

IDUHeS, 2023; 6(3): 445-459

Doi: 10.52538/iduhes.1339320

Review Paper – Derleme Makalesi

ARTIFICIAL INTELLIGENCE IN OPHTHALMOLOGY CLINICAL PRACTICES

OFTALMOLOJİ KLİNİK UYGULAMALARINDA YAPAY ZEKA

Ekrem CELİK<sup>1,2</sup>, Ezgi INAN<sup>3</sup>

Özet

Oftalmolojinin klinik uygulamalarında yüksek kaliteli ve tekrarlanan çok sayıda dijital görüntüler oftalmolojide yapay zekâ çalışmalarının küresel düzeyde gelişmesine olanak sağlamıştır. Direkt fotoğraf, fundus fotoğrafı ve optik koherens tomografinin başını çektiği dijital verileri kullanarak hastalıkları teşhis etmek, verileri izlemek, görüntüleri analiz etmek ve tedavi etkinliğini değerlendirmek amacıyla yapay zekâ algoritmaları kullanılabilir. Başta diyabetik retinopati, glokom ve yaşa bağlı makula dejenerasyonu olmak üzere oftalmolojinin tüm alanlarında klinik uygulamalarda hızlı ve doğru karar vermek için bu programlar geniş kullanım alanı bulmuştur. Bu derleme ile yapay zekanın oftalmolojinin klinik uygulamalarındaki güncel durumu, klinik uygulamadaki yaygınlığı ve potansiyel zorluklarını ortaya koymak amaçlanmıştır.

**Anahtar Kelimeler:** Oftalmoloji, Yapay Zekâ, Dijital Görüntüleme.

Abstract

A large number of high-quality and repeated digital images in clinical applications of ophthalmology have allowed the development of artificial intelligence studies in ophthalmology at a global level. Artificial intelligence algorithms can be used to diagnose diseases, monitor progression, analyze images, and evaluate treatment effectiveness by using digital data led by direct photography, fundus photography and optical coherence tomography. These programs can be used to make quick and accurate decisions in clinical applications in all areas of ophthalmology, especially diabetic retinopathy, glaucoma and age-related macular degeneration. This review, aims to reveal the current status of artificial intelligence in clinical applications of ophthalmology, its prevalence and potential difficulties in clinical practice.

**Keywords:** Ophthalmology, Artificial Intelligence, Digital Imaging.

Geliş Tarihi (Received Date): 07.08.2023, Kabul Tarihi (Accepted Date): 01.11.2023, Basım Tarihi (Published Date): 31.12.2023. <sup>1</sup> Tekirdag Namik Kemal University, Faculty of Medicine, Department of Ophthalmology, Tekirdag, Türkiye, <sup>2</sup> Tekirdag İsmail Fehmi Cumaloğlu City Hospital, Department of Ophthalmology, Tekirdag, Türkiye, <sup>3</sup> Tekirdag Namik Kemal University, Faculty of Medicine, Tekirdag, Türkiye. **E-mail:** ekelik@gmail.com, **ORCID ID's:** E.C.; <https://orcid.org/0000-0002-1455-4931>, E.I.; <https://orcid.org/0009-0008-0490-4732>.

## 1. INTRODUCTION

Artificial intelligence (AI) is a type of intelligence that imitates natural intelligence by processing information with the help of machines. A technological device using AI can perform certain tasks such as learning, processing information, problem-solving, and developing behavior by making spontaneous decisions. The first automatic device, the symbol of the beginning of AI developments, was a calculator produced at Harvard University in 1938 (Aiken and Hopper, 1946, pp. 449-454).

The pioneering studies in the development of the concept of AI are the efforts to solve the algorithm of the crypto cipher program called Enigma, created by the German Nazis during World War II. The famous mathematician of the period, Alan Turing, conducted intensive studies on solving these codes in England and laid the foundation of today's computer technologies (Morris and Jones, 1984, pp. 139-143). In 1948, with Turing's famous article "The Functioning of Machines and Intelligence", the idea of advanced AI computers was defined (Turing, 2009, pp. 23-65). The first emergence of the concept of AI in its current meaning is based on a conference held at Dartmouth College in 1956 (Howard, 2019, pp. 917-926). The association of health and AI started with the production of personal computers (personnel computer-pc) by large companies such as Microsoft, Apple, Xerox, Hewlett-Packard and IBM in the early 1970s, and since then, AI has been widely used in various forms in the field of health (Greene and Lea, 2019, pp. 480; Reiner and McKinley, 2012, pp. 325-329).

AI algorithms can be classified according to the device's self-operation and learning ability. These devices imitate natural intelligence by working with machine learning or deep learning. The ability to measure in machine learning is managed by the user and the results are left to the user's evaluation. AI-based devices based on machine learning methods cause a certain level of workload to the user today. For example, systems that provide automatic inference by processing data are examples of AI based on machine learning methods. Devices that perform functions such as image acquisition, processing, and editing, which are used to diagnose in the field of health, work with the principle of machine learning. Devices working with the principle of the deep neural network, which we call deep learning, reduce the workload by the self-decision method of the trained algorithm. Visual identification and recall applications form the working principle of convolutional neural networks (CNN). For example, when you upload a photo to Facebook, this convolutional network determines who the person is and is asked to tag him. The CNN is developed from the artificial neural network infrastructure and mimics the neural network working principle in the human brain (Hamet and Tremblay, 2017, pp. 36-40). This network enables the machine to learn and think like the human brain and to make decisions by distinguishing the data. AI algorithms for artificial neural network-based automatic diagnosis, which are widely used in ophthalmology today, were created with CNN software.

## 2. USE OF ARTIFICIAL INTELLIGENCE IN OPHTHALMOLOGY

AI is used in various fields such as diagnosing ophthalmological diseases, monitoring data, analyzing images and evaluating treatment efficacy. Today, AI algorithms can evaluate using images and data obtained on age-related macular degeneration, retinopathy of prematurity,

diabetic retinopathy, strabismus, cataract, glaucoma, uveitis, ocular oncological diseases, and corneal ectasia (Kapoor et al., 2019, pp. 233-240; Ting et al., 2021, pp. 158-168; Valente et al., 2017, pp. 295-305). With teleophthalmology methods, retinopathy of prematurity, diabetic retinopathy, ocular injuries, age-related macular degeneration and glaucoma can be diagnosed remotely (Li et al., 2015, pp. 276-282; Sim et al., 2016, pp. 308-317). Since the diagnosis and treatment of retinopathy of prematurity require experience, it is possible for ophthalmologists specialized in this field to reach patient with teleophthalmology (Rathi et al., 2017, pp. 1729-1934).

