The Royal Australian and New Zealand College of Ophthalmologists

Retinopathy of Prematurity (ROP) Screening and Treatment Guidelines

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We acknowledge the Aboriginal and Torres Strait Islander Peoples, the Traditional Owners of Country throughout Australia and recognise their continuing connection to land, waters and community. We pay our respects to them and their cultures; and to their Elders past, present and emerging.
In recognition that we are a bi-national College, we also acknowledge the Rangatiratanga of Māori as Tangata Whenua and Treaty of Waitangi partners in Aotearoa New Zealand.

1 Purpose and Scope

These clinical practice guidelines were developed by the Royal Australian and New Zealand College of Ophthalmologists (RANZCO).

The purpose of these guidelines is to provide recommendations that enable timely recognition and effective treatment of infants at risk of vision loss secondary to Retinopathy of Prematurity (ROP). These guidelines are endorsed by RANZCO for use in Australia and New Zealand.

2 Background and Context

Retinopathy of prematurity (ROP) is a potentially blinding disease seen in some premature infants.[1] ROP is the result of disordered retinal vascular development. It has strong associations with low birth weight, extreme prematurity, poor weight gain and excess administration of oxygen.[2]

ROP rates and outcomes can be used as a proxy measure of the standard of neonatal care.[3] In countries with advanced obstetric and neonatal care, ROP is very rarely seen in infants with a birth weight >1500 g and is mainly seen in those <1250 g or <30 weeks of gestation.[4-6] The International Classification of ROP (ICROP) classifies ROP in terms of location, extent, stage and severity.[7] The development of type 1 ROP and/or presence of zone 1 disease indicate a high probability of progressing to sight threatening disease. Screening to detect such disease and timely treatment has been shown to limit the number of infants suffering visual impairment.

Principles used in creating these guidelines:

- Aim: Provide guidelines for workable, safe and sustainable ROP screening and treatment programs in Australia and New Zealand.
- ROP management is a team effort requiring cooperative involvement of ophthalmologists, neonatologists, nurses, other staff and parents.
- These guidelines are not a literature review, nor a treatise on ROP and its management. This is a working document.
- These guidelines are applicable to Australia & New Zealand.
- These guidelines are evidence based where possible.
- Where appropriate, Australian and New Zealand literature is cited in support of recommendations.
- These guidelines are to be used by specific neonatal units to write or update screening protocols.
- These guidelines are not proscriptive and specific neonatal unit guidelines may vary in response to locally obtained data.
- Guidelines produced by the Paediatric Special Interest Group of RANZCO.

3 Classification and documentation of ROP

ROP is to be classified using the International Classification of ROP(ICROP). The revised classification was published in 2005.[7] A new edition, ICROP 3rd edition was published in 2021.[8]

Accurate recording of ROP findings is a vital part of the preterm infant's medical record. Documentation is to be consistent with ICROP and recorded by the examining ophthalmologist

or delegate. It is possible that appropriately trained nurse practitioners or similar may be certified to report ROP findings.[9]

Documentation must clearly indicate if the infant requires further screening examination and when this is to occur.

If treatment of ROP is indicated, this must be documented and communicated directly to the neonatal team at the time this decision is made. Plans for treatment should be formulated and documented by the ophthalmologist and neonatal team at this time.

If an infant is not able to be examined when scheduled, this fact is to be documented, as well as the reason for the examination not being undertaken. Such infants should be scheduled for future examination at a stated time.

Previous examination results should be available to the reporting ophthalmologist at the time of any subsequent examination.

Documentation of findings for each infant examined should be completed as soon as possible after the examination is concluded. When the responsible ophthalmologist is present, this should be before the next infant is assessed. In centres using telemedicine and the reporting ophthalmologist or delegate is not present, the report should be completed within 24 hours of the examination occurring.

