Retrobulbar Optic Nerve Diameter Measured by High-Speed Magnetic Resonance Imaging as a Biomarker for Axonal Loss in Glaucomatous Optic Atrophy

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PURPOSE. To assess a novel magnetic resonance imaging (MRI) protocol for quantifying the optic nerve diameter (OND) as a measure of axonal loss in the optic nerve.

METHODS. Included in the study was one eye each from 47 subjects, of whom 9 had no eye disease, 16 had preperimetric glaucoma, 11 had a glaucomatous mean visual field defect of <10 dB and 11 of >10 dB. Each subject underwent automated perimetry, scanning laser polarimetry, optic coherence tomography, scanning laser tomography, and ultrafast high-resolution MRI at 3 T. OND was determined 5, 10, and 15 mm behind the eye with a half Fourier-acquired single-shot turbo spin-echo (HASTE)-sequence requiring 1.5 seconds of data acquisition time per slice and providing a spatial resolution of 0.11 mm. A multiple linear regression model was applied to determine correlations (r) among the different techniques.

RESULTS. The correlation (r) was <0.37 for OND measurements taken 5 mm behind the eye. At 10 mm behind the eye, r increased to 0.57 and was statistically significant in four out six instances. In the orbital apex 15 mm behind the eye, r reached a maximum of 0.80 and was statistically significant in all instances. OND correlated best with the retinal nerve fiber layer thickness measured by optic coherence tomography.

CONCLUSIONS. Retina- or optic nerve head–related surrogate markers for axonal content correlated closely with the OND, although only when it was measured in the orbital apex. High-resolution MRI using an ultrafast HASTE-sequence at 3 T proved useful for OND quantification and may be a valuable asset in future neuroprotection trials. (Invest Ophthalmol Vis Sci. 2009;50:4223–4228) DOI:10.1167/iovs.08-2683

Optic neuropathies are the second most common cause of legal blindness.1 They are the result of inflammation, ischemia, and other causes, but most often of primary open-angle glaucoma (POAG). Axonal loss related to POAG results in thinning of the retinal nerve fiber layer (RNFL) and cupping of the optic nerve head, leading to visual field (VF) defects and ultimately bilateral blindness in an estimated number of 9.4 million people worldwide in 2010.2 The interrelation between structural changes and functional deficits is referred to as the structure–function relationship and has been the subject of several studies performed mostly in POAG,3–8 but in ischemic9,10 and compressive11 optic neuropathy as well. Structural parameters of the RNFL and nerve head in POAG obtained by different technologies such as scanning laser polarimetry (SLP), scanning laser tomography (SLT), and optical coherence tomography (OCT) correlate closely.3,12–15 The comparison of these methods with standard automated perimetry (SAP) as the main procedure for assessing visual function established that measurable structural changes precede measurable functional deficits in POAG.4,5 Since axonal loss is irreversible and POAG progression can be decelerated by eye-pressure–lowering treatments, early identification of patients at risk is crucial,16 and the development of more sensitive diagnostic tools is desirable. Identification is especially important with regard to future clinical trials aimed at neuroprotection. Trials may have failed because of inefficient interventions and, perhaps, the lack of sensitive quantitative outcome measures.

As retinal ganglion cell axons project to the central nervous system, their number within the retrobulbar optic nerve may be a suitable surrogate marker for optic atrophy. Histologic studies showed that optic atrophy does indeed lead to a thinning of the retrobulbar optic nerve,17 suggesting that its diameter (OND) may correlate with the extent of optic atrophy. Diameters have been quantified by sonography, computed tomography, and magnetic resonance imaging (MRI) in POAG in previous studies, all confirming nerve thinning.18–21 Dichtl and Jonas20 assessed the OND in normal subjects and patients with glaucoma and established a close correlation between OND and neuroretinal rim area of the optic disc. Beatty et al.18 found a mean OND of 2.86 mm in normal and 2.58 mm in glaucomatous eyes using B-scan sonography. Boles Carenini et al.19 applied A-scan sonography and computed tomography in two similar cohorts. Using sonography, they observed an OND of 2.50 mm in normal and 2.28 mm in glaucomatous eyes. Computed tomography yielded 3.50 mm in normal and 2.41 mm in glaucomatous eyes. Kashwagi et al.21 measured the OND with T1-weighted MRI in normal subjects and patients with glaucoma. Control subjects exhibited 2.47 mm and patients 2.25 mm, correlating with the extent of VF defects and the cup-disc ratio. Taken together, these data reveal a wide variation in OND results, thus necessitating more precise methods of orbital imaging.

