Changes in the Optic Disc Excavation of Children Affected by Cerebral Visual Impairment: A Tomographic Analysis

Giulio Ruberto,[1] *Roberto Salati,*[2] *Giovanni Milano,*[1] *Chiara Bertone,*[1] *Carmine Tinelli,*[3] *Elisa Fazzi,*[4] *Rosanna Guagliano,*[1] *Sabrina Signorini,*[3] *Renato Borgatti,*[2] *Alessandro Bianchi,*[1] *and Paolo Emilio Bianchi*[1]

Purpose. To obtain quantitative data on the optic disc excavation in children affected by cerebral visual impairment (CVI) by using the Heidelberg Retinal Tomograph (HRT)-II (Heidelberg Engineering, Heidelberg, Germany).

Methods. A total of 24 subjects affected by CVI (mean age, 7.28 years) were examined: 16 in alert conditions and 8 under general anesthesia. The following parameters of the optic nerve head were examined: disc area, cup area, rim area, cup volume, rim volume, cup-to-disc area ratio, mean cup depth, maximum cup depth, cup shape measure, and mean retinal nerve fiber layer (RNFL) thickness. The tomographic results in children with CVI were compared with those of 88 normal, alert subjects of similar age.

Results. The optic disc of patients with CVI appeared smaller than normal. Its excavation, however, was more pronounced. Several tomographic parameters were altered in CVI-affected subjects. Statistical analysis showed a highly significant probability in cup-to-disc area ratio ($P < 0.01$, both eyes), rim area ($P < 0.01$, both eyes), cup shape measure ($P < 0.01$, right eye; $P < 0.01$, left eye), and mean RNFL thickness ($P < 0.01$, right eye; $P < 0.01$, left eye). A novel observation was temporal atrophy of the optic nerve head in CVI.

Conclusions. The data provide a tridimensional, objective evaluation of the anatomic alterations of the optic nerve head in children with CVI. Furthermore, tomographic standards for optic disc shape in normal children are set for the first time. (*Invest Ophthalmol Vis Sci.* 2006;47:484–488) DOI:10.1167/iovs.05-0529

In developed countries, cerebral visual impairment (CVI) represents one of the main causes of visual loss in children,[1,2] largely because of the improvement in neonatal reanimation techniques during the last decades, which has made possible the survival of premature newborns of increasingly lower gestational age and weight.[1–3] CVI defines the visual deficit caused by damage to the retrochiasmatic visual pathways, which include the optic radiation and both striate and extrastriate higher-order cortical centers of visual processing.[2,4] The most common cause of CVI in children is perinatal hypoxia-ischemia.[5] Other mechanisms include cerebral malformations, epilepsy, and degenerative diseases of the central nervous system.[1,2]

Ophthalmic findings often associated with CVI are fundus anomalies, refraction defects, squint, and nystagmus. Any damage of the retinal ganglion cell fibers before completion of the development of the visual system results in nerve head hypoplasia,[6,7] and previous studies of CVI mention various levels of optic nerve atrophy, including pallor, hypoplasia, and excavation of the optic nerve disc.[8–10] These findings are surprising, because retrogeniculate damage of the visual pathways does not lead to peripheral modifications in the adult. To explain the peripheral alterations caused by a central lesion, a mechanism of retrograde, transsynaptic degeneration has been suggested,[11–13] similar to that observed in monkeys with damage to the visual cortex.[12,13] In humans, alterations of the optic nerve could be related to the gestational age at which the cerebral event occurred. When periventricular leukomalacia affects premature newborns at the end of the second trimester of gestation, it is typically associated with optic nerve head (ONH) hypoplasia, whereas in the third trimester, it is associated with pseudo colobomatous cupping.[9] An earlier morphologic study of the ONH[7] was based on fundus pictures of the posterior pole and included measurements of the intraocular pressure, which happened to be normal. This approach, however, could not provide tridimensional information, and therefore it did not permit the measurement the actual loss of nerve fibers. In past decades, neuroimaging techniques have been used to study CVI; transfontanel echography is commonly used during the first months of postnatal life because of its convenience, whereas computed tomography and magnetic resonance imaging are used to localize the lesions along the visual pathways.