### **2.1. Artificial intelligence in diabetic retinopathy**

Diabetic retinopathy refers to the anatomical and functional deterioration caused by changes in the retinal vascular structure, which has been exposed to hyperglycemia for many years. Clinically, deterioration in visual acuity is detected by dilated fundus examination, fundus images, and retinal changes detected by macular OCT. AI algorithms in diabetic retinopathy are being developed by training them to automatically identify and classify features in fundus photography, fundus fluorescein angiography, and optical coherence tomography images. Changes in these images, which include hemorrhages, microaneurysms, neovascularization and exudates in the retina, were taught to AI algorithms and high detection results were obtained. Gulshan et al., in 2015, used 128,000 images in a pioneering study in which they detected diabetic retinopathy with an automatic diagnosis on color fundus images. In this study, they were able to develop a program with a sensitivity of 90.3% and 87%, and a specificity of 98.1% and 98.5%, respectively, to detect moderate and severe diabetic retinopathy (Gulshan et al., 2016, pp. 2402-2410). Today, AI-based software development studies continue in many centers for the diagnosis and follow-up of diabetic retinopathy (Gargeya and Leng, 2017, pp. 825). After the American Food and Drug Administration (FDA) gave the first sales approval to AI-based software that makes automatic diagnoses for diabetic retinopathy in 2018, it started to be used daily in many centers. This system, called ID<sub>x</sub>-DR, can analyze the Topcon TRC-NW400's high-resolution non-mydratic retinal images and diagnose moderate or severe diabetic retinopathy without the need for a clinician. This clinical application is a pioneering study that enables faster screening of patients and facilitates diabetic retinopathy follow-up in many clinics. Although it has been reported that there is a certain level of efficiency in diagnosis with non-mydratic photography in studies conducted in these centers, it is reported that the rate of failure to diagnose is still high in patients with miotic pupils (Abramoff et al., 2018, pp. 39; Paul et al., 2022; Savoy, 2020, pp. 307-308).

Takahashi et al. developed a program that grades diabetic retinopathy with retinal images using the CNN-based GoogLeNet deep learning neural network. With this algorithm, they were able to diagnose diabetic retinopathy and make automatic recommendations about treatment options and prognosis (Takahashi et al., 2017). The GoogLeNet architecture can learn and describe images at the level of multiple abstractions. These features have been found suitable for developing algorithms as they can help detect and classify the subtle changes in retinal vascular structure caused by diabetic retinopathy (Salma et al., 2021, pp. 1-6). Caicho et al. compared the success of the algorithms they created with CNN-based AlexNet, GoogleNet and ResNet50 to detect diabetic retinopathy stages and claimed that the reliability of AlexNet is higher. They stated that the best results were detected by AlexNet (93.56%), while the lowest results were determined by GoogleNet (89.43%) (Caicho et al., 2022).

RetmarkerDR was developed as a machine learning-assisted program that can classify diabetic retinopathy according to the presence or absence of microvascular damage. While the rate of detection of any level of retinopathy in the deep learning algorithm, made with data obtained from more than twenty thousand patients in the United Kingdom, was 73%, this rate

was much better for proliferative diabetic retinopathy (97.9%). However, since the algorithm had a high false positive rate (47%), it was thought that it needed to be better trained to distinguish healthy participants.

## **2.2. Age-related macular degeneration and artificial intelligence**

Age-related macular degeneration (AMD) is typically diagnosed by clinician evaluation of visual acuity testing, dilated fundus examination, fundus images, and macular OCT examination. AMD is clinically divided into two types: dry (non-neovascular) and wet (neovascular). The more common type, dry AMD, occurs due to accumulated cellular damage and deposits called drusen. Wet-type AMD occurs when the fluid or blood leaks due to neovascularizations under the macula and disrupts the retinal layers. Wet AMD is less common, but more severe than dry AMD. Fundus photography, angiography, and OCT examinations can detect drusen, intraretinal fluid caused by abnormal vascularization of the macula, and changes in retinal layers (Lim et al., 2012, pp. 1728-1738). AI-assisted diagnosis and follow-up of AMD can be made using algorithms that can analyze these changes in retinal images with a single imaging method or combination (Dong et al., 2021, pp. 35).

Kermany et al. published a study that can evaluate changes in OCT images using the CNN principle to diagnose patients with choroidal neovascularization (CNV), intraretinal fluid, and drusen in AMD. In this study, using OCT images, the deep-based learning system was able to distinguish pathological diabetic macular edema, which can be confused with AMD, by diagnosing DRP. They were able to differentiate wet-AMD patients with CNV as 96.6% accuracy, 97.8% sensitivity, 97.4% specificity and 6.6% weighted error detection (Kermany et al., 2018, pp. 1122-1131). Yoo et al. were able to diagnose AMD with a program in which they evaluated OCT and fundus images together. This AI-based algorithm was able to detect AMD in fundus images with a high sensitivity of 0.983 (95% CI: 0.979–0.987) and a specificity of 0.88 (95% CI: 0.88–0.88) and was reported to be comparable to retinal experts (Yoo et al., 2019, pp. 677-687). Vaghefi et al. developed a multimodally trained CNN-based model using OCT, fundus, and angio-OCT images. This multimodal-trained algorithm was able to achieve higher accuracy than models trained with single imaging. In this study, the chance of accuracy in evaluations made with a single image was found to be low (77.8%). Combining imaging modalities into a single “multimodal” CNN resulted in 99.8% accuracy and was able to identify both progression and disease with high sensitivity and specificity (Vaghefi et al., 2020). In addition, Treder et al. used fundus autofluorescence (FAF) images in a deep learning algorithm they developed. By using this algorithm, they were able to distinguish those with signs of geographic atrophy from normal subjects and used this software to track the progression of geographic atrophy (Treder et al., 2018, pp. 2053-2060).

