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Citation: Wright, D. M., Konstantakopoulou, E., Montesano, G., Nathwani, N., Garg, A., Garway-Heath, D., Crabb, D. P. & Gazzard, G. (2020). Visual Field Outcomes from the Multicenter, Randomized Controlled Laser in Glaucoma and Ocular Hypertension Trial. *Ophthalmology*, 127(10), pp. 1313-1321. doi: 10.1016/j.ophtha.2020.03.029

This is the accepted version of the paper.

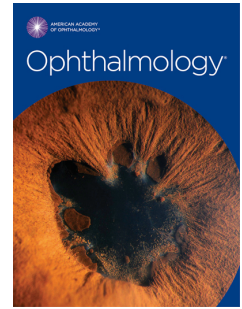
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Link to published version: <https://doi.org/10.1016/j.ophtha.2020.03.029>

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Visual Field Outcomes from LiGHT: Laser in Glaucoma and Ocular Hypertension, a multicentre, randomised controlled trial

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PII: S0161-6420(20)30313-4

DOI: <https://doi.org/10.1016/j.ophtha.2020.03.029>

Reference: OPHTHA 11182

To appear in: *Ophthalmology*

Received Date: 29 October 2019

Revised Date: 20 March 2020

Accepted Date: 23 March 2020

Please cite this article as: Wright DM, Konstantakopoulou E, Montesano G, Nathwani N, Garg A, Garway-Heath D, Crabb DP, Gazzard G, on behalf of the LiGHT Trial Study Group, Visual Field Outcomes from LiGHT: Laser in Glaucoma and Ocular Hypertension, a multicentre, randomised controlled trial, *Ophthalmology* (2020), doi: <https://doi.org/10.1016/j.ophtha.2020.03.029>.

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3

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15 Financial support: The LiGHT trial was funded by the National Institute for Health Research Health
16 Technology Assessment Panel (09/104/40) and was sponsored by Moorfields Eye Hospital NHS
17 Foundation Trust. The funding organisation or sponsor had no role in the design or conduct of this
18 research. This report presents independent research commissioned by the NIHR; the views and
19 opinions expressed by the authors in this publication are those of the authors and do not necessarily
20 reflect those of the NHS, the NIHR, MRC, CCF, NETSCC, the HTA or the Department of Health.

21 DW received funding through an MRC Innovation Fellowship (MR/S003770/1) affiliated with Health
22 Data Research UK, an initiative funded by UK Research and Innovation, Department of Health and
23 Social Care (England) and the devolved administrations, and leading medical research charities.

24 Running head: Eye drops vs SLT: visual field progression in glaucoma.

25 Acronyms

26 GPA – Guided progression analysis.

27 IOP – Intra-ocular pressure.

28 MD – Mean deviation.

29 OAG – Open angle glaucoma.

30 OHT – Ocular hypertension.

31 OR – Odds Ratio.

32 PSD – Pattern standard deviation.

33 PD – Pattern deviation.

34 SLT - Selective laser trabeculoplasty.

35 TD – Total deviation.

36 VF – Visual field.

37 Abstract

38 Objective

39 To compare visual field outcomes of ocular hypertensive and glaucoma patients treated with
40 Medicine-1st against those treated with selective laser trabeculoplasty (SLT, Laser-1st).

41 Design

42 Secondary analysis of patients from Laser in Glaucoma and Ocular Hypertension (LiGHT), a
43 multicentre randomised controlled trial.

44 Participants and controls

45 344 patients (588 eyes) treated with Medicine-1st, 344 patients (590 eyes) treated with Laser-1st.

46 Methods

47 Visual fields (VFs) were measured using standard automated perimetry and arranged in series
48 (median length and duration: 9 VFs over 48 months). Hierarchical linear models were used to
49 estimate pointwise VF progression rates, which were then averaged to produce a global progression
50 estimate for each eye. Proportions of points and patients in each treatment group with fast (< -1
51 dB/y) or moderate (< -0.5 dB/y) progression were compared using log-binomial regression.

52 Main outcome measures

53 Pointwise and global progression rates of total deviation (TD) and pattern deviation (PD).

54 Results

55 A greater proportion of eyes underwent moderate or fast TD progression in the Medicine-1st group
56 compared with the Laser-1st group (26.2% vs. 16.9%; Risk Ratio, RR = 1.55 [1.23, 1.93], $P < 0.001$). A
57 similar pattern was observed for pointwise rates (Medicine-1st 26.1% vs. Laser-1st 19.0%, RR = 1.37
58 [1.33, 1.42], $P < 0.001$). A greater proportion of pointwise PD rates were categorised as moderate or
59 fast in the Medicine-1st group (Medicine-1st 11.5% vs. Laser-1st 8.3%, RR = 1.39 [1.32, 1.46], $P <$

60 0.001). There was no statistical difference in the proportion of eyes that underwent moderate or
61 fast PD progression (Medicine-1st 9.9% vs. Laser-1st 7.1%, RR = 1.39 [0.95, 2.03], $P = 0.0928$).

62 Conclusion

63 A slightly larger proportion of ocular hypertensive and glaucoma patients treated with Medicine-1st
64 underwent rapid VF progression compared with those treated with Laser-1st.

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65 Introduction

66 Glaucoma is a progressive optic neuropathy, that left untreated can lead to loss of vision. Glaucoma
67 can have significant implications for patients and is associated with worse vision related quality of
68 life¹⁻⁴. Assessing visual function, typically done by visual field (VF) examination, is vital for clinical
69 management, especially for assessing the effectiveness of treatment in controlling the disease. VF
70 progression will usually drive treatment intensity, as lowering intra-ocular pressure (IOP) is the only
71 currently available treatment to slow the progression of glaucoma⁵.

