ORIGINAL ARTICLE

Ganglion Cell Complex Analysis as a Potential Indicator of Early Neuronal Loss in Idiopathic Intracranial Hypertension

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ABSTRACT

Reliable visual field testing is the gold standard in identifying future vision loss in patients with Idiopathic Intracranial hypertension (IIH). However, when field performance is unreliable, GCC analysis may be useful. We evaluated IIH patients over three visits: initial visit, follow-up visit and a third visit, almost 1 year later. We evaluated mean deviation (MD), GCC and RNFL at presentation and the second visit and compared it to the mean deviation (MD) on fields at the third visit. As early as the second visit, GCC loss correlated with visual field results seen at the third visit.

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Introduction

Idiopathic intracranial hypertension (IIH) is becoming an increasingly prevalent disease in our society as the rates of obesity increase.¹ It can have the devastating effect of permanent vision loss from optic nerve injury if patients are not treated in a timely and appropriate manner. Many patients with IIH have a good prognosis without permanent vision loss.² However, one of the challenges in the management of IIH is determining which IIH patients are at risk for severe, irreversible vision loss necessitating more aggressive treatment.

The majority of patients with IIH, early in the disease and with treatment have intact central vision.² Occasionally central vision is affected by sub-retinal fluid, choroidal folds and rarely choroidal neovascularization (CNV). If there is central vision loss with IIH from retinal pathology, treatment to lower intracranial pressure (ICP) or intravitreal avastin (bevacizumab) in the rare case of CNV will often improve central vision.³ Peripheral vision is minimally affected in the majority of patients as most patients present with enlarged blind spots or early arcuate defects. These visual fields often improve with treatment of increased ICP.² However, with advanced disease and inadequate treatment, IIH

patients can suffer profound symptomatic central and peripheral field loss.² Corbett et al followed 52 patients with IIH over an extended period and found that 14 patients had significant, irreversible vision loss.² Since these are not the majority of cases, the challenge is detecting when a patient is at risk for such irreversible vision loss and when to initiate more aggressive treatment or surgery.

Currently, clinicians rely on visual acuity, colour vision, visual fields, fundus examination, and optical coherence tomography (OCT) of the retinal nerve fibre layer (RNFL) and overall macular thickness in the management of IIH patients.⁴ Although these tests are helpful in the management of most cases of IIH, they have their limitations especially with more advanced disease.⁵

Automated visual field (VF) testing, when done accurately and reliably, is very useful in detecting peripheral and central field loss. However, visual field which is dependent on patient performance is prone to variability and inaccuracy.^{5,6} Often patients test poorly, especially initially, confusing the clinical picture.⁵ In addition, a further complicating factor in the interpretation of visual fields is the high prevalence of IIH and functional vision loss presenting as non-organic visual fields.^{7,8} RNFL assessment by

OCT, which has been one of the main modalities of measuring, grading, and monitoring optic nerve injury also has limitations.⁹ In cases of severe papilledema, the software algorithm is not designed to accurately measure RNFL thickness, generating inaccurate and variable results.⁹ In addition, RNFL thickness does not identify coexisting optic atrophy in the setting of papilledema.⁹

In this study, we analyzed data from patients with a recent diagnosis of IIH (within 6 months) at three points in time: presentation, a second visit (on an average 2 months after initial visit) and a third visit which occurred on an average 1 year after initial presentation. We examined visual fields, RNFL, and ganglion cell complex (GCC) thickness at each of the three different visits. We analyzed the information to determine reliability and accuracy in predicting vision loss.

Methods

A retrospective, observational, case control study was carried out in 18 patients (36 eyes) diagnosed with IIH and 18 age-matched healthy controls (36 eyes). These patients were evaluated in the neuro-ophthalmology service at the New England Eye Center, Tufts Medical Center from January 2012 to October 2015. The Tufts Medical Center Institutional Review Board approved the study in accordance with the ethical standards stated in the 1964 Declaration of Helsinki. This study is HIPAA compliant.