## **2.3. Glaucoma and artificial intelligence**

Since glaucoma is an insidious disease, vision loss can be seen even at the time of diagnosis. As the average life expectancy increases worldwide, it is predicted that the incidence of glaucoma will increase by 50% in the next 20 years (Tham et al., 2014, pp. 2081-2090). The main measurements required for diagnosis are intraocular pressure, visual acuity test, optic disc cupping ratio, OCT imaging, automatic perimetry, and visual field testing. Advanced imaging techniques and better digital recording systems have made it possible to develop effective AI algorithms for glaucoma.

The fact that optic disc evaluations can be performed with fundus images makes it possible to easily scan, diagnose and follow up glaucoma in a large population. In the evaluation of these images, the margin of error in interobserver and intraobserver increases the importance

of trained AI algorithms that make automatic diagnoses. Today, studies diagnosing glaucoma with fundus photography by using AI strategies have reached an average accuracy rate of 95% (Fan et al., 2017, pp. 224-234; Muramatsu et al., 2010, pp. 21-27; Mursch-Edlmayr et al., 2020, pp. 55). The deep learning system developed by Li et al. to detect glaucoma and distinguish it from other retinal pathologies based on 8000 fundus photographs reached an AROC value of 0.986 with 95.6% sensitivity and 92.0% specificity. The most common causes of false negative ( $n = 87$ ) were pathological myopia ( $n = 37$  [42.6%]), Glaucomatous optic neuropathy with concomitant eye pathology ( $n = 44$  [50.6%]), diabetic retinopathy ( $n = 4$  [4.6%]) and age-related macular degeneration ( $n = 3$  [3.4%]). The leading cause of false-positive results ( $n = 480$ ) was the presence of other eye conditions ( $n = 458$  [95.4%]), primarily including physiological cupping ( $n = 267$  [55.6%]). Misclassification as false-positive results in normal fundus occurred in only 22 eyes (4.6%) (Li, 2018, pp. 1199-1206). In a study evaluating the cup-disk (C/D) ratio, which expresses the ratio of cup-to-optic disc cupping, on fundus images, glaucoma could be diagnosed with a specificity of 98% on 1426 images (Raghavendra et al., 2018, pp. 41-49). Li et al., in their study called AG-CNN (attention glaucoma-convolutional neural network), reached an accuracy rate of over 95% in the algorithm they developed using the areas damaged by glaucoma in 5824 fundus images (Li et al., 2019, pp. 413-424).

Since 2005, diagnosis of glaucoma could be made by evaluating the retinal nerve fiber layer thickness in OCT images using machine learning methods. Today, the high quality and reproducibility of OCT images enable AI programs to be used effectively. Mursch-Edlmayr et al. explained that multiple AI strategies currently achieve good AROC values ( $>0.90$ ) by using OCT and visual field testing used to detect glaucoma (Mursch-Edlmayr et al., 2020, pp. 55; Zheng et al., 2019, pp. 97-103). In these studies with OCT images, deterioration in the evaluation of retinal nerve fiber layer thickness in the presence of cataract, corneal and vitreous opacity causes some high error rates to still be observed (Bussel et al., 2014, pp. 15-19; Mursch-Edlmayr et al., 2020, pp. 55)

#### **2.4. Artificial intelligence and strabismus**

Strabismus is a disease characterized by both eyes do not look in the same target direction and usually occurring before the age of 3. Timely establishment of binocular alignment in childhood improves visual acuity and binocular vision with sensorimotor stimulation (Harrad et al., 1996, pp. 373). Correction of strabismus, which affects the school-age success and lifetime visual acuity, is of great importance (Graham, 1974, pp. 224). When eyeglasses or amblyopia treatment fails to correct strabismus, surgical treatment (Mao et al., 2021; Read, 2015, pp. 214-224). Strabismus examination is done by measuring the light falling on the cornea with different tests. The prismatic cover test used to calculate the amount of strabismus can be measured with an average error of 10 prism diopters among examiners (Wright et al., 2013). Tests such as Hirschberg, Krimsky, Hess curtain and Maddox glass rod cannot be performed in young children due to difficulty in cooperation. Even ophthalmologists specializing in strabismus have difficulty reaching objective conclusions when they cannot cooperate adequately (Choi and Kushner, 1998, pp. 1301-1306; Mao et al., 2021).

Some studies based on the evaluation of corneal light reflection with direct photographs have enabled objective digital evaluations to be made even with a single photograph (de Almeida et al., 2012, pp. 135-146; Valente et al., 2017, pp. 295-305). It has been shown that the platform, which was trained using 6368 photographs in the AI-based algorithm made by Mao et al., can provide reliable results for strabismus diagnosis and surgical evaluations (Mao et al., 2021). In the study of De Figueiredo et al., a Python-based algorithm was developed using the 9-direction view photos of 110 patients with the help of the neural network architecture

Resnet50. In this way, the diagnosis of strabismus was made with high success, but it was stated that there was a need for confirmation by repeated studies (de Figueiredo et al., 2021, pp. 22).

## **2.5. Artificial intelligence applications in the cornea**

The cornea is the most refractory transparent layer of the eye and corneal disorders can cause severe visual impairment. Infectious keratitis, the most common cause of corneal opacity, is one of the leading causes of blindness worldwide and can affect the visual axis and cause severe vision loss (Ung et al., 2019, pp. 255-271). Keratoconus, the most common corneal ectasia, is a disease that needs to be treated, which may lead to severe vision loss if left untreated. Improvements in the diagnosis and follow-up of the disease are needed to apply corneal cross-linking, contact lens application, corneal ring therapy and corneal transplantation at the right time, which are the treatment options for keratoconus (Hashemi et al., 2020, pp. 263-270).

