EDITORIAL

1  New Year's greeting and overview of Artificial Intelligence in Medical Imaging in 2021
  Wu YXJ, Shen J

MINIREVIEWS

5  Artificial intelligence in ophthalmology: A new era is beginning
  Panda BB, Thakur S, Mohapatra S, Parida S
### AIMS AND SCOPE

The primary aim of *Artificial Intelligence in Medical Imaging* (AIMI, *Artif Intell Med Imaging*) is to provide scholars and readers from various fields of artificial intelligence in medical imaging with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

AIMI mainly publishes articles reporting research results obtained in the field of artificial intelligence in medical imaging and covering a wide range of topics, including artificial intelligence in radiology, pathology image analysis, endoscopy, molecular imaging, and ultrasonography.

### INDEXING/ABSTRACTING

There is currently no indexing.

### RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Yan-Xia Xing; Production Department Director: Yun-Xiaojian Wu; Editorial Office Director: Yun-Xiaojiao Wu.
Artificial intelligence in ophthalmology: A new era is beginning

Bijnya Birajita Panda, Subhodeep Thakur, Sumita Mohapatra, Subhabrata Parida

ORCID number: Bijnya Birajita Panda 0000-0002-0087-1690; Subhodeep Thakur 0000-0003-1782-3567; Sumita Mohapatra 0000-0001-7165-9572; Subhabrata Parida 0000-0002-3871-3490.

Author contributions: Panda BB and Thakur S designed the review, collected the data, analyzed the data and prepared the initial draft. Mohapatra S and Parida S revised the manuscript for important intellectual content and prepared the final draft; All authors read the manuscript and approved for the publication.

Conflict-of-interest statement: The authors declare no conflicts of interest.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/License s/by-nc/4.0/

Manuscript source: Unsolicited manuscript

Artificial intelligence in ophthalmology is not very new and its use is expanding into various subspecialties of the eye like retina and glaucoma, thereby helping ophthalmologists to diagnose and treat diseases better than before. Incorporating “deep learning” (a subfield of AI) into image-based systems such as optical coherence tomography has dramatically improved the machine’s ability to screen and identify stages of diabetic retinopathy accurately. Similar applications have been tried in the field of retinopathy of prematurity and age-related macular degeneration, a silent retinal condition that needs to be diagnosed early to prevent progression. The advent of AI into glaucoma diagnostics in analyzing visual fields and assessing disease progression also holds a promising role. The ability of the software to detect even a subtle defect that the human eye can miss has led to a revolution in the management of certain ocular conditions. However, there are few significant challenges in the AI systems, such as the incorporation of quality images, training sets and the black box dilemma. Nevertheless, despite the existing differences, there is always a chance of improving the machines/software to potentiate their efficacy and standards. This review article shall discuss the current applications of AI in ophthalmology, significant challenges and the prospects as to how both science and medicine can work together.

Key Words: Artificial intelligence; Retina; Diabetic retinopathy; Glaucoma; Retinopathy of prematurity; Image-based learning

©The Author(s) 2021. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: Artificial intelligence has improved the diagnostic ability in the ophthalmology field, thereby improving patient care. The in-depth image recognition in diabetic retinopathy, retinopathy of prematurity and age-related macular degeneration has helped in early diagnosis and prevention. The detection of visual filed...
defect even at its minute stage in glaucoma and other ocular conditions has accurately staged the disease with the prediction of its severity. Still, many challenges need to be addressed, such as image incorporation, training sets and the black box dilemma. Nevertheless, despite the existing differences, there is always a chance of improving machines to potentiate their efficacy and standards.

### Citation
Panda BB, Thakur S, Mohapatra S, Parida S. Artificial intelligence in ophthalmology: A new era is beginning. *Artif Intell Med Imaging* 2021; 2(1): 5-12