The Heidelberg Retina Tomograph (HRT; Heidelberg Engineering, Heidelberg, Germany) and its simplified version HRT-II, is a confocal scanning laser ophthalmoscope designed for acquisition and analysis of three-dimensional images of the posterior segment. Conceived originally for early detection and follow-up of glaucoma,[14–21] it has been successfully used in studies of glaucomatous optic neuropathy because of its good resolution and the reproducibility of its measurements.[14–22] The instrument provides morphometric parameters of the optic disc, such as cup area, rim area, cup volume, rim volume, and cup-to-disc ratio.[14]

In this study, the HRT-II was used for the first time to examine the optic disc in CVI with the purpose of providing a quantitative description of disc anomalies and to correlate our measurements with the visual performance of the patient.

From the [1]University Eye Clinic, the [3]Biometrics Service, IRCCS San Matteo Hospital, Pavia, Italy; the [4]Department of Child Neurology and Psychiatry, Regional Centre of Child Neurophthalmology, IRCCS (Instituti Ricovero e Cura a Carattere Scientifico) C. Mondino Institute of Neurology, Pavia, Italy; and the [2]Pediatric Ophthalmology Department and Child Neurorehabilitation Department, Scientific Institute IRCCS "E Medea," Bosisio Parini, Italy.

Submitted for publication April 28, 2005; revised September 30, 2005; accepted December 19, 2005.

Disclosure: **G. Ruberto**, None; **R. Salati**, None; **G. Milano**, None; **C. Bertone**, None; **C. Tinelli**, None; **E. Fazzi**, None; **R. Guagliano**, None; **S. Signorini**, None; **R. Borgatti**, None; **A. Bianchi**, None; **P.E. Bianchi**, None

The publication costs of this article were defrayed in part by page charge payment. This article must therefore be marked "*advertisement*" in accordance with 18 U.S.C. §1734 solely to indicate this fact.

Corresponding author: Giulio Ruberto, Clinica Oculistica IRCCS Policlinico S. Matteo, P. zzale Golgi 2, 27100 Pavia, Italy; rubertog@smatteo.pv.it.

Copyright © Association for Research in Vision and Ophthalmology

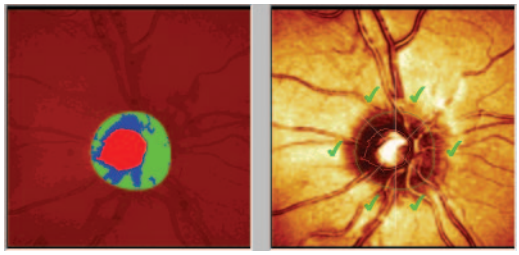

FIGURE 1. Retinal tomographic scan in an 8-year-old healthy child. Color analysis (*left*) and Moorfields analysis (*green lines*) were normal.

MATERIALS AND METHODS

We examined 24 subjects whose mean age was 7.28 ± 2.7 years. A diagnosis of CVI was confirmed after examination of the available evidence by a multidisciplinary team that included a child neurologist, an ophthalmologist, a neuroradiologist, and a psychologist. We limited our study to cerebral damage caused by hypoxia-ischemia, excluding cerebral malformations and metabolic or genetic diseases. In addition to optic disc tomography, ophthalmic tests included slit lamp and fundus examination, assessment of visual acuity (when possible), measurement of intraocular pressure with a hand-held tonometer (Tono-Pen XL; Medtronic, Jacksonville, FL) in 15 subjects, and recordings of flash-evoked visual potentials. The study was performed in 16 alert subjects. In 8 additional subjects, ophthalmic examination was particularly difficult, due to poor cooperation, roving eye movements, squint, or nystagmus. In these individuals we resorted to general anesthesia, deemed necessary because we intended to diagnose and eventually correct refractive errors that had escaped the attention of previous examiners. The parents were informed of the purpose of the procedure and their written consent was requested. Anesthesia was obtained by administering 35% nitrous oxide for 1 minute, followed by 3% sevoflurane, both in a mixture of 50% O_2-50% air through a mechanical ventilator that monitored simultaneously systemic arterial pressure and O_2 saturation in a noninvasive way. The average duration of the examination ranged from 20 to 40 minutes. On awakening, the patients were kept with their parents in the recovery room for at least 1.5 hours. The tomography results in the CVI patients were matched with those of 88 alert normal subjects of similar age (mean, 7.9 ± 2.7 years). The control subjects were selected among those referred to a Pediatric Ophthalmology Unit for suspected squint, amblyopia, or refractive errors, but otherwise found normal. All these subjects had a visual acuity of 20/20, with a refractive error ranging from +3.00 to −2.00 D; an astigmatism not higher than 2.00 D; normal anterior segment by slit lamp examination; and normal fundus by indirect ophthalmoscopy. The study was approved by the local ethics committee and was conducted according to the recommendations of Declaration of Helsinki.