The prevalence of myopia is seen up to 90% in some societies due to the increase in the use of digital screens and close working distance. Efforts to detect, follow up and correct corneal diseases and refractive errors with digital technology make AI research important. In recent years, some studies have been conducted in which infectious keratitis, pterygium and keratoconus-like ocular surface diseases have been evaluated by the AI program (Rampat et al., 2021, pp. 268; Ting et al., 2021, pp. 1537-1538; Wu et al., 2020). Even before CNN-based studies, the diagnosis of corneal ectasia, dry eye, myopia or refractive surgery history could be diagnosed at certain levels for a long time with the help of a machine and deep learning methods. Color scale and keratometry values in the corneal topography were used to diagnose and grade corneal disorders with these methods (Arbelaez et al., 2012, pp. 2231-2238; Rampat et al., 2021, pp.268). For keratoconus, some corneal topography and tomography devices had very high diagnostic power automatically to distinguish between normal and keratoconus (Smadja et al., 2013, pp. 237-246). When conventional devices are evaluated, better automatic diagnostic methods are needed for subclinical and atypical keratoconus to differentiate from normal or to decide on refractive surgery. For this purpose, CNN-based AI programs using corneal topography, tomography or anterior segment OCT data for keratoconus assessment before refractive surgery have been developed recently (Kuo et al., 2020, pp. 53; Rampat et al., 2021, pp. 268; Smadja et al., 2013, pp. 237-246). The algorithm developed by Zeboulon et al., based on the principle of showing the amount of steepening on the corneal surface map with a color scale and teaching these changes to the program, was able to diagnose a very high rate of normal, keratoconus or refractive surgery history (Zéboulon et al., 2020, pp. 33-39). Also, Kuo et al. stated that with the algorithm they developed with the artificial neural network ResNet, the diagnosis of keratoconus could be made with a sufficient level of accuracy (Kuo et al., 2020, pp. 53).

## **2.6. Artificial intelligence and cataract**

Cataract is one of the leading causes of blindness in developing countries worldwide. It is thought that the annual number of cataract surgeries, which is approximately 20 million today, will increase in parallel with the increase in the elderly population (Wang et al., 2016, pp. 5872-5881). Lens opacity, which causes a decrease in visual acuity, is removed by phacoemulsification surgery, and a transparent artificial lens is placed in its place. Innovations in phacoemulsification surgery and lens technologies have led to advances in perfect vision at all distances. Today, certain standardizations are needed to realize the vision quality at the targeted level without errors (Sudhir et al., 2019, pp. 335). For this purpose, some AI studies for automatic diagnosis with slit lamp photography or fundus images have been revealed (Gao

et al., 2015, pp. 2693-2701; Jun et al., 2019). The AI algorithm made by Xu et al. was able to diagnose cataracts with 92.7% accuracy by using two CNN-based programs together (Xu et al., 2019, pp. 556-567). Other programs with some combined algorithms that can be used in cataract diagnosis and grading of layers, which are also CNN-based, have been developed (Wu et al., 2019, pp. 1553-1560; Zhou et al., 2019, pp. 436-446).

Diagnosis of pediatric cataracts is very important for the detection of early-onset correctable vision loss. Amblyopia, strabismus, and nystagmus may develop in cases that cannot be diagnosed early. Liu et al. were able to reach a significant level of accuracy in their study in which pediatric cataract was diagnosed with slit lamp images using CNN algorithms. The AROC values in this study indicate that identification with CNN is a good method because of found classification (0.9686) and the cataract grading (0.98923), density (0.97433) and localization (0.95911) (Liu et al., 2017). The opacity of the posterior capsule, which is routinely left in cataract surgery, causes visual impairment that needs to be corrected. To determine this, some AI-based studies have been put forward, Mohammadi et al. reached an accuracy rate of 87% in their study, and Jiang et al. reached 92.2% in their study (Jiang et al., 2018; Mohammadi et al., 2012, pp. 403-408).

Telemedicine applications are widely used in ophthalmology applications and the diagnosis, imaging, and grading of cataracts are thus possible. Automatic diagnosis of cataracts with the help of AI programs over a remote connection can enable global opportunities to be used in the fight against blindness (Rampat et al., 2021, pp. 268; Ting et al., 2019, pp. 1537-1538).

## **2.7. Artificial intelligence and uveitis**

Uveitis is a disease characterized by inflammation of the uvea, the middle layer of the eye, which is still one of the leading causes of blindness in the world. Uveitis is divided into 3 groups as anterior uveitis, posterior uveitis and panuveitis, depending on the region of the eye where they are involved, and anterior uveitis is the most common, accounting for 60-90% of all uveitis (Trusko et al., 2013, pp. 259-65). The current gold standard method for detecting anterior chamber inflammation in diagnosing uveitis involves subjective counting of cells by slit lamp examination. This subjective measurement of the number of anterior chamber cells by slit lamp examination in the Uveitis Nomenclature Standardization (SUN) grading shows intraobserver and interobserver variability ( $\kappa$  range = 0.34 to 0.43) (McNeil, 2016, pp. 1-4; Jabs et al., 2018, pp. 19-24). Variation in the clarity of the biomicroscope light and lenses also prevents an objective measurement. In the early period or during the healing phase, when the number of cells is low, existing inflammation may be overlooked (Wong et al., 2009, pp. 516-520).

Sharma et al. used an automated algorithm to assess the presence or absence of cells in the AC using direct images and 3-dimensional (3D) volumetric AS-OCT scans in patients with uveitis. They stated that the total number of cells visible in both line images and 3D AS-OCT images was at the same level as subjective examination and that the automatic detection algorithm could be used efficiently (Sharma et al., 2015, pp. 1464-1470). Sorkhabi et al. developed an AI-assisted neural network-based algorithm to measure inflammation in the anterior chamber (AC) using anterior segment optical coherence tomography (AS-OCT) images. They detected cells by counting particles in the anterior chamber in AS-OCT images and showed that these can be used for uveitis diagnosis and progress monitoring. They claimed that the program had the potential to overcome the biases inherent in SUN grading and improve clinical decision-making (Sorkhabi et al., 2022, pp. 7).