Patients eligible for this study were diagnosed with IIH according to the revised, modified Dandy criteria.¹⁰ Magnetic resonance imaging (MRI), magnetic resonance venogram (MRV), and a lumbar puncture (LP) were done in all patients to confirm elevated intracranial pressure (≥ 25 cm H₂O) and rule out other potential causes of papilledema, such as venous thrombosis. Exclusion criteria included the presence of additional retinal or optic nerve pathology, or the presence of systemic diseases or venous thrombosis that could contribute to secondary causes of increased intracranial pressure. All patients had been diagnosed with IIH within 6 months of presentation to the study and showed features of active disease with papilledema confirmed on OCT. There was not an inclusion criteria based on the degree of papilledema to enter the study. Papilledema varied from RNFL thickness of 79–575 μm . At the initial

visit, 14 eyes had RNFL thickness ≤ 200 μm and 22 eyes had RNFL thickness ≥ 200 μm . All the patients with IIH were treated with either medication or surgery. The majority of patients were started on acetazolamide, typically a starting dose of at least 1 gram per day along with a weight-reduction program. Four patients underwent surgical treatment: one patient had venous sinus stenting, one had optic nerve sheath fenestration, and two had ventriculo-peritoneal shunts placed.

Three complete neuro-ophthalmological evaluations were reviewed for this study for each patient. For simplicity, the terms “initial”, “second”, and “third” visit will be used in the figures and text. The “initial” visit refers to the initial encounter. The “second” visit occurred on average 2 months after the initial visit (2.0 ± 1.4 months). The third visit occurred on average 1 year after the initial visit (14.4 ± 10.6 months). Examination included assessment of the best-corrected visual acuity (BCVA) with Snellen optotypes, color discrimination (American Optical Hardy Ritter Rand), fundus examination, automated visual fields (VF), and spectral domain OCT (SD-OCT). Age-matched control subjects recruited from workers and random subjects with no history or evidence of ocular disease underwent the same OCT evaluation in both eyes.

Automated VF of the central 30 degrees (SITA-FAST 30–2, Carl Zeiss, Dublin, CA) was performed on all patients and the mean deviation (MD) was used for statistical analysis. Visual fields were repeated on the same day if there was clear difficulty with test understanding. The number of unreliable visual fields at each visit was recorded and also removed when analyzing the data.

SD-OCT was performed using Cirrus 4000/5000 (Carl Zeiss, CA, USA). Each eye was scanned using a macular cube (512×128 line scans) and an optic disc cube (200×200 line scans) protocol. The average thicknesses of the RNFL and GCC studies expressed in micrometers (μm) were automatically obtained by the software and used for analysis. For SD-OCT quantification, automatic segmentation algorithms were used to determine the RNFL and GCC sectoral thicknesses. The scanned areas (6×6 mm) were centred on the fovea for ganglion cell complex (GCC) analysis, which is defined as the combined measurement of the Ganglion cell layer and the inner plexiform layer. The quality of

the images was evaluated by the signal strength (a value from 0 to 10 in arbitrary units) automatically provided by the system and a preference to use studies with signal strength 6 or greater. Imaging studies with signal strength less than 6 was used if the segmentation was correct. Segmentation errors were not corrected but the number of RNFL and GCC studies with segmentation errors at each visit were recorded and removed from the analysis. For SD-OCT quantification, automatic segmentation algorithms were used to determine the RNFL and GCC sectoral thicknesses. The average thicknesses of the RNFL and GCC, expressed in micrometers (μm), were automatically obtained by the software and used for analysis.

All statistical analyses were performed via Microsoft Excel (version 14.3.9, Microsoft Corp, Redmond, WA) and SPSS statistics (Version 20, IBM-SPSS, Chicago, IL, USA). Univariate analysis of variance was used to compare OCT measurements between groups, eyes, and their possible interaction. General lineal model repeated measures (one-way ANOVA with repeated measures) were used to study changes on OCT parameters over the follow up and to study differences between both eyes within the patient group. Bivariate correlation was performed to detect significant associations between MD and average GCC, RNFL thicknesses at presentation and at the second visit and MD at 1 year of follow-up (third visit). Multiple linear regressions were then used to control the possible dependency between both eyes. Finally, simple linear regression analyses were performed to quantify the relation among the parameters, using third MD as the dependent variable and the eye and the parameters previously mentioned as independent variables. Pearson correlation coefficient, R Square, unstandardized coefficient B, test of within-subjects effects with Greenhouse-Geisser correction, pairwise comparisons and 95% confidence intervals (95% CIs) were obtained. All p values were based on two-sided tests and were considered statistically significant when the values were less than 0.05.

