Role of artificial intelligence and machine learning in ophthalmology

ABSTRACT

Artificial intelligence (AI) and machine learning (ML) have entered several avenues of modern life, and health care is just one of them. Ophthalmology is a field with a lot of imaging and measurable data, thus ideal for application of AI and ML. Many of these are still in research stage, but show promising results. The ophthalmic diseases where AI is being used are diabetic retinopathy, glaucoma, age-related macular degeneration, retinopathy of prematurity, retinal vascular occlusions, keratoconus, cataract, refractive errors, retinal detachment, squint, and ocular cancers. It is also useful for intraocular lens power calculation, planning squint surgeries, and planning intravitreal antivascular endothelial growth factor injections. In addition, AI can detect cognitive impairment, dementia, Alzheimer's disease, stroke risk, and so on from fundus photographs and optical coherence tomography. We will surely see many more innovations in this rapidly growing field.

Keywords: Artificial intelligence, convolutional neural networks, deep learning, glaucoma artificial intelligence, machine learning

INTRODUCTION

John McCarthy described artificial intelligence (AI) as the "science of creating intelligent machines which replicated human behaviour." That had remained very much a part of science fiction until recently when more powerful computer hardware allowed the development of computing intensive algorithms and machine learning (ML) programming. This is now a part of the Fourth Industrial Revolution, which includes AI, autonomous vehicles, blockchain, robotics, internet of things, advanced biotechnology, and three-dimensional (3D) printing.[1] ML is a subtype of AI, where the software learns from large volumes of example data by trial and error without explicit instructions on how to derive the required output. Deep learning (DL) is a subtype of ML, which uses multiple layers of convolutional neural networks (CNNs), which are made of software-defined "neurons" which together try to figure out the instructions to process data to get information [Figure 1].

Generative adversarial networks (GANs) are a class of ML system that can generate new data based on training data.

They are paired neural networks used for unsupervised ML, where the generative neural network generates images or other data and the discriminative neural network evaluates it and gives feedback to help in the learning process. It is also useful for semi-supervised learning, fully supervised learning, and reinforcement learning. They can potentially be used to make deepfakes such as fake fundus lesions on a normal fundus photograph. Israeli researchers showed how they could insert or remove fake lung cancer lesions in a normal computed tomography (CT) scan in milliseconds.[2] They showed how the hospital's CT scan and picture archiving and communication system was easily compromised using a cheap Raspberry Pi with a fake 3D-printed logo of the CT scan

John Davis Akkara[1,2], Anju Kuriakose[3]

[1]Department of Glaucoma, Westend Eye Hospital, Kochi, [2]Department of Ophthalmology, Little Flower Hospital and Research Centre, Angamaly, [3]Department of Ophthalmology, Jubilee Mission Medical College, Thrissur, Kerala, India

Address for correspondence: Dr. John Davis Akkara, Department of Glaucoma, Westend Eye Hospital, Kacheripady, Kochi - 682 018, Kerala, India.
E-mail: johndavisakkara@gmail.com

How to cite this article: Akkara JD, Kuriakose A. Role of artificial intelligence and machine learning in ophthalmology. Kerala J Ophthalmol 2019;31:150-60.

company. This was done on high-resolution volumetric CT scans, so doing this on fundus photographs is much simpler.

Computer programming has typically depended on a series of precise sequential instructions written by a programmer. The software programmer had to know in advance what sort of input data the software would receive and how to process the data to produce the information that is required. However, with ML, the computer program figures out the instructions by itself based on example inputs and outputs. Once the software has finished learning, it is often not apparent to the programmer how exactly the ML program that they had written generates the required output. This is called the black box problem and the source of much of the trust issues with AI-generated reports. Newer AI software opens up the black box using an Integrated Gradients Explanation algorithm to show a heatmap or attention map as Google researchers demonstrated [Figure 2].[3]

A typical AI solution is a software installed on a powerful computer (ML server), which is accessed via the internet. The input data are uploaded onto the ML server, which takes some time to process it (seconds to minutes depending on complexity of data analysis and processing speed of the server). The output can be accessed via the internet.

In the medical field, ophthalmology,[4] radiology,[5] dermatology,[6] pathology,[7] pediatrics,[8] gynecology,[9] oncology,[10] endocrinology,[11] and cardiology[12] have joined the AI revolution. Most of this is because of the huge volume of nonstandardized image processing required in these fields, which is very difficult in conventional programming but much simpler to implement with ML. In addition to image processing, analysis of big data, making predictions, and finding efficient use of resources are other areas where ML can help in the medical field.

For ophthalmology in particular, the most common use of AI has been in analysis of retinal fundus[13] images for diabetic retinopathy (DR), followed by age-related macular degeneration (ARMD), glaucoma, and retinopathy of prematurity (ROP). Huge advancements have been made in this field with the advent of offline AI which can now run the final algorithm on a smartphone, whereas earlier a powerful server computer was required. However, fundus image analysis is the only part of the picture, as various other arenas of ophthalmology from intraocular lens (IOL) calculation to myopia prediction to smart electronic medical records (EMRs) are now based on AI.

Major tech companies have taken an interest in AI for ophthalmic use. Google's DeepMind Health, in a research with Moorfields Eye Hospital, showed that it can detect fifty eye diseases[14] from optical coherence tomography (OCT) scans for referral. IBM's AI can predict visual field data from OCT scans.[15] Microsoft Intelligent Network for Eyecare[16] is a collaboration to apply AI to eliminate avoidable blindness and scale eyecare delivery systems. Several authors have reviewed the current state of AI in ophthalmology, but newer applications are coming out every few months.[17-24] The current commercially available AI solutions include Netra.AI (Leben Care Technologies Pte., Ltd.),[25] Pegasus (Visulytix Ltd.),[26] Medios AI (Remidio Pvt., Ltd.),[27] and IDx-DR (IDx Technologies Inc.).[28]

Let us look at some of the applications of AI and ML in ophthalmology.
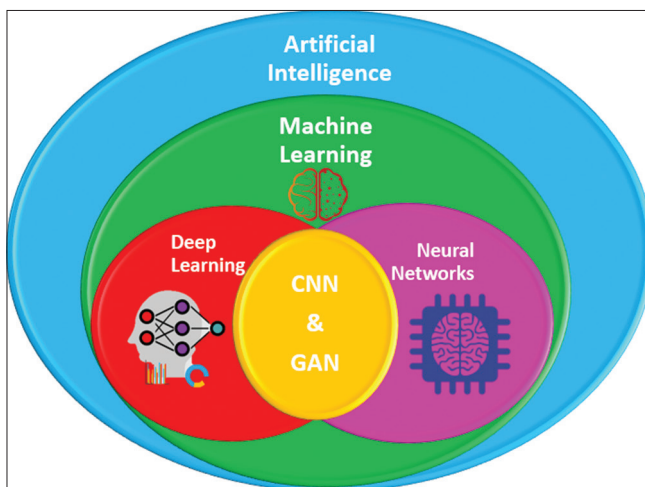