Although anterior segment involvement is the most common, vitreous opacities and posterior segment involvement can also be seen in uveitis to a certain extent. Therefore, artificial intelligence algorithms have also been made for vitreous opacities affected by uveitis, uveitic cystoid macular edema, and choroidal vascularity (Jacquot, 2023, pp. 3746). Keane et al. developed an algorithm that automatically detects the optical transmittance of the vitreous and thus the vitreous haze rate in OCT images. They claimed that by comparing a measurement of the vitreous signal intensity with that of the retinal pigment epithelium in these measurements, they could make a reliable measurement of density in uveitis patients (Keane, 2014, pp. 1706-1714).

Agrawal et al. showed that manually detecting the choroidal vascularity index using ImageJ based on posterior segment findings and detecting it as high in panuveitis patients can be used for automatic diagnosis (Agrawal, 2016). Tuğal-Tutkun et al. also developed an algorithm that will help differentiate Behçet's disease uveitis from other diseases with a high probability in a deep learning diagnosis study based only on characteristic ocular findings. This study compared the diagnosis of uveitis experts with an automatic diagnosis tool for Behçet's disease and revealed that the application could develop a diagnosis of over 95%. However, this study is only a diagnostic tool by which a single disease can be distinguished within panuveitis (Tugal-Tutkun et al., 2021, pp.1154-1163).

## **2.8. Artificial intelligence and ocular oncology**

Ocular oncology, one of the more specific sub-branches of ophthalmology, covers the diagnosis and treatment of ocular surface or intraocular tumors. Since the most definitive diagnoses in oncological diagnoses are obtained by biopsy, evisceration, enucleation or exenteration may be required for diagnosis of intraocular tumors. In recent years, especially iris tumors can be diagnosed with the fine needle aspiration biopsy method and follow-up can be done while preserving ocular survival (Correa et al., 2019, pp. 45-61, Köseoğlu et al., 2023, pp. 437-440). To date, many deep learning and machine learning studies have been conducted with artificial intelligence on uveal melanoma, retinoblastoma and ocular surface tumors in ocular oncology. Liu et al. Conducted a pilot study to develop an alternative survival prediction tool in gene expression profile prediction studies in uveal melanoma using deep learning. The study in a small group of patients (20 participants) showed that gene expression profiles could be predicted directly from digital cytopathology images with 75% accuracy in diagnosis (Liu et al., 2020, pp. 1213-1215). Zhang et al. applied deep learning techniques and included 2239 non-tumor and 778 tumor cases to predict the presence of uveal melanoma based on iris color and iris images. In this study, it was found that iris color identification was not sufficient for the CNN-based diagnosis of uveal melanoma, and this algorithm failed (Zhang, 2021).

## **3. ARTIFICIAL INTELLIGENCE AND ETHICS IN OPHTHALMOLOGY**

Ophthalmology has found a very wide field of study in the field of AI. This is mainly because there is an enormous number of operable data and images that can train the program made while creating these algorithms. The uncontrolled development of AI studies in all disciplines causes some concerns about human security. It is necessary to be transparent when developing programs that have been trained with data and are now a decision-making mechanism on their own. These studies, which begin with the claim that they are in favor of nature and humans, can be criticized, directed, and used for the right purposes thanks to

transparency. The use of personal data while training these programs and their transformation into applications that can turn into commercial purposes necessitates the establishment of a correct relationship of interest between the owners of this data and those who do the work (Balthazar et al., 2018, pp. 580-586). For this reason, it is important to inform the patients while collecting the data and to obtain full informed consent in this regard (Abdullah et al., 2021, pp. 289; Rampat et al., 2021, pp. 268).

It is predicted that in the future, artificial intelligence will reduce human errors and make faster decisions. However, it should be considered ethically that a health practice in which the human decision-making mechanism is disabled may lead to "callous" practices that are controversial and not in the interest of the person needing health care.

### 4. CONCLUSION

Currently, the overall level of use of artificial intelligence in ophthalmology is not widespread due to the lack of validation studies and ethical issues in commercial use despite extensive data. The availability of highly digital and up-to-date image processing devices such as OCT in all ophthalmology clinics and the ability to capture images at almost every check-up is a very advantageous situation for developing ophthalmological artificial intelligence devices. A multitude of comparative clinical studies are also needed to implement the developed algorithms in clinical practice, their effects on real-life diagnoses, and the desired effects on treatment and clinical workflow. Nevertheless, it is predicted that Artificial intelligence will become increasingly common in daily clinical life for monitoring and recording purposes as well as diagnosis in ophthalmology. In the coming years, AI studies may also combine with teleophthalmology, advanced communication networks, and remote robotic interventions, aiming to improve the quality of vision worldwide and facilitate human life.

### 5. REFERENCES

- Abdullah, Y. I., Schuman, J. S., Shabsigh, R., Caplan, A., Al-Aswad, L. A. (2021). Ethics of artificial intelligence in medicine and ophthalmology. *Asia-Pacific journal of ophthalmology* (Philadelphia, Pa.), 10(3), 289.
- Abràmoff, M. D., Lavin, P. T., Birch, M., Shah, N., Folk, J. C. (2018). Pivotal trial of an autonomous AI-based diagnostic system for detection of diabetic retinopathy in primary care offices, *NPJ digital medicine*, Vol. 1, 39.
- Aiken, H., Oettinger, A.G., Bartee, T.C., (1964). Proposed automatic calculating machine. *IEEE spectrum*, 1(8), pp.62-69.
- Arbelaez, M. C., Versaci, F., Vestri, G., Barboni, P., Savini, G. (2012). Use of a support vector machine for keratoconus and subclinical keratoconus detection by topographic and tomographic data. *Ophthalmology*, 119(11), 2231-2238.



