Prognostic utility of optical coherence tomography for long-term visual recovery following pituitary tumor surgery

Michael T.M. Wang, James King, R. C. Andrew Symons, Stanley S. Stylli, Joos Meyer, Mark D. Daniell, Peter J. Savino, Andrew H. Kaye, Helen V. Danesh-Meyer

PII: S0002-9394(20)30289-0

DOI: https://doi.org/10.1016/j.ajo.2020.06.004

Reference: AJOPHT 11401

To appear in: *American Journal of Ophthalmology*

Received Date: 31 March 2020

Revised Date: 2 June 2020

Accepted Date: 3 June 2020

ABSTRACT

Purpose: To investigate the association between optical coherence tomography (OCT) parameters and long-term visual recovery following optic chiasm decompression surgery.

Design: Prospective cohort study.

Methods: Consecutive patients undergoing pituitary or parasellar tumor resection, between January 2009 to December 2018, were recruited in a single-centre, two-year prospective, longitudinal cohort study. Best-corrected visual acuity, visual fields, and OCT retinal nerve fibre layer (RNFL) thickness, macular thickness and volume were assessed pre-operatively, and at 6 weeks, 6 months, and 2 years post-operatively. Long-term visual field recovery and maintenance was defined as a mean deviation greater than -3 at 24 months, and visual acuity recovery and maintenance was defined as a logMAR of 0 (Snellen 20/20) or better at 24 months.

Results: Two hundred and thirty-nine patients (129 males, 110 females; mean±SD age, 52±16 years) were included. Multiple logistic regression analysis demonstrated that increased inferior RNFL thickness (per 10μm) was associated with higher odds of long-term visual field recovery and maintenance (OR=1.26; 95% CI, 1.12-1.41; $Q<0.001$), and greater superior RNFL thickness (per 10μm) was associated with higher odds of visual acuity recovery and maintenance (OR=1.13; 95% CI, 1.03-1.27; $Q=0.031$). A multivariable risk prediction model developed for long-term visual field recovery and maintenance, incorporating age, pre-operative visual function and RNFL thickness, demonstrated C-statistics of 0.83 (95% CI, 0.72-0.94).

Conclusions: Pre-operative RNFL thickness was associated with long-term visual recovery and maintenance following chiasmal decompression. The multivariable risk prediction model developed in the current study may assist with pre-operative patient counselling and prognostication.

Manuscript title: Prognostic utility of optical coherence tomography for long-term visual recovery following pituitary tumor surgery

Short title: OCT and visual recovery following pituitary tumor surgery

Authors:

Michael T. M. Wang [1], James King [2,3], R. C. Andrew Symons [2,4], Stanley S. Stylli [2,3], Joos Meyer [2,4], Mark D. Daniell [2,5,6], Peter J. Savino,[7] Andrew H. Kaye [2,8], Helen V. Danesh-Meyer [1]

Institutional affiliations:

[1] Department of Ophthalmology, New Zealand National Eye Centre, University of Auckland, Auckland, New Zealand
[2] Department of Surgery, University of Melbourne, Parkville, Victoria, Australia
[3] Department of Neurosurgery, Royal Melbourne Hospital, Parkville, Victoria, Australia
[4] Department of Ophthalmology, Royal Melbourne Hospital, Parkville, Victoria, Australia
[5] Department of Ophthalmology, Royal Victorian Eye and Ear Hospital, Melbourne, Victoria, Australia
[6] Centre for Eye Research Australia, Melbourne, Victoria, Australia
[7] Shiley Eye Institute, University of California, San Diego, California, United States
[8] Department of Neurosurgery, Hadassah Hebrew University Medical Centre, Jerusalem, Israel

Correspondence:

Professor Helen V. Danesh-Meyer
Department of Ophthalmology
New Zealand National Eye Centre
University of Auckland
Private Bag 92019
Auckland 1142
New Zealand

Phone: +64 9 923 6254
Fax: +64 9 367 7173
Email: helendm@gmail.com

INTRODUCTION

Pituitary tumors account for approximately 15% of primary intracranial lesions,[1] and frequently cause visual impairment secondary to compression of the optic chiasm.[2] Although visual function can improve considerably following tumor resection and chiasmal decompression, the extent of recovery remains difficult to prognosticate.[2-4] A number of clinical predictors for post-operative visual recovery have been extensively investigated, with varying degrees of prognostic ability being reported.[2-4] Previous studies have demonstrated inconsistent results for the prognostic performance of age, symptom duration, tumor size, pre-operative visual function, and optic atrophy.[2-16]

In recent years, there has been growing evidence of the prognostic ability of optical coherence tomography (OCT) measurements for visual recovery following pituitary tumor resection.[2, 17] OCT facilitates rapid, non-invasive, *in vivo* cross-sectional imaging of the retinal layers, and offers a number of surrogate markers for retinal ganglion cell injury.[2, 17, 18] In particular, the predictive ability of retinal nerve fibre layer (RNFL) thickness for post-operative visual function has been confirmed by numerous reports.[3, 10, 17, 19-26]

Nevertheless, many of the earlier studies investigating the prognostic ability of OCT parameters have been limited by relatively modest sample sizes of less than fifty patients. The study follow-up periods have also generally been shorter than 12 months, although there has been increasing recognition of the potential for delayed visual recovery that might occur beyond this time period.[2, 27] In addition, the predictive ability of OCT macular parameters has received less attention.[22, 23, 28, 29] The purpose of this two-year prospective longitudinal study was therefore to investigate the prognostic ability of optical coherence tomography (OCT) parameters for long-term visual recovery and maintenance following pituitary tumor resection.