Optic Disc Tomography

HRT-II is a simplified version of the Heidelberg Retinal tomograph, which permits rapid measurements of the ONH in a clinical setting. HRT-II was described elsewhere in detail.[14] Briefly, it is an automated confocal scanning laser ophthalmoscope that consists of a 670-nm diode laser and a confocal imaging system. The laser light, deflected by oscillating mirrors, scans a 15° × 15° area at the posterior pole of the eye, 1 to 4 mm in depth, with a *Z* series of 16 to 64 consecutive and equidistant (one per 16 mm) two-dimensional optical sections, with a resolution of 384 × 384 pixels. A three-dimensional image is then obtained by integrating the optical sections acquired at different, consecutive positions of the focal plane and aligned by appropriate vertical and horizontal displacements. The resolution along the *Z*-axis at each point is approximately 20 μm. The three-dimensional image of the posterior pole is then displayed on the computer monitor, and the operator can draw the contour line of the optic disc by using a computerized mouse system. Once the disc margin has been defined, the HRT software provides a series of measurements that describe the morphology of the ONH in three dimensions. Of these measurements, the following ones were considered in this study: disc area, cup area, rim area, cup-to-disc area ratio, cup volume, rim volume, mean cup depth, maximum cup depth, mean retinal nerve fiber layer (RNFL) thickness (mean thickness of the RNFL along the contour line), and cup shape measure. The last parameter mentioned depends on the depth values relative to the curved surface of the optic disc inside the contour line.[15] Cup shape measure is expressed by a number more negative than −0.15 in normal eyes with small, flat cups, or less negative than −0.15 in glaucomatous eyes with deep cups. All HRT-II images were obtained after pupil dilation (1% tropicamide administered three times) in an operating room setting. HRT-II automatically gives a sectorial evaluation of the optic disk cupping, the so-called Moorfields regression analysis[17] (Figs. 1, 3). Since this technique has been developed to identify early glaucomatous changes, we didn't utilize it for the analysis of our sample.

Statistical Analysis

Quantitative data are shown as the mean and SD. Only images were selected for this study in which the SD for the mean position of each pixel was ≤30 μm. The Shapiro-Wilk's W test was used to evaluate the distribution of the data, and, if they were normally distributed, Student's *t*-test was used for comparisons between groups. If data distribution was not normal, the nonparametric Mann-Whitney test was used. Sensitivity (probability or percentage of positive test results among patients with disease) and specificity (probability or percentage of negative test results among patients without disease) were used to evaluate the diagnostic accuracy of HRT measures. Given the known limitations of diagnostic accuracy as a parameter for measuring the diagnostic performance of a test, the statistical analysis of sensitivity and specificity was performed by means of operating characteristic (ROC) curves[23] with the calculation of the area under the curve (and its 95% confidence interval [CI]) for all the parameters. Differences in frequencies were evaluated by means of χ^2 statistics or the Fisher exact test, as appropriate. $P < 0.05$ was assumed to indicate statistical significance. All tests were two-tailed. Analyses were performed on computer (Statistica for Windows; StatSoft Inc. 2004, Tulsa, OK, and MedCalc[24]).

