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Facilitated versus self-guided training of non-ophthalmologists for grading pre-plus and plus disease using fundus images for retinopathy of prematurity screening

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Abstract

Purpose—Retinopathy of prematurity (ROP) is an important cause of preventable blindness; barriers to screening necessitate novel approaches. While trained non-ophthalmologists can accurately grade retinal images for ROP, effective training protocols are not established. This study compares the effectiveness of facilitated versus self-guided training of non-ophthalmologists for grading retinal images for pre-plus or plus disease in ROP.

Methods—Forty-eight undergraduate and graduate students were trained to grade retinal images for the presence of pre-plus or plus disease. Students were randomly assigned to one of two training protocols. Both utilized identical electronic slideshows; one guided by an in-person facilitator, and the other was self-guided. After completing their respective training, students proficient in grading pre-plus and plus disease graded images in a telemedicine screening scenario. Accuracy of grading was compared to the reference standard of clinical examination.

Results—83% (40/48) of trained students (91% in the facilitated vs. 77% in the self-guided group, $p=0.26$) were proficient and qualified to grade the ROP telemedicine screening scenario. Median accuracy for grading normal, pre-plus or plus disease was 69% (70% in the facilitated vs. 68% in the self-guided group, $p=0.91$). When considering the designation of pre-plus or plus disease by graders as a screening test for detecting plus disease (confirmed on clinical exam), the median sensitivity and specificity of all students was 95% and 64%, respectively.

Conclusions—Both facilitated- and self-guided teaching protocols yielded similar performance in ROP image grading for pre-plus or plus disease. Self-guided training protocols may be adequate to train non-ophthalmologists to grade retinal images for pre-plus and plus disease with high sensitivity.

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Introduction

Retinopathy of Prematurity (ROP) is a major cause of avoidable blindness among prematurely born infants in both the developing and developed world.^{1,2} While timely screening and treatment decreases the risk of retinal detachment and blindness,^{3,4} a barrier to effective screening is the low percentage of ophthalmologists who are trained for and participate in screening for ROP.⁵ In fact, in 2006 the American Academy of Ophthalmology reported that only half of pediatric and retinal ophthalmology specialists treat for ROP, and a fifth plan to stop.⁶

In response to these barriers, the application of telemedicine has gained popularity for ROP screening. While indirect ophthalmoscopy remains the gold standard, alternative imaging modalities are emerging as potential tools for ROP screening.⁷ Interpretation of images obtained using the Nidek,⁸ RetCam,^{9,10} Pictor,¹¹ and Keeler indirect¹² have been evaluated as strategies for ROP screening.

The use of trained non-ophthalmologists to help screen for ROP could help address the shortage of trained ophthalmologists to screen for ROP in some areas of the world. Several studies have shown that trained non-ophthalmologists can accurately grade retinal images for ROP;^{9,13} however, *standardized* training protocols for non-ophthalmologist graders have not been developed. To date, studies that have involved training ROP graders typically employ conventional facilitated didactic instruction.^{9,13}

The purpose of this study is to compare the effectiveness of facilitated versus self-guided training of non-ophthalmologists for grading retinal images for plus and pre-plus in ROP.

Methods

This prospective study was approved by the Duke Health System Institutional Review Board and conformed to the requirements of the US Health Insurance Portability and Accountability Act.

Image Selection

The images used in this study were a subset of images used in a previous study evaluating the ability of masked ROP experts to accurately grade for the presence of pre-plus or plus disease in retinal images of prematurely-born infants obtained using the Vantage Plus LED Digital Binocular Indirect Ophthalmoscope (Keeler Instruments Inc., Broomall, PA) and a 28 D condensing lens during routine ROP rounds.¹² In the previous study, images were graded for image quality (good, fair and poor based on the ability of the grader to determine vessel dilation and tortuosity), number of gradable quadrants ("gradable" defined as at least one major vessel visible for a distance of at least one disc diameter), and the presence of pre-plus or plus disease (defined by the international classification of ROP [ICROP]-revisited¹⁴).

Image Sets

Telemedicine Screening Scenario—Starting with the 253 images used in the previous study,¹² we created an image grading set as follows: for images of plus and pre-

plus disease, we chose those where the two expert graders agreed on the diagnosis of pre-plus or plus disease and graded the images as having “good quality” with at least two gradable quadrants. For normal images, we chose those images graded as normal with “good quality” and four gradable quadrants by both graders. These criteria resulted in an imaging grading set with 59 normal, 32 pre-plus, and 16 plus images (n=107).

