Ophthalmology® Glaucoma

Volume 1, Number 1, July/August 2018
www.ophthalmologyglaucoma.org

Glaucoma Diagnosis: From the Artisanal to the Defined

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Purpose: To chronicle the history of glaucoma diagnosis from its subjective ancient origins to the modern, formerly aspirational goal of objective, precise, accurate quantitative diagnostics.

Methods: A review of the literature was performed to assess the method of diagnosis of glaucoma and determination of glaucoma progression.

Main Outcome Measures: Glaucoma diagnosis, glaucoma progression detection, and the tools and techniques used for the same.

Results: Glaucoma diagnostics have progressed from simple observation to actual quantitative measurement. In the 19th and 20th centuries, accurate, precise measurement techniques were developed and used, and by the late 20th and early 21st centuries, the presence and progression of glaucoma could be determined not only quantitatively but also objectively, and with a high degree of precision and accuracy.

Conclusions: Over the past 3 millenia, glaucoma diagnostics have evolved from subjective observation to quantitative, objective, accurate, precise measurement. Applanation tonometry has replaced finger tension intraocular pressure measurement; automated perimetry and statistical analysis have supplanted subjective assessment of manual visual field (VF) assessment; and imaging technologies, such as OCT, have provided measurable, unbiased, correct, and reproducible alternatives to clinical observation and optic disc drawings. The net effect of this innovation has been a paradigm shift from dependence on subjective physician interpretation to incorporation of objective data for discerning the presence and progression of glaucoma from health and stability. Ophthalmologists are now able to detect glaucoma and its progression earlier than ever before, enabling precise and personalized clinical decision-making that ultimately serves patients by triggering escalations of treatment even before the development of grossly detectable damage. Further, the objective, quantitative, accurate, and precise measures allow expert diagnosis to occur without the necessity of an expert observer. This permits high-quality glaucoma care in nearly any setting.

Ophthalmology Glaucoma 2018;1:3-14.

A Deep Learning-Based Algorithm Identifies Glaucomatous Discs Using Monoscopic Fundus Photographs

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Purpose: To develop and test the performance of a deep learning-based algorithm for glaucomatous disc identification using monoscopic fundus photographs.

Design: Fundus photograph database study.

Participants: Four thousand three hundred ninety-four fundus photographs, including 3768 images from previous Sydney-based clinical studies and 626 images from publicly available online RIM-ONE and High-Resolution Fundus (HRF) databases with definitive diagnoses.

Methods: We merged all databases except the HRF database, and then partitioned the dataset into a training set (80% of all cases) and a testing set (20% of all cases). We used the HRF images as an additional testing set. We compared the performance of the artificial intelligence (AI) system against a panel of practicing ophthalmologists including glaucoma subspecialists from Australia, New Zealand, Canada, and the United Kingdom.

Main Outcome Measures: The sensitivity and specificity of the AI system in detecting glaucomatous optic discs.

Results: By using monoscopic fundus photographs, the AI system demonstrated a high accuracy rate in glaucomatous disc identification (92.7%; 95% confidence interval [CI], 91.2%–94.2%), achieving 89.3% sensitivity (95% CI, 86.8%–91.7%) and 97.1% specificity (95% CI, 96.1%–98.1%), with an area under the receiver operating characteristic curve of 0.97 (95% CI, 0.96–0.98). Using the independent online HRF database (30 images), the AI system again accomplished high accuracy, with 86.7% in both sensitivity and specificity (for ophthalmologists, 75.6% sensitivity and 77.8% specificity) and an area under the receiver operating characteristic curve of 0.89 (95% CI, 0.76–1.00).

Conclusions: This study demonstrated that a deep learning-based algorithm can identify glaucomatous discs at high accuracy level using monoscopic fundus images. Given that it is far easier to obtain monoscopic disc images than high-quality stereoscopic

images, this study highlights the algorithm's potential application in large population-based disease screening or telemedicine programs.

Ophthalmology Glaucoma 2018;1:15-22.

Association between Rates of Retinal Nerve Fiber Layer Thinning and Previous Disc Hemorrhage in Glaucoma

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Purpose: To investigate the relationship between previous disc hemorrhage (DH) and subsequent rates of retinal nerve fiber layer (RNFL) thinning.

Design: Longitudinal, observational cohort study.

Participants: Twenty-eight patients with glaucoma and patients with suspected glaucoma who had a history of DH in 1 eye (unilateral DH), but not in the fellow eye, enrolled in the Diagnostic Innovations in Glaucoma Study and the African Descent and Glaucoma Evaluation Study were included.

