AI-based clinical assessment of optic nerve head robustness superseding biomechanical testing

Fabian A Braeu, Thanadet Chuangsuvanich, Tin A Tun, Shamira Perera, Rahat Husain, Alexandre H Thiery, Tin Aung, George Barbastathis, Michaël J A Girard

ABSTRACT

Background/aims To use artificial intelligence (AI) to: (1) exploit biomechanical knowledge of the optic nerve head (ONH) from a relatively large population; (2) assess ONH robustness (ie, sensitivity of the ONH to changes in intraocular pressure (IOP)) from a single optical coherence tomography (OCT) volume scan of the ONH without the need for biomechanical testing and (3) identify what critical three-dimensional (3D) structural features dictate ONH robustness.

Methods 316 subjects had their ONHs imaged with OCT before and after acute IOP elevation through ophthalmodynamometry. IOP-induced lamina cribrosa (LC) deformations were then mapped in 3D and used to classify ONHs. Those with an average effective LC strain superior to 4% were considered fragile, while those with a strain inferior to 4% robust. Learning from these data, we compared three AI algorithms to predict ONH robustness strictly from a baseline (undeformed) OCT volume: (1) a random forest classifier; (2) an autoencoder and (3) a dynamic graph convolutional neural network (DGCNN). The latter algorithm also allowed us to identify what critical 3D structural features make a given ONH robust.

Results All three methods were able to predict ONH robustness from a single OCT volume scan alone and without the need to perform biomechanical testing. The DGCNN (area under the curve (AUC): 0.76±0.08) outperformed the autoencoder (AUC: 0.72±0.09) and the random forest classifier (AUC: 0.69±0.05). Interestingly, to assess ONH robustness, the DGCNN mainly used information from the scleral canal and the LC insertion sites.

Conclusions We propose an AI-driven approach that can assess the robustness of a given ONH solely from a single OCT volume scan of the ONH, and without the need to perform biomechanical testing. Longitudinal studies should establish whether ONH robustness could help us identify fast visual field loss progressors.

INTRODUCTION

The optic nerve head (ONH) is the main site of damage in glaucoma and is exposed to various types of mechanical loads (eg, intraocular pressure (IOP), cerebrospinal fluid pressure and eye movement). It is hypothesised that excessive deformation of the lamina cribrosa might lead to glaucomatous axonal damage either through a direct or indirect pathway.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The optic nerve head (ONH) is the major site of damage in glaucoma and is exposed to various types of mechanical loads (eg, intraocular pressure (IOP), cerebrospinal fluid pressure and eye movement). It is hypothesised that excessive deformation of the lamina cribrosa might lead to glaucomatous axonal damage either through a direct or indirect pathway.

WHAT THIS STUDY ADDS

⇒ Clinical assessment of ONH robustness (ie, sensitivity to a change in IOP) from a standard optical coherence tomography (OCT) volume scan of the ONH without the need for biomechanical testing.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our proposed approach may have wide clinical interest because it does not require new hardware (it can be combined with any existing OCT device) and might help clinicians to identify fast visual field progressors earlier.

While expanding laterally,2 the cerebrospinal fluid pressure (CSFP; pushing the ONH anteriorly)3 and during eye movements, by the traction from the optic nerve generating considerable shear across all ONH tissues.3 Our group, and others, have hypothesised that excessive and cumulative deformations of the ONH from any of these loads (and their combinations) could result in glaucomatous axonal damage, either through a direct or an indirect pathway.4,5 In essence, if one could develop a test to assess the robustness of an individual’s ONH, and its sensitivity to the aforementioned loads, this may potentially help us predict who would be at risk of developing glaucoma, and for glaucoma patients, who is likely to exhibit rapid visual field loss progression. This would also motivate research to render the ONH ‘indestructible’ as a preventive treatment for glaucoma.