METHODS

Patients

This single-centre, two-year prospective, longitudinal cohort study followed the tenets of the Declaration of Helsinki and was prospectively approved by the institutional review board. Informed consent was obtained from participants after explanation of the nature and possible consequences of the study. Consecutive patients, aged 16 years or older, undergoing pituitary or parasellar tumor resection between January 2009 to December 2018 were recruited. Participants were eligible for inclusion following confirmation of magnetic resonance imaging (MRI) evidence of optic chiasm compression secondary to the pituitary or parasellar tumor, and availability for two-year post-operative follow-up. Exclusion criteria included previous anterior segment, posterior segment, or optic nerve disease (other than compressive optic neuropathy), such as glaucoma, cup disc ratio asymmetry of greater than 0.2, focal notching, or optic nerve haemorrhage; as well as spherical refractive error outside of the range of >5D or greater than 2D of astigmatism. In addition, patients with unreliable pre-operative visual field testing, defined as >25% false positive, false negative, or fixation loss rate, were also excluded.

Measurements

Best-corrected visual acuity, visual fields, and OCT parameters were assessed pre-operatively, and then 6 weeks, 6 months, and 2 years post-operatively. Best-corrected visual acuity was evaluated using a Snellen chart at 20 feet, and converted to the logMAR scale for subsequent analysis. Automated perimetry for visual field assessment was performed using the 24-2 Swedish Interactive Threshold Algorithm on the Humphrey Field Analyzer II (Carl Zeiss Meditec, Jena, Thuringia, Germany), with a Goldmann size II stimulus on a 31.5 apostilb background, and the mean deviation and pattern standard deviation measurements were recorded. Patients were able to repeat visual field testing up to three times pre-operatively to obtain more reliable results, and the most reliable pre-operative test results obtained were recorded. Quantitative OCT measurements, including RNFL thickness, macular thickness and volume, were conducted using the Spectralis® OCT machine (Heidelberg Engineering GmbH, Heidelberg, Germany) and analysed using Heidelberg eye explorer software version 1.9.14.0. Long-term visual field recovery and maintenance was defined as a mean deviation greater than -3 at the 2-year post-operative follow-up visit,[3] while long-term visual acuity recovery and maintenance was defined as a logMAR of 0 (Snellen visual acuity 20/20) or better at the 2-year post-operative follow-up visit.

Statistics

Statistical analysis was conducted using IBM SPSS Statistics version 22.0 (New York, USA) and MedCalc Statistical Software version 18.0 (Ostend, Belgium). Generalised estimating equation (GEE) modelling was performed to account for within-subject inter-eye correlation, and false discovery rate adjustment of p-values was applied and reported as Q-values to account for multiple comparisons where appropriate. Changes in visual function and OCT parameters during the study period were assessed using one-way repeated measures analysis of variance (ANOVA), and post-hoc pairwise multiplicity-adjusted Tukey's tests were conducted where significant trends were identified. The associations between pre-operative OCT parameters and long-term visual field and acuity recovery and maintenance was assessed using multiple logistic regression, adjusted for confounding variables including age, sex, and baseline mean deviation or visual acuity.

Patients were randomized into developmental (70%) and validation samples (30%) for the purposes of constructing and evaluating multivariable logit risk prediction models. A single randomly selected eye from each patient was incorporated, with no patients contributing to both the developmental and validation samples. Independent predictors ($p<0.05$) identified using multiple logistic regression analysis of the developmental sample were used to construct the multivariable logit risk prediction models. Discriminative performance in the validation sample was assessed using the concordance statistic (C-statistic) derived from the area under the receiver operating characteristic (ROC) curve, and the Youden-optimal prognostic cut-off sensitivity, specificity, positive and negative predictive values were calculated. All tests were two-tailed, and $p<0.05$ or $Q<0.05$ was considered significant.

RESULTS

A total of 462 eyes of 239 patients (129 males, 110 females; mean±SD age, 52±16 years) were included in the analysis. Two hundred and thirty-two (97%) patients underwent a trans-sphenoidal operative approach, and 216 (90%) patients presented with pituitary adenomas (Table 1).

Visual function and OCT parameters of patients during the study period are presented in Table 2 and Figure 1. Significant improvements in visual field mean deviation and pattern standard deviation were observed within 6 weeks following pituitary tumor resection (both $Q<0.001$, Table 3 and Figure 1), although no significant changes occurred between 6 weeks to 2 years (all $Q>0.20$, Table 3 and Figure 1). At the pre-operative visit, 253 (55%) eyes exhibited a visual field mean deviation greater than -3dB, and 303 (66%) eyes exhibited a best-corrected logMAR visual acuity of 0 or better. At the 2-year post-operative follow-up visit, 331 (78%) eyes exhibited a visual field mean deviation greater than -3dB, and 324 (76%) eyes exhibited a best-corrected logMAR visual acuity of 0 or better.

Multiple logistic regression results for long-term visual recovery and maintenance by OCT parameters are presented in Tables 4 and 5, and receiver operating characteristic curves are illustrated in Figure 2. Increased inferior RNFL thickness (per 10μm) was associated with higher odds of improved long-term visual field recovery and maintenance (OR=1.26; 95% CI, 1.12-1.41; $Q<0.001$), while greater superior RNFL thickness (per 10μm) was associated with higher odds of visual acuity recovery and maintenance (OR=1.13; 95% CI, 1.03-1.27; $Q=0.031$). The association between average RNFL thickness and visual field recovery and maintenance was marginally significant (OR=1.21; 95% CI, 1.06-1.39; $Q=0.053$). No significant associations were observed between OCT macular parameters and long-term visual function (all $Q>0.05$). Multivariable risk prediction models developed for long-term visual field and acuity recovery and maintenance, incorporating independent predictors, including age, pre-operative visual function and RNFL thickness, demonstrated C-statistics of 0.83 (95% CI, 0.72-0.94) and 0.69 (95% CI, 0.55-0.84), respectively in the validation sample (Table 5, Figure 2, and Supplementary Table S1).

