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# The use of digital retinal imaging in screening for retinopathy of prematurity

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## Abstract

The frequency of premature births is increasing worldwide. This factor, combined with improved survival and revised screening criteria, is resulting in an increased workload in screening for retinopathy of prematurity. Digital retinal imaging is emerging as an important alternative tool for diagnosing retinopathy of prematurity, and its use has even been extended to developing countries. Neonatal nurses and technicians can be trained to use digital imaging devices effectively. This is important in areas that do not have ready access to paediatric ophthalmologists. The ability to transfer images electronically makes it a valuable tool in telemedicine, while the ability to store and retrieve images is also advantageous from a medico-legal perspective. Image analysis software can further improve the accuracy of diagnosis. The main limitation of this technology is its high capital cost.

Key words: retinopathy of prematurity, digital retinal imaging, teleophthalmology, neonatal nurse, neonatology

## Key Points:

1. The frequency of premature births is increasing globally. With improved infant survival, more patients will have retinopathy of prematurity.
2. Digital retinal imaging is emerging as an alternative method of screening for retinopathy of prematurity.
3. Non-ophthalmologists can be trained to screen using digital retinal imaging technology.

## Quiz

1. The number of premature babies with retinopathy is expected to increase worldwide as a result of:

- a. A decline in the standards of neonatal care
- b. The increased use of oxygen at birth
- c. Improvements in standards of neonatal care
- d. A decline in the standards of obstetric care
- e. The increased use of surfactants

(Answer: c) Better neonatal care has improved the survival rate for premature infants.

2. Why is digital retinal imaging being proposed as an alternative to the traditional method of retinopathy of prematurity screening?

- a. Its reliability in producing an accurate/objective assessment
- b. It can be used by non-ophthalmologists
- c. Medico-legal advantages
- d. All of the above
- e. None of the above

(Answer: d) A combination of various factors such as accuracy, reliability, and ease of use makes this technology valuable.

3. What is the main limitation of digital retinal imaging technology?

- a. This technology is not user-friendly
- b. The availability of retinal imaging analysis software
- c. The cost of acquiring the retinal camera
- d. This technology is harmful to patients
- e. This technology is still in the experimental stage

(Answer: c) This technology is expensive.

## The use of digital retinal imaging in screening for retinopathy of prematurity

### Introduction

Preterm birth, defined as childbirth occurring at less than 37 completed weeks (259 days) of gestation, is a major cause of neonatal mortality and morbidity and has long-term adverse consequences for health [1–4]. The World Health Organization estimates that more than 12 million preterm births occur per year, with numbers continuing to increase [3]. The current joint policy statement on retinopathy of prematurity (ROP) screening produced by the American Academy of Pediatrics, the American Academy of Ophthalmology, and the American Association for Pediatric Ophthalmology and Strabismus recommends that babies with a birth weight of less than 1500 g or delivered at a gestational age of 32 weeks or less and high-risk infants undergo retinal examination for the detection of ROP [5, 6]. The rate of preterm birth has also risen in Australia [7]. In 2008, premature birth comprised 7.7% out of the 294,737 live births in Australia [8]. Approximately 19% (4384) of these premature infants would have required ROP assessment [8]. The number of infants treated for ROP in 2008 is not available but in 2006, 76 infants were treated for ROP in Australasian nurseries [9]. There is no national consensus for ROP screening in Australia but some of the neonatal units in the country have similar recommendations [10, 11]. However, the Australian and New Zealand Neonatal Network report suggest that there are local variations to the screening protocol [9].

### ROP screening

Traditionally, ROP screening is carried out by a paediatric ophthalmologist or an ophthalmologist with an interest in paediatrics or neonatology. The gold standard method for ROP screening is by using binocular indirect ophthalmoscopy (BIO) after pupillary dilatation [5]. This method is typically performed at the bedside in the neonatal intensive care unit (NICU). Although the procedure itself is non-invasive, it often requires the use of scleral depression using a scleral indenter. Scleral depression can cause systemic complications such as fluctuations in heart rate and oxygen saturation, secondary to oculocardiac reflex [12]. BIO is also labour- and time-intensive for ophthalmologists [13]. **Documentation and drawings of clinical findings in the medical records can be subjective and potentially become a problem during medico legal cases involving patients with ROP [14].**

