

# Correlation of optic neuritis and retinal nerve fibre thickness using optical coherence tomography in a cohort of multiple sclerosis patients



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## Dates:

Received: 14 Sept. 2015  
Accepted: 06 Feb. 2016  
Published: 23 June 2016

## How to cite this article:

Roos I, Budhoo R, Visser L, Bhigjee AI. Correlation of optic neuritis and retinal nerve fibre thickness using optical coherence tomography in a cohort of multiple sclerosis patients. *Afr Vision Eye Health*. 2016;75(1), a325. <http://dx.doi.org/10.4102/aveh.7511.325>

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**Background:** Optical coherence tomography (OCT) is a fast, non-invasive imaging technology that produces 3D, high-resolution images of the retina. Direct visualisation of the retina allows a unique opportunity to study the effects of multiple sclerosis (MS)-associated neurodegeneration on retinal ganglion cells as well as effects of retrobulbar demyelination on axonal and retinal architecture through measurement of retinal nerve fibre layer (RNFL) thickness and total macular volume (TMV). These findings are clinically important as axonal loss is irreversible and correlates with disability.

**Aim:** To determine the role and usefulness of OCT in a local cohort of MS patients.

**Setting:** Neurology Clinic, Inkosi Albert Luthuli Central Hospital, KwaZulu-Natal, South Africa

**Methods:** Nineteen patients with MS currently being treated with interferon  $\beta$ -1b underwent OCT examination of both eyes. RNFL thickness and macular volume were measured and correlated with clinical disease characteristics, history of optic neuritis and level of disability.

**Results:** Mean RNFL thickness was 77.3  $\mu$ m with no significant difference in mean RNFL in eyes with a history of optic neuritis (ON) and those without ( $p = 0.4$ ). Eyes with a history of ON did, however, have significantly thinner RNFL compared with the contralateral eye ( $p = 0.04$ ). Despite a strong correlation between TMV and RNFL ( $p = 0.001$ ), a subset of patients with normal RNFL had TMV that was less than 1% of what was expected. There was no correlation between RNFL and disability scores.

**Conclusion:** OCT enables a direct axonal 'optical biopsy', for monitoring disease progression and treatment response in MS. RNFL thinning occurs independently of a history of optic neuritis and may represent a chronic optic neuropathy in patients with MS.

## Introduction

Multiple sclerosis (MS) is a neuro-inflammatory disorder affecting young adults.<sup>1</sup> Any part of the central nervous system can be affected. However, most frequently affected areas are the optic nerves, pyramidal tracts, brainstem and spinal cord. The clinical presentation thus includes optic neuritis, ocular motor abnormalities, cerebellar dysfunction and partial myelopathy. The natural history of the disease in the majority of patients consists initially of relapsing and remitting episodes of acute neurological dysfunction and is referred to as relapsing remitting MS (RRMS).<sup>2</sup> About two-thirds of patients show gradually accumulating permanent deficits and enter the phase of secondary progressive MS (SPMS).

Traditionally, the pathology has focused on inflammation and demyelination. However, it has become increasingly clear that axonal degeneration occurs from an early stage.<sup>3</sup> MS disability is best correlated with axonal loss.<sup>4</sup> Attempts have been made to determine the degree of axonal loss and use this as a marker of disability and disability progression.<sup>5</sup>

Clinical scales used as a measure of disability include the Expanded Disability Status Scale (EDSS).<sup>6,7</sup> However, the EDSS measures mainly gait and is insensitive to minor but clinically important changes in disability, particularly at higher scores. Based on these shortcomings, the National MS Society's Clinical Outcomes Assessment Task Force developed an alternative scoring system, the Multiple Sclerosis Functional Composite Score (MSFCS).<sup>8</sup> This scoring system was developed based on pooled data obtained from natural history studies. Three areas are scored: leg function, based on the 25-ft walk test (25FWT); hand and arm function, based on the 9-Hole Peg Test (9 HPT); and cognition based on the Paced Serial Additions Test (PASAT).

Measuring brain atrophy on Magnetic Resonance Imaging (MRI) is another technique that may provide evidence of axonal and subsequently neuronal loss, which could be correlated with disability.<sup>9</sup> The presence of 'black holes' signify axonal loss.<sup>10,11</sup> Cerebral atrophy is a late finding, and therefore of little value, as the main aim of aggressive therapy is to avoid brain loss from occurring. Visual evoked responses (VERs) are another technique that may be used. The latency of the VER indicates demyelination while the amplitude is a measure of axonal integrity.<sup>12</sup> However, prolonged concentration required for a reliable result may be tedious for the patient.

Optical coherence tomography (OCT), first introduced in 1991,<sup>13</sup> is a non-invasive, relatively inexpensive, ocular imaging technique that produces cross-sectional or 3D images of the retina. It represents an 'optical biopsy'. OCT was originally used for primary retinal disorders. However, as the retina is an extension of the central nervous system, OCT can reflect changes that may occur in the brain in diseases such as MS. The retinal nerve fibre layer (RNFL), which is the innermost layer of the retina (Figure 1),<sup>14</sup> is composed of unmyelinated axons whose cell bodies lie in the retinal ganglion cell layer. Quantification of the RNFL provides a measure of axonal loss, which may be due to optic neuritis or a 'dying-back' phenomenon in the absence of optic neuritis, reflecting visual pathway disease in the brain.<sup>15</sup> OCT also allows for assessment of the total macular volume (TMV), which is a measure of neuronal integrity.

