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A Randomized Trial of Increasing Patching for Amblyopia

Pediatric Eye Disease Investigator Group*, David K. Wallace, MD, MPH¹, Elizabeth L. Lazar, MSPH², Jonathan M. Holmes, BM, BCh³, Michael X. Repka, MD, MBA⁴, Susan A. Cotter, OD, MS⁵, Angela M. Chen, OD⁵, Raymond T. Kraker, MSPH², Roy W. Beck, MD, PhD², Michael P. Clarke, MD⁶, Ingrid J. Lorenzana, OD⁷, David B. Petersen, MD⁸, Joan T. Roberts, MD⁹, and Donny W. Suh, MD¹⁰

¹Duke University Eye Center, Durham, North Carolina ²Jaeb Center for Health Research, Tampa, Florida ³Mayo Clinic, Rochester, Minnesota ⁴Wilmer Ophthalmological Institute, Johns Hopkins University, Baltimore, Maryland ⁵Southern California College of Optometry, Fullerton, California ⁶Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, United Kingdom ⁷Advanced Vision Center, Schaumburg, Illinois ⁸Rocky Mountain Eye Care Associates, Salt Lake City, Utah ⁹North Carolina Eye, Ear, & Throat, Durham, North Carolina ¹⁰Wolfe Eye Clinic, West Des Moines, Iowa

Abstract

Objective—After treatment with refractive correction and patching, some patients have residual amblyopia resulting from strabismus or anisometropia. We conducted a clinical trial to evaluate the effectiveness of increasing prescribed daily patching from 2 to 6 hours in children with stable residual amblyopia.

Design—Prospective, randomized, multicenter clinical trial.

Participants—A total of 169 children aged 3 to <8 years (mean, 5.9 years) with stable residual amblyopia (20/32–20/160) after 2 hours of daily patching for at least 12 weeks.

Intervention—Random assignment to continue 2 hours of daily patching or increase patching time to an average of 6 hours/day.

Main Outcome Measures—Best-corrected visual acuity (VA) in the amblyopic eye after 10 weeks.

Results—Baseline VA was 0.44 logarithm of the minimum angle of resolution (logMAR) (20/50⁻²). Ten weeks after randomization, amblyopic eye VA had improved an average of 1.2 lines in the 6-hour group and 0.5 line in the 2-hour group (difference in mean VA adjusted for acuity at randomization = 0.6 line; 95% confidence interval, 0.3–1.0; *P* = 0.002). Improvement of 2 or more lines occurred in 40% of participants patched for 6 hours versus 18% of those who continued to patch for 2 hours (*P* = 0.003).

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Correspondence: David K. Wallace, MD, MPH, c/o Jaeb Center for Health Research, 15310 Amberly Drive, Suite 350, Tampa, FL 33647. pedigal5@jaeb.org.

*A list of the members of the Pediatric Eye Disease Investigator Group participating in the study is available at <http://aaojournal.org>.

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Conclusions—When amblyopic eye VA stops improving with 2 hours of daily patching, increasing the daily patching dosage to 6 hours results in more improvement in VA after 10 weeks compared with continuing 2 hours daily.

Amblyopia is the most common cause of monocular visual impairment in both children and young and middle-aged adults.^{1,2} Partly on the basis of previous randomized amblyopia treatment trials performed by the Pediatric Eye Disease Investigator Group (PEDIG), many practitioners prescribe an initial dose of 2 hours daily patching of the fellow eye if strabismic or anisometropic amblyopia does not resolve with spectacles alone.^{3–7} Although many children are successfully treated with this regimen, some fail to attain normal visual acuity (VA) in the amblyopic eye. When improvement with initial patching therapy stops and amblyopia is still present, treatment options include maintaining the same treatment and dose, increasing the intensity of the same treatment, switching to another treatment, or combining different treatment modalities. Many clinicians will choose to increase the patching dosage, but it is unknown whether this approach is effective. Our aim was to determine whether increasing prescribed patching dosage improves amblyopic eye VA in children aged 3 to <8 years with apparently stable residual amblyopia after prescribed initial treatment with 2 hours of daily patching.