URL: https://www.wjgnet.com/2644-3260/full/v2/i1/5.htm

DOI: https://dx.doi.org/10.35711/aimi.v2.i1.5

---

## INTRODUCTION

Artificial intelligence (AI) software can perform cognitive functions like problem-solving and learning by processing and analyzing a large amount of data; in other words, the machine can gain experience as humans do. It came into existence in 1956 and in no time spread its roots into many medical fields, including ophthalmology in the late 1990s when colour fundus photography had started gaining importance in diabetic retinopathy (DR) screening. Later on, its use was not limited to but tried extensively in many subspecialties of the eye such as cataract, myopia and glaucoma screening, corneal ectasia, keratoconus, retinopathy of prematurity (ROP) and ocular reconstruction. It can also be used in calculating intraocular lens power and while planning squint surgery and intravitreal injections. AI can even detect cognitive loss, Alzheimer’s disease and cerebrovascular stroke risk from fundus photographs and optical coherence tomography (OCT). AI in ophthalmology started with machine learning (ML), which meant automatic behaviour modification after exposure to several inputs. Deep learning (DL) is a subset of ML that uses convolutional neural networks (CNN) to add decision-making capability. When incorporated into OCT, these features can help in the diagnosis of many anterior and posterior segment diseases.

## AI AND DR

The disease burden of diabetes mellitus increases day by day, and millions of people are affected. According to published data, the present disease burden is 463 million and likely to rise to 642 million by 2040. DR is a microvascular complication affecting the retina’s blood vessels, leading to progressive damage and irreversible blindness. These patients need to be diagnosed early, and prompt treatment should be started regardless of the type of diabetes. Routine dilated fundus screening in these patients with ophthalmoscopy and colour fundus photographs is the need of the hour and, therefore, eases the burden on the retina specialists. AI has shown promising results in the automated grading of DR based on ML and DL models, the CNN and the massive-training artificial neural network. The lesions in DR are recognized by ML as different colours like red (microaneurysms, haemorrhage, venous abnormalities, intraretinal microvascular abnormalities, new vessels, etc.), yellow (hard exudates, drusens) and white (cotton wool spots, fibrous proliferation, retinal oedema). Staging in DR is usually done by the Davis staging practiced worldwide. In 2017, Takahashi et al. developed a modified Davis staging adopting the DL criterion. The DL approach increases the possibility of identifying neovascularization or other features of proliferative DR (PDR) outside a 45° angle to the posterior pole by detecting non-verbalizable unclear signals. A major breakthrough in this arena was the United States Food and Drug Administration approval of IDx-DR in 2018. A CNN DL algorithm-based AI system to be used along with a Topcon fundus camera has now been proven to be an essential tool in non-ophthalmic healthcare places where it can diagnose DR in just a matter of 20 sec. Lately, the automated DR image accessing system has been applied in conditions affecting the macula such as PDR and clinically significant macular oedema. Another new entity has evolved termed as mtmDR (more than minimal DR), which is defined as the presence of Early Treatment Diabetic Retinopathy Study level 35 or higher, i.e. showing microaneurysms, hard exudates,
AI AND ROP

ROP is one of the leading causes of childhood blindness throughout the world. This vasoproliferative condition affects preterm infants with low gestational age and those with low birth weight. This condition should be diagnosed promptly so that timely intervention can be done. This can be abetted with the help of AI, which provides an automated, quantifiable and highly objective diagnosis in plus disease in ROP. A three-layer feed-forward neural network based on identifying microaneurysms and haemorrhages was proposed by Wong et al(1) to stage DR. A novel technique known as morphological component analysis was formulated by Imani et al(11) to detect oedema and haemorrhages. Yazid et al(1) used inverse surface thresholding and Lattice Neural Network with Dendritic Processing or enhancement techniques to identify hard exudates and optic disc pathologies. Akyol et al(14) tried using key point detection, texture analysis and visual dictionary techniques to detect automatically the optic disc changes from fundus images. The sensitivity and specificity of these studies ranged from 75% to 94.7%. Few studies have used the Eye Art software smartphone-based fundus photography with a sensitivity of around 98% and specificity of 91.5%. The EyeNuk software using the desktop fundus cameras to evaluate retinal images showed that EyeArt’s sensitivity for DR screening was 91.7% and specificity was 91.5%(10). Ting et al(16) validated the DL algorithm with retinal images taken with conventional fundus cameras that had high sensitivity and specificity for identifying DR and age-related macular degeneration (AMD). The intelligent retinal imaging system is another milestone achieved in the field of AI. It is a tele-retinal DR screening program that compares non-mydriatic retinal images taken by a fundus camera with a standard set of images from Early Treatment Diabetic Retinopathy Study to recommend referral in selected cases of severe non-proliferative DR or more advanced vision-threatening disease(19).