In the past, several biomechanical tests (or stress tests) have been proposed to assess the in vivo biomechanics of the human ONH. Such tests typically introduced a mechanical perturbation (eg, a change in IOP), while the ONH was continuously imaged in three dimensions using optical coherence tomography (OCT), or ultrasounds, to assess its
mechanical response. In those studies, IOP was either modulated using (1) ophthalmo-dynamometry,8–11 (2) tight-fitting swimming goggles,12 (3) the water-drinking test,13 (4) the dark room test,14 (5) trabeculectomy15 16 or (6) simply using the ocular pulse as a natural load.17 18 Others have used the traction of the optic nerve as a mechanical perturbation.19–21 In those scenarios, assessment of ONH robustness (or tissue stiffness) can be performed using the inverse finite element method or the virtual fields methods.22 23

However, none of these biomechanical tests come without drawbacks. They have yet to be optimised for their ease-of-use in a clinical setting while limiting patient discomfort. In this study, we argue that it should be possible to assess ONH robustness from a single OCT volume scan of the ONH, without performing a biomechanical test on the patient. The accuracy of such classifications can be enhanced by artificial intelligence (AI) if it was to learn from a large population on which biomechanical tests have already been performed.

In this study, we aimed to develop AI algorithms to: (1) exploit biomechanical knowledge of the ONH from a relatively large population; (2) assess ONH robustness from a single OCT volume scan of the ONH without the need for biomechanical testing and (3) identify what three-dimensional (3D) structural features of the ONH make a given ONH fragile or robust. Our work may have implications for improving the diagnosis and prognosis of glaucoma and other optic neuropathies.

METHODS

Patient recruitment

A total of 4118 subjects from two cohorts were recruited at the Singapore National Eye Centre (Singapore) and retrospectively included in this study: (1) 336 subjects of Chinese ethnicity that underwent biomechanical testing of their ONH and OCT imaging; and (2) 3782 subjects (7531 scans) of mixed ethnicity (62% Indian and 38% Chinese) with OCT imaging only. A summary of the patient population is shown in table 1.

Biomechanical testing and OCT imaging

Subjects that underwent biomechanical testing (cohort 1) had their ONH imaged with 3D spectral domain OCT (Spectralis, Heidelberg Engineering, Germany) before and after acute IOP elevation of approximately 19 mm Hg from baseline (measured with a Tono-Pen (Reichert Instruments, Munich, Germany)) through ophthalmo-dynamometry—a method to raise IOP via scleral indentation through the eyelid. More precisely, for the duration of the OCT scan acquisition (approximately 2–3 min), we applied a constant force of 0.65N to the temporal side of the lower eye lid using an ophthalmodynamometer. Additionally, subjects from cohort 2 had either one or both ONHs imaged at baseline IOP only. All subjects were seated in a dark room and if necessary, their pupil was dilated with tropicamide 1% solution. OCT volume scans (horizontal raster scans) covered the whole ONH region and were done with the same device. Each OCT volume consisted of 97 B-scans (approximately 35 µm between B-scans) with 384 A-scans per B-scan (approximately 11.5 µm between A-scans) and 496 pixels per A-scan (axial resolution of 3.87 µm/pixel) covering a rectangular area of 15° × 10° centred on the ONH. Signal averaging, TruTrack Active Eye Tracking (correcting for eye movement), AutoRescan function (for the follow-up scan at elevated IOP), and the enhanced depth imaging modality of the Spectralis OCT device were used during image acquisition.

Definition of ONH robustness

In this study, a robust ONH is thought to be less sensitive to changes in IOP and would thus exhibit relatively small lamina cribrosa (LC) strains (ie, deformations) due to an increase in IOP. The inverse (ie, relatively large LC strains) would be true for a fragile ONH. This definition of ONH robustness is based on the hypothesis that excessive deformation of the LC, due to, for example, an increase in IOP, can lead to glaucomatous axonal damage either through a direct or indirect pathway.24

