The different structure-function correlation as measured by OCT and Octopus perimetry cluster analysis in intracranial tumor and glaucoma patients

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Abstract

Background

To explore the correlation of visual field (VF) defect values and retinal nerve fiber layer (RNFL) thickness for the intracranial tumor and glaucoma patients.

Methods

Retrospective analysis is performed for the intracranial and glaucoma patients, whose VF defect values measured with Octopus perimeter cluster analysis, and RNFL thickness and optic disk parameters measured with swept source OCT. The differences between VF and RNFL (included the data of optic disc) are calculated. The correlation between VF defect values and RNFL thickness are explored.

Results

43 eyes of 29 patients with the intracranial tumor and 39 eyes of 23 patients with the glaucoma are enrolled. Thickness of RNFL not only for the whole (360°), but also for the four quadrants are thinner in the glaucoma group than those of the intracranial tumor group ($p < 0.05$). There is no significant difference of VF for those two groups. Stronger correlation for mean deviations (MD)s of VF ten clusters and RNFL thickness of OCT twelve sectors is found in the glaucoma patients, but few in the intracranial tumor patients. Logistic regression also shows the RNFL loss tending to the diagnosis of glaucoma, and the VF damage is inclined to the diagnosis of intracranial tumor.

Conclusions

Intracranial tumor has a weak correlation between the RNFL thickness and Octopus VF MD, compared with that of glaucoma. OCT and Octopus VF might provide more helpful information for the antidiastole of intracranial tumor and glaucoma.

Background

It is well-known that the intracranial tumors can cause visual field (VF) damage when affect the visual pathway. Also due to the retrograde degeneration, the compression of intracranial tumors can lead to the damage of ganglion cell axons, following the thinning of retinal nerve fiber layer (RNFL)[1]. Similar manifestations and conditions are also found in the glaucoma eyes. With the variability of RNFL and VF manifestations, intracranial tumors are sometimes misdiagnosed as other diseases, such as glaucoma[2]. A study showed that 6.5% patients diagnosed with normal tension glaucoma had clinically relevant compression of the anterior visual pathway[3]. However, for the intracranial tumors, early diagnosis is important to improve the possibilities of treatment and to reduce the mortality[4]. We strive to find an indicator to distinguish the diagnosis, between the intracranial tumor and the glaucoma.

Octopus perimeter (OP) is one of the most common used perimeters for assessing the glaucoma and many neurological disorders. Cluster analysis is a special visual field analysis program conducted by OP, and divides OP into 10 clusters according to the distribution of RNFL. The built-in program automatically calculates the arithmetic mean value of mean deviation (MD) in each cluster. The cluster analysis can identify regional visual field defects while there is a small increase of MD. Some studies had explored the relationship between VF and RNFL in intracranial tumor and glaucoma patients[5–7]. However, few were conducted with Octopus perimeter cluster analysis[8].

Our study is to analysis the structure–function correlation in the intracranial tumor and glaucoma patients, which was based on the OP ten clusters analysis and Topcon OCT twelve sectors RNFL thickness. Correlation analysis was performed to associating these VF clusters MD with RNFL sectors thickness measurements. And we try to find the difference of that correlation in the intracranial tumor and glaucoma patients.

Methods

Recruitment of Patients, and Inclusion and Exclusion Criteria

This retrospective study is conducted in the Peking University International Hospital, Beijing, China. The study is approved by the local ethical review board in accordance with the Declaration of Helsinki, and all patients provided the informed consent.

Twenty-three patients with glaucoma, and 29 patients with intracranial tumor, October 2018 to December 2020, are retrospectively enrolled in this study. For the glaucoma patients, the inclusion criteria are diagnosed with the primary open-angle or angle-closed glaucoma, and BCVA better or equal to 20/200. And the exclusion criteria is the previous intraocular surgery or any ocular diseases, which could induced the change of VF or RNFL, such as ocular trauma, corneal degeneration and dystrophy, optic nerve disease, macular or retinal disease. For the patients with the intracranial tumor, the inclusion criterion is diagnosed with pre-operative intracranial tumor, and BCVA better or equal to 20/200. And the exclusion criteria is the previous intraocular surgery or any ocular diseases, which could induced the change of VF or RNFL, such as glaucoma, ocular trauma, corneal degeneration and dystrophy, optic nerve disease, macular or retinal disease.

