anales**de**pediatría

ORIGINAL ARTICLE

Reliability of retinal imaging screening in retinopathy of prematurity[☆]

C. Navarro-Blanco[a,b,][*], J. Peralta-Calvo[c], N. Pastora-Salvador[c], L. Álvarez-Rementería[b], E. Chamorro[a], C. Sánchez-Ramos[a]

[a] Grupo de Neuro-Computación y Neuro-Robótica, Universidad Complutense de Madrid, Madrid, Spain
[b] Departamento de Oftalmología, Clínica Rementería, Madrid, Spain
[c] Departamento de Oftalmología Infantil, Hospital Universitario La Paz, Madrid, Spain

Abstract

Introduction: The retinopathy of prematurity (ROP) is a potentially avoidable cause of blindness in children. The advances in neonatal care make the survival of extremely premature infants, who show a greater incidence of the disease, possible. The aim of the study is to evaluate the reliability of ROP screening using retinography imaging with the RetCam 3 wide-angle camera and also to study the variability of ROP diagnosis depending on the evaluator.

Materials and methods: The indirect ophthalmoscopy exam was performed by a paediatric ROP-expert ophthalmologist. The same ophthalmologist and a technician specialised in digital image capture took retinal images using the RetCam 3 wide-angle camera. A total of 30 image sets were analysed by 3 masked groups: group A (8 ophthalmologists), group B (5 experts in vision), and group C (2 ROP-expert ophthalmologists).

Results: According to the diagnosis using indirect ophthalmoscopy, the sensitivity (26–93), Kappa (0.24–0.80), and the percentage agreement were statistically significant in group C for the diagnosis of ROP type 1. In the diagnosis of ROP type 1 + type 2, Kappa (0.17–0.33) and the percentage agreement (58–90) were statistically significant, with higher values in group C.

Conclusion: The diagnosis, carried out by ROP-expert ophthalmologists, using the wide-angle camera RetCam 3 has proven to be a reliable method.

© 2013 Asociación Española de Pediatría. Published by Elsevier España, S.L.U. All rights reserved.

Fiabilidad en el cribado de la retinopatía del prematuro mediante el análisis de retinografías

Resumen

Introducción: La retinopatía del prematuro (ROP) es una de las principales causas de ceguera infantil potencialmente evitable. Los avances en los cuidados neonatales consiguen la super-vivencia de niños de bajo peso extremo asociado con una mayor incidencia de la enfermedad. El objetivo de este estudio es evaluar la fiabilidad en el diagnóstico de la ROP a través de retinografías obtenidas con la cámara de campo amplio RetCam 3 y estudiar la variabilidad en el diagnóstico de ROP en función del evaluador.

Material y métodos: El examen con oftalmoscopio indirecto fue realizado por un oftalmólogo pediátrico experto en ROP. Las imágenes retinianas fueron obtenidas por el mismo oftalmólogo y un técnico especializado en la captura de imágenes digitales. Un total de 30 sets de imágenes fueron analizados por 3 grupos enmascarados: grupo A (8 oftalmólogos), grupo B (5 expertos en visión) y grupo C (2 oftalmólogos expertos en ROP).

Resultados: Acorde con el diagnóstico mediante oftalmoscopia indirecta, la sensibilidad (26-93), el índice Kappa (0,24-0,80) y el porcentaje de aciertos fueron estadísticamente signi-ficativos en el grupo C para el diagnóstico de ROP tipo 1. En el diagnóstico de ROP tipo 1 + tipo 2 el índice Kappa (0,17-0,33) y el porcentaje de aciertos (58-90) fueron estadísticamente signi-ficativos, obteniendo valores superiores en el grupo C.

Conclusiones: El diagnóstico realizado por oftalmólogos expertos en ROP con el retinógrafo móvil RetCam 3 ha demostrado ser un método fiable.