A new MRI protocol applying an ultrafast, modified HASTE sequence (half Fourier acquisition in single shot turbo spin-echo) has been recently introduced,22 which allows precise measurements of the retrobulbar OND and requiring a data acquisition time of only 1.5 seconds while providing a quantifiable spatial resolution of 0.11 mm at 3-T field strength. After establishing optic nerve diameters in normal subjects,23 we recorded data of OND in patients with POAG and correlated these measurements with the aforementioned parameters. For this purpose, we used MRI, SLP, SLT, OCT, and SAP to examine a cohort of normal subjects and patients with POAG at differ-
ent stages of progression. The purpose of the study was to evaluate how MRI measurements compare with other parameters and to add new OND data to the rather inhomogeneous set of data published so far.

**METHODS**

The study was approved by the institutional review board of our university and performed in accordance with the tenets of the Declaration of Helsinki. To compare the above-mentioned techniques, we sought to have a wide as possible spectrum in axonal content. Therefore, we included one eye in each of 9 normal subjects and 38 patients with glaucoma in various stages of the disease into this cross-sectional study. Inclusion criteria comprised an age between 18 and 85 years and a previous diagnosis of POAG based on changes in the neuroretinal rim of the optic nerve head and/or RNFL, and the appearance of VF defects, regardless of intraocular pressure. Exclusion criteria were optically significant cataract, optic nerve diseases other than glaucoma, intracranial lesions, orbital diseases, claustrophobia, metallic implants, foreign bodies, or insufficient cooperation during perimetry and fundus morphometry. All patients were informed about the purpose of the evaluation and gave informed consent. Within a 1-month period, all patients were investigated using all the following diagnostic procedures.

SAP within the central 30° was performed on a perimeter (Octopus 101; Haag-Streit AG, Kôniz, Switzerland) with the G2 glaucoma raster in a threshold-determining fashion. The mean defect (MD) was documented in each patient. Among the 38 patients with glaucoma, 16 had preperimetric glaucoma without visual field defects, 11 had an MD of <10 dB or at least three neighboring points deviating from the age-adapted norm by >4 dB, and another 11 had an MD of ≥10 dB. The healthy control subjects had a mean age of 54 years ± 16 SD, the preperimetric patients of 55 years ± 15 SD, the less progressed patients of 63 years ± 7 SD, and those ≥10 dB of 68 years ± 8 SD. According to the Aulhorn-classification,24 16 individuals had no defect and 8 had stage 1; 2 stage 2; 2 stage 3; 8 stage 4; and 2 stage 5.

The RNFL was investigated with SLP and OCT. The mean RNFL thickness was measured with SLP (GDx VCC; Laser Diagnostic Technologies, San Diego, CA) within a 0.4-mm broad band laid concentrically around the optic disc, having an internal diameter of 2.4 and external diameter of 3.2 mm. Patients with a quality index under 8 were excluded. The nerve fiber index (NFI) was recorded as well. With OCT (Glaucoma module RNFL thickness; Stratus OCT, Zeiss Humphrey, Dublin, CA) the mean RNFL thickness was determined three times in a circular scan of 3.4 mm diameter around the optic disc. Optic nerve head tomography was performed by SLT (HRT II, Heidelberg Engineering, Heidelberg, Germany). The rim area, linear cup-disc ratio, and third moment were documented.

MRI of the retrolubar optic nerve was performed 5, 10, and 15 mm behind the eye with a 3-T whole body scanner (Magneton Trio; Siemens, Munich, Germany). The OND was measured with the HASTE protocol, as published previously.22 In brief, subjects were placed in an eight-channel phased-array head coil. Inside the scanner, they fixated on a target with the right eye in primary gaze. Then an ultrafast T2-weighted HASTE sequence was applied with the following characteristics: TR, 1500 ms; TE, 146 ms; number of excitations, 1; bandwidth, 195 Hz/pixel; fast sync pulses (duration 1 ms); field of view (FOV), 23 × 18 cm²; matrix, 512 × 367; nominal spatial resolution, 0.45 × 0.49 mm²; and slice thickness, 3 mm. Interpolation to a higher matrix size of 2048 × 1468 and use of the partial volume effect of MRI22 allowed for a spatial resolution of 0.11 × 0.12 mm². In these HASTE images, cerebrospinal fluid yields a hypointense “white” signal, and the optic nerve a hypointense “dark” signal (Fig. 1). The outer diameters of the optic nerve were determined twice in masked fashion by two board-certified radiologists on a radiologic work station (J-Vision; Tiani, Vienna, Austria) by placing a circle around their outline so that the best possible fit was achieved.