Materials and Methods

The study was supported through a cooperative agreement with the National Eye Institute of the National Institutes of Health and conducted by the PEDIG. The protocol and Health Insurance Portability and Accountability Act–compliant informed consent forms were approved by institutional review boards, and a parent or guardian (referred to subsequently as parent) of each study participant gave written informed consent. The study adhered to the tenets of the Declaration of Helsinki, oversight was provided by an independent data and safety monitoring committee, and the study is listed on www.clinicaltrials.gov (NCT00945100, accessed November 27, 2012). The study protocol is available on the PEDIG website (www.pedig.net, accessed November 27, 2012) and is summarized next.

Synopsis of Study Design

Before being considered for the randomized trial, participants who had not already completed at least 12 weeks of 2 hours of daily patching, with demonstrated VA stability, were enrolled into a run-in phase and treated with 2 hours of daily patching (and spectacles if needed), with follow-up every 6 weeks until no improvement. The minimum amount of time in spectacles (if needed) before randomization was 6 weeks, with the majority of participants undergoing such optical treatment for at least 12 weeks.

Major eligibility criteria for the randomized trial included (1) age 3 to <8 years; (2) treatment of amblyopia with 2 hours of prescribed daily patching for at least 12 weeks, with no improvement in VA at 2 visits at least 6 weeks apart (confirmed by a retest), during which there was no change in spectacle correction; (3) best amblyopic eye VA of 20/40 to 20/160 inclusive with an interocular difference (IOD) of 2 lines or an amblyopic eye VA of 20/32 with 3 lines of IOD; (4) the presence of strabismus or anisometropia meeting study-specific criteria (Table 1, available at <http://aaojournal.org>); (5) fellow eye VA of 20/32 or better; and (6) reported compliance of 10 hours per week when prescribed 2 hours of daily patching.

Data were entered on the PEDIG website, and participants were randomly assigned (using a permuted block design stratified by site) with equal probability to continue 2 hours of daily patching (subsequently referred to as the 2-hour group) or to increase treatment intensity to 42 hours of weekly patching (subsequently referred to as the 6-hour group).

Participants assigned to the 6-hour group were instructed to patch 6 hours every day, but if that was not possible because of activities and so forth, they were allowed to vary the number of daily patching hours to meet the overall goal of 42 hours per week.

Testing Procedures and Follow-up

Follow-up consisted of a primary outcome examination at 10 ± 1 weeks after randomization and additional visits every 10 ± 1 weeks until there was no improvement in VA of at least 1 line, confirmed by a retest.

At each visit, VA was measured in each eye without cycloplegia using the participant's optimal spectacle correction (if applicable) by a study-certified tester using the ATS-HOTV⁸ protocol on the Electronic Visual Acuity Tester⁹. Ocular alignment was measured with a simultaneous prism and cover test at distance and near at randomization and each follow-up visit, and stereoacuity was measured with the Randot Preschool Stereoacuity Test (Stereo Optical Co., Chicago, IL) at randomization and the 10-week visit. The 10-week outcome VA was the primary study end point and was obtained by a study-certified tester who was masked to the participant's assigned treatment. Participants whose 10-week amblyopic eye VA improved at least 1 line since randomization (based on the better of the test and retest VA) continued in the study with visits every 10 ± 1 weeks until there was no further improvement in VA, confirmed by a retest.

At each follow-up visit, investigators judged compliance with patching treatment to be excellent ($>75\%$), good ($51\%–75\%$), fair ($26\%–50\%$), or poor ($<25\%$). This was based on discussions with the parent and on review of the study calendars maintained by the parent, who recorded the numbers of hours the child patched each day.

Statistical Methods

The primary outcome measure was the masked 10-week amblyopic eye VA score. The sample size for the randomized trial was computed to be 158 participants to have 90% power with a type I error rate of 5% and no more than 5% loss to follow-up to reject a null hypothesis of no difference between groups, assuming the true treatment group difference in 10-week VA was as small as 0.75 logarithm of minimum angle of resolution (logMAR) line and a standard deviation of 1.4 logMAR lines (based on a prior PEDIG study using patching for the treatment of amblyopia).³

The primary analysis was a treatment group comparison of the masked 10-week amblyopic eye VA using an analysis of covariance (ANCOVA) model, adjusting for VA at randomization. The primary analysis included data from 10-week VA examinations completed between 8 and 15 weeks (inclusive), with no imputation for missing data. Alternative analyses yielded similar results (data not shown) and consisted of the following: exclusion of 10-week VA examinations outside the 10 ± 1 week protocol window, adjustment for baseline covariates imbalanced between treatment groups, and imputation of 10-week VAs for participants with missing 10-week scores. The treatment effect in subgroups according to baseline factors of sex, race/ethnicity, cause of amblyopia, age, and amblyopic eye VA at randomization was assessed by including interaction terms in the ANCOVA models.