We undertook a cross-sectional study on a cohort of MS patients to determine the extent of RNFL loss and its correlation with optic neuritis, MRI changes and disability.

## Research methods and design

### Study design

This study was designed as a cross-sectional analysis of the RNFL and macular volume OCT findings in patients with MS.

### Setting

The study was performed in the Neurology Clinic at Inkosi Albert Luthuli Central Hospital (IALCH) in Durban, KwaZulu-Natal (KZN). This clinic, together with the one at Greys Hospital in Pietermaritzburg (90 km away) provides adult neurological service to the public sector in KZN and the northern part of the Eastern Cape (total adult population [over the age of 15] of 13.6 million.<sup>16</sup>)

### Study population and sampling strategy

All patients diagnosed with MS and being treated with IFN $\beta$ -1b between August 2013 and February 2014 were included in the study population. Minimum follow-up period of 6 months was required prior to inclusion in the study.

### Data collection

A retrospective chart analysis was performed to extract demographic data, clinical presentations (including history of optic neuritis), timing of diagnosis and treatment, assessment

of disability at commencement of therapy and results of investigations performed to establish the diagnosis of MS according to the 2010 revised McDonald Criteria.<sup>17</sup>

Each patient was assessed during a routine follow-up clinic appointment at the Neurology Clinic, IALCH between July 2013 and February 2014.

EDSS scoring was performed by a Neurostatus-certified examiner to rate the current degree of MS-related disability and compare this to disability present at commencement of IFN $\beta$ -1b therapy. The MS Severity Score was calculated with the use of the international online MSBase Registry<sup>18,19</sup> and the MS Curves tool in order to rank the severity of a patient's disability by the duration of disease. The Multiple Sclerosis Functional Composite Score (MSFCS) (consisting of the 25-ft walk test, 9 hole peg test and PASAT-3) was administered.<sup>8</sup> Disease subtype was categorised as remitting relapsing MS, primary progressive MS or secondary progressive MS.

Zeiss Cirrus third-generation time domain OCT with software version 4.5.1.11 was utilised to perform retinal imaging. Peripapillary RNFL analysis was obtained with the Optic Disc Cube 200 x 200 protocol. Data regarding average RNFL thickness, quadrants and 12 clock hours were obtained. Macular data were obtained using the Macular Cube 512 x 128 protocol. A trained technician, who ensured that fixation was reliable and signal strength was adequate, performed OCT scanning. Scans were excluded if signal strength was less than 7/10 or there was significant artefact present.

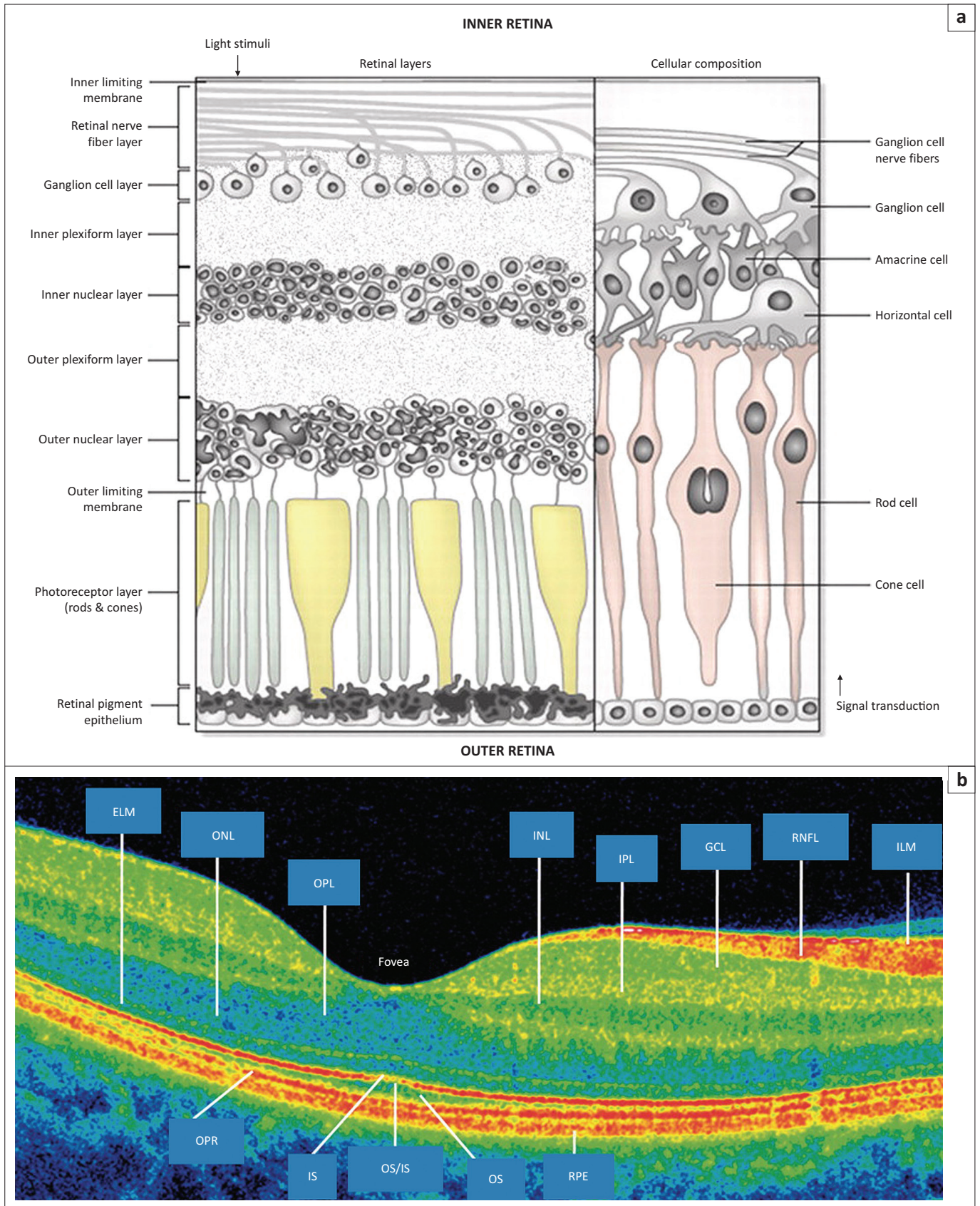
For each eye, RNFL and total macular volume values were matched with the inbuilt normative age and sex-matched computerised database. The internal database was developed with data from 284 individuals with an age range of 18–84 years.<sup>20</sup> Due to similar racial distribution in the cohort compared to the normative database, and an absence of any African patients, the normative database was felt to be applicable to our group. Measurements were then divided into the following categories: normal (5–95th percentile), below normal (< 5th percentile) and markedly below normal (< 1st percentile). The < 5th percentile and < 1st percentile groups were also collectively referred to as abnormal.

