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Visual Fields at Follow-up in the Ischemic Optic Neuropathy Decompression Trial:

Evaluation of Change in Pattern Defect and Severity Over Time

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Abstract

Purpose—To evaluate change from baseline to 12 months follow-up in study and nonstudy (fellow) eye visual fields from the Ischemic Optic Neuropathy Decompression Trial (IONDT).

Design—Randomized controlled trial and observational study.

Participants—The IONDT enrolled patients >50 years with acute nonarteritic ischemic optic neuropathy (NAION). Randomized patients (n = 258) had visual acuity <20/64; nonrandomized patients (n = 160) had visual acuity >20/64 or refused randomization.

Interventions—Optic nerve decompression surgery (n = 127) or careful follow-up (n = 131).

Main Outcome Measures—We measured visual fields at baseline and at 6 and 12 months follow-up. Using a computerized system, we classified visual field defects by pattern, location, and severity. We examined changes over time by treatment group, age, baseline comorbidities, and change in visual acuity. In fellow (nonstudy) eyes, we assessed change by whether NAION was present at baseline and also incidence of NAION by whether a visual field defect was present at baseline.

Results—We analyzed 245 study eye visual field pairs (179 and 66, randomized and nonrandomized, respectively) for change from baseline to 12 months. We observed significant changes in defect distribution within the central field ($P = 0.02$) for randomized eyes. Superior and inferior altitudinal defects were less severe at follow-up in both randomized and nonrandomized eyes. We observed an association between change in central field severity and change in visual acuity from baseline ($P < 0.001$ at 6 months; $P = 0.01$ at 12 months; Kendall's tau-b), but no association between visual field change and treatment group, age, or baseline comorbidities.

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Superior and inferior visual field defects present at baseline in nonstudy eyes improved at follow-up. Fellow (nonstudy) eyes with normal fields did not have an increased risk of developing NAION compared with eyes with 1 defects.

Conclusions—Visual fields of NAION patients enrolled in the IONDT were relatively stable from baseline to follow-up. A visual field defect in the nonstudy eye at baseline was not associated with development of NAION during follow-up compared with eyes with normal fields.

Nonarteritic anterior ischemic optic neuropathy (NAION) is second only to optic neuritis as the most common acute cause of optic nerve related visual loss. NAION is characterized by sudden onset of unilateral visual field loss in patients, with or without a reduction in visual acuity, and increased incidence with older age. The Ischemic Optic Neuropathy Decompression Trial (IONDT), a multicenter randomized controlled trial,¹ found no evidence supporting the effectiveness of optic nerve decompression surgery compared with careful follow-up alone, in improving visual acuity by 3 lines, as measured using Lighthouse charts in patients with NAION and visual acuity of 20/64 at baseline.² This finding persisted at 24 months of follow-up.³

From the study planning stages forward, we considered visual field to be an important secondary outcome in the IONDT and obtained visual fields, using the Humphrey Field Analyzer (San Leandro, CA) and 24-2 program, at baseline and follow-up visits for all patients enrolled in the IONDT. At the 6-month follow-up visit, we observed no difference in the Humphrey global index of mean deviation between the 2 randomized treatment groups.²

We previously described a method we developed for classifying defect and severity of NAION visual fields in the context of a research study using a computerized system.^{4,5} At baseline, superior and inferior arcuate defects with central depression were the most commonly encountered defects in study eyes of randomized patients with visual acuity of 20/64. Nonrandomized patients in the IONDT had similar visual field defects but no central depression in study eyes at baseline. Unexpectedly, mild superior and/or inferior arcuate defects were present in about three quarters of nonstudy eye visual fields.⁵

Longitudinal follow-up of visual fields of eyes with NAION enrolled in the IONDT is important in understanding both the natural history of the disease and determining the effect of surgical intervention on visual function. In this article, we report on change in the type of defect (pattern shift) and change in the density or sensitivity of individual defects that do not change in pattern (severity change) in visual fields of study and nonstudy eyes of randomized and nonrandomized IONDT participants, observed at 12 months of follow-up. We also compare the presence of a visual field defect pattern at baseline for study participants who developed NAION in the nonstudy eye with participants who did not.