Revisions to the screening recommendations of ROP that came into effect in 2006 have increased the proportion of premature infants eligible for screening [5]. More ophthalmologists are required to cope with this revision; however, the lack of availability of ophthalmologists continues to be a problem around the world [15, 16]. In the United States, only 11% of all ophthalmologists can perform ROP screening examinations and only 6% can provide treatment for ROP [17]. The risk of medico-legal liabilities, logistical difficulties, and the lack of financial incentives make this screening an unpopular specialty for ophthalmologists [17, 18]. In Australia, more than 75% of ophthalmologists have their primary practices in a capital city, with only approximately 10% located in regional and rural areas. Only capital cities have paediatric ophthalmologists [19]. In New Zealand, there is a growing gap between the number of ophthalmologists and the demand for their services [15].

Studies have shown that the early treatment of threshold ROP improves visual outcomes; therefore, screening programs must focus on identifying the infants that

require treatment or exhibit high-risk characteristics for progression to severe ROP [20, 21]. Current treatment recommendations include two variables that are visualised in the retina: the presence of plus disease (vascular tortuosity) (Figure 1) and the staging of the severity. Such retinal characteristics can be visualised by using retinal imaging. The images generated by this procedure also play a role in recording the treatment provided and evaluating the response to treatment (Figure 2).

### Digital retinal imaging

One of the earliest studies on the use of retinal photography in newborn babies was published 42 years ago [22]. This study by Hammersmith Hospital correctly predicted the potential of retina photography in the management of premature infants. In the past 10 years, retinal imaging has become more popular, perhaps because of an exponential increase in the computing power of microchips and the availability of digital imaging [23–25]. Digital retinal imaging, also known as wide-field digital retinal imaging, has since been proposed for ROP screening [14, 18, 26]. Digital retinal cameras that can be used in the NICU are now commercially available. In general, they can be categorised as either wide-angle cameras (for example, RetCam of Clarity Medical Systems, Inc. Pleasanton, CA, USA) or narrow-angle cameras (for example, NM-200D of NIDEK, Inc. Fremont, CA, USA). Wide-angle cameras provide a wider view of the retina and have a  $130^\circ$  field of view in contrast to narrow-angle cameras, which provide a  $30^\circ$  field of view. However, compared with narrow-angle cameras, wide-angle cameras are more expensive, less portable, and require that the camera lens be in direct contact with the cornea. That said, both types of cameras can produce digital images that are appropriate for remote transfer for later evaluation [27, 28].



In 2010, Salcone and colleagues reviewed the current evidence on the use of retinal digital imaging for ROP screening [18]. The authors identified six prospective studies that evaluated the sensitivity and specificity of digital images in the use of ROP screening [29–33]. From these studies, the sensitivities of detecting ROP were found to range from 0.46 to 0.97 and the specificity for detecting ROP was uniformly high, ranging from 0.89 to 1.00. Inter-observer reliability (kappa) ranged from 0.67 to 0.89. Importantly, the researchers concluded that they could not identify any major complications from this procedure.

Other researchers have proposed that the most important parameter is the negative predictive value (NPV). An NPV of 100% indicates that each infant with ROP has been successfully identified [34, 35]. Furthermore, the sensitivity and specificity of this technique have improved over the past 10 years, which has attributed to improvements in imaging and lens technology [34, 35].

In a New Zealand study, Dai and colleagues retrospectively evaluated the efficacy of digital retinal imaging in screening for ROP in a quaternary public NICU [14]. Retrospective chart and photo reviews were carried out for 108 participants who had been screened by both digital retinal imaging and concurrent BIO. Treatment-requiring ROP (defined as type 1 pre-threshold disease) was detected in 11 infants by both techniques. The investigators calculated digital retinal imaging to have a sensitivity of 100% and a specificity of 97.9% in detecting infants with treatment-requiring ROP. The positive and NPVs of digital retinal imaging were 84.6% and 100%, respectively. The authors thus concluded that digital retinal imaging is accurate, reliable, and efficient in detecting treatment-requiring ROP.