RESULTS

Clinical Findings and Visual Acuity

The prevalent neurologic diagnoses in our CVI sample were spastic diplegia (10 cases), tetraparesis (8 cases) and hemiparesis (5 cases). Only one subject showed less severe neurologic signs. It was possible to determine visual acuity only in 12 subjects. To this end, we used either Early Treatment Diabetic Retinopathy (ETDRS) charts (seven cases) or Teller acuity cards

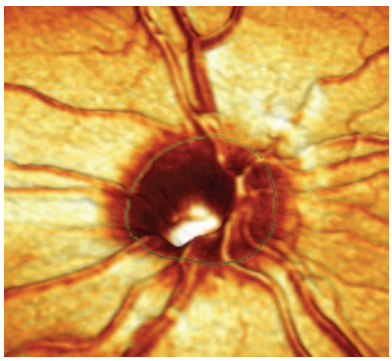

FIGURE 2. Tridimensional retinal tomographic imaging of the subject in Figure 1: the cupping was within normal limits.

TABLE 1. Optic Disc Parameters and Statistical Significance in CVI-Affected Subjects Compared with Healthy Controls

	CVI Subjects (n = 24)				Control Subjects (n = 88)					
	Mean		SD		Mean		SD		P	
	OD	OS	OD	OS	OD	OS	OD	OS	OD	OS
Disc area	2.05	1.97	0.48	0.38	2.48	2.42	0.46	0.50	0.000075	0.000163
Cup area	0.64	0.60	0.48	0.42	0.41	0.41	0.35	0.38	0.016224	0.005800
Rim area	1.40	1.30	0.49	0.41	2.03	2.01	0.47	0.44	0.000001	0.000000
Cup volume	0.23	0.13	0.50	0.12	0.09	0.10	0.13	0.15	0.045874	0.080435
Rim volume	0.42	0.29	0.28	0.18	0.52	0.52	0.23	0.32	0.032521	0.000140
Cup/disc ratio	0.30	0.33	0.21	0.19	0.16	0.16	0.11	0.12	0.001874	0.000147
Mean cup depth	0.25	0.17	0.26	0.09	0.16	0.17	0.10	0.12	0.009064	0.413672
Maximum cup depth	0.69	0.48	0.66	0.22	0.50	0.53	0.30	0.36	0.081090	0.962876
Cup shape measure	−0.15	−0.16	0.11	0.08	−0.22	−0.23	0.10	0.08	0.001681	0.000711
Mean RNFL thickness	0.15	0.10	0.16	0.11	0.21	0.24	0.08	0.13	0.003430	0.000022

(five cases). In these subjects, visual acuity ranged from 0.05 to 1 (mean, 0.46 ± 0.49).

Tomography

In normal children, tomography showed that, in general, the optic disc had lesser physiological cupping than in adults (Figs. 1, 2; Table 1).

In fact, the mean cup-to-disc area ratio was 0.16, whereas in adults the reported ratio was 0.22.[14] In patients with CVI, the mean optic disc area was smaller, the cup-to-disc ratio larger, the rim area reduced, and the optic nerve fiber layer thinner (Figs. 3, 4; Table 1).

In 14 subjects with CVI, we found an increase in the cup volume, and this alteration was especially marked in two of them. In addition, we noted that the cupping was more pronounced on the temporal side in nine of the subjects, an alteration that in the rest of this article will be referred to as temporal atrophy. Increased cup volume and temporal atrophy were present in six subjects. In patients with CVI, the mean and the maximum cup depths were deeper than in normal subjects. As expected, in patients with CVI, the rim area was smaller than in normal subjects (1.40 ± 0.49 in the right eye, 1.30 ± 0.41 in the left eye, $P < 0.000001$ and $P < 0.000000$, respectively) respect to normal children 2.03 ± 0.47 and 2.01 ± 0.44 (Table 1), suggesting a loss of fibers. The rim volume was decreased too. The cup shape measure, the number that expresses the shape of the excavation, represents one of the most important parameters in early glaucoma diagnosis. The more negative the number, the more flat and small is the cup and the shallower its depth. The cutoff for glaucoma is approximately −0.15.[16] In our CVI sample this measure was −0.15 ± 0.11 and −0.16 ± 0.08 in right and left eyes, respectively (−0.22 ± 10 and −0.23 ± 0.08 in normal children, see Table 1). Other significant probabilities were those regarding the mean RNFL thickness and the cup-to-disc ratio.

