

Macular thickness reduction in eyes with unilateral optic atrophy detected with optical coherence tomography

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Abstract

Aims To assess the changes in macular and peripapillary retinal nerve fibre layer (RNFL) thickness in eyes with unilateral optic atrophy and to evaluate the relationship between retinal thickness and visual function.

Methods Enrolled were 22 patients with unilateral optic atrophy. Macular thickness at the divided nine areas and peripapillary RNFL thickness in quadrant sections were measured by optical coherence tomography. Thickness values in the affected eyes were compared with those in the contralateral unaffected eyes. The correlation of foveal thickness with best-corrected visual acuity (BCVA) was evaluated. The correlation between retinal thickness and the remaining visual field area circumscribed with I-4-e isopter in superior and inferior hemifield was assessed.

Results Macular thinning was observed in all areas ($P < 0.001$ in each area) other than the fovea ($P = 0.068$). Peripapillary RNFL thickness decreased in all quadrant sections ($P < 0.001$ in each section). The affected to unaffected eye ratio of retinal thickness was more than 0.6 in each area. BCVA did not correlate with foveal thickness (correlation coefficient = 0.094, $P = 0.668$). Although not statistically significant ($P = 0.281$, superior hemifield; $P = 0.053$, inferior hemifield), there was a tendency that eyes with severe visual field loss show more marked retinal thinning.

Conclusions Macular thinning with the preserved foveal thickness is a hallmark of eyes with optic atrophy. Together with no correlation between foveal thickness and BCVA, this finding would help in

differential diagnosis of macular and optic nerve diseases.

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Introduction

Optic atrophy is a common end point finding of pathologies affecting the anterior visual pathway up to the lateral geniculate body and essentially reflects loss of retinal ganglion cell axons.¹ Axonal damage retrogradely degenerates ganglion cell body. Since the ganglion cells and retinal nerve fibre layer (RNFL) contribute to retinal thickness in the macula,² macular thickness is expected to be reduced to some degree in eyes with optic atrophy.

Optical coherence tomography (OCT) is an imaging device and confers both objective and quantitative information on macular and RNFL thickness with 10–15 μm vertical resolution.^{3,4} OCT has been mainly used for evaluating various types of retinal diseases, glaucoma, and optic nerve diseases.^{5–14} In eyes with macular disease such as occult macular dystrophy, and various types of macular oedema, foveal thickness have shown a correlation with visual acuity, and alterations of macular thickness have been adopted in assessing progress of disease.^{15–18} On the other hand, some studies remarked and demonstrated the decrease in peripapillary RNFL thickness in eyes with glaucoma, traumatic optic neuropathy, and compression optic neuropathy using OCT.^{9–14,19,20}

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Although it has been reported that peripapillary RNFL thickness represents the severity of visual field loss and would be of clinical use,^{14,21} little attention have been paid to the relationship between visual function and macular thickness in eyes with optic nerve disease. The purpose of the current study was to clarify the detailed characteristics of retinal damages in the macular regions due to optic nerve diseases. For this purpose, we evaluated the reduction of OCT-measured macular and peripapillary RNFL thickness in eyes with unilateral optic atrophy and assessed the relationship between retinal thickness and visual acuity or visual field.

Materials and methods

After obtaining written informed consent, 22 patients with unilateral optic atrophy were enrolled between June 2003 and December 2004. All participants underwent visual acuity test, Goldmann kinetic perimetry, stereoscopic slit-lamp examination for the macula and optic disc evaluations, and OCT. Patients were excluded from this study if they had severe opacification of optic media, previous and/or coexisting macular disease or glaucoma, or systemic diseases or drug intake that may affect the retinal or RNFL thickness.

This study was performed in accordance with the Tenets of Declaration of Helsinki and was approved by the ethical committee of Kobe University Graduate School of Medicine.

Best-corrected visual acuity (BCVA) was measured by standard Snellen visual acuity charts and converted to the logMAR scale in statistical analyses. In this conversion, visual acuities of hand motion and light perception were assigned to 20/2000 and 20/20 000 of the Snellen fraction, respectively.

Macular thickness and RNFL thickness around the optic disc were measured by OCT (OCT1, Zeiss-Humphrey, Dublin, California), as reported previously.^{13,22} In brief, retinal thickness was calculated using OCT retinal mapping software (version 6.1a), which measured thickness of nine divided macular regions (A0–A8) after six scans with 6 mm long under pupillary dilation and expressed as a colour-coded map. RNFL thickness was measured by 3.4-mm-diameter circle scans centred on the optic disc. RNFL thickness was obtained and averaged from the values of three scans in each quadrant section. Internal fixation was essentially selected due to better reproducibility, although external fixation was chosen in six subjects with severely impaired visual acuity, equal to or less than 20/200, in the affected eye. Defined area location in the OCT measurement is presented in Figure 1.

