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Imaging in Retinopathy of Prematurity: Where Are We, and Where Are We Going?

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Diagnosis and management in retinopathy of prematurity (ROP) have undergone remarkable evolution during the past 30 years, largely because of findings from multi-center randomized controlled trials such as the Cryotherapy for ROP (CRYO-ROP) and Early Treatment for ROP (ETROP) studies [1,2]. More recently, developments in wide-angle retinal imaging, computing, and information technology are continuing to advance the state of the art in ROP management. Within the overall field of general ophthalmology, similar developments in imaging such as angiography, optical coherence tomography (OCT), and ultra-widefield imaging have dramatically transformed the delivery of ophthalmic care during the past several decades. Understanding the ongoing evolution of ROP management due to wide-angle retinal imaging will help pediatric ophthalmologists not only better care for premature infants, but also provide a broader appreciation for how to incorporate a broader range of ophthalmic imaging modalities into their clinical practices in the future.

The past: where have we been with ROP examination and documentation?

Originally, ROP diagnosis was completely unstructured, with documentation of examination findings using hand-drawn sketches accompanied by qualitative description [3]. In 1984, the International Classification of ROP (ICROP) developed a standard framework and nomenclature for examination findings through the definition of parameters such as zone, stage, clock hour extent, and plus disease [4]. This greatly improved the standardization of examination and clinical documentation, and established the essential infrastructure to support multi-center clinical trials.

As a result, the gold standard for ROP examination has long been considered to be indirect ophthalmoscopy at the neonatal intensive care unit (NICU) bedside, with documentation of findings in the medical record using ICROP parameters with accompanying hand-drawn sketches [5]. However, this is challenging because examination at the NICU bedside is time-consuming and logistically-difficult [6], because documentation of clinical findings is often subjective and qualitative with high levels of inter-observer variability [7-11], and because ROP care is associated with significant medicolegal liability [12].

The past: how has technology evolved?

During the late 1990s, the development of wide-angle retinal imaging devices (e.g. RetCam; Natus Medical, Pleasanton, CA) created opportunities for more objective documentation of examination findings. Documentation of clinical observations using imaging techniques is widespread throughout general ophthalmology, particularly within subspecialties such as retina and glaucoma. In ROP, this may be particularly useful because identification of subtle vascular changes signifying disease progression or regression is essential [13].

Meanwhile, dramatic improvements in computer, information, and Internet technologies have created the potential for addressing many of the above limitations of traditional ROP care using remote telemedicine diagnosis. The premise of these telemedicine systems is that wide-angle retinal images may be taken by trained NICU nurses or other personnel, and sent for remote diagnosis and management by ophthalmologists. Infants with clinically-significant findings would be referred for detailed evaluation and possible treatment using traditional methods.

Over 30 published studies have demonstrated that telemedicine has very high accuracy for diagnosing clinically-significant ROP [14-18]. Other studies have suggested that imaged-based diagnosis may even be superior to ophthalmoscopy in certain situations because it provides the opportunity for careful scrutiny of images to identify morphological features such as presence of zone I disease [19]. Finally, other studies have suggested that telemedicine may be more cost-effective and faster than bedside ophthalmoscopy for ROP management [6, 20-21]. However, contact photography using current wide-angle imaging devices is unable to reproducibly visualize the far peripheral retina, and may cause variation in the appearance of clinically-significant peripheral findings and vascular appearance if not performed cautiously [22-23].

The present: where are we now?

As a result of this work, major real-world ROP telemedicine programs have been implemented in the United States and throughout the world [24-29], often as a strategy for improving delivery of care to rurally and medically-underserved areas.

From a policy-making perspective, the most recent version of the screening guidelines published in 2013 by the American Academy of Pediatrics (AAP), American Academy of Ophthalmology (AAO), and American Association for Pediatric Ophthalmology & Strabismus (AAPOS) has evolved to state that “digital retinal imaging may also be a useful tool for objective documentation of retinal findings and for teaching NICU staff and parents” [30]. Furthermore, these guidelines suggest that telemedicine is an acceptable method of ROP screening, but only if performed cautiously: “The use of digital photographic retinal images that are captured and sent for remote interpretation is a developing approach to ROP screening ... at minimum, programs that employ this method should comply with the timing and other recommendations outlined in the preceding guidelines” [30]. In 2015, the AAP and AAO published a joint report detailing recommendations for implementation of real-world ROP telemedicine systems [31].

The future: where are we headed?

Overall, there has been a dramatic evolution in ROP care through standardized classification of examination findings (ICROP), multi-center clinical trials to develop methods and criteria for treatment (e.g. CRYO-ROP, ETROP, BEAT-ROP), improvements in imaging technology, and clinical telemedicine research. This highlights the importance of a multi-disciplinary approach to clinical care. It also demonstrates the pathway by which gaps in the delivery of clinical care motivate research and knowledge discovery, which eventually leads to technology adoption and gradual changes in health care policy.

The future of imaging in ROP will likely involve additional modalities such as OCT, which have already been shown to identify structural retinal changes that are not visible by ophthalmoscopic examination [32-34]. Another rapidly emerging area is the development and application of computer-based image analysis methods to assist ophthalmologists through automated identification of retinal vascular abnormalities consistent with plus disease or pre-plus disease [35]. These computer-based image analysis systems have already been shown to have potential to identify plus disease with comparable or better accuracy than experts [36-41], and might eventually be integrated into imaging devices or electronic health record systems in the same way that computer-based algorithms routinely provide automated analysis of electrocardiograms.

In general, the field of pediatric ophthalmology has been slow to adopt the same imaging technologies that have revolutionized the practice of general ophthalmology. The nature of ROP care is now being gradually transformed by some of these technologies. By evaluating other emerging imaging technologies, understanding their benefits and limitations, and gradually implementing them into practice when warranted, pediatric ophthalmologists will be able to enhance the care they provide to patients for a broader range of problems in the future.

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