Erlangen Glaucoma Registry:

Prospective observational clinical study including 861 eyes of 454 Caucasian subjects (239 normal eyes of 121 subjects, 250 ocular hypertensive eyes of 118 patients, 372 eyes of 215 patients with chronic open-angle glaucoma).
For 567 eyes (304 patients) with ocular hypertension or chronic open-angle glaucoma, follow-up examinations were performed with a mean follow-up time of 62.7 ± 33.2 months (median 60.8 months; range 6.2 to 124.9 months).
All patients underwent qualitative and morphometric evaluation of color stereo optic disc photographs and white-on-white visual field examination.
Progression of glaucomatous visual field damage was defined by point wise regression analysis for each of the 59 locations in the visual field. Outcome measures were qualitative and quantitative morphologic optic nerve head parameters.
Progression with respect to the optic nerve head appearnace was defined as loss of neuroretinal rim.
Central corneal thickness was measured by corneal pachymetry.
confocal laser scanning flowmetry (Heidelberg Retinal Flow Meter) in the neuroretinal rim inside of the optic disc, and in the retina close to the temporal and nasal border of the optic nerve head was performed

Purpose I. To evaluate whether the amount of glaucomatous optic nerve damage at presentation of the patient and the rate of progression of glaucoma during follow-up are related to central corneal thickness.
Results I. Central corneal thickness was significantly ($p<0.001$) and positively correlated with the area of the neuroretinal rim and negatively correlated with the loss of visual field. Development or progression of glaucomatous visual field defects detected in 119 (21.0%) eyes was statistically independent of central corneal thickness, in a univariate ($p=0.99$) as well as in a multivariate Cox regression analysis ($p=0.19$).
Conclusions I. At the time of patient referral, the amount of glaucomatous optic nerve damage was significantly correlated with a thin central cornea. Progression of glaucomatous optic nerve neuropathy was independent of central corneal thickness suggesting that central corneal thickness may not play a major role in the pathogenesis of progressive glaucomatous optic nerve damage.

Purpose II. To evaluate which morphologic features of the optic disc are predictive factors for the development, or progression, of visual field loss in chronic open-angle glaucoma.
Results II. Development or progression of glaucomatous visual field defects were detected in 106 (13.9%) eyes. At baseline of the study, neuroretinal rim area was significantly ($P<0.002$) smaller, beta zone of parapapillary atrophy ($p<0.003$, nasal sector) was significantly larger, and age was significantly higher ($p<0.003$) in the progressive study group compared with non-progressive study group. Both study groups did not vary significantly in size of the optic disc and alpha zone of parapapillary atrophy. Cox proportional hazard regression analysis revealed that the progression of glaucomatous visual field loss depended significantly on the area of the neuroretinal rim ($p<0.001$), and age ($p<0.001$). It was independent of diameter of the retinal arterioles and veins.
Conclusions II. Morphologic predictive factors for development or progression of glaucomatous visual field defects in Caucasians are small size of neuroretinal rim and large area of beta zone of parapapillary atrophy. Age is an additional non-morphological parameter. Progression of glaucomatous optic nerve head changes is independent of size of the optic disc and alpha zone of parapapillary atrophy, and retinal vessel diameter.

Purpose III. To evaluate whether various types of chronic open-angle glaucoma differ in predictive factors for progression of glaucomatous optic nerve damage.
Results III. For patients with elevated intraocular pressure, significantly predictive factors for eventual progression were older age, advanced perimetric damage, smaller neuroretinal rim, and larger area of beta zone of parapapillary atrophy. In contrast, in the normal intraocular pressure group, a significant predictive factor was presence of disc hemorrhages at baseline. Within the patients with elevated intraocular pressure, the primary open-angle glaucoma group and the secondary open-angle glaucoma group did not differ in predictive factors for progression of glaucoma.
Conclusions III. Open-angle glaucoma patients with normal intraocular pressure and open-angle glaucoma patients with elevated intraocular pressure differ in predictive factors for eventual progression of glaucomatous optic nerve damage. It may have clinical importance and may be helpful in the discussion of the pathogenesis of the glaucomas.

