Semi-automated Optical Coherence Tomography in Clinical Practice

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Background

- Recent reports suggest retinal and macular thickness is a biomarker of neurodegenerative disease progression within the eyes of patients with multiple sclerosis (MS) without optic neuritis (ON)
- Optical Coherence Tomography (OCT) can be a useful clinical measure obtained as part of regular clinical care for monitoring prognosis and disease activity
- Traditional OCT scanners require considerable technical skill to perform, and are not very portable
- We tested a compact, semi-automated OCT scanner for routine use within an MS center

Objectives

- Assess feasibility of a portable OCT device (Optovue iScan 500) as a tool for measuring retinal nerve fiber layer (RNFL) thickness, retinal (macular) thickness and volume, and ganglion cell complex (GCC) thickness in multiple sclerosis patients with and without self reported ON
- Assess the relationship of the Pelli-Robson contrast scores and thickness measures obtained from OCT

Methods

- Cross-sectional study of 89 MS patients (178 eyes) with and without prior self-reported history of optic neuritis
- RNFL thickness, macular thicknesses and volumes, and GCC thicknesses collected using the Spectral-Domain Optovue iScan 500 OCT scanner
  - 15 patients (30 eyes) excluded due to prior ophthalmologic conditions
  - 7 eyes excluded due to insufficient scan quality
  - 4 eyes excluded due to missing scans
- RNFL and Macular Volumes were available from 71 MS patients (137 eyes)
- GCC scans were introduced later within the protocol; pilot data was acquired for 23 patients (46 eyes)
  - 4 patients (8 eyes) excluded due to prior ophthalmologic conditions; 19 patients (38 eyes) analyzed
- Contrast sensitivity measured for each eye with a Pelli-Robson (PR) contrast chart
- Mean group differences in Pelli-Robson scores, average RNFL Thickness, average Inner GCC Thickness, and Macular Volume were assessed by ANOVA
- Correlations between OCT measurements and Pelli-Robson scores were analyzed using Spearman correlations

Table 1: Demographic summary statistics of Retinal Nerve Fiber Layer (RNFL) and Ganglion Cell Complex (GCC) eyes

	Age in years, mean ± SD (range)	Disease Duration in years, mean ± SD (range)	Female, n (%)	Ethnicity (Caucasian, African-American, Other), n (%)	Types of MS (RR/SP/PP/ Unknown), n (%)	Number of ON episodes: n = 0, n= 1, n > 1 1. Right Eye 2. Left Eye	ON History Classification: No ON/ON+/ON- 1. Right Eye 2. Left Eye
RNFL n = 71 (137 eyes)	48 ± 11 (23 - 74)	11 ± 9 (0.2 - 34)	49 (69%)	57/12/2 (80/17/3)	63/3/4/1 (89/4/6/1)	1. 50/14/4 2. 50/16/3	1. 41/18/9 2. 43/19/7
GCC n = 19 (38 eyes)	48 ± 10 (32 - 65)	13 ± 10 (0.6 - 34)	14 (74%)	15/2/2 (79/11/11)	16/1/2/0 (84/5/11/0)	1. 15/3/1 2. 12/6/1	1. 12/4/3 2. 12/7/0

Figure 1: Optovue OCT iScan 500

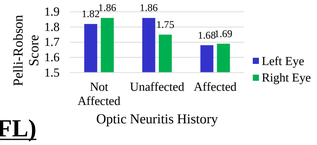
Results

Tables 2, 3, & 4: Means and Standard Deviations of Group differences between MS Patients' Affected Eyes of Pelli Robson scores, RNFL & GCC stratified by prior ON history

	No ON	ON-	ON+	Sig
Pelli-Robson	1.84 ± 0.20	1.80 ± 0.21	1.68 ± 0.24	**0.001**[a]
RNFL (µm)	92.6 ± 10.6	91.8 ± 5.8	78.4 ± 15.6	**<0.001**[a], **<0.01**[b]
GCC (µm)	87.7 ± 9.2	81.1 ± 7.4	77.2 ± 9.1	**<0.01**[a]

Mean differences evaluated using one-way ANOVA between Not Affected (No ON), Unaffected (ON-), and Affected (ON+) eyes of MS patients
Bold values indicate statistically significant differences by post-hoc analysis with Bonferroni correction.
a = Significant mean difference between No ON and ON+; b = Significant mean difference between ON- and ON+