Figure 1: Relationship between artificial intelligence, machine learning, deep learning, convolutional neural networks, and generative adversarial networks
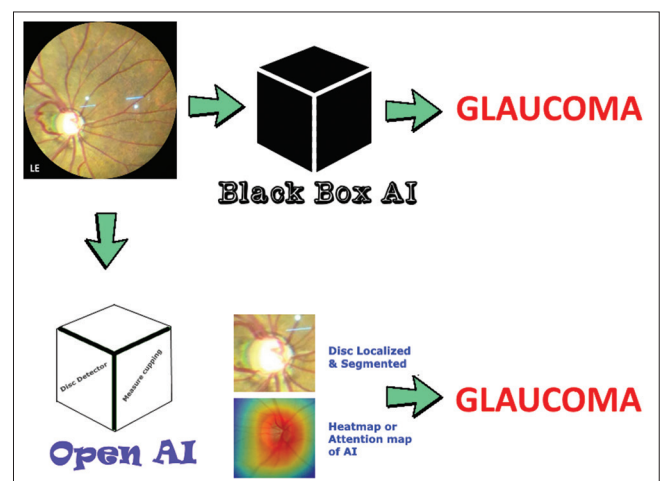

Figure 2: Representation of black box problem in artificial intelligence. Typical artificial intelligence does not show how the analysis works. By modifying the internal working, "Open" artificial intelligence shows the segmentation and heatmap by which the image was analyzed and arrived at a diagnosis

Diabetic retinopathy

The most widely known use of AI in ophthalmology is for the evaluation of DR from fundus photographs, which has several studies and reviews [Figure 3].[29-36]

The first US Food and Drug Administration-approved autonomous AI diagnostic device was IDX-DR for detecting "more than mild" DR and diabetic macular edema.[37]

Typically, ML systems run on a powerful server computer. Fundus images taken using a fundus camera are collected and evaluated later or they are uploaded through the internet to the powerful server which generates the report and sends it back to the device. With the advent of low-cost smartphone-based fundus cameras such as DIYretcam,[38] T3retcam,[39] MIIretcam,[40] JaizRetcam, and Hopescope, quick image analysis would be invaluable. In a recent study, Sosale et al. evaluated an offline AI (Medios AI) on a Remidio Fundus-on-Phone (Remidio Innovative Solutions Pvt. Ltd., Bengaluru, Karnataka, India) and showed a high sensitivity (93%) and specificity (92.5%).[41] Offline AI would make this technology accessible in areas with poor network connectivity.

Glaucoma

Glaucoma evaluation involves measurement of intraocular pressure, optic disc cupping, visual fields, gonioscopy, and optical coherence tomography for retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL) thickness. We fail to recognize that the regular OCT machines automatically measure disc size, cupping, neuroretinal rim area, RNFL thickness, and GCL thickness and all such parameters using AI image processing techniques called segmentation. A comprehensive AI for glaucoma should evaluate all the parameters including IOP, disc, gonioscopy, fields, and OCT together; however, such an AI system is not ready yet. Several studies evaluated various AI and ML systems for glaucoma.[42,43]

Martin et al. analyzed pooled data from 24 prospective clinical trials of a contact lens sensor for intraocular pressure monitoring (SENSIMED Triggerfish, Sensimed AG, Lausanne, Switzerland).[44] They used an ML approach called random forest modeling to identify the parameters associated with the primary open-angle glaucoma patients.

Niwas et al. evaluated a fully automated model to classify angle closure glaucoma from anterior segment OCT scans and showed an accuracy of 89.2%.[45]

For fundus photographs, Li et al. evaluated a DL algorithm that showed a high sensitivity (95.6%) and specificity (92%) to detect referable glaucomatous optic neuropathy.[46] The disadvantage was that high myopia caused false negatives and physiological cupping caused false positives. Al-Aswad et al. evaluated Pegasus (Visulytix Ltd., London, UK), a DL system to detect glaucomatous optic neuropathy from color fundus photographs and showed that it outperformed 5 out of 6 ophthalmologists in the study.[47] Netra.AI (Leben Care Technologies Pte., Ltd.) is another AI that evaluates glaucomatous fundus photographs [Figure 4]. Several other studies also looked at different techniques to detect glaucomatous optic neuropathy from disc photographs [Figure 5].[48-50]

Muhammad et al. showed that a hybrid deep learning method on a single, wide-field swept-source OCT had 93.1% sensitivity in detecting glaucoma suspects.[51] Asaoka et al. evaluated a DL algorithm with pretraining that diagnosed glaucoma based on macular OCT for RNFL and GCL.[52] Other studies evaluated unsupervised ML, ML classifiers (MLCs), artificial neural networks (ANNs), support vector machines, and segmentation methods for glaucoma OCT.[53-56]
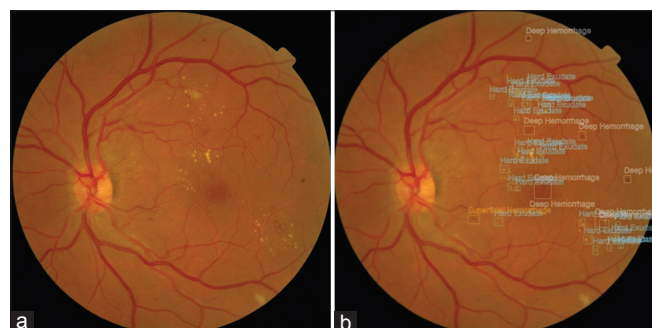

Figure 3: (a) Retinal fundus photo of the left eye of a diabetic patient. (b) Same image after artificial intelligence analysis by Netra.AI (Leben Care Technologies Pte., Ltd.) with the superficial hemorrhages, deep hemorrhages, and hard exudates

Figure 4: Retinal fundus photo of the left eye of a glaucoma patient in which the vertical disc and cup margins have been demarcated by the Netra. AI (Leben Care Technologies Pte., Ltd.)
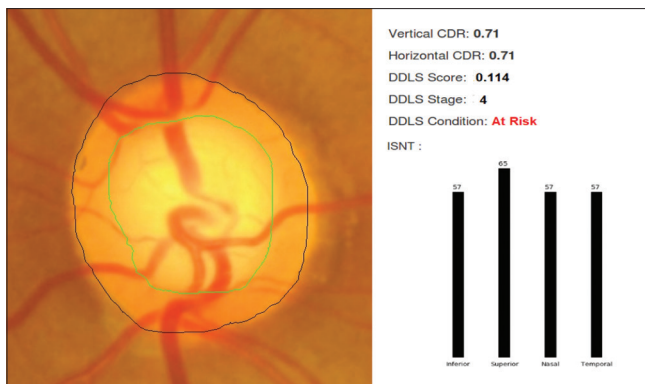
Figure 5: Localized and segmented image of disc from previous fundus image in which disc and cup margins are segmented. On the right, vertical cup: disc ratio, horizontal cup: disc ratio, and disc damage likelihood stage are shown along with the violated ISNT rule graph (inferior superior nasal and temporal neuroretinal rim) (Image courtesy: Leben Care Technologies Pte., Ltd.)