Pre- and Post-Test—We also selected a set of images for use in both a “pre-test” and a “post-test”. These images were selected from images obtained by the Keeler system during routine ROP rounds during the same time period as the previous study,¹² but were not used in that study. Ten images were approved and classified as normal, pre-plus, or plus disease by consensus agreement of 3 fellowship-trained pediatric ophthalmologists (DKW, SFF, SGP) after meeting the following criteria: good quality, 4 gradable quadrants, and a diagnosis of normal (n=4), pre-plus (n=3), or plus (n=3) disease as determined by clinical examination. Both the “pre-test” and “post-test” contained the same images, but the image order differed.

Teaching Slideshow

An 18-slide ROP teaching electronic slideshow was constructed to provide basic education in the diagnosis of pre-plus and plus disease in ROP to a participant with no former training in ophthalmology. We defined terms important to the understanding and grading of pre-plus and plus disease, such as dilation and tortuosity, but did not include the classification of zone or stage. We also provided a normal retinal image depicting quadrants and normal vessel architecture. We then created slides defining and describing plus and pre-plus disease, specifically pointing out the vessel architecture. These slides included the ICROP-revisited pre-plus and plus standardized photographs, both with animated arrows/labels indicating examples of tortuosity and dilation (Figure 1A and 1B).^{14,15} The slideshow also provided users with an animated algorithm to help them decide if a retinal image fulfilled criteria for pre-plus or plus disease. The slideshow ended with three example retinal images whose diagnoses (normal, pre-plus and plus) and explanations appeared when participants advanced through the slideshow (Figure 1C). Importantly, this slideshow was created to engage participants by requiring them to advance through the individual images, comments, arrows/labels, and diagnoses.

Subject selection and enrollment (Figure 2)

We aimed to enroll a convenience sample of 40 participants to complete the telemedicine screening scenario, 10 from each of four majors: engineering, nursing, physician assistant programs, and global health. The participants were required to be full-time degree-seeking students at Duke University enrolled in one of the above programs.

Study Protocol

Before any instruction was given, participants were given the pre-test electronic slideshow. This began with brief definitions of ROP, normal posterior pole, pre-plus and plus disease followed by a 10-slide grading scenario, each slide including 4 images as was shown to expert graders in a previous study¹²: (1) standard plus disease image from ICROP-revisited, (2) standard pre-plus disease image from ICROP-revisited, (3) normal posterior pole image,

and (4) an “unknown” image to be graded (layout similar to Figure 1C). Participants were instructed to grade each unknown posterior pole image as normal, pre-plus or plus disease. Plus disease was defined according to the ICROP-revisited definition as “the presence of sufficient vascular dilation and tortuosity as compared to a standard photograph in 2 quadrants of the eye.”¹⁴ Pre-plus disease was defined as “vascular abnormalities of the posterior pole that are insufficient for the diagnosis of plus disease but that demonstrate more arterial tortuosity and more venous dilation than normal.”¹⁴

Subsequently, participants within each major were assigned using block randomization to complete the electronic ROP teaching slideshow either with a study facilitator or self-guided. The study facilitator, a medical student (NNR) with comprehensive training in ROP classification and diagnosis, guided all facilitated training, teaching only the information contained in the slideshow without providing any additional information, thus acting solely as a guide through the slides.

Immediately following the completion of the ROP teaching slideshow, participants were given a 10-slide post-test. A score of 90% correct was required on the post-test for participants to continue to the telemedicine screening scenario. We continued recruiting until 10 students from each of the above majors passed the post-test in order to move onto the telemedicine screening scenario.

As soon as they completed and passed the post-test, each qualified participant independently completed the telemedicine screening scenario. Participants were asked to grade the images for posterior pole disease as (1) normal, (2) pre-plus, or (3) plus disease.

Statistical Analysis

We calculated the accuracy of each participant grader to correctly grade the presence of normal vessels vs pre-plus vs plus disease compared to the reference standard of clinical exam findings by indirect ophthalmoscopy performed on the same day as images were acquired. We calculated sensitivity and specificity of participants’ grades of pre-plus *or* plus disease to detect the presence of plus disease as diagnosed on clinical examination. We chose to include the diagnosis of pre-plus as a positive test for plus disease in order to increase sensitivity for detection of plus disease. Sensitivity, specificity, and accuracy were calculated for each major and for the group of students as a whole. For comparison, these statistics were also calculated for the two expert graders who graded this subset of images in a previous study.¹²

Results

Forty-eight students were recruited from the majors of engineering (n=10), nursing (n=14), physician assistant program (n=12), and global health (n=12).

Forty (83%) of the 48 participants passed the post-test. Of those who passed the post-test, 77% (20/26) completed the slideshow as a self-guided exercise and 91% (20/22) completed the teaching slideshow with a study facilitator (p=0.26).

In the post-test, one image (Figure 3) was incorrectly graded by 52% of participants compared to the next most incorrectly graded image, which was graded incorrectly by 13%. Figure 3 was taken from an infant clinically diagnosed with pre-plus, and it was graded as normal by 18% and plus by 33% of all students in the post-test.