To extract the 3D deformation of the ONHs of cohort 1 (those that underwent biomechanical testing via an acute elevation in IOP), we used a commercial digital volume correlation (DVC) module (Amira (V.2020.3), Thermo Fisher Scientific, USA). In brief, we divided each ONH geometry into approximately 4000 cubic elements (edge length of 110 µm) and used a finite element-based tracking algorithm (also known as DVC) to extract a continuous (non-overlapping and smooth) 3D displacement field resulting from acute IOP elevation. No additional smoothing or filtering of the resulting 3D displacement field was needed. More details about the DVC algorithm (including the stopping criteria) and a validation on several artificial deformation scenarios can be found in our previous study.11 From the extracted 3D deformation map, we then derived the volume-averaged effective strain in the LC ($E_{\text{eff}}$). The effective strain is a positive scalar value summarising the complex 3D strain state and is defined as follows:

$$E_{\text{eff}} = \sqrt{\frac{(E_1-E_2)^2+(E_1-E_3)^2+(E_2-E_3)^2}{2}}$$

Here, $E_1$, $E_2$ and $E_3$ are the principal components of the Green-Lagrange strain tensor. Based on the effective LC strain, we finally split the biomechanical data set into two groups: the ONH that were considered robust ($E_{\text{eff}} < 4\%$) and those fragile ($E_{\text{eff}} > 4\%$). The threshold of $E_{\text{eff}} = 4\%$ approximately corresponds to the median of the data set. The approach is summarised in figure 1. Subsequently, we used this binary classification (based on the effective LC strain) as ground truth to train and test the here developed AI algorithms.

Algorithms to predict ONH robustness without performing biomechanical testing

In the following sections, we present three AI algorithms (with gradually increasing complexity) that were able to learn from the already-acquired biomechanical data (from cohort 1). Such algorithms aimed to predict ONH robustness solely from a single OCT volume scan of the ONH without the need for any additional hardware or observations of mechanical deformations. More precisely, we used the baseline OCT volume scan of each ONH from cohort 1 as input for the AI algorithms to classify a given ONH as robust ($E_{\text{eff}} < 4\%$) or fragile ($E_{\text{eff}} > 4\%$). The first algorithm was a random forest classifier—a well-established machine learning algorithm in the field of ophthalmology.25 26 The second was an autoencoder—a method that gained popularity in recent years.29 30 It was tuned herein with additional unlabelled data (cohort 2) to improve the final classification.
Automated extraction of ONH structural parameters

The following ONH structural parameters (for both neural and connective tissues) were automatically extracted from the segmented OCT volumes of cohort 1 using the software REFLECTIVITY: (1) the average minimum rim width in each octant defined as the minimum distance from a BMO point to a point on the inner limiting membrane (ILM); (2) the average RNFL thickness in each octant measured at a distance equal to 1.5 times the radius of BMO from the centre of BMO (ie, the centroid of the BMO points); (3) the average GCL+IPL thickness in each octant evaluated at the same location as that used for RNFL thickness; (4) the prelamina depth defined as the distance from the BMO centre to a point on the ILM (perpendicular to the BMO plane); (5) the minimum prelamina thickness; (6) the LC depth defined as the distance from the BMO plane to a point on the anterior LC boundary; (7) the LC global shape index that summarises the shape of the anterior LC boundary into a single number\(^{36}\) and (8) the BMO area.

**Robustness assessment**

All ONH structural parameters were used as inputs for the random forest classifier in order to assess whether a given ONH was robust or fragile. Optimal performance was achieved with a random forest consisting of 100 individual decision trees.

**Algorithm 2 for AI-based robustness assessment: autoencoder as classifier**

We used an autoencoder (first introduced by Rumelhart et al\(^{37}\)) in combination with a multilayer perceptron (MLP) classification network to distinguish robust (\(E_{\text{eff}} < 4\%\)) from fragile ONHs (\(E_{\text{eff}} > 4\%\)) solely using six equally spaced segmented radial OCT B-scans for each ONH.

**Automated segmentation of central OCT B-scans**

We automatically segmented all baseline (undeformed) OCT volumes of cohorts 1–2 with the same segmentation approach as that presented above. Subsequently, we selected the segmented OCT B-scan that was closest to the BMO centre (defined as the segmented central OCT B-scan). Additionally, we extracted five radial OCT B-scans (centred on the BMO centre) at 30°, 60°, 90°, 120° and 150° from the central OCT B-scan.