Figure 2: Bar graph of mean Pelli-Robson score broken down by Optic Neuritis History and Eye



Retinal Nerve Fiber Layer (RNFL)

Figure 3: RNFL Thickness stratified by prior ON history and quadrant

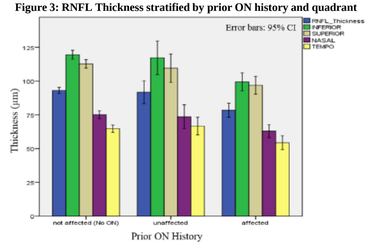
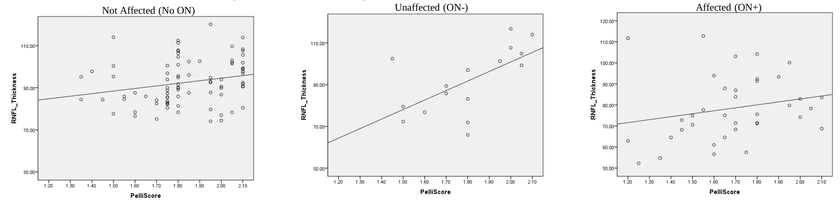


Table 5: Spearman's Correlations between RNFL Thickness and Pelli-Robson score

Subgroups	N	Spearman's Correlations
All Eyes (Patients)	137 (71)	**ρ = 0.38****
Not Affected Eyes (No ON)	84	**ρ = 0.33****
Unaffected Eyes (ON-) • Inferior • Superior • Temporal	16	**ρ = 0.59*** **ρ = 0.55*** **ρ = 0.52*** **ρ = 0.54***
Affected Eyes (ON+) • Inferior • Nasal	37	**ρ = 0.33*** **ρ = 0.42**** **ρ = 0.38***

Non-significant correlations not reported.
** Correlation is significant at the 0.01 level (2-tailed)
* Correlation is significant at the 0.05 level (2-tailed)

Figure 4: Correlation scatter plots between Pelli-Robson score and RNFL Thickness



Ganglion Cell Complex (GCC)

Table 6: Spearman's Correlations between GCC Thickness and Pelli-Robson score

Subgroups	N	Spearman's Correlations
All Eyes (Patients)	38 (19)	**ρ = 0.47****
Not Affected Eyes (No ON)	24	ρ = 0.31
Unaffected Eyes (ON-)	3	ρ = 0.87
Affected Eyes (ON+)	11	ρ = 0.51

** Correlation is significant at the 0.01 level (2-tailed)

Figure 5: RNFL Thickness stratified by prior ON history and quadrant

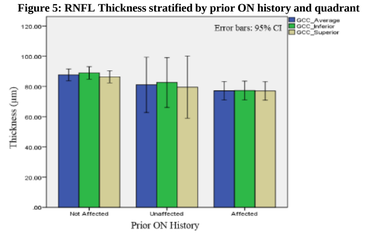
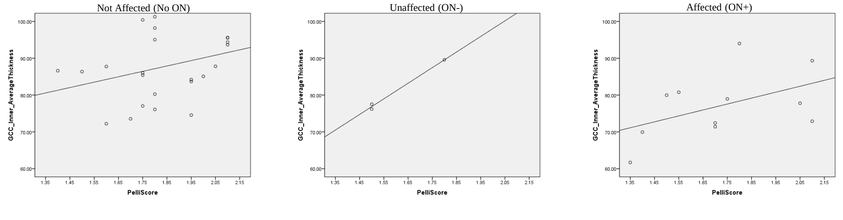


Figure 6: Correlation scatter plots between Pelli-Robson score and GCC Thickness



Results Continued

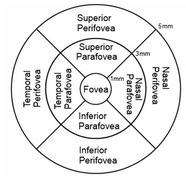
Macula of Retina

Table 6: Means±Standard Deviations of Full Retinal Total Volume and Average Thickness