Secondary analyses compared (1) the amblyopic eye VA at the visit of best VA after randomization (10-week examination or later) using the same analysis methods as the primary treatment group comparison; (2) the proportion of participants with ≥ 2 logMAR lines of improvement in amblyopic eye VA from randomization to the 10-week examination and to the visit of best VA after randomization between each group using logistic regression,

adjusting for VA at randomization; and (3) the 10-week IOD using an ANCOVA model, adjusting for IOD at randomization.

Fisher exact test was used to compare the proportions in each treatment group with a loss of 2 or more lines in the better of the initial test and retest (if indicated) fellow eye VAs at the 10-week examination and final visit since randomization. Exact Wilcoxon rank-sum tests were used to compare change in Randot Preschool stereoacuity levels from randomization to the 10-week examination by treatment group. Analyses followed the intent-to-treat principle and were conducted using SAS version 9.3 (SAS Inc, Cary, NC). If a retest was performed, then the amblyopic eye efficacy analyses were performed using the initial VA, and the retest was used only to determine whether the participant continued in the study.

Results

Between September 2009 and December 2012, 45 sites randomized 169 participants to increase patching time to an average of 6 hours per day ($n=86$) or continue 2 hours of daily patching ($n=83$). The average age was 5.9 years, and the average amblyopic eye VA was 0.44 logMAR ($\sim 20/50^{-2}$). Table 2 provides the baseline characteristics at randomization according to treatment group.

Visit Completion and Treatment

The 10-week primary outcome examination was completed by 83 (97%) and 82 participants (99%) in the 6-hour and 2-hour groups, respectively (Fig 1). The vision tester was masked to treatment group for 97% of VA examinations (98% and 96% in the 6-hour and 2-hour groups, respectively).

Treatment compliance during the initial 10 weeks of patching was judged to be excellent in 72%, good in 17%, fair in 6%, and poor in 5% of participants randomized to the 6-hour group and was excellent in 85%, good in 13%, fair in 0%, and poor in 3% of those in the 2-hour group (Table 3, available at <http://aaojournal.org>). One participant in the 6-hour group received atropine treatment off protocol 2 weeks before the 10-week primary outcome examination.

Amblyopic Eye Visual Acuity: Primary Analysis at 10 Weeks

At the 10-week primary outcome visit, amblyopic eye VA improved from randomization by an average of 1.2 lines and 0.5 line in the 6-hour and 2-hour groups, respectively (Table 4). The treatment group difference in mean VA after 10 weeks, adjusted for VA at randomization, was 0.6 line (2-sided 95% confidence interval [CI], +0.3 to +1.0 line; $P=0.002$), favoring the 6-hour group. Amblyopic eye VA met the prespecified secondary outcome of 2 lines improvement for 33 participants (40%) and 15 participants (18%) in the 6-hour and 2-hour groups, respectively (difference, 22%; 2-sided 95% CI, +8% to +35%; $P=0.003$). The treatment group difference in mean IOD after 10 weeks, adjusted for IOD at randomization, was 0.5 line (2-sided 95% CI, +0.1 to +1.0 line; $P=0.01$), favoring the 6-hour group (Table 4).

Adjustment for treatment group imbalances in amblyopia cause and degree of amblyopic eye spherical equivalent at enrollment did not affect the results of the primary outcome analysis (data not shown). In subgroup analyses, there was an indication of a greater treatment effect, favoring 6 hours, among female participants compared with male participants ($P=0.04$) (Table 5).

One additional randomized participant had not reached the 10-week outcome by the time of submission of this article, but imputing data as either the extremes of no change or maximal improvement did not influence the results.

Follow-up after 10-Week Primary Outcome

At the 10-week primary outcome evaluation, 63 participants (76%) in the 6-hour group and 55 participants (67%) in the 2-hour group met the study criteria for continued treatment (amblyopic eye VA improved ≥ 1 line from previous visit) (Fig 1). Follow-up continued for 1 additional study visit for 41 participants in the 6-hour group and 33 participants in the 2-hour group, 2 visits for 12 and 16 participants, and 3 or more visits for 4 and 3 participants, respectively.