Wong et al(1) pointed out certain limitations of DL technology in AI for the screening of DR. There is no simple, standardized algorithm to follow. The technology can talk about the referral cases but fail to detect severe sight-threatening DR that need urgent attention. The software may fail to detect associated glaucoma and AMD while screening for DR. The most severe problem is the development of the faith of the physicians on the machine. The heterogeneous population, different races and variability in pupil dilatation, cataract severity and media opacities may baffle the machine and can be one of the reasons for refusal of the technology by the physicians(20).

ROP can be evaluated by a trained retina specialist sitting at another location. Earlier systems of computer-based ROP diagnosis as described by Wittenberg et al(21)
Glaucoma is a progressive optic neuropathy caused by high intra-ocular pressure leading to retinal nerve fibre loss and irreversible blindness. Early treatment can retard the progression of the disease. AI can help in identifying the borderline cases and stratify the disease’s progression. AMD is clinically characterized by the presence of drusens and retinal pigment epithelium changes progressing into geographic atrophy and neovascularization.

Many of the studies related to incorporating AI in the screening of AMD have used colour fundus images as input materials and then extract features of early, intermediate and late AMD to differentiate from the healthy ones with relatively high accuracy and sensitivity ranging from 87%-100%[24-27]. They found this technique much cheaper than using OCT to stage the disease. Fang et al[28] proposed a spectral-domain OCT combined with DL system that could determine the macular fluid quantity of neovascular AMD and the segmentation of the retinal layers of dry AMD and validated the accuracy as 100%. Bogunovic et al[29] developed an algorithm to evaluate the response to treatment using OCT images. More recently, Bhuiyan et al[30] did pioneer research in creating and validating AI-based models for AMD screening (accuracy 99.2%) and predicting late dry and wet AMD progression within 1 and 2 years (accuracy 66%-83%). They used the DL screening methods on the Age-related Eye Disease Study (AREDS) dataset to classify their colour fundus photos into no, early, intermediate or advanced AMD and further classified them along the AREDS 12 Level severity scale[31]. They combined the AMD scores with sociodemographic, clinical data and other automatically extracted imaging data by a logistic model tree ML technique to predict risk for progression to late AMD.

A comprehensive AI for glaucoma should be able to evaluate all the necessary parameters such as optic disc changes, intraocular pressure (IOP), gonioscopy, retinal nerve fiber layer thickness, visual fields etc. However, such a comprehensive package is yet to come to the real-time world. The application of AI in measuring IOP is now limited to the Sensimed Triggerfish, a contact lens-based continuous IOP monitoring device that measures the corneal strain changes induced by IOP fluctuations. Martin et al[32] used data from 24 prospective studies of Triggerfish using Random Forest Modelling (a ML method) to identify the parameters associated with glaucoma patients.

Omodaka et al[33] developed a ML algorithm based on the segmentation technique where the parameters such as optic disc cupping, neuroretinal rim thickness and
ganglion cell thickness could be quantified with the help of swept-source OCT to the accuracy as high as 87%. Other studies by Christopher et al\(^\text{40}\), Barella et al\(^\text{41}\), Bizios et al\(^\text{42}\) and Larrosa et al\(^\text{43}\) evaluated unsupervised ML, ML classifiers, artificial neural networks, support vector machines and segmentation methods for glaucoma OCT.

Many studies have evaluated a DL algorithm to detect glaucomatous optic disc changes from colour fundus photographs with high sensitivity and specificity\(^\text{40,42}\). The available AI devices for detecting glaucomatous optic neuropathy from fundus photos are the Pegasus (Orbis Cybersight Consult Platform), NetraAI (Leben Care Technologies Pte Ltd) and the Retinal Image Analysis - Glaucoma (RIA-G). RIA-G is the AI device based on DL made by the Indian startup Kalpah Innovations (Vishakapatnam, India). It is a cloud-based software that uses advanced image processing algorithms to measure the cup disc size and ratio, NeuroRetinal Rim Thickness and Disc Damage Likelihood Score\(^\text{42}\).

