Evaluation of an indirect ophthalmoscopy digital photographic system as a retinopathy of prematurity screening tool

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PURPOSE To determine whether digital retinal images obtained from an indirect ophthalmoscopy imaging system (Keeler) can be accurately graded for clinically significant retinopathy of prematurity (ROP) by masked experts.

METHODS The medical records of infants screened for ROP who had posterior pole images acquired using the Keeler system during routine ROP examinations were retrospectively reviewed. Two reviewers, masked to patient demographics and clinical examination findings, graded the images for: (1) quality (good, fair, poor); (2) number of gradable quadrants, from 0 to 4; and (3) posterior pole disease (none, pre-plus, plus). The accuracy of grading Keeler images for clinically significant ROP (defined as pre-plus or plus disease) was compared to results of clinical examination.

RESULTS One eye each of 253 infants was included. The mean postmenstrual age at examination was 35 weeks (range, 30-42). Grader 1 found the quality of 94% of images to be fair or good; grader 2, 83% of images. Grader 1 judged 87% of images to have ≥3 gradable quadrants; grader 2, 77% of images. The sensitivity and specificity of grading pre-plus or worse disease on Keeler images were 100% and 86%, respectively, for grader 1, and 94% and 89%, respectively, for grader 2.

CONCLUSIONS Digital retinal images obtained by the Keeler system can be read with high sensitivity and specificity to screen for clinically important ROP. The Keeler system may be a valuable tool for ROP screening at remote locations (ie, via telemedicine). (J AAPOS 2014;18:36-41)

Retinopathy of prematurity (ROP) remains an important cause of blindness, especially in the developing world.[1] Appropriate screening and treatment could reduce the burden of childhood blindness due to ROP, but there are many barriers to effective ROP screening, including the shortage of ophthalmologists trained to screen for ROP[2] and the lack of access to these ophthalmologists. According to current guidelines in the United States, retinal screening examinations should be performed by an ophthalmologist trained to screen for ROP using binocular indirect ophthalmoscopy with a lid speculum, with or without scleral depression.[3]

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The Vantage Plus LED Digital Binocular Indirect Ophthalmoscope system (Keeler Instruments Inc, Broomall, PA) consists of a binocular indirect ophthalmoscope with an integrated camera that can capture still and/or dynamic images during the examination, which can be stored in various digital formats for later review. The field of view obtained by the Keeler system is similar to that seen during the standard examination with binocular indirect ophthalmoscopy. The field of view of images obtained by the Keeler system should theoretically be adequate for evaluating the posterior pole for the presence of pre-plus or plus disease.

Currently, the presence of plus disease drives the decision to treat ROP.[4] In the absence of plus disease, type 1 ROP (ie, treatment-requiring ROP) can be present only if there is stage 3 in zone 1, which is not only unusual but also would not be expected with a completely normal posterior pole.[5] Thus it might not be necessary for a true ROP "screening test" (versus a diagnostic examination performed by a trained ophthalmologist) to include views of the peripheral retina if the objective is to identify infants requiring a standard examination with indirect ophthalmoscopy by an experienced ophthalmologist to evaluate need for treatment. Obtaining and interpreting images of the vessels of the posterior pole alone may be a reasonable method to screen for those infants with type 1 ROP.

The purpose of this study was to evaluate whether digital retinal images obtained using an indirect ophthalmoscopy imaging system could be accurately graded by masked experts for clinically significant ROP (CSROP), defined for purposes of this study as pre-plus or plus disease.

Methods and Materials

This 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 of 1996. The medical records of all infants screened for ROP over a 2-year period (November 2009-November 2011) at the Duke University Neonatal Intensive Care Unit (NICU) were retrospectively reviewed. Demographic data of eligible patients were extracted, including date of birth, gestational age, birth weight, and date of ROP examinations. Postmenstrual age was calculated based on date of examination and date of birth. As part of our routine screening for ROP, we digitally recorded every examination using the Vantage Plus LED Digital Binocular Indirect Ophthalmoscope and a 28 D condensing lens. All examinations were performed by one of two pediatric ophthalmologists (SFF or DKW), both of whom have extensive experience with ROP examination and classification and have been certified investigators in multicenter ROP clinical trials.[4,6,7] Prior to examination, all infants were dilated. At our institution, ROP examinations occurred starting at 30 weeks postmenstrual age or 4 weeks of age, whichever was later, for infants with birth weight <1500 g or gestational age ≤30 weeks, and for selected infants with birth weight 1500-2000 g or gestational age >30 weeks who had an unstable clinical course, per recommended guidelines at the time of screening.[8] Follow-up examinations occurred according to current published guidelines at the time of the examination.[4,8] The presence or absence of ROP and the zone, stage, and presence or absence of plus or pre-plus disease were documented for each eye according to current international classification guidelines.[7] Our criterion for laser treatment was the development of type 1 ROP as established by the Early Treatment for ROP study.[4]