72 Thus far, IOP lowering eye drops have been used as a 1st-line treatment for glaucoma and ocular
73 hypertension (OHT), but a recent report from the Laser in Glaucoma and Ocular Hypertension
74 (LiGHT) trial showed that selective laser trabeculoplasty (SLT), an outpatient laser procedure for the
75 reduction of IOP, provides better clinical effectiveness and lower treatment intensity among newly
76 diagnosed glaucoma and OHT patients compared to IOP lowering eye drops, and comparable health
77 related quality of life, whilst also being cost-effective⁶.

78 Although the IOP lowering efficacy of SLT has been extensively compared to that of eye drops⁷⁻¹¹
79 and despite a substantial body of research into VF progression in glaucomatous patients, little
80 evidence exists comparing SLT and IOP lowering eye drops in terms of VF outcomes. This study aims
81 to compare VF progression between patients who received SLT to those who received IOP lowering
82 eye drops, as a 1st-line treatment for glaucoma and OHT in the LiGHT trial.

83 Methods

84 Analysis cohort

85 Details of the LiGHT trial design and baseline characteristics are described elsewhere^{12,13}. Briefly, the
86 LiGHT trial is a multi-centre, randomised controlled trial comparing IOP lowering eye drops to SLT. A
87 total of 718 newly diagnosed, previously untreated OHT or open angle glaucoma (OAG) patients
88 were randomised to one of two treatment pathways. Patients in the Medicine-1st group received

89 topical IOP lowering eye drops to reduce IOP, whereas patients in the Laser-1st group received SLT
90 (followed by medication if required as the trial progressed). Subsequent treatment decisions
91 surrounding treatment escalations, repeated SLT or trabeculectomy were conducted according to
92 the study protocol with the aid of a computerised decision algorithm to avoid bias in clinical decision
93 making. The decision support algorithm used in the LiGHT trial has been described in detail
94 previously^{12,14}. Patients were treated to eye-specific IOP targets that were determined according to
95 the computer algorithm. Recruitment lasted two years and ended in October 2014. Primary
96 outcomes were reported at three years and additional funding allowed the trial to extend for a
97 further three years.

98 At each study visit, visual fields (VFs) were measured using the Humphrey Field Analyzer (HFA) with
99 Swedish interactive threshold algorithm standard 24-2 programme (Carl Zeiss Meditec, Dublin, CA,
100 USA). VF measurements were used primarily as an input (along with IOP and optic disc imaging
101 measurements) into decision support software (DSS), which generated eye-specific treatment
102 recommendations at each study visit. The secondary analysis reported here used VFs extracted from
103 the DSS database on 13th December 2018, as the trial approached the six-year mark. We constructed
104 a longitudinal series of VFs for each study eye and these formed the basis for all analyses. A total of
105 11,823 VFs were extracted from the database. Of these, we excluded 86 VFs with false positive rates
106 > 14% as potentially unreliable, and 56 eyes with very short series (< 5 VFs) as these contained little
107 information from which to estimate progression. Following these exclusions there remained 11,563
108 VFs, approximately equally distributed between treatment groups. A total of 1178 eyes from 688
109 patients (95.8% of those randomised) were included in this analysis; treatment groups had similar
110 patient baseline characteristics both to each other and to previously reported analyses^{6,13} (Table 1).
111 Median follow-up time (Medicine-1st 47 months, Laser-1st 49 months) and VF series length
112 (Medicine-1st 5630 VFs, 9 VFs per eye; Laser-1st 5933 VFs, 10 VFs per eye) were similar across
113 treatment groups.

114 Statistical analysis

115 We compared VF outcomes between groups by constructing hierarchical linear models describing
116 change in VF measures over time using the visual field data described above. A trend based method
117 of comparison was chosen because it is potentially more sensitive than event based methods such as
118 Guided Progression Analysis (GPA) for detecting progression^{15,16}, especially where the number of
119 events is expected to be small as in these early cases. We examined change at each of the 52
120 measured locations (excluding the blind spot) in each VF series, specifying a random effects
121 structure nesting locations within eyes, within individuals¹⁷. This accounted for variation in response
122 among locations, due to eye level variation and correlation between eyes within individuals,
123 respectively, whilst pooling information across the entire cohort to produce the most accurate
124 estimates. Fixed effects terms represented baseline values (equivalent to y-axis intercept [dB]) and
125 rate of change per year (slope; dB/year) in each treatment group, enabling us to simultaneously
126 evaluate (using the slope by group interaction term) the statistical evidence for a difference in
127 progression rates between groups and to estimate effect size (i.e. difference in slopes)^{16,18}.

128 Two outcome variables were modelled. Total deviation (TD) is the difference of the measured
129 sensitivity at each location from that expected for a patient of that age with no pathology. Pattern
130 deviation (PD) is the TD value at each location adjusted for generalised depression of sensitivity
131 across the VF¹⁹. Both PD and TD values were extracted from the HFA. Generalised depression and
132 changes in TD may be caused by several non-glaucomatous conditions including cataract, whereas
133 PD is designed to highlight the more localised VF changes found in glaucoma. However, glaucoma
134 almost always has a diffuse component which is ignored by PD, so it is a less sensitive measure than
135 TD and is prone to underestimation of glaucomatous damage than TD²⁰. Models were fitted in R
136 version 3.5 (R Development Core Team, R Foundation for Statistical Computing, Vienna, Austria).

137 Alongside pointwise estimates, global estimates of TD and PD progression for each study eye were
138 extracted from the models. For each eye, the estimated rate at each location was extracted; the

139 mean of these pointwise rates was calculated to give the global estimate for that eye. Pointwise
140 estimates enable better detection of spatially localised changes, whereas global estimates are useful
141 for describing diffuse changes in sensitivity.