Sensitivity and Specificity

The parameter of the optic disc that exhibited the highest sensitivity (i.e., the greatest power to identify sick subjects) was the rim volume in the right eye (78.3, Table 2) and the rim area in the left eye (87.5). The parameter that had the highest specificity (i.e., the greatest power to identify healthy subjects), was the cup volume in the right eye (95.5, Table 2) and the mean RNFL thickness in the left eye (96.2). Sensitivity and specificity of each parameter decreased in parallel with the reduction of the optic disc area (in agreement with previous studies on glaucoma[15,21,22]). In our sample, 12 of 23 right eyes had hypoplastic optic discs (disc area, <1.9–2 mm) and 10 of 21 left eyes exhibited the same pathology. In only in five subjects was this finding related to low gestational age (<32 weeks). In addition, when we analyzed the data of the rim area in 23 right eyes, we noted that it was significantly reduced in 12 (<1.5 mm), and, of 21 left eyes, it was significantly reduced in 11. These findings are therefore at variance with a previous report,[9] in which the small size of the optic disc appeared correlated with lower gestational age in premature newborns, whereas an optic disc of normal size with cup excavation was associated with higher gestational age. Finally, of 23 right eyes, 9 had a significant cup excavation (>0.8 mm) and, of 21 left eyes, 9 showed the same modification. Thus, in our sample, the alteration of the optic disc is not related to the gestational age at which the pathologic event produced the anatomic and functional damage.

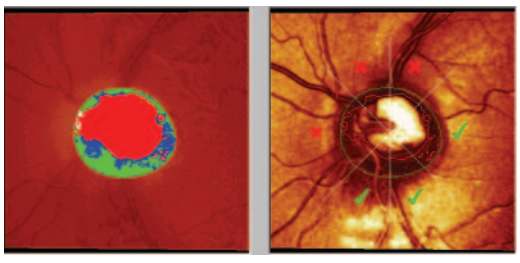

FIGURE 3. Retinal tomographic imaging in a 13-year-old CVI-affected child. Note the pronounced cupping confirmed by Moorfields analysis to be irregular at three points (*red lines*).

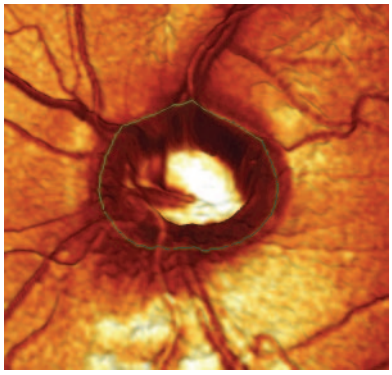

FIGURE 4. Tridimensional retinal tomographic imaging of the subject in Figure 3.

TABLE 2. Diagnostic Accuracy

	Sensibility (%)		Specificity (%)		ROC Area			
	OD	OS	OD	OS	OD	95% CI	OS	95% CI
Disc area	65.2	71.4	83.0	74.7	0.79	0.71–0.87	0.77	0.67–0.85
Cup area	52.2	76.2	78.4	53.2	0.65	0.55–0.73	0.70	0.60–0.78
Rim area	*47.8*	**87.5**	87.5	59.5	0.69	0.60–0.78	0.76	0.66–0.84
Cup volume	56.5	81.0	**95.5**	79.7	**0.83**	0.74–0.89	**0.88**	0.80–0.94
Rim volume	**78.3**	*47.6*	39.8	78.5	0.62	0.52–0.71	0.62	0.52–0.72
Cup/disc ratio	47.8	61.9	87.5	82.3	0.63	0.53–0.72	0.77	0.67–0.85
Mean cup depth	78.3	57.1	*38.6*	60.3	0.66	0.56–0.75	0.56	0.45–0.66
Maximum cup depth	78.3	71.4	*38.6*	*40.5*	*0.60*	0.50–0.69	*0.50*	0.39–0.60
Cup shape measure	60.9	81.4	73.9	68.4	0.71	0.62–0.79	0.74	0.64–0.82
Mean RNFL thickness	47.8	57.1	92.0	**96.2**	0.68	0.59–0.77	0.80	0.71–0.87

Data show sensibility, specificity, and ROC area Curves for the HRT main parameters. Bold type: maximum; italic type: minimum.