DISCUSSION

The results of this study demonstrated that pre-operative RNFL thickness was associated with long-term visual function. Greater inferior RNFL thickness was associated with higher odds of visual field recovery and maintenance, while increased superior RNFL thickness was associated with higher odds of visual acuity recovery and maintenance. Multivariable risk prediction models were then developed, incorporating independent predictors for visual recovery and maintenance, including age, pre-operative visual function and RNFL thickness. The risk prediction model for visual field recovery and maintenance exhibited moderate discriminative ability, and may potentially assist with pre-operative prognostication and patient counselling.

In agreement with the findings reported in earlier studies,[3, 10, 17, 19-26] pre-operative RNFL thickness was associated with greater odds of visual recovery and maintenance following pituitary decompression in the current cohort. RNFL thickness provides an anatomical measurement of the structural integrity of the retinal ganglion cell axons.[2, 17, 30-36] Retrograde axonal degeneration resulting from chiasmal compression secondary to pituitary tumor enlargement can result in thinning of the RNFL, and might indicate decreased reserve for visual recovery following decompression surgery.[2, 17, 23, 26, 37-40] However, inferior RNFL thickness was a more robust predictor for visual field recovery and maintenance than average RNFL thickness in the current study, which contrasts with the findings of earlier studies.[3, 10, 17, 19-26] In addition, independent associations with visual acuity recovery and maintenance were limited to superior RNFL thickness in the current study. It is possible that the longer follow up period of 2 years in the current prospective longitudinal study, as well as the multivariable analysis adjusted for confounding pre-operative variables and multiple comparisons, might have contributed to this discrepancy. Nevertheless, our results might appear somewhat surprising, especially in the context of crossing nasal fibres of the optic chiasm arising predominantly from the nasal and temporal quadrants of the optic disc, while the maculopapillary bundle responsible for central visual acuity enters through the temporal sector.[2] However, diffuse thinning of the RNFL across all sectors have also been reported to occur with chiasmal compression, even among patients with strict bitemporal hemianopic field loss, and is thought to infer the presence of crossing fibres originating from the nasal hemiretina in all quadrants of the optic disc.[2, 23, 26, 38-40] Although a number of earlier studies have reported that RNFL thinning is more prominent in the temporal and nasal quadrants with chaismal compression,[2, 26, 38-41] it has also been hypothesised that the greater reduction in RNFL thickness in these quadrants can contribute to a more narrow range of measurements, which might compromise the discriminative ability to differentiate between patients exhibiting eventual visual recovery from those that do not.[3, 24] Inferior quadrant thickness has been previously identified as the strongest OCT RNFL predictor of visual field recovery in two smaller cohorts,[3, 24] and these trends are consistent with the findings reported in the current study.

The current study did not identify macular thickness and volume measurements to be independently associated with long-term visual field and visual acuity recovery and maintenance, in contrast to the findings of earlier studies.[22, 23, 28, 29, 42-45] It is possible that the contribution of non-retinal ganglion cell components, as well as the relatively more retrograde location of the macula,[2, 18] might partially explain the poorer overall discriminative ability of macular measurements in predicting long-term visual recovery and maintenance.

Advancing age was identified to be a negative predictor of long-term visual recovery and maintenance in both of the multivariable risk prediction models developed in the current study. These findings are consistent with a number of earlier studies,[6, 24, 46] as well as a recent meta-analysis which reported a weighted mean age difference of 12.32 years between patients exhibiting post-operative visual field improvement and those that did not.[5] It has been hypothesised that the lower neuronal density in the retina associated with ageing, as well as the decreased capacity for axonal remyelination, might contribute to a decreased reserve for visual recovery.[2, 47, 48]

The longer follow up period of two years in the current study was intended to investigate the potential for delayed long term visual recovery. Interestingly, post-hoc analysis of visual field mean deviation and pattern standard deviation demonstrated that improvements occurred during the first 6 weeks post-operatively, and no significant changes were observed between 6 weeks to 2 years. These findings would suggest that the majority of visual recovery occurs in the early post-operative phase during the first 6 weeks.

Overall, the multivariable risk prediction models developed in the current study, incorporating age, pre-operative visual function and RNFL thickness, demonstrated moderate discriminative abilities. The visual field recovery and maintenance prediction model demonstrated comparable discriminative ability with a previously developed nomogram which included MRI chiasmal compression grade but not age (C-statistics, 0.83 and 0.84, respectively).[3] However, the discriminative ability of the visual acuity recovery and maintenance prediction model developed in the current study was relatively more modest (C-statistic, 0.69), and further research investigating clinical and imaging prognostic factors for visual acuity recovery and maintenance following pituitary tumor resection is required.

This study has several limitations. The single-centre setting has the potential to introduce selection bias, and external validation of the risk prediction model in future studies is required. The unavailability of data on the duration of symptoms prior to surgery is acknowledged to be a study limitation. However, pituitary adenomas are a heterogeneous group of tumors, with variable clinical presentations that can be influenced by the presence of hormone secretion or mass effect, and even patients with the same histological tumour classification may present with different symptoms.[2] Moreover, pituitary tumors are often incidental findings.[2] Patients referred to our institution were usually tertiary referrals and therefore it was not possible to accurately determine the initial presentation or how long symptoms were present. Future studies are required to investigate whether the incorporation of symptom duration might further augment the prognostic performance of risk prediction models for long-term visual recovery and maintenance. In addition, craniopharyngiomas and astrocytomas were present in a small proportion of cases, while none of the patients presented with meningiomas. It remains unclear whether the study findings are generalizable to these rarer etiologies, and caution should be applied when applying the risk prediction models in the clinical setting. The Spectralis OCT device used in the current study does not segment the ganglion cell complex (GCC), which is acknowledged to be a study limitation. A number of earlier reports have suggested that GCC thickness might be more sensitive than RNFL measurements,[22, 23, 28, 29] and future studies are required to confirm the prognostic utility of OCT GCC measurements for long-term visual recovery following chiasmal decompression.