142 To assess the clinical importance of differences between treatment groups, we categorised
143 estimated progression rates of each location and eye into one of six categories (fast progression: $-1 >$
144 slope dB/y , moderate progression: $-1 \leq \text{slope} < -0.5 \text{ dB/y}$, slow progression: $-0.5 \leq \text{slope} < 0 \text{ dB/y}$,
145 slow improvement: $0 \leq \text{slope} < 0.5 \text{ dB/y}$, moderate improvement: $0.5 \leq \text{slope} < 1 \text{ dB/y}$, fast
146 improvement: $\text{slope} \geq 1 \text{ dB/y}$. Category boundaries in the progression end (i.e. $\text{slope} < 0$) of the rate
147 distribution were based on those previously reported in studies of glaucoma progression in clinical
148 populations^{21,22}. A symmetrical set of boundaries were applied to the improvement end of the
149 distribution as a measure of variability. A tendency towards faster progression and also faster
150 improvement in one treatment group (i.e. a fatter tailed distribution) would indicate greater
151 variability in rates rather than a shift towards faster progression. We used log-binomial (relative risk)
152 regression to compare the proportion of locations and eyes in each group undergoing fast or
153 moderate progression, representing patients at the greatest risk of vision loss. These models were
154 non-hierarchical, with treatment group as the predictor and the outcome being a binary variable
155 indicating whether the estimated rates (from the hierarchical model) were above or below -0.5 dB/y .
156 At the other end of the rate distribution, the proportions of locations and eyes undergoing fast or
157 moderate improvement were compared in a similar manner.

158 We conducted a sensitivity analysis to further investigate the influence of cataract, refitting our
159 models to exclude eyes that underwent cataract removal. Similarly, eyes that underwent
160 trabeculectomy may have experienced a step increase in sensitivity after surgery. We censored VF
161 series for these eyes at time of surgery and refitted the models.

162 The study adhered to the tenets of the Declaration of Helsinki. Ethical approval was obtained from
163 local boards at each participating centre. All patients provided written informed consent before

164 participation. The study is registered at controlled-trials.com (ISRCTN32038223) and the protocol is
165 available online¹².

166 Results

167 Total deviation

168 Estimated mean pointwise total deviation decreased in both the Medicine-1st and Laser-1st groups
169 over time (mean and 95%CI: Medicine-1st = -0.25 dB/y [-0.31, -0.19]; SLT = -0.19 dB/y [-0.25, -0.13]).
170 There was little evidence for a difference in mean rates of progression between groups (slope by
171 group interaction term, $t = 1.41$, $P = 0.157$) but the distribution of estimated progression rates did
172 vary by group. Distributions of both pointwise and global estimates were more strongly left skewed
173 in the Medicine-1st group than in the Laser-1st group (Figure 1, global estimates), indicating that
174 greater proportions of locations and eyes in the Medicine-1st group showed evidence of more rapid
175 progression (Table 2).

176 One in four eyes underwent moderate or fast progression in the Medicine-1st group compared with
177 approximately one in six eyes in the Laser-1st group (Risk Ratio, RR = 1.55 [1.23, 1.93], $P < 0.001$).

178 Similarly, a greater proportion of locations was categorised as having moderate or fast progression
179 in the Medicine-1st group (RR = 1.37 [1.33, 1.42], $P < 0.001$). There was no evidence for a difference
180 between treatment groups in the proportion of eyes that underwent moderate or fast improvement
181 (RR 1.29 [0.83, 2.04], $P = 0.266$). A greater proportion of locations was categorised as having
182 moderate or fast improvement in the Medicine-1st group (RR = 1.31 [1.24, 1.39], $P < 0.001$).

183 Following exclusion of eyes that underwent cataract removal, the differences between treatment
184 groups were attenuated: eyes that underwent moderate or fast progression (RR = 1.43 [1.11, 1.83],
185 $P = 0.005$); locations (RR = 1.25 [1.21, 1.29], $P < 0.001$). Censoring VF series at trabeculectomy had
186 almost no influence on estimated differences between treatment groups (RRs not shown).

187 Pattern deviation

188 The distribution of progression estimates was similar for pattern deviation but estimated rates were
189 lower and differences between treatment groups were less pronounced than for total deviation.
190 Estimated mean pointwise pattern deviation decreased in both the Medicine-1st and Laser-1st groups
191 over time (mean and 95%CI: Medicine-1st = -0.12 dB/y [-0.16, -0.09]; Laser-1st = -0.09 dB/y [-0.13, -
192 0.06]). There was no evidence for a difference in mean rates of progression between groups ($t =$
193 1.19, $P = 0.236$) but both pointwise and global estimates were more strongly left skewed in the
194 Medicine-1st group than in the Laser-1st group (Figure 2).

195 There was no evidence for a statistical difference between treatment groups in the proportion of
196 eyes that underwent moderate or fast progression (Table 3, RR = 1.39 [0.95, 2.03], $P = 0.0928$). A
197 greater proportion of locations was categorised as having moderate or fast progression in the
198 Medicine-1st group (Table 3, RR = 1.39 [1.32, 1.46], $P < 0.001$). There was no evidence for a
199 difference between treatment groups in the proportion of eyes that underwent moderate or fast
200 improvement (RR 1.86 [0.75, 4.64], $P = 0.181$). A greater proportion of locations were categorised as
201 having moderate or fast improvement in the Medicine-1st group (RR = 1.37 [1.24, 1.51], $P < 0.001$).
202 Following exclusion of eyes that underwent cataract removal, the differences between treatment
203 groups were attenuated: eyes that underwent moderate or fast progression (RR = 1.18 [0.78, 1.77],
204 $P = 0.436$); locations (RR = 1.29 [1.22, 1.35], $P < 0.001$). Censoring VF series at trabeculectomy had
205 almost no influence on estimated differences between treatment groups (RRs not shown).