4. Method of examination

Binocular indirect ophthalmoscopy (BIO) has historically been the most common examination method used to screen for ROP. Wide-field digital retinal photography (WFDRP) is now considered to be an acceptable method of screening and in many centres is being used as the main screening modality with BIO as an ancillary procedure.[10] These guidelines make no recommendation as to the preferred method of examination and leave that choice to the supervising ophthalmologist at each centre. It is now recognised that ROP examinations performed with BIO and WFDRP have comparable accuracy for the detection of clinically significant ROP.[11] If WFDRP is used, some guidelines recommend BIO examination be used before undertaking treatment or terminating examination for acute phase ROP.[12]
Adequate pupil dilatation is needed for examination, with Cyclomydril (cyclopentolate hydrochloride 0.2% and phenylephrine hydrochloride 1%) used as a proprietary combination eyedrop for pupillary dilatation. Local units may have a differing eye drop regimen. A comprehensive examination may require the use of a lid speculum and scleral depressor. Measures to reduce infant discomfort during the screening examination should be undertaken (including infant feeding, topical anaesthesia and oral sucrose).[13-15]
Given the importance of plus disease and the subjectivity in diagnosing plus disease[16-18], it may be appropriate to have the ICROP III[8] standard photographs of plus disease available to the reporting ophthalmologist at the time of examination.

4.1 Who should examine?

Examination of preterm infants for ROP should be undertaken or supervised by an ophthalmologist. Ideally such ophthalmologists should have completed training in ROP screening supervised by an experienced ROP screener. Subspecialty training in paediatric ophthalmology or vitreoretinal diseases, including a period of supervised training in ROP screening and treatment, would fulfil such a training requirement.
If WFDRP is used to document retinal findings, the images may be acquired by nursing or other allied health staff. Such digital images are to be interpreted by the supervising ophthalmologist and this individual is responsible for ensuring the findings are documented in the medical record. When considered necessary, the retinal findings may be confirmed by BIO.

If screening examinations are undertaken by trainee ophthalmologists (registrar or fellowship trainee), the supervising ophthalmologist should be available to confirm findings. If this is not possible, the supervising ophthalmologist should confirm significant findings (zone 1 disease, pre-plus disease, plus disease or stage 3 disease) within 1 day.
Trainee ophthalmologists should not be left in the situation of making decisions with respect to treatment of ROP.

4.2 Who should be screened?

In Australia and New Zealand there is some variation in recommendations regarding gestational age and/or birth weight of infants to be referred for ROP screening. Some centres use birth weight of 1500 g or gestational age of 32 weeks, while others use a cut off of 1250 g or 30 weeks. It is recommended that such decisions be left to the discretion of individual neonatal units, or state neonatal network and be determined by the relevant neonatologists and ophthalmologists. It is noted that the currently accepted guideline for ROP screening in New Zealand is gestational age ≤ 30 weeks or birth weight ≤ 1250 g.[5]
Ideally the decision to limit screening to less mature infants (1250 g or 30 weeks) should be made on the basis of unit specific audits that have confirmed that more mature infants have been shown to be at no significant risk of requiring treatment for ROP. Examples of such audits are the reports of Keith & Doyle.[6] and Dai et al.[5] It is recognised that gestational age and birth weight recommendations may change over time as indicated by more recent publications, such as Binenbaum et al.[19]
Infants outside the above screening criteria may be referred for screening at the discretion of the treating neonatology team. Such referral may include larger infants who have been particularly unwell or have received oxygen beyond usual expectations.[5]

4.3 Commencement of examinations

Screening examinations generally commence between 31 and 32 weeks of postmenstrual age, or 4-6 weeks post-natal age. An evidence-based screening criteria table is included in Appendix 1.[20]

4.4 Frequency of examination

Frequency of repeat examinations should be determined by the ophthalmologist and is commonly at intervals of 1 to 2 weeks. On occasions it may be advisable to examine an infant more frequently than weekly.

Repeat examination should be scheduled in 1 week or less if there is no ROP, but vascularisation extends only to posterior zone 2, stage 1 or 2 disease in zone 1, pre-plus disease, the diagnosis of aggressive ROP (A-ROP) is suspected[9] or stage 3 disease in zone 2 or 3.

Examination frequency can often extend to 1 -2 weeks for stage 2 in zone 2. This will depend on how posterior the disease is and the age of the child. For more posterior stage 2 zone 2 disease, a review in 1 week would be appropriate, while in older children with more anterior disease, review in 2 weeks would be acceptable.
Examination in 2 weeks is appropriate if there is no ROP or stage 1 ROP and vascularisation has advanced beyond posterior zone 2.
On occasions it may be appropriate to leave an interval between examinations of 3 weeks.

