



HAL
open science

Long-term perimetric fluctuation in patients with different stages of glaucoma

Paolo Fogagnolo, Chiara Sangermani, Francesco Oddone, Paolo Frezzotti, Michele Iester, Michele Figus, Antonio Ferreras, Simona Romano, Stefano Gandolfi, Marco Centofanti, et al.

► **To cite this version:**

Paolo Fogagnolo, Chiara Sangermani, Francesco Oddone, Paolo Frezzotti, Michele Iester, et al.. Long-term perimetric fluctuation in patients with different stages of glaucoma. *British Journal of Ophthalmology*, 2010, 95 (2), pp.189. 10.1136/bjo.2010.182758 . hal-00560856

HAL Id: hal-00560856

<https://hal.science/hal-00560856>

Submitted on 31 Jan 2011

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

1 Long-term perimetric fluctuation in patients with different stages of glaucoma

2
3 Paolo Fogagnolo, MD,¹ Chiara Sangermani, MD,² Francesco Oddone, MD,¹ Paolo Frezzotti,
4 MD,³ Michele Iester, MD,⁴ Michele Figus, MD, PhD,⁵ Antonio Ferreras, MD, PhD,⁶ Simona
5 Romano, MD,⁷ Stefano Gandolfi, MD,² Marco Centofanti, MD, PhD,¹ Luca Rossetti, MD,⁷ Nicola
6 Orzalesi, MD.⁷

7
8 ¹G. B. Bietti Foundation - IRCCS, Rome, Italy; ² Eye Clinic, University of Parma, Parma, Italy;
9 ³Dipartimento di Scienze oftalmologiche e Neurochirurgiche, Università degli Studi di Siena, Siena,
10 Italy; ⁴ Clinica Oculistica, Università di Genova, Genova, Italy; ⁵ Eye Clinic, Department of
11 Neuroscience, University of Pisa, Pisa, Italy; ⁶ Department of Ophthalmology, Miguel Servet
12 University Hospital, University of Zaragoza, Zaragoza, Spain; ⁷ Eye Clinic, Department of Medicine,
13 Surgery and and Dentistry, San Paolo Hospital, University of Milan, Milano, Italy.

14
15 Preliminary results presented at ARVO, Fort Lauderdale, USA, May 2007.

16 Corresponding author: Paolo Fogagnolo, MD

17 Eye Clinic, San Paolo Hospital, Via di Rudini' 8, 20142 Milano, Italy

18 t +390281844301; f +390250323150; e-mail: fogagnolopaolo@googlemail.com

19 Running title: Long-term fluctuation and GSS

20 Keywords: primary open-angle glaucoma (POAG); perimetry; visual field; long-term fluctuation;
21 long-term variability; progression; glaucoma staging system.

22 Word count: abstract: 234; manuscript: 2246.

23 Licence for Publication. The Corresponding Author has the right to grant on behalf of all authors
24 and does grant on behalf of all authors, an exclusive licence (or non exclusive for government
25 employees) on a worldwide basis to the BMJ Publishing Group Ltd to permit this article (if
26 accepted) to be published in BJO and any other BMJ PGL products and sublicences such use and
27 exploit all subsidiary rights, as set out in our licence (
28 <http://group.bmj.com/products/journals/instructions-for-authors/licence-forms>).

29 Competing Interest: None declared.

30

31

32 **ABSTRACT**

33 Purpose: To evaluate the long-term perimetric fluctuation (LF) in patients with different stages of
34 glaucoma according to the Glaucoma Staging System 2 (GSS2).

35 Methods: This multicenter retrospective study included 161 eyes of 161 stable glaucoma patients
36 undergoing 4 visual field tests (Humphrey SITA-Standard program over the central 24° or 30°) over
37 a 2-year period. For each patient, the stage of the disease was classified according to GSS2. LF
38 was then calculated as the mean of the standard deviations of point-to-point threshold sensitivities
39 in the four repetitions. LF in GSS2 stages was compared using *t*-test.

40 Results: LF progressively increased from stage 0 to stage 4, and then decreased at stage 5. Stage
41 4 had a peak of 3.19 ± 0.94 dB, with statistically significant differences compared with all the other
42 stages. The lowest LF (1.65 ± 0.60 dB) was found for normal subjects, whereas similar data were
43 found for borderline patients and those at stages 1 and 5 (2.09 ± 0.58 , 2.13 ± 0.57 , and 2.22 ± 0.89
44 dB, respectively; $P > 0.13$). Visual fields with generalized defects had lower LF (1.90 ± 0.81) than
45 those with mixed (2.84 ± 0.87 , $P = 0.0003$) and localized (2.63 ± 0.72 , $P = 0.004$) defects.

46 Conclusions: In this study we showed that the lower was the visual field defect the lower was LF,
47 except at stage 5 of GSS2. As test-retest changes exceeding LF could represent a sign of
48 progression, we suggest to clinicians using this classification system to calculate LF, in order to
49 better differentiate true progression from variability.