206 Baseline sensitivity, IOP and progression rates

207 Eyes that underwent fast progression or improvement had lower average sensitivity at baseline than
208 those with intermediate progression or improvement rates (Figure 3). Similarly, eyes that underwent
209 fast progression or improvement had slightly lower IOP targets set at baseline than those with

210 intermediate rates (Figure 4). There was no evidence that the distributions of baseline sensitivity or
211 IOP targets differed between treatment groups (Table 1).

212 Discussion

213 This study reports on the VF progression differences between glaucoma/OHT patients treated with
214 Medicine-1st and patients treated with Laser-1st in the LiGHT trial. Using TD values, we estimated
215 that one in four eyes had moderate or fast VF progression in the Medicine-1st group whereas in the
216 Laser-1st group this value was about one in six. The difference between groups was less pronounced,
217 with no statistical evidence for a difference, when using PD values. The proportion of pointwise rates
218 that were moderate or fast was slightly greater in the Medicine-1st group using both PD and TD.
219 These differences were not reflected at the upper ends of the rate distributions for either eyes or
220 locations, indicating that our findings were not the result of greater variability in one or other
221 treatment group.

222 The results of this study suggest that treating patients with Laser-1st may delay VF progression in
223 comparison to Medicine-1st. IOP control with eye drops may rely upon patient concordance with
224 treatment; indeed IOP lowering drops have been reportedly available to patients only 69% of the
225 time, whilst concordance may range between 76-86% with even lower figures reported for more
226 complex instillation regimes²³⁻²⁵. Although self-reported concordance in the LiGHT trial has been
227 high¹⁴, the possibility of poor concordance having a significant adverse effect on disease control
228 cannot be ruled out as actual dose monitoring was not carried out. However, patients in clinical trials
229 are reported to have higher rates of concordance than those in routine care²⁶. Thus the true
230 magnitude and clinical importance of the slowing of VF progression in the Laser-1st group may be
231 much greater. SLT has also been proposed to provide better diurnal IOP stability, as a result of a
232 continuous effect on the trabecular meshwork²⁷⁻³⁰. This is in contrast to the episodic (and sometimes
233 erratic) administration of medication that may allow greater diurnal fluctuation in IOP, and in turn

234 faster disease progression. Even with exact concordance with instillation regimes, there are likely to
235 be long gaps between doses overnight, during which IOP may rise.

236 We observed differences in VF progression between treatment groups despite the fact that both
237 groups were treated to similar IOP targets. This indicates that monitoring of IOP reduction alone
238 (usually measured during office hours and so potentially unrepresentative of diurnal pressure
239 variation) may be insufficient to predict functional changes indicative of progression. This suggests
240 that clinical trials of new glaucoma treatments should include both IOP and VF related outcomes.
241 Greater differences were observed for TD, hinting that non-glaucomatous changes may have also
242 contributed towards differences between groups. Changes in TD may be caused by a number of non-
243 glaucomatous conditions, such as cataract. Were there higher rates of cataract in the Medicine-1st
244 group it could partially explain the tendency towards faster TD progression. During the period
245 covered by this analysis, cataracts were removed from 10.9% of eyes in the Medicine-1st group and
246 7.1% of eyes in the Laser-1st group. Assuming that cataracts not yet requiring surgery follow this
247 distribution, generalised depression of sensitivity due to lens opacity have contributed towards the
248 differences in TD rate between the two treatment groups. This is consistent with the higher rates of
249 cataract after topical medical treatment of glaucoma previously reported by landmark glaucoma
250 studies³¹⁻³⁴ and itself may contribute to a significant clinical advantage of a Laser-1st compared to a
251 Medicine-1st protocol. Our sensitivity analysis showed that differences between treatment groups
252 were narrowed when eyes that underwent cataract removals were excluded. PD models were as
253 strongly influenced by the exclusions as TD models. For example, following the exclusions there was
254 no statistical evidence for a difference in the proportion of eyes undergoing fast or moderate PD
255 progression (there remained strong evidence for a difference in the proportion of locations with
256 moderate or fast progression). This may indicate that as well as having lower sensitivity than TD²⁰,
257 PD may not be immune to the influence of cataract. Alternatively, the similar responses of TD and
258 PD following exclusions may indicate that cataract was not driving the between group differences.
259 Instead, cataract formation may be associated with faster glaucoma progression (with oxidative

260 stress a potential biological basis for the association) and by excluding cataract removal eyes much
261 of the glaucoma signal may have been excluded also. Considering that we still found clinically
262 relevant differences between treatment groups following exclusion of eyes from which cataracts
263 were removed, and recognising the limitations of both TD and PD, we conclude that greater
264 incidence of both cataract-related and glaucomatous progression in the Medicine-1st group is likely
265 to have contributed towards the observed differences between treatment groups.

