The “Eyes Have It” What’s New in Pediatric Ophthalmology?

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WREIC 2019

Low vision center with early intervention services in India, Aravind Eye Hospital, Madurai

What you need to know:

1. ***Back of the EYE***

OCT: Optical Coherent tomography

Lebers congenital amaurosis

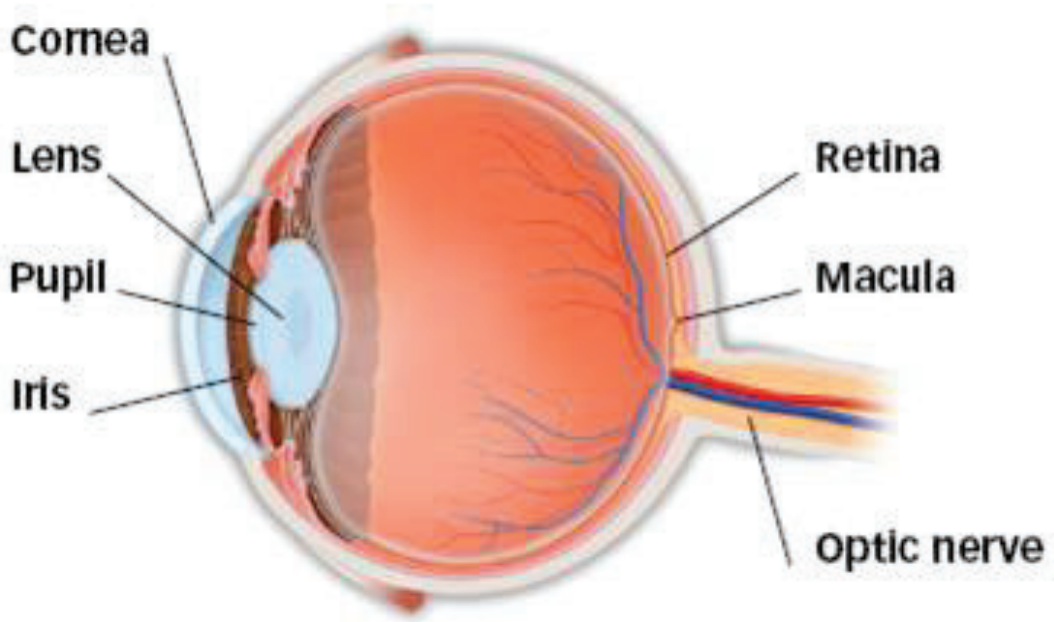
Avastin and ROP

2. ***Front of the EYE***

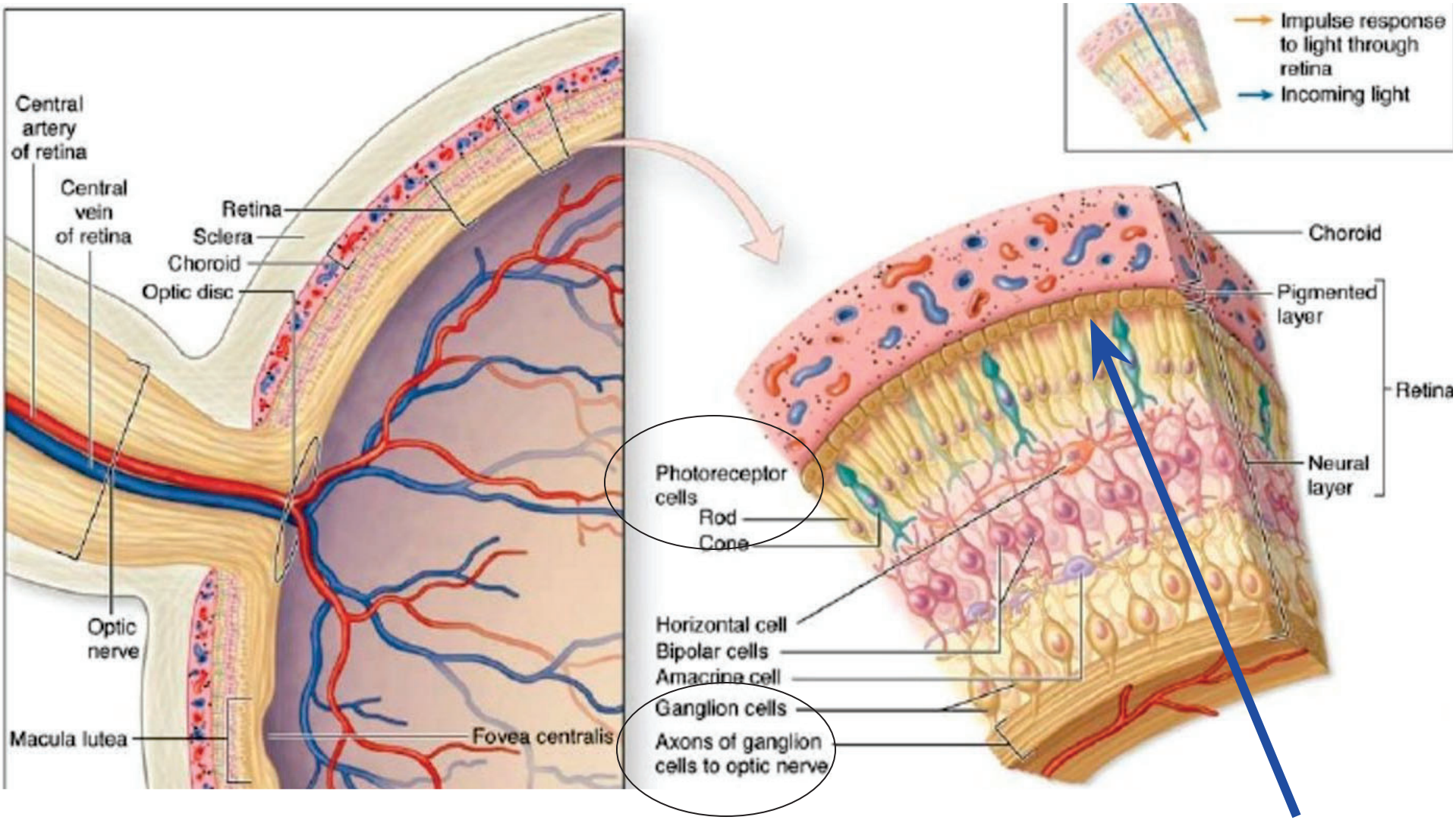
Corneal crosslinking

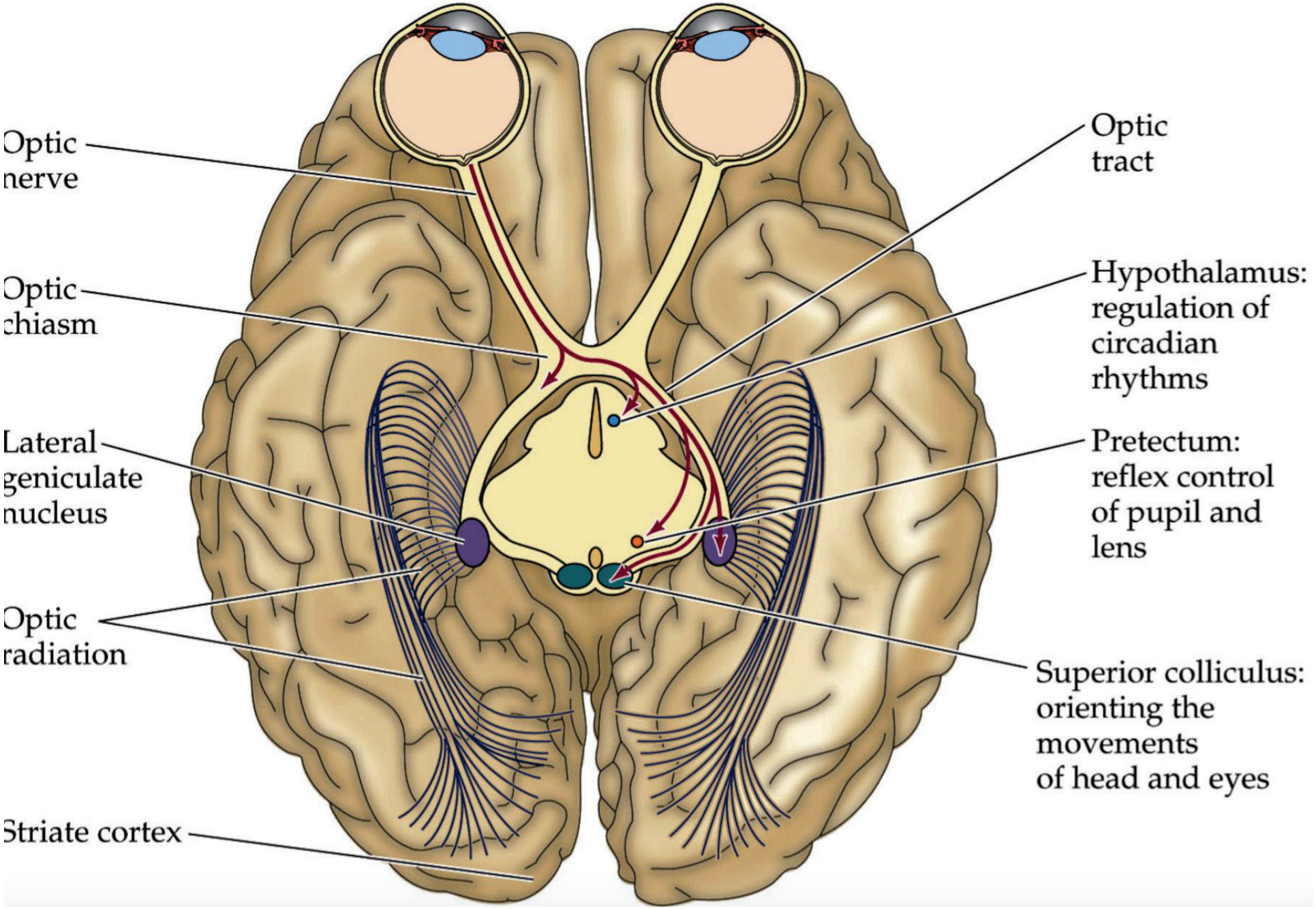
Refractive surgery for children

Glasses for infants(new little book)



Normal Retinal and Optic Nerve Anatomy




Optic nerve
Optic chiasm
Lateral geniculate nucleus
Optic radiation
Striate cortex
Optic tract
Hypothalamus: regulation of circadian rhythms
Pretectum: reflex control of pupil and lens
Superior colliculus: orienting the movements of head and eyes