Methods

Details of the methods used in the IONDT for collection and analysis of visual fields are described elsewhere.¹ Briefly, the IONDT enrolled patients aged 50 years between October 1992 and October 1994 at 1 of 25 Clinical Centers in the United States if they had experienced a unilateral acute loss of vision attributable to NAION within the 14 days previous to presentation. Patients were administered a series of baseline tests, including visual acuity and visual field. Patients were eligible for randomization to surgery or careful follow-up if the baseline best-corrected visual acuity in the study eye was 20/64 using the Lighthouse chart (“regular entry” group). Eyes of patients with visual acuity >20/64 at baseline were eligible for randomization if vision loss progressed to 20/64 within 30 days after the onset of symptoms (“late entry” group). Surgery took place within 14 days of acute

vision loss for the regular entry group and within 30 days for the late entry group. Patients with acuity that remained $>20/64$ and who fulfilled all other eligibility criteria, and patients who refused randomization, were not randomized and received careful follow-up. Nonstudy (fellow) eyes in both groups were tested for visual acuity and visual field at baseline and the results recorded. Institutional review boards at participating institutions approved the study protocol and all study participants provided signed informed consent. Baseline and incident NAION in the nonstudy eye during the study were classified based on best clinical judgment by the study neuroophthalmologist, surrogate provider, or patient report, as previously described.⁶

Acquisition of Visual Fields

Visual fields were performed in a standardized fashion according to the protocol.⁷ Trained, certified visual field technicians at the IONDT Clinical Centers obtained fields in the IONDT with the Humphrey Field Analyzer, using the 24-2 program with stimulus size III, full threshold strategy, and foveal sensitivity measured concurrently. Visual fields for the study eye were measured before those for the nonstudy eye. For randomized patients, visual fields were obtained at the baseline examination; if randomization took place >24 hours after the baseline examination, visual fields were remeasured and these fields were considered as “baseline.” Visual field technicians measured visual fields of randomized patients at 3, 6, and 12 months of follow-up, and at the time the patient completed participation in the study. We initially planned for a minimum duration of patient follow-up of 2 years with a common close-out date. We increased the minimum follow-up to 5 years in the IONDT Follow-up Study. This strategy resulted in different lengths of follow-up for individual patients. Visual fields of both eyes of nonrandomized patients were obtained at the baseline examination, at either 6 or 12 months (although some patients completed visual fields at both 6 and 12 months), and then annually after the 12-month visit, and at study closeout.

Preparation of Visual Fields for Classification

Before beginning analyses, the Coordinating Center evaluated visual fields for compliance with the protocol, that is, that the field was performed using the 24-2 program on a Humphrey Automated Visual Field Analyzer using test stimulus size III with the fixation test switch “on.” Visual fields performed using the 30-2 program, which otherwise corresponded with the protocol ($n = 6$), were analyzed by utilizing only those points also represented on the 24-2 Humphrey test (per protocol).

For each IONDT visual field, the Coordinating Center extracted the following information from the Humphrey visual field printout and entered it into a Microsoft 97/00 Excel database using double-entry verification: patient and visit identifiers; eye examined; number of fixation losses; false positives; false negatives; short-term fluctuation; foveal sensitivity; highest point of sensitivity for the whole field (dB); and dB loss at each of the 52 data points on the total deviation plot. If the initial computer-based classification of defect for an eye was “diffuse depression,” the absolute sensitivity of each of the 52 Humphrey 24-2 points was also entered into Excel to distinguish between defects of absolute and diffuse depression.

Classification of Ischemic Optic Neuropathy Decompression Trial Visual Fields

The methods for computerized analysis of the visual fields are described elsewhere.^{4,5} Briefly, rules for classifying the type of defect (pattern) and density (severity) of visual field defects were developed, tested, and validated by an expert panel of 6 neuroophthalmologists participating in the IONDT. Patients could have 1 defect, each assigned its own type and severity. The rules developed by the expert panel were incorporated into a computerized system built on a Microsoft Excel platform running on a PC. We used the methodology

developed by the Collaborative Initial Glaucoma Treatment Study to evaluate the reliability of IONDT visual fields.⁸ Visual fields scoring 4 points using the CIGTS system were classified as unreliable and were excluded from analyses. Visual fields that could not be assessed for reliability were also excluded.