We used the model suggested by Petzold et al.<sup>15</sup> to evaluate the relationship between RNFL thickness and MS pathology on MRI where relevant (Figure 2). MRI scans performed as close to possible to the date of OCT were reviewed.

Patients were excluded for OCT analysis if there was a history of any other ophthalmologic disorder, diabetes, hypertension or a history of optic neuritis in the 3 months prior to assessment.

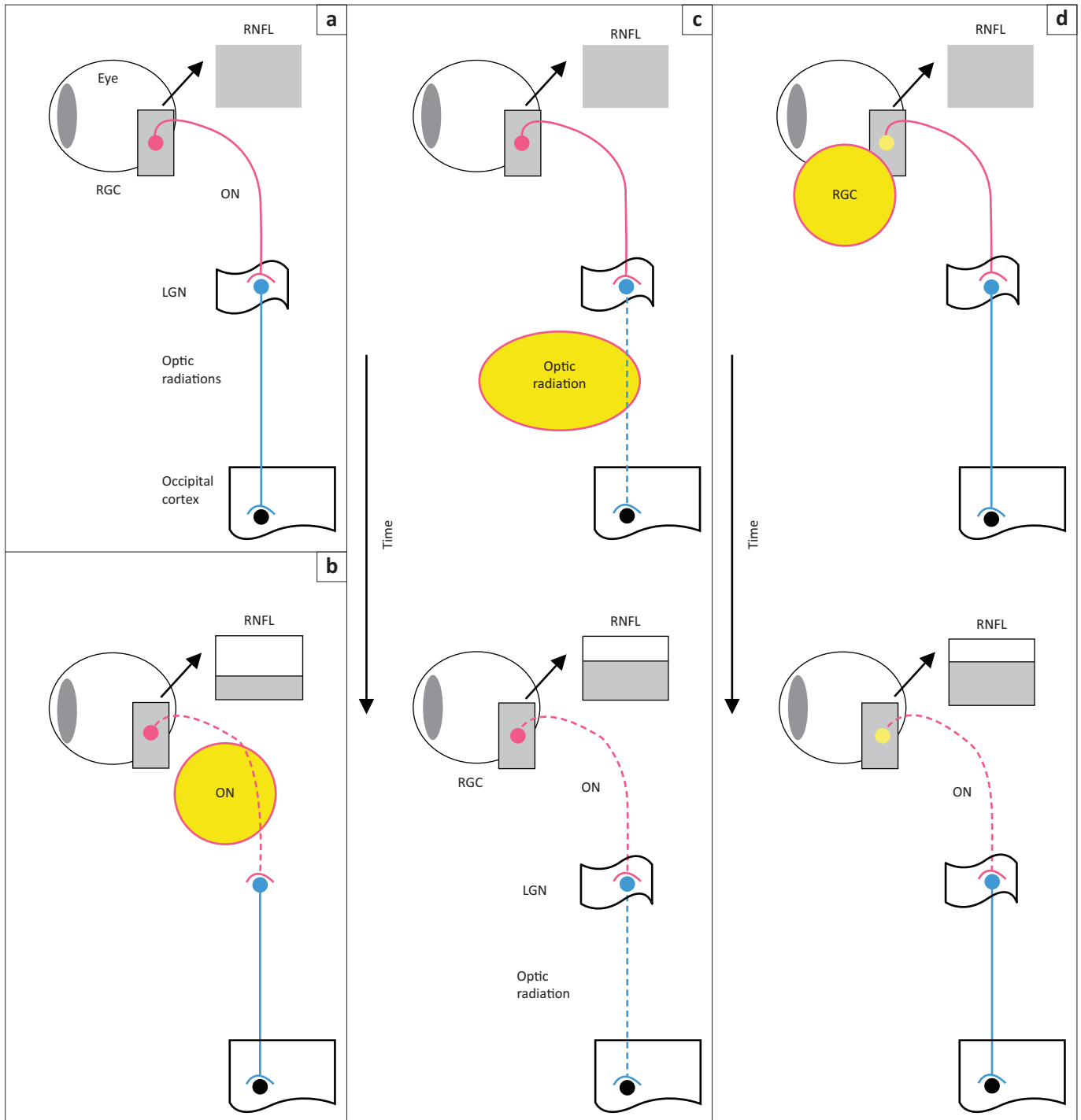
### Data analysis

Data was entered into a computer database using Microsoft Excel and imported on Statistical Package for Social Sciences (SPSS; version 22) for analysis. The data were analysed using descriptive statistics. The student *t*-test was used for continuous variables and the chi-square test for categorical variables.  $p < 0.05$  was considered statistically significant.



Source: Syc et al.<sup>14</sup> Reproduced by permission of Oxford University Press on behalf of the Guarantors of Brain. All rights reserved. For Permissions, please email: journals.permissions@oup.com  
 Note: Please note that the reflectivity of the ganglion cell layer and inner plexiform layer are very similar, which makes these layers almost indistinguishable from one another.  
 ELM, external limiting membrane; ILM, inner limiting membrane; INL, inner nuclear layer; IS, inner photoreceptor segments; IS/OS, IS/OS junction; ONL, outer nuclear layer; OPL, outer plexiform layer; OPR, outer photoreceptors; OS, outer photoreceptor segments; RPE, retinal pigment epithelium.

**FIGURE 1:** (a) Illustration of the retina. The optic nerve is formed by the fibres of the retinal nerve fibre layer which exit the retina at the optic disc. The nerve fibres of the retinal nerve fibre layer originate from the ganglion cells in the ganglion cell layer. (b) Cirrus HD-Optical coherence tomography B-scan. A false colour scheme is shown, which is generated by the differences between the retinal layers in tissue reflectivity.



Source: Reprinted from Petzold et al.,<sup>15</sup> with permission from Elsevier

Note that (c) and (d) both occur in the absence of optic neuritis.

RNFL, retinal nerve fibre layer; MS, multiple sclerosis; RGC, retinal ganglion cell; ON, optic nerve; LGN, lateral geniculate nucleus.

**FIGURE 2:** A model of the presumed relation between RNFL thickness and MS pathology: (a) A simplified sketch of the human visual pathway. RGCs send unmyelinated axons into the eye, where they form the RNFL (grey inlay), travel to the optic disc, and leave the orbit. Once the axons pass the sclera, they become myelinated and form the ON. After passing through the chiasma, where the temporal fibres cross (not shown), they are called the optic tract. The optic tract wraps around the midbrain and enters