The best VA after randomization at the 10-week primary outcome or any subsequent visit improved by an average of 1.5 lines from randomization in the 6-hour group and 0.9 line in the 2-hour group (treatment group difference adjusted for baseline VA $+0.5$ line; 2-sided 95% CI, $+0.04$ to $+1.0$ line) (Table 6). Forty-two participants (51%) in the 6-hour group and 32 participants (39%) in the 2-hour group improved ≥ 2 lines in amblyopic eye VA at the best visit after randomization (difference, $+12\%$; 2-sided 95% CI, -3 to $+27\%$).

Two randomized participants (1 described earlier in the primary outcome analysis) had not reached best VA after randomization by the time of submission of this article, but imputing data as either the extremes of no change or maximal improvement did not influence the results.

Amblyopic eye VA did not improve from randomization for 25 participants (30%) in the 6-hour group and 29 participants (35%) in the 2-hour group. For those who did show improvement in VA, the time point of best amblyopic eye VA was at the 10-week primary outcome for 42 participants (51%) and 29 participants (35%) in the 6-hour and 2-hour groups, respectively; 18 to <25 weeks for 10 participants (12%) and 20 participants (24%), respectively; and ≥ 25 weeks for 6 participants (7%) and 4 participants (5%), respectively.

Stereoacuity

Randot Preschool Stereoacuity scores did not differ between the treatment groups at the 10-week primary outcome relative to randomization for the overall cohort ($P = 0.28$) and when limited to participants with no history of strabismus ($P = 0.45$) (Table 7, available at <http://aaojournal.org>).

Adverse Events

The fellow eye VA tested ≥ 2 lines worse from randomization for 2 participants at the 10-week outcome (1 in each group; $P > 0.99$ for comparison between groups) and for 3 participants at the final visit (all 3 in the 2-hour patching group, $P = 0.12$) (Table 8, available at <http://aaojournal.org>). During the randomized trial, there were no treatment group differences in the number of participants who developed new-onset strabismus or had an increase in a preexisting strabismus (data not shown). No participants developed diplopia.

Discussion

We studied the effect of increasing the intensity of prescribed patching for children aged 3 to <8 years with residual amblyopia from strabismus or anisometropia who had stopped improving after wearing spectacles (if needed) and patching 2 hours daily for at least 12 weeks. We found that continuing patching at both doses led to further improvement. Increasing the daily patching dose to 6 hours resulted in an average of 1.2 lines additional

improvement at 10 weeks compared with 0.5 line of additional improvement when continuing 2 hours. Forty percent of participants in the 6-hour group improved by 2 or more lines at 10 weeks compared with 18% of those in the 2-hour group.

A potential limitation of our study is that some participants were unable to comply with their prescribed patching regimen. This study was designed as an effectiveness study, in which we compared prescribed patching regimens and did not formally measure treatment compliance. However, patching compliance was judged to be excellent or good for 90% and 96% of participants in the 6-hour and 2-hour groups, respectively, based on discussions with the parent and by reviewing daily dosage calendars maintained by the parent. One reason for the good compliance observed in this study is that participants were ineligible if they did not patch at least 10 of the 14 prescribed weekly hours for at least 12 weeks before randomization.

We know of no prior studies that have evaluated the effectiveness of increased patching when amblyopic VA stops improving with an initial treatment of 2 hours daily patching (and period of spectacle wear if required). The results of this study differ from those of a previous PEDIG study in which initial treatment outcomes (after spectacles) were similar with 2 or 6 hours of prescribed patching.⁴ However, the previous study differed from the current study because it evaluated patching dosage as the *initial* treatment for amblyopia and enrolled children with no patching within the previous 6 months. In addition, children in the current study were eligible only if they demonstrated good compliance with 2 hours of daily patching before randomization.

In another PEDIG study, children with an amblyopic eye VA of 20/32 to 20/63 who had stopped improving with 6 hours of prescribed daily patching or with daily atropine did not demonstrate better VA outcomes after a 10-week intensive final push of combined treatment with patching and atropine compared with a control group in whom treatment was gradually discontinued.¹⁰ However, these participants had more intensive treatment before randomization than those in the current study, possibly reducing the chance for further improvement.