AI can also augment the interpretation of visual fields in studies showed by Asaoka et al\(^\text{44}\) and Andersson et al\(^\text{45}\) using a Feed-Forward Neural Network to identify pre-perimetric visual fields (VF). Goldbaum et al\(^\text{46}\) used unsupervised ML and variational Bayesian independent component analysis mixture model (vB-ICA-mm) to analyze VF defects. Bowd et al\(^\text{43}\) used the variational Bayesian independent component analysis-mixture model, which is an unsupervised machine-learning classifier and can be used in the analysis of frequency doubling technology perimetry data\(^\text{43}\).

**AI AND CATARACT**

Studies have described techniques to grade nuclear cataracts by the help of AI using algorithms based on ML or DL systems that work as efficiently as a clinician's grading. Gao et al\(^\text{47}\) proposed a system that could process slit-lamp images to grade cataracts. Liu et al\(^\text{43}\) focused on identifying and categorizing pediatric cataracts with excellent accuracy and sensitivity. Wu et al\(^\text{48}\) developed a universal AI platform and multilevel collaborative pattern that could perform effectively in diagnostic and referral service for pediatric and age-related cataracts. Dong et al\(^\text{49}\) have proposed the automated detection and grading of cataracts from colour fundus photographs using a combination of a DL system to extract images (Caffe software) followed by a ML algorithm (called as Softmax function) for severity grading. AI has also been tried in residents’ cataract surgery training due to recognizing different phases of cataract surgery\(^\text{50,51}\). Some researchers have derived new AI-based calculation formulae for pre-cataract surgery intraocular lens power, e.g., the Hill-Radial basis function method and the Kane formula, which are reported to be able to estimate individual eye's intraocular lens power with promising results with further improvements needed for short axial length eyes\(^\text{52}\).

**CONCLUSION**

AI-assisted screening and diagnosis of high incidence diseases will help in better medical care and reduce the limitations to access ophthalmic care at remote areas devoid of ophthalmologists. In doing so, it will also reduce the overburdened healthcare system. However, this project at its infancy is nonetheless riddled with certain limitations. The assessment is highly dependent on image quality. Hence, patient factors such as head and eyeball movement and poor fixation may lead to a substandard image and a wrong assessment. However, this is the basis of ML, and in future, we expect a much more robust system. A certain degree of human supervision is required to find the subtle variations and atypical findings missed by AI. Computational cost and running expenses could be over the roof. AI mainly targets diseases with high incidence and morbidity, but not much effective for rare diseases with fewer incidences.

**Future outlook**

Not only for screening and diagnosis, AI has also been found to be instrumental in maintaining Electronic Health Record (EHR) data. Given the plethora of diagnostic tests that patients undergo, these collected EHR data could be fed into the AI system and trained through exposure to normal and pathological clinical data. Therefore, it could be used for risk assessment as well as to predict postoperative complications and outcome.
REFERENCES

1. Ruamviboonsuk P, Cheung CY, Zhang X, Raman R, Park SJ, Ting DSW. Artificial Intelligence in Ophthalmology: Evolutions in Asia. *Asia Pac J Ophthalmol (Phil)* 2020; 9: 78-84 [PMID: 32349114 DOI: 10.1097/1.APO.000066904.41191.0b]

2. Sinclair A, Saeedi P, Kaundal A, Karuranga S, Malanda B, Williams R. Diabetes and global ageing among 65-99-year-old adults: Findings from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract* 2020; 162: 108078 [PMID: 32060807 DOI: 10.1016/j.diabres.2020.108078]

3. Pady SK, Takkar B, Chawla R, Kumar A. Artificial intelligence in diabetic retinopathy: A natural step to the future. *Indian J Ophthalmol* 2019; 67: 1004-1009 [PMID: 31238395 DOI: 10.4103/ijo.IJO_1989_18]

4. Meyer M, Wiedorn KH, Hofschneider PH, Koshy R, Caselmann WH. A chromosome 17:7 translocation is associated with a hepatitis B virus DNA integration in human hepatocellular carcinoma DNA. *Hepatology* 1992; 15: 665-671 [PMID: 1312986]

5. Takahashi H, Tampo H, Arai Y, Inoue Y, Kawashima H. Applying artificial intelligence to disease staging: Deep learning for improved staging of diabetic retinopathy. *PLoS One* 2017; 12: e0179790 [PMID: 28640840 DOI: 10.1371/journal.pone.0179790]