In conclusion, this prospective longitudinal study showed that pre-operative RNFL thickness was associated with two-year post-operative visual field and acuity recovery and maintenance following pituitary tumor resection. The multivariable risk prediction model developed for visual field recovery and maintenance demonstrated moderate discriminative ability, and might assist in providing tailored pre-operative prognostication and patient counselling.

ACKNOWLEDGEMENTS AND DISCLOSURES

A. Funding and support

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

B. Financial disclosures

The authors have no conflicts of interest to declare.

C. Other acknowledgements

None.

REFERENCES

1. Ostrom QT, Gittleman H, Truitt G, Boscia A, Kruchko C, Barnholtz-Sloan JS. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2011-2015. Neuro Oncol 2018;20:iv1-iv86.
2. Danesh-Meyer HV, Yoon JJ, Lawlor M, Savino PJ. Visual loss and recovery in chiasmal compression. Prog Retin Eye Res 2019;73:100765.
3. Lee J, Kim SW, Kim DW, et al. Predictive model for recovery of visual field after surgery of pituitary adenoma. J Neurooncol 2016;130:155-164.
4. Gnanalingham KK, Bhattacharjee S, Pennington R, Ng J, Mendoza N. The time course of visual field recovery following transphenoidal surgery for pituitary adenomas: predictive factors for a good outcome. J Neurol Neurosurg Psychiatry 2005;76:415-9.
5. Sun M, Zhang ZQ, Ma CY, Chen SH, Chen XJ. Predictive factors of visual function recovery after pituitary adenoma resection: a literature review and Meta-analysis. Int J Ophthalmol 2017;10:1742-1750.
6. Barzaghi LR, Medone M, Losa M, Bianchi S, Giovanelli M, Mortini P. Prognostic factors of visual field improvement after trans-sphenoidal approach for pituitary macroadenomas: review of the literature and analysis by quantitative method. Neurosurg Rev 2012;35:369-78; discussion 378-9.
7. Anik I, Anik Y, Cabuk B, et al. Visual Outcome of an Endoscopic Endonasal Transsphenoidal Approach in Pituitary Macroadenomas: Quantitative Assessment with Diffusion Tensor Imaging Early and Long-Term Results. World Neurosurg 2018;112:e691-e701.
8. Chohan MO, Levin AM, Singh R, et al. Three-dimensional volumetric measurements in defining endoscope-guided giant adenoma surgery outcomes. Pituitary 2016;19:311-21.
9. Dutta P, Gyurmey T, Bansal R, et al. Visual outcome in 2000 eyes following microscopic transsphenoidal surgery for pituitary adenomas: Protracted blindness should not be a deterrent. Neurol India 2016;64:1247-1253.
10. Yoneoka Y, Hatase T, Watanabe N, et al. Early morphological recovery of the optic chiasm is associated with excellent visual outcome in patients with compressive chiasmal syndrome caused by pituitary tumors. Neurol Res 2015;37:1-8.
11. Chabot JD, Chakraborty S, Imbarrato G, Dehdashti AR. Evaluation of Outcomes After Endoscopic Endonasal Surgery for Large and Giant Pituitary Macroadenoma: A Retrospective Review of 39 Consecutive Patients. World Neurosurg 2015;84:978-88.
12. Ho RW, Huang HM, Ho JT. The influence of pituitary adenoma size on vision and visual outcomes after trans-sphenoidal adenectomy: a report of 78 cases. J Korean Neurosurg Soc 2015;57:23-31.

13. Prieto R, Pascual JM, Barrios L. Optic chiasm distortions caused by craniopharyngiomas: clinical and magnetic resonance imaging correlation and influence on visual outcome. World Neurosurg 2015;83:500-29.
14. Yu FF, Chen LL, Su YH, Huo LH, Lin XX, Liao RD. Factors influencing improvement of visual field after trans-sphenoidal resection of pituitary macroadenomas: a retrospective cohort study. Int J Ophthalmol 2015;8:1224-8.
15. Jahangiri A, Lamborn KR, Blevins L, Kunwar S, Aghi MK. Factors associated with delay to pituitary adenoma diagnosis in patients with visual loss. J Neurosurg 2012;116:283-9.
16. Monteiro ML, Zambon BK, Cunha LP. Predictive factors for the development of visual loss in patients with pituitary macroadenomas and for visual recovery after optic pathway decompression. Can J Ophthalmol 2010;45:404-8.
17. Zhang J, Zhang S, Song Y, et al. Predictive value of preoperative retinal nerve fiber layer thickness for postoperative visual recovery in patients with chiasmal compression. Oncotarget 2017;8:59148-59155.
18. Raz N, Bick AS, Klistorner A, et al. Physiological Correlates and Predictors of Functional Recovery After Chiasmal Decompression. J Neuroophthalmol 2015;35:348-52.
19. Danesh-Meyer HV, Wong A, Papchenko T, et al. Optical coherence tomography predicts visual outcome for pituitary tumors. J Clin Neurosci 2015;22:1098-104.
20. Park HH, Oh MC, Kim EH, et al. Use of optical coherence tomography to predict visual outcome in parachiasmal meningioma. J Neurosurg 2015;123:1489-99.
21. Loo JL, Tian J, Miller NR, Subramanian PS. Use of optical coherence tomography in predicting post-treatment visual outcome in anterior visual pathway meningiomas. Br J Ophthalmol 2013;97:1455-8.
22. Moon CH, Hwang SC, Kim BT, Ohn YH, Park TK. Visual prognostic value of optical coherence tomography and photopic negative response in chiasmal compression. Invest Ophthalmol Vis Sci 2011;52:8527-33.
23. Moon CH, Hwang SC, Ohn YH, Park TK. The time course of visual field recovery and changes of retinal ganglion cells after optic chiasmal decompression. Invest Ophthalmol Vis Sci 2011;52:7966-73.
24. Jacob M, Raverot G, Jouanneau E, et al. Predicting visual outcome after treatment of pituitary adenomas with optical coherence tomography. Am J Ophthalmol 2009;147:64-70.e2.
25. Danesh-Meyer HV, Papchenko T, Savino PJ, Law A, Evans J, Gamble GD. In vivo retinal nerve fiber layer thickness measured by optical coherence tomography predicts visual recovery after surgery for parachiasmal tumors. Invest Ophthalmol Vis Sci 2008;49:1879-85.
26. Danesh-Meyer HV, Carroll SC, Foroozan R, et al. Relationship between retinal nerve fiber layer and visual field sensitivity as measured by optical