Visual fields are difficult to interpret, so AI help would be appreciated in this context. Asaoka et al. used a feedforward neural network to identify preperimetric visual fields which did not meet Anderson–Patella's criteria from healthy visual fields.[57] Li et al. evaluated a CNN to automatically differentiate glaucoma VF from nonglaucoma VF.[58] Goldbaum et al. used unsupervised ML and variational Bayesian independent component analysis mixture model (vB-ICA-mm) to analyze VF defects.[59] Andersson et al. showed that a trained ANN obtained 93% sensitivity and 91% specificity in evaluating glaucoma VF and performed at least as well as clinicians.[60] Bowd et al. successfully used vB-ICA-mm, an unsupervised MLC, to analyze frequency-doubling technology perimetry data.[61]

For visual field progression analysis, Goldbaum et al. used progression of patterns, an MLC algorithm.[62] Yousefi et al. showed that ML detects VF progressing consistently, without confirmation visits and even slow progression.[63] All these methods would ideally run on portable perimetry devices like the smartphone-based virtual reality perimetry such as PeriScreener, VirtualEye, and C3FA.[64]

Wen et al. trained a DL system with 32,443 visual fields (24-2 HVFs) taken between 1998 and 2018, and the resulting CascadeNet-5 model was able to predict future visual fields for up to 5.5 years based on a single input visual field.[65] Kazemian et al. developed and validated Kalman filters, which could predict personalized trajectory of progression of mean deviation of visual fields at different target IOPs.[66] This would guide ophthalmologists in choosing a specific patient's target IOP.

Retinopathy of prematurity
AI tools for ROP screening[67-69] from fundus images from cameras such as RetCam (Massie Research Laboratories, Inc., Dublin, California) include ROPTool,[70] retinal image multiscale analysis,[71] computer-assisted image analysis of the retina,[72] and imaging and informatics in ROP (i-ROP).[73] Diagnostic accuracy of the i-ROP system (95%), which incorporated tortuosity of arteries and veins, was comparable to expert ophthalmologists.[73]

Age-related macular degeneration
Some ML algorithms have been trained to detect and grade ARMD from color fundus photographs.[74-78] Some other ML algorithms can detect ARMD from OCT scans.[79-82] A few other ML systems can predict visual acuity[83,84] and requirement of antivascular endothelial growth factor (VEGF)[85] from OCT scans.

Retinal vascular occlusions
ML algorithms can detect central retinal vein occlusion[86] and branch retinal vein occlusion[87] from wide-field fundus photographs or from fluorescein angiograms[88] and quantify the resulting macular edema[81] by OCT. Another study also used ML to evaluate the impact of vitreomacular adhesion on anti-VEGF therapy for retinal vein occlusions.[89]

Optical coherence tomography
Inbuilt segmentation of scans in OCT machines is a type of AI. OCT scans can be evaluated for glaucoma, DR, and several other retinal diseases. Kuwayama et al. showed the feasibility of automated detection of macular diseases such as epiretinal membrane, DR, and ARMD from OCT and found that image augmentation is effective when the number of training images is low.[90]

Sumaroka et al. used a supervised ML to predict perimetry results from OCT scans of retinitis pigmentosa and Leber congenital amaurosis patients.[91]

Fluid intelligence is a mobile AI app that runs on Android or iPhone, which allows you to take a photo of an OCT scan and detect macular edema or subretinal fluid. Odaibo et al. evaluated this app and found a sensitivity of 89.3% and specificity of 81.25% [Figure 6].[92]

Other retinal diseases
Ohsugi et al. showed that DL can detect rhegmatogenous retinal detachment from ultra-wide-field fundus photographs with a sensitivity of 97.6% and specificity of 95.6%.[93]

Xu et al. evaluated a dual-stage DL system to identify and segment pigment epithelial detachment (PED) in polypoidal choroidal vasculopathy (PCV) from OCT scans.[94]
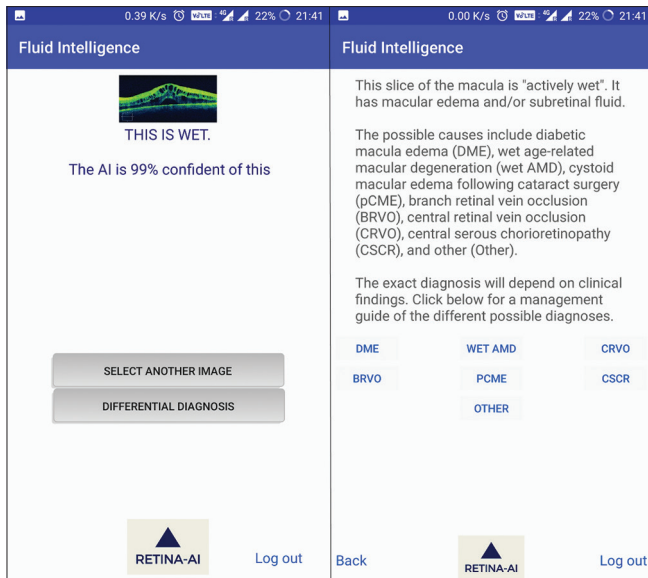
Figure 6: Screenshots of Fluid Intelligence App on Android after evaluating optical coherence tomography scans uploaded from mobile (Image courtesy: Fluid Intelligence App)

Keratoconus

AI has been used to detect keratoconus and forme fruste keratoconus[95] from Placido topography, Scheimpflug tomography,[96] SD-ASOCT, and biomechanical metrics (Corvis ST, corneal hysteresis).[97] Data from Pentacam,[98] Sirius,[99] Orbscan II,[100] Galilei,[101] and TMS-1[102] topographers and tomographers have been studied using ML algorithms to detect early keratoconus.

Other corneal diseases

Ambrósio et al. evaluated AI-based tomographic and biomechanical index (TBI), which combines Scheimpflug-based corneal tomography and biomechanics (Corvis ST) for enhancing ectasia detection.[103] Sharif et al. showed that confocal microscopy images of the cornea can be evaluated in detail using a committee machine formed from ANNs and adaptive neuro-fuzzy inference systems that can detect abnormalities with high accuracy and can visualize in 3D.[104]

Cataract grading

Mahesh Kumar and Gunasundari developed a computer-aided diagnosis system to detect corneal arcus and cataract from the photographs of eyes taken with a standard digital camera.[105] Gao et al. proposed a system to automatically grade cataract from slit-lamp images.[106]

Caixinha et al. proposed grading of cataract hardness using ultrasound in an animal model using ML.[107] Yang et al. demonstrated grading of cataract from clarity of retinal fundus photographs with an accuracy of 93.2% in detecting cataract and 84.5% in grading cataract.[108] Zhang et al.

reported a similar accuracy of 93.52% for detecting cataract and 86.69% for grading cataract with their method using fundus photographs.[109]

Mohammadi et al. predicted the risk for posterior capsule opacification (PCO) using AI with an accuracy of 87%.[110]

Gillner et al. demonstrated automated segmentation of an accommodative intraocular lens in a biomechanical eye model using OCT.[111] This can potentially be used to study the working of accommodative lens and design better IOLs.

Pediatric ophthalmology

AI and ML have been used for congenital cataract diagnosis,[112] collaborative management,[113] and prediction of surgical complications of pediatric cataract surgery.[114]

It can also be used to detect strabismus[115] and refractive error, predict future high myopia, and diagnose reading disability.[116] There have also been studies to automatically detect leukocoria in children from recreational smartphone or digital camera photographs, which suggests ocular pathology that requires screening.[117,118]

Almeida et al. presented a methodology based on support vector regression for planning surgical resections and recessions for horizontal strabismus surgeries which showed good accuracy.[119]

Ocular oncology

A technique to demarcate the boundary of ocular surface squamous neoplasia from unstained biopsy specimens using multispectral imaging and ML was described by Habibalahi et al.[120] This can potentially be used intraoperatively for rapid assessment of cancer-free margins.