Very Basic Embryology

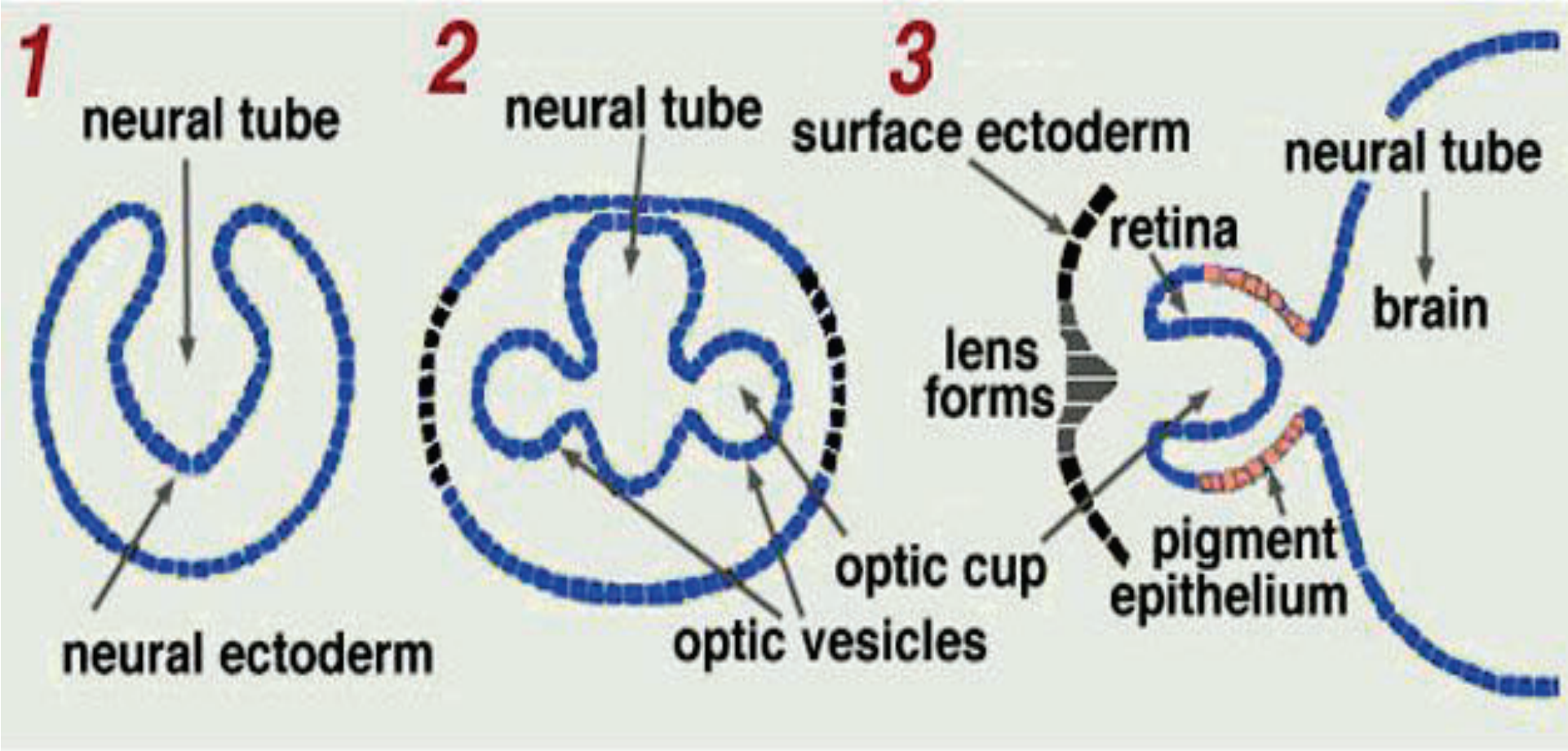
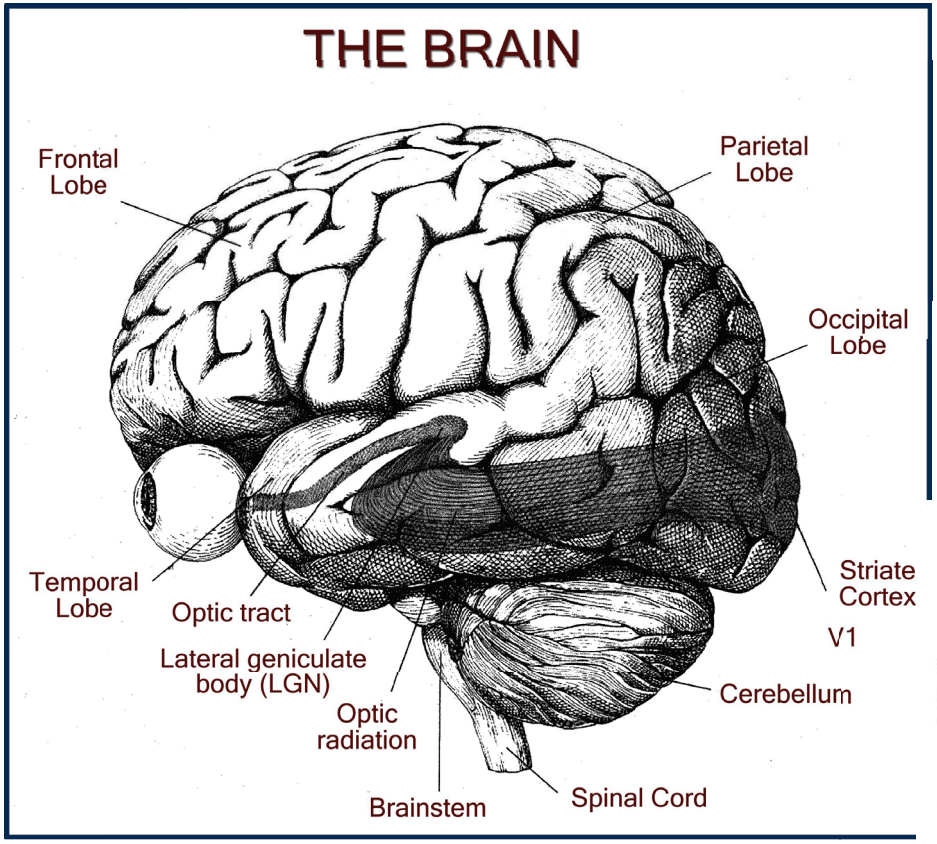
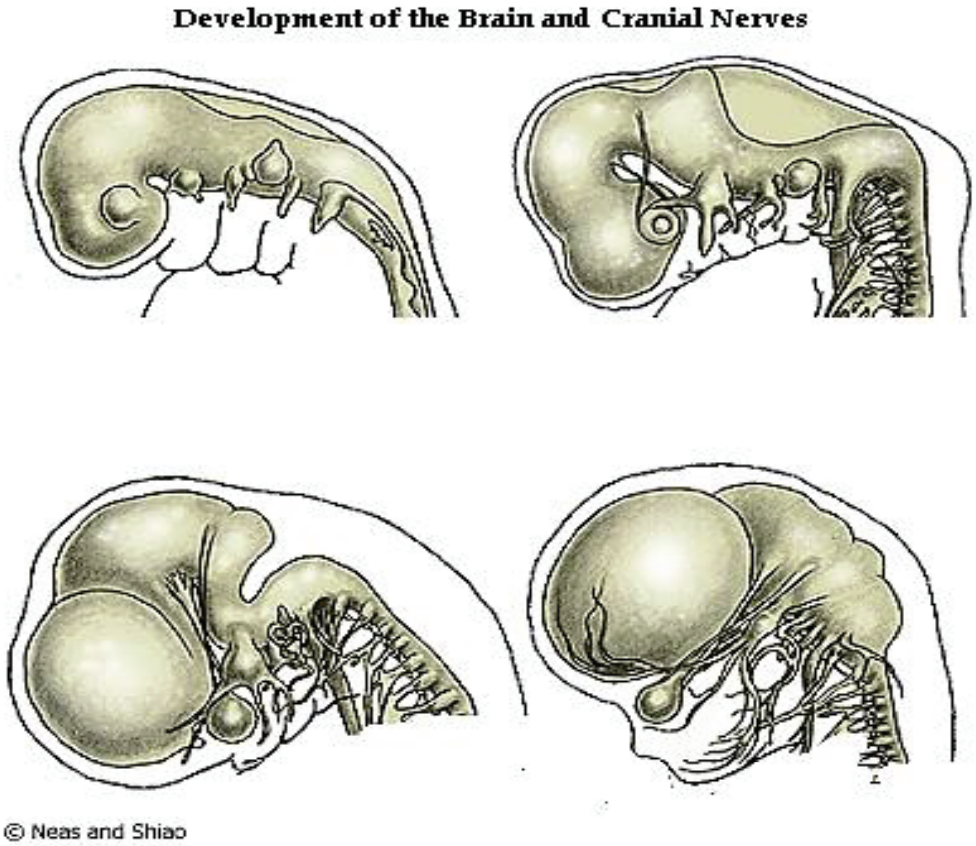


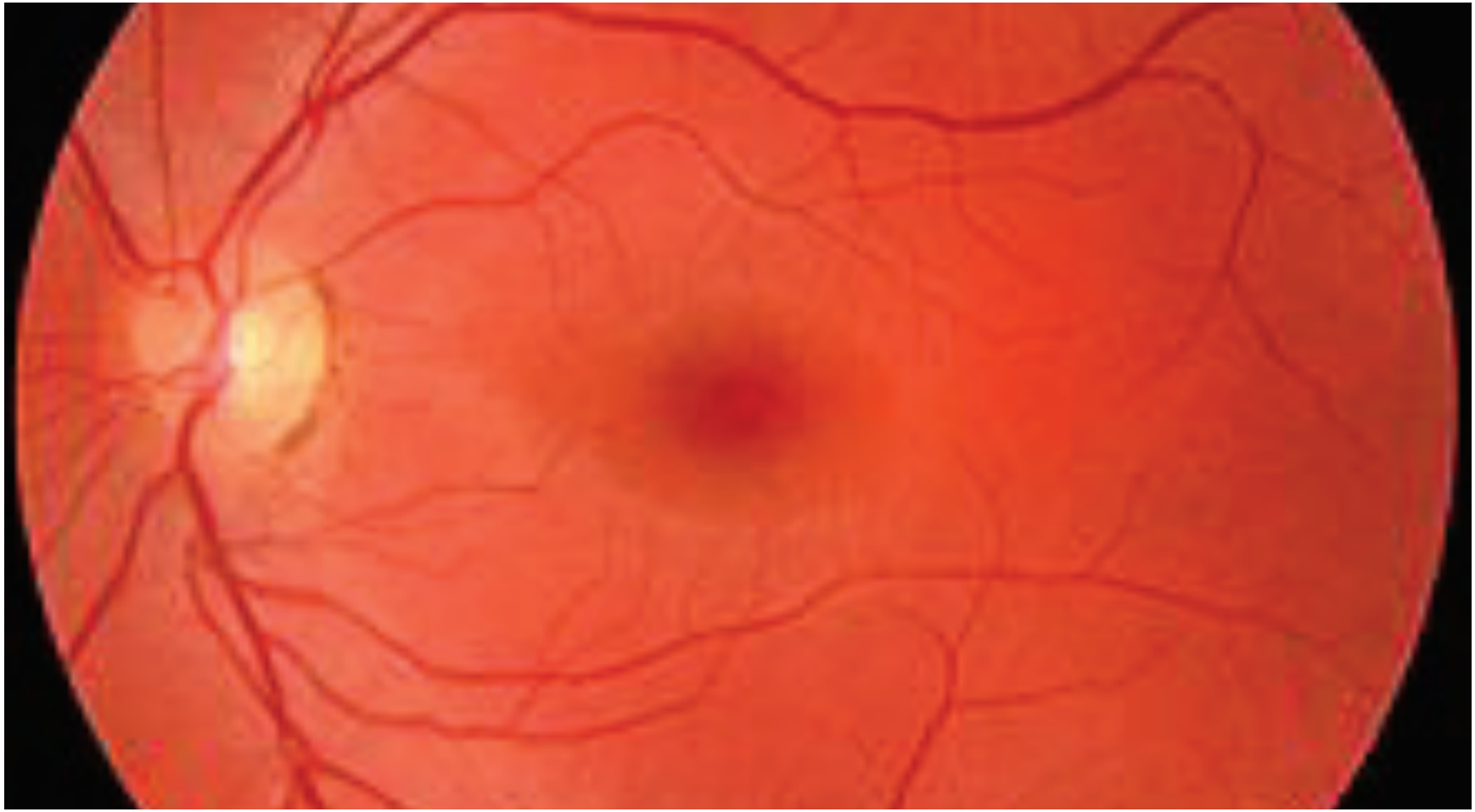
Fig. 4. Development of the eye from the neural tube though the optic vesicles and the inverted optic cup forming the retina.