50

51

52 **INTRODUCTION**

53 The analysis of changes in standard automated perimetry (SAP) over time is a key element to
54 detect glaucoma progression. Four main approaches to evaluate perimetric progression are
55 available: clinical judgment of a series of tests, classification systems, event analysis, and trend
56 analysis. All these approaches are limited by the “noise” of variability, which is the result of
57 changes in the nature of the visual system, the testing situation, the features of the perimetric
58 program, and the condition of the patient.¹

59 In a regression model of any perimetric parameter over time, regression line represents the
60 expected change, whereas long-term fluctuation (LF) is an area of uncertainty both below
61 (apparent worsening) and above (apparent improvement) this line. In the clinical practice,
62 improvement of results due to LF has limited relevance (this is clearly an artefact because
63 glaucoma cannot improve by definition), whereas worsening of results due to fluctuation is
64 extremely important because LF can mask progression or even mimic glaucomatous
65 deterioration.¹

66 Several mathematical models have been proposed for measuring LF;¹⁻³ studies of normal
67 subjects, suspect glaucoma, and glaucoma patients have also shown that LF is predictable on the
68 basis of mean defect (MD).¹⁻⁶

69 Among the strategies used to evaluate the amount of visual field defect and its changes
70 over time, the Glaucoma Staging System (GSS) is gaining popularity due to its simplicity of use. By
71 plotting MD against the pattern standard deviation (PSD) or the corrected PSD (CPSD), GSS
72 classifies visual field results into 6 stages (from 0 to 5) and three types of defects (localized, mixed,
73 generalized).⁷ Recently, the system has been implemented (GSS2) by introducing a borderline
74 stage between stages 0 and 1.⁸

75 Although GSS2 may be useful in evaluating glaucoma changes at follow-up,⁹ currently
76 there are no studies measuring LF at different stages of GSS2, which is the aim of this multicenter
77 study.

78

79 **MATERIALS AND METHODS**

80 This retrospective study involved seven University Eye Clinics: Genoa, Milan (San Paolo Hospital),
81 Parma, Pisa, Roma (G.B. Bietti Foundation), Siena (Italy) and Zaragoza (Spain). It was in
82 adherence to the tenets of the Declaration of Helsinki; patients were informed about the study and
83 gave informed consent for data treatment.

84 *Patient selection*

85 This study included patients with ocular hypertension (OH) or primary open-angle glaucoma
86 (POAG), pseudoexfoliative glaucoma (PEG) or pigmentary glaucoma (PG) who fulfilled inclusion
87 and exclusion criteria. Each of the 7 centers recruited 25 cases. One eye per subject was randomly
88 selected if both eyes met the inclusion criteria.

89 The inclusion criteria were: 18 years of age or older; patients with OH, POAG, PEG, PG;
90 stability of the disease during the study period (see below for definition); visual fields performed
91 using the Humphrey Field Analyzer (HFA) II 750 (Zeiss Humphrey Systems, Dublin, Ca, USA) 24-2
92 or 30-2 test with Standard Swedish Interactive Threshold Algorithm (SITA) strategy; presence of at
93 least 4 reliable tests (<25% false-positive responses, <25% false-negative responses, and <25%
94 fixation losses) over a 2-year period. The exclusion criteria were: normal tension glaucoma;
95 secondary glaucomas; the development of cataract or any pathology affecting visual acuity and
96 visual field at any time during the study period; any change in the program used to test the patient
97 at follow-up; learning effect at visual field during the study period; neurological disorders; systemic
98 and ophthalmic disorders affecting SAP results or reliability. Diagnosis was based on chart review
99 of medical history, biomicroscopy, gonioscopy, Goldmann applanation tonometry, and indirect
100 fundus ophthalmoscopy.

101 POAG eyes were defined as having intraocular pressure (IOP) higher than 21 mmHg prior
102 medication, glaucomatous optic neuropathy (diffuse neuroretinal rim narrowing with concentric
103 enlargement of the optic cup, localized notching, or both)¹⁰ and repeatable abnormal results at
104 SAP. OH were defined as having an IOP > 21 mmHg prior medication, no ocular pathologies and
105 normal optic nerve head appearance and visual field results.

106 *Stability of the disease*

107 To be included, patients had to have no changes in mean IOP, medical regimen, optic
108 nerve head appearance at ophthalmoscopy and SAP for the duration of the study. IOP was
109 arbitrarily considered stable if changes of less than 20% in mean value (obtained from office-hour
110 curves, i.e. 4 measurements between 8 AM and 4 PM) occurred compared with the first visit.