the LGN, where all these axons synapse. After the LGN, the axons fan out through the deep white matter (optic radiations) to reach the occipital cortex. (b) In MS, optic neuritis directly causes acute axonal loss in the ON (red dotted line), leading to thinning of the RNFL (small grey box). (c) MS lesions within the optic radiations (blue dotted line) do not immediately result in RNFL thinning. This outcome is thought to be a chronic consequence of trans-synaptic axonal loss through the LGN. With time, trans-synaptic axonal degeneration causes a smaller amount of axonal loss in the ON (red dashed line), with a quantifiable degree of RNFL loss (grey box). (d) Progressive loss of RGCs (yellow dot) is a probable result of chronic changes in the anterior visual pathways themselves in MS, and causes a small amount of RNFL loss (grey box).

## Ethical considerations

Ethical approval was granted by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (<http://www.doh.gov.za/nhrec/>) (NHREC REC 290408-009).

Written informed consent was obtained prior to participation in the study. The patient group was not required to attend any additional clinic visits as all investigations were done as a part of routine patient care. Participation in this study was voluntary.

## Results

Twenty-two patients with MS were identified for study inclusion. Three of these patients were excluded in the final study population: one patient declined study participation, one had transferred to care of a neurologist in private practice and another had stopped treatment with IFN $\beta$ -1b and discontinued follow-up. The group therefore consisted of 19 patients, with 38 eyes analysed. One patient did not meet adequate signal strength for RNFL measurements and was thus excluded. The final number thus consisted of 36 eyes analysed for RNFL thickness and 38 eyes for TMV.

The mean (SD) age of participants was 45.2 ( $\pm$ 13.7) years with a range of 18–78 years. Eighty-four per cent of patients were female (Table 1). Eleven patients (57.9%) were of Indian ethnicity, four (21.1%) were white British, three (15.8%) were white Dutch and one patient (5.3%) was of mixed ethnicity. Fifteen (78.9%) patients were of South African birth. The remaining four patients were born in Zimbabwe (three of white British and one of White Dutch descent). One patient had a positive family history for MS in her mother. Patients were diagnosed with MS at a mean age of 35 years with mean disease duration of 11.2 years at study inclusion (Table 1). The two patients aged more than 60 years had no vascular risk factors. Fourteen patients were in the secondary progressive phase of MS. Mean EDSS at study inclusion was 5.08 with a range from 0 to 8.5, mean MSSS was 78.5 and MSFCS was 2.2 (Table 2).