At the 10-week primary outcome visit in the current study, 24% of participants in the 6-hour group and 33% of those in the 2-hour group had not improved, which was confirmed by a retest. Those participants whose VA had improved at least 1 line continued in their randomized treatment groups and were reexamined every 10 weeks until there was no further improvement. On average, both groups continued to show improvement with longer follow-up. At the visit with the best-measured VA after randomization, the amblyopic eye had improved from baseline an average of 1.5 lines in the 6-hour group and 0.9 line in the 2-hour group. This difference between groups was similar in magnitude to that found at the primary outcome visit. However, the comparison of best VA after randomization of the amblyopic eye is possibly biased because not all participants were followed beyond the 10-week primary outcome examination.

On the basis of the primary outcome data, it is reasonable to increase patching to 6 hours daily when improvement seems to stall after patching 2 hours daily. Nevertheless, it is noteworthy that 39% of children who continued patching 2 hours per day improved by 2 or more lines at their best VA after randomization (Table 6). As such, it would not be unreasonable to continue 2 hours of daily patching for 1 or more cycles, even when VA seems to have stopped improving. Such a treatment plan would be particularly applicable for a family who is unable to patch their child 6 hours every day.

We found female participants to be more responsive to increased patching. This finding of a greater difference in effect for female participants is most likely due to chance, although it is

possible that female participants were more compliant with 6 hours of daily patching than male participants.

Even with the stringent prerandomization requirement of at least 12 weeks of 2 hours of daily patching and no improvement measured between 2 visits at least 6 weeks apart (confirmed by a retest), some children continued to improve with 2 hours of daily patching. One possible explanation for improvement despite apparent stability is that the Amblyopia Treatment Study VA testing protocol⁹ used provides acuity measurements in 0.1-logMAR (1 line of VA) increments, which may be larger than a child's actual improvement between tests. If a child's VA improved at a rate of less than 1 line between visits, then it might have seemed to be stable at randomization when in fact it was still slowly improving. Another possibility is that although we required 2 acuity tests on the same day to confirm lack of improvement, some children may have tested below their true VA on the day of randomization because of lack of effort, inexperience, fatigue, or test—re-test variability, again masking real improvement in VA. These or other factors could give the impression of lack of improvement from the previous visit before randomization, when in fact some of these children were still improving and not stable at randomization. We have observed apparent stability in VA in previous PEDIG studies only to discover that some children continued to improve, indicating that our definitions of “stability” may not be robust.^{6,10} In the present study, randomization is likely to have equally distributed children who were not yet truly stable with 2 hours of daily patching between the treatment groups, and therefore our primary findings would not have been influenced by whether VA was stable before randomization.

In conclusion, when amblyopic eye VA stops improving with 2 hours of daily patching, increasing the daily patching intensity to 6 hours results in more improvement in VA after 10 weeks compared with continuing 2 hours daily. This approach of increasing patching when VA seems to stop improving with lower-dose patching can now be incorporated into an evidence-based, stepwise management strategy for amblyopia (Fig 2). Amblyopia treatment may begin with spectacles alone, followed by a choice of low-dose patching, weekend atropine, or a Bangerter filter. If significant amblyopia persists, we now know that it is reasonable to increase the dose of patching therapy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Visit completion by treatment group. *One participant in the 6-hour patching group did not complete the 10-week visual acuity exam within the analysis window (8 to 15 weeks after randomization), and therefore the visual acuity exam will be considered missed for the 10-week primary outcome analyses.

Figure 2.

Evidence-based approach to management of amblyopia. * Alternative approaches include changing treatment modality to atropine or Bangerter filter have yet to be studied.

Table 2

Baseline Characteristics of All Randomized Participants According to Treatment Group

	2Hrs (N = 83)		6Hrs (N = 86)	
	<i>n</i>	%	<i>n</i>	%
Female sex	43	52	43	50
Race/ethnicity				
White	57	69	66	77
Black/African American	8	10	2	2
Hispanic	14	17	14	16
Asian	2	2	3	3
>1 race	2	2	1	1
Age at randomization, yrs				
3–<4	5	6	8	9
4–<5	15	18	15	17
5–<6	27	33	19	22
6–<7	17	20	25	29
7–<8*	19	23	19	22
Mean (SD)	5.9 (1.3)		5.9 (1.2)	
Enrollment disposition				
No current treatment	48	58	49	57
On treatment	18	22	18	21
Ready for randomization	17	20	19	22
Duration of patching before randomization (wks)				
12–<16	14	17	21	24
16–<25	39	47	31	36
>25	30	36	34	40
Mean (SD)	24.5 (10.7)		24.4(11.9)	
Amblyopia cause				
Strabismus	16	19	16	19
Anisometropia	41	49	34	40
Strabismus and anisometropia	26	31	36	42
Best distance VA in the amblyopic eye at randomization				
20/160	2	2	3	3
20/125	3	4	1	1
20/100	2	2	7	8
20/80	6	7	6	7
20/63	17	20	21	24
20/50	26	31	24	28
20/40	21	25	18	21
20/32	6	7	6	7
Mean (SD) logMAR	0.43 (0.15)		0.45 (0.16)	