6. US Food and Drug Administration. FDA permits marketing of artificial intelligence-based device to detect certain diabetes-related eye problems, 2018. [Cited December 21, 2020]. Available from: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm604357.htm

7. Optometry Times. Pros and Cons of Using an AI-Based Diagnosis for Diabetic Retinopathy. [Cited December 21, 2020]. Available from: http://www.optometrytimes.com/article/pros-and-cons-using-ai-based-diagnosis-diabetic-retinopathy

8. Abràmoff MD, Lou Y, Erginay A, Clarida W, Amelon R, Folk JC, Niemeijer M. Improved Automated Detection of Diabetic Retinopathy on a Publicly Available Dataset Through Integration of Deep Learning. *Invest Ophthalmol Vis Sci* 2016; 57: 5200-5206 [PMID: 27701631 DOI: 10.1167/iovs.14-199964]

9. Gargeya R, Leng T. Automated Identification of Diabetic Retinopathy Using Deep Learning. *Ophthalmology* 2017; 124: 962-969 [PMID: 28359545 DOI: 10.1016/j.ophtha.2017.02.008]

10. Abràmoff MD, Lavin PT, Birch M, Shah N, Folk JC. Pivotal trial of an autonomous AI-based diagnostic system for detection of diabetic retinopathy in primary care offices. *NPJ Digit Med* 2018; 1: 39 [PMID: 31304320 DOI: 10.1038/s41746-018-0040-5]

11. Wong LY, Acharya R, Venkatesh YV, Chee C, Min LC. Identification of different stages of diabetic retinopathy using retinal optical images. *Inf Sci* 2008; 178: 106-121

12. Imani E, Pourreza HR, Banaee T. Fully automated diabetic retinopathy screening using morphological component analysis. *Comput Med Imaging Graph* 2015; 43: 78-88 [PMID: 25863517 DOI: 10.1016/j.compmedimag.2013.05.004]

13. Yazid H, Arof H, Isa HM. Automated identification of exudates and optic disc based on inverse surface thresholding. *J Med Syst* 2012; 36: 1997-2004 [PMID: 21318328 DOI: 10.1007/s10977-011-9559-4]

14. Akkol K, Sen B, Bayir S. Automatic Detection of Optic Disc in Retinal Image by Using Keypoint Detection, Texture Analysis, and Visual Dictionary Techniques. *Comput Math Methods Med* 2016; 2016: 6814791 [PMID: 27110272 DOI: 10.1556/2016.6814791]

15. Niemeijer M, Abràmoff MD, van Ginneken B. Fast detection of the optic disc and fovea in color fundus photographs. *Med Image Anal* 2009; 13: 859-870 [PMID: 19782633 DOI: 10.1016/j.media.2009.08.003]

16. Rajalakshmi R, Subashini R, Anjana RM, Mohan V. Automated diabetic retinopathy detection in smartphone-based fundus photography using artificial intelligence. *Eye (Lond)* 2018; 32: 1138-1444 [PMID: 29520050 DOI: 10.1038/s41433-018-0064-9]

17. Bhaskaranand M, Ramachandra C, Bhat S, Cuadros J, Nittala MG, Sadda S, Solanki K. Automated Diabetic Retinopathy Screening and Monitoring Using Retinal Fundus Image Analysis. *J Diabetes Sci Technol* 2016; 10: 254-261 [PMID: 26889872 DOI: 10.1172/jdast.2016.10.01.11-9659]

18. Ting DSW, Cheung CY, Lim G, Tan GSW, Quang ND, Gan A, Hamzah H, Garcia-Franco R, San Yeo IF, Lee SY, Wong EYM, Sabanayagam C, Baskaran M, Ibrahim F, Tan NC, Finkelstein EA, Lamoureux EL, Wong LY, Arof H, Isa HM. Automated identification of exudates and optic disc based on inverse surface thresholding. *J Med Syst* 2012; 36: 1997-2004 [PMID: 21318328 DOI: 10.1007/s10977-011-9559-4]

19. Huemer J, Wagner SK, Sim DA. The Evolution of Diabetic Retinopathy Screening Programmes: A Chronology of Retinal Photography from 35 mm Slides to Artificial Intelligence. *Clin Ophthalmol* 2020; 14: 2021-2035 [PMID: 32764868 DOI: 10.2147/OPHT.S261629]

