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ORIGINAL ARTICLE

Visual Outcomes, Visual Fields, and Optical Coherence Tomography in Paediatric Craniopharyngioma

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ABSTRACT

Ten patients with craniopharyngioma treated for the first time when younger than 18 were included. This study reviews the visual outcomes and provides information on visual field (VF) and optical coherence tomography (OCT) examination of craniopharyngioma. The best kappa concordance coefficients between VF and OCT parameters of atrophy were obtained for the ganglion cell (GC) thickness and the mean retinal nerve fibre layer (RNFL) thickness. The agreement between GC colour maps and VF defects was good. Optic nerve compression may be detected by RNFL measurement and GC analysis, and this may be valuable to predict visual recovery and in uncooperative patients to evaluate visual damage.

Keywords: Craniopharyngioma, ganglion cell colour map, optical coherence tomography, optic neuropathy children, visual field

INTRODUCTION

Craniopharyngioma is a tumour that develops from squamous cell nests derived from the primitive Rathke pouch.[1–5] It is the most common suprasellar tumour in childhood and the second most common, after pituitary adenoma, in adults.[1] Its incidence has been estimated to be of 1.4 cases per million children per year.[6] Despite its histological classification as a benign tumour, it may be locally aggressive, with frequent extension and damage to adjacent structures and a high recurrence rate.[4,5]

Patients with craniopharyngioma are often diagnosed relatively late after the onset of the first symptoms.[1] Children present with systemic symptoms more often than adults; these symptoms may include headache and nausea due to raised intracranial pressure, as well as diabetes insipidus, growth retardation, and delayed sexual development due to the disruption of the hypothalamic-pituitary pathway.[1,5,7] Some patients present with visual loss as a result of compression of the visual pathways, with blurred vision being the most common visual complaint.[1–7]

Computed tomography (CT) usually shows an heterogeneous suprasellar mass with calcification and extension into the chiasm or third ventricle.[1] Magnetic resonance imaging (MRI) can better determine tumour extension[1] and is recommended for follow-up, although ophthalmic examinations are also considered useful for early detection of anterior visual pathway compression by recurrent tumour growth.[1] However, children affected may find it hard to perform visual fields (VF). Furthermore, VF damage reflects impairment in optic nerve function that may or may not improve after treatment. In other compressive neuropathies, optical coherence tomography (OCT) has been shown to detect anatomical damage to the optic pathway and provide prognostic information.[8] It requires only limited cooperation on the part of the patient in order to provide reliable

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measurements and therefore may be useful in patients unable to perform reliable VF.

Temporal retinal nerve fibre layer (RNFL) loss reflects damage to the papillomacular bundle, and it has been reported to be related to visual acuity loss.[9,10] Mean RNFL loss is more often associated with visual field damage. Several studies have found that the ganglion cell layer (GC) is more strongly correlated with visual field defects than with the RNFL thickness.[11]

The purpose of this paper is to review visual outcomes in children with craniopharyngioma and to evaluate the correlation between visual field testing and OCT, as well as to evaluate the role of OCT for the prediction of visual outcomes after surgery.

MATERIALS AND METHODS

The charts of patients with craniopharyngioma who had been treated for the first time when younger than 18 were reviewed and considered for inclusion in the study. This first therapeutic procedure was not always performed in our hospital; therefore, symptoms and signs at presentation were not always available. This study was started when the Cirrus-HD model 4000 (Carl Zeiss Meditec) became available in our centre in 2010. Therefore, the first time the patients could be explored with this device will be considered the baseline visit.

These patients are followed in the neuro-ophthalmology department. At every visit, an extensive ophthalmic examination is performed, including at least best-corrected visual acuity (BCVA), pupillary responses, external ocular motor examinations, and anterior and posterior pole biomicroscopy and funduscopy. When patients are 7 or older, automated perimetry (Humphrey Field Analyser 750, Zeiss/Humphrey Systems, Dublin, CA) is performed, usually 24-2 tests, SITA (Swedish interactive threshold algorithm) standard strategy. Visual fields are considered reliable when false positives and fixation losses are lower than 10%. Type of visual field defect and mean deviation (MD) were recorded. When BCVA is less or equal to counting fingers, perimetry is not performed. In these cases, MD was considered −30 dB for statistical analysis. BCVA was considered normal if $\geq$0.9 (decimal scale).