Analyses of the obtained data were carried out as follows. First, to verify whether ganglion cell loss in

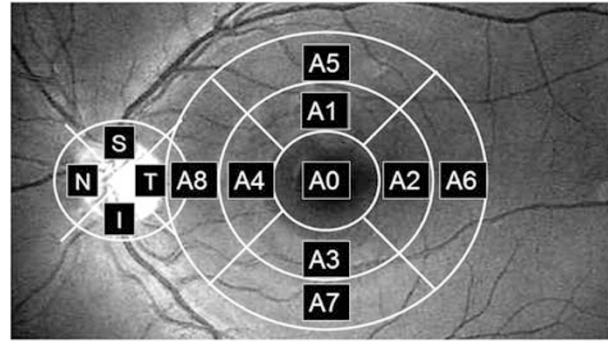


Figure 1 Defined area location in the analyses. The macula is divided into three concentric areas. A0 is the foveal region measuring 1.00 mm in diameter. The inner and outer rings are each divided into four quadrants (A1–A4 and A5–A8); the rings have diameters of 2.22 and 3.45 mm, respectively. A 3.4-mm-diameter circle centred on the optic disc is divided into four quadrant sections (S, superior; T, temporal; I, inferior; N, nasal).

optic atrophy affects macular thickness, comparison of macular thickness as well as peripapillary RNFL thickness between affected and unaffected eyes was performed. Next, to quantify the degree of decrease in macular thickness of eyes with optic atrophy, the ratio of retinal thickness in affected eyes relative to that in unaffected eyes was calculated in each area. Third, whether foveal thickness is responsible to visual acuity in eyes with optic atrophy was determined by assessing the relationship between logMAR BCVA and foveal thickness. Finally, we assessed the relationship between the degree of visual field loss and retinal thickness at the corresponding area. The degree of field loss was scored in superior and inferior hemifields as the remaining area circumscribed with I-4-e isopter within 15°, approximately comparable to the OCT-measured circle area with a diameter of 6 mm, that is, 0–25% ($n = 6$, superior hemifield; $n = 6$, inferior hemifield), 25–50% ($n = 1$, superior hemifield; $n = 2$, inferior hemifield), 50–75% ($n = 1$, superior hemifield; $n = 2$, inferior hemifield), and 75–100% ($n = 14$, superior hemifield; $n = 12$, inferior hemifield). Retinal thickness at the area corresponding to each hemifield was obtained.

Statistical analyses were performed using Stat View version 5.0 software (SAS Institute, Cary, NC, USA). Wilcoxon's signed-rank test was used to compare averages of parameters between affected and unaffected eyes. Association between foveal thickness and BCVA was evaluated by Spearman's analysis. Comparison of retinal thickness among eyes with various residual visual fields was assessed by Kruskal–Wallis test. *P*-value less than 0.05 was considered to be statistically significant.

Results

Of the 22 patients, 12 (54.5%) were female and 10 (45.5%) were male. The mean age and standard deviation (SD) was 56.3 (4.33) years, ranging 11–79, and the mean (SD) duration after the onset of optic neuropathy was 5.09 (4.26) years, ranging 1–14. Aetiology of optic neuropathy was unknown in seven cases (31.8%), ischaemia in six (27.3%), trauma in three (13.6%), retrobulbar optic neuritis in three (13.6%), and others in three (13.6%).

BCVA ranged from light perception to 20/20, and the mean (SD) logMAR-converted BCVA was 0.701 (1.177). The patterns of visual field defect were central or cecocentral scotoma in five eyes (22.7%), peripheral island in four eyes (18.2%), altitudinal hemianopia in four eyes (18.2%), quadrantic hemianopia in four eyes (18.2%), normal visual field in four eyes (18.2%), and temporal hemianopia in one eye (4.5%). Clinical characteristics of the participants are described in Table 1. In all subjects, unaffected fellow eyes had BCVA of 20/20 (0 logMAR unit) and unimpaired visual field.

