REVERSAL OF OPTIC DISC CUPPING WITH IMPROVEMENT OF VISUAL FIELD AND STEREOMETRIC PARAMETERS AFTER TRABECULECTOMY IN YOUNG ADULT PATIENTS. (TWO CASE REPORTS)

SWINNEN S., STALMANS I., ZEYEN T.

ABSTRACT

The authors report two cases of mid- to long-term reversal of optic disc cupping after trabeculectomy with mitomycine-C in young adult patients suffering from secondary glaucoma. The cup to disc ratio reversed from 0.80 and 0.60 to 0.65 and 0.40 respectively and remained unchanged until the last follow-up visit at 6 and 36 months respectively. Concomitantly, there was an improvement of the visual field and of the optic disc stereometric parameters on the Heidelberg Retina Tomograph.

KEYWORDS

Intraocular pressure, optic disc imaging, reversal of optic disc cupping, secondary glaucoma, young adult

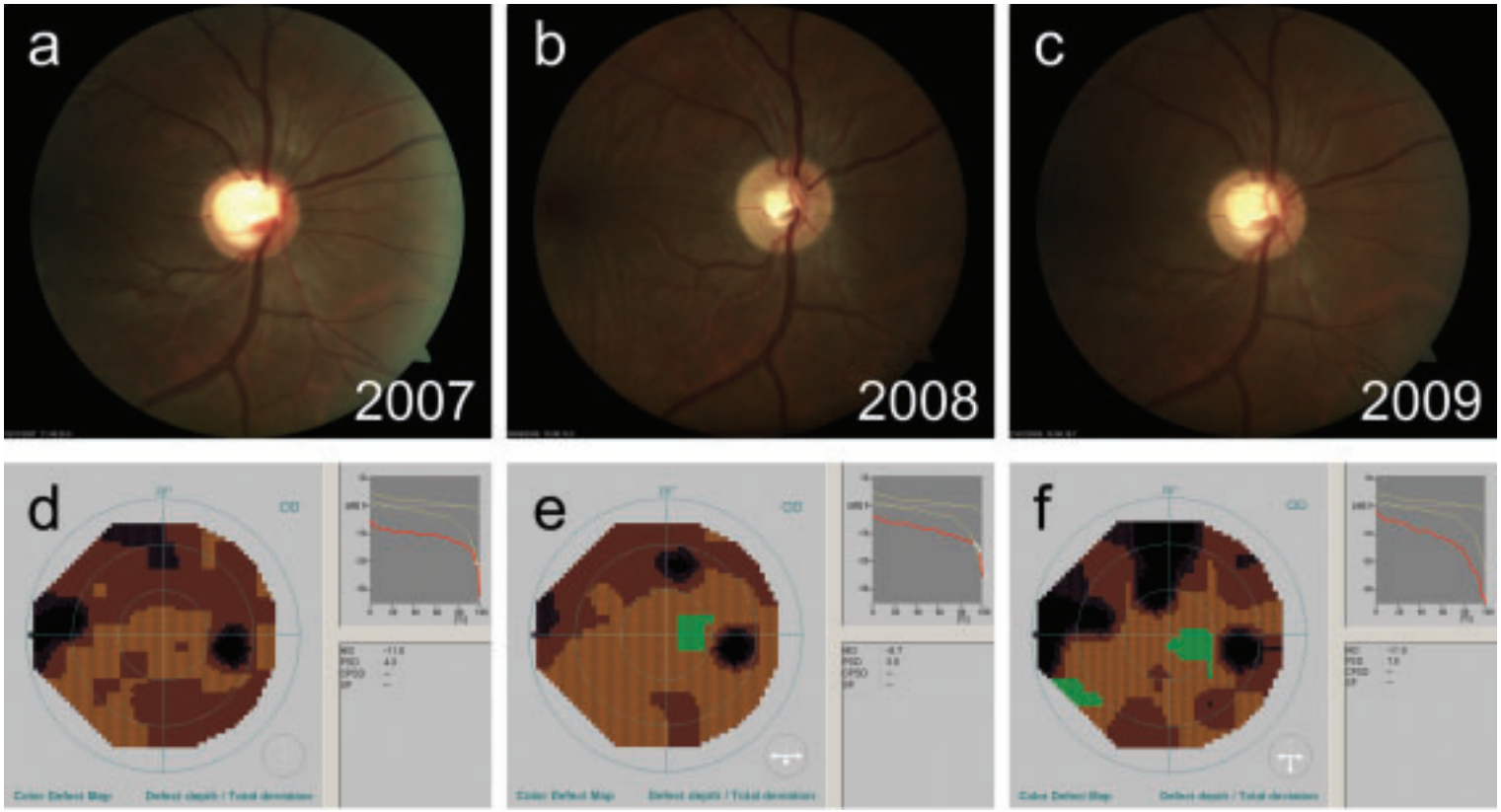
INTRODUCTION

Cup to disc reversal is a phenomenon that results in a smaller cup to disc ratio. It has been described after intraocular pressure (IOP) reduction in children with developmental and/or secondary glaucoma, but it happens less frequently in adults and is then in most cases transient. We present two patients, a 33-year-old woman and a 14-year-old boy, with secondary glaucoma and documented optic disc reversal after trabeculectomy for 6 and 36 months respectively. The reversal of optic disc cupping in these patients was combined with improvement of the visual field, transiently in one patient and long-term in the other one.

CASE REPORT 1

A 33-year-old woman with bilateral recurring idiopathic hypertensive uveitis was referred in 2000 with secondary glaucoma and intraocular pressures (IOP) up to 46 mmHg in both eyes. The IOP normalised with a combination of Timolol 0.5% and Dorzolamide 2% (Cosopt®) + Brimonidine 0.1% (Alphagan®) eye drops twice daily OU and Acetazolamide (Diamox®) 2 × 250 mg per day. The cup to disc ratio was 0.3 in the RE and 0.9 in the LE.