OCT scanning was performed in patients at least 4 years old, after mydriasis with 1% cyclopentolate, using Cirrus-HD model 4000 (Carl Zeiss Meditec). An internal fixation target was used whenever possible. To evaluate the RNFL thickness, macular thickness, and the GC, the optic disc cube protocol and the macular cube 512 × 128 acquisition protocols were performed. Mean average and temporal quadrant RNLF thickness, central foveal thickness, the total macular volume in the 6-mm ETDRS (Early Treatment Diabetic Retinopathy Study) ring, and the average GC thickness were recorded.

The Cirrus OCT compares the values for each exploration with the values of a built-in normative database; however, this database does not include children. Thus, OCT in children is harder to interpret; in daily practice, most physicians change the date of birth in order to have something with which to compare the values obtained. However, several groups have published OCT values for normal children. We compared the values for each patient with those of one such study designed to compile a normative database for healthy children in our country.[12,13] As in adults, we considered values under 5th percentile (P_5) and 1st percentile (P_1) to be abnormally reduced.

The study was approved by our institutional review board and adhered to the tenets of the Declaration of Helsinki. Statistical analysis was performed using the Statistical Package for Social Sciences software (version 20.0; IBM, Armonk, NY). Agreement between affected visual fields and decreased OCT parameters was evaluated with the kappa coefficient.

RESULTS

Ten patients with craniopharyngioma were included in the study. There were four girls and six boys, with a median age at the time of the initial therapeutic procedure of 5 years (range from 3 to 16 years). All children underwent surgery for the removal of the tumour; case 8 also received adjuvant radiotherapy. So far, they have required between one and four procedures to control the tumour (mean of two procedures per child). Three cases needed additional surgical interventions to treat complications derived from the tumour (intracranial hypertension) or from surgery (cerebrospinal fluid fistula) (Table 1).

Although two cases have been diagnosed and treated in the last year, the median time from the first surgical procedure to the last visit was 6 years. Tables 2 and 3 show the ophthalmic assessment at the last follow-up visit. There were no visual fields available for two children because at the last follow-up visit they were still younger than 7. Five eyes could not be tested due to amaurosis. MD ranged from −3.04 to −30 dB, with a mean MD for the 14 tested eyes of −16.53 dB (SD = 11.58 dB). Table 3 shows OCT parameters in the last visit. Only 3 out of 16 eyes had a mean RNFL thickness above the 1st percentile (P_1 = 78.6 μm; P_5 = 82.4 μm). Thus, most eyes had severe optic nerve damage according to the Cirrus OCT. However, only 8 out of 16 had a temporal quadrant RNFL thickness below P_1 (P_1 = 48.4 μm; P_5 = 51.8 μm).[12] The 18 eyes in which macular

TABLE 1 Baseline characteristics of study patients.

Child	Sex	Age at time of first surgery (years)	Time from surgery to the last visit (years)	Total number of surgical procedures	Systemic complications
1	Female	3	4	3	Obesity Panhypopituitarism
2	Male	3	12	2 (plus a third one due to IH)	Obesity Diabetes insipidus ACTH deficit
3	Male	4	3	2	Short stature (GH) Diabetes insipidus
4	Female	4	15	1 (plus a second one due to IH)	Panhypopituitarism Obesity
5	Female	5	9	4	Panhypopituitarism
6	Male	5	0.5	1	
7	Male	5	0.5	2	Short stature
8	Female	10	8	1 (plus radiotherapy)	Panhypopituitarism
9	Male	10	22	1	Obesity Panhypopituitarism
10	Male	16	1	2 (plus a third one due to CF fistula)	Panhypopituitarism

IH = intracranial hypertension; CF = cerebrospinal fluid; ACTH = adrenocorticotropic hormone; GH = growth hormone.

TABLE 2 Ophthalmic examination at the last visit, including visual field results.