Data were first analyzed via descriptive statistics. Correlations were determined among the different parameters in a Pearson correlation matrix. We then performed a multilinear regression analysis with the mean defect as the dependent variable. Since it is likely that the variability of the parameters measured in this study does not depend solely on the number of axons in the optic nerve, we performed a factor analysis of the entire data set to identify other as yet unknown factors that also contribute to overall variability. All calculations were performed with (SAS 9.1 software, applying the PROC CORR, the PROC FACTOR, and PROC REG modules; SAS, Cary, NC). Single regression analyses were performed with commercial software (Prism; Graph Pad, San Diego, CA). To assess the neuroradiologic test-retest variability of both measurements in the same MRI scans, we calculated the coefficient of variation (SD/mean).53

**RESULTS**

The extent of axonal damage varied widely, since we included both normal and glaucomatous eyes at various stages of progression. We included both on purpose, to allow for a potentially high correlation among the different parameters we were testing. In our cohort, the extent of axonal damage resulted in mean VF defects of up to 20.9 dB and an RNFL loss up to approximately 30%, as shown in Table 1. Unsurprisingly, the OND varied as well, which is shown in Table 2. Diameters were generally smaller in the orbital apex when compared to a cross-section closer to the eye. Normal individuals had a mean OND of 3.11 mm behind the eye and 2.64 mm in the orbital apex. Patients with advanced POAG in the ≥10-dB MD group showed a mean OND of 2.82 mm behind the eye and 1.96 mm in the orbital apex. This corresponds to a 26% decrease in OND in the apex and of 9% 5 mm behind the eye when comparing these two groups. The coefficients of variation as a measure of test–retest reliability were 7% when measured 5 mm behind the eye and 10% when measured 10 or 15 mm behind the eye.

To analyze the correlations among different parameters, we calculated a Pearson correlation matrix. The r-values presented in Table 3 permit the following main conclusions: With regard to the structure-function relationship, the highest correlation between the functional VF parameter and any morphologic parameter was found between the MD and the RNFL thickness measured by OCT (r = 0.80). Correlation coefficients between MD and OND were lower (r max = 0.63). Of interest, the correlations were higher in the orbital apex than 5 mm behind the eye. With regard to a correlation among the morphologic perimeters themselves, the OND correlated highest with the two SLP parameters: RNFL thickness (r = 0.72) and NFI (r = 0.73). Again, correlation coefficients were higher when the diameter of the optic nerve had been determined 15 mm behind the eye.
Table 1. Descriptive Statistics

<table>
<thead>
<tr>
<th>Test</th>
<th>n</th>
<th>Minimum</th>
<th>25% Quartile</th>
<th>Median</th>
<th>Mean</th>
<th>75% Quartile</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>SP MD (dB)</td>
<td>35</td>
<td>-2.10</td>
<td>0.20</td>
<td>2.60</td>
<td>5.30</td>
<td>10.10</td>
<td>20.90</td>
</tr>
<tr>
<td>MRI 5 (mm)</td>
<td>46</td>
<td>2.50</td>
<td>2.80</td>
<td>3.00</td>
<td>3.02</td>
<td>3.50</td>
<td>3.80</td>
</tr>
<tr>
<td>MRI 10 (mm)</td>
<td>45</td>
<td>1.60</td>
<td>2.20</td>
<td>2.40</td>
<td>2.44</td>
<td>2.75</td>
<td>3.60</td>
</tr>
<tr>
<td>MRI 15 (mm)</td>
<td>41</td>
<td>1.50</td>
<td>2.10</td>
<td>2.30</td>
<td>2.31</td>
<td>3.60</td>
<td>3.00</td>
</tr>
<tr>
<td>SLT RA (mm²)</td>
<td>47</td>
<td>0.41</td>
<td>1.03</td>
<td>1.31</td>
<td>1.29</td>
<td>1.45</td>
<td>2.64</td>
</tr>
<tr>
<td>SLT CDR</td>
<td>47</td>
<td>0.04</td>
<td>0.49</td>
<td>0.63</td>
<td>0.61</td>
<td>0.73</td>
<td>0.92</td>
</tr>
<tr>
<td>SLT 3M</td>
<td>47</td>
<td>-0.29</td>
<td>-0.20</td>
<td>-0.10</td>
<td>-0.11</td>
<td>-0.04</td>
<td>0.08</td>
</tr>
<tr>
<td>SLP NFL (µm)</td>
<td>44</td>
<td>30.49</td>
<td>41.26</td>
<td>51.98</td>
<td>50.16</td>
<td>56.98</td>
<td>68.37</td>
</tr>
<tr>
<td>SLP NFI</td>
<td>44</td>
<td>5.00</td>
<td>17.50</td>
<td>25.50</td>
<td>25.23</td>
<td>53.00</td>
<td>98.00</td>
</tr>
<tr>
<td>OCT NFL (µm)</td>
<td>45</td>
<td>21.00</td>
<td>47.00</td>
<td>83.00</td>
<td>73.96</td>
<td>96.00</td>
<td>118.00</td>
</tr>
</tbody>
</table>

