A Randomized Trial Comparing Bangerter Filters and Patching for the Treatment of Moderate Amblyopia in Children

*Pediatric Eye Disease Investigator Group Writing Committee**

Objective: To determine whether visual acuity improvement with Bangerter filters is similar to improvement with patching as initial therapy for children with moderate amblyopia.

Design: Randomized, clinical trial.

Participants: We enrolled 186 children, 3 to <10 years old, with moderate amblyopia (20/40–20/80).

Methods: Children were randomly assigned to receive either daily patching or to use a Bangerter filter on the spectacle lens in front of the fellow eye. Study visits were scheduled at 6, 12, 18, and 24 weeks.

Main Outcome Measures: Visual acuity in amblyopic eyes at 24 weeks.

Results: At 24 weeks, amblyopic eye improvement averaged 1.9 lines in the Bangerter group and 2.3 lines in the patching group (difference in mean visual acuities between groups adjusted for baseline acuity = 0.38 line). The upper limit of a 1-sided 95% confidence interval was 0.76 line, which slightly exceeded a prespecified noninferiority limit of <0.75 line. Similar percentages of subjects in each group improved ≥3 lines (Bangerter group 38% vs patching group 35%; $P = 0.61$) or had ≥20/25 amblyopic eye acuity (36% vs 31%, respectively; $P = 0.86$). There was a lower treatment burden in the Bangerter group as measured with the Amblyopia Treatment Index. With Bangerter filters, neither a fixation switch to the amblyopic eye nor induced blurring in the fellow eye to worse than that of the amblyopic eye was required for visual acuity improvement.

Conclusions: Because the average difference in visual acuity improvement between Bangerter filters and patching was less than half a line, and there was lower burden of treatment on the child and family, Bangerter filter treatment is a reasonable option to consider for initial treatment of moderate amblyopia.

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Although patching and atropine are well established as effective treatments for amblyopia,[1-3] Bangerter filters or foils (Ryser Optik AG, St. Gallen, Switzerland) placed on the spectacle lens of the fellow eye have also been used. These transparent filters, available since the 1960s, were designed as a method to modulate the degree of deprivation from occlusion, by producing diffuse image defocus that degrades the fellow eye visual acuity to predicted levels.[4,5] Bangerter filters have been used mostly as secondary treatment after either patching or atropine.[5,6] The potential advantages of using Bangerter filters compared with patching include the ability to change the density of the filter to modulate the degree of deprivation, the possibility of better compliance because the filter is applied to the glasses and not the skin, the possibility of higher parental and child acceptance because the filter is not readily apparent to casual observers, and the possibility that the filter may be less disruptive to binocular function. Potential disadvantages of the filters are that glasses must always be worn properly during treatment; peeking around the filters is relatively easy, and the filters may not uniformly degrade visual acuity to the predicted level reported by the manufacturer.

The effectiveness of the filters as primary treatment for amblyopia has not yet been studied rigorously. Iacobucci et al[6] reported successful treatment in a small case series and Bonsall found similar improvement with patching and filters in a small, randomized trial (Bonsall, unpublished data, March 2006). We designed a randomized trial to determine whether visual acuity improvement with Bangerter filters was similar to daily patching when initiating therapy for moderate amblyopia in children ages 3 to <10 years.

Methods

The study was supported through a cooperative agreement with the National Eye Institute of the National Institutes of Health and was conducted by the Pediatric Eye Disease Investigator Group (PEDIG) at 39 clinical sites. The protocol and Health Insurance Portability and Accountability Act compliant informed consent forms were approved by institutional review boards, and a parent

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or guardian (referred to subsequently as "parent") of each study subject gave written informed consent. The subject gave assent as required. Study oversight was provided by an independent data and safety monitoring committee. The study is listed on www.clinicaltrials.gov, under identifier NCT00525174 (accessed September 10, 2009). The protocol, which is available on the PEDIG website (www.pedig.net, accessed September 10, 2009), is summarized below.

Synopsis of Study Design

Screening/Eligibility. At baseline, visual acuity was measured in each eye, without cycloplegia using optimal spectacle correction, by a study-certified examiner using either the Amblyopia Treatment Study single–surround HOTV protocol (ATS-HOTV) for children aged 3 to <7 years[7] or the Electronic Early Treatment Diabetic Retinopathy Study (E-ETDRS) protocol for subjects aged 7 to <10 years.[8] Additional testing at enrollment included an ocular examination; a cycloplegic refraction using cyclopentolate 1%; measurement of ocular alignment with a simultaneous prism and cover test at distance and near; assessment of binocularity with the Randot Preschool Stereoacuity Test (Stereo Optical Co., Chicago, IL); fixation preference with and without a Bangerter filter; and the fellow eye visual acuity through a Bangerter filter.

Major eligibility criteria for the trial included: age 3 to <10 years, visual acuity in the amblyopic eye 20/40–20/80 (54–71 letters if E-ETDRS used), fellow eye visual acuity 20/40 or better (≥69 letters if E-ETDRS used), interocular acuity difference ≥3 lines (≥15 letters if E-ETDRS used), and the presence of or a history of an amblyogenic factor meeting study-specified criteria for strabismus and/or anisometropia. In addition, all subjects had to be currently wearing spectacles. Spectacles had to provide optimal correction for a minimum of 16 weeks or until stability of visual acuity was documented (no improvement in amblyopic eye visual acuity at 2 consecutive visits ≥4 weeks apart). Exclusion criteria included myopia >6.00 diopters (D) spherical equivalent in either eye, treatment for amblyopia (other than spectacle correction) within the 6 months before enrollment, or inability to complete either the ATS-HOTV test (3 to <7 years old) or the E-ETDRS test (7 to <10 years old). A complete list of eligibility and exclusion criteria is provided in Table 1 (available online at http://aaojournal.org).

Randomization. Each subject was randomly assigned with equal probability, using a permutated block design stratified by age group (3 to <7 years and 7 to <10 years) and site, to receive either daily patching or a Bangerter filter over the fellow eye spectacle lens.

Follow-up Visits. Follow-up visits were conducted at 6, 12, 18, and 24 weeks (±2 weeks), with the 24-week visit specified as the primary outcome visit. At each visit, visual acuity was measured in each eye by a study-certified examiner using the same testing protocol used at enrollment (ATS-HOTV or E-ETDRS). The examiner was masked to treatment group at the 24-week visit. The fellow eye visual acuity was evaluated through a Bangerter filter for all subjects at baseline and for subjects randomized to the Bangerter filter group at follow-up visits using the previously prescribed Bangerter filter. Ocular alignment was assessed at each visit and stereoacuity was measured at the 24-week outcome visit using the Randot Preschool Stereoacuity Test (Stereo Optical Co.).