	BCVA				Pallor disc		VF RE		VF LE	
Child	RE	LE	RAPD	Strabismus	RE	LE	MD	Defect	MD	Defect
1	0.6	0.025	LE	Exotropia	Diffuse	Diffuse	−18.23	Temporal hemianopia		NP
2	0.6	0.5	—	Orthotropia	No pallor	No pallor	−3.71	Normal	−3.75	Normal
3	1	0.13	LE	Exotropia	Temporal	Diffuse	−15.71	Temporal hemianopia		NP
4	0.7	0.7	—	Orthotropia	Temporal	Band atrophy	−7.12	Left hemianopia	−6.17	Left hemianopia
5	0.3	0	LE	Esotropia	Temporal	Diffuse	−20.42	Temporal		NP
6	1	1	—	Orthotropia	No	No		NP		NP
7	0.9	0.4	—	Orthotropia	No	Diffuse		NP		NP
8	1	0.025	LE	Orthotropia	Temporal	Diffuse	−3.04	Temporal	−26.71	Diffuse
9	0.006	0.0125	RE	Exotropia	Diffuse	Diffuse		NP		NP
10	1	1	—	Orthotropia	Temporal	Temporal	−5.40	Left hemianopia	−4.15	Left hemianopia

BCVA = best-corrected visual acuity; RE = right eye; LE = left eye; RAPD = relative afferent pupillary defect; MD = mean deviation; NP = not performed.

examination was performed showed a foveal thickness above P_1 and only 3 eyes had values below P_5 ($P_1 = 206\,\mu m$; $P_5 = 220.1\,\mu m$). The macular volume was below P_1 in 6 eyes and below P_5 in 11 eyes ($P_1 = 9.1\,mm^3$; $P_5 = 9.4\,mm^3$).[12] Macular GC thickness was below P_5 and P_1 in 12 out of 16 explored eyes ($P_1 = 72\,\mu m$; $P_5 = 75\,\mu m$).[13] Kappa concordance coefficients between visual fields (affected or not) and OCT parameters below normal values were statistically significant for the GC thickness (kappa = 1; $p < 0.001$ for P_1 and P_5) and the mean RNFL thickness (kappa = 0.632; $p = 0.011$ for P_1 and P_5).

At least three reliable sequential visual fields could be performed in eight eyes of five children. Visual fields are difficult to perform and the MD values varied greatly, even in patients in whom there was no tumour recurrence. The variance of the VF MD of each eye during follow-up ranged from 0.124 to 7.441 in those without recurrence and from 26.184 to 75.381 in those with recurrences (Figure 1). OCT values fluctuated less. In patient 10, who presented with papilloedema, RNFL thickness decreased 49 and 50 μm in each eye, respectively. The variance ranged from 0.5 to 7.9 μm in all other cases. GC thickness values also showed less variation between visits. In case 10, GC thickness decreased 22 and 16 μm in each eye, respectively. The variance ranged from 0 to 0.81 in all other cases. Figure 1 shows the evolution of the MD of the visual fields and of the mean RNFL and GC thicknesses in those affected eyes with both tests available. Figure 2 shows the correspondence between VF and GC colour map. The agreement between GC colour maps and VF for the detection of diffuse or hemianopic defects was good. The kappa concordance coefficient was 0.667 ($p = 0.014$).

TABLE 3 OCT parameters in the last visit.

	RNFL thickness (µurn)				Macular parameters				GC thickness	
	RE		LE		RE		LE		(µm)	
Child	Mean	Temporal	Mean	Temporal	MV (mm^3)	FT (µm)	MV (mm^3)	FT (µm)	RE	LE
1	54	36	57	49	8.6	225	8.3	223	54	48
2	78	61	86	70	9.9	289	10.1	285	78	85
3	67	42	55	53	9.8	264	8.7	259	67	53
4	51	50	60	37	9.2	231	9.3	237	70	67
5	76	39	53	54	9.2	243	7.6	216	64	42
6					9.9	297	10.1	279	79	88
7	97	56	85	77	9	273	9	239		
8	76	36	72	35	9.4	243	9.3	235	69	67
9										
10	64	29	77	44	8.7	215	9.5	220	55	63

RNFL = retinal nerve fibre layer; RE = right eye; LE = left eye; FT = foveal thickness; GC = ganglion cell.