Tan et al. showed that a supervised ML decision tree model was able to predict the complexity of reconstructive surgery after excision of periocular basal cell carcinoma.[121]

Refractive error prediction

Das et al. from LV Prasad Eye Institute, India, presented a study that predicted the progression of myopia and refractive error in children using ML on data such as age, gender, onset of refractive error, current refractive error, visual acuity, and other clinical information.[122] Zhang et al. validated the accuracy of a model to predict onset of myopia in children using ocular biometry, height, weight, and presenting visual acuity.[123] Lin et al. developed an algorithm to use refraction data from EMRs to predict refraction values at future time points.[124]

Surprisingly, Varadarajan *et al*. from Google used DL using TensorFlow for predicting refractive error from only retinal fundus photographs.[125] The attention map which opens up the black box of the ML algorithm showed that features on the fovea were important to predict refractive error including spherical equivalent, spherical, and cylindrical powers. Liu *et al*. presented the Pathological Myopia Detection Through Peripapillary Atrophy system to detect pathological myopia from retinal images by the detection of parapapillary atrophy.[126] Zhang *et al*. further demonstrated the diagnosis of pathological myopia by combining heterogeneous biomedical data, including demographic data, fundus imaging data, and single-nucleotide polymorphism data.[127]

Koprowski *et al*. demonstrated the use of ANNs to predict the corneal power after myopic refractive surgery with good accuracy (0.16 ± 0.14 diopters).[128]

Intraocular lens power calculation

IOL power calculations have always been an approximate estimate from several parameters and are thus suited for ML algorithms. AI-powered IOL calculations include Hill-Radial Basis Function (RBF),[129] Ladas Super Formula,[130,131] Clarke Neural Network,[132] and FullMonte Method. A few other studies have also attempted to use AI for IOL calculation.[133-135] Kane *et al*., in 2017, had compared the accuracy of Hill-RBF, Ladas Super Formula, and FullMonte with that of Holladay 1 and Barrett Universal II, but did not find them to be more accurate.[136]

The best known AI formula is the Hill-RBF formula[129] by Dr. Warren Hill, available online at https://rbfcalculator.com/online/, which uses pattern recognition and data interpolation. It is currently in version 2.0 and uses data from 12,419 eyes. Biometry data required include axial length, anterior chamber depth, and keratometry values and their axes. Optional data which can improve accuracy include central corneal thickness, lens thickness, and white-to-white [Figure 7].

Dementia and Alzheimer's disease

Retinal vascular changes not detectable by human ophthalmologists are present in neurological diseases[137] such as cognitive impairment,[138] dementia,[139-141] and Alzheimer's disease,[142-144] which can be detected by ML algorithms from fundus photography and OCT. Carl Zeiss Meditech holds a patent for a method and system for detecting the effects of Alzheimer's disease in the human retina.[145]

Predicting cardiovascular and stroke risk

In a study by Google, Poplin *et al*. trained a DL AI using data from 284,335 patients and validated on two independent datasets of 12,026 and 999 patients. From fundus photographs, the AI was able to predict age (mean error of 3.26 years), gender (AUC = 0.97), smoking status (AUC = 0.71), systolic blood pressure (mean error of 11.23 mmHg), and major adverse cardiac events (AUC = 0.70). They noted that AI used anatomical features of the fundus photo such as optic disc and blood vessels to make the predictions. This can potentially help humans to learn from the AI regarding how to predict these from fundus photos.

Figure 7: Website of artificial intelligence based Hill-Radial Basis Function intraocular lens power calculator showing the parameters entered (image courtesy: rbfcalculator.com)

Automatic retinal image analysis of fundus photos by an ML algorithm can predict the presence of white matter hyperintensities on magnetic resonance imaging brain, which is a risk for cerebral small vessel disease and stroke.[146]

CONCLUSION

The age of AI and ML has definitely arrived. However, the accuracy and reliability of the systems in a real-world clinical scenario is questionable. AI and ML should augment the clinician skill and can only be considered a tool. AI in ophthalmology would probably find the best application in screening camps and teleophthalmology.[147] This could also be applied in virtual clinics[148] to reduce the number of onward referrals to higher centers. Currently available medical diagnosis apps include Ada (available on Android and Apple phones), Babylon, and Your.MD, and though they sometimes give correct diagnosis, they cannot be relied on for critical decisions. Fundus photographs can be analyzed on Orbis Cybersight Consult website in the clinical cases section. Many newer fundus cameras and OCT machines might come inbuilt AI software. EMRs may be integrated with a cloud AI system.

Ophthalmologists should know about the AI resources available to them and make judicious use of them when understanding their limitations.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Akkara J, Kuriakose A. The magic of three-dimensional printing in ophthalmology. Kerala J Ophthalmol 2018;30:209-15.
2. Mirsky Y, Mahler T, Shelef I, Elovici Y. CT-GAN: Malicious tampering of 3D medical imagery using deep learning. arXiv preprint arXiv:1901.03597. 2019. Available from: http://arxiv.org/abs/1901.03597. [Last accessed on 2019 Jul 10].
3. Sayres R, Taly A, Rahimy E, Blumer K, Coz D, Hammel N, *et al.* Using a deep learning algorithm and integrated gradients explanation to assist grading for diabetic retinopathy. Ophthalmology 2019;126:552-64.
4. Akkara JD, Kuriakose A. Commentary: Rise of machine learning and artificial intelligence in ophthalmology. Indian J Ophthalmol 2019;67:1009-10.
5. Hosny A, Parmar C, Quackenbush J, Schwartz LH, Aerts HJ. Artificial intelligence in radiology. Nat Rev Cancer 2018;18:500-10.
6. Hogarty DT, Su JC, Phan K, Attia M, Hossny M, Nahavandi S, *et al.* Artificial intelligence in dermatology-where we are and the way to the future: A Review. American Journal of Clinical Dermatology 2019;5:1-7.
7. Colling R, Pitman H, Oien K, Rajpoot N, Macklin P, Snead D, *et al.* CM-Path AI in Histopathology Working Group, Bachtiar V, Booth R. Artificial intelligence in digital pathology: A roadmap to routine use in clinical practice. The Journal of pathology 2019.
8. Liang H, Tsui BY, Ni H, Valentim CC, Baxter SL, Liu G, *et al.* Evaluation and accurate diagnoses of pediatric diseases using artificial intelligence. Nat Med 2019;25:433-8.
9. Desai GS. Artificial intelligence: The future of obstetrics and gynecology. J Obstet Gynaecol India 2018;68:326-7.
10. Rattan R, Kataria T, Banerjee S, Goyal S, Gupta D, Pandita A, *et al.* Artificial intelligence in oncology, its scope and future prospects with specific reference to radiation oncology. BJR Open 2019;1:20180031.
11. Gubbi S, Hamet P, Tremblay J, Koch CA, Hannah-Shmouni F. Artificial intelligence and machine learning in endocrinology and metabolism: The dawn of a new era. Front Endocrinol (Lausanne) 2019;10:185.
12. Johnson KW, Soto JT, Glicksberg BS, Shameer K, Miotto R, Ali M, *et al.* Artificial intelligence in cardiology. J Am Coll Cardiol 2018;71:2668-79.
13. Schmidt-Erfurth U, Sadeghipour A, Gerendas BS, Waldstein SM, Bogunović H. Artificial intelligence in retina. Prog Retin Eye Res 2018;67:1-29.
14. De Fauw J, Ledsam JR, Romera-Paredes B, Nikolov S, Tomasev N, Blackwell S, *et al.* Clinically applicable deep learning for diagnosis and referral in retinal disease. Nat Med 2018;24:1342-50.
15. AI Holds Promise for Glaucoma, a Leading Global Cause of Blindness. IBM Research Blog; 2019. Available from: https://www.ibm.com/blogs/research/2019/05/ai-glaucoma/. [Last accessed on 2019 Jul 12].
16. Microsoft, LV Prasad Eye Institute and Global Experts Collaborate to Launch Microsoft Intelligent Network for Eyecare. Microsoft News Center India; 2016. Available from: https://news.microsoft.com/en-in/microsoft-l-v-prasad-eye- institute-and-global-experts- collaborate-to-launch-microsoft- intelligent- network-for-eyecare/. [Last accessed on 2019 Jul 12].
17. Ting DS, Pasquale LR, Peng L, Campbell JP, Lee AY, Raman R, *et al.* Artificial intelligence and deep learning in ophthalmology. Br J Ophthalmol 2019;103:167-75.
18. Kapoor R, Walters SP, Al-Aswad LA. The current state of artificial intelligence in ophthalmology. Surv Ophthalmol 2019;64:233-40.
19. Hogarty DT, Mackey DA, Hewitt AW. Current state and future prospects of artificial intelligence in ophthalmology: A review. Clin Exp Ophthalmol 2019;47:128-39.
20. Lu W, Tong Y, Yu Y, Xing Y, Chen C, Shen Y. Applications of artificial intelligence in ophthalmology: General overview. J Ophthalmol 2018;2018:5278196.
21. Rahimy E. Deep learning applications in ophthalmology. Curr Opin Ophthalmol 2018;29:254-60.
22. Ting DS, Peng L, Varadarajan AV, Keane PA, Burlina PM, Chiang MF, *et al.* Deep learning in ophthalmology: The technical and clinical considerations. Prog Retin Eye Res 2019. pii: S1350-9462(18)30090-9.
23. Balyen L, Peto T. Promising artificial intelligence-machine learning-deep learning algorithms in ophthalmology. Asia Pac J Ophthalmol (Phila) 2019;8:264-72.
24. Du XL, Li WB, Hu BJ. Application of artificial intelligence in ophthalmology. Int J Ophthalmol 2018;11:1555-61.
25. Leben Care Technologies – AI Imaging Diagnostics and Screening for Ophthalmology, Diabetic Retinopathy, Glaucoma, Age Related Macular Degeneration. Available from: https://www.leben.ai/. [Last accessed on 2019 Jul 14].
26. Pegasus. Available from: https://pegasus.visulytix.com/#!/. [Last accessed on 2019 Jul 14].
27. Medios AI- Remidio. Available from: https://www.remidio.com/medios.php. [Last accessed on 2019 Jul 14].
28. IDx-DR EU. Available from: https://www.eyediagnosis.co/idx-dr-eu-1. [Last accessed on 2019 Jul 14].
29. Padhy SK, Takkar B, Chawla R, Kumar A. Artificial intelligence in diabetic retinopathy: A natural step to the future. Indian J Ophthalmol 2019;67:1004-9.
30. Sosale AR. Screening for diabetic retinopathy – Is the use of artificial