DISCUSSION

In this article, we provide the first tomographic description of the morphology of the ONH in children affected by CVI. In addition, because existing standards for optic disc tomography in healthy populations are exclusively concerned with adults 18 to 80 years of age, we report data obtained from a large sample of normal subjects of pediatric age (mean, 8 years; range, 4–12). Thus, our work represents the first database of optic disc tomography in children. Optic disc analysis based on bidimensional images generates useful descriptive data, but it does not provide quantitative information on the precise tridimensional anatomy of the ONH. In agreement with previous studies based on fundus examination,[8–10] we observed in subjects affected by CVI a marked hypoplasia of the optic nerve associated with a significant percentage of reduction in disc area (16% and 17% the right and left eyes, respectively; $P < 0.01$ in both eyes). Significant reductions of rim area (30% in OD, 35% in OS, $P < 0.01$) and rim volume (20% and 40% the right and left eyes, respectively; $P < 0.01$) were also found—probably due to expression of a reduced number of nerve fibers, as a result of optic nerve damage. These findings are also most likely related to a smaller scleral hole in a smaller and malformed ocular globe in CVI-affected children. Our findings confirm the observation that the ONH of children affected by CVI exhibits a more prominent pseudocolobomatous excavation.[8] In addition, we show an enlargement in the area and volume of the excavation and a significant increase in both the cup-to-disc area ratio and cup shape measure. Taking into account a mean cup shape measure of approximately −0.15 in the patient group, we could suppose that such data points out a more pronounced excavation, but a rather small one, in these subjects. This finding could represent differences in the morphologic characteristics of CVI-induced optic nerve damage compared with that in glaucomatous neuropathy. In contrast, however, with this study we show that hypoplasia and excavation may coexist in the same ONH (5/12 subjects), rather than being mutually exclusive. The reduction in both area and volume of the neuroretinal rim and in the mean nerve fiber thickness show that the central cerebral damage causes a loss of axons in the optic disc of children affected by CVI. Particularly interesting is the novel observation of a temporal atrophy, either isolated (3 subjects, 6 eyes) or associated with excavation (6 subjects, 10 eyes). This finding may be a sign of a loss of fibers of the papillomacular bundle, suggesting a severe functional damage. Compared with the glaucomatous disc, the excavation of the ONH in CVI-affected children is oriented in a more horizontal direction. Maybe the injury that occurs in the optic radiations mostly reverberates along temporal–nasal axis. Hence, for a better understanding of the correlation along the visual pathway between the damaged cerebral area and the fiber loss in the optic disc, a comparison between magnetic resonance findings, and optic tomography data in the same subjects could provide further information. If the temporal atrophy is indeed caused by a lesion of the papillomacular bundle, it should be emphasized that this tomographic finding may be a sign of a more severe visual loss. In fact, visual acuity could not be tested or was very low in all but one of the subjects with temporal atrophy (8/9), whereas in individuals who exhibited cupping alone (5/12), it ranged between 0.2 and 1. In conclusion, this study stresses the usefulness of the tomographic analysis of the ONH in diseases other than glaucoma.