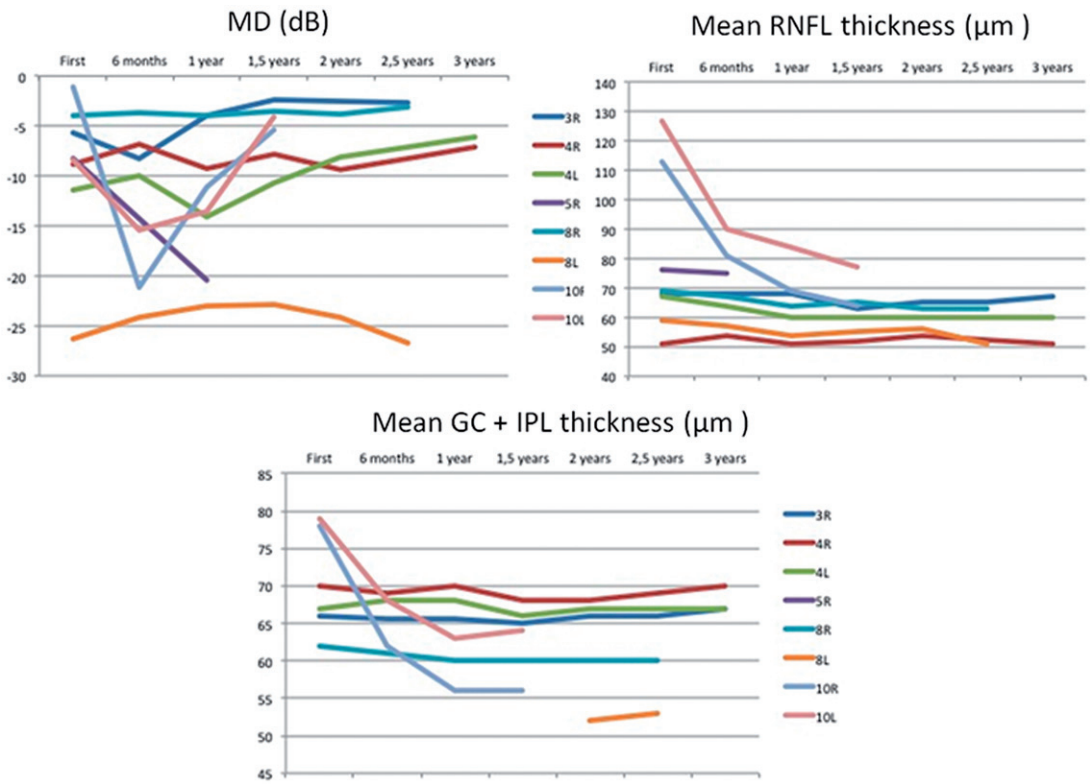


FIGURE 1 Visual field and RNFL and GC thickness changes during the follow-up period of three years. Case 5 and 10 showed significant worsening of their visual fields due to recurrent tumoral growth. RNFL and GC thickness remained stable save for case 10 who initially showed papilledema that disappeared after surgery.

In case 10, Cirrus OCT was available before and after surgical treatment of a tumour recurrence. RNFL thickness was 81 µm in the right eye and 90 µm in the left eye, and the patient recovered most of the VF defect, as shown in Figure 3. Case 3 also had a recurrence before Cirrus OCT was available. The left eye was already blind at that time with a Stratus-OCT RNFL thickness of 47 µm; vision did not improve after surgery. The right eye showed a temporal hemianopia (−15.71 dB) with a Stratus-OCT RNFL thickness before surgery of 79 µm. After surgery, the VF only showed a mild superior temporal defect (−2.68 dB).