intelligence and cost-effective fundus imaging the answer? Int J Diabetes Dev Ctries 2019;39:1-3.

31. Rajalakshmi R, Subashini R, Anjana RM, Mohan V. Automated diabetic retinopathy detection in smartphone-based fundus photography using artificial intelligence. Eye (Lond) 2018;32:1138-44.

32. Keel S, Lee PY, Scheetz J, Li Z, Kotowicz MA, MacIsaac RJ, et al. Feasibility and patient acceptability of a novel artificial intelligence-based screening model for diabetic retinopathy at endocrinology outpatient services: A pilot study. Sci Rep 2018;8:4330.

33. 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.

34. Wong TY, Bressler NM. Artificial intelligence with deep learning technology looks into diabetic retinopathy screening. JAMA 2016;316:2366-7.

35. Ting DS, Carin L, Abramoff MD. Observations andlessons learned from the artificial intelligence studies for Diabetic retinopathy screening. JAMA Ophthalmology. 2019. Available from: https://jamanetwork.com/journals/jamaophthalmology/fullarticle/2734989. [Last accessed on 2019 Jul 05].

36. Kanagasingam Y, Xiao D, Vignarajan J, Preetham A, Tay-Kearney ML, Mehrotra A. Evaluation of Artificial intelligence–based grading of diabetic retinopathy in primary care. JAMA Netw Open 2018;1:e182665.

37. 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.

38. Raju B, Raju NS, Akkara JD, Pathengay A. Do it yourself smartphone fundus camera – DIYretCAM. Indian J Ophthalmol 2016;64:663-7.

39. Chandrakanth P, Ravichandran R, Nischal NG, Subhashini M. Trash to treasure retcam. Indian J Ophthalmol 2019;67:541-4.

40. Sharma A, Subramaniam SD, Ramachandran KI, Lakshmikanthan C, Krishna S, Sundaramoorthy SK. Smartphone-based fundus camera device (MII ret cam) and technique with ability to image peripheral retina. Eur J Ophthalmol 2016;26:142-4.

41. Sosale B, Sosale AR, Murthy H, Narayana S, Sharma U, Gowda SG, et al. 51-OR: Medios – A smartphone-based artificial intelligence algorithm in screening for diabetic retinopathy. Diabetes 2019;68 Suppl 1:51.

42. Kapoor R, Whigham BT, Al-Aswad LA. The role of artificial intelligence in the diagnosis and management of glaucoma. Curr Ophthalmol Rep 2019;7:136-42.

43. Zheng C, Johnson TV, Garg A, Boland MV. Artificial intelligence in glaucoma. Curr Opin Ophthalmol 2019;30:97-103.

44. Martin KR, Mansouri K, Weinreb RN, Wasilewicz R, Gisler C, Hennebert J, et al. 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.

45. Niwas SI, Lin W, Bai X, Kwoh CK, Jay Kuo CC, Sng CC, et al. Automated anterior segment OCT image analysis for angle closure glaucoma mechanisms classification. Comput Methods Programs Biomed 2016;130:65-75.

46. Li Z, He Y, Keel S, Meng W, Chang RT, He M. Efficacy of a deep learning system for detecting glaucomatous optic neuropathy based on color fundus photographs. Ophthalmology 2018;125:1199-206.

47. Al-Aswad LA, Kapoor R, Chu CK, Walters S, Gong D, Garg A, et al. Evaluation of a deep learning system for identifying glaucomatous optic neuropathy based on color fundus photographs. Journal of glaucoma 2019.

48. Cerentini A, Welfer D, Cordeiro d'Ornellas M, Pereira Haygert CJ, Dotto GN. Automatic identification of glaucoma using deep learning methods. Stud Health Technol Inform 2017;245:318-21.

49. Haleem MS, Han L, Hemert JV, Li B, Fleming A, Pasquale LR, et al. A novel adaptive deformable model for automated optic disc and cup segmentation to aid glaucoma diagnosis. J Med Syst 2017;42:20.

50. Thompson AC, Jammal AA, Medeiros FA. A deep learning algorithm to quantify neuroretinal rim loss from optic disc photographs. Am J Ophthalmol 2019;201:9-18.

51. Muhammad H, Fuchs TJ, De Cuir N, De Moraes CG, Blumberg DM, Liebmann JM, et al. Hybrid deep learning on single wide-field optical coherence tomography scans accurately classifies glaucoma suspects. J Glaucoma 2017;26:1086-94.