Clinical Observations

Clinical history and routine clinical examination was performed by slit-lamp microscopy, indirect ophthalmoscopy, uncorrected (UCVA) and best-corrected visual acuity (BCVA) logMAR were tested, besides intraocular pressure (IOP), VF and RNFL. IOP was measured by noncontact tonometer (Canon TX-10/TX-F, Tokyo, Japan), slit lamp examination (Topcon SL-1E, Tokyo, Japan), and fundus examination (90 Dioptre, Volk Optical, Mentor, OH) with undilated pupil.

VF measurement

VF was tested with Octopus 900 perimeter (Haag-Streit AG, formerly Interzeag AG, Schlieren, Switzerland). The program of White-on-White TOP strategy with 4/1000 asb III 100ms, and Octopus G Standard distribution of points was performed for those included patients. The acceptable criterion of reproducible test are both of false-positive and false-negative response rates less than 15%. The manufacturer-provided ten visual field clusters were used (Figure 1), and set as VF01-VF10, with calculated MD values. The clusters of the left eyes were mirrored and numbered as those of the right eyes, to ensure uniform handling of all data.

RNFL measurement

Peripapillary RNFL thickness was measured at the same time without dilating the pupil, using DRI OCT Trion (Topcon Corp., Tokyo, Japan). RNFL measurements were categorized by clock-hours, and labeled such that left eye sectors mirrored right eye sectors (Figure 1), set as Clock 1-12.

Statistical analysis

The Kolmogorov–Smirnov test was used to verify the normality of the data distribution. For quantitative comparisons between groups, we used the Student *t*-test for independent samples for parametric variables. Pearson correlation coefficients were calculated to assess the relation between continuous variables. Binary logistic regression is calculated to assess the influence of VF and RNFL changes on the diagnosis of glaucoma or intracranial tumor. Statistical analyses were performed using SPSS statistical software for Windows (version 20.0, IBM-SPSS, Chicago, IL). The level of statistical significance was set at $p < 0.05$.

Results

Included patients are divided as two groups of intracranial tumor and glaucoma due to the diagnosis. Intracranial tumor group has 43 eyes of 29 patients (11 with pituitary adenoma, eight with meningioma, two with craniopharyngioma, three with glioma, one with ependymoma, one with metastatic tumor, one with cerebellar hemangioblastoma, one with cavernous hemangioma, and one with inflammatory pseudotumor). And the location of these intracranial tumors is post-lateral geniculate body for 13 patients. Glaucoma group has 39 eyes of 23 patients (15 with primary open-angle glaucoma, and eight with primary angle-closed glaucoma). The mean ages of glaucoma and intracranial tumor groups are 55.39 ± 14.90 and 51.97 ± 14.11 years ($p = 0.400$).

As the results of RNFL measured by TOPCON OCT in Table 1, the thickness of RNFL not only for the whole (360°), but also for the superior, inferior, nasal and temporal quadrants are thinner in the glaucoma group than those of the intracranial tumor group ($p < 0.05$). Moreover, the rim area, linear CDR, vertical CDR and cup volume of optic disc measured by OCT all have the significant differences for the two groups ($p < 0.05$).

Table 1
Data of VF and RNFL for the glaucoma and intracranial tumor groups

Groups	Glaucoma	Intracranial tumor
N (eyes)	39	43
RNFL (360°) (μm)**	78.03 ± 21.41	113.58 ± 33.78
Superior quadrant of RNFL (μm)**	97.67 ± 30.14	145.28 ± 48.67
Inferior quadrant of RNFL (μm)**	89.26 ± 37.56	150.12 ± 43.98
Nasal quadrant of RNFL (μm)**	58.25 ± 17.61	81.14 ± 31.27
Temporal quadrant of RNFL (μm)*	66.02 ± 19.94	78.21 ± 23.16
Rim area (μm ²)**	0.61 ± 0.40	1.59 ± 0.90
Disc area (μm ²)	1.90 ± 0.43	7.34 ± 33.37
Linear CDR**	0.79 ± 0.19	0.51 ± 0.23
Vertical CDR**	0.80 ± 0.21	0.49 ± 0.23
Cup volume (μm ³)**	0.40 ± 0.28	0.12 ± 0.14
MD of VF (dB)	18.28 ± 6.98	16.89 ± 5.40
MS of VF (dB)	9.54 ± 6.75	10.97 ± 5.35
sLV of VF (dB)	5.08 ± 2.58	6.15 ± 2.56
Visual field (VF); Retinal nerve fiber layer (RNFL); Square root of loss variance (sLV);		
*p < 0.05; **p < 0.01;		

On the contrary, the results (global MD, MS, sLV) of VF measured with Octopus perimeter (Table 1), for the glaucoma group, have no statistical significant difference ($p > 0.05$) with those of the intracranial tumor group.