Introduction

Despite advances in retinopathy of prematurity (ROP), this disorder is one of the main potentially avoidable causes of childhood blindness.[1] ROP is a vasoproliferative retinopathy, characterised by the presence of an immature and partially vascularised retina, affecting low birth-weight preterm infants. The spectrum of possible results for patients with ROP ranges from mild cases, where the sequelae are minimal and do not affect vision, to more aggressive, bilateral cases, with total and irreversible blindness.[2] Prompt intervention is critical to maximise the chance of a favourable outcome[3]; without treatment, at least 50% of eyes with severe ROP will suffer serious and permanent visual loss.[3]

Recent studies show that in the last 20 years the num-ber of children requiring monitoring has risen constantly.[1,4-7] Advances in neonatal care enable very low weight newborns to survive; low weight and gestational age are associated with a higher incidence of severe ROP.[4,8-10] The incidence of the disorder in developed countries varies compared to developing countries,[11,12] partly due to greater use of assisted conception, increasing maternal age, possible genetic aetiologies and other socioeconomic issues.[13] Preva-lence in Spain, during the last decade and the beginning of the present one,[11] was similar to that of other devel-oped countries in the European Community and the United States.[7,14] Currently, according to the available data from the Instituto Nacional de Estadística (INE: National Statis-tics Institute), the number of newborns whose weight was less than 1500 g in Spain in 2011 was 4178, of whom 682 were in the Autonomous Community of Madrid.

The current method of diagnosis, binocular indirect ophthalmoscopy (BIO), has serious limitations.[5] The exam-iner's interpretations are transcribed onto ophthalmological examination sheets, where the interpretation is assumed to be correct and cannot be revised.[15] Another worrying factor is the shortage of trained ophthalmologists capable of per-forming examinations for diagnosis of ROP.[5,6,10] As a result, a large number of untrained ophthalmologists are carrying out screening and treatment of ROP.[10,16,17] Several studies show that inexperienced ophthalmologists are less skilled than trained ophthalmologists at identifying clinically sig-nificant ROP by analysing digital images.[10,17,18] Because of the shortage of trained ophthalmologists, long delays can occur in screening; another alternative is for the infants to be transferred, with the considerable cost this entails and the potential risk to which the premature baby is subjected.[3]

Telemedicine makes it possible to capture images and send them for subsequent interpretation by a remote expert,[6] thereby solving many of the limitations in diagno-sis of ROP performed by means of the ''gold standard''. By using wide-angle cameras, telemedicine has demonstrated high precision and reliability in the diagnosis of ROP,[6,19-26] and may be more cost-effective than the current method of diagnosis.[6,27]

The main objectives of this study are:

- To assess the reliability of diagnosis of ROP through ocular fundus images obtained with a RetCam 3 mobile retinal camera (Clarity Medical Systems Inc.) via telemedicine.
- To explore the variability in diagnosis of ROP according to the training profile of the evaluator.

Materials and methods

This study followed the principles of the Helsinki Declaration and was approved by the Ethics Committee of the Hospital Clínico San Carlos and the Hospital Universitario La Paz in Madrid. All the parents of the preterm infants at risk of ROP who participated in the study signed an informed consent document.

Patients

Digital images were taken of children at risk of ROP admitted to the neonatal intensive care unit (NICU) of the Hospital Universitario La Paz in Madrid. The screening criterion applied was that laid down in the NICU protocol, which includes all infants with a gestational age of less than 31 weeks ($\leq30+6$), those of less than 34 weeks (31–33) with unstable clinical course or a weight of less than 1250 g. Thirty retinal photographs were captured (15 right eyes and 15 left eyes) of 9 preterm infants between January 2012 and April 2012. A total of 24 preterm infants were examined, but only the cases with ROP were included in the study. Excluded from the study were the preterm infants who, in the neonatologist's opinion, had an unstable clinical evolution and those whose retinopathy had previously been treated by laser. In three low birth-weight preterm infant the initial examination could not be performed owing to the poor quality of the images obtained, two of them because of corneal oedema and one because of insufficient pupillary dilation.

Schedule of care

The first ocular fundus examination is carried out at the age of 4 weeks for newborns with a gestational age at birth of 27 weeks or more. For newborns with a gestational age of less than 27 weeks, the first examination is performed at the postmenstrual age of 31 weeks. Depending on the results found in the ocular fundus exploration by BIO, the scheduling of the follow-up examinations will adhere to the guidelines published by the Academy of Paediatrics, the American Association for Paediatric Ophthalmology and Strabismus and the American Academy of Ophthalmology.[28] The check-ups are continued until (a) the retina is fully vascularised; (b) the vessels reach zone III without previous ROP in zone I or II (a confirmatory examination would be indicated in very low-weight infants) or (c) absence of ''pre-threshold'' disease by 45 weeks post-conceptional age (zone I: any stage with plus, stage 3 without plus; zone II: stage 2 ''plus'' or stage 3).