For the telemedicine screening scenario, mean accuracy for grading normal, pre-plus or plus disease was 69% (70% in the facilitated vs. 68% in the self-guided group ($p=0.91$)) (Table 1). When considering the designation of plus or pre-plus disease by participants as a screening test for detecting plus disease (as diagnosed on clinical exam), the mean sensitivity of all students was 95% and the mean specificity was 64% (Table 1). Comparing facilitated and self-guided groups, the sensitivities were 93% and 96% ($p=0.25$), respectively, and specificities were 65% and 64% ($p=0.98$), respectively. For the two expert graders who graded this subset of images in a previous study¹², when considering their grading of plus or pre-plus disease, sensitivity and specificity for detecting plus disease was 100% and 76–78%, respectively.

Discussion

This study compared the effectiveness of facilitated versus self-guided training of non-ophthalmologists to grade retinal images for ROP screening. We found that trained non-ophthalmologists can grade retinal images with high sensitivity to screen for plus disease and that grading performance (i.e. sensitivity and specificity) of the self-guided vs. facilitated training groups were similar. Non-ophthalmologists were able to screen retinal images for plus disease with a sensitivity comparable to that of ophthalmologists expert at ROP screening.

In this study we trained non-ophthalmologists to screen for ROP by having them grade for the presence of pre-plus or plus disease, *but not zone or stage*, for several reasons. Currently, the presence of plus disease largely drives the decision to treat severe ROP, and previous studies have shown that screening for plus disease may be sufficient for true ROP screening.^{3,16,17} Pre-plus is predictive of future need for treatment, especially when present between 33–36 weeks post-menstrual age.¹⁸ The ETROP study established that the indication for treatment is type 1 ROP, defined as zone I disease (any stage) with plus, zone I (stage 3) without plus, or zone II (stage 2 or 3) with plus. Although type 1 ROP included stage 3 in zone I without plus disease, one study found that normal retinal vasculature reliably signifies a lack of stage 3 disease.¹⁷ In addition, ROP characterization into zones and stages can be difficult, especially for non-ophthalmologists, which would decrease sensitivity and specificity in grading retinal images for ROP.^{13,16} Thus, the ideal training protocol for non-ophthalmologists to help screen for treatment-warranted (type 1) ROP could be focused on posterior pole vessel characteristics rather than zone and stage.³ In an ideal screening protocol, sensitivity for plus disease would be 100%, at the expense of some specificity. To increase the sensitivity of detecting premature infant eyes with plus disease, we considered a grade of pre-plus *or* plus to be a “positive test” for ROP screening. Thus, if a non-ophthalmologist judges an image to be pre-plus or plus disease, an exam by an ophthalmologist trained in ROP screening using indirect ophthalmoscopy would be warranted.

Previous studies have shown that non-ophthalmologists can be trained to grade retinal images for ROP with high sensitivity and specificity.^{9,13} When grading for treatment-requiring ROP (defined as type 1 ROP³ or threshold ROP (defined as at least five contiguous or eight cumulative clock hours of stage 3 ROP in zone I or II, in the presence of plus disease)⁴), William et al. reported a sensitivity of 82% and specificity of 92% for non-expert medical students.¹³ When grading for referral-warranted ROP (any ROP in zone I, plus disease, or any stage 3 ROP)¹⁹, Quinn et al. report sensitivity of 82% and specificity of 90% for trained non-experts.⁹ When grading for presence of pre-plus or plus disease, our study found a sensitivity of 95% and specificity of 64% for trained non-ophthalmologists to detect the presence of plus disease seen on clinical exam.

ROP screening algorithms should have a high sensitivity so as not to miss treatment-requiring disease and a high specificity to decrease the number of unnecessary exams. While the non-ophthalmologist student graders in our study had a high sensitivity for plus disease, they had specificity that was lower than desired, suggesting there is room for improvement in our training protocol. Our low specificity has many possible causes. In order to minimize the number of missed cases, we included the grade of pre-plus or plus disease as a positive test for plus disease. This intentionally decreases specificity as these pre-plus eyes (if graded correctly as pre-plus) increase the number of false positives. The low specificity may also result from the teaching slideshow's implicit warning that a missed case of ROP could lead to blindness. This fear by non-ophthalmologist graders may prompt over-grading of normal posterior vasculature as pre-plus or plus disease which would also increase the number of false positives. Another possibility is that some retinal images were out of focus, which could give the impression of wider caliber retinal vessels due to edge blur, thereby leading to over-diagnosis of pre-plus and plus disease.