Mean RNFL thickness was 77.3  $\mu$ m ( $\pm$ 13.5). Nine patients (47.4%) reported a previous episode of optic neuritis (ON).

**TABLE 1:** Demographic data of patients with multiple sclerosis.

Demographic data	Variable	Data number	%
Age (years)	Mean (s.d.)	45.2 $\pm$ 13.7	-
	Median	43	-
	Range	18–78	-
Age groups	0–29	2	10.5
	30–39	5	26.3
	40–49	5	26.3
	50–59	5	26.3
	60–69†	1	5.3
	70–79†	1	5.3
Gender	Female	16	84.2
Ethnicity	Indian	11	57.9
	White British	4	21.1
	White Dutch	3	15.8
	Mixed ancestry	1	5.3
Country of birth	South Africa	15	78.9
	Zimbabwe	4	21.1
Family history of MS	Positive	1	5.3
Disease stage	Relapsing remitting MS (RRMS)	5	26.3
	Secondary progressive MS (SPMS)	14	73.7
Age at MS diagnosis (years)	Mean (s.d.)	35.8 $\pm$ 13.4	-
	Median	35	-
	Range	15–67	-
Duration of MS (years)	Mean (s.d.)	11.2 $\pm$ 7.9	-
	Median	8	-
	Range	4–30	-

†, No history of any vascular risk factors such as diabetes mellitus or hypertension.

There was no difference in mean RNFL in eyes with a history of ON (75.5  $\mu$ m  $\pm$ 12.9  $\mu$ m) and those without (79.1  $\mu$ m  $\pm$ 14.2  $\mu$ m) with a *p*-value of 0.4 (Table 3). Eyes with a history of ON did however have significantly thinner RNFL (70.1  $\mu$ m  $\pm$ 10.7  $\mu$ m) compared with the contralateral eye (79.5  $\mu$ m  $\pm$ 11.5  $\mu$ m) (*p* = 0.04) (Figure 3). There was no increase in the presence of a relative afferent pupillary defect (RAPD) in eyes with a history of ON (*p* = 0.9). VER abnormalities were also not more frequent in those with a reported history of ON. Patients with abnormal VER were however more likely to have a RAPD (*p* = 0.03).

Six of the fourteen patients with SPMS had a previous history of ON. Patients with SPMS had significantly thinner RNFL (74.8  $\mu$ m  $\pm$  13.9  $\mu$ m) compared to those with RRMS (83.9  $\mu$ m  $\pm$  10.1  $\mu$ m) (*p* = 0.04) (Table 3). There was, however, no correlation between disease duration and mean RNFL thickness or abnormally thinned RNFL. The temporal quadrant was most frequently and severely affected, being abnormally thinned in 17 eyes (47%), and less than 1% expected thickness in 16 (44%) eyes tested (Figures 3 and 4).

Mean TMV was 9.2 mm<sup>3</sup>  $\pm$  0.6 mm<sup>3</sup>. There was a strong correlation between TMV and RNFL (*p* = 0.001). There were, however, two patients with normal RNFL and TMV that was less than 1% than expected. Patients with SPMS had thinner TMV (9.01  $\pm$  0.5) than those with RRMS (9.5  $\pm$  0.5) (*p* = 0.04). There was, however, no relationship between disease duration and TMV (*p* = 0.09).