- Balthazar, P., Harri, P., Prater, A., Safdar, N. M. (2018). Protecting your patients' interests in the era of big data, artificial intelligence, and predictive analytics. *Journal of the American College of Radiology*, 15(3), 580-586.
- Bussel, I. I., Wollstein, G., Schuman, J. S. (2014). OCT for glaucoma diagnosis, screening and detection of glaucoma progression. *British Journal of Ophthalmology*, 98(Suppl 2), ii15-ii19.
- Caicho, J., Chuya-Sumba, C., Jara, N., Salum, G. M., Tirado-Espín, A., Villalba-Meneses, G., Alvarado-Cando, O., Cadena-Morejón, C., Almeida-Galárraga, D. A. (2022). Diabetic retinopathy: detection and classification using AlexNet, GoogleNet and ResNet50 convolutional neural networks. Paper presented at the Smart Technologies, Systems and Applications: Second International Conference, SmartTech-IC 2021, Quito, Ecuador, December 1–3, 2021, Revised Selected Papers.
- Choi, R. Y., Kushner, B. J. (1998). The accuracy of experienced strabismologists using the Hirschberg and Krimsky tests. *Ophthalmology*, 105(7), 1301-1306.
- Corrêa, Z. M., Augsburger, J. J. (2019). Indications for Fine Needle Aspiration Biopsy of Posterior Segment Intraocular Tumors. *American journal of ophthalmology*, 207, 45–61.
- de Almeida, J. D. S., Silva, A. C., de Paiva, A. C., Teixeira, J. A. M. (2012). Computational methodology for automatic detection of strabismus in digital images through Hirschberg test. *Computers in biology and medicine*, 42(1), 135-146.
- de Figueiredo, L. A., Dias, J. V. P., Polati, M., Carricondo, P. C., Debert, I. (2021). Strabismus and artificial intelligence app: optimizing diagnostic and accuracy. *Translational Vision Science & Technology*, 10(7), 22-22.
- Dong, L., Yang, Q., Zhang, R. H., Wei, W. B. (2021). Artificial intelligence for the detection of age-related macular degeneration in color fundus photographs: A systematic review and meta-analysis. *EclinicalMedicine*, 35, 100875.
- Fan, Z., Rong, Y., Cai, X., Lu, J., Li, W., Lin, H., Chen, X. (2017). Optic disk detection in fundus image based on structured learning. *IEEE journal of biomedical and health informatics*, 22(1), 224-234.
- Gao, X., Lin, S., Wong, T. Y. (2015). Automatic feature learning to grade nuclear cataracts based on deep learning. *IEEE Transactions on Biomedical Engineering*, 62(11), 2693-2701.
- Gargeya, R., Leng, T. (2017). Automated identification of diabetic retinopathy using deep learning. *Ophthalmology*, 124(7), 962-969.
- Graham, P. (1974). Epidemiology of strabismus. *The British journal of ophthalmology*, 58(3), 224.
- Greene, J. A., Lea, A. S. (2019). Digital futures past the long arc of big data in medicine. *The New England journal of medicine*, 381(5), 480.
- Gulshan, V., Peng, L., Coram, M., Stumpe, M. C., Wu, D., Narayanaswamy, A., Venugopalan, S., Widner, K., Madams, T., Cuadros, J. (2016). Development and validation of a deep learning algorithm for detection of diabetic retinopathy in retinal fundus photographs. *Jama*, 316(22), 2402-2410.
- Hamet, P., Tremblay, J. (2017). Artificial intelligence in medicine. *Metabolism*, 69, S36-S40.

- Harrad, R., Sengpiel, F., Blakemore, C. (1996). Physiology of suppression in strabismic amblyopia. *The British journal of ophthalmology*, 80(4), 373.
- Hashemi, H., Heydarian, S., Hooshmand, E., Saatchi, M., Yekta, A., Aghamirsalim, M., Valadkhan, M., Mortazavi, M., Hashemi, A., Khabazkhoob, M. (2020). The prevalence and risk factors for keratoconus: a systematic review and meta-analysis. *Cornea*, 39(2), 263-270.
- Howard, J. (2019). Artificial intelligence: Implications for the future of work. *American Journal of Industrial Medicine*, 62(11), 917-926.
- Jabs, D. A., Dick, A., Doucette, J. T., Gupta, A., Lightman, S., McCluskey, P., Okada, A. A., Palestine, A. G., Rosenbaum, J. T., Saleem, S. M., Thorne, J., Trusko, B. (2018). Standardization of Uveitis Nomenclature Working Group Interobserver Agreement Among Uveitis Experts on Uveitic Diagnoses: The Standardization of Uveitis Nomenclature Experience. *American journal of ophthalmology*, 186, 19–24.
- Jacquot, R., Sève, P., Jackson, T. L., Wang, T., Duclos, A., Stanescu-Segall, D. (2023). Diagnosis, Classification, and Assessment of the Underlying Etiology of Uveitis by Artificial Intelligence: A Systematic Review. *Journal of clinical medicine*, 12(11), 3746.
- Jiang, J., Liu, X., Liu, L., Wang, S., Long, E., Yang, H., Yuan, F., Yu, D., Zhang, K., Wang, L. (2018). Predicting the progression of ophthalmic disease based on slit-lamp images using a deep temporal sequence network. *PLoS One*, 13(7), e0201142.
- Kapoor, R., Walters, S. P., Al-Aswad, L. A. (2019). The current state of artificial intelligence in ophthalmology. *Survey of ophthalmology*, 64(2), 233-240.
- Kermany, D. S., Goldbaum, M., Cai, W., Valentim, C. C., Liang, H., Baxter, S. L., McKeown, A., Yang, G., Wu, X., Yan, F. (2018). Identifying medical diagnoses and treatable diseases by image-based deep learning. *cell*, 172(5), 1122-1131. e1129.
- Koseoglu, N. D., Corrêa, Z. M., Liu, T. Y. A. (2023). Artificial intelligence for ocular oncology. *Current opinion in ophthalmology*, 34(5), 437–440.
- Kuo, B.-I., Chang, W.-Y., Liao, T.-S., Liu, F.-Y., Liu, H.-Y., Chu, H.-S., Chen, W.-L., Hu, F.-R., Yen, J.-Y., Wang, I.-J. (2020). Keratoconus screening based on deep learning approach of corneal topography. *Translational Vision Science & Technology*, 9(2), 53-53.
- Leng, T., Gargeya, R. (2017). A deep learning approach for automatic identification of referral-warranted diabetic retinopathy. *Investigative Ophthalmology & Visual Science*, 58(8), 825-825.
- Li, B., Powell, A.-M., Hooper, P. L., Sheidow, T. G. (2015). Prospective evaluation of teleophthalmology in screening and recurrence monitoring of neovascular age-related macular degeneration: a randomized clinical trial. *JAMA ophthalmology*, 133(3), 276-282.
- Li, L., Xu, M., Liu, H., Li, Y., Wang, X., Jiang, L., Wang, Z., Fan, X., Wang, N., (2019). A large-scale database and a CNN model for attention-based glaucoma detection. *IEEE transactions on medical imaging*, 39(2), pp.413-424.
- Li, Z., He, Y., Keel, S., Meng, W., Chang, R. T., He, M. (2018). Efficacy of a Deep Learning System for Detecting Glaucomatous Optic Neuropathy Based on Color Fundus Photographs. *Ophthalmology*, 125(8), 1199–1206



Lim, L. S., Mitchell, P., Seddon, J. M., Holz, F. G., Wong, T. Y. (2012). Age-related macular degeneration. *The Lancet*, 379(9827), 1728-1738.