Treatment. Subjects in the patching group initially were assigned 2 hours of daily patching (Coverlet/3M Opticlude/Ortopad). Subjects assigned to the Bangerter group had a Bangerter filter density of 0.3 (for 20/40–20/63 amblyopic visual acuity) or 0.2 (for 20/80 amblyopic acuity) placed on the spectacle lens over the fellow eye, and the spectacles were to be worn full time. A Grade-Level Reading Assessment Test was administered to subjects ≥7 years old to ensure that they could read grade-appropriate text while using the filter (all subjects could). At each follow-up visit, children in the Bangerter group received a new filter. In both groups, parents were instructed to have their child spend ≥1 hour each day performing near activities while wearing the Bangerter filter or during patching.

A refraction was performed and new spectacles prescribed if indicated at the 12-week visit when amblyopic eye acuity had not improved from baseline by ≥1 line. If the refraction was unchanged, then the treatment intensity was increased to 6 hours of patching a day in the patching group or to a higher density filter in the Bangerter group (0.2 density filter for subjects using the 0.3 filter and 0.1 for subjects using the 0.2 filter.) At the 18-week visit if visual acuity had not improved ≥2 lines from baseline and treatment had not been increased at the 12-week visit, treatment was increased similarly. If Bangerter filter density was increased during the study, subjects again had a reading test and were given glasses without a filter for school work when needed.

Parents recorded the child's level of compliance with the treatment and spectacle use on calendars, which were returned at each visit. Investigators judged compliance as excellent (76%–100%), good (51%–75%), fair (26%–50%), or poor (≤25%) based on the calendars and conversations with the child's parent at each visit. At each visit, the parent was queried about any potential side effects of treatment. At the 6- and 24-week visits, parents completed the Amblyopia Treatment Index questionnaire,[9,10] consisting of 18 Likert-type questions with 5 choices ranging from "strongly agree" to "strongly disagree," that evaluate the impact of treatment on the child and family using predefined subscales consisting of adverse effects, compliance, and social stigma.

Statistical Methods. The trial was designed as a non-inferiority study. The sample size was computed to be 170 subjects to have 90% power and a type 1 error rate of 5% for a noninferiority limit of 0.075 logarithm of the minimum angle of resolution (logMAR), equivalent to 0.75 line, based on the following assumptions from prior PEDIG studies;[1,11–13] a standard deviation of 24-week visual acuity scores of 0.16 logMAR, a correlation between baseline and final acuities of 0.20, and 10% noncompletion of the study primary outcome examination.

The primary outcome measure was the masked 24-week amblyopic eye visual acuity score. An analysis of covariance (ANCOVA) model, in which the logMAR acuity scores were adjusted for baseline amblyopic eye acuity, was used to compute the upper limit of a 1-sided 95% confidence interval constructed on the difference between adjusted mean visual acuity scores for both treatment groups. If the upper limit of this 95% confidence interval was less than the predetermined noninferiority limit, the conclusion of the primary outcome would be that Bangerter filters are noninferior to patching. To be included in the primary analysis, the 24-week examination must have been completed between 20 and 28 weeks (inclusive).

Secondary analyses were conducted using logistic regression for the following 24-week success definitions: amblyopic visual acuity ≥ 20/25, amblyopic eye acuity improvement ≥3 lines (≥15 letters for E-ETDRS testing) from baseline, and amblyopic eye acuity within 1 line (≤+4 letters for E-ETDRS testing) of the fellow eye or better. One subject in the patching group who was treated with a Bangerter filter was considered a failure in these analyses. A similar analysis (post hoc) was performed comparing the proportions of patients in each group who had no improvement or worsening in amblyopic eye acuity from baseline to 24 weeks (change from baseline ≤+4 letters for E-ETDRS testing).

Methods used to analyze the amblyopic eye acuity scores in subgroups and at the 6-, 12-, and 18-week visits paralleled the analysis conducted on the 24-week outcome visit data. In addition, the treatment group difference in the rate of improvement was evaluated using a population averaged linear mixed model after performing an inverse transformation of time to obtain linearity[14]

and in the time to first achieve ≥20/25 acuity was evaluated using a Cox proportional hazard model.[15]

In the Bangerter filter group, the association of fixation preference while the Bangerter filter was over the fellow eye at baseline (amblyopic eye, fellow eye, alternates) with 24-week amblyopic eye acuity was evaluated in an ANCOVA model. Similarly, the relationship between the fellow eye blur from the Bangerter filter at baseline and amblyopic improvement at the 24-week outcome was evaluated with an ANCOVA model with the acuity in the fellow eye being categorized as better than versus equal to or worse than the acuity in the amblyopic eye.

A treatment group difference in the fellow eye visual acuity at 24 weeks was evaluated in an ANCOVA model, adjusted for the baseline fellow eye acuity. Wilcoxon rank-sum tests were used to evaluate change in Randot Preschool stereoacuity levels (from baseline to the 24-week outcome examination) by treatment group and *t*-tests were used to evaluate the parent questionnaire at 6 weeks and at 24 weeks by treatment group using overall and individual subscale scores.

Analyses followed the intent-to-treat principle and were conducted using SAS Version 9.1 (SAS Institute, Cary, NC).

Results

Baseline Characteristics

Between November 2007 and July 2008, 39 sites enrolled 186 subjects (average age, 6.3 years), with 89 randomized to the Bangerter group and 97 to the patching group. The cause of amblyopia was strabismus in 27%, anisometropia in 44%, and a combination of strabismus and anisometropia in 30%. Table 2 provides the baseline characteristics according to treatment group.