266 To our knowledge this is the first study to robustly compare VF outcomes between IOP lowering
267 drops and SLT, as previous research has focused on IOP lowering alone as a surrogate for disease
268 control. In the absence of a universally accepted, standardised classification of rates of visual field
269 progression we have adopted that used by Chauhan et al.²¹: fast progressors as <-1dB/year (-
270 1dB/year is approximately ten times faster than age related decay). Although statistical methods
271 differ among studies, our estimates of global TD progression are broadly comparable with MD rates
272 in clinical glaucoma populations, which report median progression rates ranging from -0.62dB/year
273 to -0.05dB/year)^{21,35,36}. For the formal comparisons of Medicine-1st vs. Laser-1st we reported the
274 proportion of eyes with moderate or fast progression, combining these categories to ensure
275 reasonable data support for each outcome. These figures are not directly comparable with the
276 number of VF progressions reported in the recent paper on the primary outcomes of LiGHT⁶, where
277 progression was detected using GPA. The proportions reported here are larger, possibly because
278 trend based methods are more sensitive for detecting progression than event based methods such
279 as GPA¹⁵, especially given the relatively high upper threshold of the moderate/fast classification (-
280 0.5dB/year). Also, this analysis covers a longer follow-up period, extending beyond the 36-month
281 point reported previously and so a larger proportion of eyes would be expected to show evidence of
282 VF progression in our study. Despite these methodological differences, both analyses report higher
283 risks of VF progression in the Medicine-1st group, that may be related to the higher rates of disease
284 deterioration previously reported⁶.

285 This VF analysis is more detailed than those previously reported for LiGHT^{6,14,37} in that pointwise
286 rates were modelled and then averaged to produce global rate estimates, retaining more
287 information than if global VF measures such as MD or Pattern Standard Deviation (PSD) had been
288 used. Furthermore, we considered the overall shapes of the progression rate distributions rather
289 than using the mean of each distribution as the single point of comparison. We show that
290 differences between treatment groups were manifest only towards the more rapidly progressing
291 end of the rate distribution. If we had concentrated solely on mean TD and PD we would have found
292 no differences between treatment groups, consistent with the MD and PSD results reported at 36-
293 months¹⁴.

294 The data derived for this study were drawn from a carefully conducted, randomised controlled trial.
295 Patients were monitored according to routine clinical care; the trial used eye specific IOP targets
296 which were objectively defined and adjusted by a computerised decision algorithm to avoid bias¹².
297 Similarly, to avoid bias in clinical decision making, treatment escalation decisions were initiated by
298 the computerised decision algorithm, which followed a robust protocol developed according to
299 international guidelines by the EGS, American Academy of Ophthalmology Preferred Practice Pattern
300 and the and the South-East Asia Glaucoma Interest Group³⁸⁻⁴⁰. The decision support algorithm used
301 in the LiGHT trial has been described in detail before^{12,14}. The success of this strategy is highlighted
302 by the well matched distributions of baseline damage and IOP targets between treatment groups
303 (Table 1, Figures 3 and 4). As a result, any differences in VF progression between treatment groups
304 reflect genuine change, in the presence of identical IOP control practices between the two groups.
305 Patients treated with Laser-1st exhibited slower VF progression, as shown in this study, in addition to
306 better IOP control, less intense medical and surgical treatment and lower rates of disease
307 deterioration⁶.

308 The data presented here support the use of SLT as a first line treatment for glaucoma and OHT as
309 suggested by the previously reported improved clinical outcomes, lower treatment intensity and

310 cost-savings for the NHS. With slower VF deterioration SLT may delay or completely avert the need
311 for more intense medical and surgical intervention in a significant proportion of patients.

312 Acknowledgements

313 We thank Dr Amanda Davis for supporting trial management, Emily Dowse and Karine Girard-
314 Claudon for clinical support. We also thank the LiGHT participants and all recruiting sites.

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425

426 Figure legends

427 Figure 1. Distribution of estimated global total deviation progression rates by treatment group.

428 Histogram with median and 10th percentiles indicated. Curved line represents a smoothed density
429 estimate to the histogram.

430 Figure 2. Distribution of estimated global pattern deviation progression rates by treatment group.

431 Histogram with median and 10th percentiles indicated. Curved line represents a smoothed density
432 estimate to the histogram.