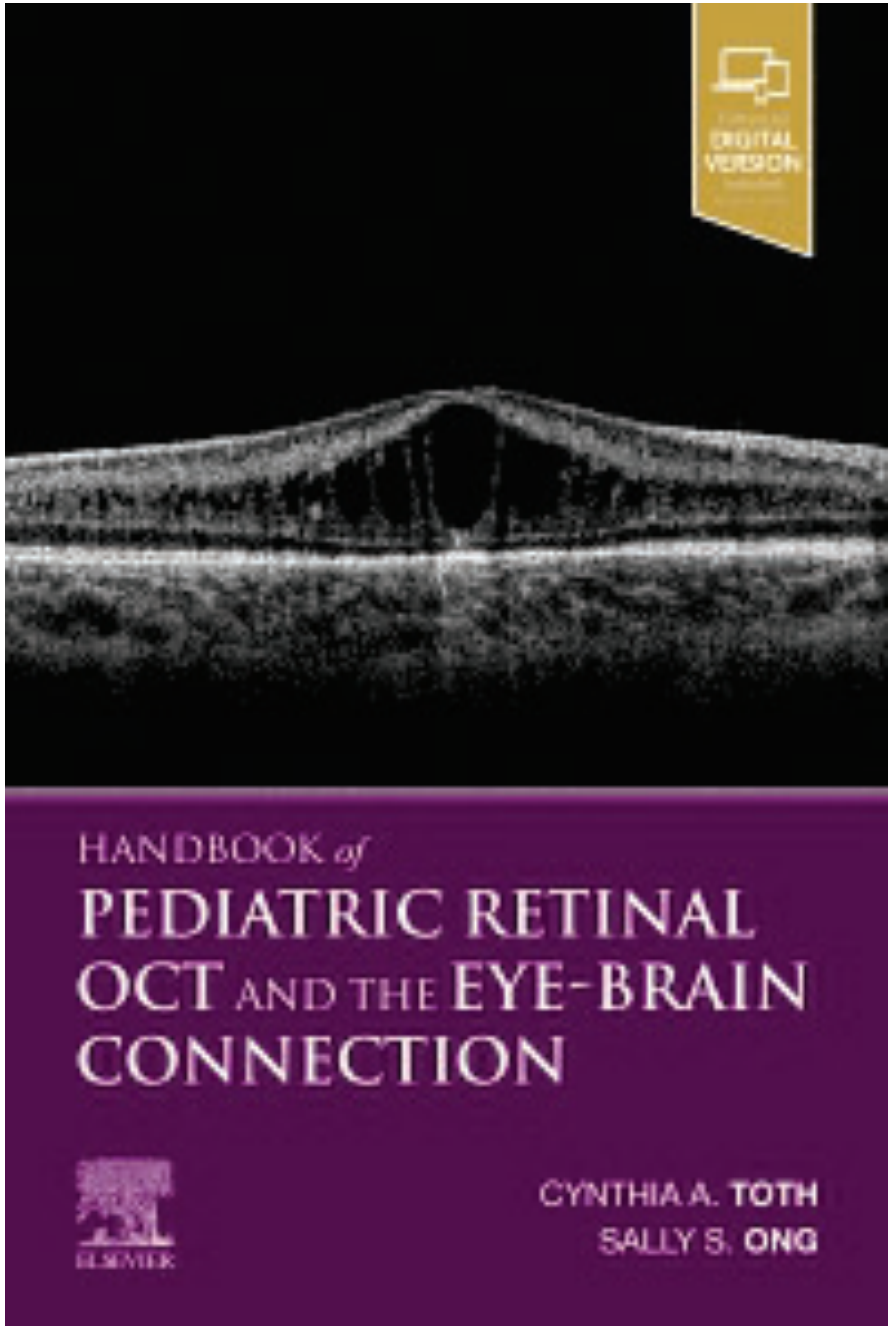

THE BRAIN
Frontal Lobe
Parietal Lobe
Occipital Lobe
Temporal Lobe
Optic tract
Lateral geniculate body (LGN)
Optic radiation
Striate Cortex
V1
Cerebellum
Brainstem
Spinal Cord

Embryology


Development of the Brain and Cranial Nerves
© Neas and Shiao

Back of the Eye





New Book on Pediatric OCT

From: Pediatric Optical Coherence Tomography in Clinical Practice—Recent Progress
Invest. Ophthalmol. Vis. Sci.. 2016;57(9):OCT69-OCT79. doi:10.1167/iovs.15-18825

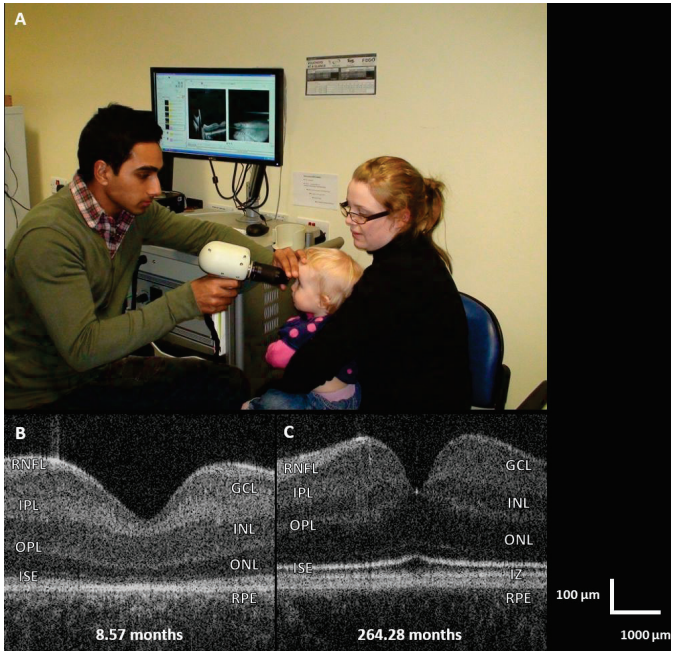


Figure Legend:

(A) Example of using HH-SDOCT to acquire a retinal tomogram in a child and two foveal tomograms taken at the foveal center illustrating normal retinal anatomy and the morphologic differences between the neonatal (B) and adult retina (C). Both participants were born at term, and the ages of the participants are given in months postmenstrual age. During normal foveal development, there is migration of the IRLs (GCL, IPL, INL, and OPL) away from the central fovea, migration of the cone photoreceptors into the central fovea, and elongation of the ORLs (ONL, IS, and OS) with increasing age. This explains the presence of the IRLs and absence of cone photoreceptors at the central fovea on the neonatal OCT (B). In contrast, the IRLs are absent and the cone photoreceptors are present at the central fovea on the adult OCT (C). The presence of the interdigitation zone in (C) is an additional marker of retinal maturity.

- The use of OCT (optical coherence tomography) is now becoming instrumental in the diagnosis and management of many pediatric conditions.

- Uses infrared light to provide micron-scale resolution of in vivo tissue

- OCT angiography (OCTA)

Images retinal microvasculature

How can we use? Optic Nerve

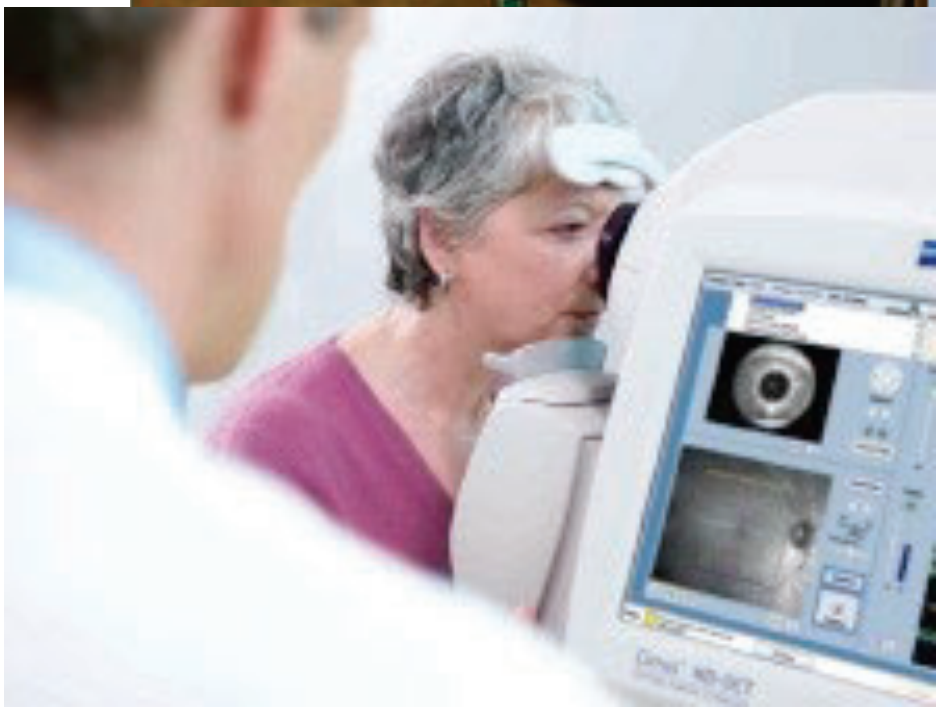
- Glaucoma vs. physiologic cupping
- Optic atrophy post trauma
- Optic nerve hypoplasia
- Progression of nerve fiber loss (optic nerve gliomas)
- Optic neuritis/papilledema
- Optic nerve drusen/pseudopapilledema
- Track increase ICP from VP shunt

How can we use? Retina

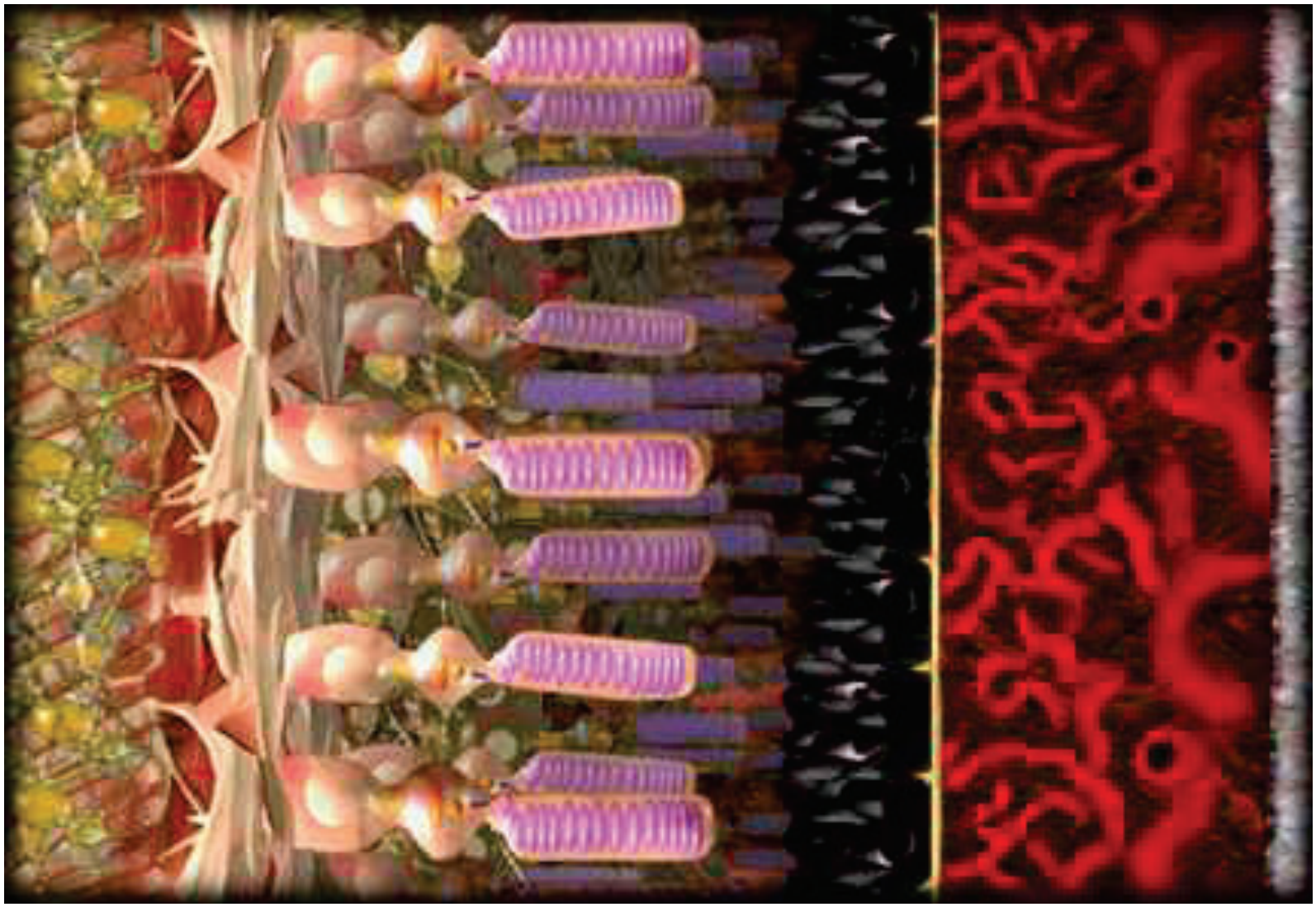
- Foveal Hypoplasia
- Cystoid macular edema
- Macular holes/trauma
- Structural causes of amblyopia
- Retinal dystrophies
- Hereditary retinal dystrophies
- Toxicity (plaquenil, ?vigabatrin)
- tumors

Technical challenges in Kids

- No official norms for kids: soon
- Difficult technically in kids, nystagmus, fixation
- Hand held expensive
- Built for adults