SP, static perimetry; MD, mean defect; MRI 5–15, magnetic resonance imaging 5 to 15 mm behind the eye; RA, rim area; CDR, cup disc ratio; 3M, third moment; NFL, nerve fiber layer thickness; NFI, nerve fiber index.

behind the eye in the orbital apex. To test for nonlinearity, we recalculated the matrix using the Spearman correlation coefficients. In general, the r values did not increase (data not shown).

Since the correlation between OND and any other morphologic parameter was strongest for RNFL thickness measured by SLP, this correlation is shown as a linear regression analysis in Figure 2. The OND 15 mm behind the eye is the dependent and the NFI the independent variable.

To analyze the structure-function relationship further, we used a multilinear regression analysis approach with the MD acting as the dependent variable and single or combinations of structural parameters being independent variables. Table 4 indicates the highest coefficient of determination for the NFI obtained by SLP. The second highest coefficient of determination was found for the RNFL thickness measured by OCT. The coefficients of determination increased when different morphologic parameters were combined. Combining two parameters, the highest correlation was identified with RNFL thickness measured by OCT and retrobulbar OND measured 5 mm behind the eye. A coefficient of the determination of even 0.73 was obtained with three parameters combined, namely RNFL thickness measured by SLP and OCT and optic nerve diameter measured 5 mm behind the eye by MRI. OND measured at 5 mm yielded a higher correlation because the OND at 15 mm was already incorporated in the OCT and SLP data.

A rotated factor pattern analysis identified three factors loading differently on all on the investigated parameters, as shown in Table 5. These three factors together explain 97% of the overall variance. Factor 1, which primarily loads on the MD, the OND in the orbital apex, and the RNFL, explains 44% of the variance. Factor 2 accounts for 30% of the overall variance and loads mainly on parameters obtained by SLT. Factor 3 explains 25% of the variance. It seems likely that Factor 1 represents axonal loss. Factor 2 seems related to SLT parameters, and factor 3 relates to MRI-inherent properties.

Discussion

According to our literature search, this is the first investigation to apply a high-resolution MRI-protocol to the measurement of OND at different retrobulbar locations and to the evaluation of OND as a surrogate marker for glaucomatous optic atrophy by comparing it to established parameters. Obtaining these measurements became feasible with the recent introduction of HASTE sequences to orbital imaging. As MRI protocols based on HASTE sequences employ high echo times and thus detect signals mainly from water, this MRI protocol uses the fact that the optic nerve is surrounded by cerebral spinal fluid, thus allowing delineation of the optic nerve parenchyma. Another advantageous property of HASTE sequences compared to conventional sequences is their very short recording time. This results from the fact that the image is acquired from just one excitation pulse (i.e., a single shot sequence). We observed that the OND correlated with the extent of VF damage. Moreover, it correlated closely with other structural parameters such as RNFL thickness. In comparison, the OND correlated just slightly less with the MD than with RNFL-related parameters. However, there are no indications for it to replace RNFL-related parameters, also because it is incapable of detecting localized loss in the optic nerve. With regard to the structure-function relationship, multilinear regression analysis indicated that the combined consideration of different structural parameters increases the relationship. However, the addition of MRI increased this relationship only slightly. Furthermore, our investigation revealed high correlations only when the OND was measured in the orbital apex compared with measurements taken closer to the eye.