One of the goals of the study was to determine the reliability of the tests at each visit. Fields were

felt to be unreliable based on the gaze tracker and reliability standards of fixation losses greater than 33% and false positive results greater than 15%. False negative errors were not included in determination of reliability as this number increased with increased field loss. OCT RNFL and GCC studies were determined to be unreliable if there were clear segmentation errors.

Results

Of the 108 patients with a diagnosis code of papilledema evaluated at Tufts Medical Center from 2012–2015, 18 met the inclusion criteria and had testing and follow-up required to be part of the study. Comparisons were made with an age-matched control group (36 eyes).

There were 4 men and 14 women (36 eyes) and 18 age-matched controls 5 men and 13 women (36 eyes) with a mean age of 30.6 ± 9.6 years and 30.7 ± 9.7 , respectively. The mean weight was 244.66 ± 58.63 lbs, the mean body mass index was 33 ± 3.08 kg/m² and the mean lumbar pressure was 424.72 ± 93.60 mmH₂O in the patient group.

11 out of the 36 visual fields (30.5%) were unreliable on the initial visit, 4 (11%) at the second visit and 1 (2.7%) at the last visit based on the reliability standards mentioned above. RNFL and GCC studies also had most unreliable data at the initial visit, though there was not a correlation with the ones with unreliable fields and those with unreliable OCT studies. With RNFL, seven studies (19.4%) initially versus 0 at the second and third visit were found to be unreliable. Although RNFL results did not have clear segmentation errors on the second and third visit, it was difficult to determine if there was a comitant optic atrophy in the setting of papilledema. With GCC, 5 studies (13.8%) initially versus 3 (8.3%) at the second and 0 at the third visit were found to be unreliable. There was not a correlation between less reliable GCC studies initially and worse visual outcomes.

The mean RNFL, GCC, BCVA, and MD on VF at presentation, second, and third visits are presented in [Figure 1](#). The second visit occurred on average 2 months after the initial visit (2.0 ± 1.4 months). The third visit occurred on average 1 year after the initial visit (14.4 ± 10.6 months). The mean RNFL and mean GCC values of the control group were

$95.67 \pm 7.05 \mu\text{m}$ and $83.81 \pm 4.35 \mu\text{m}$, respectively. Univariate analysis of variance showed that the mean RNFL was significantly greater in the IIH patients group compared to controls at presentation and the second visit ($p = 0.00$), but not at the third visit ($p = 0.69$), with no differences between eyes (all p values > 0.05). The mean GCC was thinner in IIH patients compared to controls at all three visits (all p values < 0.01) with no differences between eyes (all p values > 0.05).

General linear model repeated measures showed statistically significant changes of mean RNFL and MD values over time within the papilledema group (Greenhouse-Geisser, $F = 24.562$; $p = 0.00$; $F = 4.163$, $p = 0.04$), whereas there were no significant changes of GCC and BCVA values (Greenhouse-Geisser, $F = 0.644$; $p = 0.37$; $F = 0.003$, $p = 0.99$). Pairwise comparisons revealed statistically significant differences between the three RNFL values over the 1-year of follow-up (all p values < 0.05). There were no

significant differences of mean RNFL, GCC, MD, and BCVA between right and left eyes (all p values > 0.05).

Bivariate correlation analysis was performed to study possible associations between the MD on the third visit and MD, RNFL, and GCC thicknesses at diagnosis and the second visit. MD at first and second visit were significantly associated with final MD (both $p = 0.00$). GCC thickness at the second visit was significantly associated with MD ($p = 0.01$) on the third visit, whereas GCC at time of diagnosis and RNFL thicknesses were not associated with the MD on the third visit ($p > 0.05$) (Table 1).

Multiple linear regressions were performed with the MD at the third visit as the dependent variable and MD at first and second visit, GCC at the second visit, and the eye as independent variables. The third visit MD was significantly correlated with MD at initial visit ($R^2 = 0.63$, $p = 0.00$; Durbin-Watson = 2.32), MD at second visit

Figure 1, Athappilly

Figure 1. RNFL = Retinal nerve fibre layer thickness, GCC = Ganglion cell complex thickness, MD = mean deviation, BCVA = Best corrected visual acuity. Graph depicting RNFL, GCL, Mean Deviation (MD) and BCVA in IIH patients throughout course of disease. RNFL had the most significant change over time followed by MD, BCVA, and GCC, respectively.