111 A battery of visual fields was considered stable if the first and the last tests showed
112 absence of: 1) the development of a new scotoma (defined as three or more contiguous points with
113 $P < 5\%$, or two or more contiguous points with $P < 1\%$); 2) the expansion of an existing scotoma into
114 previously normal regions (defined as three or more contiguous points with $P < 5\%$, or two or more
115 contiguous points with $P < 1\%$); 3) the deepening of an existing scotoma (defined as a decrease in
116 the probability value or a reduction in sensitivity of at least 5 dB in three or more contiguous points,
117 or 10 dB or more in at least two contiguous points¹¹); and 4) a worsening probability value for any
118 perimetric index. Any change occurring in the second and third test was considered as variability.¹
119 Being stability a key point for a correct study conduction, all SAP were reviewed by an independent
120 evaluator (PF), and 5 cases were excluded for progression.

121 The stage of the disease was classified according to the GSS2 using the mean of MD and
122 PSD of the four tests. For each patient, all four tests were plotted into GSS2, and cases with
123 borderline stage (ie. two tests falling into different stages) were excluded, a fact which occurred in
124 9 cases (Figure 1).

125 *Statistical analysis.*

126 LF was calculated as the mean of the standard deviations of point-to-point threshold
127 sensitivities in the four repetitions using the following formula:

$$128 \quad LF = \frac{1}{r} \sum_{i=1}^r \sqrt{\frac{\sum_{j=1}^n (x_j - \bar{x})^2}{n-1}}$$

129 where i (ranging from 1 to r , which was 54 for 24-2 program and 76 for 30-2 program)
130 identifies the locations of the test, and j (ranging from 1 to n) is the number of tests per patient.

131 LF was then plotted against MD and PSD for each patient, Regression analysis was
132 performed and correlation was calculated for the whole dataset. Thereafter, mean LF, standard
133 deviation, and confidence intervals were calculated for each stage.

134 The analysis was performed with SPSS (version 13.0; SPSS Science Inc., Chicago, IL,
135 USA). The *t*-test was used for comparisons; $P \leq 0.05$ was considered significant. Models of linear
136 and second-degree regression were also used to inspect data associations.

137

138 **RESULTS**

139 The study was conducted on 161 Caucasian patients, whose demographics and perimetric data
140 are given in Tables 1 and 2. The populations in the 7 sites had similar characteristics (similar age,
141 MD, PSD, LF; $P > 0.10$).

142 MD was similar in patients with generalized and mixed defects ($P = 0.65$) and lower in
143 patients with localized defects ($P < 0.001$). PSD was similar in patients with mixed and localized
144 defects ($P = 0.39$) and lower in patients with generalized ($P < 0.001$, Table 2).

145 LF was plotted against MD and PSD. As shown by regression analyses in Figures 1 and 2,
146 the best fitting curves for these variables were quadratic. LF had a trough of about 1.5 dB at MD of
147 about +2 dB, it progressively increased to 3 dB, reaching a plateau for MD of about -12/-15 dB,
148 and it progressively decreased to 1.5 dB when MD worsened up to -30 dB ($y = -0.0065x^2 - 0.1719x$
149 $+ 1.9054$; $R^2 = 0.30$). Similar findings were shown for PSD: LF had a trough of 1.5 dB for null PSD;
150 it increased to 3 dB for PSD of 10 dB, and it progressively decreased to about 2 dB ($y = -0.0159x^2$
151 $+ 0.3214x + 1.3256$; $R^2 = 0.26$).

152 LF mean values and 95% intervals of confidence are given in Table 3, box plot diagrams
153 are given in Figure 4. LF progressively increased from stage 0 to stage 4, and then decreased at
154 stage 5. Stage 4 had a peak of 3.19 ± 0.94 dB, with statistically significant differences compared
155 with all the other stages ($P < 0.05$). Visual fields with generalized defects had lower LF (1.90 ± 0.81)
156 than those with mixed (2.84 ± 0.87 , $P = 0.0003$) and localized (2.63 ± 0.72 , $P = 0.004$) defects. Table
157 4 also reports the details of LF for stage and type of defects; at each stage, mixed defects had the
158 highest LF values.

159

160 **DISCUSSION**

161 Many strategies have been developed over the last years with the aim of providing an early and
162 accurate diagnosis of functional progression of glaucoma, but this task still remains tricky in a
163 number of cases due to the inability to distinguish true change from fluctuation. This clinical
164 problem is very relevant, as shown in the rigorous settings of a multicenter randomized study such
165 as the Normal Tension Glaucoma Study, on which a false call of progression of more than 50%
166 was found.¹²

167 LF is inborn on a psychophysical test such as perimetry, and it is therefore impossible to
168 get over it even at optimal clinical conditions. Mathematical models to soften the effect of LF and to
169 stabilize a series of visual fields have been recently reported,¹³ but the best way to reduce
170 variability is to reduce the clinical sources of the problem. Efforts should focus on adopting ideal
171 testing conditions (calm and comfortable room, mild illumination, use of standard operating
172 procedures) and the same perimetric strategy over time (LF largely varies between perimetric
173 strategies¹⁴).