With regard to the absolute variation of OND in normal subjects among different studies, we believe that our data closely approximate the real OND, because MRI devices are calibrated, and the HASTE sequence depicts the optic nerve in high contrast. Other methods such as sonography, computed tomography and T₁-weighted MRI, do not provide such high contrast. ONDs of the normal eyes in this study are similar to the histologically determined OND, which yields a mean of 3.04 ± 1.00 mm.

That observation that optic atrophy leads to thinning of the retrobulbar portion of the optic nerve is not new. Jonas et al. demonstrated that glaucomatous optic nerves in postmortem specimens were thinner than those of normal subjects. This was reproduced several times using noninvasive imaging techniques such as A-scan sonography, B-scan sonography, computed tomography, and MRI. The corresponding publications yielded the following OND in normal subjects and patients with glaucoma, respectively: with A-scan sonography 2.87 mm versus 2.61 mm (9% loss) by Dichtl and Jonas; with B-scan sonography 2.86 mm versus 2.58 (10% loss) by Beatty et al.; with computed tomography 3.50 mm versus 2.41 mm (31% loss) again by Boles Careenini et al.; and finally with MRI 2.47 mm versus 2.25 mm (9% loss) by Kashiwagi et al. Except
for the computed tomography study, which did not explicitly
differentiate between dura and nerve parenchyma, the extent
of loss is rather uniform; however, absolute ONDs vary. All
those measurements were taken in the anterior third of the
optic nerve. The percentages of OND thinning just listed are
relatively similar to those in our investigation, which yielded a
loss of 7% in the anterior part of the nerve and 20% in the
orbital apex when comparing normal subjects with patients
with perimetric glaucoma.

The finding that is more pronounced in the orbital apex may
result from a decreased ratio of connective tissue over axonal
loss of 7% in the anterior part of the nerve and 20% in the
orbital apex when comparing normal subjects with patients
with glaucoma progression very likely results from axonal loss.

The OND decrease with glaucoma progression very likely results from axonal loss. The finding that is more pronounced in the orbital apex may result from a decreased ratio of connective tissue over axonal tissue in the orbital apex. In fact, that has been shown in histologic studies.25,26

Volumetric change in neuronal tissue within the visual path-
ways is not confined to the optic nerve. In a primate model of
glaucoma, Weber et al.27 showed that the lateral geniculate
body suffers volumetric loss as well. Similarly, the afore-
mentioned study by Kashiwagi et al.21 also reported a shortening of
the optic nerve close in the intracranial part.

Others have also identified correlations between OND and
other glaucoma-related, clinical parameters: Among the photo-
graphically determined neuroretinal rim areas and OND mea-
sured by A-scan sonography, Dichtl and Jonas20 found a corre-
lation coefficient of \( r = 0.82 \); however, their data were derived
from twice as many individuals as in our study, which revealed
\( r = 0.44 \) based on SLT. Compared with their investigation, our
study has the weakness that it did not involve more subjects.
Hence, it remains unknown whether a larger sample size
would have yielded more robust correlations. Kashiwagi et
al.21 found statistically significant correlations between ONDs
with mean VF defects \( r = 0.55 \) and the cup-to-disc ratio \( r = 0.41 \).
The correlation coefficients observed in our investiga-
tion were slightly higher: 0.63 and 0.43, respectively. A likely
source of variability of our data is the variability of OND
measurements with a coefficient of variation ranging between
7% and 10% depending on the cross-sectional plane in the
orbit. This coefficient was calculated from repeated measure-
ments of the same MRI scans and not from repeated scanning
procedures. A previous study on repeated OND scans by MRI
applying HASTE sequences in normal subjects yielded a coef-
ficient of variation between 3% and 7%.23 Further studies
applying the HASTE sequence of the optic nerve should con-
sider and evaluate this variability.

