Guest Editorial

The many challenges in automated glaucoma diagnosis based on fundus imaging

Glaucoma is a leading cause of irreversible blindness. Though early diagnosis and therapeutic intervention are key to prevent glaucoma blindness, detection is challenging in early stages due to its asymptomatic nature. In most developing nations, including India, less than 10% of those with glaucoma are detected. Population-based screening for glaucoma is impractical owing to its low prevalence in the communities, lack of cost effectiveness, and other logistic barriers. Automated glaucoma detection, especially when combined with teleglaucoma approach, may enable large-scale glaucoma screening in high-risk, targeted populations.[1] Clinical optic nerve head evaluation and optic disc photography remain the cornerstone in glaucoma screening. Disc photography read by experienced observers achieve similar diagnostic performance as that of advanced imaging methodology, such as optical coherence tomography. A major concern with this approach, however, is its subjective nature and interobserver disagreements even among experienced glaucoma specialists. Fundus photography-based qualitative glaucoma screening may be feasible through automated detection utilizing artificial intelligence and deep learning algorithms (DLA). Earlier machine learning algorithms were primarily based on cup to disc ratio estimation, evaluation of retinal nerve fiber layer, and peri papillary atrophy without adjustment for disc size or other physiological variations in disc appearance.[2] A major advance in this area in recent times has been the development of DLA, in particular, the use of convolutional neural network (CNN), which facilitates improved image analysis with an enhanced capability to extract low-level coarse features or high-level fine features to diagnose glaucoma from fundus images. CNN-based algorithm achieved a high diagnostic accuracy in differentiating the glaucomatous discs from the healthy fundus.[3,4] DLA that interpret the fundus-based biomarkers characterizing glaucomatous optic nerve damage similar to or more reliably than humans can facilitate early diagnosis of glaucoma by quickly screening several individuals at any given time.

DLA can learn the features associated with a specific diagnosis, such as glaucoma without having the features of the disease preprogrammed. When presented with a new unlabeled image, DLA can produce probability output with a possible diagnosis of glaucoma. Since unambiguity in labeling disease in training phase is critical, accuracy of image labeling is pivotal. With exponential advances in computational abilities and digitization, large aggregated data sets available for training the algorithms can enable modern DLA to predict possibility of diseases such as glaucoma based on image analysis that often exceeds human capability. The most commonly employed deep learning inputs include fundus images, spectral domain optical coherence tomography and static threshold perimetry. Despite the unreliability of using fundus images alone for establishing glaucoma diagnosis, it is possible to acquire large training data sets of fundus images with varying ONH features to optimize DLA. However, cross-sectional information from fundus photos may be inadequate to provide highly sensitive or specific biomarkers or characteristic clinical features for automated glaucoma diagnosis with sufficient confidence.

Experienced human graders of optic disc features provide the ground truth essential for accurate training of DLA. However, extreme level of interobserver disagreement in grading or labeling optic discs[5] is one of the significant challenges in evolving DLA to diagnose glaucoma from fundus images most accurately. Although glaucoma experts are expected to provide the best possible ground truth, the absence of reliable diagnostic indicators or biomarkers in disc evaluation, especially in early glaucoma and immense physiologic variations in the appearance of the optic nerve head challenges the subjective interpretation of the changes in fundus images. Definitive diagnosis of glaucoma often depends upon longitudinal observations and progressive changes in the characteristics of the optic disc over time, a vital information that cannot be made available on cross-sectional images. As most experienced clinicians would agree, glaucoma diagnosis relies on a holistic assessment by a trained human mind, of evaluation of both structural and functional tests, detailed history as well as clinical evaluation of the optic nerve and peri papillary retina. Yet another major drawback of automated algorithms has been that these are not trained to recognize borderline or early glaucoma; nevertheless, these are designed to identify typical, more advanced disc damage or those with the typical features of glaucoma. Performance of DLA in glaucoma seems to vary with severity of glaucoma.[6] In this context, it would be useful to establish what is "referable" ground truth rather than established glaucoma alone, so that the essence of such automated diagnostic DLA are to refer those with suspected disease rather than identify true disease. There is high likelihood of exaggerated false positives, burdening an already overstretched health care system.

In conclusion, it is no gainsaying that there is a critical need for a cost effective, easily accessible, and a reliable screening algorithm with the potential for being employed in large populations to facilitate glaucoma diagnosis. Though several algorithms for automated glaucoma diagnosis have been tested and found to be highly sensitive and specific, what is required is a longitudinal registry with consistent inputs across the varying stages of well-defined glaucoma to overcome the challenges with the existing input data set of fundus images. To date the major challenges to develop a robust DLA to diagnose glaucoma include a lack of an unambiguous definition of glaucoma, subjective bias among human experts to define what would form the ground truth for glaucoma diagnosis, and inadequacy of real world data with diverse population characteristics that could be uniformly applied. Automated DLA-based glaucoma diagnosis would continue to be a holy grail amid the many practical challenges the investigators continue to face in evolving robust, fool proof algorithms.

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Dr. R Krishnadas graduated from Kilpauk Medical College in Chennai in the year 1987 and pursued post graduate training in Ophthalmology at the Aravind Eye Hospital and Post Graduate Institute of Ophthalmology, Madurai from 1988-1993, which included fellowship training in Glaucoma. After initially serving as a Consultant in Glaucoma Services, he headed the Department of Glaucoma at the Aravind Eye Hospital in Madurai from the year 1997- 2004. Subsequently, he had been the Chief Medical Officer of the Aravind Eye Hospital, Madurai until 2010 and is now officiating as the Director of Human Resources Development of the Aravind Eye Care System, a large network of eye care hospitals in the state of Tamil Nadu. Dr Krishnadas has collaborated in many research initiatives pertaining to epidemiology, genetics and treatment outcomes of glaucoma and has contributed to close to 40 international peer reviewed publications in glaucoma research. Dr Krishnadas is part of the IJO Editorial Board and is an the avid reviewer for the Journal.