Definition of Change Across Time

To measure change across time, namely, from baseline to a follow-up visit, we analyzed fields at both time points and compared defect type and severity. Because there could be spurious changes in visual fields caused by patient learning effects or by short-term fluctuation (SF), when we found a change in defect type we used the Humphrey global index SF, a measure of intratest variability, as a measure of the normal variation within an individual's visual field at different points in time to assess if the change was spurious. We calculated an adjustment factor, corrected SF (SF^c),⁴ for each set of baseline and follow-up fields⁴ equal to half of the 95% confidence interval on the pooled estimate of SF across the 2 visits. This factor was then used to temporarily "adjust" the follow-up visit Humphrey visual field at those specific test points used by the computerized system to differentiate between specific defects (e.g., points 21 and 22 to distinguish between superior arcuate and superior altitudinal defects, and points 29 and 30 to distinguish between inferior arcuate and inferior altitudinal defects). To err on the side of not overcalling change, adjustment was made in the direction that would decrease the probability of detecting a pattern change from baseline to follow-up. The temporarily adjusted data were then used for the evaluation of change as described. If the difference in field pattern persisted despite this manipulation, then the follow-up field was determined to be "changed." If the difference in field pattern disappeared with this manipulation, the follow-up visual field was determined to be "not changed."

To define improvement, no change, or worsening of the visual field of an individual, we first used the computerized system to classify baseline and follow-up visual fields in the superior, inferior, and central locations, and compared defect patterns across time within each of these locations separately. We defined an improvement in pattern for a superior or inferior defect as a change in classification from (1) an arcuate defect to normal (defined as no defect in superior region), or (2) an altitudinal defect to an arcuate defect or normal. We defined a worsening in pattern for a superior or inferior defect as a change in classification from (1) an arcuate to an altitudinal defect, or (2) a normal to an arcuate or altitudinal defect. For the central location of the visual field, we defined improvement in pattern as a change from (1) a central to a paracentral scotoma or a normal region, or (2) a paracentral scotoma to a normal region. We defined worsening in pattern as a change from (1) a paracentral to central scotoma or (2) a normal region to either paracentral or central scotoma. A change in severity was assessed only when no pattern change was observed, using the difference in average dB loss for the points in the area involved.

Comparison of Baseline and Follow-up Visual Fields

In this report, we compare visual fields measured at baseline (or at the last visit before randomization for late entry patients) with visual fields measured at 12 months of follow-up. Comparison of baseline visual fields with visual fields measured at 6 months of follow-up has previously been reported.⁵ We also examined fields measured at the patient's closeout visit, but because we obtained similar findings and follow-up times varied for the close-out examination, we do not present those analyses here. We examined the distribution of defect types in the study eye of randomized patients by treatment group and in the study eye of nonrandomized patients. We compared the baseline and follow-up visual fields by defect location (superior, inferior, or central), defect type, and direction of change, if any. We also examined change across the entire visual field, by assessing the overall proportion of visual

fields that improved or worsened in 1 locations of the visual field. We compared changes by patient age (<65 versus ≥65 years); presence of ≥1 self-reported vascular risk factor (i.e., hypertension, diabetes mellitus, myocardial infarction, cerebrovascular accident, or transient ischemic attack) versus none; study group (randomized versus nonrandomized); and treatment group (surgery versus careful follow-up). We examined the association between visual field change and visual acuity change, defined as a change of ≥3 lines using the Lighthouse chart, our primary outcome. Finally, we examined change in nonstudy eyes from baseline to 6 and 12 months. We also compared the proportion of nonstudy eyes developing NAION, by whether a baseline visual field defect was present.

Statistical Analyses

Visual field data and other patient data were analyzed using STATA statistical software for Windows (STATA Statistical Software, Release 7.0, College Station, TX). All statistical tests were 2 sided. The Stuart Maxwell chi-square test of homogeneity, a generalization of the McNemar test for homogeneity of 2×2 tables, was used to test for within-participant pattern shifts.⁹ Score test for trend of odds, an approximate chi-square test for linear trend of the log odds across ordinal visual field categories (see STATA'S "tabodds" command in epitab) was used to test for differences in visual field change among subgroups.¹⁰ The degree of association comparing change in visual acuity with change in visual field was measured using Kendall's tau-b. We classified $P < 0.05$ as statistically significant. We chose not to make formal adjustment for multiple comparisons, presenting the results of statistical tests, and leaving inferences to the reader.