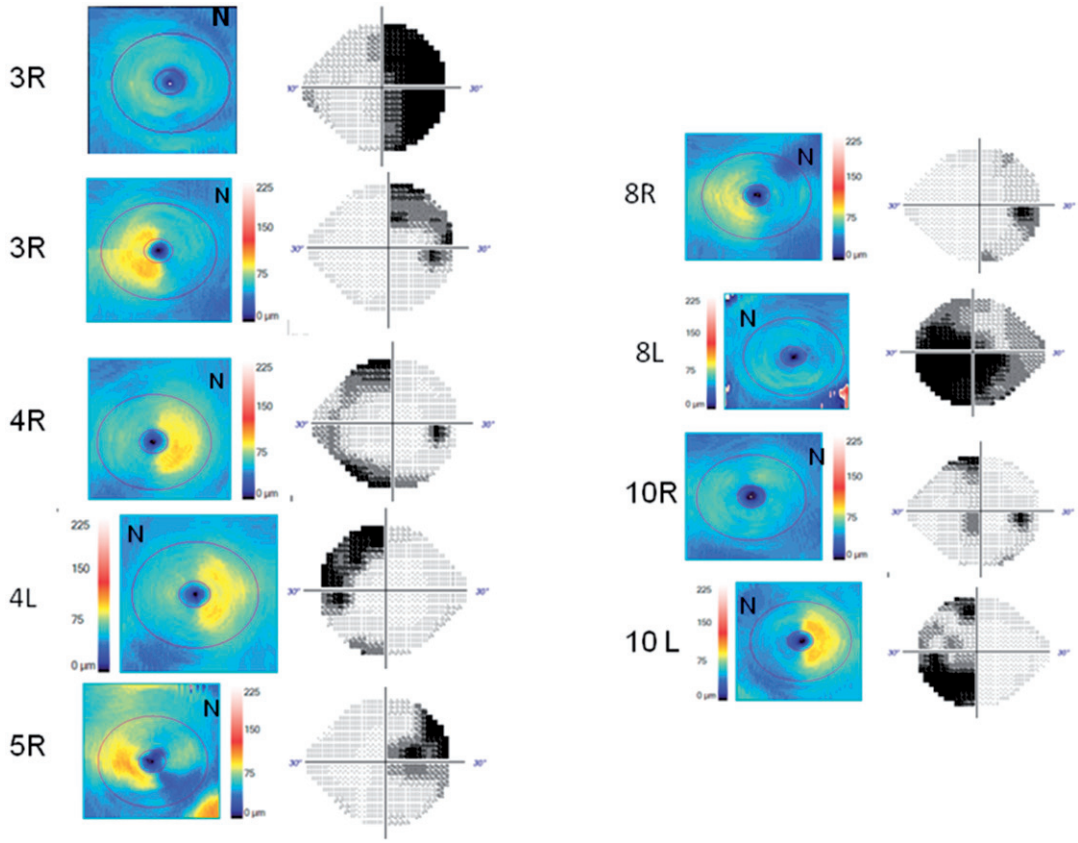


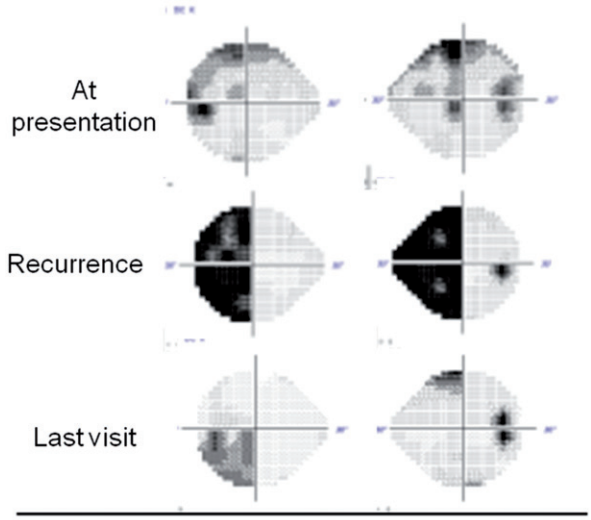
FIGURE 2 Correspondance of VF with its GC color-map to identify diffuse or hemianopic defects.

DISCUSSION

Optic neuropathy is a frequent result of craniopharyngioma in children despite the low rate of cases presenting with visual complaints.[7,14,15] Optic nerve damage may be due to chronic papilloedema, radiotherapy, direct compression, or manipulation during surgery. Direct compression is considered the main cause of visual loss.[16]

OCT in sellar tumours may predict visual recovery after surgery. In patients with visual field defects, if the RNFL thickness is not under normal values, visual recovery is frequent. However, if the RNFL thickness is already decreased before surgery, the chances of visual recovery are lower. The explanation for this may be that compression initially leads to impaired function, which is reflected as visual field damage. Retinal ganglion cell death occurs after prolonged compression, and there is a time delay before RNFL thinning is detected on OCT. Thus, RNFL thinning reflects irreversible ganglion cell damage. This predictive role has been established in adults with pituitary adenoma.[8] Although OCT may also have a similar predictive role in children, craniopharyngioma may behave differently than adenomas because complete resection is difficult and the risk of recurrence is high (34–75%).[17–21] In this case series, pretreatment OCT was available in four subjects. Two were children too young to perform visual fields. In the two patients who had reliable presurgical VF and OCT, visual fields improved in both eyes in patient 10 and in only one eye of patient 3. This eye was the only one that had severe RNFL damage on OCT.