4.5 When to cease examination

It is generally accepted that examinations can be discontinued once retinal vascularisation has reached zone 3 in infants who have not had any evidence of ROP. This degree of vascularisation is rarely seen before 37 weeks postmenstrual age. Infants who have had ROP, but which has not required treatment, should be followed until the ROP has been observed to

clearly regress and vascularisation has entered zone 3. It may be necessary to continue screening examinations well beyond 40 weeks of postmenstrual age.

In the era of VEGF inhibitors, frequent ongoing examinations may be required up to 65 weeks post-menstrual age, so institutions need to provide facilities to occasionally examine infants under sedation or general anaesthesia.

4.6 Follow-up

There is no uniform agreement as to when and what follow-up examinations for ex-premature infants who have not required treatment for ROP. It is recognised that there is an increased rate of strabismus, refractive error and amblyopia in such surviving infants and some form of follow-up is strongly recommended. It is suggested that these infants be reviewed at least between 6 and 12 months of corrected age with further follow-up as required.
Infants who have required treatment have an increased risk of late ophthalmic complications and require life-long follow-up.[21,22] This should commence within 3-6 months of treatment and continue periodically, depending on the nature of any problems that are subsequently detected.

5 Treatment

5.1 Which infants require treatment?

The development of type 1 ROP as described in the Early Treatment of ROP (ETROP) Trial indicates the need for treatment. Type 1 ROP includes: Zone 1 disease of any stage with plus disease, zone 1 stage 3 disease without plus disease, and zone 2 stage 2 or 3 with plus disease.

A-ROP requires urgent treatment and may not follow the more typical progression of ROP requiring treatment. A-ROP is characterised by "… its location(posterior or peripheral), prominence of plus disease, and the ill-defined nature of the retinopathy." and rapid progression.[7]

There are a small number of infants that have stage 3 disease with extensive fibrovascular proliferation into the vitreous, but do not develop plus disease. These infants may be at risk of developing retinal traction and some ophthalmologists will recommend treatment in this situation.

5.2 Timing of treatment

Treatment should be undertaken within 72 hours of the diagnosis of type 1 ROP (in accordance with ETROP protocol) and within 24-48 hours for A-ROP).

5.3 Methods of treatment

Ablation of the peripheral avascular retina with transpupillary laser photocoagulation is the recommended treatment unless the child has: A-ROP, zone 1 disease, is too sick to tolerate laser treatment or in cases where the view of the retina is inadequate to allow safe laser treatment. In these cases, intravitreal injection of a VEGF inhibitor (such as bevacizumab or ranibizumab) is preferred.[23,24] Treatment should be undertaken by a paediatric ophthalmologist or vitreoretinal surgeon experienced in the treatment of ROP. Laser retinal burns should be confluent or near confluent in the avascular region. Some authorities recommend photocoagulation immediately posterior to the vascular ridge in more severe cases of type 1 ROP.[25] It is recognised that the treatment of ROP is steadily evolving and modalities such as fundus fluorescein angiography and optical coherence tomography may be integrated in to the standard of care.[26,27]

VEGF inhibitors are used as the primary treatment in the indications described above. They are also used as a rescue treatment if laser treatment has failed to control type 1 disease or A-ROP.[23,24] The long-term potential side effects of VEGF inhibitors on the premature infant are

not well understood and are still under investigation.[28] The choice of drug and dosage are also constantly changing, so the most recent evidence-base should be consulted prior to administering treatment. Treatment with VEGF inhibitors should be subject to individual institutional policy with appropriate informed consent obtained from the guardians. VEGF inhibitors without laser ablation, require far more intensive follow-up for the infant and family, which may not be appropriate in certain geographical locations.
Cryotherapy to the peripheral avascular retina is not an acceptable treatment for ROP in Australia and New Zealand. Its use has been superseded by laser.

These guidelines make no recommendation with respect to where ROP treatment should occur. It is recognised that the least movement and medical intervention that is required to safely undertake treatment is in the best interest of the infant. Common locations for treatment include dedicated laser rooms in Neonatal Intensive Care Units or in the Operating Theatre. All infants having treatment should have a repeat examination within 1 week of this treatment. Additional treatment is at the discretion of the treating ophthalmologist. Indications for further treatment may include no evidence of regression (or indeed deterioration) of ROP, worsening plus disease or the presence of laser skip areas. Such treatment may include further laser or VEGF inhibitors.