20. Wong TY, Bressler NM. Artificial Intelligence With Deep Learning Technology Looks Into Diabetic Retinopathy Screening. *JAMA* 2016; 316: 2366-2367 [PMID: 27898977 DOI: 10.1001/jama.2016.17563]

21. Aata-Cansizoglu E, Bolon-Canedo V, Campbell JP, Bozkurt A, Erdoganus D, Kalpathy-Cramer J, Patel S, Jonas K, Chan RV, Ostmo S, Chiang MF; i-ROP Research Consortium. Computer-Based Image Analysis for Plus Disease Diagnosis in Retinopathy of Prematurity: Performance of the "i-
ROP System and Image Features Associated With Expert Diagnosis. *Transl Vis Sci Technol* 2015; 4: 5 [PMID: 26644965 DOI: 10.1167/tvst.4.6.5]

22 **International Committee for the Classification of Retinopathy of Prematurity.** The International Classification of Retinopathy of Prematurity revisited. *Arch Ophthalmol* 2005; 123: 991-999 [PMID: 16609843 DOI: 10.1001/archopht.123.7.991]

23 **Wittenberg LA, Jonsson NJ, Chan RV, Chiang MF.** Computer-based image analysis for plus disease diagnosis in retinopathy of prematurity. *J Pediatr Ophthalmol Strabismus* 2012; 49: 11-9; quiz 10, 20 [PMID: 212366159 DOI: 10.3928/01913913-20110222-01]

24 **Brown JM, Campbell JP, Beers A, Chang K, Ostro S, Chan RVP, Dy J, Ergodmus D, Ioannidis S, Kalpathy-Cramer J, Chiang MF; Imaging and Informatics in Retinopathy of Prematurity (i-ROP) Research Consortium.** Automated Diagnosis of Plus Disease in Retinopathy of Prematurity Using Deep Convolutional Neural Networks. *JAMA Ophthalmol* 2018; 136: 803-810 [PMID: 29801159 DOI: 10.1001/jamaophthalmol.2018.1934]

25 **Taylor S, Brown JM, Gupta K, Campbell JP, Ostro S, Chan RVP, Dy J, Ergodmus D, Ioannidis S, Kim SJ, Kalpathy-Cramer J, Chiang MF; Imaging and Informatics in Retinopathy of Prematurity Consortium.** Monitoring Disease Progression With a Quantitative Severity Scale for Retinopathy of Prematurity Using Deep Learning. *JAMA Ophthalmol* 2019 [PMID: 31268518 DOI: 10.1001/jamaophthalmol.2019.243]

26 **Mookiah MR, Acharya UR, Fujita H, Koh JE, Tan JH, Noronha K, Bhandary SV, Chua CK, Lim CM, Laude A, Tong L; Local configuration pattern features for age-related macular degeneration characterization and classification.** *Comput Biol Med* 2015; 63: 208-218 [PMID: 26993788 DOI: 10.1016/j.compbiomed.2015.05.019]

27 **Burlina P, Pacheco KD, Joshi N, Freund DE, Bressler NM.** Comparing humans and deep learning performance for grading AMD: A study in using universal deep features and transfer learning for automated AMD analysis. *Comput Biol Med* 2017; 82: 80-86 [PMID: 28167406 DOI: 10.1016/j.compbiomed.2017.01.018]

28 **Fang L, Cunefare D, Wang C, Guymer RH, Li S, Farsiu S.** Automatic segmentation of nine retinal layer boundaries in OCT images of non-exudative AMD patients using deep learning and graph search. *Biomed Opt Express* 2017; 8: 2732-2744 [PMID: 28663902 DOI: 10.1364/BOE.8.002732]

29 **Bogunovic H, Waldstein SM, Schlegl T, Langs G, Sadeghpour A, Liu X, Gerendas BS, Osborne A, Schmidt-Erfurth U.** Prediction of Anti-VEGF Treatment Requirements in Neovascular AMD Using a Machine Learning Approach. *Invest Ophthalmol Vis Sci* 2017; 58: 3240-3248 [PMID: 28660277 DOI: 10.1167/ios16.21-0153]

30 **Bhuiyan A, Wong TY, Ting DSW, Govindiaiah A, Souied EH, Smith RT.** Artificial Intelligence to Stratify Severity of Age-Related Macular Degeneration (AMD) and Predict Risk of Progression to Late AMD. *Transl Vis Sci Technol* 2020; 9: 25 [PMID: 32818086 DOI: 10.1167/tvst.9.2.23]

