnal IOP fluctuations and distinguishing eyes with open-angle glaucoma from healthy eyes. Analysis showed that combining ambulatory IOP assessment with a 24-hour profile of ocular shape changes recorded by contact lenses provides a better indicator for detecting open-angle glaucoma than using either method alone. This finding suggests the potential use of Triggerfish as a novel biomarker in glaucoma diagnostics [11]. However, several aspects of such devices still require further development, including the rigidity and bulkiness of embedded circuits, the inability to detect minor IOP fluctuations, and the complexity involved in manufacturing these lenses [12].

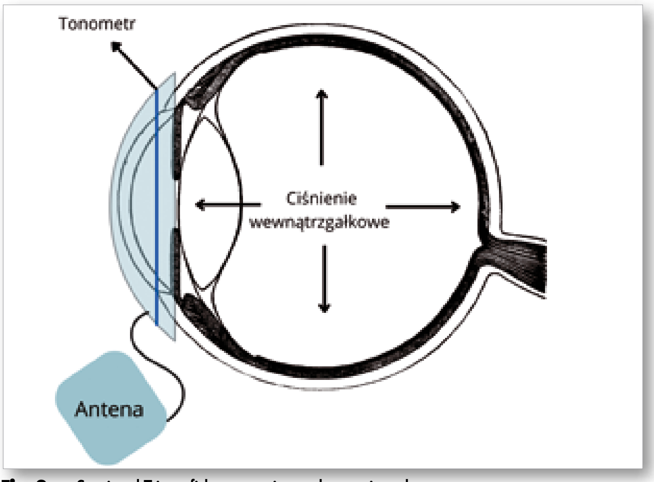

Fig. 2. Sensimed Triggerfish construction and operation scheme.

4.2 Fundus examination

Ophthalmoscopy, or fundoscopy, allows assessment of the internal posterior part of the eye. This examination enables evalu-

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ation of the retina, optic disc, and retinal vessels. Characteristic changes in these areas help in the diagnosis of various diseases, including glaucoma. In the course of this disease, morphological changes occur, including distinctive hollowing of the optic disc, indicative of nerve tissue loss (glaucomatous cupping), glaucomatous neuropathy, alterations in the RNFL, and peripapillary atrophy. The cup-to-disc ratio (CDR) is also assessed based on the ratio of the vertical cup diameter (VCD) to the vertical disc diameter (VDD), expressed as a decimal fraction [13]. One method of fundus imaging involves color images captured by cameras [4]. The first publication investigating the application of AI in this technique appeared in 1999, when Sinthanayothin et al. reported successful anatomical localization of the optic disc, optic cup, and retinal blood vessels. The study demonstrated that automatic recognition of the optic disc, blood vessels, and the fovea centralis can aid disease detection by analyzing changes in these retinal areas [14]. Building on this, several authors later evaluated the usefulness of AI-based analysis of color fundus photographs for glaucoma detection. Some of these publications evaluated AI models based on optic nerve head analysis, while others relied on detecting features suspected of glaucomatous neuropathy, such as a high vertical cup-to-disc ratio, retinal nerve fiber layer defects, peripapillary atrophy, disc hemorrhages, and rim thinning [15]. Li et al. evaluated the effectiveness of a deep learning (DL) algorithm in detecting glaucomatous neuropathy based on color fundus photographs. The study found that the DL model achieved very high effectiveness in detecting glaucomatous neuropathy, reaching a sensitivity of 95.6% and a specificity of 92%. It was observed that the algorithm most often made errors in glaucoma detection when other ocular conditions were present, such as pathological myopia, or in cases of physiological cupping of the optic disc [16]. Bhuiyan et al. conducted a study with the aim of developing and validating an AI-based CDR assessment system to support effective screening of individuals suspected of having glaucoma. Unfortunately, the effectiveness of AI in detecting glaucoma was lower than in the case of diabetic retinopathy, which was also examined in the study. While the technology has the potential to improve diagnostic accessibility and reduce unnecessary referrals, it still requires further validation and integration with other diagnostic methods. Once refined, the system may facilitate early glaucoma detection and help mitigate the risk of vision loss – especially in regions facing a shortage of ophthalmic specialists [17]. Additionally, Al-Aswad et al. assessed the effectiveness of the Pegasus system, an AI-based tool, for glaucoma screening using color fundus photographs. The results of the assessments performed by professionals and AI were compared with the reference clinical diagnosis established before in the Singapore Malay Eye Study, which served as the gold standard. The Pegasus system demonstrated superior diagnostic performance compared to five of the six physicians involved in the study, achieving an accuracy comparable to the gold standard. These findings suggest its potential utility in screening for glaucomatous neuropathy. To validate its effectiveness further, analyses on a larger patient cohort are planned [18]. In a related approach, Masumoto et al. employed a deep learning algorithm that integrated both fundus image analysis and visual field testing. This combination enabled more effective detection of glaucomatous eyes. The comprehensive evaluation of multiple parameters remains an active area of research in the application of AI [19].