For the glaucoma group, the correlation coefficient between VF cluster MD and RNFL sector thickness is shown as Table 2, the clusters of VF and sectors of RNFL are set in Fig. 1. And the strong correlations (value more than 0.45) could be observed in Fig. 2. As shown in Table 3, few correlations were observed between VF cluster MD and RNFL sector thickness for the intracranial tumor group, the figure of correlation is not drawn.

Table 2
The correlation coefficient of VF and RNFL for the glaucoma group

	Clock01	Clock02	Clock03	Clock04	Clock05	Clock06	Clock07	Clock08	Clock09	Clock10	Clock11	Clock12
VF01	-0.363*	-0.267	-0.120	0.148	-0.005	-0.259	-0.286	-0.306	-0.549**	-0.483**	-0.537**	-0.427**
VF02	-0.489**	-0.468**	-0.208	0.084	-0.165	-0.495**	-0.417**	-0.332*	-0.460**	-0.465**	-0.517**	-0.666**
VF03	-0.510**	-0.509**	-0.275	-0.022	-0.185	-0.480**	-0.335*	-0.255	-0.348*	-0.348*	-0.362*	-0.632**
VF04	-0.519**	-0.508**	-0.313	-0.078	-0.161	-0.424**	-0.167	-0.166	-0.297	-0.261	-0.220	-0.429**
VF05	-0.357*	-0.341*	-0.233	-0.081	-0.063	-0.177	0.011	-0.127	-0.223	-0.141	-0.041	-0.166
VF06	-0.322*	-0.392*	-0.240	-0.097	-0.153	-0.338*	-0.174	-0.312	-0.307	-0.213	-0.172	-0.260
VF07	-0.331*	-0.422**	-0.226	0.045	-0.148	-0.393*	-0.476**	-0.506**	-0.458**	-0.277	-0.310	-0.397*
VF08	-0.307	-0.361*	-0.165	0.106	-0.085	-0.353*	-0.516**	-0.575**	-0.560**	-0.318*	-0.313	-0.390*
VF09	-0.310	-0.354*	-0.124	0.123	-0.074	-0.321*	-0.525**	-0.674**	-0.649**	-0.444**	-0.420**	-0.440**
VF10	-0.311	-0.317*	0.044	0.195	-0.029	-0.229	-0.383*	-0.561**	-0.691**	-0.530**	-0.416**	-0.383*
Visual field (VF); Retinal nerve fiber layer (RNFL); Square root of loss variance (sLV);												
The clusters of VF and sectors of RNFL are set in Fig. 1												
*p < 0.05; **p < 0.01;												

Table 3
The correlation coefficient of VF and RNFL for the intracranial group

	Clock01	Clock02	Clock03	Clock04	Clock05	Clock06	Clock07	Clock08	Clock09	Clock10	Clock11	Clock12
VF01	-0.128	-0.196	-0.099	0.001	0.103	0.025	0.326*	-0.190	-0.189	-0.211	-0.110	-0.096
VF02	-0.118	-0.117	-0.073	0.002	0.202	0.106	0.167	-0.048	-0.012	0.027	0.018	-0.071
VF03	-0.143	-0.201	-0.089	-0.043	0.154	0.059	0.161	0.017	0.043	0.040	0.038	-0.023
VF04	-0.110	-0.231	-0.079	0.000	0.189	0.072	0.270	-0.018	-0.071	-0.098	-0.056	-0.032
VF05	-0.206	-0.302*	-0.164	-0.081	0.163	-0.007	0.228	-0.207	-0.254	-0.215	-0.197	-0.169
VF06	-0.160	-0.258	-0.100	-0.051	0.029	-0.044	0.221	-0.217	-0.374*	-0.336*	-0.159	-0.110
VF07	-0.086	-0.225	-0.083	-0.081	0.109	-0.030	0.262	-0.090	-0.319*	-0.267	-0.143	-0.088
VF08	-0.007	-0.077	-0.064	0.012	0.205	0.051	0.380*	0.004	-0.184	-0.091	0.016	0.007
VF09	-0.091	-0.015	0.016	0.130	0.296	0.138	0.322*	-0.043	-0.072	0.023	0.039	-0.067
VF10	-0.187	-0.277	-0.149	-0.126	-0.070	-0.200	0.330*	-0.383*	-0.494**	-0.468**	-0.335*	-0.267
Visual field (VF); Retinal nerve fiber layer (RNFL); Square root of loss variance (sLV);												
The clusters of VF and sectors of RNFL are set in Fig. 1												
*p < 0.05; **p < 0.01;												