52. Asaoka R, Murata H, Hirasawa K, Fujino Y, Matsuura M, Miki A, et al. Using deep learning and transfer learning to accurately diagnose early-onset glaucoma from macular optical coherence tomography images. Am J Ophthalmol 2019;198:136-45.

53. Christopher M, Belghith A, Weinreb RN, Bowd C, Goldbaum MH, Saunders LJ, et al. Retinal nerve fiber layer features identified by unsupervised machine learning on optical coherence tomography scans predict glaucoma progression. Invest Ophthalmol Vis Sci 2018;59:2748-56.

54. 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.

55. Bizios D, Heijl 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.

56. 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;24:672-8.

57. Asaoka R, Murata H, Iwase A, Araie M. Detecting preperimetric glaucoma with standard automated perimetry using a deep learning classifier. Ophthalmology 2016;123:1974-80.

58. Li F, Wang Z, Qu G, Song D, Yuan Y, Xu Y, et al. Automatic differentiation of glaucoma visual field from non-glaucoma visual filed using deep convolutional neural network. BMC Med Imaging 2018;18:35.

59. Goldbaum MH, Sample PA, Zhang Z, Chan K, Hao J, Lee TW, et al. Using unsupervised learning with independent component analysis to identify patterns of glaucomatous visual field defects. Invest Ophthalmol Vis Sci 2005;46:3676-83.

60. 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;91:413-7.

61. Bowd C, Weinreb RN, Balasubramanian M, Lee I, Jang G, Yousefi S, et al. Glaucomatous patterns in frequency doubling technology (FDT) perimetry data identified by unsupervised machine learning classifiers. PLoS One 2014;9:e85941.

62. Goldbaum MH, Lee I, Jang G, Balasubramanian M, Sample PA, Weinreb RN, et al. Progression of Patterns (POP): A machine classifier algorithm to identify glaucoma progression in visual fields. Invest Ophthalmol Vis Sci 2012;53:6557-67.

63. Yousefi S, Kiwaki T, Zheng Y, Sugiura H, Asaoka R, Murata H, et al. Detection of longitudinal visual field progression in glaucoma using machine learning. Am J Ophthalmol 2018;193:71-9.

64. Akkara JD, Kuriakose A. Review of recent innovations in ophthalmology. Kerala J Ophthalmol 2018;30:54.

65. Wen JC, Lee CS, Keane PA, Xiao S, Rokem AS, Chen PP, et al. Forecasting future Humphrey visual fields using deep learning. PLoS One 2019;14:e0214875.

66. Kazemian P, Lavieri MS, Van Oyen MP, Andrews C, Stein JD. Personalized prediction of glaucoma progression under different target intraocular pressure levels using filtered forecasting methods. Ophthalmology 2018;125:569-77.

67. Brown JM, Campbell JP, Beers A, Chang K, Donohue K, Ostmo S, et al. Fully automated disease severity assessment and treatment monitoring

in retinopathy of prematurity using deep learning. In: Medical Imaging 2018: Imaging Informatics for Healthcare, Research, and Applications. International Society for Optics and Photonics; 2018. p. 105790Q. Available from: https://www.spiedigitallibrary.org/conference-proceedings-of-spie/10579/105790Q/Fully-automated-disease-severity-assessment-and-treatment-monitoring-in-retinopathy/10.1117/12.2295942.short. [Last accessed on 2019 Jul 13].

68. Worrall DE, Wilson CM, Brostow GJ. Automated retinopathy of prematurity case detection with convolutional neural networks. Deep Learning and Data Labeling for Medical Applications. Springer, Cham; 2016. p. 68-76.

69. Brown JM, Campbell JP, Beers A, Chang K, Ostmo S, Chan RVP, et al. Automated diagnosis of plus disease in retinopathy of prematurity using deep convolutional neural networks. JAMA Ophthalmol 2018;136:803-10.

70. Abbey AM, Besirli CG, Musch DC, Andrews CA, Capone A Jr., Drenser KA, et al. Evaluation of screening for retinopathy of prematurity by ROPtool or a lay reader. Ophthalmology 2016;123:385-90.

71. Gelman R, Martinez-Perez ME, Vanderveen DK, Moskowitz A, Fulton AB. Diagnosis of plus disease in retinopathy of prematurity using retinal image multiScale analysis. Invest Ophthalmol Vis Sci 2005;46:4734-8.

72. Wilson CM, Cocker KD, Moseley MJ, Paterson C, Clay ST, Schulenburg WE, et al. Computerized analysis of retinal vessel width and tortuosity in premature infants. Invest Ophthalmol Vis Sci 2008;49:3577-85.

73. Campbell JP, Ataer-Cansizoglu E, Bolon-Canedo V, Bozkurt A, Erdogmus D, Kalpathy-Cramer J, et al. Expert diagnosis of plus disease in retinopathy of prematurity from computer-based image analysis. JAMA Ophthalmol 2016;134:651-7.

74. Ting DSW, Cheung CY, Lim G, Tan GSW, Quang ND, Gan A, et al. Development and validation of a deep learning system for diabetic retinopathy and related eye diseases using retinal images from multiethnic populations with diabetes. JAMA 2017;318:2211-23.

75. Burlina PM, Joshi N, Pekala M, Pacheco KD, Freund DE, Bressler NM. Automated grading of age-related macular degeneration from color fundus images using deep convolutional neural networks. JAMA Ophthalmol 2017;135:1170-6.

76. Grassmann F, Mengelkamp J, Brandl C, Harsch S, Zimmermann ME, Linkohr B, et al. A deep learning algorithm for prediction of age-related eye disease study severity scale for age-related macular degeneration from color fundus photography. Ophthalmology 2018;125:1410-20.

77. 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;82:80-6.

78. Peng Y, Dharssi S, Chen Q, Keenan TD, Agrón E, Wong WT, et al. DeepSeeNet: A deep learning model for automated classification of patient-based age-related macular degeneration severity from color fundus photographs. Ophthalmology 2019;126:565-75.

79. Lee CS, Baughman DM, Lee AY. Deep learning is effective for the classification of OCT images of normal versus age-related macular degeneration. Ophthalmol Retina 2017;1:322-7.

80. Treder M, Lauermann JL, Eter N. Automated detection of exudative age-related macular degeneration in spectral domain optical coherence tomography using deep learning. Graefes Arch Clin Exp Ophthalmol 2018;256:259-65.

81. Schlegl T, Waldstein SM, Bogunovic H, Endstraßer F, Sadeghipour A, Philip AM, et al. Fully automated detection and quantification of macular fluid in OCT using deep learning. Ophthalmology 2018;125:549-58.

82. Chakravarthy U, Goldenberg D, Young G, Havilio M, Rafaeli O, Benyamini G, et al. Automated identification of lesion activity in neovascular age-related macular degeneration. Ophthalmology 2016;123:1731-6.

83. Schmidt-Erfurth U, Bogunovic H, Sadeghipour A, Schlegl T, Langs G, Gerendas BS, et al. Machine learning to analyze the prognostic value of current imaging biomarkers in neovascular age-related macular degeneration. Ophthalmol Retina 2018;2:24-30.

84. Aslam TM, Zaki HR, Mahmood S, Ali ZC, Ahmad NA, Thorell MR, et al. Use of a neural net to model the impact of optical coherence tomography abnormalities on vision in age-related macular degeneration. Am J Ophthalmol 2018;185:94-100.