Inclusion criteria included hospitalization at the Duke University NICU, birth weight <1500 g or gestational age ≤30 weeks, ROP screening from November 1, 2009 to November 16, 2011, and availability of digital images obtained by the Keeler system at the time of screening. Infants were excluded if they had received laser or anti-vascular endothelial growth factor (VEGF) treatment prior to having an examination recorded by the Keeler system during the study period.

The images from one examination date were chosen for each infant (Figure 1). The images were chosen in order to enhance the sample by including an adequate number of posterior pole images representing pre-plus and plus disease. If an infant required treatment (ie, laser or anti-VEGF treatment), the latest eligible examination date prior to treatment was selected. Otherwise, for each infant, the examination date with the most severe posterior pole disease (plus > pre-plus > normal) was selected. If there were several examination dates that contained the most severe posterior pole disease, the date closest to when the infant had a postmenstrual age of 36 weeks was selected. If two examinations were performed equidistant from 36 weeks, the earlier examination date was chosen. Any examination performed after treatment was excluded.

After the examination date was chosen, we reviewed the images recorded on that date by the Keeler system for the infant. If a video recording was obtained on the selected screening date, still images were created using a video converter (Windows Movie Maker 2.6, Microsoft, Redmond, WA). To be eligible for inclusion, images had to include a view of the optic nerve. Only images from one eye for each infant were included. Images of the right eye were selected unless no eligible image was available, in which case left eye images of the same examination date were selected. Up to 3 images for the selected eye could be included because not all of the images of the posterior pole were centered on the optic nerve and our goal was to provide graders with at least 1 disk diameter length of a major vessel in each quadrant.

An electronic slide show was created with one "unknown" image per slide. If more than 1 image was included per subject, these images were placed in the slide show consecutively and labeled A, B, and C, as appropriate, to indicate that the images belonged to the same subject (up to 3 slides for each eye/infant). These slides, along with a sample of repeat images, were randomly placed in a slide show without any demographic or clinical information for the graders. Twenty repeat slides were randomly selected from all slides proportional to the number of those with normal, pre-plus, and plus disease in the original study population in order to assess intra-grader reliability. Graders were provided with standard reference images for pre-plus and plus disease from the International Classification of ROP (ICROP) revisited paper,[7,9] cropped to display a field of view similar to that captured by the Keeler system through a 28 D lens and with similar magnification to the study images. The standard photographs and the study images were displayed on the same interface to allow for direct comparison (Figure 2).

Two ROP experts masked to demographic information and clinical findings (SFF and DKW) independently reviewed the slide show and evaluated the images for: (1) quality, (2) number of gradable quadrants, and (3) posterior pole disease. Based on the ability of the grader to determine the dilation and/or tortuosity of the vessels in all images selected from one examination date for each infant, image quality was graded as follows: "good," providing a clear view of both the optic nerve and vessels such that the grader could easily discern the dilation and tortuosity of the vessels; "fair," in which either dilation or tortuosity was difficult to discern; or "poor," in which both dilation and tortuosity could not be clearly discerned. The number of gradable quadrants (0-4) was scored based on the visibility of at least 1 disk diameter length of a major vessel in a given quadrant. Posterior pole disease was graded as: (1) normal, (2) pre-plus, or (3) plus disease. In this study, pre-plus disease was defined according to the ICROP revisited definition of "vascular abnormalities of the posterior pole that are insufficient for the diagnosis of plus disease but that demonstrate more arterial tortuosity and more venous dilatation than normal,"[7] and plus disease was defined as the presence in ≥2 quadrants of the eye of sufficient vascular dilation and tortuosity as compared to a standard photograph.[7,10] Because both