**Robustness assessment**

We first trained the autoencoder (without the MLP network) in an unsupervised manner using all segmented radial OCT B-scans of each OCT volume from cohort 2. By training the autoencoder on such a relatively large unlabelled dataset (ie, cohort 2), we hoped to increase the quality of the compressed representation that is subsequently used for classifying ONH robustness. To assess the performance of the autoencoder (ie, its ability to encode/compress a segmented radial OCT B-scan), we reported the Dice coefficient as mean±SD for all reconstructed OCT B-scans from the test set (figure 2A). We then discarded the decoder and fixed the weights of the encoder. Finally, we used the encoder (fixed weights) to transform each segmented radial OCT B-scan from cohort 1 into its corresponding compressed representation that was subsequently used to train the MLP network in a supervised manner (figure 2B). To predict the robustness of a given ONH from cohort 1, we averaged the prediction results from all six segmented radial OCT B-scans of the corresponding baseline (undeformed) OCT volume. As compared with directly using the segmented radial OCT B-scans to train the MLP network, using a compressed representation facilitated the learning process and
reduced overfitting. The architecture of the autoencoder and the MLP network were adopted from. However, in contrast to, optimal performance was achieved with a compressed representation of dimension $D=64$.

**Algorithm 3 for AI-based robustness assessment: DGCNN**
The DGCNN was used to predict whether a given ONH was considered robust ($E_{\text{eff}} < 4\%$) or fragile ($E_{\text{eff}} > 4\%$) due to an acute increase in IOP. Contrary to the other two algorithms, DGCNN can learn from complex 3D shapes, as long as they are represented as 3D point clouds. Our goal was to describe a given ONH as a 3D point cloud (from the OCT volume scan) which then served as an input for DGCNN.

**Representing a given ONH as a 3D point cloud**
From the ONH segmentations (see section above and figure 3A,B), we identified the anterior boundaries of all aforementioned tissues, plus the posterior boundaries of the sclera and LC. All points were transformed to the physical space (‘true’ scanning area) using the respective voxel resolution provided by the Spectralis OCT device that corrects for ocular magnification due to, for example, different axial lengths or refractive errors. Approximately 20,000 points were randomly selected from those boundaries to represent the final 3D point cloud (figure 3C,D). In addition, for each tissue, the local thickness was mapped (minimum distance between anterior and posterior boundaries) and values were assigned to points from the anterior tissue boundary. In total, each point was assigned four values: its coordinates $(x, y, z)$ and a local tissue thickness (whenever applicable or 0 otherwise). To homogenise the data across subjects, the origin of the coordinate system $(x=0, y=0, z=0)$ was situated at the centre of BMO (centroid of the BMO points) and the BMO plane (best-fit plane to the BMO points) was aligned horizontally. In addition, we performed a cylindrical crop around the centre of BMO (radius of 1.75 mm and aligned with the axial direction) to further homogenise the data.

**Robustness assessment**
The DGCNN was specifically designed to take 3D point clouds (or unordered sets of points) as input such as those represented in figure 3D. By dynamically computing local graphs for each point in the input point cloud (through edge convolutions or ‘EdgeConv’), the DGCNN can capture fine structural features of an object, such as small changes in curvature (figure 3D). To predict robustness from a given ONH point cloud, we used the same DGCNN architecture as in, except that we used a max pooling layer of dimension 256 and set the number of k-nearest neighbours for all EdgeConv layers to 20.
Identification of critical 3D structural features of the ONH

The specific architecture of the DGCNN inherently allowed us to identify the critical structural landmarks of a given ONH that make it robust or fragile. This was summarised as a subset of 3D points (ie, critical points) for each ONH. When all critical points from all ONHs were pooled, a density map was obtained, thus revealing important ONH regions contributing to ONH robustness. Using the best performing hyperparameters (determined by...
Performance comparison: random forest, autoencoder and DGCNN

To assess and compare the overall performance of the three classification algorithms, the biomechanical data set was split in training (70%), validation (15%) and test (15%) sets, respectively. A fivefold cross-validation study was performed (using the train and validation set) and we reported the receiver operating characteristic (ROC) curves and the area under the curves (AUCs) of the model with the best performing hyperparameters as mean±SD. Each of the three methods used the same split of data and was trained on a Nvidia RTX A5000 GPU card until optimum performance was reached in the validation set.