Table 2. Baseline Data According to Treatment Group

	Bangerter (N = 89) n (%)	Patching (N = 97) n (%)
Gender: Female	36 (40%)	48 (49%)
Race/ethnicity		
White	69 (78%)	67 (69%)
African-American	1 (1%)	13 (13%)
Hispanic or Latino	15 (17%)	11 (11%)
Asian	0	3 (3%)
More than 1 race	3 (3%)	2 (2%)
Unknown/not reported	1 (1%)	1 (1%)
Age at enrollment (yrs)		
3 to <7	57 (64%)	62 (64%)
7 to <10	32 (36%)	35 (36%)
Mean (SD)	6.3 (1.67)	6.3 (1.62)
Prior treatment for amblyopia at enrollment		
None	72 (81%)	83 (86%)
Patching	5 (6%)	8 (8%)
Atropine	3 (3%)	2 (2%)
Patching and atropine	9 (10%)	4 (4%)
Cause of amblyopia		
Strabismus	23 (26%)	27 (28%)
Anisometropia	39 (44%)	42 (43%)
Strabismus and anisometropia	27 (30%)	28 (29%)
Distance visual acuity in amblyopic eye		
20/80 (0.62–0.56 logMAR)	16 (18%)	23 (24%)
20/63 (0.54–0.46 logMAR)	27 (30%)	31 (32%)
20/50 (0.44–0.36 logMAR)	24 (27%)	22 (23%)
20/40 (0.34–0.28 logMAR)	22 (25%)	21 (22%)
Mean (SD) logMAR	0.44 (0.10)	0.46 (0.10)
Snellen equivalent	$20/50^{-2}$	$20/50^{-3}$
Distance visual acuity in fellow eye		
20/40 (0.32 to 0.26 logMAR)	3 (3%)	2 (2%)
20/32 (0.24 to 0.16 logMAR)	9 (10%)	16 (16%)
20/25 (0.14 to 0.06 logMAR)	19 (21%)	17 (18%)
20/20 (0.04 to −0.04 logMAR)	40 (45%)	42 (43%)
20/16 (−0.06 to −0.14 logMAR)	18 (20%)	20 (21%)
Mean (SD) logMAR	0.03 (0.10)	0.04 (0.10)
Snellen Equivalent	$20/20^{-2}$	$20/20^{-2}$
Intereye acuity difference		
Mean (SD) lines	4.1 (1.1)	4.2 (1.1)
Spherical equivalent in amblyopic eye (D)		
<0.00	8 (9%)	3 (3%)
0 to < +1.00	2 (2%)	2 (2%)
+1.00 to <+2.00	1 (1%)	8 (8%)
+2.00 to <+3.00	10 (11%)	6 (6%)
+3.00 to <+4.00	13 (15%)	10 (10%)
≥+4.00	55 (62%)	68 (70%)
Mean (SD) spherical equivalent	+4.15 (2.57)	+4.41 (2.21)
Spherical equivalent in fellow eye (D)		
<0.00D	5 (6%)	1 (1%)
0 to < +1.00D	16 (18%)	18 (19%)
+1.00 to <+2.00D	21 (24%)	25 (26%)
+2.00 to <+3.00D	12 (13%)	13 (13%)
+3.00 to <+4.00D	13 (15%)	8 (8%)
≥+4.00D	22 (25%)	32 (33%)
Mean (SD) spherical equivalent	+2.49 (2.13)	+2.81 (2.14)

D = diopters; logMAR = logarithm of the minimum angle of resolution; SD = standard deviation.

Visit Completion

The 24-week primary outcome examination was completed by 81 of 89 (91%) subjects in the Bangerter group and 88 of 97 (91%) subjects in the patching group (Fig 1). The vision tester was masked to treatment group for 96% of these examinations (95% in the Bangerter group and 98% in the patching group). Visit completion rates were similar between the 2 treatment groups at the 6, 12, and 18-week examinations (Fig 1).

Treatment

In the Bangerter group, spectacles were changed at the 12- or 18-week visit in 14 (16%) subjects. The density of the filter was increased in 14 (16%) subjects at the 12-week visit and in 29 (33%) at the 18-week visit. In 3 of these subjects the filter density was increased even though amblyopic eye acuity had improved (Table 3; available online at http://aaojournal.org). Adherence with the prescribed regimen using the Bangerter filter over follow-up was judged by the investigator to be excellent in 88%, good in 8%, fair in 4%, and poor in 1% of subjects, and adherence with wearing spectacles over follow-up was judged by the investigator to be excellent in 90%, good in 6%, and fair in 4% of subjects.

In the patching group, spectacles were changed at either the 12- or 18-week visit in 11 (11%) subjects. Patching was increased to 6 hours per day for 7 (7%) subjects at the 12-week visit and 21 (22%) at the 18-week visit. In 2 of these subjects patching was increased even though amblyopic eye acuity had improved and in 6 additional subjects, patching hours were not increased even though visual acuity had not improved (Table 3; available online at http://aaojournal.org). Adherence with the prescribed patching was judged by the investigator to be excellent in 82%, good in 14%, fair in 3%, and poor in 1% of subjects, and adherence with wearing spectacles over follow-up was judged to be excellent in 94% and good in 6% of subjects.

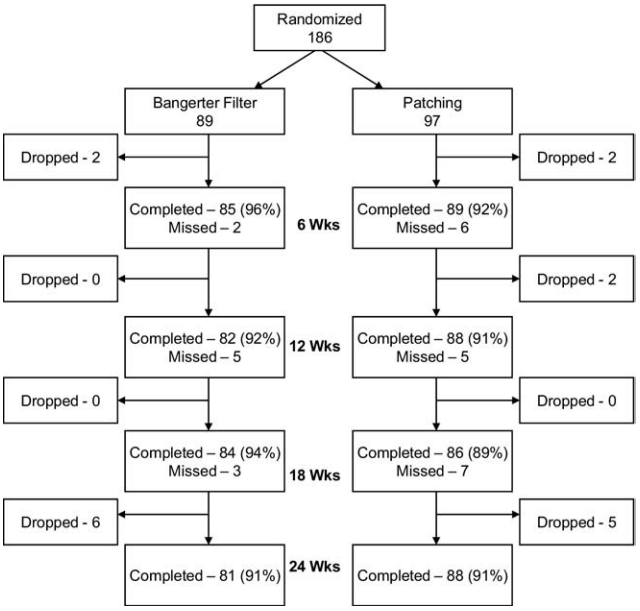

Figure 1. Visit completion by treatment group. Flow chart showing study completion in each treatment group.

Amblyopic Eye Visual Acuity

At 24 weeks, visual acuity was improved from baseline by an average of 1.9 lines in the Bangerter group and 2.3 lines in the patching group (Table 4). The mean difference between groups adjusted for baseline acuity was 0.38 line favoring the patching group. The upper limit of the 1-sided 95% confidence interval was computed to be 0.76 line, which exceeded the predefined upper limit of noninferiority of 0.75 line. However, patching was not statistically superior to Bangerter treatment (95% confidence interval for difference between groups = −0.06 to +0.83 line; P = 0.09). Results of exploratory subgroup analyses are shown in Table 5 (available online at http://aaojournal.org).

Five subjects in the Bangerter group had acuity ≥1 line worse at 24 weeks than at baseline and 13 had the same acuity at both time points compared with 1 and 7, respectively, in the patching group (P = 0.02 for difference in proportions of subjects not improved between treatment groups adjusting for baseline acuity). This is reflected in Figure 2 by noting that a few more subjects in the Bangerter group than the patching group had 24-week amblyopic eye acuity of ≤20/63.

For the prespecified, secondary, 24-week outcomes, ≥20/25 amblyopic eye acuity was achieved by 29 subjects (36%) in the Bangerter group and 27 subjects (31%) in the patching group (P = 0.86); ≥3 lines improvement occurred in 31 subjects (38%) and 31 subjects (35%) in the 2 groups, respectively (P = 0.61); and an interocular difference of <1 line was present in 15 (19%) and 10 (11%), respectively (P = 0.27). The rate of amblyopic eye improvement (Fig 3) and time to 20/25 or better amblyopic eye acuity were not statistically different between treatment groups (P = 0.20 and 0.28, respectively).