Examination techniques

Pupillary dilation is necessary to perform an ophthalmological examination. Mydriasis is achieved by instillation of one drop of cyclopentolate 0.25% and one drop of phenylephrine 1% 1 h before the examination, repeated after 10 min. The presence or absence of ROP, its location, its extent and plus disease were documented according to the criteria established in the International Classification of ROP.[29] During the ophthalmological examination a nurse immobilises the premature infant and monitors his or her vital signs; if there is any sudden alteration in the low birth-weight preterm infant cardiorespiratory indicators the examination is interrupted until the infant stabilises. To avoid retinal phototoxicity, ambient lighting is kept to a minimum and the lowest light intensity that allows a reliable examination is used in the ophthalmoscope.

Indirect ophthalmoscopic examination (the ''gold standard'') was performed by a paediatric ROP-expert ophthalmologist. The eyelids are kept open with special blepharostats for premature infants. Viewing of the peripheral retina is carried out using scleral indentation and a 28-D lens. Immediately after the BIO examination, the same ophthalmologist and a technician specialising in capture of digital images (Certificate of Completion. Training Module Series: RetCam Practice, Ocular Anatomy and Imaging ROP Presented by Clarity Medical Systems Inc., Pleasanton, CA) captured the images of each eye using the RetCam 3 wide-angle camera (Clarity Medical Systems, Pleasanton, CA, USA) equipped with a special 130° lens for premature infants. In the methodology employed the ophthalmologist holds the camera while the technician controls the lighting and focus. A minimum of 3 photos per eye was captured (posterior pole, nasal retina and temporal retina); a group of images of the same eye in the same session was called a ''set''.

Reading and coding of digital images

The retinal photographs obtained were sent to the storage centre, where they were coded. A total of 30 sets were interpreted independently by 3 masked groups: group A, comprising 8 ophthalmologists (3 anterior pole surgeons, 3 retinologists, and 2 general ophthalmologists); group B, composed of 5 vision experts from the Universidad Complutense in Madrid (graduates with official master's degrees in optics, optometry and vision) and group C, consisting of 2 ophthalmologist experts in diagnosis and treatment of ROP. Groups A and B were informed about the diagnosis of ROP by means of a 4-page guide compiled by the authors. All those surveyed were asked about the diagnosis of ROP; each set of photos was classified by ROP, stage, zone, plus, referral to paediatric ophthalmologist (type 1 + type 2) and observations. The interpretation of the retinal photographs was based on the criteria laid down in the study *Early Treatment for Retinopathy of Prematurity* (ETROP).[30] The images transmitted were coded at the storage centre and classified using a system of 4 levels, as in the study by Myung et al.[17]:

(1) *Type 1 ROP*: zone I, any stage with plus disease or stage 3 without plus disease; zone II, stages 2 or 3 with plus disease.
(2) *Type 2 ROP*: zone I, stages 1 or 2 without plus disease; zone II, stage 3 without plus disease.
(3) *Moderate ROP*: defined as ROP less severe than type 2.
(4) *No ROP*.

No time limit was set for interpreting the images. The diagnosis and recommendations for control examinations were returned by email to the storage centre.

Analysis of data

The validity of the new diagnosis system was determined by comparing the results obtained by the three groups, and the diagnosis performed using BIO by a paediatric ophthalmologist specialising in ROP was taken as a reference. The results obtained with BIO and RetCam for each set were collected in separate columns using statistical software (Microsoft Excel 2010, Redmond, WA, USA). The calculations for the statistical analysis were performed with SAS 9.2 software. Sensitivity, specificity, Kappa index and percent success rate of each group were calculated for detection of type 1 ROP and referral (type 1 + type 2 ROP). We used ANOVA and Duncan's test to compare the results between groups.