Results

In the IONDT, 258 NAION patients were randomized and 160 enrolled in the nonrandomized study. We obtained reliable visual fields at both baseline and 6 months for 203 randomized and 75 nonrandomized study participants, and reliable visual fields at both baseline and 12 months for 179 randomized and 66 nonrandomized participants (Fig 1). All patients with reliable 6-month visual fields received treatment as assigned and were analyzed according to randomized assignment. Two patients with reliable 12-month visual fields underwent surgery instead of careful follow-up and were analyzed as part of the surgical group. There were no differences in patients who completed visits associated with reliable visual fields compared with those who did not in terms of age, gender, baseline visual acuity, presence of NAION or optic neuropathy in the nonstudy eye at baseline, or treatment group.

Change in Visual Fields Over Time for Ischemic Optic Neuropathy Decompression Trial Patients

We found a significant pattern shift toward improvement in defect type within the central visual field location between the baseline and the 12-month visit (Stuart Maxwell; $P = 0.002$), for study eyes of randomized IONDT patients (Table 1). No pattern shifts were observed in superior or inferior defects; however, we found that superior and inferior altitudinal defects were less severe compared with baseline (paired t test; $P = 0.008$ for superior altitudinal defect and $P = 0.001$ for inferior altitudinal defects; Table 2).

Study eyes of nonrandomized IONDT participants showed no pattern shift between baseline and the 12-month follow-up visit (Table 3), but we did note an improvement in severity of altitudinal field defects from both inferior ($P = 0.02$) and superior fields ($P = 0.03$; Table 4).

We compared the visual fields of randomized with those of nonrandomized study eyes by comparing the distribution of fields that showed improvement, worsening, or no change in

pattern shift by visual field location. Proportionately more eyes improved by 12 months in the central location of the visual field (20.7% versus 12.1%) and fewer eyes worsened (9.5% versus 25.8%) in the randomized group compared with the nonrandomized group ($P=0.002$). There were no differences in the distributions of eyes improving or worsening by pattern shift in the inferior location of the visual field of randomized compared with nonrandomized study eyes. (Tables 4 and 2, respectively).

Overall Change

We also looked at the aggregation of change within an individual eye. We classified eyes as “improving” overall if 1 location of the field improved and none worsened, and as “worsened” overall if no location improved and 1 location worsened, using previously described definitions for improvement or worsening for pattern changes. Overall, for all study eyes (randomized plus nonrandomized) at the 6-month visit, visual fields of 19.8% of patients improved in 1 location, 48.2% were unchanged, 6.1% improved in 1 area and worsened in another, and 25.9% worsened in 1 location. Results at the 12-month visit were similar (22.5%, 49.4%, 4.5%, and 23.3% improved, showed no change, improved in 1 location and worsened in another, or worsened, respectively; Fig 2). Overall changes in visual fields of randomized eyes alone from baseline to both the 6 and 12-month follow-up visits were similar (data not shown).

Comparison of Change in Visual Fields with Change in Visual Acuity

For eyes showing change in visual acuity (defined as a change of 3 lines on the Lighthouse chart) from baseline to follow-up at 6 and from baseline to 12 months, we observed a concomitant pattern shift in the central location of the visual field measured at the same follow-up visit. Approximately one third of eyes that showed an improvement in visual acuity of 3 lines also showed improvement in the central location of the visual field. In contrast, <15% of these eyes showed improvement in the superior or inferior location of the visual field. Eyes showing a worsening of visual acuity by 3 lines seemed to show worse visual fields at any location. For randomized eyes, we observed a statistically significant association between improvement or worsening in visual acuity and the pattern shift in the central location of the visual field ($P<0.001$ at 6 months and $P=0.001$ at 12 months; Kendall's tau-b); in the pattern shift in the superior visual field at 6 and at 12 months ($P=0.008$ and $P=0.04$, respectively; Kendall's tau-b); and in the pattern shift in the inferior visual field at 6 months ($P=0.003$; Kendall's tau-b; Fig 3).

Effect of Treatment

No differences in proportion of visual field locations showing worsening or improvement in pattern were observed between eyes undergoing surgery compared with those receiving careful follow-up ($P=0.61$, 0.66, and 0.68 for superior, inferior, and central locations, respectively; Score test for trends of odds). Similarly, the average dB loss in defects that did not change pattern (severity shift) was no different for the surgery group compared with the careful follow-up group for any defect type.