Liu, X., Jiang, J., Zhang, K., Long, E., Cui, J., Zhu, M., An, Y., Zhang, J., Liu, Z., Lin, Z. (2017). Localization and diagnosis framework for pediatric cataracts based on slit-lamp images using deep features of a convolutional neural network. *PloS one*, 12(3), e0168606.

Mao, K., Yang, Y., Guo, C., Zhu, Y., Chen, C., Chen, J., Liu, L., Chen, L., Mo, Z., Lin, B. (2021). An artificial intelligence platform for the diagnosis and surgical planning of strabismus using corneal light-reflection photos. *Annals of Translational Medicine*, 9(5).

McNeil, R. (2016). Grading of ocular inflammation in uveitis: an overview. *Eye news*, 22(5), 1-4.

Mohammadi, S.-F., Sabbaghi, M., Hadi, Z., Hashemi, H., Alizadeh, S., Majdi, M., Taei, F. (2012). Using artificial intelligence to predict the risk for posterior capsule opacification after phacoemulsification. *Journal of Cataract & Refractive Surgery*, 38(3), 403-408.

Morris, F.L., Jones, C.B., (1984). An early program proof by Alan Turing. *IEEE Annals of the History of Computing*, 6(02), pp.139-143.

Muramatsu, C., Hayashi, Y., Sawada, A., Hatanaka, Y., Hara, T., Yamamoto, T., Fujita, H. (2010). Detection of retinal nerve fiber layer defects on retinal fundus images for early diagnosis of glaucoma. *Journal of biomedical optics*, 15(1), 016021-016021-016027.

Mursch-Edlmayr, A. S., Ng, W. S., Diniz-Filho, A., Sousa, D. C., Arnould, L., Schlenker, M. B., Duenas-Angeles, K., Keane, P. A., Crowston, J. G., Jayaram, H. (2020). Artificial intelligence algorithms to diagnose glaucoma and detect glaucoma progression: translation to clinical practice. *Translational vision science & technology*, 9(2), 55-55.

Paul, S., Tayar, A., Morawiec-Kisiel, E., Bohl, B., Großjohann, R., Hunfeld, E., Busch, M., Pfeil, J. M., Dähmcke, M., Brauckmann, T. (2022). Use of artificial intelligence in screening for diabetic retinopathy at a tertiary diabetes center. *Der Ophthalmologe: Zeitschrift der Deutschen Ophthalmologischen Gesellschaft*.

Raghavendra, U., Fujita, H., Bhandary, S. V., Gudigar, A., Tan, J. H., Acharya, U. R. (2018). Deep convolution neural network for accurate diagnosis of glaucoma using digital fundus images. *Information Sciences*, 441, 41-49.

Rampat, R., Deshmukh, R., Chen, X., Ting, D. S., Said, D. G., Dua, H. S., Ting, D. S. (2021). Artificial intelligence in cornea, refractive surgery, and cataract: basic principles, clinical applications, and future directions. *Asia-Pacific journal of ophthalmology (Philadelphia, Pa.)*, 10(3), 268.

Rathi, S., Tsui, E., Mehta, N., Zahid, S., Schuman, J. S. (2017). The current state of teleophthalmology in the United States. *Ophthalmology*, 124(12), 1729-1734.

Read, J. C. (2015). Stereo vision and strabismus. *Eye*, 29(2), 214-224.

Reiner, B. I., McKinley, M. (2012). Application of innovation economics to medical imaging and information systems technologies. *Journal of digital imaging*, 25, 325-329.



Salma, A., Bustamam, A., Sarwinda, D. (2021). Diabetic Retinopathy Detection Using GoogleNet Architecture of Convolutional Neural Network Through Fundus Images. *Nusantara Science and Technology Proceedings*, 1-6.

Savoy, M. (2020). IDx-DR for diabetic retinopathy screening. *American family physician*, 101(5), 307-308.

Sharma, S., Lowder, C. Y., VasANJI, A., Baynes, K., Kaiser, P. K., Srivastava, S. K. (2015). Automated Analysis of Anterior Chamber Inflammation by Spectral-Domain Optical Coherence Tomography. *Ophthalmology*, 122(7), 1464–1470.

Sim, D. A., Mitry, D., Alexander, P., Mapani, A., Goverdhan, S., Aslam, T., Tufail, A., Egan, C. A., Keane, P. A. (2016). The evolution of teleophthalmology programs in the United Kingdom: beyond diabetic retinopathy screening. *Journal of diabetes science and technology*, 10(2), 308-317.

Smadja, D., Touboul, D., Cohen, A., Doveh, E., Santhiago, M. R., Mello, G. R., Krueger, R. R., Colin, J. (2013). Detection of subclinical keratoconus using an automated decision tree classification. *American journal of ophthalmology*, 156(2), 237-246. e231.

Sorkhabi, M. A., Potapenko, I. O., Ilginis, T., Alberti, M., Cabrerizo, J. (2022). Assessment of anterior uveitis through anterior-segment optical coherence tomography and artificial intelligence-based image analyses. *Translational Vision Science & Technology*, 11(4), 7-7.