After surgery, OCT reflects the damage sustained by the optic nerve and is correlated with visual acuity and visual fields. Bialer *et al*. evaluated 20 children with craniopharyngioma with OCT.[14] The RNFL thickness was evaluated in 16 cases, with follow-up examinations available in 10 cases.[22–24] They found a correlation between RNFL thickness and BCVA; RNFL thickness was also significantly thinner in those eyes with visual field defects.[14] In Bialer *et al*.'s study, among the 15 children who were able to perform visual fields, 4 showed bilateral temporal defects, 3 unilateral temporal defects, 1 inferior homonimous quadrantopia, and 1 a severe unilateral defect.[14] These were the visual defects that children showed at presentation; therefore, they were less severe than our results after a mean of 5 years of



	RNFL thickness	GCL thickness
At presentation	113 / 127 µm	78 / 79 µm
Recurrence	81 / 90 µm	62 / 68 µm
Last visit	64 / 77 µm	56 / 64 µm

FIGURE 3 Case 10 presented with severe left homonimous hemianopia that recovered after surgery as predicted by his OCT study.

follow-up. In our series, 60% of eyes had a BCVA below 0.5, although only in 20% of the children were both eyes similarly affected. This rate is similar to that reported previously.[1,14,25] More frequent than decreased acuity was the presence of a visual field defect, which is consistent with the higher prevalence of decreased mean RNFL thickness as compared with temporal RNFL damage that we observed. In our case series, only one out of eight tested cases showed normal visual fields. The most common defect was a temporal hemianopia in one eye and a diffuse and severe loss in the fellow eye (50%), which would be consistent with previous studies that report bitemporal hemianopia to be the most common initial visual field defect.[1,2] The second-most frequent defect was homonymous hemianopia (25%).

Recently, several studies have focused on GC analysis in sellar tumours. Moon *et al*. studied the relationship between visual field recovery and changes in the retinal GC layer in 19 adults with sellar tumours, including two patients with craniopharyngioma. They found that the GC layer was more strongly correlated with visual field defects than mean RNFL thickness, and they concluded that the selective measurement of the GC layer can be a useful parameter for evaluating the damage induced by chiasmal compression.[11] Although our case series is small and therefore our data should be interpreted with caution, in our study visual field defects were correlated with mean RNFL thickness and even more strongly with GC layer thickness.

Trans-synaptic retrograde degeneration of retinal ganglion cells following retrogeniculate visual pathway lesions has been reported.[26,27] Initially, progressive thinning of the RNFL following occipital lobe/optic radiation damage due to stroke was described.[27] Thinning of the RNFL was asymmetric and topographically congruent with lesions of the visual pathway located between the chiasm and the occipital lobe.[26,28–31] There also is also evidence supporting the correlation between the pattern of both RNFL loss and macular GC thinning and the type of visual field defect in other optic neuropathies.[32–36] Kanamori *et al*. showed how colour-coded maps could help to visualize the pattern of GC thinning in four cases of optic tract syndrome.[31] Our colour maps (Figure 2), also reflected a good topographic concordance between visual field damage and the areas represented in cold colours (blue). Only in two eyes was the visual field defect milder and more limited than would be expected in the presence of diffuse GC atrophy (1R and 10R). Since OCT can be performed in younger children than visual fields, and macular protocols are easier to perform than optic nerve protocols, these maps would allow us to estimate visual field damage in young children.

Figure 1 shows some examples of visual field and RNFL and ganglion cell thickness changes during the follow-up period of 3 years. During follow-up, cases 5 and 10 showed significant worsening of their visual fields, which prompted us to repeat MRI. In both cases, recurrent tumour growth was detected. Case 10 was operated quickly and, as predicted by the analysis of the RNFL thickness, recovered most of the visual field (Figure 3). Case 5 has not received further treatment yet. It must be borne in mind that as mentioned before, there is a time delay between retinal GC death and detection of RNFL or ganglion cell layer thinning on OCT. Thus, correlations between visual damage and OCT parameters in acute phases of the disease are not as clear as in stable nerves.

In summary, young children who may not perform reliable visual fields can be scanned with OCT. Optic nerve damage may be detected both by RNFL measurement and GC analysis, and this information may be valuable in patients still untreated to predict visual recovery and in uncooperative patients after surgery to estimate visual damage. Although we consider that visual fields are irreplaceable to detect compression of the visual pathway in time to avoid irreversible damage, OCT may be a valid substitute when patients are unable to perform perimetry. Therefore, both visual fields and OCT should be performed in patients with craniopharyngioma whenever possible. Although the absence of a

built-in normative database for children in commercially available OCT scanners can represent a problem for interpreting OCT examinations, normative data are now available in the literature.

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***Note*:** Figures 1 and 2 of this article are available in colour online at www.informahealthcare.com/oph.

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