174 Our study aimed at calculating the amount of LF in glaucoma patients with different GSS2
175 stages, which is, to the best of our knowledge, an unexplored issue. In theory, clinicians using this
176 classification system would find our data helpful to discriminate early glaucoma progression to
177 fluctuation.¹

178 As expected, patients with normal fields had low LF values (CIs ranging from 1.40 to 1.90
179 dB), with small overlap with borderline cases (inferior CIs of 1.80 dB) and glaucoma cases at stage
180 1 (1.86 dB).

181 An interesting finding of our paper was that borderline patients had MD similar to normal
182 subjects (Stage 0), and LF comparable with stage 1 (Table 3), despite a difference of more than 2
183 dB in MD and of more than 0.5 dB in PSD (Table 2). In other words, high LF values might be used
184 to predict the presence of early disease in borderline cases with normal MD. This finding needs
185 verification by properly designed studies.

186 Our paper confirmed that the relation between MD and LF is curvilinear and not linear
187 (Figure 2).^{2,15} LF progressively increased from stage 0 to stage 4, it reached a plateau for MD of
188 about -13 dB,,and then decreased when glaucoma defect became more diffuse (stage 5 had
189 intervals of confidence similar to stage 1). This curve resembles the curvilinear relation between
190 MD and PSD described by Pearson et al.,¹⁶ because they share at least two common determining
191 factors.

192 The first factor is the asymmetry of the Bebie curve, which increases as long as the
193 glaucoma defect becomes more localized, and progressively decreases in more advanced stages
194 of the disease, when both hemifields are involved. PSD is a direct measure of the asymmetry of
195 the hill of vision with respect to normal, age-matched fields. As locations on the edge of the defect
196 have higher variability,¹⁷ when a localized defect enlarges, the edge of the scotoma becomes
197 larger and LF increases, as shown by several studies.^{2,3,5,15,18-20}

198 When the defects involve both hemifields, the edge of the scotomas becomes even larger,
199 and one would therefore expect LF to increase. Actually, based on our data, LF progressively
200 decreases, probably because the effect of the enlargement of the absolute scotoma (which
201 fluctuates less than a relative scotoma¹⁷) is prevalent as both hemifields progressively deteriorate.

202 The second factor is a limitation of perimetry for high MD values. At the “bottom of the
203 scale”, very deep scotomas may be judged absolute by the perimeter; this is due to insufficient
204 stimulus size and luminance to stimulate the damaged ganglion cells. As a consequence, the
205 corresponding points can fluctuate only above their average sensitivity but not below it (inferior
206 fluctuation is not tested being sensitivity null for the perimeter). Also for this reason, both LF and
207 PSD get reduced for high MD values.

208 Caution is required when using our data in the clinical settings. Although our dataset was
209 clinical-based (the study was a retrospective analysis of data collected in glaucoma patients
210 undergoing routine visits and visual field tests every 6 months), a fixed number of tests was
211 chosen. Different LF values would be found if a variable number of tests was considered. Also, we
212 excluded patients with different GSS2 stages at the beginning and the end of the study, although
213 changes of type and stage can occur even in stable patients. Subgroup analysis was of limited

214 relevance due to the small number of cases ($n < 5$) falling in stages 1L, 2G, 3G, 4G, 5L. Our study is
215 not informative on patients with normal tension glaucoma or secondary glaucoma, although GSS2
216 is useful also to monitor these patients.

217 A strength of the study was the multicenter design; tests were double-checked to exclude
218 progression and similar inter-site demographics, perimetric and variability data were found. As
219 opposite to other studies on perimetric fluctuation which used computer-simulated dataset or visual
220 fields obtained over a short period of time, in our study routine intervals of time of 6 months were
221 maintained between tests repetitions.

222 In summary, LF is a key-point to ascertain perimetric stability or progression, regardless of
223 the strategy used to analyze visual field tests. This parameter can be easily calculated for each
224 patient and it may provide useful information in a number of cases. We suggest to clinicians using
225 GSS2 to calculate LF at least in patients with suspect progression, in order to obtain an earlier and
226 more accurate diagnosis.

227

228

229

230 **Table 1. Demographics of study participants.**

231

232		Ocular hypertension	Glaucoma
233			
234	Number of patients (%)	41(25%)	120 (75%)
235	Female/Male, n	9/12	66/54
236	Age, mean±SD (years)	53±12	64±10
237	Range (years)	34-70	46-85
238	Diagnosis (n=161)		
239	Ocular hypertension (n, %)		41 (25%)
240	Primary open-angle glaucoma (n, %)		100 (87%)
241	Pseudoexfoliative glaucoma (n, %)		15 (8%)
242	Pigmentary glaucoma (n, %)		6 (5%)

