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Mini Review

AI/ ML, machine learning and DL, deep learning In Ophthalmology Key Diseases and Challenges

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Introduction, AI Groups and Vision Impairment Diagnosis

AI is comprised of: 1. Machine Learning, ML, (central branch of AI) that develops algorithms to learn from data to identify patterns and make decisions based on data like fraud detection; 2. Deep learning, DL, (a subset of machine learning), uses convolutional neural networks, CNN, to model and solve complex problems like image recognition; 3. Natural Language Processing, (e.g. Virtual Assistants) allow AI systems to process text and speech and make them more responsive to human needs and activities; 4. Robotics, AI helps robots move and make decisions in real time, like drones; 5. Fuzzy logic, handles uncertainty in AI decision making, e.g. weather prediction [1].

AI works by gathering data and organizing data for analysis, (texts, images, video, voice). AI systems then use and further develop algorithms to train, test and validate the data to learn relationships and make predictions from the patterns and iterative learning and reinforcement learning it uses to come to conclusions. The repetitive reinforcement of learning strengthens the validity of iterative outcomes and can be checked for individual iterative level accuracy [1].

The five leading causes of vision impairment and blindness in the world are: uncorrected refractive error, cataracts, diabetic retinopathy, age-related macular degeneration, and glaucoma [2]. Approximately 1billion individuals of the 2.2 billion who have near vision impairment may have been prevented [2].

AI Examples in Uncorrected Refractive Errors

Several papers recently illustrated AI helping improve vision care in uncorrected refractive errors, with respect to (1) general optometry correction in a clinical setting [3].

(2) predicting refractive error from retinal fundus images: e.g. Using 30 and 45degree field images from the UK Biobank and Age-related Eye Disease Study, AREDS, clinical trials, for a total of 226,870 images and validated on 24,007 UK Biobank and 15,750 AREDS images, the AI algorithm had a mean absolute error of 0.56 diopters for estimating spherical equivalent on the UK Biobank data and 0.91diopters on the AREDS data set in a total of 70,000 participants [4].

(3) Myopia, (defined as spherical equivalence less than or equal to -.5 diopters), globally is estimated to be 49.8% (or 4.758 billion) of the world population. 938 million will have high myopia by 2050 [5]. Over 80% of high school students in some Asian countries are myopic and a larger portion of younger individuals go on to high myopia, spherical equivalence of 6 diopters or more, which carries a higher risk of visual impairment or blindness [5-16].

Lin et al using refraction data with a random forest machine learning AI model endeavored the prediction of high myopia onset

[17]. The AUC ranged from .903 to .986 for 3 years, 0.875 to 0.901 for 5 years and 0.852 to 0.888 for 8 years [17].

Rampat, et al. with three ML (gradient boosted tree) algorithms, on wavefront aberrometry data, predicted subjective refractions of 350 other eyes, unknown to the model [18]. The machine learning models were significantly better than the paraxial matching method with a mean error of .30 diopters for the M vector, 0.12 diopters for the JO vector and 0.094 for the J45 vector, for predicting subjective refraction from polynomial wavefront data [18].

Using machine learning-based algorithms, (six types were implemented in the model), with input variables including: age, sex, central corneal thickness, spherical equivalence, mean K and white to white corneal diameter, the best-performing algorithm was applied to predict axial length to estimate the physiological elongation of ocular length in myopic children. Based on the partial derivatives of the axial length predicted age curves, the estimated elongation varied from 0.003 to 0.110 mm/year in female subjects. The model found that physiological elongation of axial length decreased with increasing age and was negatively correlated with spherical equivalent and K mean [19].

Table 1: Ocular Disease vs Number Worldwide vs AI Methodology Used.

Ocular Disease	Disease World Prevalence in Millions	AI Study Methodology and Reference #
Uncorrected Refractive Errors	By 2050: 938, Ref 5	Ref 17, Lin et al, high myopia prediction in children, Random Forest ML; 3yrs:.903-.986 AUC
Cataracts	57.1, ref 21	Ref 20, KY Son et al, cataract classification: DL, ResNet18, WideRes-Net50-2; Resnext50, prediction performance AUC.95
Diabetic Retinopathy, DR	3.2, ref 21	Ref 30, MAdos Reis et al, DL with CNN vs ophthalmologist on fundus images, DL, specificity 96.41%
Adult-Onset Macular degen-eration	58, ref 21	Ref 35, N Motozawa et al, DL CNN +transfer learning OCT model distin-guishing exudative from non-exudative, sensitivity 100%
Glaucoma	4, ref 21	Ref 37, Yu et al, DL CNN classifiers for OCT with Angle Closure Glaucoma, .928 AUC detection

AI Examples in the Management of Cataracts

Using slit lamp and retro-illumination lens photos based on the Lens Opacities Classification System, LOCS III, a convolutional neural network was trained and tested on 1335 slit lamp images and 637 retro illumination images from 596 patients to detect and grade cataracts. The images were also graded by two trained graders using LOCS III. Four key strategies were trained and validated in the AI domain: (1) region detection for redundant information of inside data, (2) data augmentation and transfer learning for the small data set problem, (3) generalized cross-entropy loss for the small dataset size problem and (4) class balanced loss for class imbalance problems. The AI platform performance was strengthened by an ensemble of 3 AI algorithms: ResNet18, WideResNet50-2, and ResNext50. The AI platform AUC was 0.99, accuracy 98.82%, and 98.51% and LOCSIII based grading prediction performance AUC 95%, accuracy 91.22% and 90.26% for nuclear opalescence and nuclear color. AUC and accuracy for cortical opacity and posterior subcapsular opacity in slit lamp and retro illumination categories were also quite good but slightly less. [20].