	No ON	ON-	ON+	Sig
Macular Volume (mm^3)	5.29 ± 0.30	5.28 ± 0.47	5.10 ± 0.33	**0.02**[a]
• Parafovea	1.88 ± 0.12	1.89 ± 0.17	1.81 ± 0.12	**0.03**[a]
• Perifovea	3.41 ± 0.19	3.39 ± 0.30	3.28 ± 0.22	**0.01**[a]
Macular Thickness (µm)	285 ± 22	285 ± 30	275 ± 23	**<0.01**[a]
• Parafovea	299 ± 18	300 ± 28	289 ± 18	**0.03**[a]
• Perifovea	271 ± 15	270 ± 24	261 ± 17	**<0.01**[a]

Mean differences evaluated using one-way ANOVA between Not Affected (No ON), Unaffected (ON-), and Affected (ON+) eyes of MS patients
Bold values indicate statistically significant differences by post-hoc analysis with Bonferroni correction.
a = Significant mean difference between No ON and ON+

Figure 7: Representative map of macular regions



Tables 7 and 8: Means and Standard Deviations of Full Retinal Volumes and Thicknesses of macular quadrants stratified by prior ON history

	Parafovea Volume (mm^3) (mean ± SD)				Perifovea Volume (mm^3) (mean ± SD)			
	No ON	ON-	ON+	Sig	No ON	ON-	ON+	Sig
Inferior	0.47 ± 0.03	0.47 ± 0.04	0.45 ± 0.03	**0.03**[a]	0.83 ± 0.05	0.82 ± 0.07	0.80 ± 0.05	**<0.01**[a]
Superior	0.47 ± 0.03	0.47 ± 0.04	0.46 ± 0.03	**0.04**[a]	0.86 ± 0.05	0.86 ± 0.08	0.84 ± 0.06	NS
Nasal	0.48 ± 0.03	0.48 ± 0.04	0.46 ± 0.03	NS	0.89 ± 0.06	0.89 ± 0.09	0.85 ± 0.06	**<0.01**[a]
Temporal	0.46 ± 0.03	0.46 ± 0.04	0.44 ± 0.03	**0.02**[a]	0.83 ± 0.05	0.82 ± 0.07	0.80 ± 0.05	**0.03**[a]

	Parafovea Thickness (µm) (mean ± SD)				Perifovea Thickness (µm) (mean ± SD)			
	No ON	ON-	ON+	Sig	No ON	ON-	ON+	Sig
Inferior	296 ± 18	298 ± 28	286 ± 18	**0.02**[a]	265 ± 16	262 ± 23	254 ± 17	**<0.01**[a]
Superior	300 ± 19	301 ± 28	290 ± 20	**0.04**[a]	272 ± 15	273 ± 25	266 ± 19	NS
Nasal	306 ± 20	309 ± 28	296 ± 19	NS	284 ± 19	284 ± 27	270 ± 20	**<0.01**[a]
Temporal	294 ± 18	293 ± 28	283 ± 19	**0.02**[a]	264 ± 17	261 ± 23	255 ± 16	**0.03**[a]

Mean differences evaluated using one-way ANOVA between Not Affected (No ON), Unaffected (ON-), and Affected (ON+) eyes of MS patients
Bold values indicate statistically significant differences by post-hoc analysis with Bonferroni correction.
a = Significant mean difference between No ON and ON+

Discussion

- Optovue iScan 500 is a reliable evaluation tool in measuring retinal parameters within an MS center
  - Capable of stratifying patients based on prior optic neuritis history
  - GCC thickness is available at the time of acquisition, and requires no further analysis or post-processing
- Pelli-Robson is feasible to acquire as a single contrast assessment in MS patients' eyes with and without optic neuritis
- Pelli-Robson score, RNFL Thickness, GCC Thickness, and Macular Thickness (Parafovea and Perifovea) were all significantly reduced in Affected (ON+) eyes in patients with prior ON
  - Unaffected (ON-) eyes were relatively spared in thinning during an ON episode except in RNFL
- Optovue is a semi-automated device which can provide detailed information about RNFL, GCC, and macular volume in approximately 10 minutes

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ZG: None, SL: None, GA: None, CD: None, PK: Optovue, RTN: Alkermes, Acorda, Bayer, Biogen, Genentech, Genzyme, EMD Serono, Mallinckrodt, Novartis, Pfiser, Teva
Optovue provided the OCT scanner for evaluation. This investigation was conducted independently from the manufacturer.