Results

A total of 30 sets of images were analysed by 15 observers (8 ophthalmologists, 5 vision experts and 2 paediatric ophthalmologists specialising in ROP). According to the diagnosis with BIO performed by the reference observer (the ''gold standard''), 47% of the digital images showed type 1 ROP, 3% type 2 ROP, and 50% moderate ROP.

Table 1 shows sensitivity, specificity, Kappa index and percent agreement in the diagnosis of type 1 ROP and type 1 + type 2 (referral) by group C, comprising two ophthalmologists expert in the diagnosis of ROP.

Tables 2 and 3 show sensitivity, specificity, Kappa index and percent agreement in the diagnosis of type 1 ROP and type 1 + type 2 (referral) by three groups of specialists compared with the reference diagnosis performed by a paediatric ROP-expert ophthalmologist. Sensitivity, Kappa index and percent success rate were statistically significant in group C for diagnosis of type 1 ROP. In the diagnosis of type 1 + type 2 ROP the Kappa index and percent success rate were statistically significant, producing higher values in group C. No statistically significant differences were found between groups A and B in the diagnosis of type 1 ROP and type 1 + type 2 ROP.

Discussion

The results of this study confirm, firstly, the efficacy of the RetCam 3 wide-angle camera through images obtained by trained staff. In addition, the study demonstrates the viability of telemedicine for the diagnosis of type 1 ROP and type 1 + type 2 ROP (referral) when performed by paediatric ROP-expert ophthalmologists.

The viability of telemedicine in the assessment of low birth-weight preterm infant is a point of great interest given the gradually increasing number of children at risk of ROP[4,8] in developed countries. Digital images offer an innovative strategy for detecting infants with severe ROP,[31,32] and several studies show excellent sensitivity and specificity in the diagnosis of ROP.[5,18–20,24,25,33–36] In most research studies an ophthalmologist[5,19,26,32,33,36–38] or a nurse[17,21,22,25,34,35,39,40] carried out the test, although occasionally an ophthalmological photographer[18,20,23] obtained the images. Our conclusions coincide with the results published by Skalet et al.,[40] in which two trained nurses captured the images with the NIDEK NM200-D camera and subsequently sent them to five ROP experts. The conclusions of Skalet et al. show that images obtained by trained staff and sent to specialists can be useful for identifying infants who require evaluation by a ROP-expert ophthalmologist.

In 2008 Kemper et al.[16] showed that there was a high proportion of untrained ophthalmologists carrying out screening and treatment of ROP. Moreover, Paul Chan et al.,[18] in 2010, assessed the reliability of inexperienced ophthalmologists in the diagnosis of ROP; they demonstrated a clinically significant underestimation of ROP, which raises important questions about the quality of ROP screening performed by non-expert ophthalmologists. We therefore agree with the suggestion of Wong et al.[10] that an ophthalmologists' training should include a minimum number of ROP examinations and treatments.

The results of this research are similar to those obtained in the study by Myung et al.,[17] which shows a sensitivity of approximately 50% in the detection of type 1 and type 2 ROP by paediatric ophthalmologists inexperienced in ROP; it is equivalent, in this study, to the sensitivity in referral (type 1 + type 2) of groups A and B, consisting of non-ROP experts. The results also coincide for type 1 ROP, where low sensitivity and high specificity were obtained in groups A and B. Unlike the study by Myung et al.,[17] in which the diagnosis made by a paediatric retina expert using digital images is taken as a reference, the ''gold standard'' used here is the diagnosis obtained using indirect ophthalmoscopy performed by an expert in ROP, following the recommendations of the Section on Ophthalmology of the American Academy of Pediatrics, the American Academy of Ophthalmology and the American Association for Pediatric Ophthalmology and Strabismus.[7]

The advantages of telemedicine have already been described by several authors. It has been shown to be reliable for the diagnosis of ROP and to save costs compared with the conventional method of diagnosis,[27] but this is not enough; the opinion of the parents must be taken into account. The research of Lee[6] concludes that parents have a positive impression of ROP diagnosis by telemedicine, but express a preference for face-to-face contact. The current

Table 1 Sensitivity, specificity, Kappa index and percent agreement for diagnosis of type 1 ROP and type 1 + type 2 ROP (referral) in group C (ROP-expert ophthalmologist).