coherence tomography in chiasmal compression. Invest Ophthalmol Vis Sci 2006;47:4827-35.
27. Kerrison JB, Lynn MJ, Baer CA, Newman SA, Biousse V, Newman NJ. Stages of improvement in visual fields after pituitary tumor resection. Am J Ophthalmol 2000;130:813-20.
28. Tieger MG, Hedges TR, 3rd, Ho J, et al. Ganglion Cell Complex Loss in Chiasmal Compression by Brain Tumors. J Neuroophthalmol 2017;37:7-12.
29. Ohkubo S, Higashide T, Takeda H, Murotani E, Hayashi Y, Sugiyama K. Relationship between macular ganglion cell complex parameters and visual field parameters after tumor resection in chiasmal compression. Jpn J Ophthalmol 2012;56:68-75.
30. Costa-Cunha LV, Cunha LP, Malta RF, Monteiro ML. Comparison of Fourier-domain and time-domain optical coherence tomography in the detection of band atrophy of the optic nerve. Am J Ophthalmol 2009;147:56-63.e2.
31. de Araujo RB, Oyamada MK, Zacharias LC, Cunha LP, Preti RC, Monteiro MLR. Morphological and Functional Inner and Outer Retinal Layer Abnormalities in Eyes with Permanent Temporal Hemianopia from Chiasmal Compression. Frontiers in neurology 2017;8:619.
32. Monteiro ML, Moura FC. Comparison of the GDx VCC scanning laser polarimeter and the stratus optical coherence tomograph in the detection of band atrophy of the optic nerve. Eye (London, England) 2008;22:641-8.
33. Monteiro ML, Cunha LP, Vessani RM. Comparison of retinal nerve fiber layer measurements using Stratus OCT fast and regular scan protocols in eyes with band atrophy of the optic nerve and normal controls. Arquivos brasileiros de oftalmologia 2008;71:534-9.
34. Monteiro ML, Cunha LP, Costa-Cunha LV, Maia OO, Jr., Oyamada MK. Relationship between optical coherence tomography, pattern electroretinogram and automated perimetry in eyes with temporal hemianopia from chiasmal compression. Invest Ophthalmol Vis Sci 2009;50:3535-41.
35. Monteiro ML, Hokazono K, Cunha LP, Oyamada MK. Correlation between multifocal pattern electroretinography and Fourier-domain OCT in eyes with temporal hemianopia from chiasmal compression. Graefe's archive for clinical and experimental ophthalmology = Albrecht von Graefes Archiv fur klinische und experimentelle Ophthalmologie 2013;251:903-15.
36. Sousa RM, Oyamada MK, Cunha LP, Monteiro MLR. Multifocal Visual Evoked Potential in Eyes With Temporal Hemianopia From Chiasmal Compression: Correlation With Standard Automated Perimetry and OCT Findings. Invest Ophthalmol Vis Sci 2017;58:4436-4449.
37. Zhang X, Sun P, Wang J, Wang Q, Song SK. Diffusion tensor imaging detects retinal ganglion cell axon damage in the mouse model of optic nerve crush. Invest Ophthalmol Vis Sci 2011;52:7001-6.
38. Kanamori A, Nakamura M, Matsui N, et al. Optical coherence tomography detects characteristic retinal nerve fiber layer thickness corresponding to band atrophy of the optic discs. Ophthalmology 2004;111:2278-83.

39. Monteiro ML, Leal BC, Rosa AA, Bronstein MD. Optical coherence tomography analysis of axonal loss in band atrophy of the optic nerve. Br J Ophthalmol 2004;88:896-9.
40. Monteiro ML, Medeiros FA, Ostroscki MR. Quantitative analysis of axonal loss in band atrophy of the optic nerve using scanning laser polarimetry. Br J Ophthalmol 2003;87:32-7.
41. Leal BC, Moura FC, Monteiro ML. Retinal nerve fiber layer loss documented by Stratus OCT in patients with pituitary adenoma: case report. Arquivos brasileiros de oftalmologia 2006;69:251-4.
42. Moura FC, Medeiros FA, Monteiro ML. Evaluation of macular thickness measurements for detection of band atrophy of the optic nerve using optical coherence tomography. Ophthalmology 2007;114:175-81.
43. Monteiro ML, Hokazono K, Fernandes DB, et al. Evaluation of inner retinal layers in eyes with temporal hemianopic visual loss from chiasmal compression using optical coherence tomography. Invest Ophthalmol Vis Sci 2014;55:3328-36.
44. Monteiro ML, Costa-Cunha LV, Cunha LP, Malta RF. Correlation between macular and retinal nerve fibre layer Fourier-domain OCT measurements and visual field loss in chiasmal compression. Eye (London, England) 2010;24:1382-90.
45. Moura FC, Costa-Cunha LV, Malta RF, Monteiro ML. Relationship between visual field sensitivity loss and quadrantic macular thickness measured with Stratus-Optical coherence tomography in patients with chiasmal syndrome. Arquivos brasileiros de oftalmologia 2010;73:409-13.
46. Rivoal O, Brezin AP, Feldman-Billard S, Luton JP. Goldmann perimetry in acromegaly: a survey of 307 cases from 1951 through 1996. Ophthalmology 2000;107:991-7.
47. Franklin RJ, Zhao C, Sim FJ. Ageing and CNS remyelination. Neuroreport 2002;13:923-8.
48. Wei Y, Jiang H, Shi Y, et al. Age-Related Alterations in the Retinal Microvasculature, Microcirculation, and Microstructure. Invest Ophthalmol Vis Sci 2017;58:3804-3817.

