Digital imaging and Telemedicine in ROP

Retinopathy of Prematurity

Prof Nicoline Schalij-Delfos, MD, PhD
Paediatric Ophthalmology
LEIDEN UNIVERSITY MEDICAL CENTRE
THE NETHERLANDS
Data Monitoring Committee Novartis Rainbow studies

RAntibizumab compared with laser therapy for the treatment of INfants BOrn prematurely With retinopathy of prematurity
Outline

• Digital imaging (DI) and Telemedicine (TM)
  • Current practice
  • Advantages and pitfalls
  • Opportunities
  • Review literature on grading accuracy
  • Training
  • Systemised algorithms
ROP-screening: Why?

Visual disability is largely preventable when treatment requiring ROP is detected and treated in time.
Screening technique

• Gold standard screening
  • (Binocular) Indirect Ophthalmoscopy ((B)IO) by trained ophthalmologists

• Reports
  • Drawings
  • Written (EPD)

• Okay for the majority of screening examinations

• Comparison of FU examinations subjective
  • Personal interpretation
  • Dependent on expertise
  • Issue in case of transfer to another hospital / screener

• Transportation for expert opinion (babylance)
Screening with camera

- **Widefield Digital imaging (WFDI)**
- **Objective** information for disease detection
- Facilitates comparison with previous images and retrospective analysis
- Easy to ask expert opinion by secured mail, app etc: **Telemedicine** (TM)
- Timing of treatment more exact
- Less transport of often critically ill infants

- Most used and evaluated: Retcam (Natus Medical)
Additional advantages DI

• Can be done by ophthalmologist, neonatologist, physician assistant, nurse (practitioner), paramedic or other trained personnel

• Extension of diagnostic expertise to underserved areas
  • Local scarcity (available or willing) of qualified ophthalmologists
  • Remote location of some NICU’s or High Care Centers

• Valuable for:
  • ROP education and training (screeners and residents)
  • Communication with parents
  • Medico legal issues

• Facilitates computer based analysis of plus disease, THE hallmark for treatment
Early initiative

- Wide Field Digital Imaging (WFDI) based TM: Retcam® 120
- 5 hospitals in the South of Germany
- Coded transfer of data to reading center
- Evaluation by experienced paediatric ophthalmologists
- (S)TR-ROP: suspected treatment requiring ROP

- N=1222
- 6 years FU
- 3.5% TR-ROP
- Sensitivity 100%, PPV 82.4%
- All TR-ROP detected in time

Pitfalls DI / TM

• Digital imaging
  • RetCam expensive (US$95 000 / €120.000)
    • Number of infants per hospital with severe ROP relatively small
    • Lack of or marginal insurance coverage and reimbursement
    • Cost effectiveness studies are scarce and are not universally applicable

• Telemedicine
  • Limited internet access
  • Secure server
  • Timely review
  • Training of imagers and graders
  • Certification process and licensing
  • Medicolegal issues: final responsibility
Technical Pitfalls

• Image quality may limit ability for accurate diagnosis
  • Hazy vitreous in extremely immature babies

• Temporary morphological changes
  • Plus disease masked by camera compression on the eye
  • Retinal hemorrhages
  • Influenced by experience of imager
Alternatives for Retcam

- Panocam LT / Pro (Visunex Medical Systems, Fremont CA)
- Optomap (Optos PLC, Scotland, UK)
- Spectralis (Heidelberg, Germany)
- 3nethra (Forus Health PVT, Bangalore, India)
- I-phone with 20D (D-EYE)
- Indirect ophthamoscopic digital photographic system (Keeler)

Issues:

- Portable and accessible for NICU population
- Review system
- Field of view (30 - 130°)
- Image quality
- Validation
- Pricing
Review of literature

Sensitivity and specificity of grading

Pubmed and Cochrane search

- 486 papers
- 11 suitable for review
- 8 level 1 evidence (independant masked comparison)
- Sensitivity and specificity are high but differ dependant on
  - Study design
  - Population
  - Time of screening / imaging
  - Item graded (plus or type 1 or Zone or ROP stage)