($R^2 = 0.88$, $p = 0.00$; Durbin-Watson = 2.63) and the second visit follow-up GCC ($R^2 = 0.22$, $p = 0.03$), independent of the eye studied. Simple linear regression was also used to measure the correlation between second visit GCC and third visit MD. The analysis showed a positive correlation between the second GCC visit and the third visit MD ($R^2 = 0.22$; $p = 0.01$). When the data were split depending on the RNFL thickness at diagnosis, regression analyses showed stronger positive correlation between the second visit GCC and the third visit MD, when RNFL is less or equal to $200\text{ }\mu\text{m}$ ($R^2 = 0.52$; $p = 0.01$). Statistically significant correlation between the second visit GCC and third visit MD was not present when RNFL was higher than $200\text{ }\mu\text{m}$ ($p = 0.14$) (Figure 2).

Discussion

Although MD on automated VF is routinely used to monitor IIH patients clinically and in clinical trials, it is subject to variability.⁵ The thresholds obtained from automated perimetry depend on the technician administering the study and a variety of physical and behavioural

factors dependant on the patient.^{5,7,8,11,12} The performance failures caused by this variability have been detected in 21% of patients with IIH on at least one VF examination.⁵

In this study of 18 IIH patients, we observed that visual fields when reliable, are predictive of future vision loss. Both the first and second mean deviation correlated with the final mean deviation on visual fields when unreliable data were removed from the analysis. The visual fields, however, had the greatest number of unreliable tests at the first visit compared to RNFL and GCC studies. The performance on visual fields did improve with time, with the third visit having only 1 unreliable field result, compared to 11 at the first visit. However, patients with advanced disease on presentation may require more aggressive and potentially surgical intervention. This can make dependence on fields difficult for management.

Spectral-domain OCT may not accurately define the borders of the RNFL when the peripapillary retinal layers are thickened due to edema.¹³ In addition, as mentioned previously, RNFL is not able to detect comitant optic atrophy in the setting of papilledema making it difficult to predict vision loss. In

Table 1. Correlations between ganglion cell complex, retinal nerve fibre layer, mean deviation on visual field and mean deviation on third visit.

		Initial RFNL	Initial MD	Initial GCC	Second Visit RNFL	Second Visit MD	Second Visit GCC
Third MD	Pearson Correlation	0.012	0.778	0.209	-0.070	0.938	0.473
	P value	0.950	0.000	0.258	0.695	0.000	0.007

RNFL = Retinal nerve fibre layer thickness, GCC = Ganglion cell complex thickness, MD = mean deviation on the third, 30-2 visual field, BCVA = Best corrected visual acuity. A value of $p < 0.05$ was considered statistically significant.

Figure 2. A: Dispersion graph showing significant linear relation between average MD at third visit and average GCC at the second visit ($R^2 = 0.224$). B: In patients with initial RNFL equal or lower than $200\text{ }\mu\text{m}$ ($R^2 = 0.518$) the model fits the data better, suggesting a stronger correlation.

contrast, in patients with mild papilledema, peripapillary RNFL thickness abnormalities have been demonstrated to be better correlated with VF sensitivity loss.¹⁴

RNFL data followed a similar pattern with data being most unreliable at the initial visit and improvement with subsequent visits. In the cases with more severe papilledema, initial RNFL values could not be reliably obtained due to algorithm failure. RNFL thickness on initial presentation and follow-up were increased in the majority of our patients, despite probable concomitant optic nerve injury. This made RNFL measurements also difficult to guide management in cases where there was a concern for early, impending vision loss.

GCC reliability also improved over the visits. Compared to RNFL and HVF there was less unreliable data at the initial visit. On the second visit, there were a few studies that had unreliable GCC results due to segmentation errors, but there was still a statistical correlation to final visual fields even when including unreliable GCC studies. Though the correlation was stronger when GCC studies with artifact were removed. The correlation between final MD and GCC at 2 months was even stronger in the 14 eyes with initial RNFL less than or equal to 200 μm in whom the RNFL thickening did not obscure the GCC (Figure 2a–b). Of those patients in whom RNFL thickness was greater than 200 μm , GCC analysis was not reliable possibly because of axon swelling as well as subretinal and intraretinal fluid obscuring the GCC. Although one may expect more GCC atrophy with increased RNFL thickness making GCC assessment easier, there may not be a correlation with increased RNFL thickness and GCC atrophy. In follow up, despite the presence of papilledema affecting accuracy of RNFL, patients had less distortion from edema and fluid in the retina allowing for more accurate measurements of the GCC. GCC, in contrast to RNFL, could more reliably indicate optic nerve injury and symptomatic vision loss earlier in the course of disease (Figure 3).