To improve performance and reduce overfitting, we used data augmentation techniques such as random cropping, random rotations, random rigid translations, random sampling (ie, randomly picking a subset of points from the input point cloud) and additive Gaussian noise where applicable.

RESULTS

Assessment of ONH robustness: biomechanical testing

We were able to extract the volume-averaged effective strain in the LC following an acute IOP elevation for all 336 subjects of the biomechanical test dataset (cohort 1). A total of 162 ONHs were classified as fragile (\( E_{\text{eff}} > 4\% \)) and 174 ONHs were classified as robust (\( E_{\text{eff}} < 4\% \)) with a resulting average LC effective strain of 5.65%±1.48% and 2.97%±0.65%, respectively.

Assessment of ONH robustness: performance comparison

All three AI-based methods were able to assess ONH robustness from a single 3D OCT volume scan. The DGCNN (AUC: 0.76±0.08) outperformed the autoencoder (AUC: 0.72±0.09) and the random forest classifier (AUC: 0.69±0.05). The corresponding ROC curves are shown in figure 4. Furthermore, the autoencoder was able to accurately reconstruct a segmented central OCT B-scan with a Dice coefficient of 0.91±0.03.

Critical 3D structural features of the ONH for the assessment of ONH robustness

The DGCNN allowed us to directly extract critical points that were important for the assessment of ONH robustness. Using the model with the best performing hyperparameters, we extracted and pooled all critical points from all ONHs of the test set and displayed them as a density map (figure 5). The critical points formed a circle around the optic disc with points mainly located near the connective tissues (peripapillary sclera and LC) in the deeper part of the ONH (~80%). More precisely, we found that points mainly concentrated in the superior quadrant of the ONH around the scleral canal and near the LC insertion sites.

DISCUSSION

In this study, we developed an AI-driven approach that can predict the robustness of a given ONH solely from information derived from an OCT volume scan. This was done without the need to perform any form of biomechanical testing on the unseen OCT volumes. Among the three AI approaches, the DGCNN provided the best performance. It had the advantage of identifying what key structural landmarks (or critical points) most contributed to make a given ONH robust, thus increasing the interpretability of the method. Most critical points formed a ring that closely matched the location of the scleral canal boundary, while others were found near the LC insertion sites. With such a technology, our goal is to understand whether ONH robustness...
could help us identify glaucoma patients at risk of fast visual field loss progression.

In this study, we provided a proof of principle for assessing ONH robustness solely from information extracted from a single OCT volume scan. Specifically, it appears that ONH morphology (ie, the size, shape and structure of the ONH) can code for its biomechanical behaviour, but most likely through an intricate relationship. Our work is a preliminary step and provides a foundation to ultimately refine such a relationship. Overall, our concept is not unfamiliar to the field of biomechanics; for instance, it has been shown that it was possible to predict the apparent elastic modulus (ie, elastic stiffness) of trabecular bone simply from a quantitative CT scan (through assessment of the apparent density) and without performing biomechanical testing. Biomechanical finite element models have also predicted that a simple change in tissue morphology could considerably alter the biomechanical environment of the ONH. In this context, it is thus not surprising that AI might be able to pick up such relationships.

We found that geometric deep learning provided the best performance in predicting ONH robustness. Due to the vast amount of data in a raw 3D OCT volume scan of the ONH, several machine learning-based algorithms considered reducing the amount of input data by: (1) extracting characteristic structural parameters of the ONH; (2) using two-dimensional OCT B-scans instead of the whole OCT volume or (3) down-sampling the raw 3D OCT volume scans. All these preprocessing methods involve an inherent loss of fine local 3D structural features of the ONH. In contrast, the DGCNN takes a 3D point cloud as input that can represent the complex 3D structure of the ONH in an efficient way without losing fine local structural features, such as small changes in curvature. This could explain the boost in performance of the DGCNN (AUC: 0.76±0.08) as compared with the autoencoder (AUC: 0.72±0.09) or the random forest (AUC: 0.69±0.05).