433 Figure 3. Distribution of mean deviation (MD) at baseline by estimated total deviation progression
434 rates.

435 Figure 4. Distribution of target IOP at baseline by estimated total deviation progression rates.

Figure 1

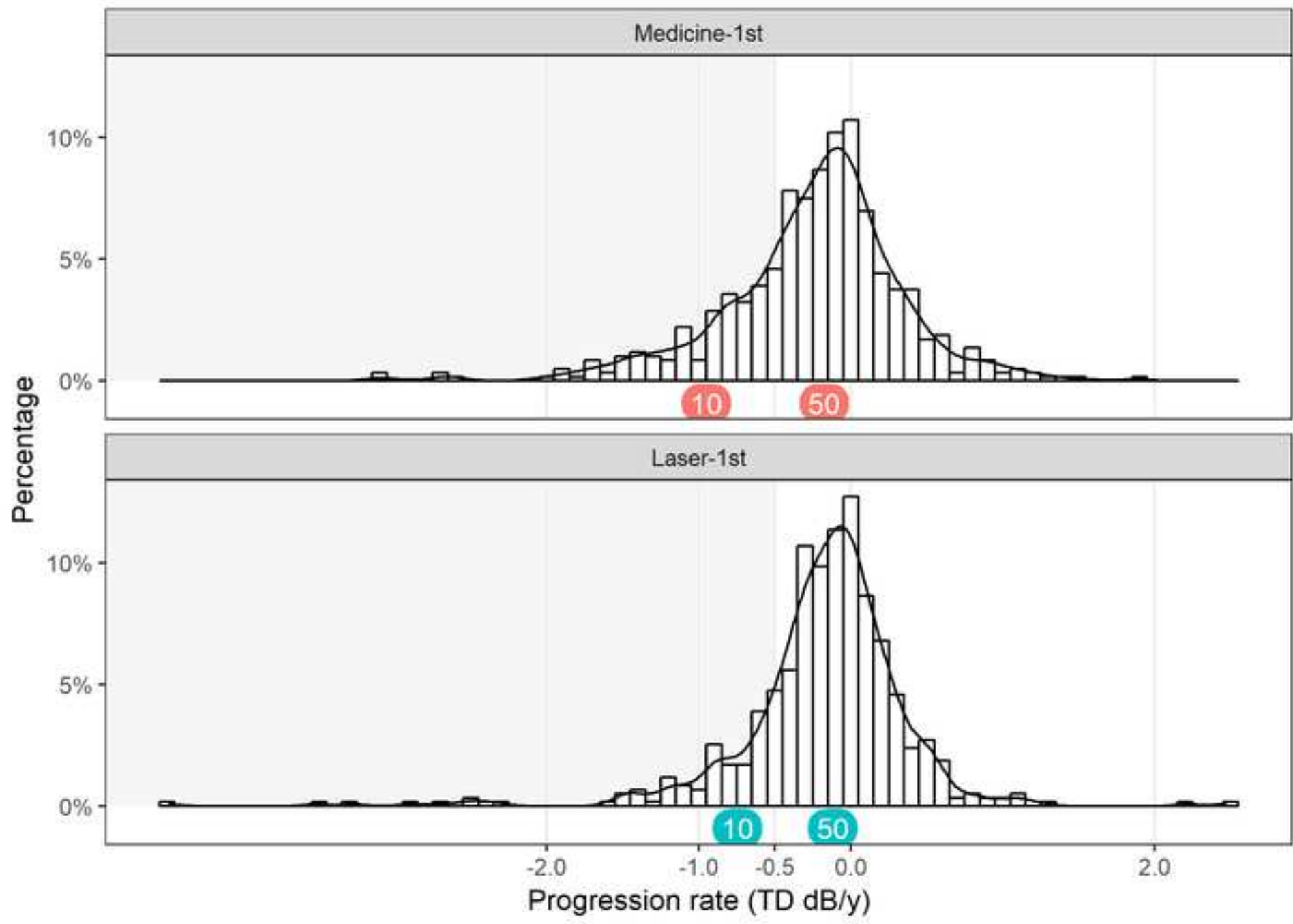
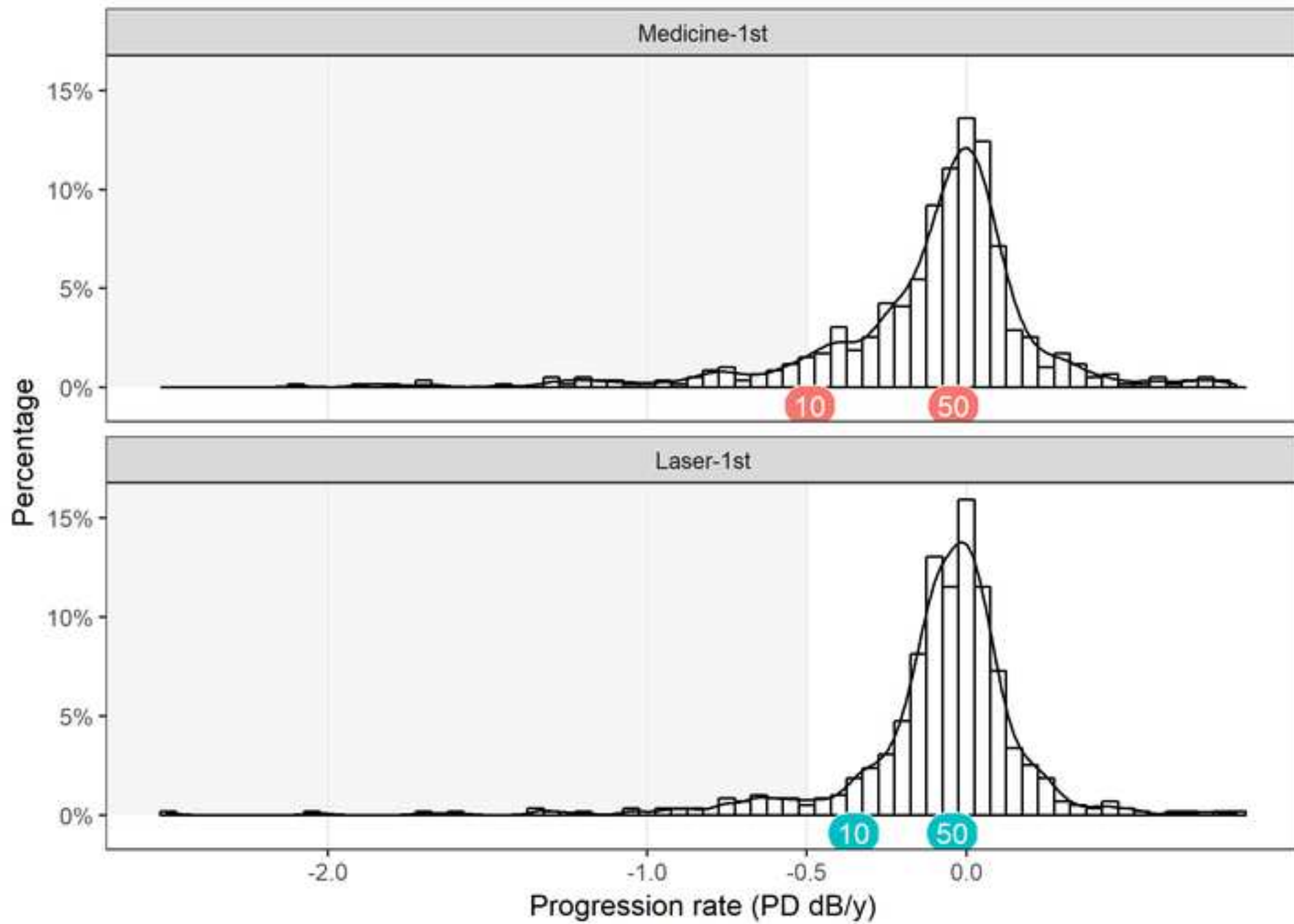