Factors Predictive of Improvement in Bangerter Group

Mean visual acuity improvement from baseline to 24 weeks was 1.8 lines in the 53 subjects whose fellow eye acuity with the Bangerter filter at enrollment was equal to or worse than the amblyopic eye and 2.1 lines in the 28 subjects with the fellow eye acuity still better than the amblyopic eye (P = 0.49). However, variability in the degree of the fellow eye degradation induced by the Bangerter filter at baseline was evident as only 111 (60%) of 186 enrolled children were blurred within 1 line of the predicted manufacturer's visual acuity. Similarly, with baseline fixation preference testing while the filter was in front of the fellow eye, mean acuity improvement was 1.6 lines when the amblyopic eye was preferred (n = 20), 1.7 lines when the fellow eye was preferred (n = 33), and 2.3 lines when fixation preference alternated (n = 28; P = 0.21).

Amblyopia Treatment Index

The Parental Amblyopia Treatment Index was completed by 79 of 89 (89%) in the Bangerter group and by 81 of 97 (84%) of the parents in the patching group at the 6-week visit and by 75 of 89 (84%) and 75 of 97 (77%), respectively, at the 24-week visit (Table 6, available online at http://aaojournal.org). Overall, the negative impact of treatment was less among the Bangerter group compared with the patching group at both the 6-week visit (2.1 vs 2.3; P = 0.03) and at the 24-week visit (1.9 vs 2.3; P<0.001). Questionnaire scores on the adverse effects subscale were similar between treatment groups at 6 weeks (mean = 2.2 vs 2.2; P = 0.90), but favored the Bangerter group at 24 weeks (mean = 1.9 vs 2.2; P = 0.01). Questionnaire scores for the compliance subscale were not significantly different at 6 weeks (mean = 2.3 vs 2.5; P = 0.12), but favored the Bangerter group at 24 weeks (mean = 2.1 vs 2.6; P = 0.001). The questionnaire scores favored the Bangerter group at both time points on the social stigma treatment subscale (at 6 weeks, mean = 1.7 vs 2.4 [P<0.001] and at 24 weeks, mean = 1.6 vs 2.4 [P<0.001]).

Stereoacuity

There was no difference between treatment groups in Randot Preschool Stereoacuity scores at the 24-week outcome relative to baseline either overall or among those with anisometropic amblyopia (P = 0.90 and P = 0.88, respectively; Table 7, available online at http://aaojournal.org).

Adverse Events

At 24 weeks, the mean change in the fellow eye visual acuity from baseline was 0.09 line in the Bangerter group and 0.36 line in the patching group (P = 0.07 for difference between treatment groups in the mean fellow eye acuity, adjusted for baseline acuity; Table 8). One subject (1%) in the Bangerter group and 5 (6%) subjects in the patching group tested ≥2 logMAR lines worse in the fellow eye at 24 weeks compared with baseline (Fisher exact test, P = 0.21). Follow-up beyond the end of the study revealed that the fellow eye was ≥20/25 in 4 of the 6 subjects (all in the patching group), and no further follow-up was available in the remaining 2 subjects (1 in the patching group and 1 in the Bangerter group.)

During the study, there were no differences between treatment groups in the number of subjects who developed new-onset strabismus or had an increase or decrease in a preexisting strabismus (data not shown). There were no subjects diagnosed with reverse amblyopia or constant symptomatic diplopia.

Discussion

The current study compared visual acuity improvement using a Bangerter filter with daily patching when initiating therapy for moderate amblyopia (20/40–20/80) over a 24-week period in children ages 3 to <10 years. The study was designed to

Table 4. Visual Acuity in the Amblyopic Eye at Each Study Visit

	6-Week Examination		12-Week Examination		18-Week Examination		24-Week Examination	
	Bangerter *N = 85* *n (%)*	*Patching* *N = 89* *n (%)*	*Bangerter* *N = 82* *n (%)*	*Patching* *N = 88* *n (%)*	*Bangerter* *N = 84* *n (%)*	*Patching* *N = 86* *n (%)*	*Bangerter* *N = 81* *n (%)*	*Patching* *N = 88* *n (%)*
Distribution of visual acuity*								
20/125	0	1 (1%)	1 (1%)	0	0	0	1 (1%)	0
20/100	2 (2%)	0	0	1 (1%)	3 (4%)	1 (1%)	3 (4%)	0
20/80	6 (7%)	4 (4%)	5 (6%)	0	2 (2%)	3 (3%)	3 (4%)	1 (1%)
20/63	7 (8%)	18 (20%)	9 (11%)	8 (9%)	7 (8%)	7 (8%)	7 (9%)	8 (9%)
20/50	17 (20%)	14 (16%)	8 (10%)	14 (16%)	8 (10%)	9 (10%)	5 (6%)	12 (14%)
20/40	28 (33%)	21 (24%)	18 (22%)	16 (18%)	25 (30%)	16 (19%)	19 (23%)	19 (22%)
20/32	20 (24%)	20 (22%)	24 (29%)	24 (27%)	15 (18%)	18 (21%)	14 (17%)	20 (23%)
20/25	4 (5%)	7 (8%)	13 (16%)	16 (18%)	18 (21%)	19 (22%)	20 (25%)	17 (19%)
20/20	1 (1%)	4 (4%)	4 (5%)	8 (9%)	5 (6%)	12 (14%)	9 (11%)	7 (8%)
20/16	0	0	0	1 (1%)	1 (1%)	1 (1%)	0	4 (5%)
Mean (SD) logMAR Snellen Equivalent	0.33 (0.14) $20/40^{-1}$	0.32 (0.16) $20/40^{-1}$	0.28 (0.17) $20/40^{+1}$	0.25 (0.16) $20/32^{-2}$	0.26 (0.17) $20/40^{+2}$	0.23 (0.17) $20/32^{-1}$	0.25 (0.19) $20/32^{-2}$	0.23 (0.16) $20/32^{-1}$
Change from baseline*								
≥3 lines worse	0	0	1 (1%)	0	1 (1%)	0	1 (1%)	0
2 lines worse	1 (1%)	1 (1%)	1 (1%)	0	0	0	2 (2%)	0
1 line worse	7 (8%)	1 (1%)	3 (4%)	2 (2%)	3 (4%)	2 (2%)	5 (6%)	1 (1%)
0 lines	15 (18%)	15 (17%)	11 (13%)	4 (5%)	10 (12%)	6 (7%)	8 (10%)	4 (5%)
1 line better	33 (39%)	31 (35%)	22 (27%)	18 (20%)	19 (23%)	19 (22%)	12 (15%)	19 (22%)
2 lines better	21 (25%)	27 (30%)	18 (22%)	29 (33%)	25 (30%)	20 (23%)	20 (25%)	27 (31%)
≥3 lines better	8 (9%)	14 (16%)	26 (32%)	35 (40%)	26 (31%)	39 (45%)	33 (41%)	37 (42%)
Mean (SD) lines change	1.1 (1.2)	1.4 (1.1)	1.6 (1.4)	2.1 (1.2)	1.8 (1.4)	2.3 (1.4)	1.9 (1.6)	2.3 (1.3)
Proportion ≥20/25 (≥78 letters)	5 (6%)	11 (12%)	17 (21%)	25 (28%)	24 (29%)	32 (37%)	29 (36%)	28 (32%)
Mean (SD) IOD (lines)	2.9 (1.4)	2.9 (1.6)	2.4 (1.9)	2.3 (1.6)	2.4 (1.8)	2.2 (1.7)	2.3 (2.0)	2.3 (1.5)
Proportion IOD <1 line (resolved)	2 (2%)	3 (3%)	13 (16%)	12 (14%)	12 (14%)	13 (15%)	15 (19%)	11 (13%)