	2Hrs (N = 83)		6Hrs (N = 86)	
	<i>n</i>	%	<i>n</i>	%
Snellen equivalent	~20/50 ⁻²		~20/63 ⁺²	
Best distance VA in the fellow eye at randomization				
20/32	5	6	5	6
20/25	17	20	21	24
20/20	27	33	26	30
20/16	34	41	34	40
Mean (SD) logMAR	-0.01 (0.09)		0.00 (0.09)	
Snellen equivalent	~20/20		~20/20	
Best interocular eye VA difference at randomization				
Mean (SD) logMAR lines	4.4	(1.6)	4.5	(1.7)
Refractive error in amblyopic eye at enrollment, D				
0-<+1.00	9	11	3	3
+ 1.00-<+2.00	5	6	3	3
+2.00-<+3.00	2	2	4	5
+3.00- +4.00	13	16	6	7
>+4.00	54	65	70	81
Mean (SD)	4.58 (2.26)		5.27 (1.94)	
Refractive error in fellow eye at enrollment, D				
<0	1	1	1	1%
0-<+1.00	22	27	14	16
+ 1.00-<+2.00	30	36	19	22
+2.00-<+3.00	10	12	14	16
+3.00-<+4.00	4	5	12	14
+4.00	16	19	26	30
Mean (SD)	2.10 (1.86)		2.89 (2.06)	

D = diopters; logMAR = logarithm of the minimum angle of resolution; SD — standard deviation; VA — visual acuity.

* Seven participants (5 in the 2-hour group and 2 in the 6-hour group) were aged <8 years at time of enrollment into the run-in phase and 8 years at time of randomization (8.1, 8.1, 8.2, 8.2, and 8.6 in 2-hour group, and 8.0 and 8.5 in 6-hour group).

Table 4**Amblyopic Eye Visual Acuity at 10-Week Primary Outcome**

	2Hrs (n=82)	6Hrs (n=82)
Change in VA from randomization		
3 lines worse	1(1)	0(0)
2 lines worse	3(4)	2(2)
1 line worse	13 (16)	7(9)
No change (0)	19 (23)	17 (21)
1 line improved	31 (38)	23 (28)
2 lines improved	13 (16)	19 (23)
3 lines improved	2(2)	14(17)
Mean (SD) change in lines	0.5 (1.2)	1.2 (1.4)
Distribution of VA		
20/200	1(1)	0(0)
20/160	0(0)	0(0)
20/125	3(4)	3(4)
20/100	3(4)	2(2)
20/80	8(10)	4(5)
20/63	6(7)	9(11)
20/50	19 (23)	15 (18)
20/40	23 (28)	20 (24)
20/32	14(17)	15 (18)
20/25	3(4)	12(15)
20/20	2(2)	2(2)
20/16	0(0)	0(0)
Mean (SD) logMAR VA	0.38 (0.19)	0.33 (0.18)
(Snellen equivalent)	-20/50+ ¹	~20/40~ ²
Mean (SD) IOD (lines)	3.7 (2.2)	3.2 (2.1)
Difference between treatment groups (2-sided 95% CI), lines of IOD *	+0.5 (+0.1-+1.0) <i>P</i> = 0.01	
Difference between treatment groups (2-sided 95% CI), logMAR lines *	+0.6 (+0.3-+1.0) <i>P</i> = 0.002	

CI = confidence interval; IOD = interocular difference; logMAR = logarithm of the minimum angle of resolution; SD = standard deviation; VA = visual acuity. Values shown as n (%) unless otherwise indicated. One participant in the 6-hour patching group was excluded from the primary outcome analysis because the 10-week VA was tested more than 15 weeks after randomization.

* Positive difference indicates favorable outcome for 6-hour daily patching group.