Skau et al. reported that changes in RNFL thickness correlated with improvements in MD at 3 months of follow up.¹⁵ In our study there was a greater degree of papilledema initially

and in follow-up compared to Skau's study. New techniques to measure optic nerve volume and height have been reported to be better diagnostic markers in IIH and may correlate better with intracranial pressure changes than RNFL thickness.¹⁶

In a study of 20 IIH patients, Bianchi et al. evaluated RNFL and GCC with different stages of optic nerve involvement with papilledema.¹³ They noted that in 10% of their patients, GCC was reduced when the RNFL thickness was still elevated, indicating retrograde nerve damage. They concluded GCC analysis could be a valuable early predictor of vision loss.¹³ The NORDIC trial, which measured IIH patients with mild visual field loss, did find a correlation between reduced GCC-IPL complex values in the lower 5% of their IIH patients and higher mean deviations on visual fields but did not find correlations with higher mean deviations on visual fields and increased RNFL thickness.^{9,17} Unlike the Nordic trial, our patients were not limited to those with mild visual loss. The average mean deviation on initial visual fields in our study was -9.90 dB (range: -0.17 to -32.80 , median: -2.62) compared to PMD of -2.00 to -7.00 dB in the NORDIC trial. Most of our patients had a RNFL thickness greater than 200 μm on initial presentation, and two patients showed atrophic papilledema on presentation (sectoral thinning of more than 5%). The spectrum of severity of disease in our IIH patients may reflect what occurs in the broader population of patients with IIH. In a recent study, Chen et al. found that in patients with irreversible vision loss from optic nerve injury, the GCC, specifically in follow-up, was predictive of vision loss.⁴ However, a custom GCC analysis program was used, whereas in our study a commercially available algorithm was used to simulate what typically occurs in most clinical practices.

Our study was retrospective, and there was some variability in the time of the follow-up visits. Since only a few patients underwent surgical intervention, we were not able to categorize results based on treatment modality. In addition, the use of MD is not a reliable measurement of symptomatic, central vision loss as

Figure 3. Case illustration with pattern deviation from VF 30–2, OCT RNFL and OCT GCC values. This Case illustrates findings from the left eye of an IIH patient with mild vision loss. Initial fields are deceptively constricted and unreliable. Initial GCC was affected by algorithm failure from severe RNFL thickening (indicated by white arrows). RNFL thickness is elevated at initial and slightly on the second visit, therefore, did not provide early information regarding optic nerve injury compared to GCC studies. GCC studies at the second and third visit were reliably measured as indicated by the white arrows. The GCC analysis demonstrated sectoral thinning, suggestive of mild optic nerve injury correlating with visual field loss at the third visit. The second visit and third visit fields became more reliable. The pattern deviation visual fields correspond to second and third visit GCC studies, which show sectoral thinning.

the MD includes measurements of the total field, including areas of the visual field whereby patients may not be symptomatic.

Visual fields when reliable are still the gold standard to predicting future vision loss in IIH. When fields are unreliable and there is a concern for early, progressive visual loss in certain IIH patients, GCC may aid in detection of optic nerve injury earlier than RNFL analysis. Therefore, GCC studies may be a valuable tool in aiding management of IIH.

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References

1. Kilgore KP, Lee MS, Mokri B, et al. Re-evaluating the incidence of idiopathic intracranial hypertension in an era of increasing obesity. *Ophthalmology*. 2017;124(5):697–700. doi:10.1016/j.ophtha.2017.01.006.
2. Corbett JJ, Savino PJ, Thompson HS, et al. Visual loss in pseudotumor cerebri. Follow-up of 57 patients from 5 to 41 years and a profile of 14 patients with permanent severe visual loss. *Arch Neurol*. 1982;39:461–474. doi:10.1001/archneur.1982.00510200003001.
3. Lee IJ, Maccheron LJ, Kwan AS. Intravitreal bevacizumab in the treatment of peripapillary choroidal neovascular membrane secondary to idiopathic intracranial hypertension. *J Neuroophthalmol*. 2013 Jun;33(2):155–157. doi:10.1097/WNO.0b013e31827c6b49.
4. Chen JJ, Thurtell MJ, Longmuir RA, et al. Causes and prognosis of visual acuity at the time of initial presentation in idiopathic intracranial hypertension. *Invest Ophthalmol Vis Sci*. 2015 Jun;56(6):3850–3859. doi:10.1167/iovs.15-16450.