	Sensitivity (%) (standard error)	Specificity (%) (standard error)	Kappa (standard error)	CD (%) (maximum–minimum)
Type 1	93 (0)	88 (13)	0.80 (0.14)	88 (95–81)
Type 1 + type 2	90 (3)	90 (10)	0.80 (0.09)	90 (95–85)

Table 2 Sensitivity, specificity, Kappa index and percent agreement for diagnosis of type 1 ROP by 3 groups of specialists compared with the reference diagnosis performed by a paediatric ROP-expert ophthalmologist.

Type 1	Sensitivity (%) (standard error)	Specificity (%) (standard error)	Kappa (standard error)	CD (%) (maximum−minimum)
Group A	26 (10)	93 (2)	0.24 (0.20)	57 (68−40)
Group B	39 (5)	92 (3)	0.29 (0.12)	56 (65−47)
Group C	93 (0)	88 (13)	0.80 (0.14)	88 (95−81)
Value of p	0.0114[a]	0.6944	0.0046[a]	0.0053[a]

CD, correct diagnoses.
[a] Group C different from the other groups.

Table 3 Sensitivity, specificity, Kappa index and percent agreement for diagnosis of type 1 + type 2 ROP (referral) by 3 groups of specialists compared with the reference diagnosis performed by a paediatric ROP-expert ophthalmologist.

Type 1 + type 2	Sensitivity (%) (standard error)	Specificity (%) (standard error)	Kappa (standard error)	CD (%) (maximum−minimum)
Group A	47 (10)	86 (7)	0.33 (0.23)	66 (78−55)
Group B	59 (11)	59 (13)	0.17 (0.07)	58 (61−55)
Group C	90 (3)	90 (10)	0.80 (0.09)	90 (95−85)
Value of p	0.1358	0.1101	0.0048[a]	0.0045[a]

CD, correct diagnoses.
[a] Group C different from the other groups.

benefits of new technologies are indisputable, but it should not be forgotten that information must be as widely available as possible, both to patients and to those accompanying them.

In our review of the literature we found few studies that evaluated the training of ophthalmologists who carry out the examination, assessment and treatment of ROP.[10,16–18] As has been shown, differences in the diagnosis of ROP lead to different outcomes of the disease, and therefore future research should propose a minimum number of examinations for untrained ophthalmologists. We also wish to highlight the potential risk involved in untrained staff carrying out the diagnosis and treatment of ROP. This study found no significant differences in the results between ophthalmologists (group A) and vision experts (group B). Future projects could analyse the role of opticians and optometrists for screening of ROP, which would save the cost of transferring the premature infant and avoid having specialists perform the test.

We recognise that one of the limitations of this study is the number of premature infants examined and the small number of experts performing the diagnosis of ROP. In this phase, only retinal photographs of premature infants with some stage of retinopathy were captured. This was done to avoid the stress for the infant caused by the additional test with the RetCam. Future research could be conducted, as in the study by Skarlet et al.,[40] with several experts on premature infants, comparing them with a series of ophthalmologists without experience of ROP. As in previous studies, the principal limitations were the assessment of zone III and the quality of the images;[17] in particular, serious difficulties were encountered in the examination of patients with CPAP both by BIO and by RetCam; the view of the retina is slightly better with digital images.

In conclusion, use of the RetCam 3 mobile retinal camera by ophthalmologist experts in ROP has proved to be reliable for diagnosis.

Conflicts of interest

The authors have no conflicts of interest to declare.

Acknowledgments

References

1. Gilbert C, Fielder A, Gordillo L, Quinn G, Semiglia R, Visintin P, et al. Characteristics of infants with severe retinopathy of prematurity in countries with low, moderate, and high levels of development: implications for screening programs. Pediatrics. 2005;115:518–25.
2. Casteels I, Cassiman C, van Calster J, Allegaert K. Educational paper: retinopathy of prematurity. Eur J Pediatr. 2012;171:887–93.
3. Ells A. A telemedicine approach to screening for retinopathy of prematurity: implications for improved diagnosis and resource utilization. Neonatal Intensive Care. 2005;18:52–4.
4. Tasman W. Retinopathy of prematurity: do we still have a problem? The Charles L. Schepens lecture. Arch Ophthalmol. 2011;129:1083–6.
5. Dai S, Chow K, Vincent A. Efficacy of wide-field digital retinal imaging for retinopathy of prematurity screening. Clin Exp Ophthalmol. 2011;39:23–9.