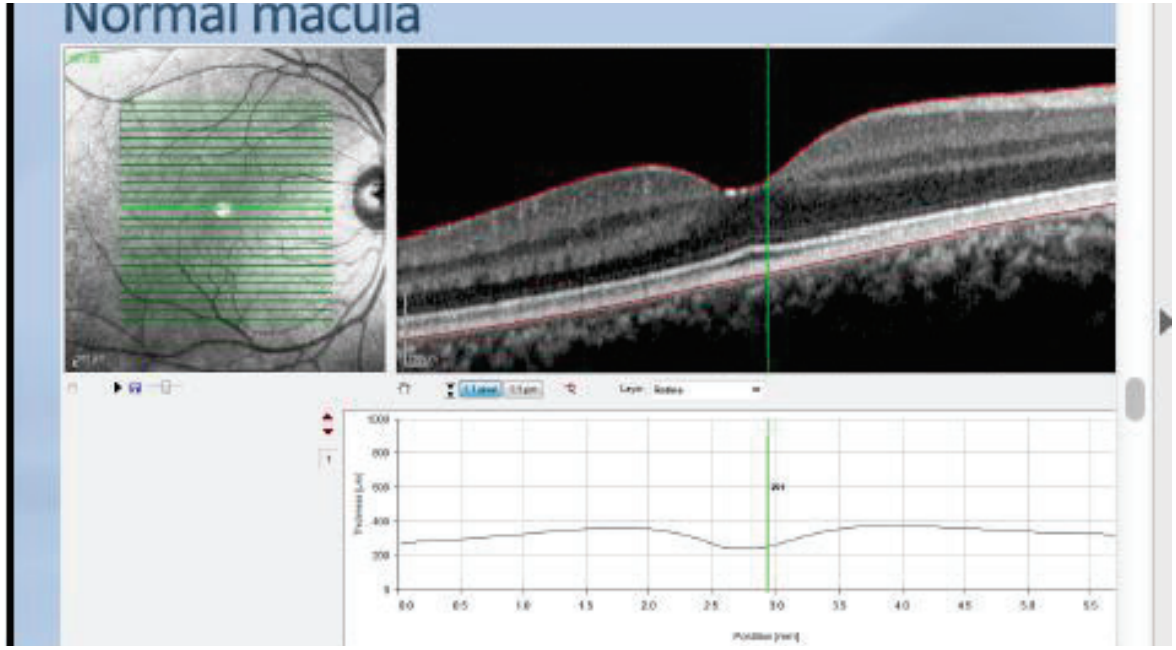


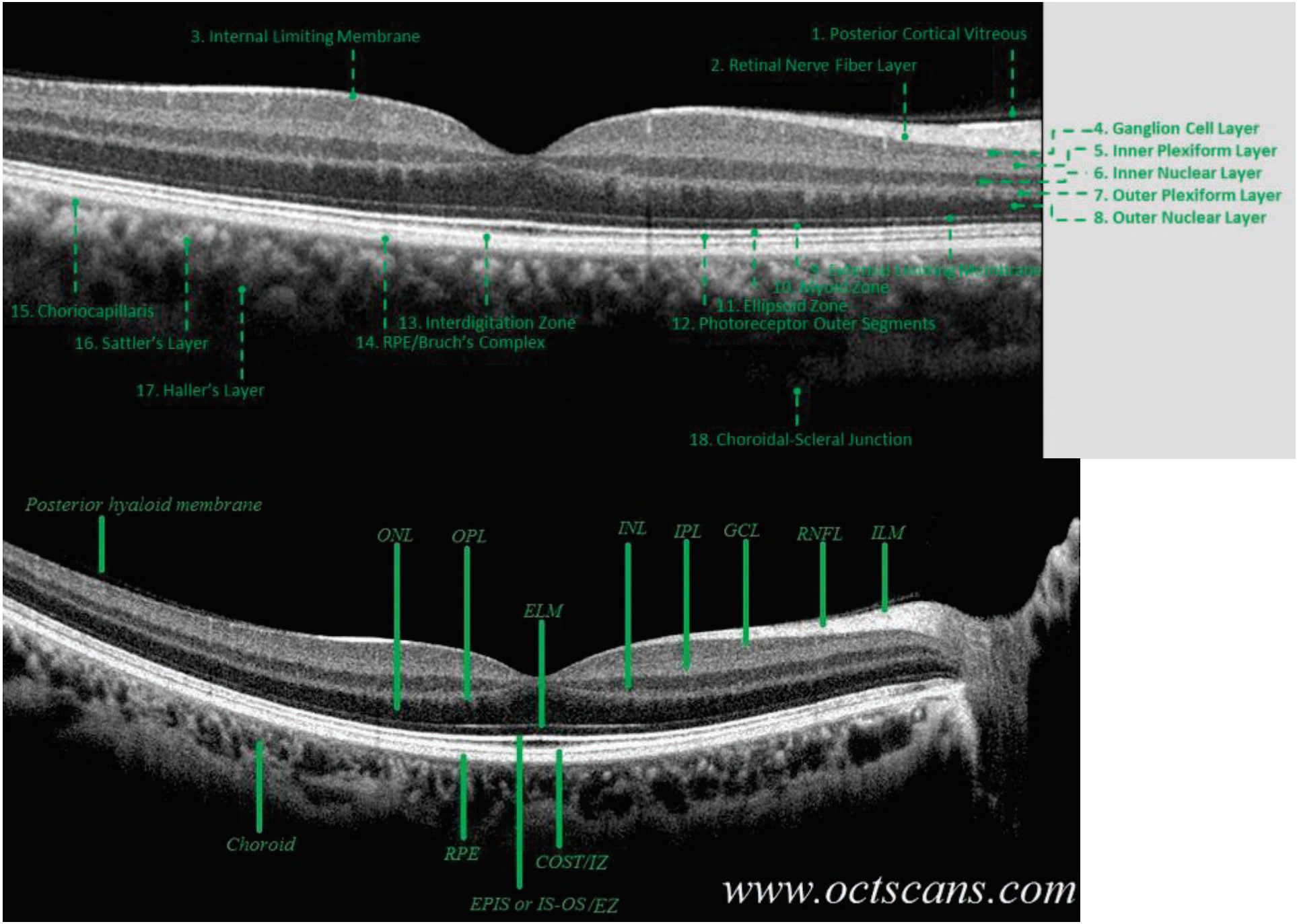
ANATOMY OF THE RETINA



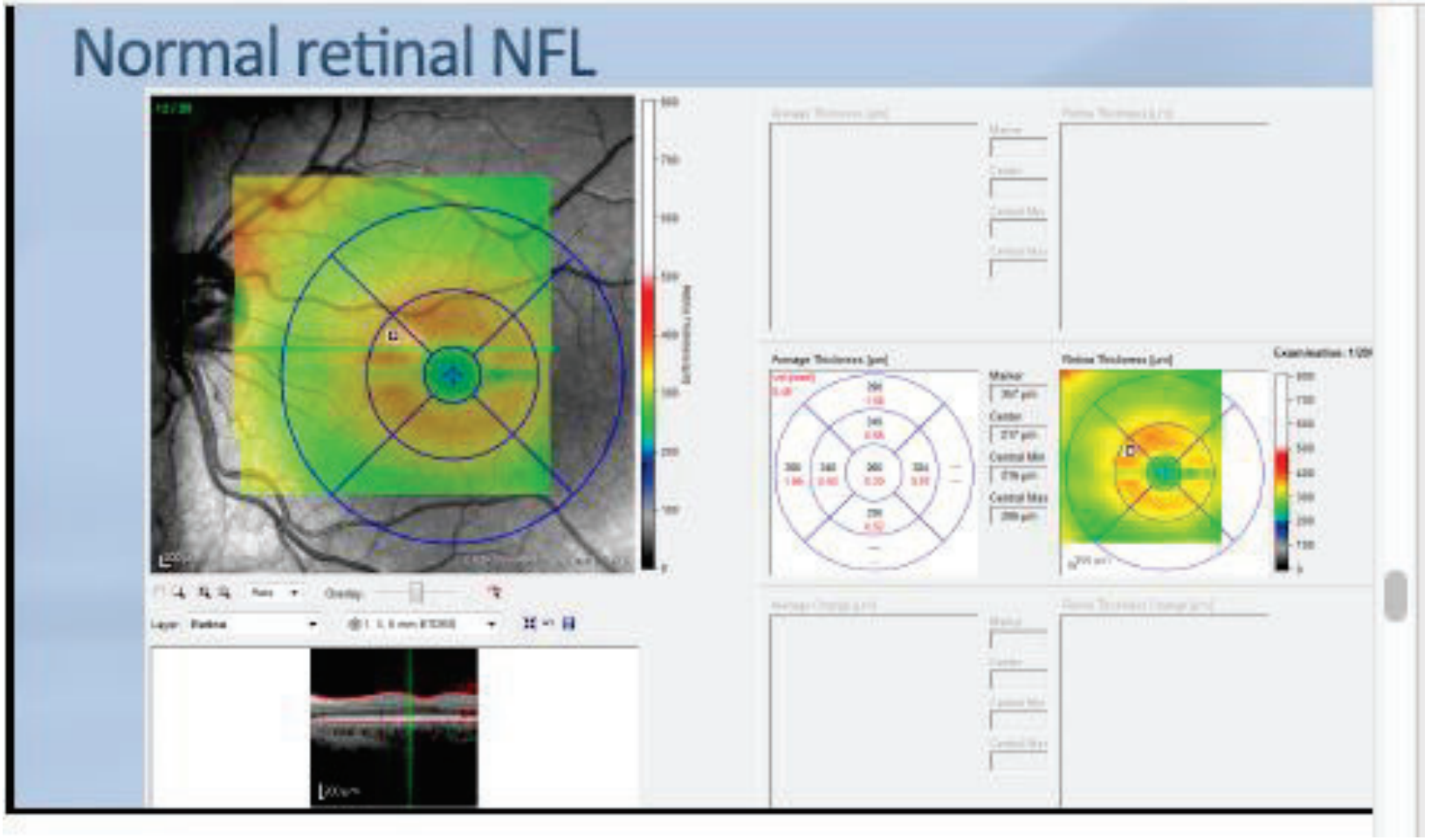
Normal Retina

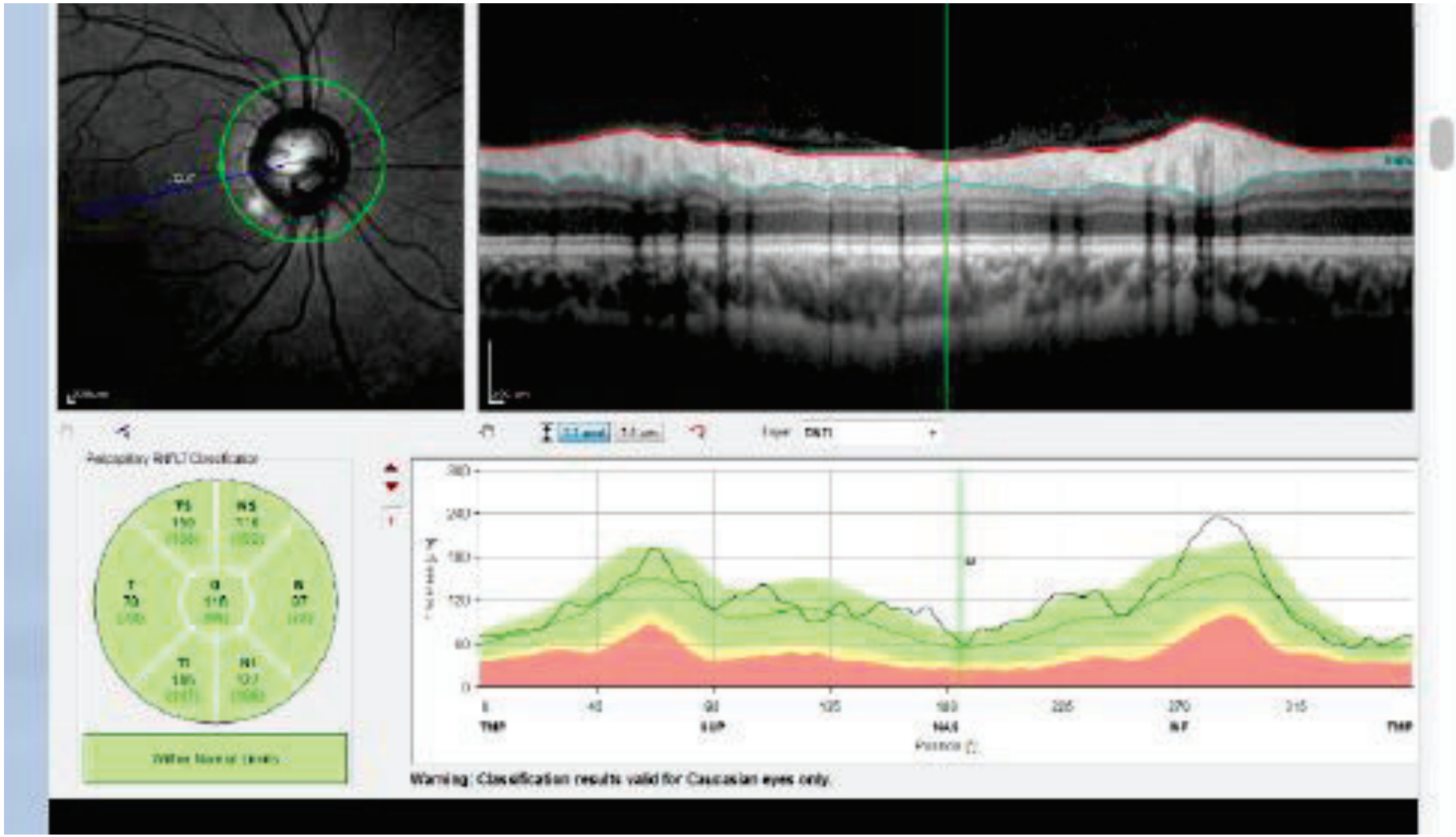
Vitreous
Inner retina
  Internal limiting membrane
  Nerve fiber
  Ganglion cell
Central retina
  inner plexiform
  inner nuclear
  outer plexiform
  outer nuclear
Outer Retina
  external limiting membrane
  rods and cones
  retinal pigment epithelial
  Bruch's membrane
Choroid
  choriocapillaris/choroid