5. Cello KE, Keltner JL, Johnson CA, Wall M. Factors affecting visual field outcomes in the idiopathic intracranial hypertension treatment trial. *J Neuroophthalmol*. 2016;36(1):6–12. doi:[10.1097/WNO.0000000000000327](https://doi.org/10.1097/WNO.0000000000000327).
6. Wall M, Johnson CA, Cello KE, Zamba KD, McDermott MP, Keltner JL. Visual field outcomes for the Idiopathic Intracranial Hypertension Treatment Trial (IIHTT). *Invest Ophthalmol Vis Sci*. 2016;57(3):805–808. doi:[10.1167/iovs.15-18626](https://doi.org/10.1167/iovs.15-18626).
7. Ney JJ, Volpe NJ, Liu GT, Balcer LJ, Moster ML, Galetta SL. Functional visual loss in idiopathic intracranial hypertension. *Ophthalmology*. 2009 Sep;116(9):1808–1813.e1. doi:[10.1016/j.ophtha.2009.03.056](https://doi.org/10.1016/j.ophtha.2009.03.056).
8. Kutzko KE, Brito CF and Wall M. Effect of instructions on conventional automated perimetry. *Invest Ophthalmol Vis Sci*. 2000;41:2006–2013.
9. Optical Coherence Tomography Substudy Committee, NORDIC Idiopathic Intracranial Hypertension Study Group. Papilledema outcomes from the optical coherence tomography substudy of the idiopathic intracranial hypertension treatment trial. *Ophthalmology*. 2015;122(9):1939–1945. doi:[10.1016/j.ophtha.2015.06.003](https://doi.org/10.1016/j.ophtha.2015.06.003).
10. Friedman DI, Jacobson DM. Diagnostic criteria for idiopathic intracranial hypertension. *Neurology*. 2002;59(10):1492–1495. doi:[10.1212/01.WNL.0000029570.69134.1B](https://doi.org/10.1212/01.WNL.0000029570.69134.1B).
11. Zalta AH. Lens rim artifact in automated threshold perimetry. *Ophthalmology*. 1989;96(9):1302–1311. doi:[10.1016/S0161-6420\(89\)32722-9](https://doi.org/10.1016/S0161-6420(89)32722-9).
12. Lindenmuth KA, Skuta GL, Rabbani R, Musch DC. Effects of pupillary constriction on automated perimetry in normal eyes. *Ophthalmology*. 1989;96(9):1298–1301. doi:[10.1016/S0161-6420\(89\)32723-0](https://doi.org/10.1016/S0161-6420(89)32723-0).
13. Bianchi S, Ciasca P, Curone M, et al. Quantitative analysis of optic nerve damage in idiopathic intracranial hypertension (IIH) at diagnosis. *Neurol Sci*. 2013;34(s1):143–145. doi:[10.1007/s10072-013-1373-1](https://doi.org/10.1007/s10072-013-1373-1).
14. Rebolleda G, Muñoz-Negrete FJ. Follow-up of mild papilledema in idiopathic intracranial hypertension with optical coherence tomography. *Invest Ophthalmol Vis Sci*. 2009;50(11):5197–5200. doi:[10.1167/iovs.08-2528](https://doi.org/10.1167/iovs.08-2528).
15. Skau M, Sander B, Milea D, Jensen R. Disease activity in idiopathic intracranial hypertension: a 3-month follow-up study. *J Neurol*. 2010;258(2):277–283. doi:[10.1007/s00415-010-5750-x](https://doi.org/10.1007/s00415-010-5750-x).
16. Kaufhold F, Kadas EM, Schmidt C, et al. Optic nerve head quantification in idiopathic intracranial hypertension by spectral domain OCT. *PLoS ONE*. 2012;7(5):e36965. doi:[10.1371/journal.pone.0036965](https://doi.org/10.1371/journal.pone.0036965).
17. OCT Sub-Study Committee for the NORDIC Idiopathic Intracranial Hypertension Study Group. Baseline OCT measurements in the idiopathic intracranial hypertension treatment trial, part I: quality control, comparisons, and variability. *Invest Ophthalmol Vis Sci*. 2014;55(12):8180–8188. doi:[10.1167/iovs.14-14960](https://doi.org/10.1167/iovs.14-14960).