КЛИНИЧЕСКИЕ ИССЛЕДОВАНИЯ

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TELEMEDICINE WITH SMART SOFTWARE FOR RETINOPATHY OF PREMATURITY SCREENING: EXPERIENCE FROM A PROGRAM IN THE USA AND PROSPECTS FOR USE

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Retinopathy of prematurity (ROP) remains a leading cause of preventable blindness in premature infants worldwide. ROP screening is the most important part of ROP care, which determines proper timing for treatment. The standard method for diagnosis of ROP — bedside binocular indirect ophthalmoscopy (BIO) has many limitations. Effectiveness of a telemedicine approach, using wide angle remote digital fundus imaging and Smart Software for ROP screening, was demonstrated. Telemedicine can supplant BIO examination as a primary approach for ROP screening, reduce human error, provide better care, reduce physician time and therefore reduce cost for ROP screening.

Key words: *retinopathy of prematurity; screening; telemedicine*

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ТЕЛЕМЕДИЦИНА С ПРИМЕНЕНИЕМ СОВРЕМЕННОГО ПРОГРАММНОГО ОБЕСПЕЧЕНИЯ ДЛЯ ДИАГНОСТИКИ РЕТИНОПАТИИ НЕДОНОШЕННЫХ: ОПЫТ ИСПОЛЬЗОВАНИЯ В США И ПЕРСПЕКТИВЫ ПРИМЕНЕНИЯ

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Ретинопатия недоношенных (РН) остается ведущей причиной устранимой слепоты недоношенных детей во всем мире. Выявление (скрининг) РН является чрезвычайно важным, так как позволяет своевременно определить показания к лечению. Стандартный метод диагностики РН — непрямая бинокулярная офтальмоскопия имеет много ограничений. Эффективным методом скрининга РН является телемедицина с дистанционным анализом широкоугольных цифровых изображений глазного дна и использованием современного программного обеспечения. Телемедицина может заменить диагностику РН с помощью непрямой бинокулярной офтальмоскопии, что позволяет снизить частоту диагностических ошибок, улучшить результаты лечения, уменьшить трудозатраты врачей офтальмологов и общую стоимость выявления РН.

Ключевые слова: *ретинопатия недоношенных; скрининг; телемедицина*

Retinopathy of prematurity (ROP) is a vasoproliferative retinopathy affecting premature infants that may progress to retinal detachment and blindness. ROP remains a leading cause of preventable blindness in premature infants worldwide [1—4]. As premature infant survival increases worldwide, the incidence of ROP also continues to rise. In Russia 93200—108200 babies are born prematurely (with a birth weigh 2500 g or less per year) [5]. The total ROP screening population in Russia is approximately 30000 babies per year. In the USA the premature baby is examined in average 6 times beginning at 31 weeks postmenstrual age prior to discharge from the hospital. This means approximately 180000 exams per year. It is unlikely that there are enough experienced examiners to do these exams.

The International Classification of Retinopathy of Prematurity (ICROP) [6, 7], the Cryotherapy for Retinopathy of Prematurity (CRYO- ROP) [8] and Early Treatment for Retinopathy of Prematurity (ETROP) trials [9] have had a profound impact on the way in which we screen, treat, and discuss ROP.

ROP is a time sensitive disease, which can progress rapidly. ROP screening is the most important part of ROP care. A lot of children have poor screening or no screening done, which results in poorly timed treatment or no treatment that leads to blindness.

The standard method for diagnosis of ROP has been bedside binocular indirect ophthalmoscopy (BIO) for both routine clinical care and clinical trials. Yet indirect ophthalmoscopic screening has limitations. The exam is

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Figure 1. Focus ROP Homepage.

best performed by an ophthalmologist. The examiner's interpretations of the clinical findings, rather than the actual retinal features, are transcribed onto grading sheets. The interpretation of fundus findings is presumed to be correct without opportunity for actual review. It is difficult to coordinate care with multiple doctor's drawings. Besides that bedside screening involves much wasted doctor's time to and from neonatal intensive care units (NICU) as well as examination of eye that do not need treatment (80%). Geography can create areas, where it is difficult to perform timely screening exams. There are manpower limitations to providing the number of screening exams required to at-risk infants as well. Many physicians do not perform ROP screening for the fear of litigation. In peripheral centres there may be no physician with expertise in ROP diagnosis and management. Bedside screening with BIO isolates Neonatologist, Nurse and family from understanding the changes in the eye and reason for treatment.