In November 2007, she was referred again because of elevated IOP. Her best-corrected visual acuity (BCVA) was 7/10 in the RE and 4/10 in the LE. The BCVA for near vision was Snellen 1 in both eyes. Slit lamp examination showed no inflammation in the anterior segment, and lens opacities in the LE more than in the RE. Gonioscopy revealed partial secondary angle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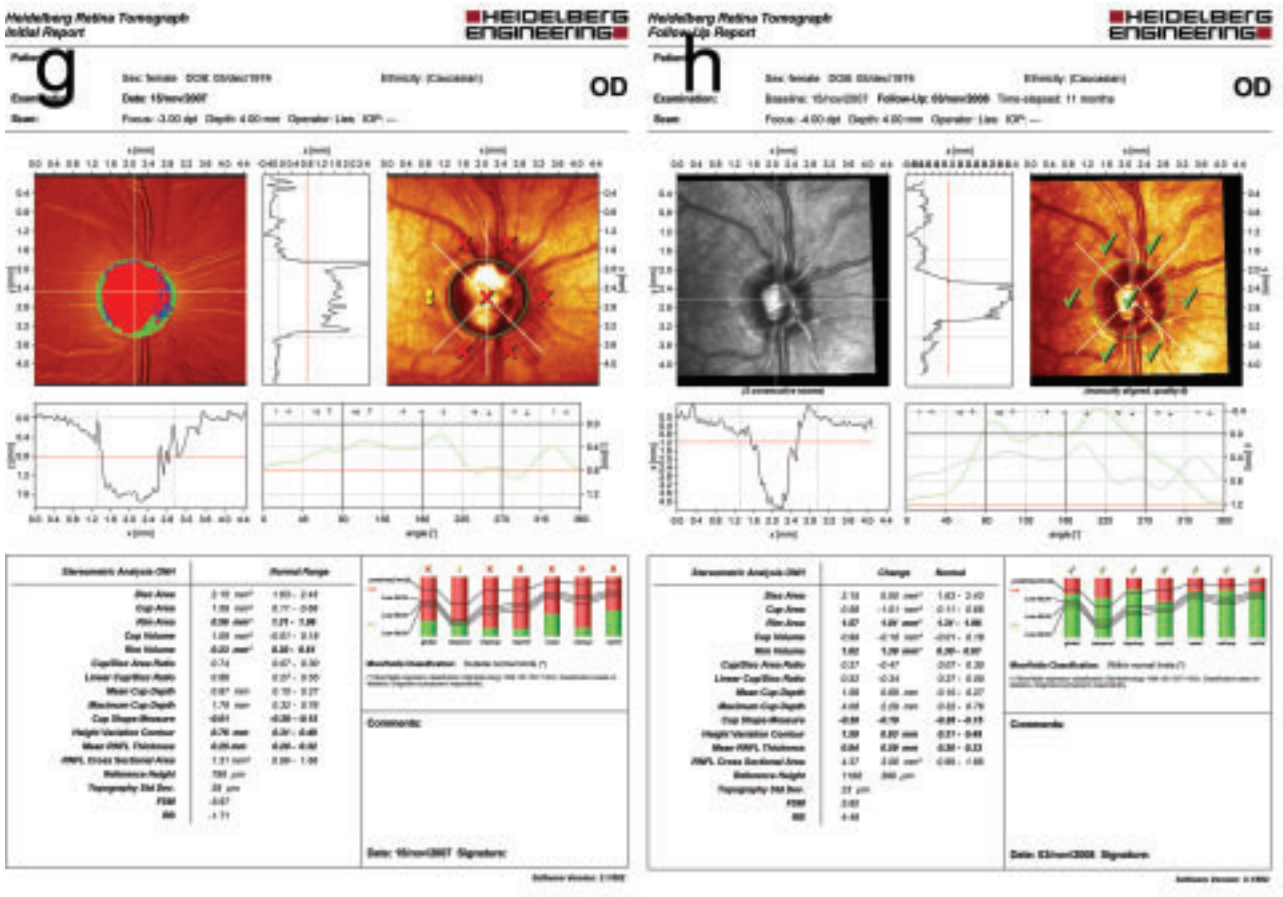
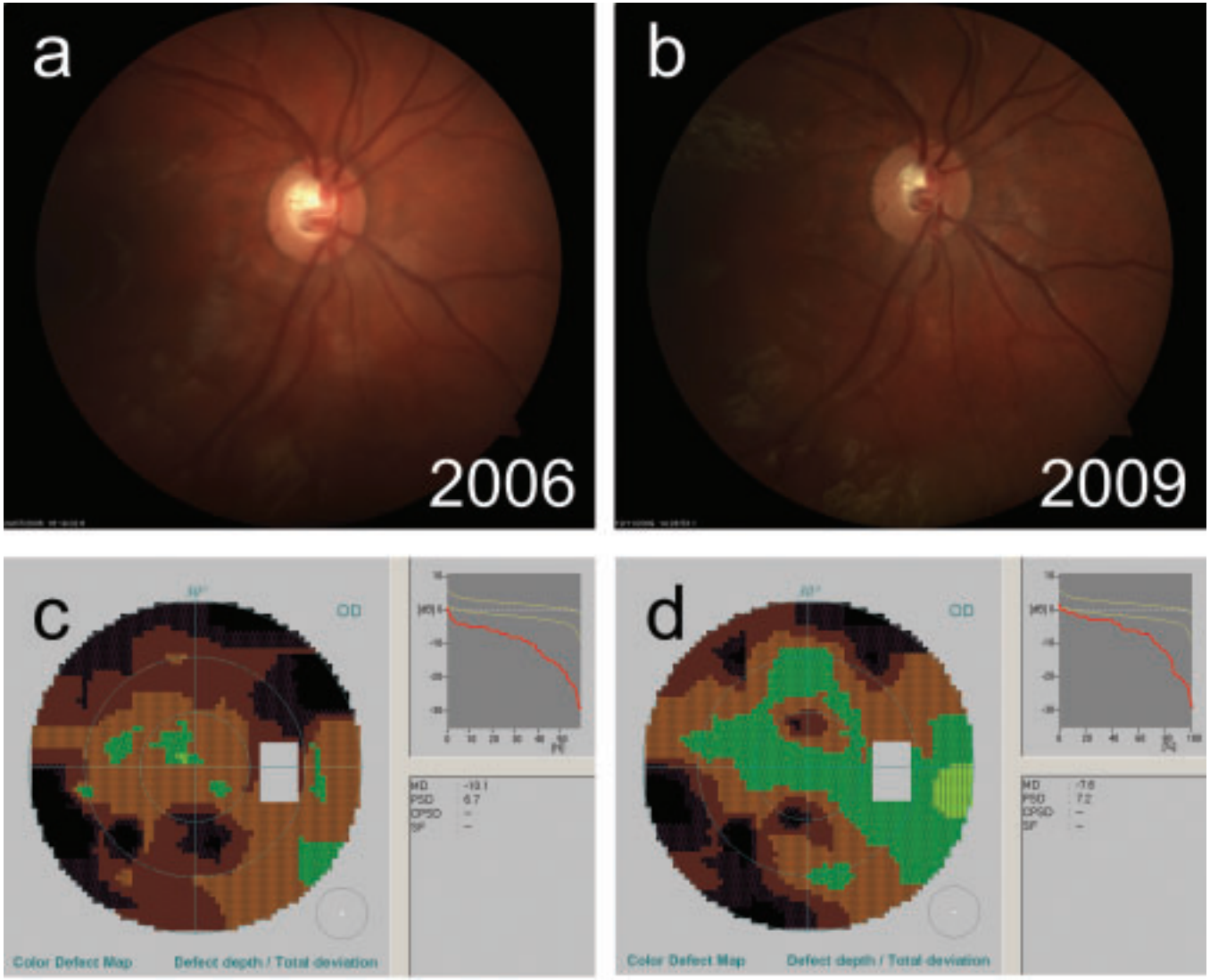