IOD = interocular difference; logMAR = logarithm of the minimum angle of resolution; SD = standard deviation.
*Values are rounded to nearest logMAR line.

determine whether Bangerter filters provide essentially the same therapeutic benefit as patching with respect to visual acuity. In a noninferiority study, to use the correct statistical terminology, "essentially the same" must be a priori defined by selecting a noninferiority limit. For this study, a noninferiority limit of 0.75 line was chosen based on consensus from the study planning committee. For the Bangerter filter treatment to meet this definition of noninferiority to patching, the end of the 95% 1-sided confidence interval on the mean difference in change in visual acuity between treatment groups would need to be less than this limit. In our study, although the mean difference between groups was only 0.38 line, the end of the confidence interval on the difference was 0.76 line, and thus, treatment with Bangerter filters did not quite meet the prespecified definition of noninferiority to patching when initiating therapy for moderate amblyopia. However, we also did not find that patching was statistically superior to Bangerter filters. Therefore, we cannot conclude that the Bangerter filter treatment effect is similar to that seen with patching (based on our predefined definition of noninferiority), but we also cannot conclude that patching is definitely better. Compliance assessment was based on parents' diaries and judgment by the researchers. Because we did not use an objective method to measure occlusion or spectacle wear, we cannot guarantee that the patients adhered to their prescribed regimens. For secondary outcomes, the proportions of subjects in the 2 groups for 3 definitions of success (≥20/25 acuity, ≥3 line improvement, and amblyopic eye within 1 line of the fellow eye or better) were similar. Burden of treatment, as assessed with the Amblyopia Treatment Index, was less in the Bangerter group than the patching group with respect to adverse events, compliance,

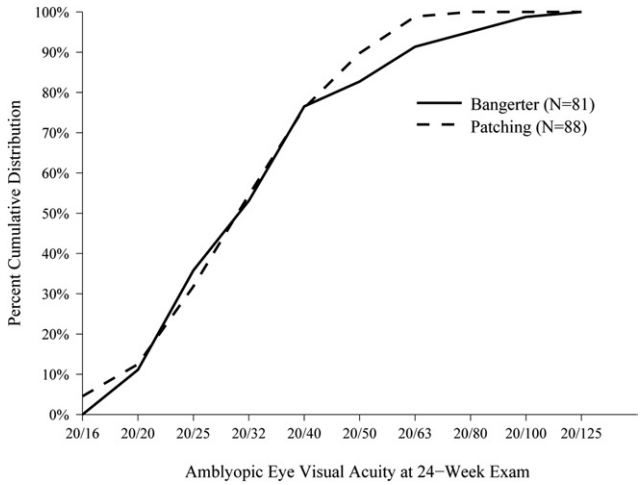

Figure 2. Cumulative distribution of visual acuity at 24-week masked examination. Cumulative distribution of amblyopic eye visual acuity scores at 24-week outcome examination according to treatment group.

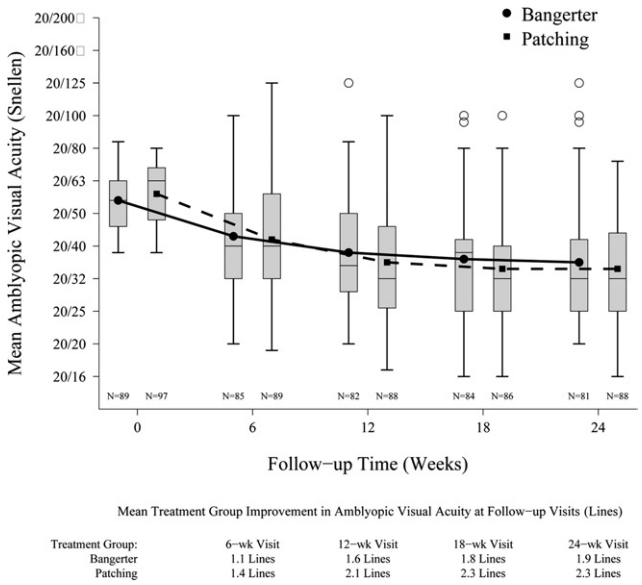

Figure 3. Mean visual acuity in amblyopic eyes from baseline to 24 weeks. At each time point, the box on the left is the distribution of amblyopic eye visual acuity scores for the Bangerter group and that on the right represents the patching group. The top and bottom of each box represents the 25th and 75th percentiles of the data and the line in the box is the median. The treatment group means are represented by a dot (Bangerter) or a square (patching) and are connected across the visits with lines. The bars extending above and below each box represent 1.5 times the interquartile range (difference between the 25th and 75th percentiles). The open circles are outlier values.

and social stigma subscales after 24 weeks of treatment. There was no clear impact of treatment on the fellow eye; more eyes in the patching group had a ≥2-line improvement in acuity, but more in the patching group had a ≥2-line worsening. There also was no difference between treatment groups in the worsening or improvement in stereoacuity.

The slightly better mean amblyopic eye acuity at 24 weeks in the patching group compared with the Bangerter group was largely because more subjects in the Bangerter group having ≥1 more logMAR lines worse acuity (n = 5) or no improvement (n = 13) at 24 weeks compared with baseline acuity than in the patching group (n = 1 and 7, respectively). Of interest, all 5 Bangerter subjects whose acuity worsened ≥1 lines had significant anisometropia ranging from 3 to 6 D and 4 had poor compliance scores for the question specifically relating to the child peeking over the filter on the 6- or 24-week Amblyopia Treatment Index. Thus, it seems plausible that in these subjects amblyopia worsened because of the substantial refractive error in the amblyopic eye, which was not being corrected when the child either did not wear the spectacles or looked over them. When prescribing Bangerter filters for amblyopic patients with high anisometropia, clinicians should carefully monitor spectacle compliance, because visual acuity might worsen if the spectacles are either looked over or not worn.