Effect of Age

We found few differences in the defect patterns for study eyes of randomized patients <65 years compared with those ≥65 years. Eyes from patients aged ≥65 years, but not for those <65 years, showed worsening by pattern shifts from baseline to 6 months in the superior ($P=0.034$), central ($P=0.048$), and inferior ($P=0.054$) visual field locations. At 12 months, only the change in distribution in defects in the inferior visual field remained statistically significant ($P=0.047$).

Effect of Vascular Condition at Baseline

We also compared visual fields for eyes of randomized patients by presence of a vascular condition at baseline, defined as patient report of ≥ 1 vascular conditions at the baseline visit versus no report. We found no changes in the distribution of defect pattern type from baseline to either the 6- or the 12-month follow-up visit by vascular condition.

Visual Fields of Nonstudy Eyes

We obtained reliable baseline visual fields for the nonstudy eye of 300 of 326 study participants without NAION or an optic neuropathy at baseline. The proportion of nonstudy eyes with baseline visual field defects subsequently developing NAION was 38/255 (14.9%), whereas the proportion of nonstudy eyes with no field defect developing NAION was 4/45 (8.9%). This difference was not statistically different ($P = 0.357$, Fisher's exact test); that is, the presence of a visual field defect at baseline was not associated with a decreased risk of subsequent development of NAION.

We obtained reliable visual fields at both baseline and 6 months for 271 nonstudy eyes, and reliable visual fields at both baseline and 12 months for 235 nonstudy eyes. We assessed change separately for eyes by the presence of NAION at baseline: 216 eyes at 6 months and 181 eyes at 12 months did not have NAION at baseline. Nonstudy eyes without NAION at baseline showed improvement in pattern from baseline to 6 months or 12 months in the superior and inferior portions of the field, but not in the central portion of the visual field (Table 5). There was no or little change resulting in a worsening pattern shift in any field location. In contrast, nonstudy eyes with NAION at baseline showed a pattern shift similar to study eyes, with improvement in the central, but not in the superior or inferior, visual field (Table 6). Twenty-four percent (47/195) of nonstudy eyes that had ≥ 1 defects at baseline improved so that the visual field was classified as normal at the 6-month follow-up visit.

Discussion

Visual fields of study eyes of NAION patients randomized to surgery or careful follow-up in the IONDT remained remarkably stable over 12 months, with only small pattern and severity changes compared with baseline. We found improvement in both pattern and severity in the central visual field. Superior and inferior altitudinal defects were less severe at 12 months compared with baseline in patients without pattern shifts. These results are similar with the results previously reported on visual field defect change from baseline to 6 months follow-up,⁵ emphasizing the stability of visual field defects in NAION patients. We also found no effect of study intervention (surgery versus careful follow-up) on visual field changes after 12 months follow-up, as reported for 6 months follow-up.

In study eyes of nonrandomized patients (the majority of which tested with visual acuity $>20/64$ at baseline), similar changes were seen except that there was no pattern shift for central defects from baseline to follow-up. For study eyes of both randomized and nonrandomized patients, visual fields of approximately one quarter of all patients improved in pattern, one quarter worsened, and the rest were unchanged or had improvement in one location and worsening in another. About 30% of visual fields with defects in the central location showed improvement from baseline in both visual acuity and overall visual field at 6 and 12 months. We observed no difference in visual field changes at 6 and 12 months by age or presence of a vascular condition.

Although we found some statistically significant pattern shifts in visual fields of study eyes from baseline to 6 and 12 months, these changes are unlikely to be clinically meaningful, except perhaps for central field improvement, which parallels acuity improvement. We previously reported 43.7% of randomized patients showed improvement in visual acuity at 6

months.^{2,3} Although an association between visual acuity and foveal sensitivity has been reported,¹¹ exact concordance of central field change with acuity change is not expected because the 2 measures are determined through different testing methods based on different psychophysical principles. Furthermore, with many defects splitting or otherwise only partially affecting foveal function, scanning strategies used by patients for assessment of acuity might differ from fixation strategies (e.g., eccentric fixation) used for assessment of visual fields.