Purpose IV. To evaluate which morphologic features of the optic disc are predictive factors for progressive neuroretinal rim loss in chronic open-angle glaucoma.
Results IV. Progression of glaucomatous optic nerve changes was detected in 42 (11%) eyes. At baseline of the study, neuroretinal rim area was significantly (total area P=0.03) smaller and beta zone of parapapillary atrophy (total area P=0.04) was significantly larger in the progressive study group compared with non-progressive study group. Both study groups did not vary significantly in size and shape of the optic disc, optic cup depth, alpha zone of parapapillary atrophy, and diameter of the retinal arteries and veins (P>0.05). Multiple Cox-regression analysis revealed that the progression of glaucoma depended significantly on the area of the neuroretinal rim (temporal sector, P=0.003) and beta zone of parapapillary atrophy (temporal upper sector P=0.02).
Conclusions IV. Important morphologic predictive factors for progression of the glaucomatous appearance of the optic nerve head in Caucasians are small size of neuroretinal rim and large area of beta zone of parapapillary atrophy. Progression of glaucomatous optic nerve head changes is independent of size and shape of the optic disc, size of alpha zone of parapapillary atrophy, retinal vessel diameter, and optic cup depth.

Purpose V. To evaluate which optic disc parameters are predictive factors for the development of disc hemorrhages in chronic open-angle glaucoma.
Results V. At baseline of the study, neuroretinal rim area was significantly (P<0.03) smaller and beta zone of parapapillary atrophy (temporal lower sector) was significantly (P<0.03) larger in the hemorrhagic group than in the stable group. Both study groups did not vary significantly (P>0.05) in optic disc size and shape, optic cup depth, alpha zone of parapapillary atrophy, and retinal vessel diameter. In multivariate analysis, neuroretinal rim area was the only significant predictor of hemorrhages. The hemorrhagic group and the rim loss group did not differ significantly (P>0.05) in any optic disc parameter measured.
Conclusions V. In chronic open-angle glaucoma, morphologic predictive factors for the development of disc hemorrhages are small size of neuroretinal rim and, possibly, large area of parapapillary beta zone. Development of disc hemorrhages is independent of optic disc size and shape, size of alpha zone of parapapillary atrophy, retinal vessel diameter, and optic cup depth. Eyes with eventual development of disc hemorrhages and eyes with eventual progressive rim loss without observed disc hemorrhages do not differ markedly in the optic nerve head appearance.

Purpose VI. To evaluate the potentials of sequential classification strategies for individually adapted diagnostic programs in glaucoma screening.
Methods VI. In a cross-sectional clinical study, a sequential diagnostic strategy, based on several psychophysical and electrophysiological tests, was evaluated on measurements from 595 eyes from 310 patients with primary open-angle glaucoma, and 419 eyes from 213 control subjects (18-70 years either). Diagnostic reference criteria included applanation tonometry and optic disc morphometry. Patients and controls successively underwent up to five psychophysical and electrophysiological diagnostic tests. Optic disc morphometry was taken as gold standard. Adapting group sequential techniques, sensitivity and specificity for the whole diagnostic program were controled, allotting overall error rates of 10%. The criteria for the diagnostic process were developed in a learning sample (677 eyes) and verified in a validation sample (337 eyes).
Results VI. In the validation sample, 62.0% of the examined eyes could be classified, using a sequential 15-minute two-step program. An overall "gain" of saved time, compared to non-sequential discriminant analysis, of 13.6% was reached without loss of diagnostic accuracy. A sequential 45-minute five-step program classified 68.8% of the whole sample before morphometry, saving approximately 39% of examination time, compared to taking the complete discriminant score.
Conclusions VI. Especially in screening, where the use of time consuming and complicated diagnostics is restricted, the implementation of testing programs based on group sequential strategies might be a promising tool for saving personnel resources and patients' inconvenience.

Purpose VII. Examining patients with normal-pressure glaucoma, it was the study purpose to look for a relationship between morphologic optic disc parameters and hemodynamic parameters as measured by confocal laser scanning Doppler flowmetry.
Results VII. Mean confocal laser scanning flowmetric measurements in the neuroretinal rim, in the temporal parapapillary retina and the nasal parapapillary retina were significantly ($p<0.03$) lower in the normal-pressure glaucoma group than in the control group. Correspondingly, mean confocal laser scanning flowmetric measurements within the neuroretinal rim decreased significantly, with relatively low correlation coefficients, with decreasing neuroretinal rim area ($p=0.016$; correlation coefficient $r^2 = 0.026$), and increasing mean visual field

defect ($p=0.011$; $r^2 = 0.029$). They were statistically independent of alpha zone ($p=0.38$; $r^2 = 0.004$) and beta zone ($p=0.57$; $r^2 = 0.002$) of parapapillary atrophy.
Conclusions VII. In eyes with normal-pressure glaucoma, confocal laser scanning flowmetric measurements within the neuroretinal rim are lower than in an age-matched normal control group. Confocal laser scanning flowmetric measurements decrease with increasing glaucomatous optic nerve damage. There is, however, a marked variability preventing a clear relationship between stage of glaucoma and decrease in confocal laser scanning flowmetric measurements. Parapapillary atrophy is not statistically significantly correlated with confocal laser scanning flowmetric measurements in normal-pressure glaucoma.