Jackson and colleagues used cost/utility analysis to evaluate the cost-effectiveness of digital imaging with telemedicine compared with BIO for ROP

management [36]. Cost/utility analysis is a method that measures costs against the value generated by medical interventions. The value resulting from an intervention is expressed in quality-adjusted life years (QALYs), which are defined as improvement in utility multiplied by the duration of the benefit [37], and quantified in dollars spent per QALY gained. The investigators found that the costs per QALY were \$3193 with telemedicine/digital imaging and \$5617 with BIO. They thus concluded that digital imaging with telemedicine is more cost-effective than is BIO for ROP management.

The use of digital retinal imaging has been shown to be less stressful on premature infants. Mukherjee and colleagues carried out a study on a cohort of 86 preterm infants and compared the impact of ROP screening examination between a digital retinal camera and BIO using cardio-respiratory indices as a measure of distress [38]. Increases in heart rate and respiratory rate were significantly higher in the BIO group than in the digital camera group. The investigators concluded that screening for ROP using a digital retinal camera was associated with a significantly lower stress-related response than that observed using the conventional technique.

Moreover, digital retinal images can be used to inform parents about the nature and importance of eye assessment. These images could also be used to teach neonatal staff.

#### Imaging by non-ophthalmologists

There are no published data on the use of digital retinal imaging by neonatologists or paediatricians, but there are increasing numbers of studies on the use of this technology by neonatal nurses and trained technicians [34, 35, 39, 40]. Silva and colleagues published the largest study to date on the benefit of having

neonatal nurses lead ROP screening programmes using digital retinal imaging [41]. This programme aimed to provide quaternary ROP screening services to the larger San Francisco Bay Area community [34, 35, 41]. All infants fulfilling the criteria for screening [5] in this network were evaluated remotely via digital images collected using the RetCam II system without a simultaneous BIO examination. Retinal imaging was conducted using a predetermined protocol, in which images of various parts of the retina were captured. In a 36-month retrospective audit of 230 infants, the investigators found that the programme missed no treatment-warranted ROP [41].

**Ten infants were identified to have referral-warranted ROP.** Nine of these infants underwent laser photocoagulation and one regressed spontaneously. The sensitivity of this technique was 100%, with a specificity of 99.5%. No patient progressed to retinal detachment or experienced any other adverse outcomes. The NPV was 100%. Similar outreach programmes involving trained technicians have been adopted in developing countries [40].

In order to determine whether retinal images can be safely reviewed and assessed by non-ophthalmologists, Williams and colleagues compared the accuracy of telemedical ROP diagnosis by trained non-experts and experts [42]. In this study, 248 eye examinations on 67 infants were carried out using digital retinal photography (RetCam II). Non-experts attended two one-hour-long training sessions for image-based ROP diagnosis. The investigators found that for the detection of type 2 or worse ROP, the mean sensitivities and specificities were 95% and 93% for experts and 87% and 73% for non-experts, respectively. For the detection of treatment-requiring ROP, they were 100% and 93% for experts and 88% and 84% for non-experts. The investigators concluded that the mean sensitivity and specificity of trained non-

experts were lower than were those of experts. Thus, input from expert ophthalmologists is still needed for accurate diagnosis.

In the Department of Neonatology at Townsville Hospital, which is a tertiary perinatal centre in regional Queensland, this technology has been available for ROP screening since 2007 [43]. Images are acquired using the retinal camera and are reviewed by resident ophthalmologists. Images of concern are sent electronically to a paediatric ophthalmologist in the state capital, 1500 km away. Infants requiring laser treatment are then transferred by the neonatal transport team. Owing to the increase in workload, this department has recently adopted a neonatal nurse-assisted ROP screening model to complement the ophthalmology team. Two neonatal nurses are now qualified to screen premature babies using the digital retinal camera. The outcome of this model of care will be reviewed in due course.

Another exciting development in this field is the availability of image analysis software that can help clinicians diagnose ROP [44–46]. Programmes such as ROPtool [46], Retinal Image Multiscale Analysis [47], and Computer-Aided Image Analysis of the Retina [48] can measure retinal vessel dilatation and tortuosity automatically. These measurements are then used to determine the severity of the disease. Although this technology is not widely used, the increase in computing power in the future will enable it to become more accurate and reliable.