This combination of challenges has fuelled research into a telemedicine approach to ROP screening over the last several years. Originally proposed in 1999 [10], proof of concept was demonstrated in

2000 for telemedicine use in ROP. The ROP screening telemedicine is using wide angle remote digital fundus imaging (RDFI) [11]. The basic premise is a store-and-forward, hub-and-spoke model: images are obtained locally in the NICU, stored in the camera, uploaded to the Internet in a Health Insurance Portability and Accountability Act (HIPAA)-compliant fashion and then received, interpreted and adjudicated by the reader and a report returned to the NICU.

Extensive evaluation of RDFI in ROP has been performed. Investigators introduced two important concepts: (i) referral-warranted ROP (RW-ROP) defined as zone 1, plus, or stage 3 and (ii) standardized fundus imaging [12]. The RW-ROP concept built upon the idea of clinically significant ROP proposed earlier [13] in that it was ROP that merited serious consideration for treatment, as opposed to being any ROP within a specified area. The authors utilized a series of five standard images per eye with respect to optic nerve: centred, superior, nasal, inferior and temporal [12]. Later six standard photographs were introduced: one external iris photograph and five fundus views previously described [14]. The iris view allows the visualization of any media opacity, iris neovascularization, and/or inadequate visualization that may hamper RDFI.

The recent iteration of the RetCam (Clarity Medical Systems, Inc. Pleasantion, CA), most widely employed in ROP screening, utilizes a 130-degree wide angle digital fiberoptic lens, gets at least a 100-degree field in every infant, which is 50-degree radius around the optic nerve. According to ICROP, this will include all of zone 1 and much of zone 2 [6, 7]. Therefore, it became obvious that we have an objective method for ascertaining the key determinant of treatment warranted ROP (TW-ROP) i.e. posterior location of the disease.

Observations suggested that the RDFI had greater ability for accurate longitudinal comparisons compared to the BIO [13]. Wu C. et al. demonstrated that RDFI had 100% sensitivity in identifying prethreshold and threshold ROP when compared with contemporaneous bedside BIO [15]. Besides that benefits highlighted were objective documentation, indisputable evidence to the location of the disease, longitudinal review, educational opportunities and the opportunity of a detailed review of photographic findings [16]. The concept that RDFI images could be safely and reproducibly obtained by a trained neonatal nurse was made and confirmed [17].

SMART SOFTWARE

Smart Software for ROP screening: Focus ROP and ROP tool. A reliable software system such as Focus ROP system (www.focusrop.com) is needed to transfer images (Figure 1). Images are taken by nurses or other trained personnel who have certification in the use of the camera. The images are sent to trained RDFI reader who interprets the images in regard to the necessity of continuation of exam and arrangement for future screening or treatment or termination of ROP screening. A Portable Document Format (PDF) printable report or Electronic Medical Record (EMR) compatible report, which is HIPAA compliant, is sent back to NICU in as little as one hour (within 24 hours) and stores the images for 22 years as needed. The exam schedule is not changeable determined by the Focus ROP program based on fundus findings. The