Purpose VIII. To compare the amount of optic nerve damage in relation to intraocular pressure in highly myopic eyes with chronic open-angle glaucoma versus non-highly myopic eyes with chronic open-angle glaucoma.
(Methods VIII. The comparative clinical observational study included 1841 eyes of 1100 Caucasian patients with chronic open-angle glaucoma. The highly myopic study group consisted of 25 eyes with a myopic refractive error equal to or higher than –8 diopters. It was subdivided into eyes with an optic disc size larger than 2.7 mm^2 and eyes with an optic disc smaller than 2.7 mm^2. The control group included the remaining, non-highly myopic, eyes ($n=1816$). For all patients, a morphometric analysis of color stereo optic disc photographs was performed. Main outcome measures were morphometric optic disc measurements and intraocular pressure.)
Results VIII. In the highly myopic, large-optic-disc study group compared with the control group, maximal and minimal intraocular pressure readings were significantly ($p<0.05$) lower and neuroretinal rim area corrected for optic disc size was slightly ($p=0.16$) smaller. Comparing the total highly myopic study group with a control group adjusted for optic disc area, neuroretinal rim area was significantly ($p=0.039$) smaller in the study group with no significant difference in intraocular pressure measurements between the groups.
Conclusions VIII. At a given intraocular pressure in chronic open-angle glaucoma, optic nerve damage may be more pronounced in highly myopic eyes with large optic discs than in non-highly myopic eyes. It may suggest a higher susceptibility for glaucomatous optic nerve fiber loss in highly myopic eyes than in non-highly myopic eyes.

Purpose IX. To evaluate whether an optic disc hemifield test comparing the superior half of the optic disc with the inferior disc half, is useful for glaucoma diagnosis.
(Methods IX. The clinical observational study included 1268 patients with primary or secondary open-angle glaucoma and 649 normal subjects. The glaucoma group was divided into 1118 patients with glaucomatous visual field defects ("perimetric glaucoma"), and 150 patients with optic nerve head changes and normal visual fields („preperimetric glaucoma"). Color stereo optic disc photographs were morphometrically evaluated. The optic disc area was divided into four sectors: temporal horizontal (60°), superotemporal (90°), inferotemporal (90°), and nasal (120°). Area and width of the neuroretinal rim were measured, and the ratio of superotemporal-to-inferotemporal rim area, the ratio of superior (12 o'clock) - to - inferior (6 o'clock) rim width, the difference of inferotemporal minus superotemporal rim area, and the difference of inferior rim width minus superior rim width were calculated.)
Results IX. For the differentiation between the normal group and the whole glaucoma group, and for the differentiation between the normal group and the preperimetric glaucoma group, respectively, areas under the ROC curves were significantly smaller for the parameters of the optic disc hemifield test (superior-to-inferior rim width ratio: 0.448 and 0.412, resp.; and superotemporal-to-inferotemporal rim area ratio: 0.395 and 0.434, resp.) than for any other rim parameter tested such as inferotemporal rim area (0.827 and 0.745, reps.), total rim area (0.814 and 0.741, resp.), and superotemporal rim area (0.781 and 0.705, resp).
Discussion IX. An optic disc hemifield test with the parameters superior-to-inferior rim width ratio and superotemporal-to-inferotemporal rim area ratio is not markedly helpful for the morphometric diagnosis of glaucomatous optic nerve damage, neither in the preperimetric stage nor in the perimetric stage of the disease.

Background X. Since the central retinal vessel trunk usually located in the nasal optic disc sector can render difficult the delineation of the neuroretinal rim and optic disc, purpose of the present study was to evaluate whether the nasal region of the optic nerve head is important, or can be left out, for the morphometric glaucoma diagnosis.
Results X. Highest diagnostic power for the separation between the normal group and the perimetric glaucoma group, and for the differentiation between the normal group and the preperimetric glaucoma group, had the sum of inferotemporal rim area plus superotemporal rim area, the sum of inferotemporal rim area plus superotemporal

rim area plus temporal rim area, and the inferotemporal rim area as single parameter. The lowest diagnostic precision had the nasal rim area as single parameter or in combination with rim measurements in other disc sectors.

Discussion X. Excluding the nasal optic disc sector does not markedly decrease the diagnostic power of morphometric optic disc analysis in glaucoma diagnosis. It may have importance for an automated computerized morphometric detection of glaucomatous optic nerve damage.