Statistically significant decrease in RNFL thickness of the affected eyes was observed in all quadrantic sections ($P < 0.001$). Decrease in retinal thickness of the affected eye was significant in all areas except for A0, foveal area ($P < 0.001$; Table 2, Figures 2 and 3). Retinal thickness in the affected eyes was at least 60% of the value of that in

the unaffected fellow eyes (Table 3), whereas RNFL thickness reduction in some cases exceeded 90% of contralateral eyes. There was no significant correlation between logMAR BCVA and foveal thickness (correlation

Table 2 Mean values (SD) of macular or RNFL thickness (μm) in each segment for the 22 eyes with optic atrophy and 22 unaffected fellow eyes

	Optic atrophy (n = 22)	Fellow eye (n = 22)	P-value*
<i>RNFL quadrants</i>			
Superior	87.2 (42.9)	138.0 (28.8)	0.0001
Temporal	53.1 (35.0)	93.1 (25.1)	<0.0001
Inferior	87.2 (34.5)	140.6 (20.9)	<0.0001
Nasal	49.3 (32.1)	84.3 (36.0)	<0.0001
<i>Macular area</i>			
A0	192.7 (25.9)	205.9 (28.7)	0.0680
A1	225.4 (35.0)	260.5 (27.5)	0.0001
A2	217.1 (25.8)	244.2 (28.7)	0.0002
A3	224.4 (29.7)	261.5 (21.3)	<0.0001
A4	227.5 (39.0)	264.1 (26.7)	0.0005
A5	218.1 (35.6)	250.4 (24.2)	<0.0001
A6	209.4 (37.2)	228.1 (40.7)	0.0078
A7	209.6 (29.7)	240.3 (26.3)	0.0001
A8	223.5 (34.7)	260.0 (21.7)	<0.0001

*Wilcoxon's signed-rank test.

Table 1 Patient demographics

Case no.	Age (years)	Sex	Eye	Diagnosis	Duration (years)	Visual acuity	Visual field	Systemic disease
1	72	M	OD	ION	12	20/30	Altitudinal hemianopia	Hyperlipidaemia
2	65	F	OS	RON	12	LP	Peripheral island	
3	68	M	OD	ION	2	20/25	Quadrantic hemianopia	
4	66	F	OD	TON	14	20/30	Altitudinal hemianopia	
5	68	M	OS	CON	1	20/20	Normal	Brain infarction, DM, HT
6	57	M	OS	Papillitis	1	20/20	Normal	DM
7	42	F	OD	ION	1	20/100	Altitudinal hemianopia	HT
8	40	M	OS	OA	5	HM	Peripheral island	
9	67	M	OS	ION	5	20/20	Cecocentral scotoma	Tuberculosis, TAO
10	74	F	OD	RON	4	20/20	Normal	Hyperlipidaemia
11	11	M	OD	OA	4	20/20	Relative central scotoma	
12	42	M	OD	OA	5	20/20	Normal	
13	79	F	OS	OA	5	20/500	Central scotoma	HT
14	21	F	OS	Meningioma	5	20/20	Quadrantic hemianopia	
15	70	F	OD	OA	13	HM	Peripheral island	
16	66	F	OS	RON	3	20/25	Quadrantic hemianopia	Aplastic anaemia
17	19	F	OD	OA	1	20/20	Cecocentral scotoma	
18	66	F	OD	TON	5	20/20	Quadrantic hemianopia	HT
19	52	F	OS	OA	1	20/500	Temporal hemianopia	
20	68	F	OD	ION	1	20/200	Peripheral island	
21	51	M	OS	ION	1	20/20	Cecocentral scotoma	DM, HT
22	71	M	OD	TON	7	20/30	Altitudinal hemianopia	

F = female; M = male; OD = right eye; OS = left eye; ION = ischaemic optic neuropathy; RON = retrobulbar optic neuritis; TON = traumatic optic neuropathy; CON = compressive optic neuropathy; OA = optic atrophy of unknown origin; meningioma = parasellar meningioma; LP = light perception; HM = hand motion; HT = hypertension; DM = diabetes mellitus; TAO = thromboangiitis obliterans. Durations indicate the period from the onset of disease to OCT examination.

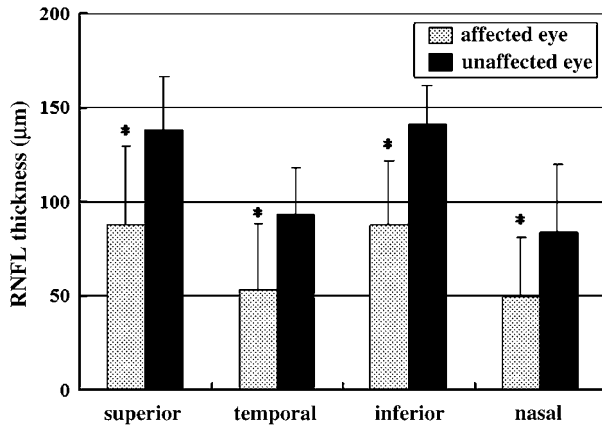


Figure 2 Comparison of peripapillary RNFL thickness in the 22 tested cases. Significant decrease in RNFL thickness is observed in the affected eyes compared with the fellow eyes (* $P < 0.001$, Wilcoxon's signed-rank test).