**TABLE 2:** Measures of disability in patients with multiple sclerosis.

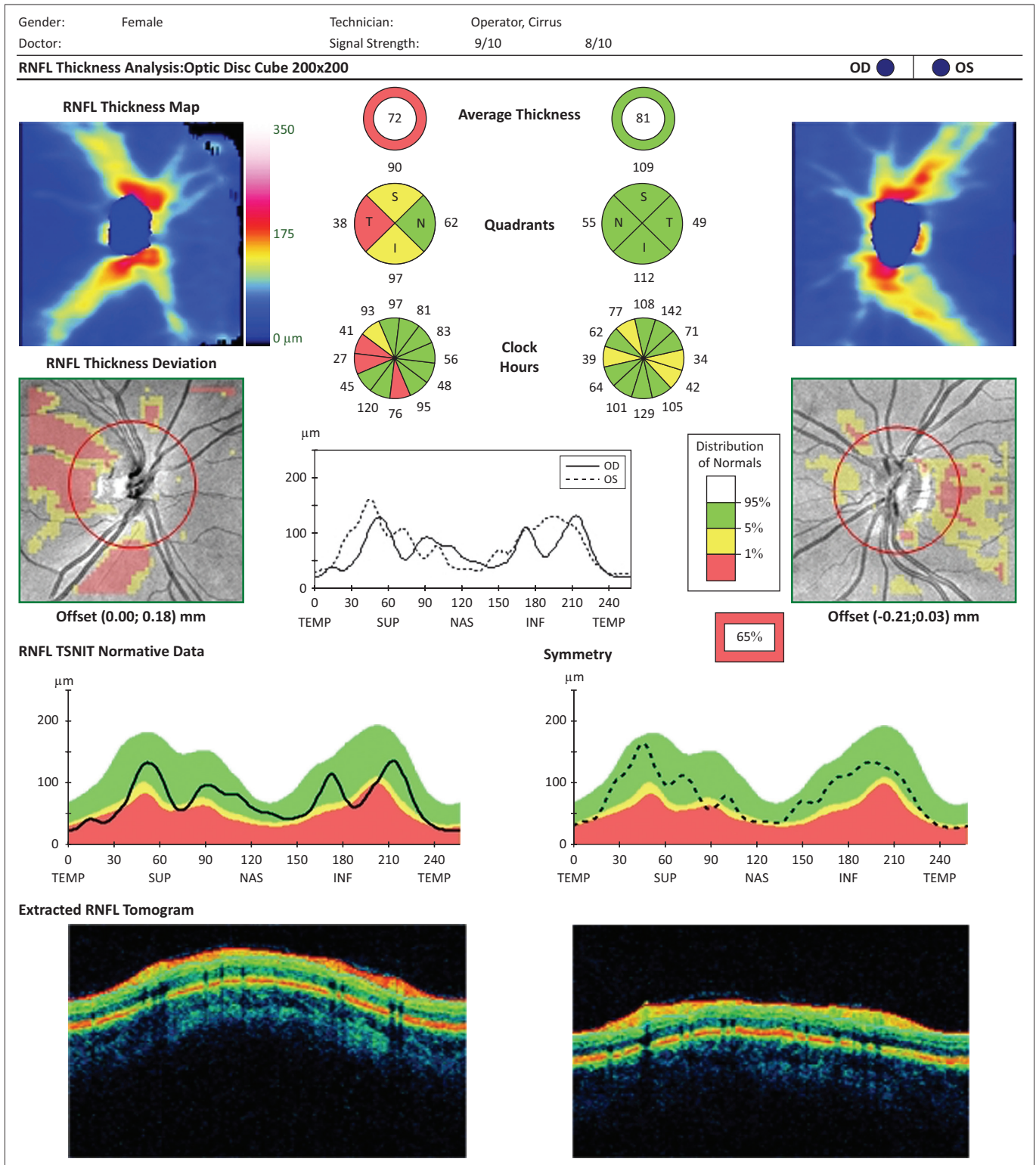
Description	Variable	Data number (%)
EDSS	Mean (s.d.)	5.08 $\pm$ 2.2
	Median	6
	Range	0–8.5
MSSS	Mean (s.d.)	78.5 $\pm$ 24.6
	Median	91
	Range	10–97
MSFCS	Mean (s.d.)	-2.2 $\pm$ 2.5
	Median	-1.17
	Range	-7.0–0.64

EDSS, expanded disability status score; MSSS, multiple sclerosis severity status score; MSFCS, multiple sclerosis functional composite score.

**TABLE 3:** Retinal nerve fibre layer thickness and changes with optic neuritis and disease stage as measured by optical coherence tomography in patients with multiple sclerosis.

Description	Variable	RNFL ( $\mu$ m)	<i>p</i> -value
RNFL – all eyes tested	Mean (s.d.)	77.3 $\pm$ 13.5	-
	Median	79	-
	Range	43–103	-
RNFL – eyes with previous ON	Mean (s.d.)	75.5 $\pm$ 12.9	-
RNFL – eyes without previous ON	Mean (s.d.)	79.1 $\pm$ 14.2	0.04
RNFL in eye with previous ON compared with contralateral eye	Affected eye	-	-
	Mean (s.d.)	70.1 $\pm$ 10.7	-
	Median	66	-
	Range	54–84	-
	Contralateral eye	-	0.04
	Mean (s.d.)	79.5 $\pm$ 11.5	-
	Median	78	-
	Range	64–103	-
Disease stage	RRMS	83.9 $\pm$ 10.1	0.04
	SPMS	74.8 $\pm$ 13.9	-