6. Lee JY, Du YE, Coki O, Flynn JT, Starren J, Chiang MF. Parental perceptions toward digital imaging and telemedicine for retinopathy of prematurity management. Graefes Arch Clin Exp Ophthalmol. 2010;248:141–7.

7. Section on Ophthalmology AAoP, American Academy of Ophthalmology, American Association for Pediatric Ophthalmology and Strabismus. Screening examination of premature infants for retinopathy of prematurity. Pediatrics. 2006;117:572–6.

8. Gunn DJ, Cartwright DW, Gole GA. Incidence of retinopathy of prematurity in extremely premature infants over an 18-year period. Clin Exp Ophthalmol. 2012;40:93–9.

9. Austeng D, Kallen KB, Hellstrom A, Jakobsson PG, Johansson K, Tornqvist K, et al. Screening for retinopathy of prematurity in infants born before 27 weeks' gestation in Sweden. Arch Ophthalmol. 2011;129:167–72.

10. Wong RK, Ventura CV, Espiritu MJ, Yonekawa Y, Henchoz L, Chiang MF, et al. Training fellows for retinopathy of prematurity care: a web-based survey. J AAPOS. 2012;16:177–81.

11. Conde JRC, Urcelay IE, Mussons FB, Alonso CRP, Narbona E, Luna MS, et al. Retinopathy of prematurity. Prevention, screening and treatment guidelines. An Pediatr. 2009;71:514–23.

12. Gilbert C, Rahi J, Eckstein M, O'Sullivan J, Foster A. Retinopathy of prematurity in middle-income countries. Lancet. 1997;350:12–4.

13. Richter GM, Williams SL, Starren J, Flynn JT, Chiang MF. Telemedicine for retinopathy of prematurity diagnosis: evaluation and challenges. Surv Ophthalmol. 2009;54:671–85.

14. O'Connor AR, Stephenson T, Johnson A, Tobin MJ, Moseley MJ, Ratib S, et al. Long-term ophthalmic outcome of low birth weight children with and without retinopathy of prematurity. Pediatrics. 2002;109:12–8.

15. Trese MT. What is the real gold standard for ROP screening? Retina. 2008;28 3 Suppl.:S1–2.

16. Kemper AR, Freedman SF, Wallace DK. Retinopathy of prematurity care: patterns of care and workforce analysis. J AAPOS. 2008;12:344–8.

17. Myung JS, Paul Chan RV, Espiritu MJ, Williams SL, Granet DB, Lee TC, et al. Accuracy of retinopathy of prematurity image-based diagnosis by pediatric ophthalmology fellows: implications for training. J AAPOS. 2011;15:573–8.

18. Paul Chan RV, Williams SL, Yonekawa Y, Weissgold DJ, Lee TC, Chiang MF. Accuracy of retinopathy of prematurity diagnosis by retinal fellows. Retina. 2010;30:958–65.

19. Ells AL, Holmes JM, Astle WF, Williams G, Leske DA, Fielden M, et al. Telemedicine approach to screening for severe retinopathy of prematurity: a pilot study. Ophthalmology. 2003;110:2113–7.

20. Chiang MF, Keenan JD, Starren J, Du YE, Schiff WM, Barile GR, et al. Accuracy and reliability of remote retinopathy of prematurity diagnosis. Arch Ophthalmol. 2006;124:322–7.

21. Chiang MF, Wang L, Busuioc M, Du YE, Chan P, Kane SA, et al. Telemedical retinopathy of prematurity diagnosis: accuracy, reliability, and image quality. Arch Ophthalmol. 2007;125:1531–8.

22. Scott KE, Kim DY, Wang L, Kane SA, Coki O, Starren J, et al. Telemedical diagnosis of retinopathy of prematurity intraphysician agreement between ophthalmoscopic examination and image-based interpretation. Ophthalmology. 2008;115:1222–8.

23. Chiang MF, Starren J, Du YE, Keenan JD, Schiff WM, Barile GR, et al. Remote image based retinopathy of prematurity diagnosis: a receiver operating characteristic analysis of accuracy. Br J Ophthalmol. 2006;90:1292–6.