Our results confirm our original finding that optic nerve decompression surgery is not beneficial for treatment of NAION.^{2,3} This report also extends the finding we reported previously, showing no difference in change in visual fields by treatment assignment at 6 months follow-up. To our knowledge, these are the first reports of a prospective long-term evaluation of visual fields from patients with incident cases of NAION. Arnold and Hepler¹² examined visual fields of 27 patients with NAION using the Octopus perimeter Program 32 within 30 days of onset and again after 3 months. Using a change of >2 dB to define change, these investigators found that visual field performance worsened in 22.2% and improved in 24% of patients. Looking at the nonprogressive subgroup of 21 patients separately, they found that 31.6% showed a visual field improvement.¹² We had previously reported no change in mean deviation of visual fields at 6 months between surgery and careful follow-up groups.² Our finding of only a modest correlation between mean deviation or corrected pattern standard deviation and pattern defect severity at baseline suggests that these global measures have limited value for comparing visual fields in a longitudinal study, however.⁵

We are unable to explain the high prevalence of visual field defects present at baseline in nonstudy eyes without prior evidence of NAION. These defects were mild, usually superior and/or inferior arcuate defects⁵; about one quarter of defects present at baseline resolved to normal during follow-up. These data could suggest the presence of a testing or learning artifact, but many other defects persisted through the 6 and 12 month visits, suggesting that for the most part, we identified true defects. The underlying cause of nonstudy eye field defects is unknown, although some might be explained by media opacity or other unknown comorbidities. Another possibility is that these defects represent past subclinical episodes of NAION. In this case, our data suggest that previous episodes, as suggested by the presence of a baseline defect, have no effect on the development of subsequent, clinically apparent NAION.

Our interpretation emphasizes results that seem to be consistent between the 6- and 12-month visits and that are clinically plausible. Simple comparisons of number and type of change in individual visual fields are remarkably consistent with findings by superior, inferior, or central locations. We believe our findings are generalizable, encouraged by the consistency of our findings with visual acuity outcomes and the persistence of most changes at both 6 and 12 months. Still, some of our statistically significant findings may be due to chance. We performed many comparisons and many of these involved only a small number of observations (e.g., each defect type), which may lead to an unreliable finding of statistical significance.¹³ The small improvements that we observed in the eyes with altitudinal defects may also be due to a learning effect; many of the IONDT patients were inexperienced in performing visual field tests before baseline. We also cannot rule out regression to the mean as contributing explanation for improvements observed.

Using a computerized system that corrects for SF, we have found that visual fields of patients with NAION are relatively stable, with the majority improving or remaining the same over the 6- to 12-month period from disease onset. For visual fields of eyes that show improvement or worsening, these changes are not associated with treatment group, age, or

presence of a self-reported vascular condition at baseline. An improvement in a central visual field defect is associated with a corresponding improvement in visual acuity. Visual field defects, mostly mild, were discovered at baseline in evaluation of many non-study eyes, but were not associated with incidence of NAION in the nonstudy eye during the study follow-up period.

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* Non-randomized IONDT patients were required to have 6 or 12 month follow-up visual field.

Figure 1. IONDT CONSORT (Consolidated Standards of Reporting Trials) flow chart. The IONDT protocol required nonrandomized patients to have a 6-or a 12-month follow-up visual field. A total of 102 of 160 nonrandomized patients with reliable baseline visual fields also had a 6 or 12 month reliable visual field. IONDT = Ischemic Optic Neuropathy Decompression Trial; Mo = month; VA = visual acuity.

Visual Field Change between Baseline and 6 and 12 Months

Figure 2.

Pattern shift between baseline and 6 and 12 months in randomized and nonrandomized eyes. Number of fields by number of areas (inferior, superior, or central) showing improvement or worsening. One visual field may have 1 location for which change is assessed. Change from baseline to 6 months was evaluated for randomized and nonrandom-ized eyes in 261 of 278 visual fields (black bars), and from baseline to 12 months in 233 of 245 visual fields (gray bars). Visual fields not included in the graph include those in which 1 areas improved and 1 areas worsened ($n = 17$ at 6 months and 11 at 12 months). In addition, 1 visual field at 12 months had a nasal step defect that we did not define as improvement or worsening. Numbers of visual fields shown at top of each bar.

Figure 3.