Figure 2



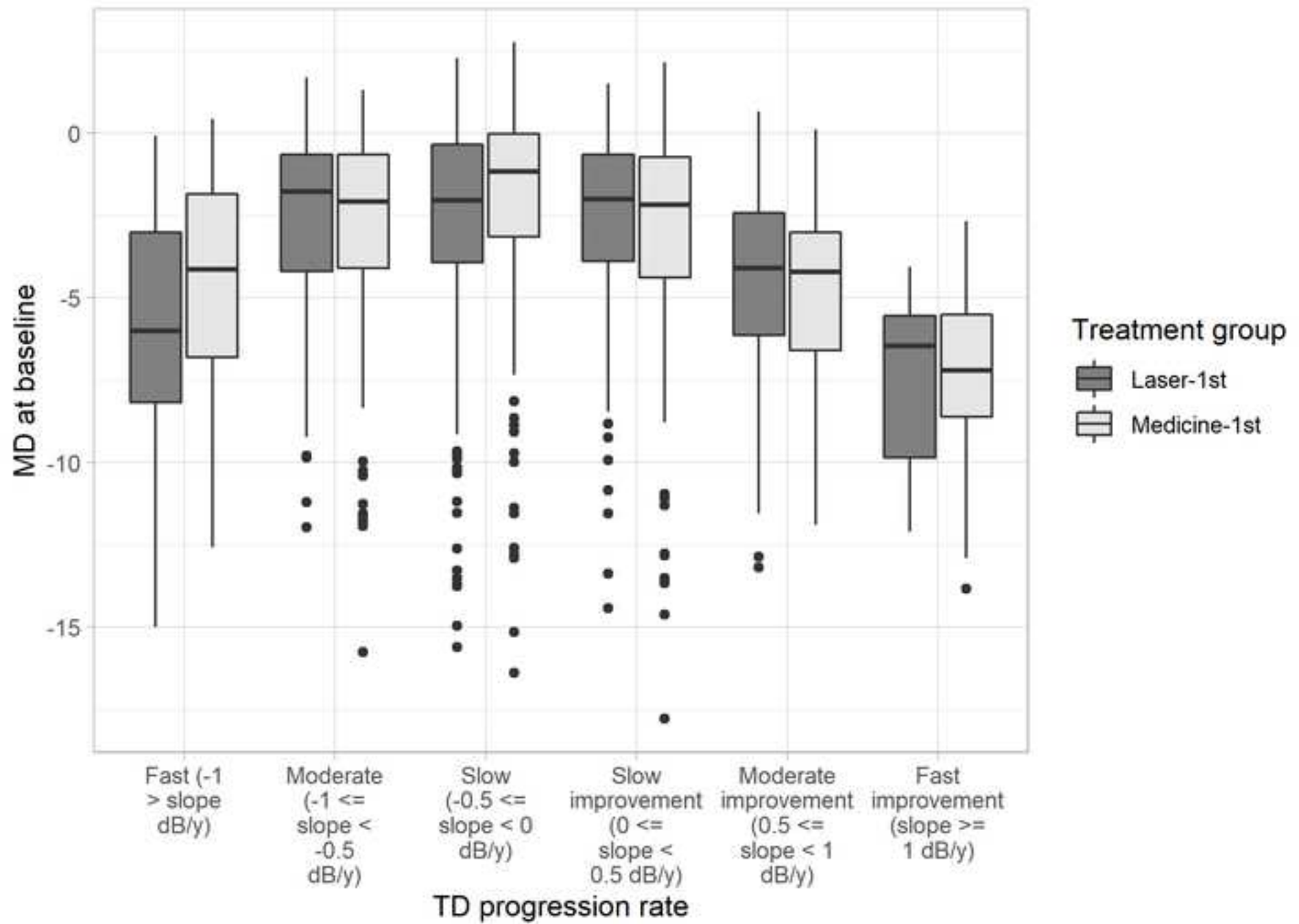


Figure 4

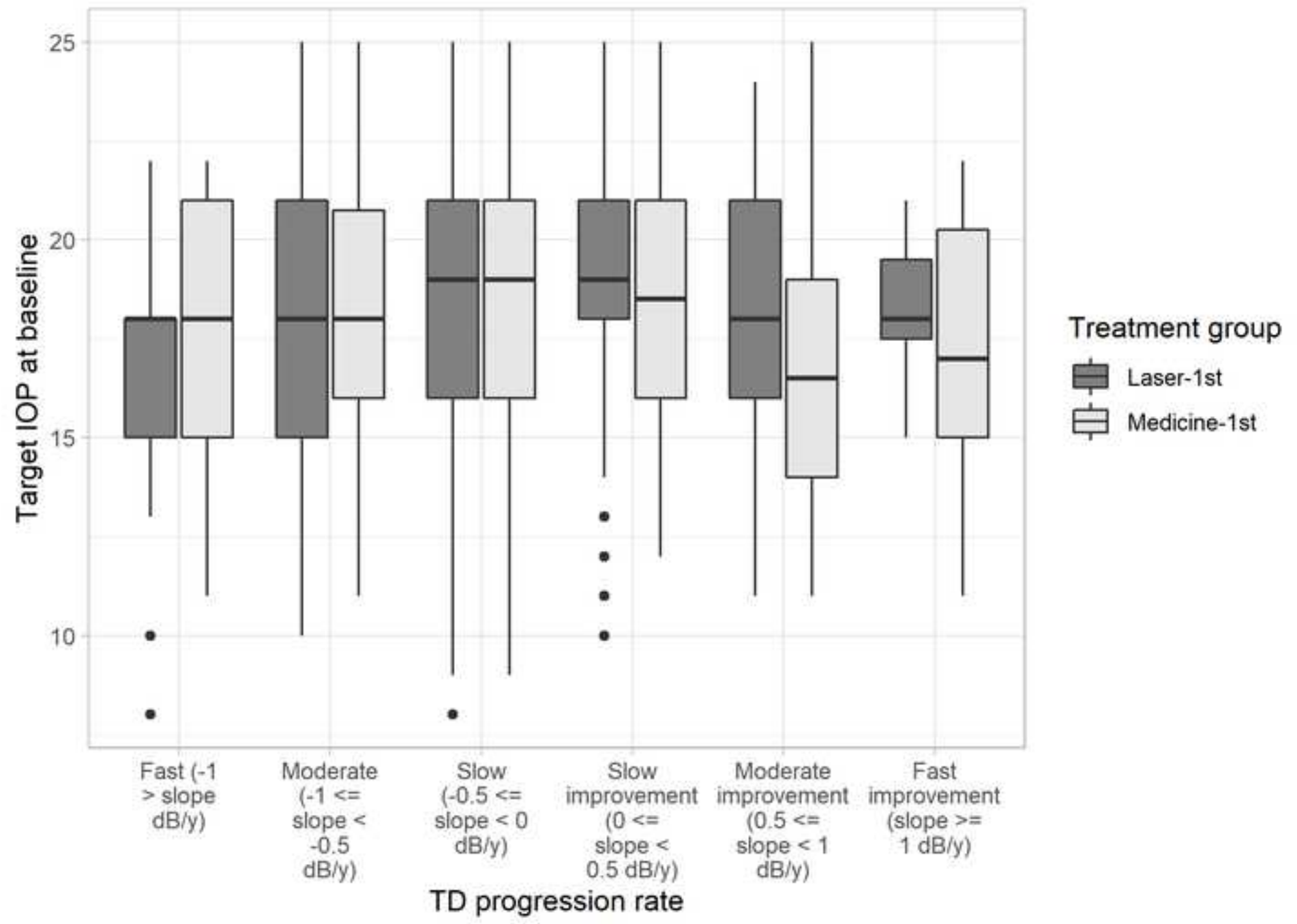


Table 1. Distribution of cohort characteristics by treatment group. Values given are frequencies unless otherwise marked.

	Medicine-1st	Laser-1st
Patients	344	344
Male	180 (52.3%)	193 (56.1%)
Female	164 (47.7%)	151 (43.9%)
Age in years, mean (SD)	62.9 (11.6)	63.4 (12.0)
OAG	271 (78.8%)	266 (77.3%)
OHT	73 (21.2%)	78 (22.7%)
Eyes	588	590
Bilateral cases	245 (71.2%)	249 (72.4%)
Follow up duration in months, median (IQR)	47 (39, 54)	49 (42, 56)
Visual fields	5630	5933
Visual fields per eye, median (IQR)	9 (8, 11)	10 (8, 12)
Interval between fields in days, median (IQR)	135 (83, 189)	140 (94, 189)
Visual field mean deviation at baseline in dB, median (IQR)	-2.0 (-4.5, -0.5)	-2.2 (-4.4, -0.6)
IOP target at baseline in mmHg, median (IQR)	18 (16, 21)	18 (16, 21)
Number of cataract removals performed	64	42

Table 2. Distribution of estimated total deviation progression rates by treatment group.

Progression rate	Locations		Eyes	
	Medicine-1st	Laser-1st	Medicine-1st	Laser-1st
Fast ($-1 > \text{slope dB/y}$)	10.2% (3115)	6.0% (1848)	9.5% (56)	5.4% (32)
Moderate ($-1 \leq \text{slope} < -0.5 \text{ dB/y}$)	15.9% (4864)	13.0% (3980)	16.7% (98)	11.5% (68)