Fig. 1: **a.** Optic disc photo RE, Nov 2007, pre-trabeculectomy; **b.** Optic disc photo RE, Sept 2008, 1 month post-trabeculectomy; **c.** Optic disc photo RE, Febr 2009, 6 months post-trabeculectomy; **d.** HFA* RE, Nov 2007, pre-trabeculectomy; **e.** HFA RE, Sept 2008, 1 month post-trabeculectomy; **f.** HFA RE, Febr 2009, 6 months post-trabeculectomy; **g.** HRT** RE, Nov 2007, pre-trabeculectomy; **h.** HRT RE, Sept 2008, 1 month post-trabeculectomy.

** HFA: Humphrey Field Analyzer*
*** HRT: Heidelberg Retina Tomograph*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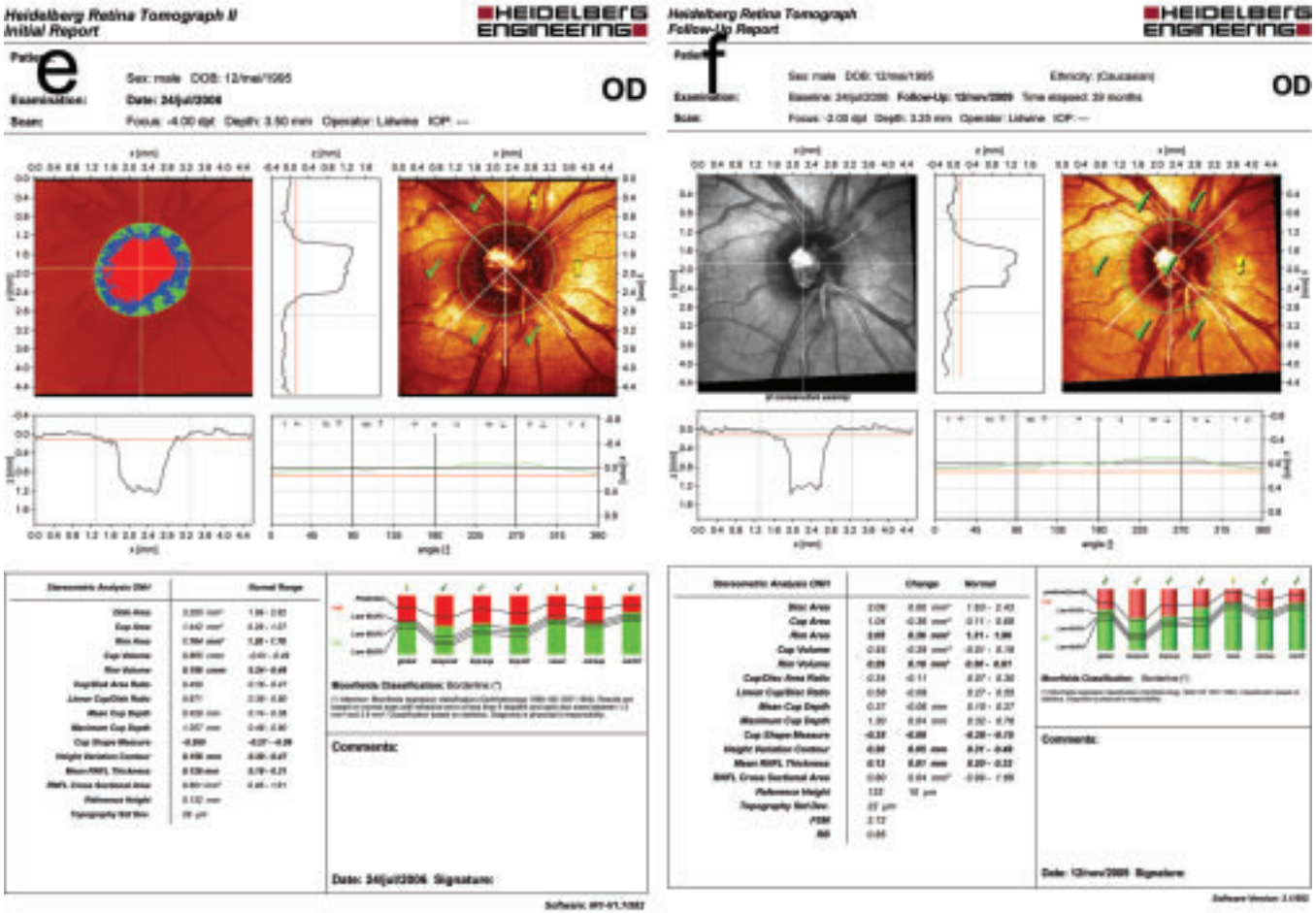

Fig. 2: **a.** Optic disc photo RE, June 2006, pre-trabeculectomy; **b.** Optic disc photo RE, Nov 2009, 36 months post-trabeculectomy; **c.** Octopus RE, June 2006, pre-trabeculectomy; **d.** Octopus RE, Nov 2009, 36 months post-trabeculectomy; **e.** HRT* RE, June 2006, pre-trabeculectomy; **f.** HRT RE, Nov 2009, 36 months post-trabeculectomy.