4.3 Visual field (VF)

Currently, one of the primary methods used to monitor visual function during glaucoma progression is VF testing [1]. The most common types of VF deficits in this condition result from localized damage to retinal nerve fibers and their spatial distribution. Nasal fibers and the papillomacular bundle are typically spared until the late stages of the disease, which is why eyes with advanced glaucoma often retain a central or temporal island of vision. Damage to the arcuate fibers is commonly observed, and the deficits correspond to the anatomy of these fibers – most glaucomatous VF defects do not cross the horizontal midline [20]. When DL systems are trained on large VF datasets and their models are optimized to improve the detectability of glaucomatous VF defects, artificial intelligence algorithms become capable of predicting, diagnosing, and monitoring the disease with high accuracy, at low cost, and with increased efficiency [21]. Since 1994, numerous publications have confirmed the effectiveness of DL machines trained on standard perimetric data from automated perimetry in distinguishing glaucomatous VF patterns from normal ones and in classifying the severity of glaucomatous VF loss [15]. Heijl et al. conducted a study aimed at comparing the precision and certainty of VF assessments made by physicians and those made by a constructed artificial neural network (ANN) in the context of glaucoma diagnosis. Among physicians, the sensitivity in assessing VF ranged from low to high values, and specificity also showed a wide range. On average, the sensitivity was approximately 83%, and the specificity reached 90%. The ANN demonstrated higher sensitivity than the physicians while maintaining comparable specificity. The study results indicate that the constructed neural network may serve as an effective alternative to traditional, subjective VF evaluation performed by specialists, and its integration with diagnostic tools could improve the quality of patient care. The main limitation of this study is the relatively small number of glaucoma experts involved. Moreover, even though the ANN demonstrated high accuracy in classifying VF test results, its interpretation should not be regarded as a definitive diagnosis, as glaucoma identification requires consideration of other clinical parameters such as IOP, risk factors, and observations of the optic disc. Consequently, the final diagnosis should be made by a specialist based on a comprehensive analysis of these parameters [22]. In 2018, a smartphone application called iGlaucoma was developed, incorporating a DL system trained to detect glaucomatous VF changes. It was found to be a clinically effective tool for detecting glaucomatous neuropathy, indicating promising potential for clinical application. However, the study focused on a specific population and relied solely on VF test results. Future analyses should integrate clinical data, test outcomes, and structural images to enable more accurate glaucoma diagnosis [23].