## Limitations

The main limiting factor that is preventing the widespread use of this technology is the cost of acquiring a retinal camera (each device costs more than A\$100,000). However, despite this high capital cost, the technology is increasingly being used in developing countries [40, 49, 50]. The devices can also be used for the

assessment and documentation of conditions such as non-accidental injuries and other neonatal and paediatric ophthalmological conditions [51]. There is also a possibility that ophthalmologists might no longer have regular working relationships with a neonatal unit, with babies with other ocular conditions may not have ready access to ophthalmological assessment. These babies are very much a minority in most neonatal units, thereby reducing this concern [52].

## Conclusion

Digital retinal imaging is emerging as an alternative tool in the worldwide diagnosis of ROP, and its use has even extended to developing countries. Neonatal nurses can be trained to use these imaging devices. This use of non-ophthalmologist staff is important in areas where paediatric ophthalmologists are not readily available. The ability to transfer digital images electronically also makes it a valuable telemedicine tool, while the ability to store and retrieve images is advantageous from a medico-legal perspective. Although image analysis software may further improve the accuracy of diagnosis, continued participation from ophthalmologists in the diagnosis and subsequent management of ROP is essential.

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Figure 1: Retinal image of a premature infant with Plus disease (vascular tortuosity)

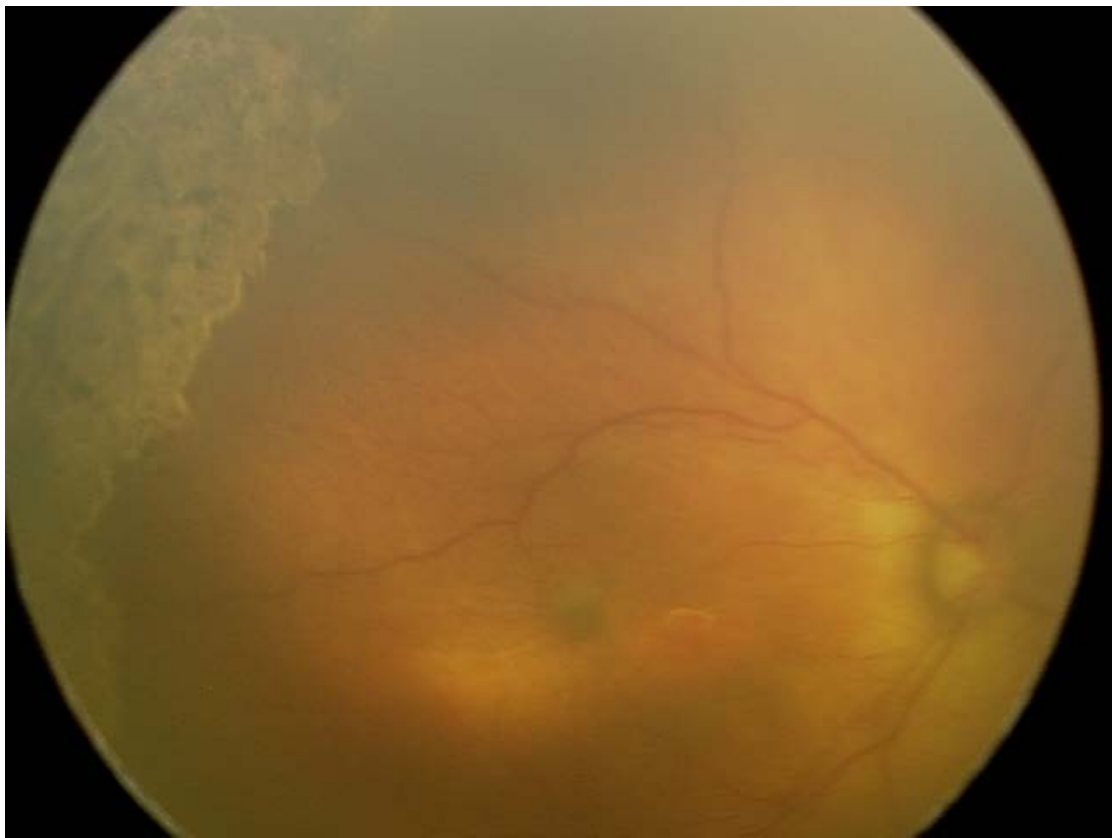


Figure 2: Retinal image from the same infant (**opposite eye**) after laser treatment  
(characterized by retinal burn scars on the periphery)