Overall, for robustness classification, we found that our AUCs remained in the acceptable range from 0.7 to 0.8. While the AUCs may appear moderate, it should be emphasised that it would almost be impossible for a human observer to discriminate robust from fragile ONHs based on a standard 3D OCT volume scan. Additionally, the performance of our AI algorithms might be negatively influenced by the way we created the ground truth. The median of the average effective LC strain \( (E_{\text{eff}} = 4\%) \) was used as the cut-off value to discriminate robust from fragile ONHs (binary classification). However, more than 50% of the subjects in the biomechanical test dataset (cohort 1) exhibited an average effective LC strain between 3% and 5%, close to the cut-off value of 4%. This alone could have strongly impacted the AUC values. In the near future, we could consider the LC strain as a continuous variable and predict its ‘true’ value, instead of a binary classification, as this might give us a boost in performance.

Interestingly, to decide whether a given ONH was robust, our geometric deep learning algorithm especially used information from the scleral canal and LC insertion sites. Previous studies have reported the presence of a highly anisotropic (circumferentially aligned) ring of collagen fibres in the scleral flange surrounding...
the LC, but also with the presence of through-thickness variations. Computational studies suggested that this is an optimal fibre alignment protecting the LC from large deformations due to for example a change in IOP. Therefore, pathological or age-related alterations of the collagen microstructure in the peripapillary sclera/scleral canal might have a major impact on LC strains—our definition of ONH robustness. Additionally, local LC defects or alterations like posterior movement of the LC insertion zones and LC disinsertions were observed in glaucomatous eyes. Prior to these defects, the ONH tissues of these glaucomatous eyes often underwent excessive remodelling leading to a change in the biomechanics of the ONH and its robustness. Therefore, the position and the structure of the LC insertion sites might be a good indicator for ONH robustness.

In this study, we defined ONH robustness based on LC effective strains alone for several reasons. First, we used strain because it is a quantity that can be measured experimentally (as opposed to stress) in humans. In a controlled biomechanical test environment with the application of a constant force (like in our study), strain also grossly reflects the structural stiffness of a structure as it is both affected by morphology and biomechanical properties. Second, we used effective strain for simplicity because it nicely summarises the 3D state of local deformations into a single number. Third, we focused on the LC because it is the major known site of axonal damage in glaucoma. However, the term ‘robustness’ does not have a strong theoretical foundation in the field of soft tissue biomechanics. We purposely used this terminology (and its antonym, here ‘fragile’) because it has clinical value and it can be understood by both, medical practitioners and patients alike. Also note that we fully acknowledge that ONH robustness may require an improved definition, and we hope to be able to refine it once we better understand how the ONH responds to IOP, optic nerve tracton and CSFP in a longitudinal context.

Whether ONH robustness could be used to predict visual field loss progression remains controversial. From a pure biomechanical point of view, it makes sense: a given ONH exhibiting more strains in its LC may be at greater risk of visual field loss progression. But this assumption somehow underpins the complex tissue remodelling changes that are known to occur with age, and the development and progression of glaucoma. With age, the sclera gets stiffer, which may in some configurations reduce LC strains. With the development and progression of glaucoma, the ONH exhibits a hypercompliance phase in the early stages, followed by a stiffening phase in the more advanced stages. Taken together, these results, although only evaluated in primates and human donor eyes, suggest strong variations in ONH robustness throughout the course of the disease. This may need to be considered when making a prediction about visual field loss progression. We aim to better understand such implications by applying our technology to a longitudinal cohort.