As the binary logistic regression, the thickness of RNFL, MD and MS of VF, are included (Table 4). It shows the loss of RNFL tending to the diagnosis of glaucoma, and the damage of VF is inclined to the diagnosis of intracranial tumor.

Table 4
The influence of VF and RNFL on the diagnosis

	B	Wals	Sig.	Exp (B)	95% C.I. of EXP(B)	
					lower	upper
RNFL	0.154	19.549	0.000	1.167	1.090	1.249
MD of VF	1.985	7.439	0.006	7.277	1.748	30.293
MS of VF	2.311	8.866	0.003	10.080	2.203	46.131
Constant	-72.632	9.929	0.002	0.000		
Visual field (VF); Retinal nerve fiber layer (RNFL);						

Discussion

Visual field and OCT are two most commonly used clinical examine methods for nerve injury disorder, such as glaucoma and intracranial tumor. And the Cluster analysis program in Octopus perimeter, which is designed according to the distribution of RNFL, can sensitively detect regional dysfunction when there are minimal visual field abnormalities. Perdicchi's study showed within normal VF and abnormal ganglion cell complex (GCC) eyes of hypertension or early stage glaucoma, all of the 23 eyes showed abnormal results with cluster analysis[8]. Some studies had shown the correlation between the structure and function in glaucoma patients with Humphrey or Octopus perimeter and OCT[9–11]. Generally these studies all found a topographic correlation in VF and OCT. But few studies have explored the topographic correlation in intracranial tumor patients with Octopus perimeter and OCT, fewer are about cluster analysis.

Our study shows a relative weak correlation between the MD of OP clusters with the thickness of RNFL in seven of ten OP clusters in those intracranial tumor patients (cluser1, 5, 6–10), most correlation coefficient absolute value is less than 0.45. While in the glaucoma patients, with each OP cluster, we find moderate correlations in more than one RNFL sector, which is similar with other studies[12–14]. Also the map (Fig. 2) shows the topographic structure-function relationship in glaucoma. Previous studies also showed a moderate association between RNFL thickness in each sector with VF region either in Octopus or Humphrey perimetry in glaucoma patients[9–11], a structure-function map which is similar with ours was created.

We assume the result may correlate with the different retinal ganglion cells (RGCs) damage mechanisms in glaucoma and intracranial tumor. It is well-known that glaucoma is characterized by the damage to RGCs axons initialing at the optic nerve head with different mechanisms, such as

intraocular pressure mechanical compression, vascular disorders, immunologic influence, and oxidative stress. That may lead to the direct retrograde damage to the RGCs, following with the RNFL thinning and VF defect. Also some studies show glaucoma optic disk change correlated with the intraorbital optic nerve measurement and chiasmal size[15–17], which suggest glaucoma may also lead to anterograde degeneration post optic disk. Therefore, glaucoma may produce a bidirectional nerve injury from the optic nerve head.

While intracranial tumors cause the retrograde degeneration on the visual pathway, the pathologic changes starts from the distal axonal and progresses centripetally, which is also found in other central nervous system pathologies such as cerebral infarction, head trauma, multiple sclerosis[18–20]. That includes two conditions. Tumor arising near the sella turcica causing the axonal or terminal lesions between the eye and the lateral geniculate body, leads to the direct retrograde degeneration[6]. Whereas, tumors arising post lateral geniculate body cause damage to the optic radiation after the tertiary neurons in the visual pathway and lead to the trans-synaptic retrograde retinal degeneration (TRD). It also causes the RNFL thinning and the optic nerve head vessel density decrease[18, 21, 22]. This is mechanically different from the damage of RGCs and axons in glaucoma.