Comparison of change from baseline to follow-up in defect pattern of randomized study eyes by change in visual acuity of 3 lines. Percent of 200 fields at 6 months (A) and 175 fields at 12 months (B) showing improvement or worsening of visual field defect pattern from baseline by visual field location (inferior, superior, or central). The number of visual fields in each category is shown beside the bar. White bars show patients at 6 and 12 months with improved visual acuity compared with baseline. Visual acuity improvement is defined as gain of 3 lines on the Lighthouse vision chart ($n = 65$ at 6 months and 76 at 12 months); gray bars show patients with no change in visual acuity ($n = 86$ at 6 months and 92 at 12 months) and black bars patients with worse visual acuity, defined as a worsening by 3 lines on the Lighthouse vision chart ($n = 32$ at 6 months and 24 at 12 months). The association between change in visual acuity and pattern shift was statistically significant for all locations at 6 months ($P = 0.04$, 0.003 , and <0.001 for superior, inferior, and central locations, respectively; Kendall's tau-b) and for superior and central locations at 12 months ($P = 0.008$ and 0.001 , respectively; Kendall's tau-b).

Table 1

Visual Field Pattern Shift in Study Eyes of Randomized Study Participants from Baseline to the 12 Month Follow-up Visit by Location

Visual Field Location	Total No. Fields [*]	Type of Change			
		Improved [†]	Unchanged [‡]	Worse [§]	P
Superior	179	No. (%) 12 (6.7)	No. (%) 150 (83.8)	No. (%) 17 (9.5)	0.22
Inferior [¶]	178	No. (%) 15 (8.4)	No. (%) 152 (85.4)	No. (%) 11 (6.2)	0.68
Central	179	No. (%) 37 (20.7)	No. (%) 125 (69.8)	No. (%) 17 (9.5)	0.02

^{*} Patients can have defects in 1 location.

[†] Improved defined as change in defect classification from superior or inferior arcuate scotoma to normal; from superior or inferior altitudinal defect to superior or inferior arcuate scotoma or normal; from central scotoma to paracentral scotoma or normal; or from paracentral scotoma to normal.

[‡] Unchanged defined as normal at both baseline and follow-up or defect unchanged from baseline to follow-up.

[§] Worse defined as change in defect classification from superior or inferior arcuate to superior or inferior altitudinal; from normal to any defect; or from paracentral scotoma to central scotoma.

^{||} Stuart Maxwell test for marginal homogeneity.

[¶] One patient not included because visual field was classified as "other isolated defect" at 12-month visit, for which improvement or worsening from baseline was not determined (i.e., nasal step).

Visual Field Severity Shift in Study Eyes of Randomized Study Participants from Baseline to 12 Month Follow-up Visit by Defect Classification

Table 2

Defect Classification	Total No. *	Mean Severity (dB) at		Change in Severity [†]	P [‡]
		Baseline	Follow-up		
Superior arcuate	75	13.86	14.10	0.24	0.80
Superior altitudinal	73	26.96	25.46	-1.50	0.008
Inferior arcuate	63	18.22	18.96	0.74	0.35
Inferior altitudinal	86	28.80	27.42	-1.38	0.001
Paracentral scotoma	5	20.00	15.73	-4.27	0.22
Central scotoma	108	6.61	5.05	-1.56	0.08

* Patients can have defects in 1 location.

[†] Improvement is a decrease in severity (negative change in dB) and worsening is an increase in severity (positive change in dB).

[‡] Paired t test.

Table 3
Visual Field Pattern Shift in Study Eyes of Nonrandomized Study Participants from Baseline to 12 Month Follow-up Visit by Location

Visual Field Location	Total No. Fields [*]	Type of Change			p
		Improved [†]	Unchanged [‡]	Worse [§]	
		No. (%)	No. (%)	No. (%)	
Superior	66	7 (10.6)	49 (74.2)	10 (15.2)	0.15
Inferior	65 [¶]	3 (4.6)	56 (86.2)	6 (9.2)	0.22
Central	66	8 (12.1)	41 (62.1)	17 (25.8)	0.11

^{*} Patients can have defects in 1 location.

[†] Improved defined as change in defect classification from superior or inferior arcuate scotoma to normal; from superior or inferior altitudinal defect to superior or inferior arcuate scotoma or normal; from central scotoma to paracentral scotoma or normal; or from paracentral scotoma to normal.

[‡] Unchanged defined as normal at both baseline and follow-up or defect unchanged from baseline to follow-up.

[§] Worse defined as change in defect classification from superior or inferior arcuate to superior or inferior altitudinal; from normal to any defect; or from paracentral scotoma to central scotoma.