When the judgment of pre-plus or plus was considered a positive screening test for plus disease, we found that graders in the facilitated vs. self-guided training groups showed similar sensitivity (93% vs 96%, respectively) and specificity (65% vs 64%, respectively). Similarly, accuracy for grading for normal, pre-plus, and plus disease between self-guided and facilitated training groups was similar (70% vs 68%, respectively). While other studies have used didactic lectures lasting up to two hours,^{9,13} our goal was to create a more streamed-lined training protocol by simplifying the training and minimizing training time. We focused our training on information paramount to diagnose plus and pre-plus disease, such as vessel characteristics of dilation and tortuosity. From a global perspective, if graders can be trained effectively using a self-guided training protocol, there would be no need for trainers or trainees to travel for in-person training, conserving resources. Also, the trainee could complete the training process at a convenient time, which would make the training more widely available to interested trainees who may have other obligations that would otherwise deter them from participating. This would be particularly useful in inaccessible areas and in middle-income countries where the need for ROP screening is even greater.²⁰

Self-directed learning approaches have many advantages. One study indicated that most allied-health students prefer self-directed learning approaches, giving credence to the self-guided electronic slideshow used in the present study.²¹ The learning style, however, may depend on the participant's level of education; more mature participants, such as those with

work experience, tend to favor self-directed learning compared with those in the early stages of education.²² This study specifically recruited participants who, despite not having any previous training in ocular pathology, were actively pursuing degrees that may one day influence telemedicine. For example, nursing, physician assistant, global health, and engineering students may one day be involved in ROP rounds, imaging, global telemedicine, and ROP software/hardware development, respectively. Thus, not only may our participants be motivated in telemedicine screening, but their educational maturity may make them more fit for self-directed learning.

This study must be viewed in light of its limitations. Our sample size was small, so we did not have adequate power to detect a small difference between groups, and we could not stratify our analysis based on student major. In addition, because we specifically chose participants from the majors of nursing, physician assistant, engineering, and global health, our results may not be generalizable to other non-ophthalmologists. Also, the statistically insignificant difference between the facilitated and self-guided groups was possibly augmented by the intentional “weeding out” those students with poor scores on the post-test, thus creating more equal groups. Finally, it is difficult to establish “truth” when choosing a reference standard for plus disease. It has been shown that, even among experts, there is significant disagreement when diagnosing for plus disease in retinal images.^{23,24,25}

We found similar effectiveness of facilitated versus self-guided training of non-ophthalmologists to grade retinal images for ROP. Not only can non-ophthalmologists be trained to accurately grade retinal images to detect plus disease, but their training can occur without the need for an in-person training facilitator. Validated self-guided training protocols could increase our workforce to screen for ROP without adding the additional burden of in-person training. This approach could help extend care, especially to remote locations where there is a need for increased manpower for ROP screening.

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Figure 1.

Slides from the teaching slideshow. (A and B) Two slides defining plus disease with accompanying labeled standard International Classification of Retinopathy of Prematurity (ICROP)-revisited plus disease photo.¹⁴ (C) A practice slide. The unknown image is in the lower right corner. Normal and ICROP-revisited standardized images of pre-plus and plus disease are shown for comparison.^{14,15} The answer and explanation appears after the participant has formulated his or her own answer. [Plus disease images reproduced with permission from Arch Ophthalmol. 2006; 124(11): 1669–1670. Copyright©(2006) American Medical Association. All rights reserved. Pre-plus disease image reproduced with permission from Arch Ophthalmol. 2005; 123(7):991–999. Copyright©(2005) American Medical Association. All rights reserved. Normal image reprinted with permission from J AAPOS, Vol 18/1, Prakashaporn SG, Freedman SF, Wallace DK, Evaluation of an indirect ophthalmoscopy digital photographic system as a retinopathy of prematurity screening tool, 36–41,2014, with permission from Elsevier.]

Figure 2.
Schematic of study protocol. Parentheses indicate number of participants.

Figure 3.
The most incorrectly graded image in the post-test.

Table 1

Accuracy of grading normal, pre-plus or plus disease and the sensitivity and specificity for detecting plus disease (as diagnosed on clinical exam). Retinal images were graded for the presence of pre-plus or plus disease by two ophthalmologists expert in ROP examination, as well as by non-ophthalmologist student graders (divided by study major).

	Accuracy (%)	Sensitivity ¹	Specificity ¹
Engineering students	72	94	66
Nursing students	69	95	64
Physician Assistant students	66	97	58
Global Health students	68	92	68
Total for the above majors combined	69	95	64
Expert ROP grader #1 ²	80	100	78
Expert ROP grader #2 ²	82	100	76

¹We calculated sensitivity and specificity of graders' grades of pre-plus *or* plus disease to detect the presence of plus disease as diagnosed on clinical examination

²Data from Prakalapakorn SG et al. Evaluation of an indirect ophthalmoscopy digital photographic system as a retinopathy of prematurity screening tool. J AAPOS 2014;18:36–41.