### Table 4. Multilinear Regression Analysis of the Correlation of MD with Morphologic Parameters

<table>
<thead>
<tr>
<th>( r^2 )</th>
<th>Parameters in Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.57</td>
<td>SLP NFI</td>
</tr>
<tr>
<td>0.56</td>
<td>OCT NFL</td>
</tr>
<tr>
<td>0.50</td>
<td>SLP NFL</td>
</tr>
<tr>
<td>0.45</td>
<td>MRI 15</td>
</tr>
<tr>
<td>0.37</td>
<td>MRI 10</td>
</tr>
<tr>
<td>0.69</td>
<td>OCT NFL + MRI 5</td>
</tr>
<tr>
<td>0.65</td>
<td>OCT NFL + MRI 10</td>
</tr>
<tr>
<td>0.65</td>
<td>SLP NFI + MRI 10</td>
</tr>
<tr>
<td>0.65</td>
<td>SLP NFI + MRI 15</td>
</tr>
<tr>
<td>0.65</td>
<td>SLP NFI + MRI 5</td>
</tr>
<tr>
<td>0.73</td>
<td>SLP NFL + OCT NFL + MRI 5</td>
</tr>
<tr>
<td>0.72</td>
<td>OCT NFL + OCT NFL + MRI 5</td>
</tr>
<tr>
<td>0.71</td>
<td>SLT RA + SLP NFL + MRI 5</td>
</tr>
<tr>
<td>0.70</td>
<td>SLP NFL + OCT NFL + MRI 10</td>
</tr>
<tr>
<td>0.69</td>
<td>SLP NFL + OCT NFL + MRI 10</td>
</tr>
</tbody>
</table>

MRI 5–15; magnetic resonance imaging 5–15 mm behind the eye; RA, rim area; CDR, cup disc ratio; 3M, third moment; NFL, nerve fiber layer thickness.

*\( p < 0.01 \) corrected for multiple testing.

![Linear regression analysis with retinal nerve fiber layer index NFI obtained by scanning laser polarimetry as the independent variable on the x-axis and optic nerve diameter determined 15 mm behind the eye as the dependent variable on the y-axis. Solid line: the regression line; dotted lines: 95% CI. \( r^2 = 0.53 \).](chart.png)
Apart from the OND, several other previous investigations compared VF indices, mostly with the MD, with structural parameters, applying regression analyses in most instances. Among those studies, many researchers have advocated a linear model similar to that applied here, especially with regard to POAG’s progressive course. Ajtony et al. found a correlation of \( r = 0.72 \) when comparing RNFL measurements by OCT with the MD being rather similar to our findings. Another study applied a design similar to ours, except for not including MRI. Bowd et al. showed that VF sensitivity was associated with RNFL/optic disc measurements of up to \( r^2 = 0.26 \) for SLT, \( r^2 = 0.21 \) for SLP, and \( r^2 = 0.38 \) for OCT. Hood et al. found \( r = 0.82 \) for the upper hemifield and \( r = 0.70 \) for the lower hemifield when comparing SAP with OCT. Lester et al. pointed out that, among other parameters, the NFI correlated best with the MD, as we noted in our multivariate analysis. Leung et al. observed a good concordance between OCT and SLP in POAG, with a slightly better correlation between MD and RNFL thickness when measured with OCT compared with SLP. Concerning the reproducibility of morphometric measurements, other authors maintained that SLP may be superior to OCT in less advanced cases of POAG. For the RNFL measurement with the Stratus OCT, Budenz et al. calculated a coefficient of variation of 5% for overall thickness and around 10% for single quadrants, which closely resembles our coefficients of variation regarding the OND. Taken together, the aforementioned studies correspond relatively well to our findings. Our investigation has furthermore revealed that the combined consideration of different morphologic parameters enhances the structure-function relationship, confirming previous studies.

As expected, our cohort of normal individuals and patients with glaucoma revealed high variability in all tested parameters. The factor analysis was performed to identify any factors contributing to this variation. We found three factors, that together account for 97% of the overall variation. The first factor with the strongest weight loaded mainly on the VF defect and those structural measures which most likely represent axonal contents (i.e., the OND and RNFL thickness). The other two factors loaded on and grouped different parameters of single methods only—that is, SLT and MRE. Factor 2 loads on rim area, cup-disc ratio, and the third moment, all measured by SLT. Factor 3 loads on OND at different locations. Thus, device properties seem to add to the variance, which is associated with diseases of neuronal structures, but on interindividual variation and ageing as well. Especially with regard to the influence of age, the limited number of normal compared with glaucomatous subjects does not allow assessment of its influence in our data set.