6 Audit of compliance with ROP screening guidelines

It is recommended that individual units undertake internal unit audits periodically to confirm all eligible infants are screened and that there is adherence to the screening and treatment guidelines.

6.1 Responsibilities

6.1.1 Neonatal team

1. Identifies and refer infants who meet the screening criteria outlined above. The individual institution ROP policy should identify staff who are responsible for these tasks and indicate this responsibility in their job description.
2. Maintains a scheduling system that indicates when infants are due for first and subsequent examinations.
3. Notifies the ophthalmology team of any infants considered too sick for examination and the reason.
4. Ensures that appropriate pupil dilation is ordered and performed prior to the ophthalmology team attending for ROP screening ward rounds.
5. Arranges support staff appropriate for the safe conduct of ROP screening and treatment (when such treatment is undertaken in the neonatal unit). When treatment is undertaken in an operating theatre, it is the responsibility of the institution to provide staff necessary for this to occur.
6. Ensures that appropriate ongoing screening is available at the receiving unit when infants are transferred away from the current unit before ROP screening is completed. It is the responsibility of the neonatal team to ensure that all pertinent clinical information (including ROP screening and any treatment records) is passed on to the receiving unit at the time of transfer. If such ongoing screening is not available, the infant should not be transferred, or arrangements made for the infant to be transferred back to the original unit as required by the ophthalmologist for ongoing review. It is recognised that mobile WFDRP with photographs (“telemedicine”) taken by non-medical staff and interpreted by the supervising ophthalmologist may be used in such circumstances.

6.1.2 Ophthalmology team

1. Undertakes all screening, treatment and associated documentation for the safe management of ROP. This involves good communication with the neonatal team and reliable and timely attendance for screening ward rounds to minimize disruption of the neonatal unit.
2. Provide a weekly screening service. Some peripheral centres may only be able to provide fortnightly screening service. Children requiring more frequent screening should remain in the original unit as required by the ophthalmologist for ongoing review (see above 6.1.1, point 6)
3. Notifies the neonatal team of all planned leave in time to arrange appropriate leave cover.

6.1.3 Institution

1. Provides appropriate funding and staff resources for the effective and safe conduct of an ROP screening and treatment service. Resources include all equipment needed for clinical examination and treatment. This includes appropriate funding of the ophthalmology team and neonatal team members and may include the funding of dedicated nursing staff or allied health staff (such as photographers). Funding needs to have an allocation for the provision of leave funding for all team members.
2. Provides an appropriate area to undertake laser treatment safely and in compliance with relevant safety standards.
3. Is responsible for the recruitment and accreditation of all staff required to provide this service.
4. Ensures that the institution has a ROP management policy and that this policy is updated from time to time. The institutional ROP policy is to be formulated with input from the neonatal and ophthalmology teams. It is recognised that institutions may have policies that differ with respect to guidelines for referral for screening and follow-up. It is strongly recommended that an institutional ROP management policy be consistent with these guidelines, but it is recognised that the institutional policy takes precedence over these guidelines.
5. Provides clinical ethics input when required.

7 Acknowledgements

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8 Record of Amendments

Page	Details of Amendment	Date amended
Entire document	Created	October 2021

9 Abbreviations

ROP	Retinopathy of prematurity
RANZCO	Royal Australian and New Zealand College of Ophthalmologists
ICROP	International classification of retinopathy of prematurity
BIO	Binocular indirect ophthalmoscopy
WFDRP	Wide field digital retinal photography
ETROP	Early Treatment of ROP
A-ROP	Aggressive ROP
VEGF	Vascular endothelial growth factor

Appendix 1: Evidence-based screening criteria table

	Age at first ROP screening examination	
Gestational age (weeks)	**Postnatal age (weeks)**	**Postmenstrual age (weeks)**
22	8	30
23	7	30
24	6	30
25	5	30
26	4	30
27	4	31
28	4	32
29	4	33
30	4	34
31	4	35
32	3	35
33	2	35
34	2	36
35	2	37

ROP, Retinopathy of prematurity.
Adapted from reference Reynolds JD, Dobson V, Quinn GE, et al. Evidence-based screening criteria for retinopathy of prematurity: natural history data from the CRYO-ROP and LIGHT-ROP studies. Arch Ophthalmol 2002; 120: 1470–6.

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