85. Bogunovic H, Waldstein SM, Schlegl T, Langs G, Sadeghipour A, Liu X, et al. Prediction of anti-VEGF treatment requirements in neovascular AMD using a machine learning approach. Invest Ophthalmol Vis Sci 2017;58:3240-8.

86. Nagasato D, Tabuchi H, Ohsugi H, Masumoto H, Enno H, Ishitobi N, et al. Deep neural network-based method for detecting central retinal vein occlusion using ultrawide-field fundus ophthalmoscopy. Journal of ophthalmology 2018. Available from: https://www.hindawi.com/journals/joph/2018/1875431/. [Last accessed on 2019 Jul 13].

87. Zhao R, Chen Z, Chi Z. Convolutional Neural Networks for Branch Retinal Vein Occlusion recognition? In: 2015 IEEE International Conference on Information and Automation; 2015. p. 1633-6.

88. Zhang H, Chen Z, Chi Z, Fu H. Hierarchical local binary pattern for branch retinal vein occlusion recognition with fluorescein angiography images. Electron Lett 2014;50:1902-4.

89. Waldstein SM, Montuoro A, Podkowinski D, Philip AM, Gerendas BS, Bogunovic H, et al. Evaluating the impact of vitreomacular adhesion on anti-VEGF therapy for retinal vein occlusion using machine learning. Sci Rep 2017;7:2928.

90. Kuwayama S, Ayatsuka Y, Yanagisono D, Uta T, Usui H, Kato A, et al. Automated detection of macular diseases by optical coherence tomography and artificial intelligence machine learning of optical coherence tomography images. J Ophthalmol 2019;2019:6319581.

91. Sumaroka A, Garafalo AV, Semenov EP, Sheplock R, Krishnan AK, Roman AJ, et al. Treatment potential for macular cone vision in leber congenital amaurosis due to CEP290 or NPHP5 mutations: Predictions from artificial intelligence. Invest Ophthalmol Vis Sci 2019;60:2551-62.

92. Odaibo SG, MomPremier M, Hwang RY, Yousuf S, Williams S, Grant J. Mobile artificial intelligence technology for detecting macula edema and subretinal fluid on OCT scans: Initial results from the DATUM alpha Study. arXiv preprint arXiv:1902.02905. 2019. Available from: http://arxiv.org/abs/1902.02905. [Last accessed on 2019 Jul 05].

93. Ohsugi H, Tabuchi H, Enno H, Ishitobi N. Accuracy of deep learning, a machine-learning technology, using ultra-wide-field fundus ophthalmoscopy for detecting rhegmatogenous retinal detachment. Sci Rep 2017;7:9425.

94. Xu Y, Yan K, Kim J, Wang X, Li C, Su L, et al. Dual-stage deep learning framework for pigment epithelium detachment segmentation in polypoidal choroidal vasculopathy. Biomed Opt Express 2017;8:4061-76.

95. Saad A, Gatinel D. Topographic and tomographic properties of forme fruste keratoconus corneas. Invest Ophthalmol Vis Sci 2010;51:5546-55.

96. Kovács I, Miháltz K, Kránitz K, Juhász É, Takács Á, Dienes L, et al. Accuracy of machine learning classifiers using bilateral data from a Scheimpflug camera for identifying eyes with preclinical signs of keratoconus. J Cataract Refract Surg 2016;42:275-83.

97. Klyce SD. The future of keratoconus screening with artificial intelligence. Ophthalmology 2018;125:1872-3.

98. Ruiz Hidalgo I, Rodriguez P, Rozema JJ, Ní Dhubhghaill S, Zakaria N, Tassignon MJ, et al. Evaluation of a machine-learning classifier for keratoconus detection based on Scheimpflug tomography. Cornea 2016;35:827-32.

99. Arbelaez MC, Versaci F, Vestri G, Barboni P, Savini G. Use of a support vector machine for keratoconus and subclinical keratoconus detection by topographic and tomographic data. Ophthalmology 2012;119:2231-8.

100. Souza MB, Medeiros FW, Souza DB, Garcia R, Alves MR. Evaluation of machine learning classifiers in keratoconus detection from orbscan

II examinations. Clinics (Sao Paulo) 2010;65:1223-8.

101. Smadja D, Touboul D, Cohen A, Doveh E, Santhiago MR, Mello GR, *et al*. Detection of subclinical keratoconus using an automated decision tree classification. Am J Ophthalmol 2013;156:237-460.

102. Maeda N, Klyce SD, Smolek MK, Thompson HW. Automated keratoconus screening with corneal topography analysis. Invest Ophthalmol Vis Sci 1994;35:2749-57.

103. Ambrósio R Jr., Lopes BT, Faria-Correia F, Salomão MQ, Bühren J, Roberts CJ, *et al*. Integration of Scheimpflug-based corneal tomography and biomechanical assessments for enhancing ectasia detection. J Refract Surg 2017;33:434-43.

104. Sharif MS, Qahwaji R, Ipson S, Brahma A. Medical image classification based on artificial intelligence approaches: A practical study on normal and abnormal confocal corneal images. Appl Soft Comput 2015;36:269-82.

105. Mahesh K, Gunasundari R. Computer-aided diagnosis of anterior segment eye abnormalities using visible wavelength image analysis based machine learning. Journal of medical systems 2018;42:128.

106. Gao X, Lin S, Wong TY. Automatic feature learning to grade nuclear cataracts based on deep learning. IEEE Trans Biomed Eng 2015;62:2693-701.

107. Caixinha M, Amaro J, Santos M, Perdigao F, Gomes M, Santos J. *In vivo* automatic nuclear cataract detection and classification in an animal model by ultrasounds. IEEE Trans Biomed Eng 2016;63:2326-35.

108. Yang JJ, Li J, Shen R, Zeng Y, He J, Bi J, *et al*. Exploiting ensemble learning for automatic cataract detection and grading. Comput Methods Programs Biomed 2016;124:45-57.

109. Zhang L, Li J, Zhang I, Han H, Liu B, Yang J, *et al*. Automatic cataract detection and grading using Deep Convolutional Neural Network. In: 2017 IEEE 14th International Conference on Networking, Sensing and Control (ICNSC); 2017. p. 60-5.

110. Mohammadi SF, Sabbaghi M, Z-Mehrjardi H, Hashemi H, Alizadeh S, Majdi M, *et al*. Using artificial intelligence to predict the risk for posterior capsule opacification after phacoemulsification. J Cataract Refract Surg 2012;38:403-8.

111. Gillner M, Eppig T, Langenbucher A. Automatic intraocular lens segmentation and detection in optical coherence tomography images. Z Med Phys 2014;24:104-11.

112. Liu X, Jiang J, Zhang K, Long E, Cui J, Zhu M, *et al*. 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.

113. Long E, Lin H, Liu Z, Wu X, Wang L, Jiang J, *et al*. An artificial intelligence platform for the multihospital collaborative management of congenital cataracts. Nat Biomed Eng 2017;1:24.

114. Zhang K, Liu X, Jiang J, Li W, Wang S, Liu L, *et al*. Prediction of postoperative complications of pediatric cataract patients using data mining. J Transl Med 2019;17:2.

115. Almeida JD, Silva AC, Paiva AC, Teixeira JA. Computational methodology for automatic detection of strabismus in digital images through Hirschberg test. Comput Biol Med 2012;42:135-46.