243

244 **Table 2. Perimetric data of study participants based on GSS2 staging.**

245

Stage	n (%)	MD, dB (mean ± sd)	PSD, dB (mean ± sd)
0	21 (13%)	+0.51 ± 0.95	1.57 ± 0.51
borderline	17 (11%)	-0.13 ± 1.23	2.28 ± 0.73
1	17 (11%)	-2.31 ± 1.30	2.75 ± 0.94
2	18 (11%)	-4.53 ± 1.41	4.80 ± 1.59
3	31 (19%)	-7.70 ± 1.94	8.39 ± 1.90
4	32 (19%)	-12.94 ± 2.68	11.83 ± 2.56
5	25 (16%)	-22.39 ± 4.18	9.75 ± 3.78
Generalized	17 (11%)	-12.66 ± 11.96	3.41 ± 2.30
Mixed	72 (45%)	-12.35 ± 6.41	8.79 ± 3.43
Localized	34 (21%)	-6.74 ± 4.08	9.55 ± 3.94

246

247

248 **Table 3. Long-term perimetric fluctuation and intervals of confidence.**

249

Stage	LF, dB (mean ± sd)	95%-IC, dB
0	1.65 ± 0.60	1.40 – 1.90
borderline	2.09 ± 0.58	1.80 – 2.38
1	2.13 ± 0.57	1.86 – 2.40
2	2.52 ± 0.72	2.19 – 2.85
3	2.80 ± 0.68	2.56 – 3.04
4	3.19 ± 0.94	2.87 – 3.52
5	2.22 ± 0.89	1.87 – 2.57
Generalized	1.90 ± 0.81	1.51 – 2.28
Mixed	2.84 ± 0.87	2.63 – 3.04
Localized	2.63 ± 0.72	2.39 – 2.88

250

251

252 **Inter-group t-test, P-values**

Vs	0	Borderline	1	2	3	4
5	0.05	0.13	0.68	0.23	0.01	0.0002
4	<0.0001	<0.0001	<0.0001	0.007	0.05	
3	<0.0001	<0.0001	0.0007	0.19		
2	<0.0001	0.003	0.08			
1	0.15	0.62				
borderline	0.18					

253

254 Generalized v Mixed, **P=0.0003**

255 Generalized v Localized, **P= 0.004**

256 Mixed v Localized, P=0.21

257

258 **Table 4. Test-retest perimetric variability for stage and type of defects.**

259

Stage	n	LF, dB (mean ± sd)
1 localised	4	1.68 ± 0.58
mixed	5	2.43 ± 0.60
generalised	8	2.16 ± 0.44
2 localised	7	2.55 ± 0.71
mixed	9	2.58 ± 0.73
generalised	2	2.15 ± 1.03
3 localised	12	2.70 ± 0.47
mixed	18	2.88 ± 0.81
generalised	1	2.49
4 localised	10	3.07 ± 0.69
mixed	22	3.25 ± 1.05
generalised	0	n/a
5 localised	1	1.81
mixed	18	2.53 ± 0.66
generalised	6	1.37 ± 1.03

260

261 **LEGENDS TO FIGURES**

262

263 **Figure 1.** Study flow. Gray box, patients excluded from the study.

264 **Figure 2.** Regression analysis of mean defect vs long-term fluctuation.

265 **Figure 3.** Regression analysis of pattern standard deviation vs long-term fluctuation.

266 **Figure 4.** Box plot diagrams of long-term fluctuation for different GSS2 stages. G, generalized
267 defects; M, mixed defects; L, localized defects; circles, outliers.

268

269 **REFERENCES**

- 270 1. Flammer J, Drance SM, Zulauf M. Differential light threshold. Short- and long-term fluctuation in
271 patients with glaucoma, normal controls, and patients with suspected glaucoma. *Arch Ophthalmol*
272 1984;102:704-6.
- 273 2. Fogagnolo P, McNaught A, Centofanti M, Rossetti L, Orzalesi N. The effects of intraocular
274 pressure reduction on perimetric variability in glaucomatous eyes. *Invest Ophthalmol Vis Sci.*
275 2007;48:4557-63.
- 276 3. Hutchings N, Wild JM, Hussey MK, Flanagan JG, Trope GE. The long-term fluctuation of the
277 visual field in stable glaucoma. *Invest Ophthalmol Vis Sci.* 2000;41:3429–3436.
- 278 4. Heijl A, Lindgren A, Lindgren G. Test-retest variability in glaucomatous visual fields. *Am J*
279 *Ophthalmol.* 1989;108(2):130-5.
- 280 5. Henson DB, Chaudry S, Artes PH, Faragher EB, Ansons A. Response variability in the visual
281 field: comparison of optic neuritis, glaucoma, ocular hypertension, and normal eyes. *Invest*
282 *Ophthalmol Vis Sci.* 2000;41:417-21.
- 283 6. Kwon YH, Park HJ, Jap A, Ugurlu S, Caprioli J. Test-retest variability of blue-on-yellow perimetry
284 is greater than white-on-white perimetry in normal subjects. *Am J Ophthalmol* 1998;126:29-36.
- 285 7. Brusini P. Clinical use of a new method for visual field damage classification in glaucoma. *Eur J*
286 *Ophthalmol.* 1996;6:402-7.
- 287 8. Brusini P, Filacorda S. Enhanced Glaucoma Staging System (GSS 2) for classifying functional
288 damage in glaucoma. *J Glaucoma.* 2006;15:40-6.
- 289 9. Koçak I, Zulauf M, Hendrickson P, Stümpfig D. Evaluation of the Brusini glaucoma staging
290 system for follow-up in glaucoma. *Eur J Ophthalmol.* 1997;7:345-50.
- 291 10. Tuulonen A, Airaksinen PJ. Initial glaucomatous optic disk and retinal nerve fiber layer
292 abnormalities and their progression. *Am J Ophthalmol* 1991;111:485-90.
- 293 11. Caprioli, J. Automated perimetry in glaucoma. In Walsh, T. J., *Visual fields: examination and*
294 *interpretation. Ophthalmology Monographs* (pp. 71-105). San Francisco: American Academy of
295 *Ophthalmology*, 1990.