4.4 Spectral Optical Coherence Tomography (SOCT)

SOCT is a non-invasive and safe diagnostic technique that has become a standard in contemporary ophthalmic practice. Thanks to the diverse scanning protocols available in SOCT, subtle structural changes caused by glaucoma can be detected even before visual field defects appear [3]. However, the vast amount of data generated by SOCT scans, combined with the need for highly precise image interpretation, may place a significant burden on physicians – potentially leading to diagnostic delays and inaccuracies in conditions such as glaucoma. In response to these problems, many recent studies have focused on developing artificial intelligence algorithms to support the diagnosis of this condition [24]. Typical SOCT parameters used in glaucoma diagnostics include three main areas: retinal nerve fiber layer (RNFL) thickness, macular parameters – including macular cube scan, ganglion cell complex (GCC) and ganglion cell layer with inner plexiform layer (GC-IPL), as well as optic nerve head parameters such as Bruch's membrane opening and minimum rim width (BMO-MRW), and optic nerve head (ONH) cube scan. Although RNFL thickness is the most commonly used clinical parameter in SOCT, DL algorithms rely on a combination of the mentioned parameters to enhance diagnostic accuracy. During the analysis of these parameters, BMO-MRW was identified as a potentially very good and precise marker, offering comparable or even superior effectiveness in detecting glaucoma compared to RNFL thickness [25]. Researchers have also described a comprehensive deep learning (DL) algorithm designed to quantitatively assess optic nerve damage due to glaucoma, based on fundus imaging. This algorithm, trained using SOCT data, was applied to estimate RNFL thickness based on fundus images, with the aim of predicting neuroretinal damage, and achieved promising results. It has even been demonstrated that such DL algorithms perform better than human assessment in distinguishing eyes with normal and abnormal VF test results [26]. The aim of the study conducted by Mariottoni et al. [27] in 2020 was to use a residual neural network, additionally developed on their own dataset of unsegmented B-scans and RNFL thickness measurements, to predict RNFL thickness from raw B-scans. The results of the study showed that the developed DL algorithm was able to identify features of B-scans relevant for predicting RNFL thickness, without the need to rely on conventional segmentation by spectral-domain OCT machines. The system developed by the authors performed at a level comparable to conventional SOCT software for high-quality images but outperformed it for lower-quality images. Based on the results obtained, it was established that a DL algorithm operating without segmentation can provide reliable estimates of RNFL thickness in both high- and lower-quality images. Such an algorithm may be valuable in clinical practice by allowing the assessment of RNFL thickness without segmentation, thus eliminating the time-consuming process of verification and manual correction of retinal layer boundaries [25]. Another area of growing interest is the application of CNNs, which not only minimize the need for manual image review but also enable accurate detection of glaucoma in SOCT and fundus photographs. Glaucoma diagnostics based on CNNs leverages the capabilities of the algorithm in image segmentation and classification, enabling segmentation of the optic disc and its evaluation. It is also possible to identify additional features on B-scans from spectral-domain OCT that are relevant for diagnosing glaucoma or monitoring its progression. The aim of the study conducted by Zafar et al. was to compare the performance of CNN algorithms with traditional methods in detecting glaucoma, as well as to assess their ability to analyze and classify images. The study demonstrated the superiority of CNN algorithms over traditional methods, particularly in the context of image analysis and classification, with performance equal to or exceeding that of human experts. Zafar et al. highlighted the potential of CNNs to leverage large datasets collected during imaging studies, which are commonly used in ophthalmology. The study particularly highlighted the usefulness of CNN algorithms in glaucoma diagnostics, especially with respect to SOCT imaging [28].

5. Limitations and challenges in the use of artificial intelligence for glaucoma diagnosis

The use of AI to identify individuals at risk of glaucoma may help reduce the burden on medical staff, lower costs, and shorten the duration of screening procedures. Nevertheless, AI is not a self-sufficient solution, and several challenges persist – including result interpretability, legal and ethical considerations, standardization, quality control, and regulatory requirements for its use as a medical device. One notable obstacle in the clinical implementation of AI is the variability in image quality. Models are sensitive to this and may perform less effectively when the data quality is poor. The quality of imaging is influenced by a range of factors including differences in equipment, lighting, and patient positioning, which can disrupt the features used by the algorithm for classification [29]. A separate issue is related to logistical challenges, which can pose a significant barrier to the implementation of AI. Education on the use of AI should be integrated into medical training programs, and practicing clinicians will require additional instruction. In addition, employing qualified technical personnel to work alongside physicians will be essential for facilitating the integration of new systems [30]. However, it is important to recognize that the behavior of AI may still be unpredictable, even when all safety standards are followed and developers make every effort to mitigate risks. Despite the implementation of appropriate safeguards, AI systems may exhibit behaviors that are difficult to predict due to their complexity and the variability of the data on which they base their decisions. Consequently, even with careful design, there is a risk that artificial intelligence may behave in unforeseen ways, creating challenges related to supervision and control [31].

6. Conclusions

Artificial intelligence holds great potential for glaucoma detection by monitoring intraocular pressure and analyzing fundus images, visual field tests, and optical coherence tomography. The ability of AI models to process large volumes of data may support earlier detection of glaucoma. One example of AI application in early-stage glaucoma diagnosis is the use of contact lenses that can continuously monitor intraocular pressure. Their use may contribute to a faster diagnosis of the disease. Promising results have also been reported in the application of artificial intelligence to visual field testing and fundus photography, where AI demonstrates high sensitivity and specificity in detecting glaucomatous neuropathy. SOCT scans analyzed by deep learning algorithms offer physicians highly precise diagnostic insights into this condition. Despite its promise, AI also presents certain limitations – artificial intelligence models are quite sensitive to the quality of the analyzed images, which may lead to diagnostic errors when low-quality data are used. Furthermore, adapting these models to entirely new data outside the training set may prove challenging, potentially limiting their clinical utility. Yet another obstacle is the need for large and diverse datasets to implement these models in clinical practice, which may be complicated by concerns over privacy and data security. Successful integration of AI into routine clinical practice also depends on providing adequate training for medical personnel and ensuring access to professional technical support. In summary, AI holds significant potential to improve glaucoma diagnostics. However, further development is required, particularly in areas such as adapting systems to variable clinical conditions and ensuring sufficiently high-quality input data.

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