For subjects in the Bangerter group, amblyopic eye visual acuity improvement did not require that the filter reduce the fellow eye acuity to be worse than the amblyopic eye acuity and did not require a shift in fixation from the fellow eye to the amblyopic eye with the Bangerter filter over the fellow eye. These findings were analogous to those that we have reported with atropine,[1,16] where neither fixation switch to the amblyopic eye nor reduction of visual acuity in the fellow eye to worse than that of the amblyopic eye are necessary for amblyopic eye improvement. The reasons for this phenomenon are not clear. It is possible that the amblyopic eye is used preferentially for some activities while wearing the Bangerter filter or while using atropine. The topic of improvement in amblyopic eye acuity despite no detectable fixation switch is worthy of further study.

The fact that amblyopic eye acuity can improve with a Bangerter filter over the fellow eye even when the visual acuity is not reduced to below that of the amblyopic eye is reassuring, considering the reported variability of blur induced with the filters. Filters of the same manufacturer-labeled density have considerable individual variability in the degree of reduction in acuity, possibly owing to nonuniformity from 1 filter to the next (Repka MX, Gramatikov BI. The reproducibility of blur with a Bangerter filter. J AAPOS 2006:10;80). In addition, there is also variability in reduction of visual acuity with the same filter, possibly owing to nonuniformity across the surface of an individual filter or due to individual patient differences in response to blur[17] (Bustos DE, Donahue SP. Evaluation of Bangerter filters as a predictable means of blurring vision. Invest Ophthalmol Vis Sci 2006;47:E-Abstract 2457). The present study confirms marked variability of blur induced with a Bangerter filter, with 111 (60%) of 186 enrolled children blurred within 1 line of the manufacturer's predicted visual acuity at baseline.

The lower negative impact with Bangerter treatment, as measured on the Amblyopia Treatment Index, indicates that

Table 8. Fellow Eye Visual Acuity at 24-weeks by Treatment Group

	Bangerter N = 81 n (%)	Patching N = 88 n (%)
Distribution of visual acuity		
20/50	1 (1%)	0
20/40	2 (2%)	0
20/32	9 (11%)	11 (13%)
20/25	15 (19%)	16 (18%)
20/20	29 (36%)	25 (28%)
20/16	25 (31%)	36 (41%)
Mean (SD) logMAR	0.02 (0.11)	0.00 (0.10)
Snellen Equivalent	$20/20^{-1}$	20/20
Lines change from baseline		
3 lines or worse	0	0
2 lines worse	1 (1%)	5 (6%)
1 line worse	17 (21%)	8 (9%)
0 lines	39 (48%)	40 (45%)
1 line better	20 (25%)	23 (26%)
2 lines better	4 (5%)	11 (13%)
3 lines or better	0	1 (1%)
*Mean (SD) logMAR lines change	0.09 (0.84)	0.36 (1.1)

logMAR = logarithm of the minimum angle of resolution; SD = standard deviation.
Change from baseline represented rounded values.
*P = 0.07 from an analysis of covariance model in which the logMAR fellow eye acuity scores were adjusted for baseline acuity.

the filters were better accepted by the parents and children in our study when compared with part-time patching. This finding is similar to our previous findings favoring atropine over patching.[1,2,18] Unlike atropine,[1,2] the differences between Bangerter filter treatment and patching in the compliance and adverse effects subscales were not seen at 6 weeks. However, the differences were seen at 24 weeks.

A recent study by Agervi et al[19] compared spectacle correction alone to spectacle correction with Bangerter filters in 80 children with untreated anisometropic amblyopia and found a more rapid visual acuity recovery when Bangerter filters were used, but no difference after 12 months. The investigators suggested that using Bangerter filters may accelerate visual acuity improvement in some children with amblyopia. However, these results do not contribute to our understanding of the results of the current study because we compared Bangerter filters with patching in children only after visual acuity had been maximized with best spectacle correction.

In summary, Bangerter filter treatment did not meet our prespecified criterion to consider the 24-week improvement noninferior to patching when initiating treatment of moderate amblyopia. We believe that failure to meet the prespecified criterion was largely influenced by several subjects in the Bangerter group with anisometropic amblyopia that did not improve during the study, likely owing to poor compliance. Parent-reported negative impact of treatment with respect to adverse effects, compliance, and social stigma was lower with the filters than with patching. When clinicians consider what treatment to prescribe for moderate amblyopia, the impact of the treatment should be considered. Because the average difference in visual acuity improvement between Bangerter filters and patching was less than half a line, and there was less burden of treatment on the child and family, Bangerter filter treatment is a reasonable option to consider when initiating treatment of moderate amblyopia.

References

1. Pediatric Eye Disease Investigator Group. A randomized trial of atropine vs patching for treatment of moderate amblyopia in children. Arch Ophthalmol 2002;120:268–78.
2. Pediatric Eye Disease Investigator Group. Patching vs atropine to treat amblyopia in children aged 7 to 12 years: a randomized trial. Arch Ophthalmol 2008;126:1634–42.
3. Pediatric Eye Disease Investigator Group. Pharmacological plus optical penalization treatment for amblyopia: results of a randomized trial. Arch Ophthalmol 2009;127:22–30.
4. Bangerter A. Occlusion in pleoptics and orthoptics [in German]. Klin Monatsblatter Augenheilkd Augenarztl Fortbild 1960;136:305–31.
5. Lang J. An efficient treatment and new criteria for cure of strabismic amblyopia: reading and Bangerter foils. Binocul Vis Strabismus Q 1999;14:9–10.
6. Iacobucci IL, Archer SM, Furr BA, et al. Bangerter foils in the treatment of moderate amblyopia. Am Orthopt J 2001;51:84–91.
7. Holmes JM, Beck RW, Repka MX, et al, Pediatric Eye Disease Investigator Group. The Amblyopia Treatment Study visual acuity testing protocol. Arch Ophthalmol 2001;119:1345–53.
8. Beck RW, Moke PS, Turpin AH, et al. A computerized method of visual acuity testing: adaptation of the Early Treatment of Diabetic Retinopathy Study testing protocol. Am J Ophthalmol 2003;135:194–205.
9. Cole SR, Beck RW, Moke PS, et al, Pediatric Eye Disease Investigator Group. The Amblyopia Treatment Index. J AAPOS 2001;5:250–4.
10. Holmes JM, Strauber S, Quinn GE, et al, Pediatric Eye Disease Investigator Group. Further validation of the Amblyopia Treatment Index parental questionnaire. J AAPOS 2008;12:581–4.
11. Pediatric Eye Disease Investigator Group. A randomized trial of patching regimens for treatment of moderate amblyopia in children. Arch Ophthalmol 2003;121:603–11.
12. Pediatric Eye Disease Investigator Group. Randomized trial of treatment of amblyopia in children aged 7 to 17 years. Arch Ophthalmol 2005;123:437–47.
13. Pediatric Eye Disease Investigator Group. A randomized trial to evaluate 2 hours of daily patching for strabismic and anisometropic amblyopia in children. Ophthalmology 2006;113:904–12.
14. Verbeke G, Molenberghs G. Linear Mixed Models for Longitudinal Data. New York: Springer; 2000:41–2.
15. Cox DR. Regression models and life-tables. J R Stat Soc Ser B 1972;34:187–220.
16. Pediatric Eye Disease Investigator Group. A randomized trial of atropine regimens for treatment of moderate amblyopia in children. Ophthalmology 2004;111:2076–85.
17. Odell NV, Leske DA, Hatt SR, et al. The effect of Bangerter filters on optotype acuity, Vernier acuity, and contrast sensitivity. J AAPOS 2008;12:555–9.
18. Pediatric Eye Disease Investigator Group. Impact of patching and atropine treatment on the child and family in the Amblyopia Treatment Study. Arch Ophthalmol 2003;121:1625–32.
19. Agervi P, Kugelberg U, Kugelberg M, et al. Treatment of anisometropic amblyopia with spectacles or in combination with translucent Bangerter filters. Ophthalmology 2009;116;1475–80.