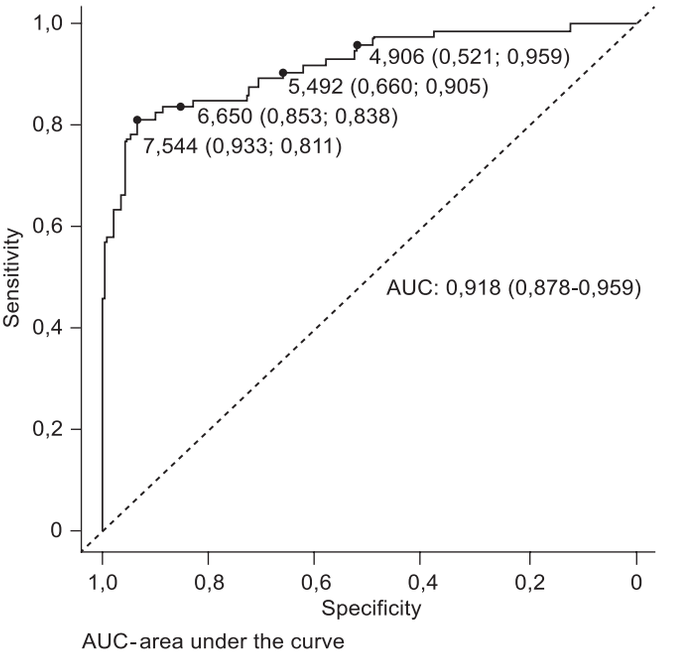

Figure 2. Receiver Operating Characteristic Curve.

most common error that doctors make while doing ROP exams is the extension of the exam schedule for too long period of time. The FocusROP system does not allow the doctor to do that: it determines the exam (if it is photo or bedside) based on the recorded findings. This removes the possibility of poorly timed exams allowing disease progression beyond a treatment window.

In Focus ROP there is an education module for ROP training and a module to train NICU nurses to download and upload images. Remote ROP graders should have an experience in interpretation of digital images for ROP. Interpretation requires not only expert knowledge about ROP but also understanding of the limitations of interpreting of digital images.

ROP tool is a software program which assigns a number to the tortuosity and dilatation of retinal vessels in the posterior pole — the area of the worse ROP — aggressive posterior ROP (APROP) and location of plus and easiest to image. If the number of these vessels increases, the risk of plus disease increases.

In the ROP tool Validation Study of tortuosity 335 eyes were read by the ROP tool and compared to doctor (M. Trese, A. Capone, K. Drenser) read photographs. The ROP tool gives a value like an experienced examiners value. It can be followed on weekly exam to see if the tortuosity is changing and give the reader a level of comfort regarding the presence or absence of plus disease. By using the tortuosity value of 4.106 the sensitivity of the ROP tool was 96% and specificity was 64%. The area under the Receiver Operating Characteristic Curve was 0.92 suggesting a very positive correlation (Figure 2).

Real-world RDFI networks proliferate with much success [18-27]. The solution for many problems facing medicine in general and for the problems specifically facing ROP is the use of digital information management and the advent of telemedicine. Nowadays telemedicine is an optimal approach, which can supplant BIO examination as a primary approach for ROP screening. Prop-

er functioning of telemedicine requires wide angle digital fundus cameras in every NICU, a reliable software system, certificated NISU nurses or other personnel to capture images and RDFI readers. Also you must indentify an individual responsibility for ROP screening in the NICU. The person responsible for ROP screening organization is the NICU nurse — a ROP coordinator. In addition to outlining each team responsibilities, the NICU contact person deals with disputes about what to do when a photographer is unavailable, when an infant needs treatment, when there is an equipment malfunction, and the like. Close collaboration among neonatologist, imaging staff and ophthalmologists is warranted. Specific responsibilities of each individual must be carefully delineated in a written protocol in advance, so that repeat imaging and/or confirmatory examinations and required, treatments can be performed without delay as ROP is a time sensitive disease.

Certainly, there are expenses on the equipment, software, personnel training, but cost for blindness is substantially higher. The one-time cost of the digital screening camera is easily off set by the reduction of physician time and medico-legal risk. Apart from that, new wide angle digital fundus cameras, which are being developed nowadays, promise to be cheaper, which allows to decrease equipment cost and overall expenses.

Telemedicine screening creates a safety net for patients, doctors and hospitals for ROP care and medical malpractice protection. It would minimize uncertainty in medico legal cases, and provide a more consistent level of screening for all at-risk infants and give a better chance for properly timed treatment. Telemedicine with smart software can reduce human error, provide better care, reduce physician time and therefore reduce cost for ROP screening.

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