In this study, several limitations warrant further discussion. First, the number of patients that underwent biomechanical testing (cohort 1) was rather small for training. In addition, the reported AUCs are only valid to this specific population and may not translate to other ethnicities. In the future, it will be crucial to validate our approach in a much larger and heterogeneous population. Second, our work was only tested with data acquired from one OCT device (Spectralis, Heidelberg Engineering, Germany). We were able to process OCT volume scans (all raster, but not diagonal) with varying resolutions and field of views, however, in the future, we must make our approach device-agnostic to be universally applicable. Third, the accuracy of the extracted point clouds might be sensitive to the performance of the segmentation algorithm. This, in turn, might influence our ONH robustness predictions. Sensitivity analyses would need to be performed to better address this issue. Fourth, our segmentations excluded some potentially relevant tissues, including, but not limited to: retinal layers (other than RNFL, GCL and IPL), the central retinal vessel trunk (and its branches), and the border tissues of Elschnig and Jacoby. A proper detection and subsequent representation of these tissues in the 3D ONH point cloud may in turn improve the assessment of ONH robustness. Finally, we labelled each ONH as robust or fragile according to a binary classification scheme. Instead, a ‘robustness score’ ranging from 0 (fragile) to 1 (robust) might be more attractive for clinical translation, and this should be considered in our next iteration.

In conclusion, we have proposed an AI-driven approach that can assess the robustness of a given ONH solely from a single OCT volume scan of the ONH, and without the need to perform biomechanical testing. This could be achieved because our group has gathered in vivo ONH biomechanical data in a relatively large population, and from which AI could learn from. In addition, AI suggested that regions located near the scleral canal opening or near the LC insertion sites might be important landmarks to drive ONH robustness or its fragility. In the future, we should evaluate whether ONH robustness could help us identify fast visual field loss progressors.

Contributors Study conception and design: FAB, TC, TA, GB and MJAG; data collection: FAB, TAT, SP, RH and TA; analysis and interpretation of results: FAB, AHT and MJAG; draft manuscript preparation: FAB and MJAG; guarantor: MJAG. All authors reviewed the results and approved the final version of the manuscript.

Funding We acknowledge funding from (1) the donors of the National Glaucoma Research, a programme of the BrightFocus Foundation, for support of this research (G2021010S (MJAG)); (2) SingHealth Duke-NUS Academy Medicine Research Grant (SRDUK4MR21A6 (MJAG)); (3) the ‘Retinal Analytics through Machine learning aiding Physics (RAMP)’ project that is supported by the National Research Foundation, Prime Minister’s Office, Singapore under its Intra-CREATE Thematic Grant “Interception Of Engineering And Health” - NRF2019-THE002-0006 awarded to the Singapore MIT Alliance for Research and Technology (SMART) Centre (MJAG/ATI GB); (4) the ‘Tackling & Reducing Glaucoma Blindness with Emerging Technologies (TARGET)’ project that is supported by the National Medical Research Council (NMRC), Singapore (MOH-OFLCG21Jun-0003 (MIAG)).

Competing interests MJAG and AHT are the co-founders of the AI start-up company Abyss Processing.

Patient consent for publication Not applicable.

Ethics approval The study adhered to the tenets of the Declaration of Helsinki and was approved by SingHealth Centralised Institutional review board (CIRB: 2016/2591). All subjects gave written informed consent.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request.

ORCID iD Michaël J A Girard http://orcid.org/0000-0003-4408-5918

REFERENCES
1 Sigal IA, Ether CR. Biomechanics of the optic nerve head. Exp Eye Res 2009;88:799–807.
2 Yan DB, Coloma FM, Methenaltart A, et al. Deformation of the lamina cribrosa by elevated intraocular pressure. Br J Ophthalmol 1994;78:643–8.
3 Fazio MA, Clark ME, Bruno L, et al. In vivo optic nerve head mechanical response to intraocular and cerebrospinal fluid pressure: imaging protocol and quantification method. Sci Rep 2018;8:12639.
4 Wang X, Beetle MR, Tun TA, et al. In vivo 3-dimensional strain mapping confirms large optic nerve head deformations following horizontal eye movements. Invest Ophthalmol Vis Sci 2016;57:3823–33.
5 Burgoyne CF, Downs IC, Belin EM, et al. The optic nerve head as a biomechanical structure: a new paradigm for understanding the role of IOP-related stress and strain in the pathophysiology of glaucomatous optic nerve head damage. Prog Retin Eye Res 2005;24:39–73.