Table 5

Visual Acuity in the Amblyopic Eye According to Baseline Characteristics

	No. of Participants		VA (logMAR) at Randomization		Change from Randomization to 10-Wk Primary Outcome Examination (logMAR Lines)		P _{value} for interaction *
	2 hrs	6 hrs	2 hrs	6 hrs	2 hrs	6 hrs	
Subgroups							
Sex							
Female	43	41	0.44 (0.17)	0.45 (0.16)	0.4 (1.3)	1.4 (1.3)	0.04
Male	39	41	0.41 (0.13)	0.44 (0.14)	0.7 (1.1)	0.9 (1.5)	
Race/ethnicity							
White (non-Hispanic)	56	63	0.42 (0.16)	0.45 (0.14)	0.5 (1.0)	1.2 (1.4)	0.89
Nonwhite/Hispanic	26	19	0.43 (0.14)	0.43 (0.17)	0.5 (1.6)	1.1 (1.3)	
Age at randomization (yrs)							
3–<5	20	23	0.45 (0.14)	0.44 (0.12)	0.9 (1.0)	1.5 (1.4)	0.49
5	62	59	0.42 (0.16)	0.45 (0.16)	0.4 (1.2)	1.0 (1.4)	
VA in amblyopic eye at randomization							
20/80	12	15			0.7 (1.4)	1.3 (1.6)	
20/63	17	21			0.7 (1.3)	1.6 (1.4)	0.37
20/50	26	24			0.4 (1.2)	1.4 (1.1)	
20/40	27	22			0.4 (1.1)	0.5 (1.3)	
Cause of amblyopia							
Strabismus	16	15	0.46 (0.17)	0.43 (0.15)	1.1 (1.2)	1.4 (1.3)	
Anisometropia	40	31	0.39 (0.11)	0.43 (0.13)	0.3 (1.2)	1.3 (1.5)	0.50
Combined mechanism	26	36	0.47 (0.19)	0.46 (0.16)	0.5 (1.1)	1.0 (1.4)	

logMAR = logarithm of the minimum angle of resolution; VA = visual acuity.

Values shown as mean (standard deviation) unless otherwise indicated. One participant in the 6-hour patching group was excluded from the primary outcome analysis because the 10-week VA was not performed within the analysis window (8–15 weeks after randomization).

* P_{value} based on the interaction between treatment group and each subgroup factor in an analysis of covariance (ANCOVA) model to evaluate change in 10-week amblyopic eye VA, adjusting for VA at randomization, and main effects corresponding to the interaction term. Age and amblyopic eye VA at randomization were treated as continuous factors in the ANCOVA models.

Table 6**Amblyopic Eye Visual Acuity at Best Visit after Randomization**

	Best VA after Randomization (10 Wks or Later*)	
	2 Hrs (n=82)	6 Hrs (n=83)
Change in VA from randomization		
3 lines worse	1(1)	0(0)
2 lines worse	3(4)	2(2)
1 line worse	12(15)	6(7)
No change (0)	13 (16)	17 (20)
1 line improved	21 (26)	16 (19)
2 lines improved	22 (27)	21 (25)
3 lines improved	10 (12)	21 (25)
Mean (SD) change in lines	0.9 (1.5)	1.5 (1.6)
Distribution of VA		
20/200	1(1)	0(0)
20/160	0(0)	0(0)
20/125	2(2)	2(2)
20/100	3(4)	3(4)
20/80	7(9)	4(5)
20/63	7(9)	7(8)
20/50	15 (18)	11 (13)
20/40	16 (20)	21 (25)
20/32	15 (18)	14(17)
20/25	12(15)	15 (18)
20/20	3(4)	5(6)
20/16	1(1)	1(1)
Mean (SD) logMAR VA	0.33 (0.21)	0.30 (0.19)
(Snellen equivalent)	~20/40~ ²	~20/40
Difference between treatment groups (2-sided 95% CI), logMAR lines [†]	+0.5 (0.04--1.0)	

CI = confidence interval; logMAR = logarithm of the minimum angle of resolution; SD = standard deviation; VA = visual acuity.

Values shown as n (%) unless otherwise indicated.

* The median number of weeks of treatment was approximately 10.1 weeks (9.0–33.0 weeks) for the 2-hour group and 10.0 weeks (8.0–51.7 weeks) in the 6-hour group

[†] Positive difference indicates favorable outcome for the 6-hour group.