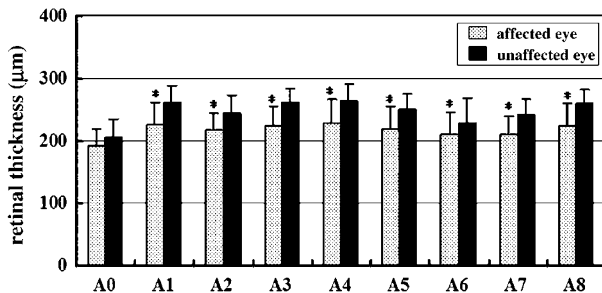


Figure 3 Comparison of macular thickness in the 22 tested cases. Decrease in retinal thickness of the affected eye is prominent in all but A0 areas (* $P < 0.001$, Wilcoxon's signed-rank test).

Table 3 Mean values (SD) of the affected to unaffected ratios of macular thickness in each area in eyes with unilateral optic atrophy ($n = 22$)

Area	Ratio	Range
A0	0.95 (0.12)	0.65–1.17
A1	0.87 (0.11)	0.70–1.08
A2	0.89 (0.09)	0.73–1.09
A3	0.86 (0.09)	0.67–1.01
A4	0.87 (0.14)	0.62–1.26
A5	0.87 (0.10)	0.68–1.08
A6	0.93 (0.25)	0.64–1.89
A7	0.87 (0.08)	0.78–1.15
A8	0.86 (0.09)	0.66–0.98

coefficient = 0.094, $P = 0.668$; Figure 4). Concerning the relationship between retinal thickness and the remaining visual field, there was a tendency that eyes with severe visual field loss have the higher degree of retinal thinning (Figure 5). Although the tendency did not reach statistical significance among the four visual field groups

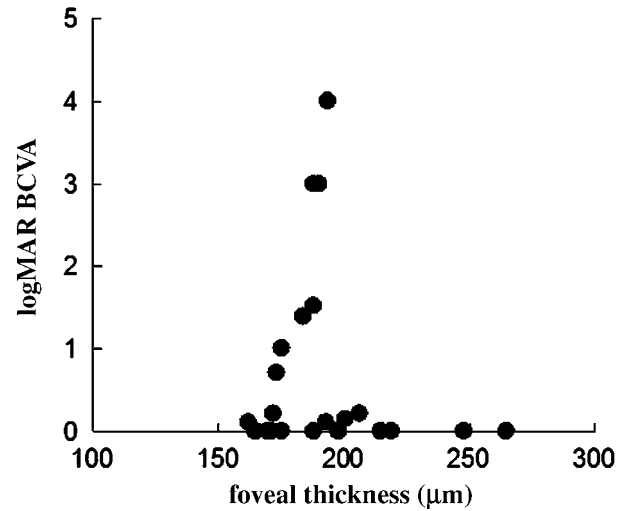


Figure 4 Relationship between foveal thickness (retinal thickness at A0) and logMAR BCVA in the 22 eyes with optic atrophy. No significant correlation was demonstrated (correlation coefficient = 0.094, $P = 0.668$, Spearman's analysis).

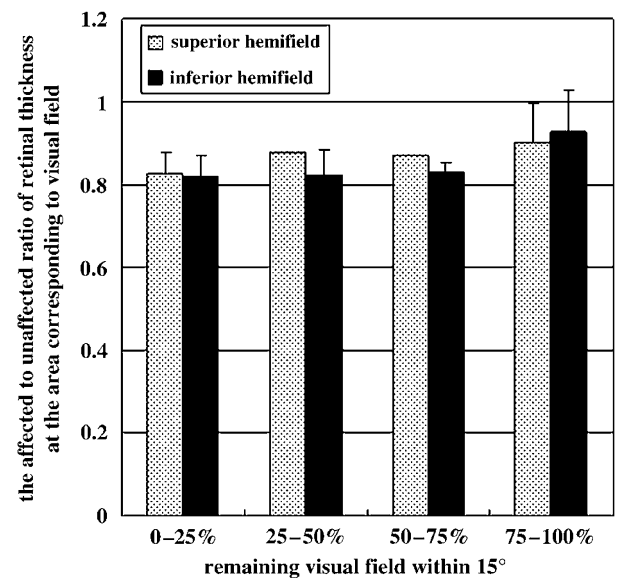


Figure 5 Relationship between the severity of visual field loss and retinal thickness at the corresponding area. The ratio of residual visual field within 15° was calculated by the area within I-4-e isopter in the superior and inferior hemifields. Note that there is a tendency that eyes with larger remaining visual field have greater retinal thickness.