Previous research showed the chiasmal lesion caused more prominent optic nerve head vessel density decrease than postgeniculate lesion, which indicated the direct retrograde degeneration might be more prominent than TRD[22]. And our study shows the RNFL thinning is less prominent than glaucoma' RGCs' degeneration, both of the direct and trans-synaptic retrograde induced by the intracranial tumor. Whether the RNFL damage extent is negative correlated with the distance from the initial site of injury to the RGCs remains unknown and need more research to prove.

Another hypothesis is that the weak structure-function correlation in intracranial tumor patients is mightly due to the less injury of RNFL caused by direct or trans-synaptic retrograde. Our study yields two age and VF matched groups, of glaucoma and intracranial tumor, and shows more severe RNFL damage, smaller rim area, larger cup volume and larger C/D ($P < 0.05$) in the glaucoma patients. Also some study showed the optic chiasmal Compression might cause the cell-inner plexiform layer thinning without RNFL changing in the early phase of some intracranial tumors[23, 24]. However, Orman's study showed, pituitary tumors might have RNFL thinning and RGCs degeneration without VF defect[25]. These inconsistencies in structure and function may also lead to the weak structure-function correlation in those intracranial tumor patients.

In the contrast to the intracranial tumor, in our study, at the same age range and VF MD levels, glaucoma patients have more severe RNFL and optic nerve head damage. The logistic regression analysis shows the RNFL loss tending to the diagnosis of glaucoma; the VF damage is inclined to the diagnosis of intracranial tumor. Few studies had ever explored the RNFL difference between those two VF-affected diseases. This may provide some information for the antidiastole.

There are some limitations in our study. First, the smaller number of participants may introduce some selection bias. Second, there are not enough post-geniculate participants to analysis the direct and transsynaptic retrograde degeneration respectively. The same problem exists in the angle-closed and open glaucoma cases. Further study should be conducted to explore more detailed information.

In conclusion, due to few correlation coefficients, intracranial tumor has a weak correlation between the RNFL thickness and Octopus visual field MD, compared with the glaucoma. RNFL and optic nerve head damage was more prominent in glaucoma patients when compared to intracranial tumor patients. OCT and Octopus visual field may provide more information for the antidiastole of intracranial tumor and glaucoma.

Conclusions

Intracranial tumor has a weak correlation between the RNFL thickness and Octopus VF MD, compared with that of glaucoma. OCT and Octopus VF might provide more helpful information for the antidiastole of intracranial tumor and glaucoma.

Declarations

Ethical approval and consent to participate: The study was in accordance with the tenets of the Declaration of Helsinki and has been approved by the institutional review board of Peking University International Hospital. All patients provided the informed consent.

Consent for publication: Not applicable.

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Competing interests: None

Availability of data and material: The datasets generated and/or analysed during the current study are not publicly available due to limitations of ethical approval involving the patient data and anonymity but are available from the corresponding author on reasonable request.

Code availability: Not Applicable

Author's contributions: Xiaochun Li, Jiayin Qin and Xiaoguang Cao wrote the main manuscript text, and prepared figures and tables. Zeqin Ren, Ting Cui and Yongzhen Bao provided the data. All authors reviewed the manuscript.

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Figures

Figure 1

The diagram of visual field (VF) clusters and retinal nerve fiber layer (RNFL) clock-hour sector map. A The ten clusters are numbered as 01 to 10 on VF graph for the right eye (OD). B The ten clusters are numbered as 01 to 10 on VF graph for the left eye (OS), mirrored as OD. C The clockwise number of twelve RNFL sectors on OCT graph for the right eye (OD). D The counter-clockwise number of twelve RNFL sectors on OCT graph for the left eye (OS), mirrored as OD.

Figure 2

The diagram of visual field (VF) clusters and retinal nerve fiber layer (RNFL) clock-hour sector map. A The ten clusters are numbered as 01 to 10 on VF graph for the right eye (OD). B The ten clusters are numbered as 01 to 10 on VF graph for the left eye (OS), mirrored as OD. C The clockwise number of twelve RNFL sectors on OCT graph for the right eye (OD). D The counter-clockwise number of twelve RNFL sectors on OCT graph for the left eye (OS), mirrored as OD.