Slow ($-0.5 \leq \text{slope} < 0 \text{ dB/y}$)	40.3% (12336)	43.4% (13311)	41.5% (244)	48.1% (284)
Slow improvement ($0 \leq \text{slope} < 0.5 \text{ dB/y}$)	25.7% (7863)	31.6% (9705)	25.5% (150)	29.7% (175)
Moderate improvement ($0.5 \leq \text{slope} < 1 \text{ dB/y}$)	5.9% (1798)	4.7% (1442)	5.1% (30)	4.1% (24)
Fast improvement ($\text{slope} \geq 1 \text{ dB/y}$)	2.0% (600)	1.3% (394)	1.7% (10)	1.2% (7)

Table 3. Distribution of estimated pattern deviation progression rates by treatment group.

Progression rate	Locations		Eyes	
	Medicine-1st	Laser-1st	Medicine-1st	Laser-1st
Fast ($-1 > \text{slope dB/y}$)	4.6% (1403)	3.2% (967)	3.4% (20)	1.7% (10)
Moderate ($-1 \leq \text{slope} < -0.5 \text{ dB/y}$)	6.9% (2103)	5.1% (1565)	6.5% (38)	5.4% (32)
Slow ($-0.5 \leq \text{slope} < 0 \text{ dB/y}$)	46.6% (14234)	48.9% (14990)	51.7% (304)	55.6% (328)
Slow improvement ($0 \leq \text{slope} < 0.5 \text{ dB/y}$)	38.9% (11900)	40.6% (12471)	36.2% (213)	36.1% (213)
Moderate improvement ($0.5 \leq \text{slope} < 1 \text{ dB/y}$)	2.6% (805)	1.8% (557)	2.2% (13)	1.0% (6)
Fast improvement ($\text{slope} \geq 1 \text{ dB/y}$)	0.4% (131)	0.4% (130)	- (0)	0.2% (1)