296 12. Schulzer M. Errors in the diagnosis of visual field progression in NTG. *Ophthalmology*.
297 1994;101:1589-94.

298 13. Gonzalez de la Rosa M, Gonzalez-Hernandez M, Diaz Aleman T, Sanchez Mendez M.
299 Stabilization and comparison of TOP and Bracketing perimetric strategies using a threshold spatial
300 filter. *Graefes Arch Clin Exp Ophthalmol*. 2007;245:1303-9.

301 14. Bengtsson B, Heijl A, Olsson J. Evaluation of a new threshold visual field strategy, SITA, in
302 normal subjects *Acta Ophthalmol Scand*. 1998;76:165–169.

303 15. Boeglin RJ, Caprioli J, Zulauf M. Long-term fluctuation of the visual field in glaucoma. *Am J*
304 *Ophthalmol*. 1992;113:396-400.

305 16. Pearson PA, Baldwin LB, Smith TJ. The relationship of mean defect to corrected loss variance
306 in glaucoma and ocular hypertension. *Ophthalmologica*. 1990;200:16-21.

307 17. Haefliger IO, Flammer J. Fluctuation of the differential light threshold at the border of absolute
308 scotomas. Comparison between glaucomatous visual field defects and blind spots. *Ophthalmology*.
309 1991;98:1529-32.

310 18. Smith SD, Katz J, Quigley HA. Analysis of progressive change in automated visual fields in
311 glaucoma. *Invest Ophthalmol Vis Sci*. 1996;37:1419–1428.

312 19. Tattersall CL, Vernon SA, Menon GJ. Mean deviation fluctuation in eyes with stable Humphrey
313 24-2 visual fields. *Eye*. 2007;21:362-6.

314 20. Werner EB, Petrig B, Krupin T, Bishop KI. Variability of automated visual fields in clinically
315 stable glaucoma patients. *Invest Ophthalmol Vis Sci*. 1989;30:1083–1089.