FIGURE CAPTIONS

Figure 1: Visual field (a) mean deviation and (b) pattern standard deviation during the study period. Points represent the mean visual field measurements, and error bars represent the standard deviation.

Figure 2: Receiver operating characteristic curves for the discriminative performance of the multivariable risk prediction models developed for long-term visual field and acuity recovery and maintenance.

SUPPLEMENTAL MATERIAL

Supplementary Table S1: Multivariable risk prediction calculator developed for long-term visual field and acuity recovery and maintenance. The white boxes allow for pre-operative parameters to be entered into the risk prediction calculator, and the yellow boxes contain formulas which will auto-populate with the percentage outcome predictions.

Table 1: Demographic and clinical characteristics of patients.

Characteristic	Value
Age (years)	52±16
Male sex	129 (54%)
Pituitary tumor classification	
Pituitary adenoma	216 (90%)
Rathke's cleft cyst	10 (4%)
Craniopharyngioma	7 (3%)
Astrocytoma	2 (0.8%)
Epidermoid cyst	1 (0.4%)
Metastatic undifferentiated carcinoma	1 (0.4%)
Solitary fibrous tumor	1 (0.4%)
Teratoma	1 (0.4%)
Surgical approach	
Trans-sphenoidal	232 (97%)
Craniotomy	7 (3%)

Data is presented as mean ± SD, or number of participants (% of participants).

Table 2: Visual function and optical coherence tomography (OCT) parameters of patients during the study period.

Parameter	Pre-operative	Post-operative			Q-value [a]
	Baseline	6-week	6-month	2-year	
Visual fields (dB)					
Mean deviation	-5.0±6.5	-3.0±4.8	-2.4±4.8	-2.3±5.0	<0.001
Pattern standard deviation	5.2±4.6	3.7±3.5	3.4±3.5	3.4±3.5	<0.001
Best-corrected logMAR visual acuity	0.087±0.267	0.081±0.306	0.080±0.356	0.078±0.325	0.929
RNFL thickness (μm)					
Average	93±21	90±20	90±21	88±19	0.103
Superior	113±27	112±26	111±29	109±26	0.322
Inferior	121±25	118±24	118±27	116±24	0.103
Temporal	65±23	62±17	62±20	62±18	0.322
Nasal	71±31	67±32	67±33	66±27	0.322
Macular thickness (μm)					
Average	286±35	287±33	287±34	283±35	0.376
Foveal	216±40	219±37	216±38	213±41	0.376
Superior	287±35	288±36	284±35	283±37	0.322
Inferior	284±35	286±32	287±32	282±33	0.376
Temporal	277±37	281±34	280±33	276±35	0.322
Nasal	294±37	294±36	296±35	292±37	0.554
Macular volume (mm^3)					
Total	7.61±0.89	7.65±0.88	7.66±0.86	7.56±0.89	0.376
Foveal	0.19±0.04	0.20±0.03	0.20±0.05	0.19±0.04	0.554
Superior	1.91±0.23	1.91±0.25	1.92±0.23	1.89±0.24	0.376
Inferior	1.88±0.22	1.89±0.21	1.89±0.21	1.87±0.22	0.322
Temporal	1.84±0.25	1.86±0.26	1.86±0.27	1.83±0.25	0.376
Nasal	1.98±0.23	1.99±0.22	1.99±0.22	1.97±0.24	0.554

LogMAR = logarithm of the minimum angle of resolution; RNFL = retinal nerve fibre layer.

Data is presented as mean ± SD.

[a] One-way repeated measures analysis of variance (ANOVA) testing.

Table 3: Post-hoc pairwise comparisons of visual function parameters of patients during the study period.

Parameter	Comparison	Q-value [a]
Visual field mean deviation	Baseline versus 6-week	**<0.001**
	6-week versus 6-month	0.247
	6-month versus 2-year	0.751
	Baseline versus 2-year	**<0.001**
Visual field pattern standard deviation	Baseline versus 6-week	**<0.001**
	6-week versus 6-month	0.504
	6-month versus 2-year	0.897
	Baseline versus 2-year	**<0.001**

[a] Post-hoc pairwise multiplicity-adjusted Tukey's test.

Table 4: Multiple logistic regression odds ratios for long-term visual recovery and maintenance by optical coherence tomography (OCT) parameters.