116. Reid JE, Eaton E. Artificial Intelligence for Pediatric Ophthalmology. ArXiv preprint arXiv:1904.08796. 2019. Available from: http://arxiv.org/abs/1904.08796. [Last accessed on 2019 Jul 05].

117. Asensio-Sánchez VM, Díaz-Cabanas L, Martín-Prieto A. Photoleukocoria with smartphone photographs. Int Med Case Rep J 2018;11:117-9.

118. Rivas-Perea P, Baker E, Hamerly G, Shaw BF. Detection of leukocoria using a soft fusion of expert classifiers under non-clinical settings. BMC Ophthalmol 2014;14:110.

119. Almeida JD, Silva AC, Teixeira JA, Paiva AC, Gattass M. Surgical planning for horizontal strabismus using support vector regression. Comput Biol Med 2015;63:178-86.

120. Habibalahi A, Bala C, Allende A, Anwer AG, Goldys EM. Novel automated non invasive detection of ocular surface squamous neoplasia using multispectral autofluorescence imaging. Ocul Surf 2019. pii: S1542-0124 (18) 30284-2.

121. Tan E, Lin F, Sheck L, Salmon P, Ng S. A practical decision-tree model to predict complexity of reconstructive surgery after periocular basal cell carcinoma excision. J Eur Acad Dermatol Venereol 2017;31:717-23.

122. Das AV, Verkicharla P, Kekunnaya R, Gullapalli R. Prediction of myopia and refractive error progression in children using machine learning – A study. Artif Intell Med 2017. Available from: https://ai-med.io/ dt_team/prediction-of-myopia-and-refractive-error-progression-in-chil dren-using-machine-learning-a-study/. [Last accessed on 2019 Jul 14].

123. Zhang M, Gazzard G, Fu Z, Li L, Chen B, Saw SM, *et al*. Validating the accuracy of a model to predict the onset of myopia in children. Invest Ophthalmol Vis Sci 2011;52:5836-41.

124. Lin H, Long E, Ding X, Diao H, Chen Z, Liu R, *et al*. Prediction of myopia development among Chinese school-aged children using refraction data from electronic medical records: A retrospective, multicentre machine learning study. PLoS Med 2018;15:e1002674.

125. Varadarajan AV, Poplin R, Blumer K, Angermueller C, Ledsam J, Chopra R, *et al*. Deep learning for predicting refractive error from retinal fundus images. Invest Ophthalmol Vis Sci 2018;59:2861-8.

126. Liu J, Wong DW, Lim JH, Tan NM, Zhang Z, Li H, *et al*. Detection of pathological myopia by PAMELA with texture-based features through an SVM approach. Journal of Healthcare Engineering. 2010;1:1. Available from: https://www.hindawi.com/journals/jhe/2010/657574/abs/. [Last accessed on 2019 Jul 14].

127. Zhang Z, Xu Y, Liu J, Wong DW, Kwoh CK, Saw SM, *et al*. Automatic diagnosis of pathological myopia from heterogeneous biomedical data. PLoS One 2013;8:e65736.

128. Koprowski R, Lanza M, Irregolare C. Corneal power evaluation after myopic corneal refractive surgery using artificial neural networks. Biomed Eng Online 2016;15:121.

129. Hill W. Hill-RBF Calculator for IOL Power Calculations. Available from: https://rbfcalculator.com/online/. [Last accessed on 2019 Jul 14].

130. Siddiqui AA, Juthani V, Kang J, Chuck RS. The future of intraocular lens calculations: Ladas Super Formula. Annals of Eye Science 2019;4. Available from: http://aes.amegroups.com/article/view/4812. [Last accessed on 2019 Jul 14].

131. Ladas JG, Siddiqui AA, Devgan U, Jun AS. A 3-D "Super surface" combining modern intraocular lens formulas to generate a "Super formula" and maximize accuracy. JAMA Ophthalmol 2015;133:1431-6.

132. Clarke GP, Burmeister J. Comparison of intraocular lens computations using a neural network versus the Holladay formula. J Cataract Refract Surg 1997;23:1585-9.

133. Yarmahmoodi M, Arabalibeik H, Mokhtaran M, Shojaei A. Intraocular lens power formula selection using support vector machines. Front Biomed Technol 2015;2:36-44.

134. Sramka M, Slovak M, Tuckova J, Stodulka P. Improving clinical refractive results of cataract surgery by machine learning. PeerJ 2019;7:e7202.

135. Findl O, Struhal W, Dorffner G, Drexler W. Analysis of nonlinear systems to estimate intraocular lens position after cataract surgery. J Cataract Refract Surg 2004;30:863-6.

136. Kane JX, Van Heerden A, Atik A, Petsoglou C. Accuracy of 3 new methods for intraocular lens power selection. J Cataract Refract Surg 2017;43:333-9.

137. Zafar S, McCormick J, Giancardo L, Saidha S, Abraham A, Channa R. Retinal imaging for neurological diseases: "A window into the brain". Int Ophthalmol Clin 2019;59:137-54.

138. Dumitrascu OM, Qureshi TA. Retinal vascular imaging in vascular cognitive impairment: Current and future perspectives. J Exp Neurosci 2018;12:1179069518801291.

139. Chan VT, Wong PP, Cheung CY. Retinal vascular changes in diabetes

and dementia. Diabet Retin Cardiovasc Dis 2019;27:86-99.

140. Cheung CY, Chan VT, Mok VC, Chen C, Wong TY. Potential retinal biomarkers for dementia: What is new? Curr Opin Neurol 2019;32:82-91.

141. Cheung CY, Chen C, Wong TY. Ocular fundus photography as a tool to study stroke and dementia. Semin Neurol 2015;35:481-90.

142. Cheung CY, Ong YT, Ikram MK, Ong SY, Li X, Hilal S, *et al.* Microvascular network alterations in the retina of patients with Alzheimer's disease. Alzheimers Dement 2014;10:135-42.

143. Sandeep C, Kumar AS. WN segmentation of retina images for the early diagnosis of Alzheimer's disease (AD). Anal Pharm Res 2018;7:2. Available from: http://medcraveonline.com/JAPLR/JAPLR-07-00225.pdf. [Last accessed on 2019 Jul 14].

144. Cabrera DeBuc D, Arthur E. Recent Developments of Retinal Image Analysis in Alzheimer's Disease and Potential AI Applications. In: Carneiro G, You S. (eds) Computer Vision – ACCV 2018 Workshops. ACCV 2018. Lecture Notes in Computer Science. Springer, Cham: Springer International Publishing; 2019;11367:261-75.

145. Zhou Q, Sinai MJ, Moore JC, Wong W. Method and system for detecting the effects of Alzheimer's disease in the human retina. US6988995B2; 2006. Available from: https://patents.google.com/patent/US6988995B2/en. [Last accessed on 2019 Jul 14].

146. Lau AY, Mok V, Lee J, Fan Y, Zeng J, Lam B, *et al.* Retinal image analytics detects white matter hyperintensities in healthy adults. Ann Clin Transl Neurol 2019;6:98-105.

147. Korot E, Wood E, Weiner A, Sim DA, Trese M. A renaissance of teleophthalmology through artificial intelligence. Eye (Lond) 2019;33:861-3.

148. Kotecha A, Brookes J, Foster PJ. A technician-delivered 'virtual clinic' for triaging low-risk glaucoma referrals. Eye (Lond) 2017;31:899-905.