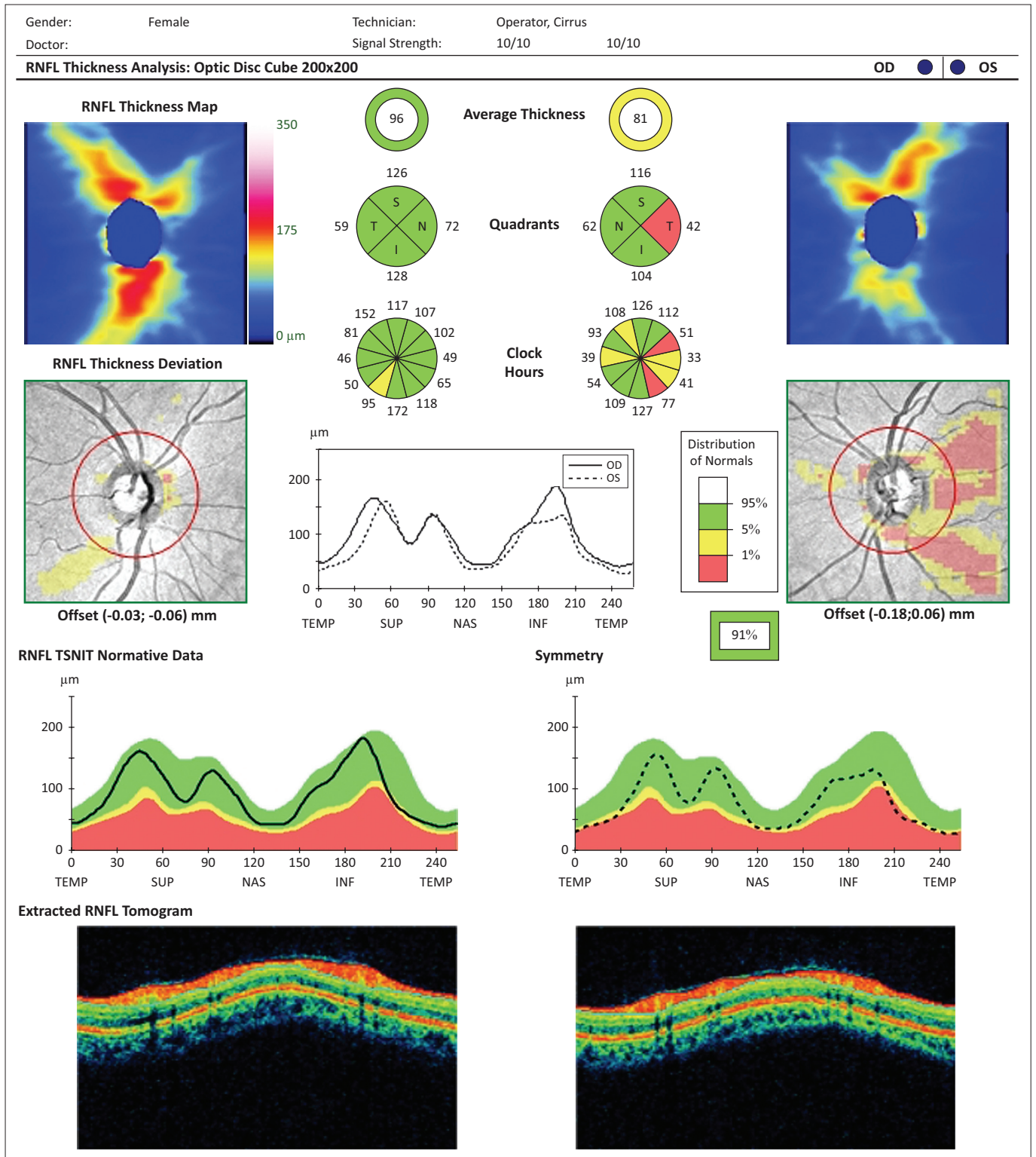
RNFL, retinal nerve fibre layer thickness; ON, optic neuritis; OCT, optical coherence tomography.



**FIGURE 3:** Optical coherence tomography findings in a patient with multiple sclerosis and a prior history of right-sided optic neuritis. The average retinal nerve fibre layer thickness in the left eye (OS) is represented in green (indicating a value within normal range), while the average RNFL thickness in the right eye (OD) is represented in red, indicating a reduced RNFL thickness (red denotes values < 1% of what would be expected when compared with a reference population). The temporal quadrant was the most severely affected, as indicated by the representation in red, followed by the superior and inferior quadrants represented in yellow (yellow denotes values between 1% and 5% of what would be expected when compared with a reference population).

On measures of disability, the RNFL did not correlate with EDSS ( $p = 0.14$ ), MSSS ( $p = 0.11$ ) or MSFCS ( $p = 0.17$ ). An abnormal RNFL did, however, predict lower scores on the 9HPT subcategory of the MSFCS ( $p = 0.02$ ) (Table 4). TMV did not correlate with EDSS or MSSS scores. TMV categorised as

abnormal was predictive for lower scores on the MSFCS ( $p = 0.02$ ) as well as the MSFCS subcategories of the 9HPT ( $p = 0.006$ ) and 25-ft walk test ( $p = 0.03$ ) (Table 5). Lower absolute TMV was predictive of lower scores on the PASAT ( $p = 0.021$ ) and 9HPT ( $p = 0.020$ ) subcategories of the MSFCS.



**FIGURE 4:** Optical coherence tomography findings in a patient with multiple sclerosis and no prior history of optic nerve. The average retinal nerve fibre layer thickness in the right eye (OD) is represented in green (indicating a value within normal range), while the average retinal nerve fibre layer thickness in the left eye (OS) is represented in yellow, indicating a reduced retinal nerve fibre layer thickness (yellow denotes values 1% – 5% of what would be expected when compared with a reference population). The temporal quadrant was the most severely affected, thereby contributing most to retinal nerve fibre layer thinning, as indicated by the representation in red, with all other quadrants being within normal range.

MRI brain findings on imaging performed on closest possible date to OCT scanning showed typical lesions supportive of the diagnosis of MS. Axial T2 FLAIR imaging showed the location of these lesions to include the chiasm, tracts and optic radiations.

## Discussion

Optic nerve and pathway are frequently affected in MS. As many as 70% of patients will develop acute optic neuritis during the course of the illness.<sup>21,22</sup> In a meta-analysis, Petzold

**TABLE 4:** Retinal nerve fibre layer thickness categories correlation with different measures of disability in patients with multiple sclerosis.

Description	Measure of significance	EDSS	MSSS	MSFCS	9HPT	25FWT	PASAT
Normal RNFL	<i>r</i>	-0.277	-0.69	0.130	-0.68	0.137	0.174
	<i>p</i>	0.26	0.81	0.67	0.79	0.59	0.49
	<i>r</i>	0.158	-0.290	0.241	0.521*	0.001	0.390
Abnormal RNFL	<i>p</i>	0.5	0.24	0.334	0.02	0.9	0.11

RNFL, retinal nerve fiber layer thickness; EDSS, expanded disability status score; MSSS, multiple sclerosis severity status score; MSFCS, multiple sclerosis functional composite score; 9HPT, 9 hole peg test; 25FWT, 25-ft walk test; PASAT, paced auditory serial addition test.