Parameter	2-year visual field recovery and maintenance [a]		2-year visual acuity recovery and maintenance [b]	
	OR (95% CI)	**Q-value**	**OR (95% CI)**	**Q-value**
RNFL thickness (per 10μm)				
Average	1.21 (1.06-1.39)	0.053	1.11 (1.01-1.24)	0.512
Superior	1.12 (1.01-1.24)	0.167	**1.13 (1.03-1.27)**	**0.031**
Inferior	**1.26 (1.12-1.41)**	**<0.001**	1.05 (0.97-1.15)	0.512
Temporal	1.02 (0.92-1.14)	0.859	1.02 (0.93-1.12)	0.776
Nasal	1.14 (1.01-1.28)	0.167	1.07 (0.98-1.18)	0.512
Macular thickness (per 10μm)				
Average	0.98 (0.91-1.05)	0.859	0.99 (0.94-1.04)	0.776
Foveal	0.94 (0.88-1.00)	0.167	0.97 (0.92-1.02)	0.512
Superior	0.98 (0.92-1.06)	0.859	0.98 (0.93-1.04)	0.776
Inferior	0.97 (0.91-1.06)	0.859	0.99 (0.92-1.04)	0.776
Temporal	0.97 (0.91-1.05)	0.859	1.00 (0.97-1.03)	0.776
Nasal	0.98 (0.93-1.04)	0.859	0.98 (0.93-1.04)	0.776
Macular volume (per 0.1mm^3)				
Total	1.00 (0.98-1.02)	0.943	0.99 (0.98-1.01)	0.512
Foveal	0.65 (0.35-1.21)	0.512	0.86 (0.55-1.33)	0.776
Superior	1.00 (0.91-1.09)	0.943	0.98 (0.90-1.07)	0.776
Inferior	1.01 (0.96-1.07)	0.859	0.94 (0.87-1.03)	0.512
Temporal	0.99 (0.90-1.09)	0.943	0.94 (0.86-1.03)	0.512
Nasal	1.00 (0.92-1.08)	0.943	0.98 (0.91-1.06)	0.917

OR = odds ratio; 95% CI = 95% confidence interval; RNFL = retinal nerve fibre layer.

[a] Generalised estimating equations (GEE) multivariable logistic regression analysis accounting for inter-eye correlation, and adjusted for confounding variables including age, sex, baseline mean deviation.
[b] Generalised estimating equations (GEE) multivariable logistic regression analysis accounting for inter-eye correlation, and adjusted for confounding variables including age, sex, baseline best-corrected visual acuity.

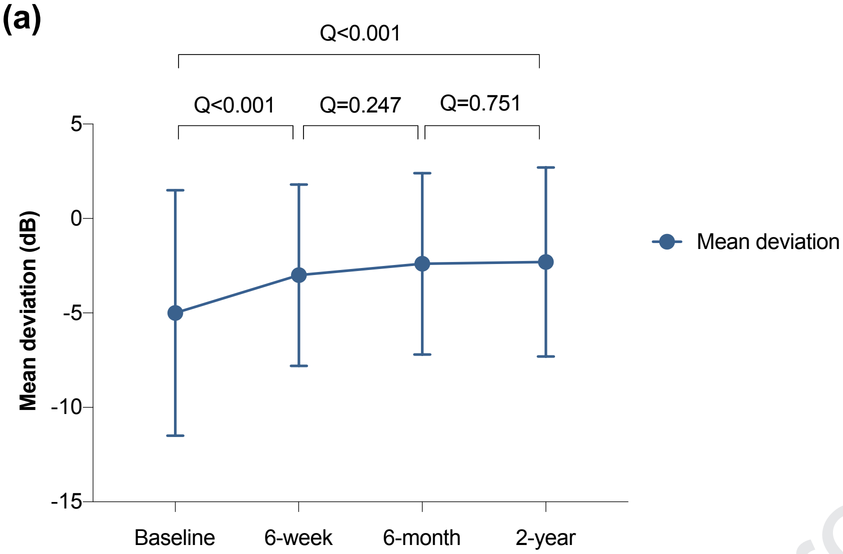
Table 5: Multiple logistic regression modelling for long-term visual recovery and maintenance prognostication.

	2-year visual field recovery and maintenance [a]		**2-year visual acuity recovery and maintenance** [a]	
	OR (95% CI)	**p-value**	**OR (95% CI)**	**p-value**
Parameter				
Age (per 10 years)	0.85 (0.72-0.99)	0.043	0.83 (0.71-0.98)	0.026
Baseline visual field mean deviation (per dB)	1.15 (1.07-1.24)	<0.001	-	-
Baseline best-corrected visual acuity (per 0.1 logMAR unit)	-	-	0.89 (0.82-0.96)	0.007
Superior RNFL thickness (per 10μm)	-	-	1.16 (1.03-1.33)	0.034
Inferior RNFL thickness (per 10μm)	1.22 (1.06-1.52)	0.001	-	-
Model summary [b]				
Risk prediction equation	Log odds = -0.173 - (0.016 × age) + (0.129 × mean deviation) + (0.020 × inferior RNFL thickness)		Log odds = 0.467 - (0.018 × age) - (1.191 × logMAR visual acuity) + (0.014 × superior RNFL thickness)	
C-statistic (95% CI)	0.83 (0.72-0.94)		0.69 (0.55-0.84)	
Youden-optimal prognostic cut-off	>0.60		>0.70	
Sensitivity (95% CI)	85% (73%-92%)		74% (60%-85%)	
Specificity (95% CI)	67% (44%-84%)		58% (39%-76%)	
Positive predictive value (95% CI)	88% (79%-94%)		78% (68%-85%)	
Negative predictive value (95% CI)	60% (42%-75%)		54% (39%-68%)	
Positive likelihood ratio (95% CI)	2.55 (1.31-4.94)		1.79 (1.08-2.95)	
Negative likelihood ratio (95% CI)	0.23 (0.11-0.46)		0.44 (0.24-0.79)	