Neonatus 2017 Poznan
Grading programs

• e-ROP: evaluation of acute phase retinopathy

• SUNDROP: Stanford University Network for Diagnosis of Retinopathy of Prematurity

• KIDROP: Karnataka Internet-assisted Diagnosis for ROP
Evaluation of TM grading for detection of Treatment Requiring (TR)- or Referral Warranted (RW)-ROP

• Trained nonphysician readers were compared to physicians
  • good intragrader and intergrader consistency for detection of TR-ROP

• The likelihood of detecting RW-ROP by telemedicine screening is decreased when a full set of retinal images (5) is not obtained
• Stanford University Network for Diagnosis of Retinopathy of Prematurity (SUNDROP)
  • 6 yrs follow up
  • Remote evaluation by ROP specialist
  • Sensitivity 100%, specificity 99.8%

• KID-ROP – India
  • Middle income countries: increased survival, scarce ROP experts
  • Trained non-physicians
  • Sensitivity 95.7%, specificity 93.2%
Conclusion

Grading DI – TM

good sensitivity and specificity

Vital issues are:

Training
Image quality
Responsibilities
Training

• No official certification or license for grading of images yet

• GEN-ROP (Global Education Network)
  • A secure web-based tele-education system for ROP education
  • 2,500 unique image sets of ROP
  • Evaluation accuracy and liability of grading results during pretest, posttest, and training chapters of 55 USA and Canadian residents

• GEN-ROP proved effective in improving diagnostic accuracy of ROP

• Tool for future certification

Timely feedback

Decisions about referral / treatment are needed in short time

• Referral for examination and consideration of treatment within 24 hrs

• Turnaround time (time from imaging to answer by reading centre)
  • 95.5% within 24 hrs

• Delay
  • Time acquisition - uploading
  • Time incoming images and capacity reading centre to grade

GE Quinn. Timely implementation of a retinopathy of prematurity telemedicine system. JAAPOS 2016;20:425-430.
Image review Netherlands

• Secured app (Siilo): password, end-2-end data encryption, images are not automatically stored and are deleted after 3 months

Work in progress:
• Secured ophthalmologist network ‘Oogartsennet’
• Screening ophthalmologist upload
  • Digital images
  • Standard background information (GA, BW, AV, SatO₂ levels etc)
  • Questions
• Expert team (5) for review
  • E-mail alert
  • At least 2 reviewers have to respond
• Screening physician
  • E-mail alert
  • Takes final decision
Algorithms to detect plus disease

- Plus disease is main criterion for treatment (ET-ROP)
- Exact measurement of retinal vessel diameter
  - provides objective information about changes in vessel width
  - can be a predictor of disease progression
- Algorithms for identification (‘segmentation’) of retinal vessels
- Assisting / replacing (?) graders
Image analysis systems

• ROP tool
  • Computer program to assess tortuosity (USA)
  • Retcam-based
  • ROP-tool and lay screeners good accuracy compared to 3 expert graders

• Oximetry (ODR and vessel width)

Retinal oximetry (ROPOXYMAP-study)

- Fundus images using dual wavelengths
- Difference in light absorbance of hemoglobin bound and unbound to oxygen
  - 633 nm **sensitive** to changes of oxygen
  - 532 nm **insensitive** to changes of oxygen
- Oxymap software processing
  - Relative oxygen saturation in the retinal vessel
  - Vessel width
- Non contact, handheld camera
Telemedicine and digital imaging increase accessibility to adequate care for a large population of infants susceptible for ROP.

High accuracy for detection of clinically significant ROP improves healthcare for premature infants.

ROP significant threat to vision

Timely detection and appropriate timing of treatment is essential for successful outcome

Comparisons of digital imaging and telemedicine to the gold standard of binocular indirect ophthalmoscopy are favorable

Some evidence that digital imaging may even be superior in some aspects

Practical and risk management considerations essential when including DI-TM in any new or existing ROP care structure
Questions and discussion