316
317
318

319 ACKNOWLEDGEMENTS

320 We are very grateful to Dr. Paolo Brusini and Dr. Marco Zeppieri for their valuable suggestions in
321 study design.

322

FIGURE

1

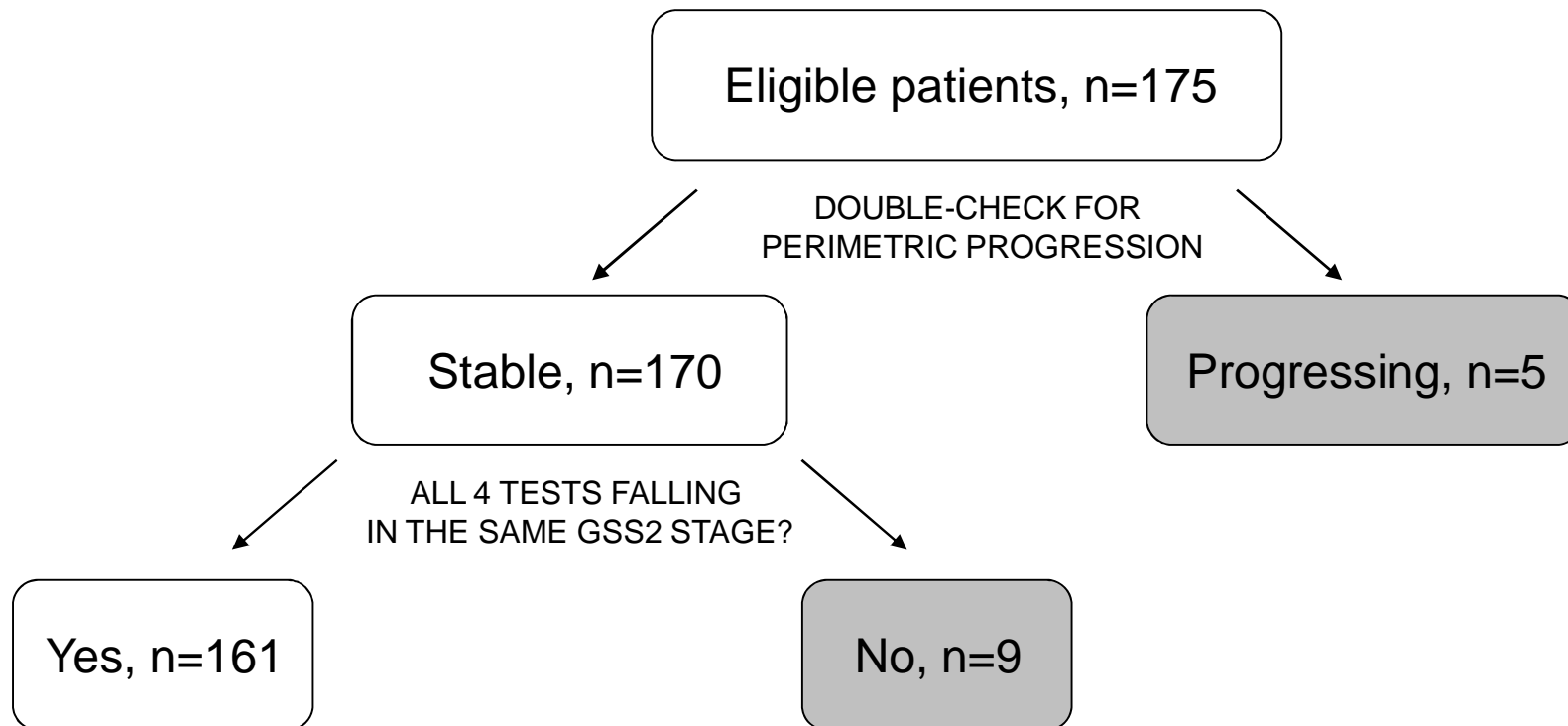


FIGURE
2

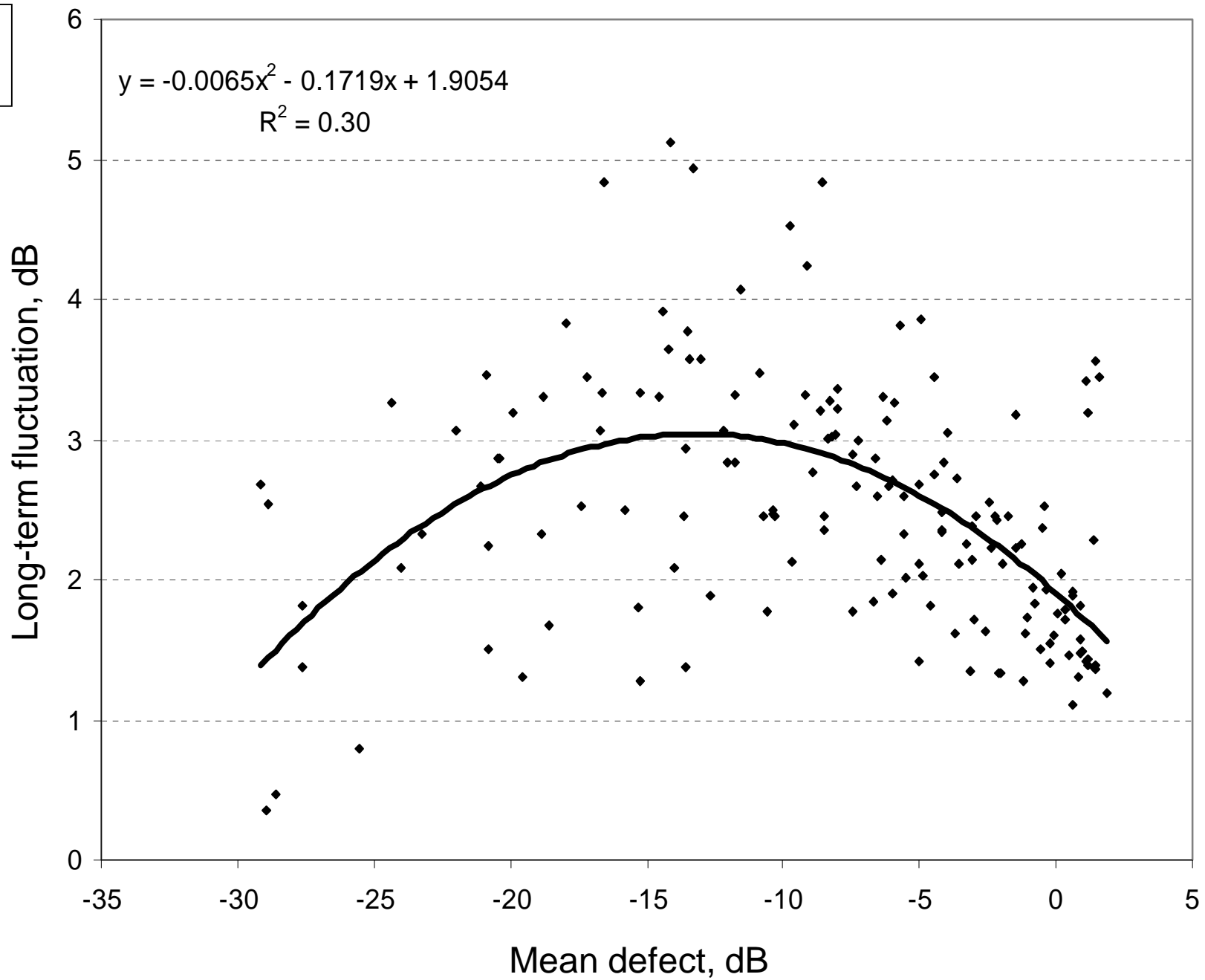


FIGURE
3

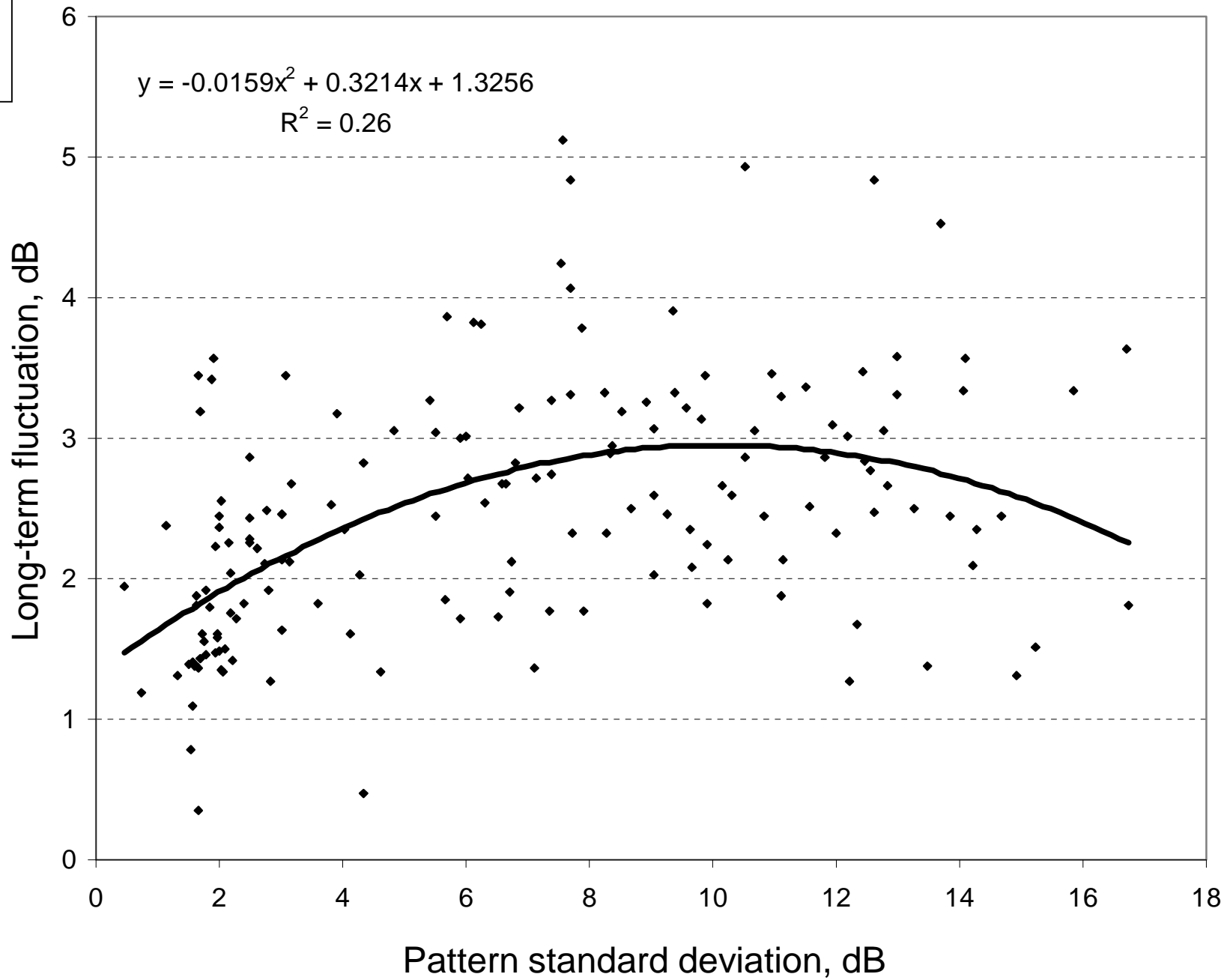


FIGURE
4