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*The writing committee (Appendix 1) appears at the end of this manuscript and a list of the members of the Pediatric Eye Disease Investigator Group (PEDIG) participating in the study is available at http://aaojournal.org.

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Table 1. Eligibility and Exclusion Criteria

Eligibility criteria
1. Age 3 to <10 years
2. Amblyopia associated with strabismus (comitant or incomitant), anisometropia, or both, meeting the following criteria:
   Strabismic amblyopia: At least one of the following criteria must be met and criteria are not met for combined-mechanism amblyopia:
   Heterotropia at distance and/or near fixation on examination (with or without spectacles)
   History of strabismus surgery (or botulinum)
   Documented history of strabismus which is no longer present (and which, in the judgment of the investigator, is the cause of amblyopia)
   Anisometropic amblyopia: At least one of the following criteria must be met:
   ≥0.50 D difference between eyes in spherical equivalent
   ≥1.50 D difference between eyes in astigmatism in any meridian
   Combined mechanism amblyopia: Both of the following criteria must be met:
   Criteria for strabismus are met (see above)
   ≥1.00 D difference between eyes in spherical equivalent or ≥1.50 D difference between eyes in astigmatism in any meridian
3. Visual acuity, measured using the ATS single-surround HOTV protocol for subjects aged <7 years and the E-ETDRS visual acuity testing protocol for subjects 7 to <10 years using the Electronic Visual Acuity Tester, meeting the following criteria:
   Best-corrected visual acuity in the amblyopic eye 20/40–20/80 inclusive (71–54 letters inclusive)
   Best-corrected visual acuity in the fellow eye ≥20/40 (≥69 letters)
   Inter-eye acuity difference ≥3 logMAR lines (i.e., amblyopic eye acuity ≥3 lines by ATS-HOTV or ≥15 letters by E-ETDRS worse than the fellow eye acuity)
4. No amblyopia treatment other than spectacles used in the past 6 months before enrollment. Any treatment >6 months before enrollment is acceptable
5. Ocular examination within 6 months before enrollment
6. Cycloplegic refraction within 6 months before enrollment
7. Spectacles must be worn currently.
8. Spectacle correction for measurement of enrollment visual acuity must meet the following criteria and be based on a cycloplegic refraction that is no more than 6 months old. Requirements for spectacle correction:
   Spherical equivalent must be within 0.50 D of fully correcting the anisometropia
   Hypermetropia must not be undercorrected by more than +1.50 D spherical equivalent, and reduction in plus must be symmetric in the 2 eyes
   Cylinder power in both eyes must be within 0.50 D of fully correcting the astigmatism
   Cylinder axis in the spectacle lenses in both eyes must be within 6 degrees of the axis of the cycloplegic refraction when cylinder power is ≥ 1.00 D
   Myopia of the amblyopic eye greater than 0.50 D by spherical equivalent
   Must be corrected, and the glasses must not undercorrect the myopia by more than 0.25 D or overcorrect it by more than 0.50 D
   Spectacles meeting above criteria must be worn either: for 16 weeks immediately before enrollment, or until visual acuity in amblyopic eye is stable (defined as 2 consecutive visual acuity measurements by the same testing method at least 4 weeks apart with no improvement of one logMAR line or more)
   An acuity measurement done any of the following ways may be considered the first of 2 consecutive measurements: 1) in current glasses, 2) in trial frames with full correction of hypermetropia with cycloplegia, or 3) by having the subject return in new glasses for first measurement. Note: since this determination is a pre-study procedure, the method of measuring visual acuity is not mandated.

Exclusion criteria
1. Presence of an ocular cause for reduced vision
2. Myopia > −6.00 D spherical equivalent in either eye
3. Prior intraocular or refractive surgery
4. Known skin allergy to patch or bandage adhesives
5. Current vision therapy or orthoptics

ATS = Amblyopia Treatment Study; D = diopters; E-ETDRS = Electronic Early Treatment of Diabetic Retinopathy; logMAR = logarithm of the minimum angle of resolution.

Table 3. Treatment Prescribed over Follow-up

	Bangerter N = 89	Patching N = 97
Treatment per protocol		
No change in assigned treatment intensity	46 (52%)	62 (64%)
Increased treatment intensity*	40 (45%)	26 (27%)
12 weeks	12 (14%)	5 (5%)
18 weeks	28 (31%)	21 (22%)
Treatment not per protocol	3 (3%)	9 (9%)
Treatment increased when amblyopic eye acuity improved†	3	2
Treatment not increased when amblyopic eye acuity was not improved	0	6
Crossover‡	0	1

*Increase density of the filter in the Bangerter group and increased patching hours in the patching group.
†Four subjects increased treatment intensity at 12 weeks (2 Bangerter and 2 patching) and 1 Bangerter subject increased treatment intensity at 18 weeks.
‡Switched to Bangerter filter immediately after randomization.