Methods: All subjects underwent annual optic disc photography and semiannual spectral-domain OCT RNFL thickness measurements. Multivariable linear mixed-effects models were used to investigate the relationship between the presence of previous DH and RNFL thinning rates while adjusting for potential confounding factors, such as race, age, mean intraocular pressure (IOP), baseline disease severity, and central corneal thickness (CCT). The relationship between the timing of DH and the rates of RNFL thinning also was investigated in eyes with a history of DH.

Main Outcome Measures: Rates of global and local RNFL thinning.

Results: Previous DH was significantly associated with faster RNFL thinning rates globally (−0.39 μm/year faster, $P = 0.010$), in DH quadrants (−0.77 μm/year faster, $P = 0.012$), and non-DH quadrants (−0.49 μm/year faster, $P = 0.038$) after adjustment for race, mean IOP, baseline age, baseline standard automated perimetry mean deviation, and CCT. Higher IOP was also significantly associated with faster thinning rates globally (−0.07 μm/year faster per 1 mmHg higher, $P = 0.047$) and in DH quadrants (−0.10 μm/year faster per 1 mmHg higher, $P = 0.044$). In eyes with a history of DH, the time elapsed from the latest DH episode to the first OCT examination was not significantly associated with the rate of RNFL thinning.

Conclusions: A history of DH is an independent risk factor for faster rates of RNFL thinning in non-DH quadrants and in DH quadrants; this risk is present even in eyes that exhibited DH several years earlier.

Ophthalmology Glaucoma 2018;1:23-31.

Position of Central Retinal Vascular Trunk and Preferential Location of Glaucomatous Damage in Myopic Normal-Tension Glaucoma

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Purpose: To investigate the spatial correlation between the central retinal vascular trunk and the preferential location of glaucomatous damage in myopic normal-tension glaucoma (NTG) eyes.

Design: Cross-sectional study.

Participants: One hundred thirty-seven subjects with myopic NTG (137 eyes).

Methods: The position of the vascular trunk was measured from the center of the Bruch membrane opening (BMO), which was delineated by optical coherence tomography imaging. The angular deviation was measured, with the horizontal nasal midline as 0° and the superior location as a positive value. The shift index was calculated as the distance of the vascular trunk from the BMO center relative to that of the BMO margin. The angular location of the midpoint of the retinal nerve fiber layer (RNFL) defect was measured from the BMO center. In cases with bi-hemispheric RNFL defects, the angular location was measured for the RNFL defect of larger width. For categorical analysis, hemispheric dominancy was determined if the RNFL defect in one hemisphere was larger than twofold that in the opposite hemisphere. In cases with no dominant hemisphere, the eye was classified as bi-equivalent involvement.

Main Outcome Measures: The vascular trunk position within the BMO and the location of glaucomatous damage.

Results: The moderate- and severe-shift groups (shift index ≥ 0.5) were associated with younger age, longer axial length, smaller angular deviation, and lesser incidence of focal lamina cribrosa (LC) defect. A multiple regression analysis showed a significant correlation between the vascular trunk position and the RNFL defect location ($P < 0.001$). A logistic regression analysis revealed that the dominant RNFL defect occurred in the opposite hemisphere of the vascular trunk ($P < 0.001$), and bi-equivalent involvement in both hemispheres was associated with a larger shift index ($P = 0.001$). A conditional inference tree analysis showed that both the angular deviation ($P < 0.001$) and the extent of vascular trunk shift ($P < 0.001$) determined the RNFL defect location.

Conclusions: In myopic NTG eyes, the vascular trunk is located in the direction opposite of the RNFL defect with reference to the BMO. Because the vascular trunk is embedded in the LC, this implies that LC shift during axial elongation is associated with greater vulnerability of myopic eyes to glaucomatous damage.

Ophthalmology Glaucoma 2018;1:32-43.

Comparison between Lamina Cribrosa Depth and Curvature as a Predictor of Progressive Retinal Nerve Fiber Layer Thinning in Primary Open-Angle Glaucoma

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Purpose: To compare the ability of lamina cribrosa (LC) depth (LCD) and LC curvature to predict the rate of progressive retinal nerve fiber layer (RNFL) thinning in patients with primary open-angle glaucoma (POAG).

Design: Observational case series.

Participants: A total of 114 eyes of 114 patients diagnosed with POAG, in which RNFL thickness had been measured by serial spectral-domain (SD) OCT for at least 2.5 years.

Methods: The optic nerves of all participants underwent enhanced depth imaging volume scanning, and their circumpapillary