* *HRT: Heidelberg Retina Tomograph*

closure due to goniosynechiae OU. The IOP was 35 mmHg in the RE and 20 mmHg in the LE without treatment. Ultrasonic corneal pachymetry was normal (RE = 532 μm and LE = 529 μm). Ophthalmoscopy showed a clear vitreous and a cup to disc ratio of 0.8 in the RE (figure 1a) and 0.95 in the LE. There were no signs of macular cystoid edema on optical coherence tomography (OCT) OU. Standard automated perimetry (SAP) (Humphrey Field Analyzer, Zeiss, Oberkochen, Germany) showed early defects in the RE (figure 1d) and a superonasal defect in the LE. The baseline confocal laser scanning ophthalmoscopy (Heidelberg Retina Tomograph [HRT], Heidelberg Germany) of the RE with abnormal Moorfields Regression Analysis (MRA) is shown in figure 1g (quality score: acceptable, standard deviation (SD) 38 μm). Stereometric analysis of the optic nerve head in the RE showed a cup area of 1.59 mm^2 (normal range 0.11-0.68), a rim area of 0.56 mm^2 (normal range 1.31-1.96), a rim volume of 0.23 mm^3(normal range 0.30-0.61) and a cup volume of 1.09 mm^3 (normal range -0.01-0.18). The mean retinal nerve fiber layer (RNFL) thickness was 0.25 mm (normal range 0.20-0.32). The IOP remained in the high twenties despite maximal medical treatment (Cosopt® + Alphagan® [we preferred not to prescribe prostaglandins in this patient with uveitis]).

In the LE the cup to disc ratio remained unchanged (0.95) after trabeculectomy and cataract surgery due to a very advanced glaucoma stage. The IOP of the RE fluctuated between the mid teens and mid twenties with Cosopt® + Alphagan®. The cup to disc ratio remained 0.8 but the visual field worsened.

In September 2008 she underwent a trabeculectomy with mitomycine-C in her RE after which the IOP in this eye stabilized between 8 and 10 mmHg. The cup to disc ratio recovered from 0.8 to 0.35 (figure 1b), with concomitant improvement of the stereometric parameters (cup area 0.58 mm^2, rim area 1.57 mm^2, rim volume 1.62 mm^3, cup volume 0.99 mm^3 and mean RNFL thickness 0.84 mm) and normalization of the MRA on the follow-up HRT (quality score: good, SD 23 μm) three months after the filtering procedure (figure 1h), whereas the MD value in SAP improved from a preoperative value of -11 dB to a value of -8.7 dB (figure 1e). In the RE the visual acuity remained 7/10 and the visual field remained stable. Three months later, in February 2009, the examination showed an IOP of 10 mmHg and 12 mmHg and a cup to disc ratio of 0.65 in the RE (figure 1c). Six months after trabeculectomy the visual field in the RE showed some deterioration to a MD value of -11.9 dB (figure 1f), but the c/d ratio was still 0.65 with stable stereometric parameters on HRT (quality score: very poor, SD 55 μm). The uveitis did not recur under Rimexolon (Vexolon®) twice daily OU.

CASE REPORT 2

A 14-year-old boy, with recurring uveitis due to chronic juvenile arthritis (Still-Chauffard syndrome), developed a secondary glaucoma and cataract in the RE in 2001. The IOP fluctuated between 11 mmHg and 29 mmHg in the RE, and was normal in the LE. In 2002 he underwent a phacoemulsification with implantation of an IOL in the RE (type Hydriol 28G, PhysIOL® hydrophilic acrylic IOL).

In July 2006 he was referred because of uncontrolled IOP in the RE despite maximal medical treatment. The BCVA was 7/10 in the RE and 10/10 in the LE. The BCVA for near vision was Snellen 1 in both eyes. The IOP was 20 mmHg and 15 mmHg, respectively in the RE and LE, under Cosopt® + Alphagan® twice daily and Ketorolactrometamol (Aculare®) three times a day in the RE. Slit lamp examination showed no inflammation in the anterior segment. Gonioscopy revealed partial secondary angle closure due to goniosynechiae in the RE. Ultrasonic corneal pachymetry was 590 μm in the RE and 604 μm in the LE. Ophthalmoscopy showed a clear vitreous and a cup to disc ratio of 0.6 in the RE (figure 2a). The LE was normal with a physiological cup to disc ratio of 0.2. There were no signs of macular cystoid edema on OCT imaging OU. SAP (Octopus Field Analysis, Haag-Streit, Koeniz, Switzerland) revealed a superior and inferior defect in the RE (figure 2c) and was normal in the LE. The baseline HRT of the RE (quality score: good, SD 29 μm), with two borderline segments on MRA, is shown in figure 2e. Stereometric analysis of the optic nerve head in the RE showed a cup area of 1.44 mm^2 (normal range 0.26-1.27),