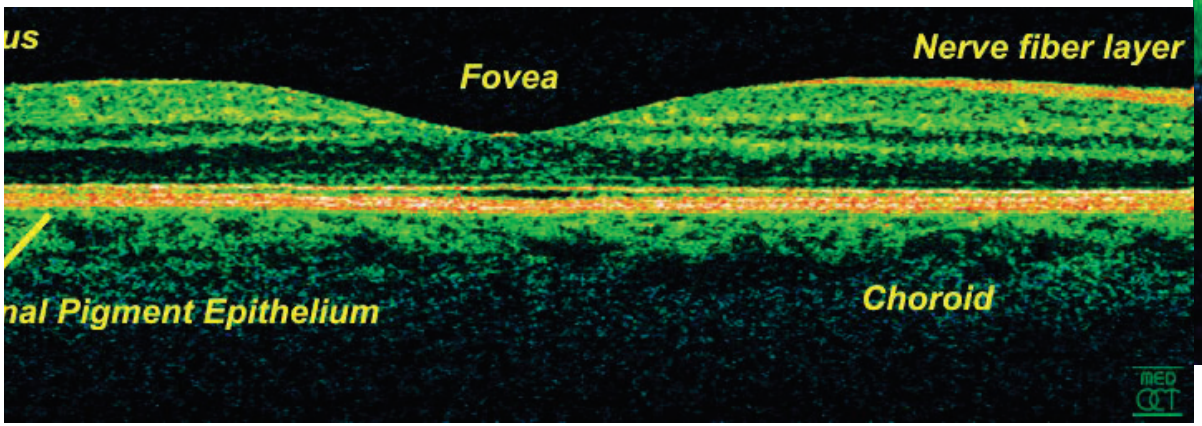

3. Internal Limiting Membrane
1. Posterior Cortical Vitreous
2. Retinal Nerve Fiber Layer
4. Ganglion Cell Layer
5. Inner Plexiform Layer
6. Inner Nuclear Layer
7. Outer Plexiform Layer
8. Outer Nuclear Layer
15. Choriocapillaris
16. Sattler's Layer
17. Haller's Layer
13. Interdigitation Zone
14. RPE/Bruch's Complex
11. Ellipsoid Zone
12. Photoreceptor Outer Segments
18. Choroidal-Scleral Junction
Posterior hyaloid membrane
ONL
OPL
ELM
INL
IPL
GCL
RNFL
ILM
Choroid
RPE
COST/IZ
EPIS or IS-OS/EZ
www.octscans.com

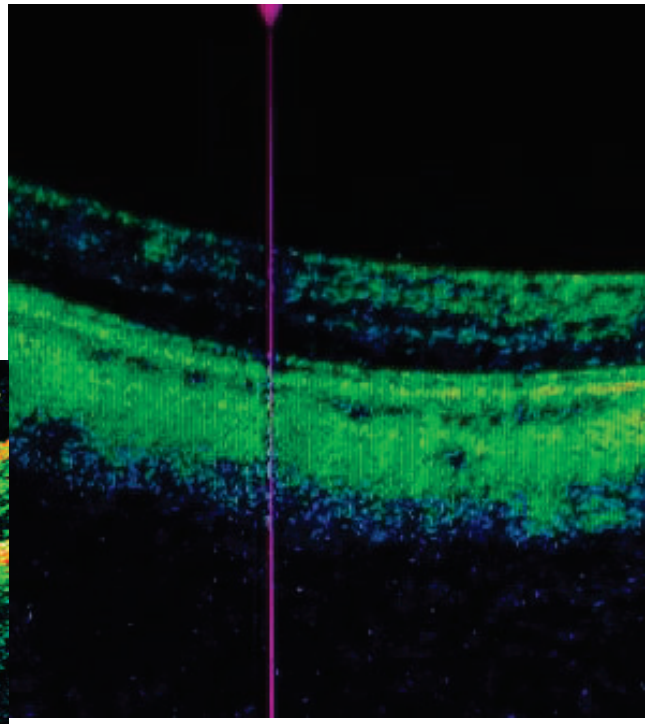
Normal retinal NFL



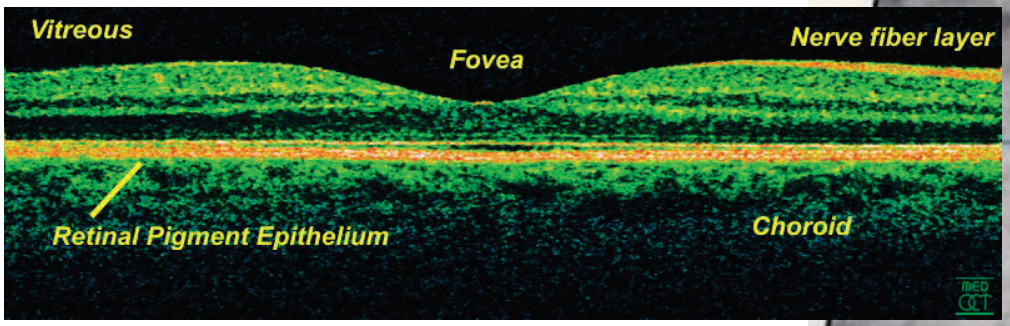

Peripapillary RNFL Classification
Warning: Classification results valid for Caucasian eyes only.

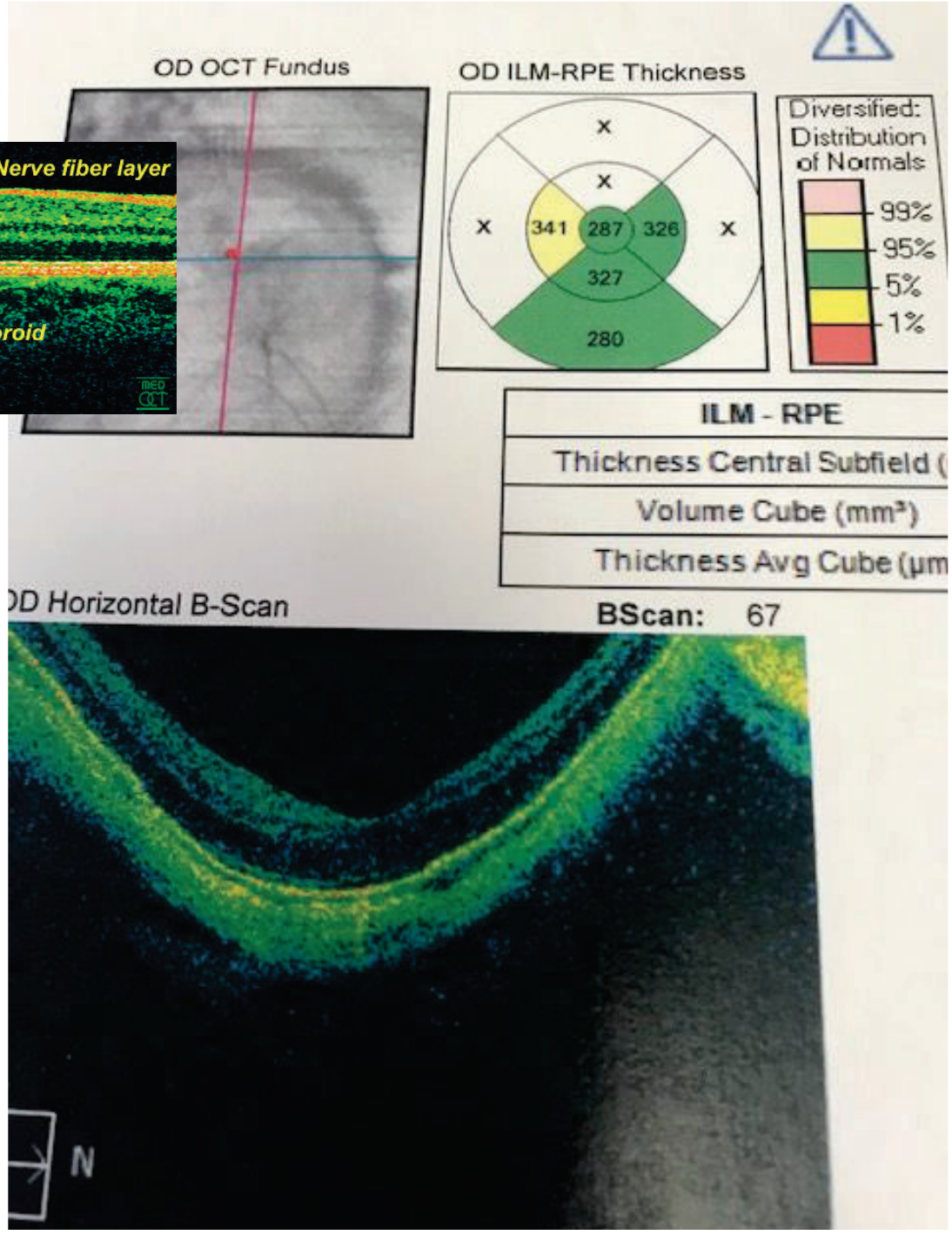
Retinopathy of Prematurity





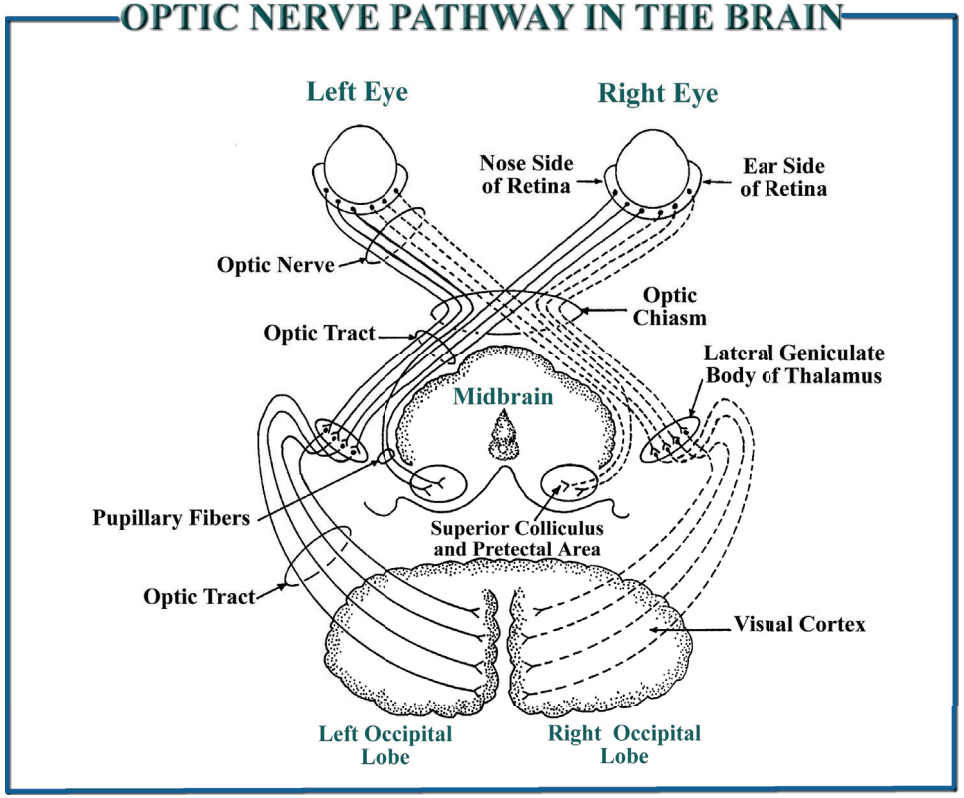
Macula OCT age 12 you


Vitreous
Fovea
Nerve fiber layer
Retinal Pigment Epithelium
Choroid


OD OCT Fundus
OD ILM-RPE Thickness
Diversified:
Distribution
of Normals
99%
95%
5%
1%
341
287
326
327
280
ILM - RPE
Thickness Central Subfield
Volume Cube (mm³)
Thickness Avg Cube (µm
OD Horizontal B-Scan
BScan: 67
N