\*. Significant: *r*, correlation coefficient; *p*, *p*-value.

**TABLE 5:** Total macular volume correlation with measures of disability in patients with multiple sclerosis.

Description	Measure of significance	EDSS	MSSS	MSFCS	9HPT	25FWT	PASAT
Normal TMV	<i>r</i>	-0.175	-0.483	0.372	0.472	0.284	0.48
	<i>p</i>	0.5	0.5	0.1	0.06	0.2	0.05
	<i>r</i>	-0.229	-0.272	0.487*	0.571**	0.459*	0.033
Abnormal TMV	<i>p</i>	0.3	0.2	0.02	0.006	0.03	0.8

TMV, total macular volume; EDSS, expanded disability status score; MSSS, multiple sclerosis severity status score; MSFCS, multiple sclerosis functional composite score; 9HPT, 9 hole peg test; 25FWT, 25 foot walk test; PASAT, paced auditory serial addition test.

\*. Significant: *r*, correlation coefficient; *p*, *p*-value.

et al.<sup>15</sup> compared eyes with MS optic neuritis with eyes of healthy controls and noted a significant RNFL loss in affected eyes of approximately 20  $\mu\text{m}$ . In our series, 9 patients reported a previous episode of ON. The mean RNFL thickness in these eyes with ON was 75.5  $\mu\text{m} \pm 12.9 \mu\text{m}$ . We were careful not to include patients with acute ON as the swollen disc would have given an erroneous result.

Eyes with a history of ON had a significantly thinner RNFL (70.1  $\mu\text{m} \pm 10.7 \mu\text{m}$ ) compared with the contralateral eye (79.5  $\mu\text{m} \pm 11.5 \mu\text{m}$ ) ( $p < 0.04$ ). This finding is consistent with the meta-analysis by Petzold et al.<sup>15</sup> Thus in the individual patient, a significant difference of the RNFL between the two eyes would be indicative of a previous optic neuritis.

An intriguing observation is that in many MS patients there may be subclinical disease of the RNFL. Two possible mechanisms may account for this observation (Figure 2). Demyelination of the optic nerve may result in secondary axonal damage leading to a 'dying-back' phenomenon of the axons of RNFL and subsequent death and thinning of the retinal ganglion cell (RGC) layer. A similar mechanism may apply when there are MS lesions in the intra-parenchymatous parts of the visual system. In this case, there would be transsynaptic RGC degeneration. The loss of RGC may be detected by a decrease in the TMV on OCT. The presence of TMV loss in the absence of RNFL reduction is suggestive of primary neuronal pathology rather than a secondary transsynaptic or 'dying-back' disease. The macula is a good marker of neuronal integrity and architecture due to the 1:1 ratio of RGC to axons. Use of macular segmentation techniques in Spectral Domain-OCT has identified selective involvement of the ganglion cell or inner plexiform layers as well as the inner and outer nuclear layers in other studies.<sup>23,24</sup>

In those patients who did not have a history of ON but had significant RNFL thinning, we examined their MRI brain scans done closest to the OCT studies to see if they had any lesions in the parenchymal pathways. We noted that all patients had lesions that supported the diagnosis of MS, including lesions involving the optic tracts and radiations. MRI tractography studies would be useful in

further delineating the exact location of these lesions in the optic pathways.

Axonal loss is considered to be the most important factor in disability and disability progression.<sup>23,25</sup> We therefore attempted to correlate RNFL as a marker of axonal loss with clinical disability using the EDSS, MSSS and MSFCS. No correlation was found. This should not be surprising as these scales focus largely on motor function and patient mobility. The scales do therefore not fully assess the wide range of disability that MS patients have. However, the RNFL did predict lower scores on the 9HPT subcategory of the MSFCS. The TMV categorised as abnormal was predictive for lower scores on the MSFCS and its subcategories of the 9HPT and 25-ft walk test. This observation probably correlates with a late-stage illness and the fact that the majority of the patients were already cases of SPMS.

The limitations of our study include the small number of patients, the fact that both RRMS and SPMS patients were grouped together and that these patients were assessed at various stages of their illness. A prospective study utilising OCT at the time of MS diagnosis (and before the institution of disease modifying therapy) has been commenced.

## Conclusion

OCT enables a direct axonal 'optical biopsy' for monitoring disease progression and treatment response in MS. RNFL thinning occurs independently of a history of optic neuritis and may represent a chronic optic neuropathy in patients with MS.

## Acknowledgements

Thanks are due to the patients who agreed to participate in the study and also to Mr S Khedun who provided statistical advice and analysis.

## Competing interests

The authors declare that they have no financial or personal relationships which may have inappropriately influenced them in writing this article.



## Authors' contributions

I.R. was the project leader, performed the retrospective chart review, all clinical testing and patient assessments. A.I.B. provided supervision, assisted with study design and manuscript preparation. L.V. assisted with critical appraisal of the manuscript. R.B. performed OCT scanning.

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