References

1. Good WV, Jan JE, Desa L, Barkovich AJ, Groenveld M, Hoyt CS. Cortical visual impairment in children. *Surv Ophthalmol.* 1994;38:351–364.
2. Good WV, Jan JE, Burden SK, Skoczenski A, Candy R. Recent advances in cortical visual impairment. *Dev Med Child Neurol.* 2001;43:56–60.
3. Hagberg B, Hagberg G, Zetterstrom R. Decreasing perinatal mortality-increasing cerebral palsy morbidity? *Acta Pediatr Scan.* 1989;78:664–670.
4. Brodsky MC, Fray KJ, Glasier CM. Perinatal cortical and subcortical visual loss. *Ophthalmology.* 2002;109:85–94.
5. Pike MG, Holmstrom G, De Vries LS et al. Patterns of visual impairment associated with lesions of the preterm infant brain. *Dev Med Child Neurol.* 1994;36:849–862.
6. Margaleth D, Jane JE, McCormick AQ, et al. Clinical spectrum of congenital optic nerve hypoplasia: review of 51 patients. *Dev Med Child Neurol.* 1984;26:311–322.
7. Jacobson L, Helström A, Flodmark O. Large cups in normal-sized optic discs. A variant of optic nerve hypoplasia in children with periventricular leukomalacia. *Arch Ophthalmol.* 1997;115:1263–1269.
8. Jacobson L. Visual dysfunction and ocular signs associated with periventricular leukomalacia in children born preterm. *Kongl Carolinska Medico Chirurg Inst.* Stockolm, Sweden; 1998. Doctoral thesis.
9. Jacobson L, Hård AL, Svensson E, Flodmark O, Helström A. Optic disc morphology may reveal timing of insult in children with periventricular leucomalacia and/or periventricular haemorrhage. *Br J Ophthalmol.* 2003;87:1345–1349.
10. Brodsky MC, Glasier CM. Optic nerve hypoplasia: clinical significance of associated central nervous system abnormalities on magnetic resonance imaging. *Arch Ophthalmol.* 1993;111:66–74.

11. Uggetti C, Egitto M, Bianchi PE, et al. Transynaptic degeneration of lateral geniculate bodies in blind children: in vivo MR demonstration. *Am J Neuroradiol.* 1997;18:233–238.
12. Cowey A. Atrophy of retinal ganglion cells after removal of striate cortex in rhesus monkey. *Perception.* 1974;3:257–260.
13. Johnson H, Cowey A. Transneuronal retrograde degeneration of retinal ganglion cells following restricted lesions of striate cortex in the monkey. *Exp Brain Res.* 2000;132:269–275.
14. Rohrschneider K, Burk RO, Volcker HE. Comparison of two laser scanning tomography systems for three-dimensional analysis of the optic papilla. *Ophthalmologe.* 1993;90:613–619.
15. Iester M, Mikelberg FS, Courtright P, et al. Correlation between the visual field indices and Heidelberg retina tomograph parameters. *J Glaucoma.* 1997;6:78–82.
16. Iester M, Mikelberg FS, Swindale NVP, Drance SM. ROC analysis of Heidelberg Retina Tomograph optic disc shape measure in glaucoma. *Can J Ophthalmol.* 1997;32:382–388.
17. Wollstein G, Garway-Heath DF, Hitchings RA. Identification of early glaucoma cases with the scanning laser ophthalmoscope. *Ophthalmol.* 1998;105:1557–1563.
18. Teesalu P, Vihanninjoki K, Airaksinen PJ, et al. correlation of blue-on-yellow visual fields with scanning confocal laser optic disc measurements. *Invest Ophthalmol Vis Sci.* 1997;38:2452–2459.
19. Weinreb RN, Zangwill L, Berry CC, Bathija R, Sample PA. Detection of glaucoma with scanning laser polarimetry. *Arch Ophthalmol.* 1998;116:1583–1589.
20. Eid TM, Spaeth GL, Katz U et al. Quantitative estimation of retinal nerve fiber layer height in glaucoma and visual field. *J Glaucoma.* 1997;6:221–230.
21. Iester M, Courtright P, Mikelberg FS. Retinal nerve fiber layer height in high-tension glaucoma and normal eyes. *J Glaucoma.* 1998;7:1–7.
22. Chauhan BC, LeBlanc RP, McCormick TA, Rogers JB. Test-retest variability of topographic measurements with confocal scanning laser tomography in patients with glaucoma and control subjects. *Am J Ophthalmol.* 1994;118:9–15.
23. Metz CE. Basic principles of ROC analysis. *Semin Nucl Med.* 1978;8:283–298.
24. Schoonjans F, Zalata A, Depuydt CE, Comhaire FH. MedCalc: a new computer program for medical statistics. *Comput Methods Programs Biomed.* 1995;48:257–262.