($P = 0.281$, superior hemifield; $P = 0.053$, inferior hemifield, respectively), a notable relationship between retinal thickness and the residual visual field was observed when the eyes with equal or more than 50% remaining visual field was compared with those less than 50% in the inferior hemifield ($P = 0.017$, Mann-Whitney test).

Discussion

Previous studies demonstrated scanning laser polarimeter and OCT detected the progressive RNFL thickness reduction in eyes with traumatic optic neuropathy and that in glaucoma, respectively.^{9–13,19,20} Recently, we and Monteiro *et al* also reported that OCT could detect RNFL thickness reduction corresponding to band atrophy in eyes with compressive lesions at the chiasmal region.^{14,21} In this study, peripapillary RNFL thickness of optic atrophy showed global reduction in all quadrant sections consistent with previous reports on compressive optic neuropathy and traumatic optic neuropathy.^{14,19–21} Taken together, biometrical assessment of RNFL thickness with OCT reflects the loss of retinal ganglion cell axons in most cases of optic neuropathy.

The measurement of macular thickness in eyes with optic atrophy demonstrated overall decrease with the foveal thickness being unaffected. Given that RNFL is composed of neuroglia, astrocytes, and axons of ganglion cells, and fovea is devoid of ganglion cells,²³ it is reasonable that macular thickness at A0, the fovea, did not show significant reduction in eyes with optic atrophy. The ganglion cells and RNFL are reported to contribute to approximately 35% of the macular thickness.² Accordingly, if ganglion cell loss is the major cause for the macular thinning, macular thickness remains at least about 65% of controls. This notion was supported by the present finding that the mean macular thickness in eyes with optic atrophy exceeded 60% of that in unaffected eyes at each area. It has been known that some artefacts in measurement using OCT might have effects on calculated retinal thickness.²⁴ However, even taken that into consideration, it would be pertinent from the current data that the degree of retinal thinning is limited. It is noteworthy that even in optic atrophy, the end point status of optic nerve disease, more than 60% of retinal thickness is preserved, which could not be seen in eyes with severe macular disease. In this regard, simultaneous measurements of macular and peripapillary RNFL thickness are of clinical significance, since these may distinguish retinal disease without fundus abnormality, in which foveal thickness is reported to be reduced,^{15,25} from optic nerve disease and would be useful for the evaluation of macular disease combined with optic neuropathy.

It is known that foveal thickness in some macular diseases demonstrates fine correlation with visual acuity.^{16–20} From this point, it would be an important feature of optic nerve disease that foveal thickness in eyes with optic atrophy does not correlate with BCVA in our study, and be helpful in differential diagnosis. In addition, there was a tendency that an area with severe

visual field loss has more marked retinal thinning at the corresponding retinal area. Therefore, measurement of retinal thickness would be useful for the objective assessment of the severity of optic nerve disease.

It is necessary to keep in mind that one of the limitations of our study is the lack of longitudinal evaluation. Additional, large-scale prospective studies are necessary to find out the relationship between the progression of optic atrophy and macular thickness reduction. Another limitation is the small number of subjects. Essentially because of this, we performed the *intraindividual* comparisons regarding the macular and RNFL thinning in unilateral optic nerve diseases. In patients with systemic diseases such as diabetes and hypertension, macular thickness may be affected by these systemic conditions irrelevant to the primary ocular pathologies. This inevitably increases the SD of macular thickness measured. Thus, *interindividual* comparisons in a small number of patients were presumed to be difficult to assess the macular thinning in patients with bilateral optic atrophy as compared with independent control subjects.

In conclusion, in eyes with optic atrophy, both macular thickness and peripapillary RNFL thickness were reduced. Macular thickness in the affected eye remained more than 60% of that in the unaffected eye, and the decrease was not significant in the fovea. Significant correlation was not recognized between foveal thickness and visual acuity. There was a trend that the area of visual field loss corresponded to the retinal thinning area. The characteristic change of macular thickness in optic atrophy would be helpful for the differential diagnosis of retinal and optic nerve diseases.

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