31 **Martin KR, Mansouri K, Woinreb RN, Wasilewicz R, Gisler C, Hennebert J, Genoud D; Research Consortium.** Use of Machine Learning on Contact Lens Sensor-Derived Parameters for the Diagnosis of Primary Open-angle Glaucoma. *Am J Ophthalmol* 2018; 194: 46-53 [PMID: 30053471 DOI: 10.1016/j.ajo.2018.07.005]

32 **Omodaka K, An G, Tsuda S, Shiga Y, Takada N, Kikawa T, Takahashi Y, Yokota H, Akiba M, Nakazawa T.** Classification of optic disc shape in glaucoma using machine learning based on quantified ocular parameters. *PLOS One* 2017; 12: e0190012 [PMID: 29261773 DOI: 10.1371/journal.pone.0190012]

33 **Christopher M, Belghith A, Woinreb RN, Bowd C, Goldbaum MH, Saunders LJ, Medeiros FA, Zangwill LM.** Retinal Nerve Fiber Layer Features Identified by Unsupervised Machine Learning on Optical Coherence Tomography Scans Predict Glaucoma Progression. *Invest Ophthalmol Vis Sci* 2018; 59: 2748-2756 [PMID: 29860461 DOI: 10.1167/ios17.23-387]

34 **Barella KA, Costa VP, Gonçalves Vidotti V, Silva FR, Dias M, Gomi ES.** Glaucoma Diagnostic Accuracy of Machine Learning Classifiers Using Retinal Nerve Fiber Layer and Optic Nerve Data from SD-OCT. *J Ophthalmol* 2013; 2013: 789129 [PMID: 24369495 DOI: 10.1155/2013/789129]

35 **Bizios D, Hejil A, Hougaard JL, Bengtsson B.** Machine learning classifiers for glaucoma diagnosis based on classification of retinal nerve fibre layer thickness parameters measured by Stratus OCT. *Acta Ophthalmol* 2010; 88: 44-52 [PMID: 20066422 DOI: 10.1111/j.1755-3768.2009.01784.x]

36 **Larrosa JM, Polo V, Ferreras A, García-Martín E, Calvo P, Pablo LE.** Neural Network Analysis of Different Segmentation Strategies of Nerve Fiber Layer Assessment for Glaucoma Diagnosis. *J Glaucoma* 2015; 24: 672-678 [PMID: 25055209 DOI: 10.1097/IJG.0000000000000071]

37 **Li Z, He Y, Keel S, Meng W, Chang RT, He M.** Efficacy of a Deep Learning System for Detecting Glaucomatous Optic Neuropathy Based on Color Fundus Photographs. *Ophthalmolology* 2018; 125: 1199-1206 [PMID: 29506863 DOI: 10.1016/j.ophtha.2018.01.023]

38 **Al-Aswad LA, Kapoor S, Walters S, Gong D, Garg A, Gopal K, Patel V, Samee T, Rogers MW, Nicolás J, De Moraes GC, Mozammali K.** Evaluation of a Deep Learning System For Identifying Glaucomatous Optic Neuropathy Based on Color Fundus Photographs. *J Glaucoma* 2019; 28: 1029-1034 [PMID: 31233461 DOI: 10.1097/IJG.0000000000001319]

39 **Akara JD, Kuriakose A.** Role of artificial intelligence and machine learning in ophthalmology. *Kerala J Ophthalmol* 2019; 31: 150-160

40 **Asaoka R, Murata H, Iwase A, Araie M.** Detecting Preperimetric Glaucoma with Standard Automated Perimetry Using a Deep Learning Classifier. *Ophthalmology* 2016; 123: 1974-1980 [PMID: 27395766 DOI: 10.1016/j.ophtha.2016.05.029]
41 Andersson S, Heijl A, Bizios D, Bengtsson B. Comparison of clinicians and an artificial neural network regarding accuracy and certainty in performance of visual field assessment for the diagnosis of glaucoma. *Acta Ophthalmol* 2013; 91: 413-417 [PMID: 22583841 DOI: 10.1111/j.1755-3768.2012.02435.x]