a rim area of 1.76 mm^2 (normal range 1.20-1.78), a rim volume of 0.20 mm^3 (normal range 0.24-0.49), a cup volume of 0.87 mm^3 (normal range -0.01-0.49) and a mean RNFL thickness of 0.13 mm (normal range 0.18-0.31).
The patient underwent a trabeculectomy with mitomycine-C in the RE in October 2006. Postoperatively the IOP remained stable with minor fluctuations between 8 and 12 mmHg.
In October 2007, one year postoperatively, the BCVA was 5/10 in the RE and 10/10 in the LE. The IOP was 10 mmHg in the RE and 8 mmHg in the LE with Aculare® three times daily OU and Cosopt® twice a day LE. Slit lamp examination of the RE showed a functional bleb, no cells nor flare, and calcification of the IOL. Ophthalmoscopy revealed an improved optic disc cupping (0.4) in the RE with a stable visual field.
In October 2008, two years postoperatively, the BCVA in the RE was diminished to 25/100 because of increased calcification of the IOL. The IOP was 9 mmHg and 11 mmHg, respectively in the RE and LE, under Aculare® OU and Cosopt® LE twice daily. Slit lamp examination showed no inflammation of the anterior segment.
In August 2009 he underwent an IOL exchange in the right eye. Postoperatively the BCVA was 8/10 in the RE, and the IOP remained in the low teens.
In November 2009, three years after trabeculectomy in the RE, the cup to disc ratio was still 0.4 in the RE (figure 2b). The IOP was 10 mmHg RE and 11 mmHg LE. The visual field in the RE improved from a mean defect (MD) of +10.1 dB in July 2006 (figure 2c) to MD of +7.6 dB in November 2009 (figure 2d). There was a concomitant improvement of the stereometric parameters of the follow-up HRT in the RE (quality score: good, SD 22 μm; cup area 1.04 mm^2, rim area 2.05 mm^2, rim volume 0.29 mm^3, cup volume 0.55 mm^3 and mean RNFL thickness 0.13 mm) with only one borderline segment on MRA (figure 2f).

DISCUSSION

We report two cases of reversal of optic disc cupping in young adults after trabeculectomy with mitomycine-C. To the best of our knowledge, these are the first published cases of young adult patients with documented long-term reversal of optic disc cupping combined with improvement of the visual field.
Reversal of optic disc cupping was first reported in 1869 by von Jaeger (1). It is well known that optic disc cupping can reverse after intraocular pressure reduction following glaucoma surgery in congenital or childhood glaucoma (2-8) but this happens to a lesser degree in adult glaucoma (9-16). In the literature, several authors hypothesized pathophysiological mechanisms to explain these findings.
Quigley et al considered that reversal of optic disc cupping in congenital glaucoma could be explained by the incomplete collagen structure of the lamina cribrosa during embryonic and neonatal development, which possibly results in compression or posterior movement of the tissues of the optic nerve head (17). Especially in the first year of life these changes are reversible and there is an increased elasticity of the optic nerve head in children compared to adults. Distension of the scleral canal in infants disappears with a successful IOP reduction after glaucoma surgery. Cup to disc reversal usually takes place around six weeks postoperatively. Non-reversal of cupping may be due to damage of the optic disc and loss of nerve fibers during IOP elevation or it can be the result of enlargement of the scleral canal with consequent enlargement of the optic disc and its cupping (18). In definite cupping there is an irreversible decrease in number of nerve fibers, glial cells and blood vessels, as it was the case in the LE of our first patient. In adult patients, any change in optic disc cupping after IOP reduction is minimal, transient in most cases and difficult to detect by the conventional methods.
A study of Park et al described short-term (follow-up of two months) reversal of optic disc cupping documented by HRT in adult glaucoma patients (mean age of 59.3±9.1 years) after IOP reduction following trabeculectomy (19). The mean cup/disc area ratio decreased from 0.62±0.17 to 0.54±0.17. Our two patients showed an improvement of cup to disc area ratio on HRT from 0.74 to 0.27, and from 0.45 to 0.34 respectively. The authors have speculated that an anterior movement of the lamina cribrosa occurred with a simultaneous reformation of neuroretinal tissue. Moreover they