Table 5. Change in Visual Acuity in the Amblyopic Eye at 24-Week Outcome Examination According to Baseline Patient Characteristics

	Bangerter N = 81		Patching N = 88	
	n	*Mean Change in Lines (SD)*	*n*	*Mean Change in Lines (SD)*
Gender				
Female	34	2.1 (1.7)	43	2.4 (1.3)
Male	47	1.7 (1.6)	45	2.2 (1.3)
Race/ethnicity*				
White, non-Hispanic	63	1.8 (1.7)	61	2.3 (1.3)
Non-white or Hispanic	17	2.1 (1.4)	26	2.4 (1.3)
Age at enrollment (yrs)				
3 to <5	21	2.1 (1.9)	23	2.7 (1.4)
5 to <7	31	2.1 (1.7)	34	2.5 (1.2)
7 to <10	29	1.5 (1.3)	31	1.8 (1.2)
Prior treatment for amblyopia at enrollment				
No	65	1.9 (1.7)	75	2.4 (1.3)
Yes	16	2.0 (1.4)	13	1.7 (1.0)
Cause of amblyopia				
Strabismus	21	2.2 (1.5)	23	2.4 (1.3)
Anisometropia	36	1.5 (1.7)	39	2.4 (1.4)
Strabismus and anisometropia	24	2.2 (1.5)	26	2.1 (1.2)
Distance visual acuity in amblyopic eye at baseline				
20/80 (53–57 letters)	15	2.3 (2.0)	22	2.3 (1.3)
20/63 (58–62 letters)	25	1.8 (1.7)	29	2.5 (1.5)
20/50 (63–67 letters)	20	1.7 (1.7)	17	2.3 (1.4)
20/40 (68–72 letters)	21	1.9 (1.0)	20	2.0 (1.1)

SD = standard deviation.
*Two subjects (1 in each treatment group) were excluded owing to unknown/not reported ethnicity classification.

Table 6. Parent Amblyopia Treatment Index Response at 24-Week Outcome

		Bangerter N = 75 (Mean = 1.9)					
	Item (abbreviated)	*Strongly Disagree 1*	*Disagree 2*	*Neither Agree nor Disagree 3*	*Agree 4*	*Strongly Agree 5*	*Bangerter Avg. Response (1–5)*
		%					
1	Child seems to mind treatment	56	27	4	12	1	1.8
2	Worry child may miss out on fun activities	41	51	4	1	3	1.7
3	Treatment affects child's learning	37	41	12	8	1	1.9
4	Treatment makes it hard for child to play	40	45	4	9	1	1.9
5	Trouble applying treatment to child	52	28	8	12	0	1.8
6	Treatment is a source of tension for me						
	a. with child	55	32	1	12	0	1.7
	b. with another family member*	55	38	5	1	0	1.5
	c. with my child's teacher†	53	37	7	1	1	1.6
7	Difficult for child to draw, color, or write	33	40	13	12	1	2.1
8	Worry child will be injured on treatment	48	43	5	4	0	1.7
9	My child cannot see well while on treatment	27	44	21	7	1	2.1
10	Child complains when it is time for treatment	41	29	8	17	4	2.1
11	Worry that child not getting enough treatment	47	32	8	11	3	1.9
12	Child clumsy on treatment	37	39	12	11	1	2.0
13	Other children stare at child	49	44	4	3	0	1.6
14	Treatment will not improve my child's vision	44	44	8	1	3	1.7
15	Treatment makes it difficult for child to play	44	40	7	7	3	1.8
16	Sometimes forget to apply treatment to child	55	33	4	8	0	1.7
17	Worry that child feels different	48	40	7	5	0	1.7
18	Notice child peeking over filter/pulling off patch	13	19	12	37	19	3.3

*"Not applicable" responses appeared on 9 questionnaires (1 Bangerter and 8 Patching).
†"Not applicable" responses appeared on 29 questionnaires (7 Bangerter and 22 Patching).

Examination (Higher scores reflect negative impact of treatment)

Patching N = 75 (Mean = 2.3)					
Patching Avg. Response (1–5)	*Strongly Disagree 1*	*Disagree 2*	*Neither Agree nor Disagree 3*	*Agree 4*	*Strongly Agree 5*
	%				
2.4	15	56	7	19	4
2.0	31	48	16	4	1
1.8	37	49	9	4	0
2.5	19	44	16	16	5
2.3	29	37	12	17	4
2.2	33	39	11	13	4
1.8	36	49	12	3	0
1.8	30	58	11	0	0
2.4	20	44	16	17	3
1.9	31	55	7	8	0
2.6	9	47	19	25	0
3.3	13	16	17	39	15
2.7	9	48	15	23	5
2.2	17	56	13	13	0
2.6	12	44	23	15	7
1.7	48	43	5	3	1
2.1	21	57	13	7	1
2.9	9	40	3	47	1
2.3	17	55	13	13	1
2.6	15	48	8	21	8

Table 7. Randot Preschool Stereoacuity at Baseline and at the 24-Week Outcome Examination by Treatment Group

	Baseline		24 Weeks	
Randot Preschool Stereoacuity (arc second)	*Bangerter (N = 89)*	*Patching (N = 97)*	*Bangerter (N = 81)*	*Patching (N = 87)*
All subjects				
Failed pretest	6 (7%)	6 (6%)	2 (2%)	2 (2%)
>800	45 (51%)	45 (46%)	40 (49%)	36 (41%)
800	11 (12%)	8 (8%)	6 (7%)	10 (11%)
400	10 (11%)	7 (7%)	4 (5%)	11 (13%)
200	9 (10%)	11 (11%)	15 (19%)	12 (14%)
100	5 (6%)	12 (12%)	9 (11%)	9 (10%)
60	3 (3%)	6 (6%)	3 (4%)	4 (5%)
40	0	2 (2%)	2 (2%)	3 (3%)

	Treatment Group	
Change in Stereoacuity (Levels)	*Bangerter (N = 76)*	*Patching (N = 80)*
≥2 levels improved	12 (16%)	15 (19%)
Within 1 level	61 (80%)	58 (73%)
≥2 levels worsened	3 (4%)	7 (9%)

P = 0.90 from Wilcoxon rank-sum test for difference between treatment groups in distribution of levels of change from baseline to 24 weeks.

	Baseline		24 Weeks	
Randot Preschool Stereoacuity (arc second)	*Bangerter (N = 39)*	*Patching (N = 42)*	*Bangerter (N = 36)*	*Patching (N = 38)*
Subjects with anisometropia and no strabismus*				
Failed pretest	5 (13%)	3 (7%)	1 (3%)	1 (3%)
>800	13 (33%)	9 (21%)	10 (28%)	6 (16%)
800	3 (8%)	2 (5%)	2 (6%)	2 (5%)
400	6 (15%)	5 (12%)	2 (6%)	5 (13%)
200	5 (13%)	8 (19%)	11 (31%)	9 (24%)
100	5 (13%)	8 (19%)	5 (14%)	8 (21%)
60	2 (5%)	5 (12%)	3 (8%)	4 (11%)
40	0	2 (5%)	2 (6%)	3 (8%)

	Treatment Group	
Change in Stereoacuity (Levels)	*Bangerter (N = 33)*	*Patching (N = 34)*
≥2 levels improved	7 (21%)	9 (26%)
Within 1 level	25 (76%)	21 (62%)
≥2 levels worsened	1 (3%)	4 (12%)

P = 0.88 from Wilcoxon rank-sum test for difference between treatment groups in distribution of levels of change from baseline to 24 weeks.
*Cause of amblyopia at time of randomization.