^{||} Stuart Maxwell test for marginal homogeneity.

[¶] One patient not included because visual field was classified as “other isolated defect” at 12 month visit, for which improvement or worsening from baseline was not determined (i.e., nasal step).

Visual Field Severity Shift in Study Eyes of Nonrandomized Study Participants from Baseline to 12 Month Follow-up by Defect Classification

Table 4

Defect Classification	Total No. *	Mean Severity (dB) at		Change in Severity [†]	P [‡]
		Baseline	Follow-up		
Superior arcuate	33	10.55	13.00	2.44	0.13
Superior altitudinal	7	21.83	18.88	-2.95	0.03
Inferior arcuate	40	18.67	18.54	-0.13	0.92
Inferior altitudinal	13	25.80	24.37	-1.43	0.05
Paracentral scotoma	8	13.27	13.31	0.04	0.98
Central scotoma	5	17.40	15.80	-1.60	0.71

* Patients can have defects in 1 location.

[†] Improvement is a decrease in severity (negative change in dB) and worsening is an increase in severity (positive change in dB).

[‡] Paired t test.

Visual Field Pattern Shift in Nonstudy Eyes without Nonarteritic Ischemic Optic Neuropathy at Baseline by Location and Follow-up Visit

Table 5

Change from Baseline Visit to	Visual Field Location	Total No. Fields*	Type of Change				P	
			Improved [†]		Unchanged [‡]			Worse [§]
			No. (%)	No. (%)	No. (%)	No. (%)		
6-Month follow-up visit	Superior	216	45 (20.8)	162 (75.0)	9 (4.2)	0.001		
	Inferior	216	46 (21.3)	159 (73.6)	11 (5.1)	0.000		
	Central	217	12 (5.5)	192 (88.5)	13 (6.0)	0.52		
12-Month follow-up visit	Superior	178	36 (20.2)	134 (75.3)	8 (4.5)	0.001		
	Inferior	181	44 (24.3)	128 (70.7)	9 (5.0)	0.001		
	Central	181	13 (7.2)	155 (85.6)	13 (7.2)	0.88		

* Patients can have defects in 1 location.

[†] Improved defined as change in defect classification from superior or inferior arcuate scotoma to normal; from superior or inferior altitudinal defect to superior or inferior arcuate scotoma or normal; from central scotoma to paracentral scotoma or normal; or from paracentral scotoma to normal.

[‡] Unchanged defined as normal at both baseline and follow-up or defect unchanged from baseline to follow-up.

[§] Worse defined as change in defect classification from superior or inferior arcuate to superior or inferior altitudinal; from normal to any defect; or from paracentral scotoma to central scotoma.

|| Stuart Maxwell test for marginal homogeneity.

Visual Field Pattern Shift in Nonstudy Eyes with Nonarteritic Ischemic Optic Neuropathy at Baseline by Location and Follow-up Visit

Table 6

Change from Baseline Visit to	Visual Field Location	Total No. Fields*	Type of Change				p	
			Improved [†]		Unchanged [‡]			Worse [§]
			No. (%)	No. (%)	No. (%)	No. (%)		No. (%)
6-Month follow-up visit	Superior	55	5 (9.1)	49 (89.1)	1 (1.8)	0.000		
	Inferior	55	2 (3.6)	52 (94.6)	1 (1.8)	0.22		
	Central	55	14 (25.5)	37 (67.3)	4 (7.3)	0.01		
12-month follow-up visit	Superior	54	3 (5.6)	48 (88.9)	3 (5.6)	1.00		
	Inferior	54	2 (3.7)	51 (94.4)	1 (1.9)	0.15		
	Central	54	16 (29.6)	31 (57.4)	7 (13.0)	0.05		

* Patients can have defects in 1 location.

[†] Improved defined as change in defect classification from superior or inferior arcuate scotoma to normal; from superior or inferior altitudinal defect to superior or inferior arcuate scotoma or normal; from central scotoma to paracentral scotoma or normal; or from paracentral scotoma to normal.

[‡] Unchanged defined as normal at both baseline and follow-up or defect unchanged from baseline to follow-up.

[§] Worse defined as change in defect classification from superior or inferior arcuate to superior or inferior altitudinal; from normal to any defect; or from paracentral scotoma to central scotoma.

^{||} Stuart Maxwell test for marginal homogeneity.