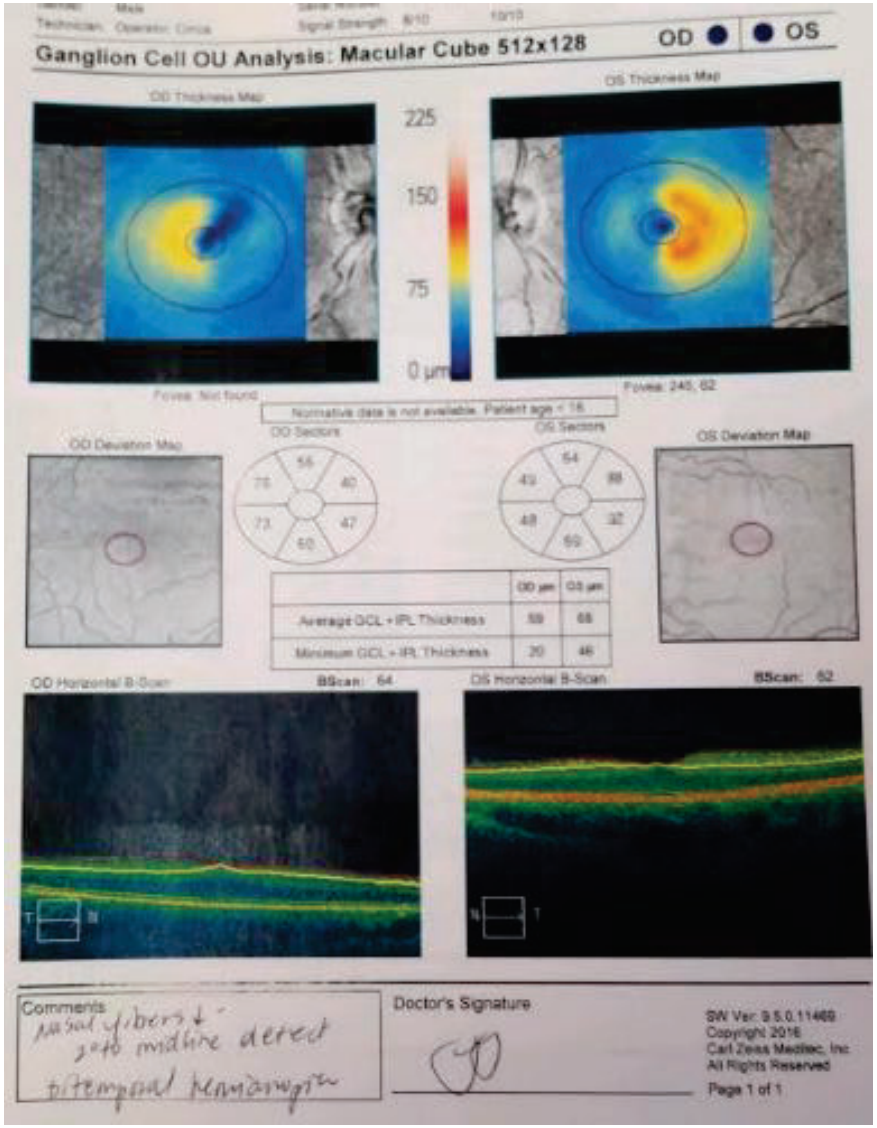
Retinotopic Organization

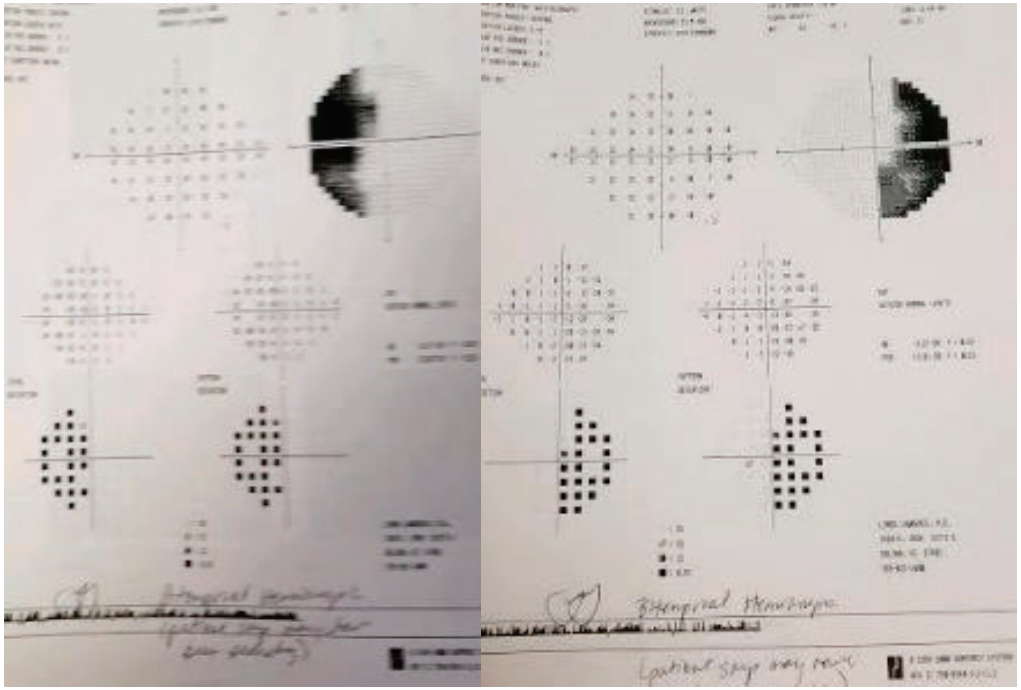
- Anatomy and Function go together
- Retinotopic organization maintained to occipital cortex



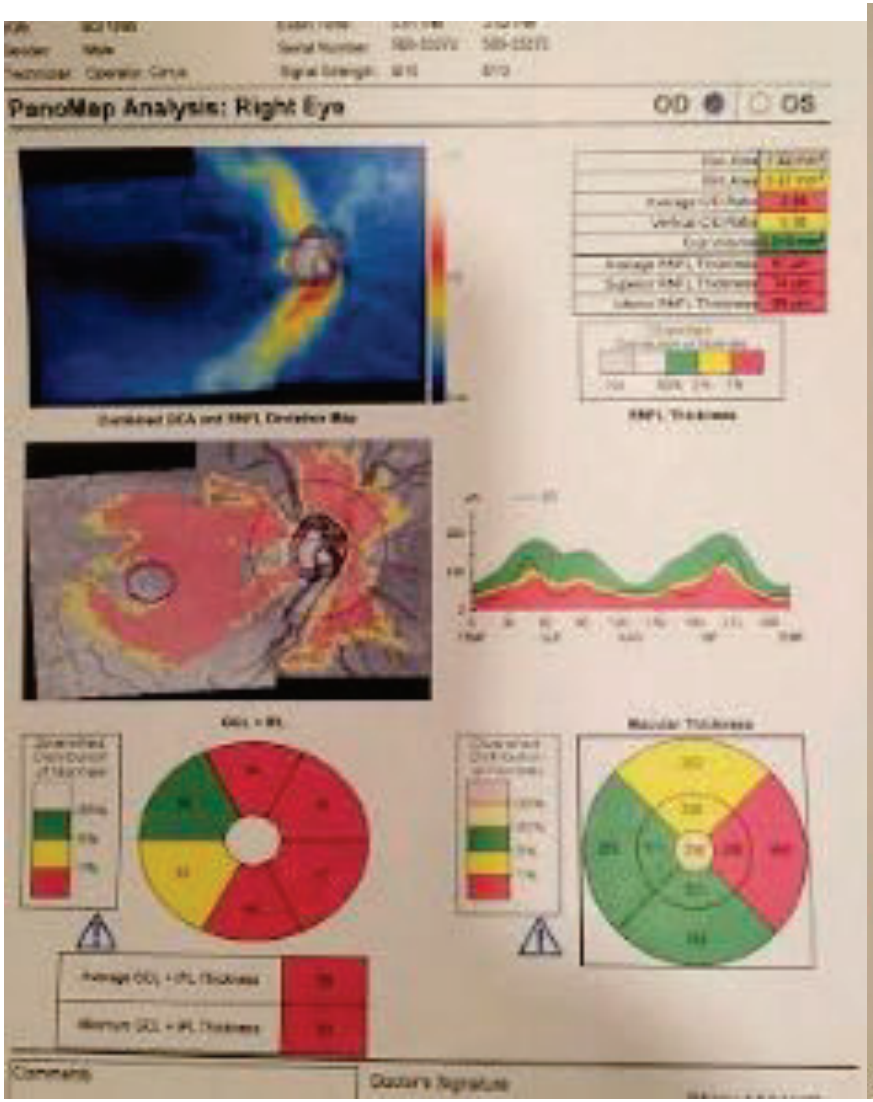
Clinical applications in small office in Kansas

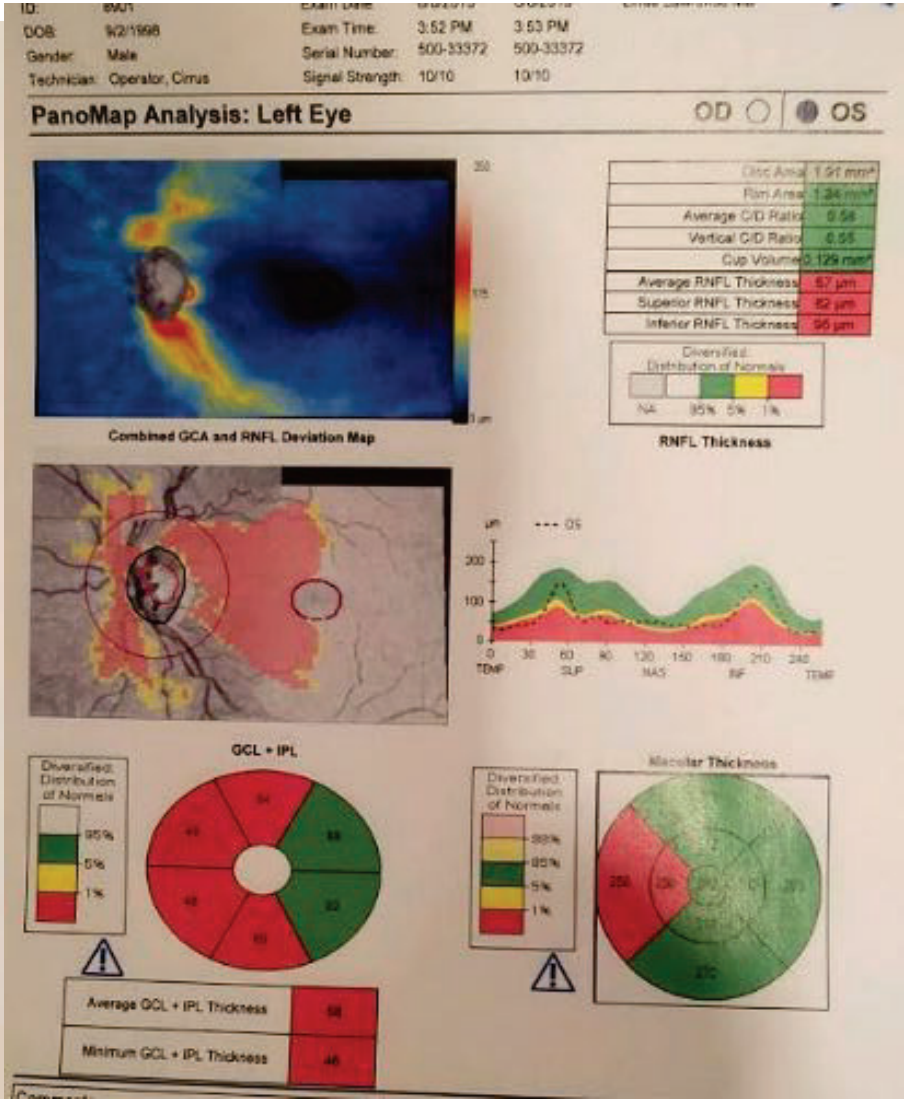
- 18yo boy
- Craniopharyngioma age 4yo
- Did fine until 4th grade difficulty reading





Nerve fiber layer los correlates with visual field defect


PanoMap Analysis: Right Eye
OD
OS
Comments
Doctor's Signature


DOB: 9/2/1998
Exam Time: 3:52 PM 3:53 PM
Gender: Male
Serial Number: 500-33372 500-33372
Technician: Operator, Cirrus
Signal Strength: 10/10 10/10
PanoMap Analysis: Left Eye
OD
OS
Average C/D Ratio 0.58
Vertical C/D Ratio 0.55
Cup Volume 0.129 mm³
Average RNFL Thickness 87 µm
Superior RNFL Thickness 82 µm
Inferior RNFL Thickness 96 µm
Combined GCA and RNFL Deviation Map
RNFL Thickness
GCL + IPL
Macular Thickness
Average GCL + IPL Thickness 58
Minimum GCL + IPL Thickness 46

Genetic conditions

Ways to think through Inherited eye disease

1. Congenital (present at birth)
2. Very early onset
3. Early onset and stable
4. Later onset and progressive

What is the pattern of expression of a genetic disorder?