Sudhir, R. R., Dey, A., Bhattacharya, S., Bahulayan, A. (2019). AcrySof IQ PanOptix intraocular lens versus extended depth of focus intraocular lens and trifocal intraocular lens: a clinical overview. *Asia-Pacific Journal of Ophthalmology (Philadelphia, Pa.)*, 8(4), 335.

Takahashi, H., Tampo, H., Arai, Y., Inoue, Y., Kawashima, H. (2017). Applying artificial intelligence to disease staging: Deep learning for improved staging of diabetic retinopathy. *PloS one*, 12(6), e0179790.

Tham, Y.-C., Li, X., Wong, T. Y., Quigley, H. A., Aung, T., Cheng, C.-Y. (2014). Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology*, 121(11), 2081-2090.

Ting, D. S. J., Ang, M., Mehta, J. S., Ting, D. S. W. (2019). Artificial intelligence-assisted telemedicine platform for cataract screening and management: a potential model of care for global eye health, Vol. 103: 1537-1538, BMJ Publishing Group Ltd.

Ting, D. S. J., Foo, V. H., Yang, L. W. Y., Sia, J. T., Ang, M., Lin, H., Chodosh, J., Mehta, J. S., Ting, D. S. W. (2021). Artificial intelligence for anterior segment diseases: Emerging applications in ophthalmology. *British Journal of Ophthalmology*, 105(2), 158-168.

Treder, M., Laueremann, J. L., Eter, N. (2018). Deep learning-based detection and classification of geographic atrophy using a deep convolutional neural network classifier. *Graefes Archive for Clinical and Experimental Ophthalmology*, 256, 2053-2060.

Trusko, B., Thorne, J., Jabs, D., Belfort, R., Dick, A., Gangaputra, S., Nussenblatt, R., Okada, A., Rosenbaum, J. (2013) Standardization of Uveitis Nomenclature (SUN) Project. The Standardization of Uveitis Nomenclature (SUN) Project. Development of a clinical evidence base utilizing informatics tools and techniques. *Methods of information in medicine*, 52(3), 259–S6..



Tugal-Tutkun, I., Onal, S., Stanford, M., Akman, M., Twisk, J. W. R., Boers, M., Oray, M., Özdal, P., Kadayifcilar, S., Amer, R., Rathinam, S. R., Vedhanayaki, R., Khairallah, M., Akova, Y., Yalcindag, F., Kardes, E., Basarir, B., Altan, Ç., Özyazgan, Y., Gül, A. (2021). An Algorithm for the Diagnosis of Behçet Disease Uveitis in Adults. *Ocular immunology and inflammation*, 29(6), 1154–1163.

Turing, A. M. (2009). *Computing machinery and intelligence*, Parsing the turing test: 23-65, Springer.

Ung, L., Bispo, P. J., Shanbhag, S. S., Gilmore, M. S., Chodosh, J. (2019). The persistent dilemma of microbial keratitis: Global burden, diagnosis, and antimicrobial resistance. *Survey of ophthalmology*, 64(3), 255-271.

Vaghefi, E., Hill, S., Kersten, H.M., Squirrell, D., (2020). Multimodal retinal image analysis via deep learning for the diagnosis of intermediate dry age-related macular degeneration: a feasibility study. *Journal of ophthalmology*, 2020.

Valente, T. L. A., de Almeida, J. D. S., Silva, A. C., Teixeira, J. A. M., Gattass, M. (2017). Automatic diagnosis of strabismus in digital videos through cover test. *Computer methods and programs in biomedicine*, 140, 295-305.

Wang, W., Yan, W., Fotis, K., Prasad, N. M., Lansingh, V. C., Taylor, H. R., Finger, R. P., Facciolo, D., He, M. (2016). Cataract surgical rate and socioeconomic: a global study. *Investigative ophthalmology & visual science*, 57(14), 5872-5881.

Wong, I. G., Nugent, A. K., Vargas-Martín, F. (2009). The effect of biomicroscope illumination system on grading anterior chamber inflammation. *American journal of ophthalmology*, 148(4), 516–520.

Wright, K. W., Spiegel, P. H., Hengst, T. (2013). *Pediatric ophthalmology and strabismus*: Springer Science & Business Media.

Wu, X., Huang, Y., Liu, Z., Lai, W., Long, E., Zhang, K., Jiang, J., Lin, D., Chen, K., Yu, T. (2019). Universal artificial intelligence platform for collaborative management of cataracts. *British Journal of Ophthalmology*, 103(11), 1553-1560.

Wu, X., Liu, L., Zhao, L., Guo, C., Li, R., Wang, T., Yang, X., Xie, P., Liu, Y., Lin, H. (2020). Application of artificial intelligence in anterior segment ophthalmic diseases: diversity and standardization. *Annals of Translational Medicine*, 8(11).

Xu, X., Zhang, L., Li, J., Guan, Y., Zhang, L. (2019). A hybrid global-local representation CNN model for automatic cataract grading. *IEEE journal of biomedical and health informatics*, 24(2), 556-567.

Yoo, T. K., Choi, J. Y., Seo, J. G., Ramasubramanian, B., Selvaperumal, S., Kim, D. W. (2019). The possibility of the combination of OCT and fundus images for improving the diagnostic accuracy of deep learning for age-related macular degeneration: a preliminary experiment. *Medical & biological engineering & computing*, 57, 677-687.

Zéboulon, P., Debellemière, G., Bouvet, M., Gatinel, D. (2020). Corneal topography raw data classification using a convolutional neural network. *American Journal of Ophthalmology*, 219, 33-39.



Zheng, C., Johnson, T. V., Garg, A., Boland, M. V. (2019). Artificial intelligence in glaucoma. *Current opinion in ophthalmology*, 30(2), 97-103.

Zhang, H., Liu, Y., Zhang, K., Hui, S., Feng, Y., Luo, J., Li, Y., Wei, W. (2021). Validation of the Relationship Between Iris Color and Uveal Melanoma Using Artificial Intelligence With Multiple Paths in a Large Chinese Population. *Frontiers in cell and developmental biology*, 9, 713209.

Zhou, Y., Li, G., Li, H. (2019). Automatic cataract classification using deep neural network with discrete state transition. *IEEE transactions on medical imaging*, 39(2), 436-446.