considered an improved blood flow in that area with restoration of axoplasmic flow. Furthermore, Spaeth et al have reported that optic disc edema that develops after sudden IOP reduction, could mimic reversal of optic disc cupping ("pseudo reversal"), but that this phenomenon only lasts for maximum two months postoperatively (21). This phenomenon of pseudo reversal may have biased the results by Park et al. In our patients, the reversal of cupping lasted for 6 and 36 months respectively, indicating that this reversal was more prolonged and thus not solely attributable to transient disc edema. Of note, the recovery was indeed transiently more pronounced in our first patient for the first postoperative months, which may be explained by the overestimation due to transient optic disc swelling.

A prospective study of Harju et al used a decrease in cup volume as the HRT indicator for cup reversal because this seems to better reflect the movements of the lamina cribrosa than HRT parameters describing the nerve fiber layer thickness (20). They followed a group of 80 patients (mean age of 70 years) with exfoliation syndrome, ocular hypertension or uncontrolled exfoliation glaucoma for 6 years. A decrease in cup volume of $>5\%$ after trabeculectomy, argon laser trabeculoplasty or medical treatment was considered as cup reversal. The cup volume of our patients, who were younger, reversed from 1.09 $mm^3$to 0.99 mm^3 (-10%), and from 0.87 $mm^3$to 0.55 mm^3 (-35%), respectively after trabeculectomy.

Another prospective study from Lesk et al also found a reversal of optic disc cupping, based on HRT parameters (cup area, rim area, c/d ratio and mean cup depth) in adult patients range 33 to 80 years following an IOP reduction of $>40\%$ (22). The amount of improvement correlated with the percentage of IOP reduction. This compares favourably with our patients who showed an improvement of HRT parameters after an IOP reduction of 60%. The authors also showed that the degree of optic nerve head compliance decreased with age. Therefore age also has significant effect on the ability of the lamina cribrosa to move adequately with IOP reduction. This might be another explanation why, in our 33-year old patient, the final reversal of optic disc cupping (0.65) was less important than the initial postoperative reversal (0.35) whereas in our second, younger patient the postoperative reversal remained stable.

Recently, Parrish et al published the results of five-year follow-up of optic disc findings in the Collaborative Initial Glaucoma Treatment Study (23). They concluded that reversal of cupping, based on stereoscopic optic disc photographs occurred more frequently in the surgical group (13%) than in the medical treatment group (1%) and that reversal was associated with lower IOP, but without any significant improvement of the visual field. Our patients improved also after trabeculectomy, but, in contrast to Parrish's findings, our first patient showed an improvement in visual field for at least 3 months, our second patient even for 3 years.

CONCLUSION

We documented two young-adult patients with reversal of optic disc cupping after trabeculectomy. Concomitantly, there was an improvement of the optic disc stereometric parameters on HRT. Our second patient showed an improvement of the visual field even after 3 years. In our first patient the visual field defects had improved transiently. To the best of our knowledge, these are the first published cases of young adult patients with documented reversal of optic disc cupping combined with improvement of the visual field, although transiently in one patient. Cup to disc reversal can be minimal in adults and difficult to detect with conventional methods. According to our experience, digitized optic disc imaging with HRT makes it easier to detect minor changes in the follow-up of cup to disc ratios.

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Adress for correspondence:
Department of Ophthalmology, University Hospitals
Kapucijnenvoer, 33, 3000 Leuven BELGIUM
Fax: +32 16 332367
Tel.: +32 16 332385
Email: thierry.zeyen@uzleuven.be