- Does it mainly affect the eye?
- Progressive or non-progressive?
- Early onset or late onset?

- Multisystem expression that happens to include the eye?
  - Ocular with hearing impairment
  - Ocular with other associated disorders
  - Cerebral visual impairment associated with genetic disorders

Leber Congenital Amaurosis (LCA)

- Group of heterogenous disorders characterized by early onset rod-cone dystrophy and severe visual loss.
- Most without associated findings
- Sporadic and inherited
- Appears normal at birth
- Total blindness develops
- Severe visual impairment, LP to NLP

LCA

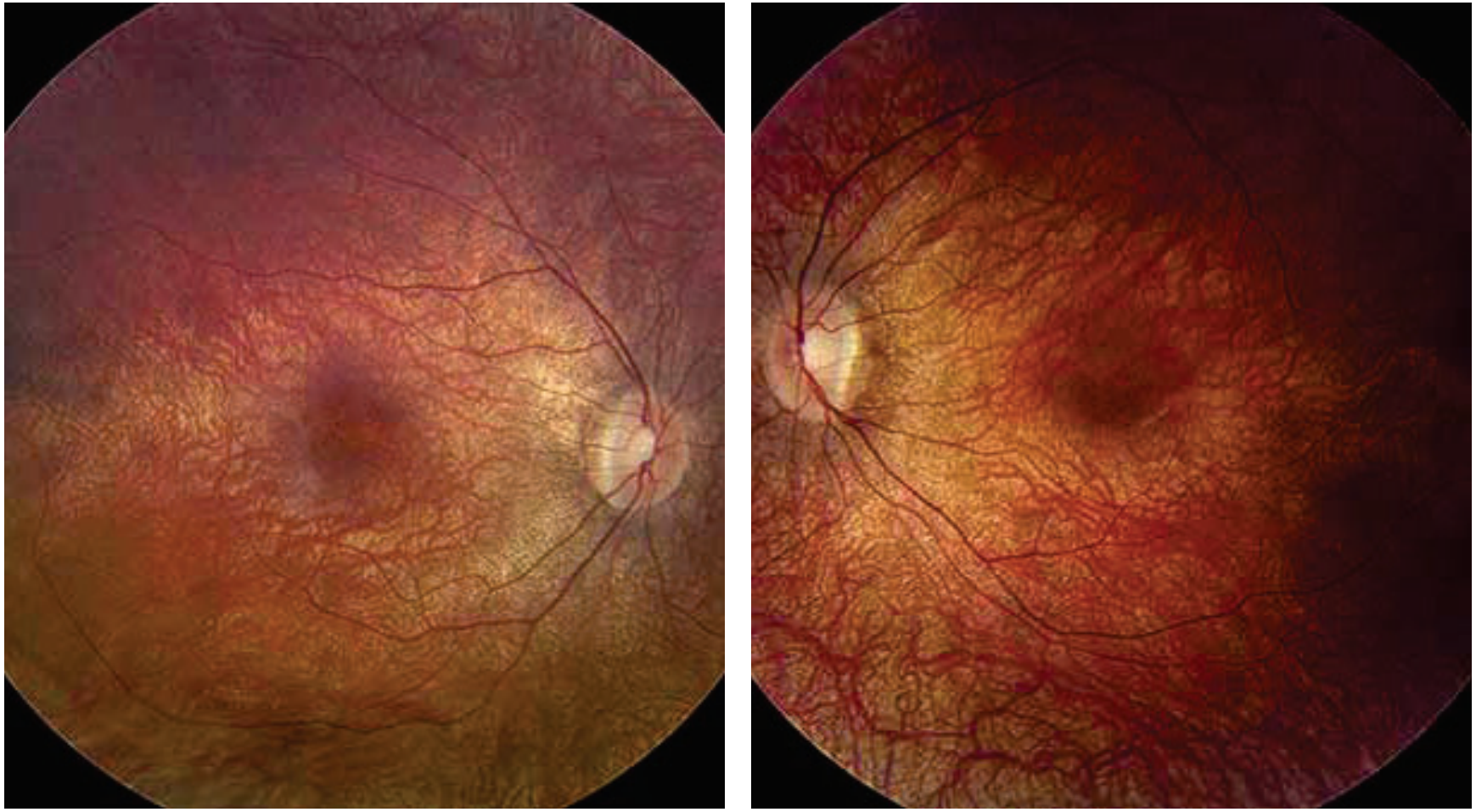
- Early age
- Severe
- Nystagmus, sluggish pupils, poor acuity, photophobia, high hyperopia
- Described by Theodor Karl Gustav von Leber in 1869
- AR, 17 phenotypes with 22 genotypes identified (about 50% identified)
- RPE65 4th most frequent (8%)

LCA

- Inability of eye to undergo phototransduction due to disruption of visual cycle between RPE and neurosensory retina to metabolize dietary vit A into 11-*cis retinal* to generate photopigment
- 2-3/100,000
- Most common inherited blindness in children
- 5% of all retinal dystrophies

Myopic-looking fundus with slight attenuation of the vasculature in this young child with RPE65 mutations. Pigmentary changes develop with age in this type of LCA

RP65-associated Leber Congenital Amaurosis



Fundus photos with punctuate yellow dots and pigment mottling of the retina pigment epithelium.

Clinical Findings and diagnostic testing

- OCT: relatively preserved central macula surrounded by retina thinning/atrophy
- FAF: reduced/absent autofluorescence signal, likely due to decreased levels of lipofuscin in the RPE layer.22

LCA Hallmarks

Early:

- Severe, early vision loss
- Sluggish pupils
- Severely abnormal ERG
- Retina may look normal!
- Mild nystagmus
- Fundus exam is characteristic for a blond translucent appearance and whitish drusen-like deposits in about 90% of cases. Later in life, patients develop chorioretinal atrophy peripheral patches in 64% of cases

Late: oculo-digital sign,, chorio-retinal degeneration, keratoconus

Pathology

Retinoid isomerohydrolase enzyme
(Retinoid visual cycle)

This enzyme normally isomerizes and hydrolyzes all-trans retinyl ester to 11-cis retinol each time a photon hits 11-cis retinal.

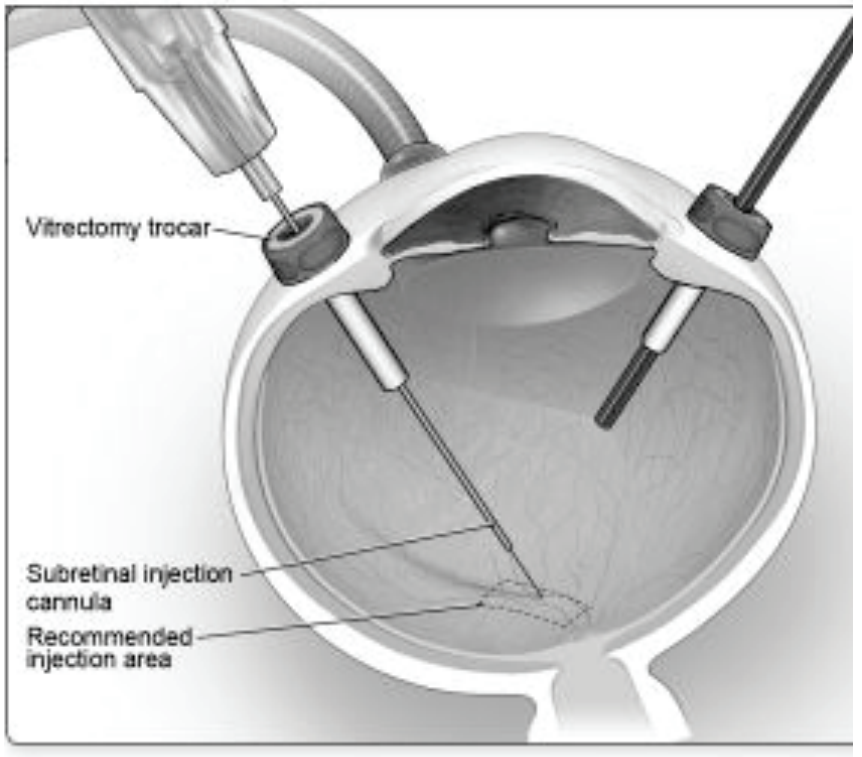
Relatively good vision early in life (due to good residual cone function and alternative supply of 11-cis-retinal18) with a possible mild improvement in visual function temporarily.

Specifically, patients have significant nyctalopia (poor rod function)

Leber Congenital Amaurosis RPE65

- Luxturna®
- Adeno-associated viral vector
- Carries a normal copy of the human RPE65 gene
- Injected into subretinal space
- General anesthesia
- Only at specific centers

Figure 5a. Subretinal injection cannula introduced via pars plana



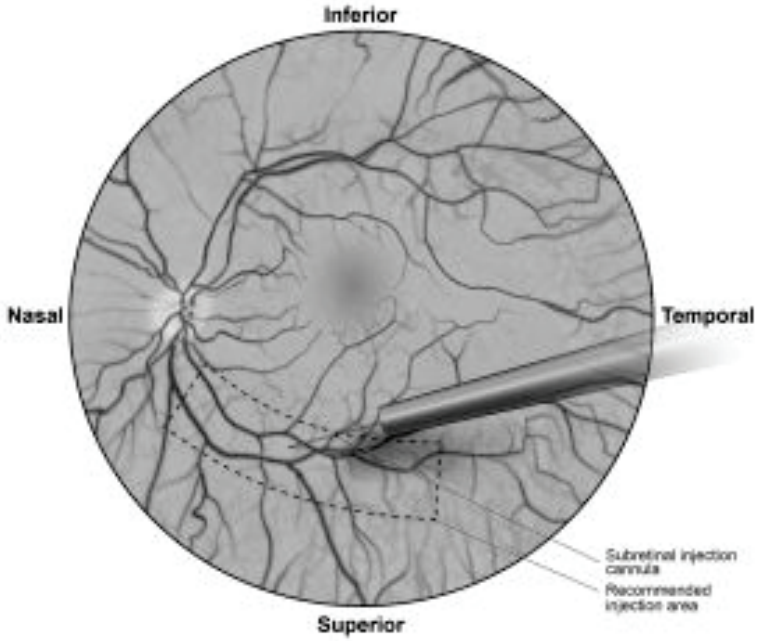
Leber Congenital Amaurosis

- Requires genetic testing to ensure have the appropriate condition for treatment
- ERG, OCT

Who pays?