By 2020 in the global population the number of people with cataracts was about 57.1 million [21]. Visual impairment from cataracts is higher in low to moderate income economies compared to developed countries [22, 23]. A diagnostic machine language platform named "CC cruiser", developed by Zhongshan Ophthalmic Center, [22-24] using a CNN algorithm to grade and diagnose cataracts on slit lamp images achieved a diagnostic accuracy of 98% [23]. However, in a multicenter randomized controlled trial only achieved an 87.4% for accuracy of cataract diagnosis [24]. Nonetheless, the time to diagnosis using "CC Cruiser" was about three times shorter than pediatric ophthalmologists and had a high level of patient satisfaction because of the reduced waiting time [25].

AI Examples in Diabetic Retinopathy, DR

DR which increased in prevalence globally between 1990 and 2015 has about 3.2 million people with moderate to severe visual impairment [21].

AI using CNN applied to photos and OCT images of diabetic retinopathy can detect edges, lines, colors and even more complex patterns. Thus, AI algorithms can automate the detection of microaneurysms and hemorrhages from fundus photos and OCT images [26].

However, because of computational complexity, accuracy questions in DR staging and maintenance cost, more advanced AI models have been suggested to examine initial stages of DR [27]. Also, although AI study in DR screening showed high sensitivity, there was low specificity, 82% for referrable DR. Thus, 4 out of 5 patients without referrable DR would still be referred to an ophthalmologist, causing unnecessary burden to patient and physicians [28].

In contrast, AI diabetic eye exams in racially and ethnically diverse youths at point of care had a considerably higher completion rate than controls, 64% vs 22% [29].

Also in contrast, a total of 4590 patients in an Endocrinology Unit, in Porto Alegre, Brazil, with an overall prevalence of 26.5% for DR, had manual diagnosing of DR performed by an ophthalmologist compared to a deep learning, DL, algorithm with CNN using images from a dilated exam photographed with a Cannon CR-2 camera. The deep learning algorithm had an area under the curve of 98%, specificity of 96.4%, and sensitivity of 93.5% [30].

AI Examples in Macular Degeneration, AMD

Despite being a common cause of visual loss, (approximately 8.8 million worldwide, 2020, with moderate to severe visual impairment) [21] early diagnosis of AMD, as well as customized treatment, cost control and efficient management of patient and doctor time remains difficult. AI by retinal and OCT image analysis can leverage large amounts of data to predict disease progression by identifying biomarkers and disease criteria and stages [31].

Dong et al, Serner et al, and Rasti et al developed machine learning and deep CNN models for classification of dry and wet AMD [32-34]. Montazawa et al, using a basic CNN and a transfer deep learning model to improve stability and efficiency, [35] found that the basic CNN model achieved the following metric significances: sensitivity = 100%, specificity = 91.8%, and accuracy = 99% in distinguishing exudative and non-exudative AMD from normal OCT images [35].

AI Examples in Glaucoma

Studies between 1980 and 2012 as well as unpublished studies through the Vision Loss Expert Group found that glaucoma was one of the diseases of vison impairment that had increased, to approximately 4 million individuals worldwide [21].

DP Rao, et al. from a tertiary glaucoma center in India, including 243 subjects with varying severity of glaucoma, evaluated an automated referable glaucoma AI detection system. 65% of the retinal images were captured using the Remidio FOP target device and 35% using desktop fundus cameras. The AI performance on the smartphone camera was the same when compared to image grading on either of the Remidio or desktop fundus camera.

76.1% of the photos were captured from a South African population and 23.9% on a Caucasian population. AI cup and disc segmentation model and a binary classification model were compared to a glaucoma specialist with full glaucoma workup and consensus imaging grading. The AI system had a sensitivity and specificity of 93.7% and 85.6% respectively in detection of referrable glaucoma. The model used ResNet 50 architecture and was pre-trained on the ImageNet dataset. Two other AI models were trained. The first provides a quality image for reliable glaucoma diagnosis. The second localized the disc center in the retinal image. These two steps represent the pre-processing for AI segmentation and classification algorithms.

Overall, the glaucoma specialists detected 67/111 true glaucoma cases or 60% using just fundus images; the AI model detected 104/111 or 94% of true glaucoma patients on the same fundus images [36].

Yu et al used large data sets with CNN classifiers to identify OCT images for angle closure glaucoma. The best CNN classifier model was ResNet-18. It was able to detect angle closure glaucoma types on AI automated anterior segment OCT images. The detection of angle closure glaucoma was .928 AUC on AI test data set. Yu et al concluded that deep learning CNN models were able to illustrate differences between angle closure, (without synechiae) vs angle closure with synechiae and this differentiation could improve eyecare in high-risk populations [37, 38].

Conclusion

This short communication endeavors to provide brief illustrations of the contribution of AI methods, machine learning and deep learning to: better identify stages and categories of the more prevalent eye diseases, consider more effective AI methods in learning about different population datasets on common eye diseases, and allow the reader to come upon challenges in the accuracy of AI outcomes vs expert ophthalmological opinions in the diagnosis of these diseases.

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Conflict of Interest

None.

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