42 Goldbaum MH, Sample PA, Zhang Z, Chan K, Hao J, Lee TW, Boden C, Bowd C, Bourne R, Zangwill L, Sejnowski T, Spinak D, Weinreb RN. Using unsupervised learning with independent component analysis to identify patterns of glaucomatous visual field defects. *Invest Ophthalmol Vis Sci* 2005; 46: 3676-3683 [PMID: 16186349 DOI: 10.1167/iovs.04-1167]

43 Bowd C, Weinreb RN, Balasubramanian M, Lee I, Jang G, Yousefi S, Zangwill LM, Medeiros FA, Girkin CA, Liebmann JM, Goldbaum MH. Glaucomatous patterns in Frequency Doubling Technology (FDT) perimetry data identified by unsupervised machine learning classifiers. *PLoS One* 2014; 9: e85941 [PMID: 24497932 DOI: 10.1371/journal.pone.0085941]

44 Gao X, Lin S, Song YM. Automatic Feature Learning to Grade Nuclear Cataracts Based on Deep Learning. *IEEE Trans Biomed Eng* 2015; 62: 2693-2701 [PMID: 26080373 DOI: 10.1109/TBME.2015.2444389]

45 Liu X, Jiang J, Zhang K, Long E, Cui J, Zhu M, An Y, Zhang J, Liu Z, Li X, Chen J, Cao Q, Li J, Wu X, Wang D, Lin H. Localization and diagnosis framework for pediatric cataracts based on slit-lamp images using deep features of a convolutional neural network. *PLoS One* 2017; 12: e0168606 [PMID: 28306716 DOI: 10.1371/journal.pone.0168606]

46 Wu X, Huang Y, Liu Z, Lai W, Long E, Zhang K, Jiang J, Lin D, Chen K, Yu T, Wu D, Li C, Chen Y, Zou M, Chen C, Zhu Y, Guo C, Zhang X, Wang R, Yang Y, Xiang Y, Chen L, Liu C, Xiong J, Ge Z, Wang D, Xu G, Du S, Xiao C, Wu J, Zhu K, Nie D, Xu F, Lv J, Chen W, Liu Y, Lin H. Universal artificial intelligence platform for collaborative management of cataracts. *Br J Ophthalmol* 2019; 103: 1553-1560 [PMID: 31481392 DOI: 10.1136/bjophthalmol-2019-314729]

47 Dong Y, Zhang Q, Qiao Z, Yang J. Classification of cataract fundus image based on deep learning. In: 2017 IEEE International Conference on Imaging Systems and Techniques; 2017 Oct 18-20; Beijing, China. IEEE; 2017: 1-5

48 Yu F, Silva Croso G, Kim TS, Song Z, Parker F, Hager GD, Reiter A, Vedula SS, Ali H, Sikder S. Assessment of Automated Identification of Phases in Videos of Cataract Surgery Using Machine Learning and Deep Learning Techniques. *JAMA Netw Open* 2019; 2: e191860 [PMID: 30951163 DOI: 10.1001/jamanetworkopen.2019.1860]

49 Zisimopoulos O, Flouty E, Luengo I, Giagaganas P, Nehme J, Chow A, Stoyanov D. Deep Phase: surgical phase recognition in CATARACTS videos. In: Frangi A, Schnabel J, Davatzikos C, Alberola-López C, Fichtinger G, editors. Medical Image Computing and Computer Assisted Intervention – MICCAI 2018. Cham: Springer; 2018: 265-272 [DOI: 10.1007/978-3-030-00937-3_31]

50 Melles RB, Kane JX, Olsen T, Chang WJ. Update on Intraocular Lens Calculation Formulas. *Ophthalmology* 2019; 126: 1334-1335 [PMID: 30980824 DOI: 10.1016/j.ophtha.2019.04.011]

51 Connell BJ, Kane JX. Comparison of the Kane formula with existing formulas for intraocular lens power selection. *BMJ Open Ophthalmol* 2019; 4: e000251 [PMID: 31179396 DOI: 10.1136/bmjophth-2018-000251]

52 Hoffer KJ. Intraocular lens power calculation after previous laser refractive surgery. *J Cataract Refract Surg* 2009; 35: 759-765 [PMID: 19304101 DOI: 10.1016/j.jcrs.2009.01.005]