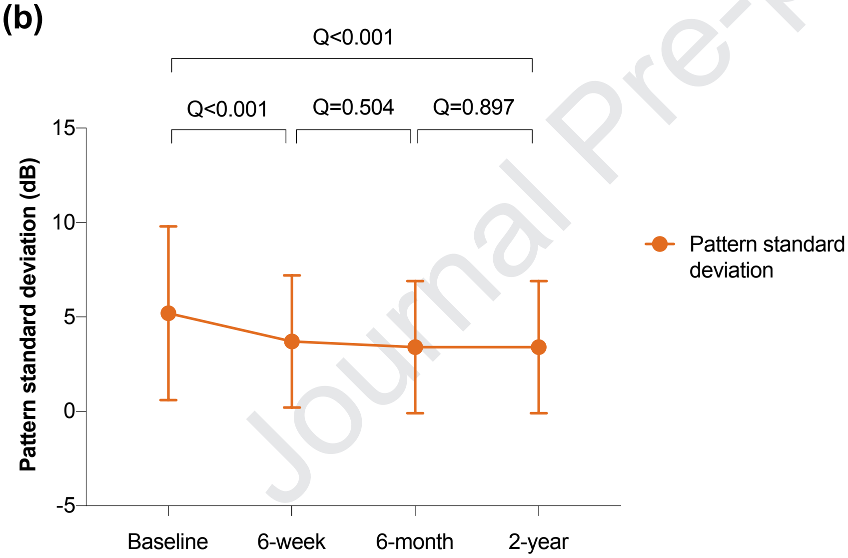
OR = odds ratio; 95% CI = 95% confidence interval; C-statistic = concordance statistic; logMAR = logarithm of the minimum angle of resolution; RNFL = retinal nerve fibre layer.

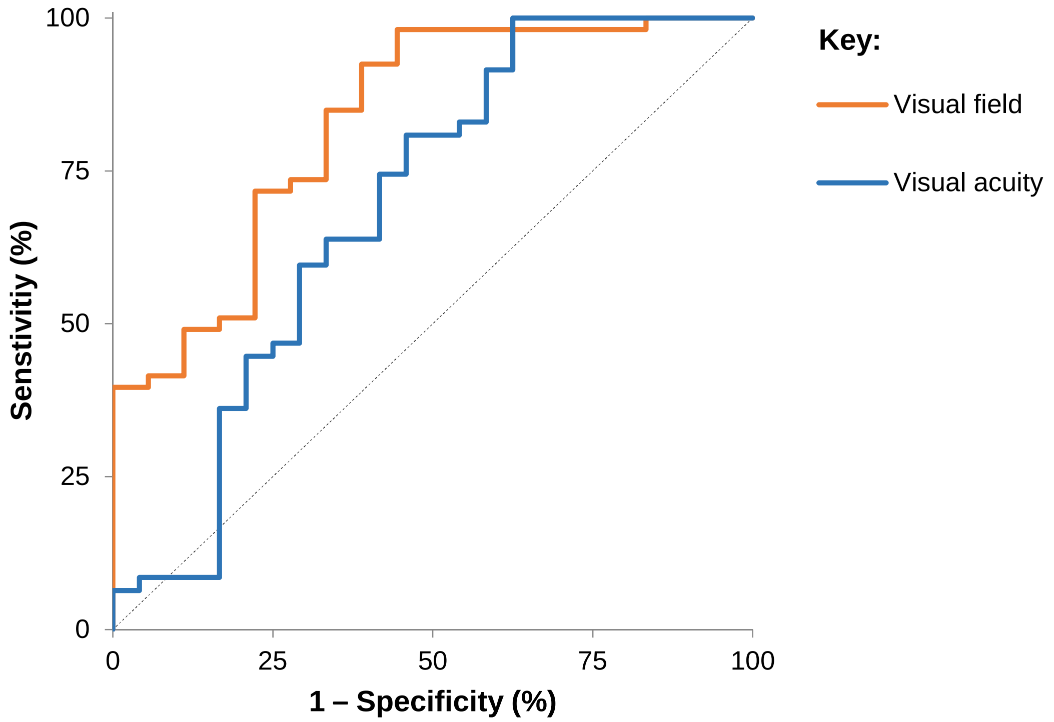
[a] Multivariable logistic regression analysis of developmental sample.
[b] Diagnostic accuracy values of risk prediction models in validation sample.

(a)


Q<0.001
Q<0.001
Q=0.247
Q=0.751
Mean deviation (dB)
5
0
-5
-10
-15
Baseline
6-week
6-month
2-year
Mean deviation

(b)


Q<0.001
Q<0.001
Q=0.504
Q=0.897
Pattern standard deviation (dB)
15
10
5
0
-5
Baseline
6-week
6-month
2-year
Pattern standard deviation


Senstivitiy (%)
100
75
50
25
0
0
25
50
75
100
1 – Specificity (%)
Key:
Visual field
Visual acuity

Biographical sketch

Michael T. M. Wang is a resident medical officer, neuro-ophthalmology research fellow, and final year PhD candidate at Auckland District Health Board and the University of Auckland, New Zealand. He received his medical degree from the University of Auckland in 2017, and has co-authored over 60 peer-reviewed publications in ophthalmology and internal medicine.

Biosketch: Helen Danesh-Meyer

Helen v Danesh-Meyer is the Sir William and Lady Stevenson Professor of Ophthalmology at the University of Auckland. She is also Head of Academic Neuro-ophthalmology and Glaucoma. She undertook both a Neuro-ophthalmology and Glaucoma Fellowship at Wills Eye Hospital in Philadelphia. She is also Director of the Optic Nerve Research Lab in Auckland, a translational research group focussed on neuroprotection strategiesShe has authored approximately 200 publications, numerous chapters and several textbooks. She has served as the international. She has served a the Neuro-ophthalmology International Consultant for the Basic and Clinical Science Course (BCSC) For the AAO. She is also Chair of Glaucoma NZ, a national charitable trust for the prevention of blindness from glaucoma.

TABLE OF CONTENTS STATEMENT

This two-year prospective cohort study of 239 patients investigated the association between optical coherence (OCT) parameters and long-term visual recovery following optic chiasm decompression surgery. Multiple logistic regression analysis demonstrated that increased inferior retinal nerve fibre layer (RNFL) thickness was associated with higher odds of long-term visual field recovery and maintenance. The multivariable risk prediction model developed in the current study may assist with pre-operative patient counselling and prognostication.