24. Wu C, Petersen RA, van derVeen DK. RetCam imaging for retinopathy of prematurity screening. J AAPOS. 2006;10:107–11.

25. Silva RA, Murakami Y, Jain A, Gandhi J, Lad EM, Moshfeghi DM. Stanford University Network for Diagnosis of Retinopathy of Prematurity (SUNDROP): 18-month experience with telemedicine screening. Graefes Arch Clin Exp Ophthalmol. 2009;247:129–36.

26. Lorenz B, Spasovska K, Elflein H, Schneider N. Wide-field digital imaging based telemedicine for screening for acute retinopathy of prematurity (ROP). Six-year results of a multicentre field study. Graefes Arch Clin Exp Ophthalmol. 2009;247:1251–62.

27. Castillo-Riquelme MC, Lord J, Moseley MJ, Fielder AR, Haines L. Cost-effectiveness of digital photographic screening for retinopathy of prematurity in the United Kingdom. Int J Technol Assess Health Care. 2004;20:201–13.

28. A Joint Statement of The American Academy of Pediatrics Taafpoas, and The American Academy of Ophthalmology. Screening examination of premature infants for retinopathy of prematurity. Pediatrics. 2001;108:809–11.

29. International Committee for the Classification of Retinopathy of Prematurity. The international classification of retinopathy of prematurity revisited. Arch Ophthalmol. 2005;123:991–9.

30. Good WV. Final results of the Early Treatment for Retinopathy of Prematurity (ETROP) randomized trial. Trans Am Ophthalmol Soc. 2004;102:233–48, discussion 48-50.

31. Fielder AR, Gilbert C, Ells A, Quinn GE. Internet-based eye care. Lancet. 2006;367:300–1.

32. Balasubramanian M, Capone Jr A, Hartnett ME, Pignatto S, Trese MT. The Photographic Screening for Retinopathy of Prematurity Study (Photo-ROP): study design and baseline characteristics of enrolled patients. Retina. 2006;26 7 Suppl.:S4–10.

33. Schwartz SD, Harrison SA, Ferrone PJ, Trese MT. Telemedical evaluation and management of retinopathy of prematurity using a fiberoptic digital fundus camera. Ophthalmology. 2000;107:25–8.

34. Yen KG, Hess D, Burke B, Johnson RA, Feuer WJ, Flynn JT. Telephotoscreening to detect retinopathy of prematurity: preliminary study of the optimum time to employ digital fundus camera imaging to detect ROP. J AAPOS. 2002;6:64–70.

35. Murakami Y, Silva RA, Jain A, Lad EM, Gandhi J, Moshfeghi DM. Stanford University Network for Diagnosis of Retinopathy of Prematurity (SUNDROP): 24-month experience with telemedicine screening. Acta Ophthalmol. 2010;88:317–22.

36. Richter GM, Sun G, Lee TC, Chan RV, Flynn JT, Starren J, et al. Speed of telemedicine vs ophthalmoscopy for retinopathy of prematurity diagnosis. Am J Ophthalmol. 2009;148:136–4200.

37. Dhaliwal C, Wright E, Graham C, McIntosh N, Fleck BW. Wide-field digital retinal imaging versus binocular indirect ophthalmoscopy for retinopathy of prematurity screening: a two-observer prospective, randomised comparison. Br J Ophthalmol. 2009;93:355–9.

38. Shah PK, Narendran V, Saravanan VR, Raghuram A, Chattopadhyay A, Kashyap M. Screening for retinopathy of prematurity—a comparison between binocular indirect ophthalmoscopy and RetCam 120. Indian J Ophthalmol. 2006;54:35–8.

39. Lajoie A, Koreen S, Wang L, Kane SA, Lee TC, Weissgold DJ, et al. Retinopathy of prematurity management using single-image vs multiple-image telemedicine examinations. Am J Ophthalmol. 2008;146:298–309.

40. Skalet AH, Quinn GE, Ying GS, Gordillo L, Dodobara L, Cocker K, et al. Telemedicine screening for retinopathy of prematurity in developing countries using digital retinal images: a feasibility project. J AAPOS. 2008;12:252–8.