- Insurance? Compassionate care?
- $450,000 per injection for medication

Figure 5b. Tip of the subretinal injection cannula placed within the recommended site of injection (surgeon's point of view)



Leber Congenital Amaurosis
RPE65

- Approved Dec. 19, 2017 by FDA
- Approved for children 12 months and older
- 5 medical centers in USA doing the treatment

Current Gene Therapy Trials

Disease	Gene	Status	Intervention	Age Limit	Contact	Comment
Leber Congenital Amaurosis (LCA)	RPE65	FDA Approved	Voretigene (Luxturna)	1 y.o (though only studied in > 3 y.o)	Spark Therapeutics 1-833-772-7577	Phase 3 completed
LCA	CEP290	Recruiting	QR-110	6 y.o.	clinical@proqr.com	Phase 1/2
Stargardt	ABCA4	Recruiting	SAR422459	6 y.o.	Contact-Us@sanfoni.com	Phase 1/2
Stargardt	ABCA4	Recruiting	ALK-001	12 y.o.	Leonide Saad, PhD trials@alkeus.com	Phase 2
Achromatopsia	CNGB3	Recruiting	AAV-CNGB3	6 y.o.	ocularinfo@meiragtx.com	UK: Phase 1/2
Achromatopsia	CNGA3	Recruiting	AGTC-402	6 y.o.	Jill Dolgin, Pharm D advocacy@agtc.com	Phase 1/2
X-Linked Retinoschisis	RS1	Recruiting	rAAV2tYF-CB-hRS1	6 y.o.	Jill Dolgin, Pharm D advocacy@agtc.com	Phase 1/2
Leber Hereditary Optic Neuroopathy (LHON)	G11778A	Recruiting	AAV2-P1ND4v2	15 y.o.	John Guy, MD jguy@med.miami.gov	Phase 1
LHON	ND4	Not yet recruiting	GS010	15 y.o.	Barrett Katz, MD bkatz@gensight-biologics.com	Phase 3

Questions

1. What is the effect of preexisting deprivational amblyopia? Do we need to look at the occipital lobe function with FMRI?

2. Can there be immunity against the vector (adenovirus)

3. How do you measure functional improvement

   light sensitivity, visual field, navigation, visual

   acuity. Each study is developing their own functional measurements, there is no standard

Will the newly FDA approved gene therapy help my child?

- On December 19, 2017, the FDA approved for the first time a gene therapy product for a type of congenital retinal blindness,
- Leber Congenital Amaurosis caused by mutations in both copies of the RPE65 gene.
- Most patients with RPE65-related inherited retinal disease have poor vision from birth, but some patients lose vision at older ages.
- Luxturna®, is an adeno-associated viral vector carrying a normal copy of the human RPE65 gene. It is injected under the retina into the subretinal space following a vitrectomy (surgical removal of the vitreous).
- This procedure is performed under general anesthesia.
- This treatment will be available at several sites across the country. Because this is a brand new therapy, insurance coverage issues currently are not known.

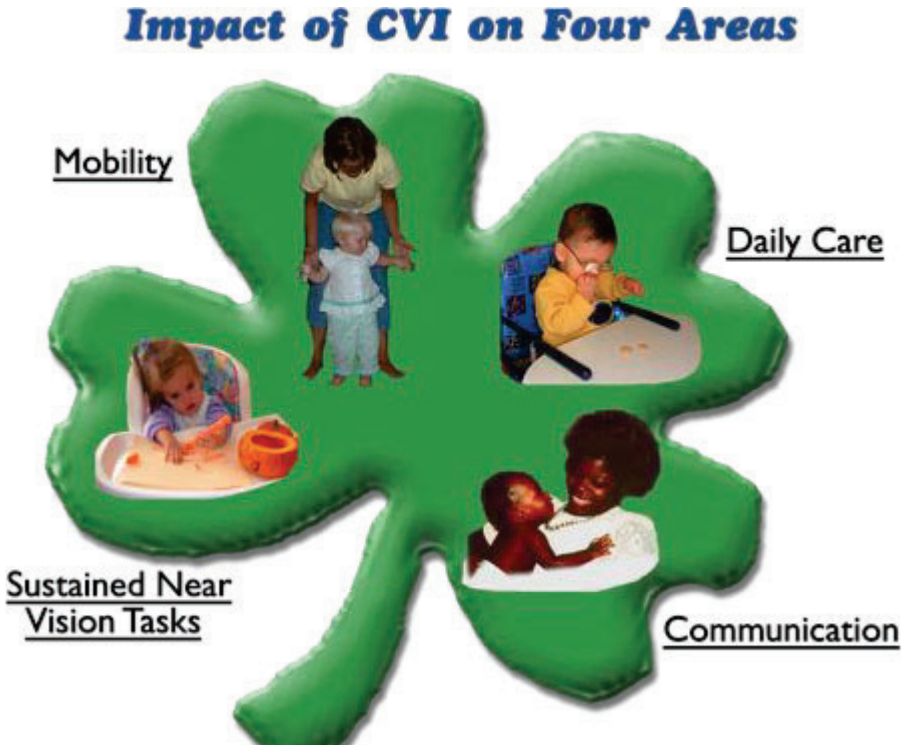
Retinopathy of Prematurity and Cerebral/Cortical Visual Impairment

Extremely premature infants and ANTIVEGF

Visual Function – describes how the **EYE** functions: VA, contrast sensitivity, VF, color vision

- **Functional Vision** – describes how the **PERSON** functions in vision-related activities (in baby)
- ETROP 14.3% with favorable structural retinal outcome but unfavorable functional vision outcome

Good, WV.Final results of the ETROP randomized trial. Trans Amer Ophth Soc. 2004: 102:233-48



Impact of Visual Impairment Starts at Birth

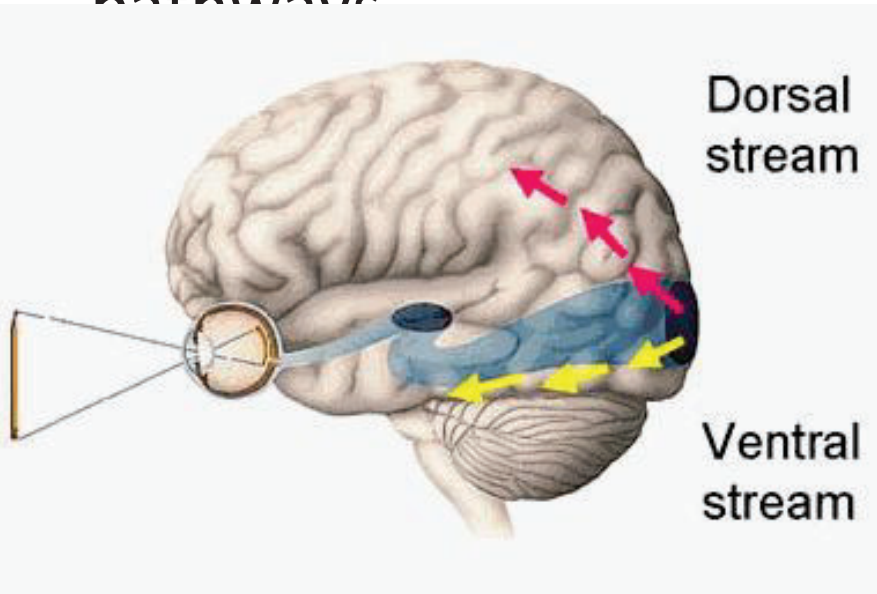
- Mutual eye gaze between the infant and families facilitates attachment.

- When vision is impaired, attachment and communication between parent and infant is challenged.

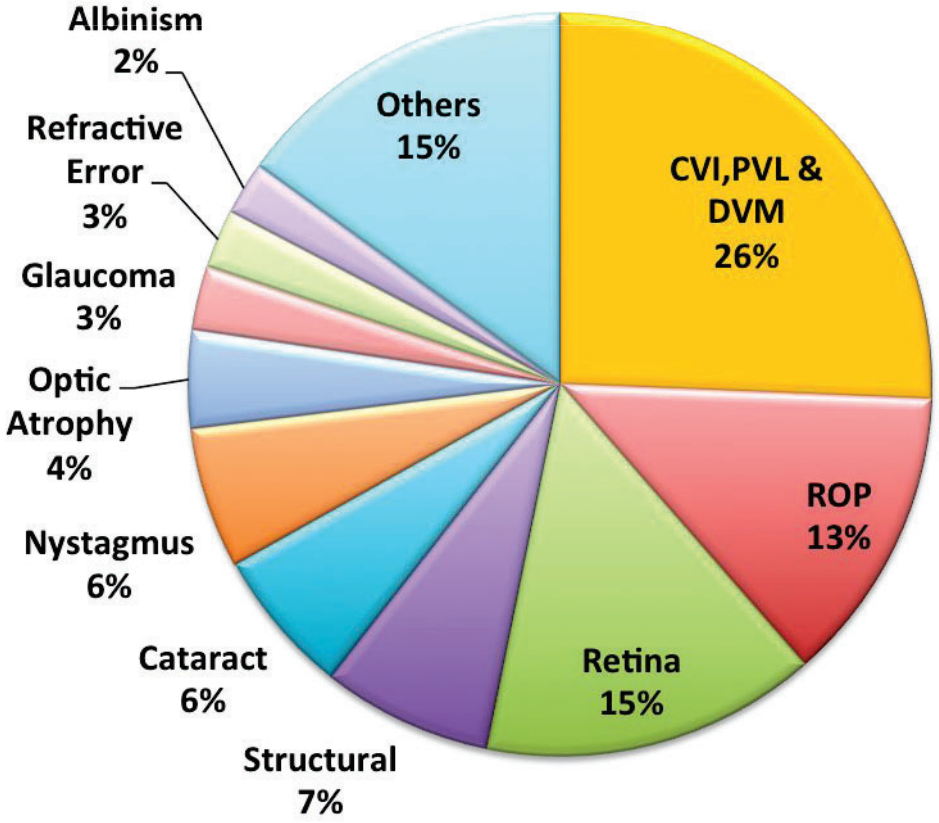
Each child will be unique

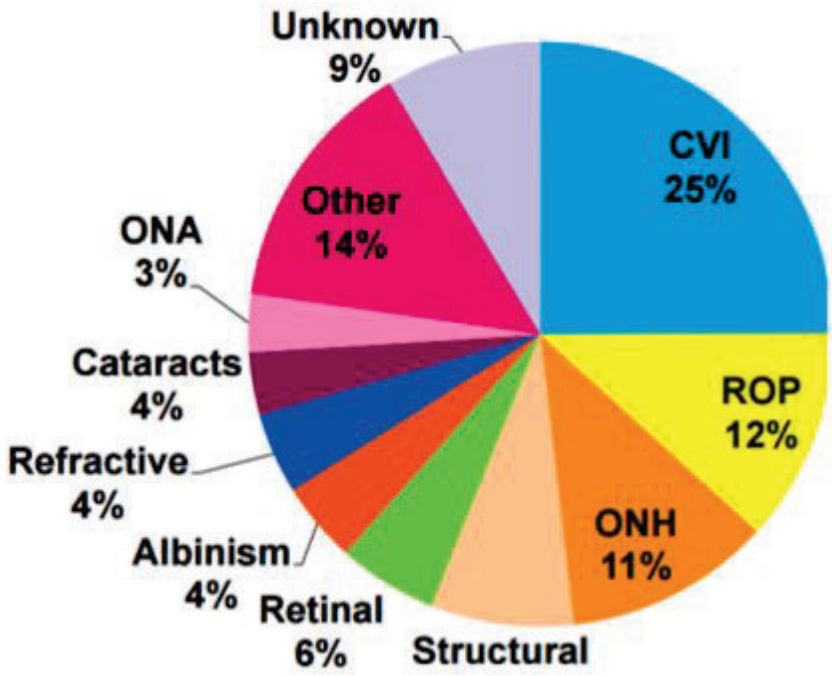
What is CVI?

- Cerebral or Cortical or Neurological?
- Ocular impairment does not explain VI.
- Dysfunction, anomaly, or injury to retro-geniculate pathways



CVI





Most common cause of visual impairment in developed countries, but also increasing in developing countries as there is improved intensive care for neonates

Babies Count
The National Registry for Children With Visual Impairments, Birth to 3 years

AMERICAN PRINTING HOUSE FOR THE BLIND, INC.

Deborah Hatton, Ph.D., & Sarah Ivy, M.Ed.
Vanderbilt University

Burt Boyer, M.A.
American Printing House for the Blind

September 2012
National Data

Additional Risks of the infant born premature for brain damage

- Perinatal asphyxia
- Intracranial hemorrhage (IVH)
- Intrauterine exposure to toxins, drugs
- Intrauterine infection (TORCH), Zika
- **Prematurity (especially <2000 g)**
- **Very low birth weight (<1500 g)**
- Kernicterus
- **Hypoglycemia**
- Syndromes/genetic disorders
- Seizure disorder

ROP: A CNS neurovascular disease?

- Retina is part of the Central nervous system
- ROP is associated with other cerebral lesions
- Neurodevelopmental disorders in 50-70% of very preterm infants

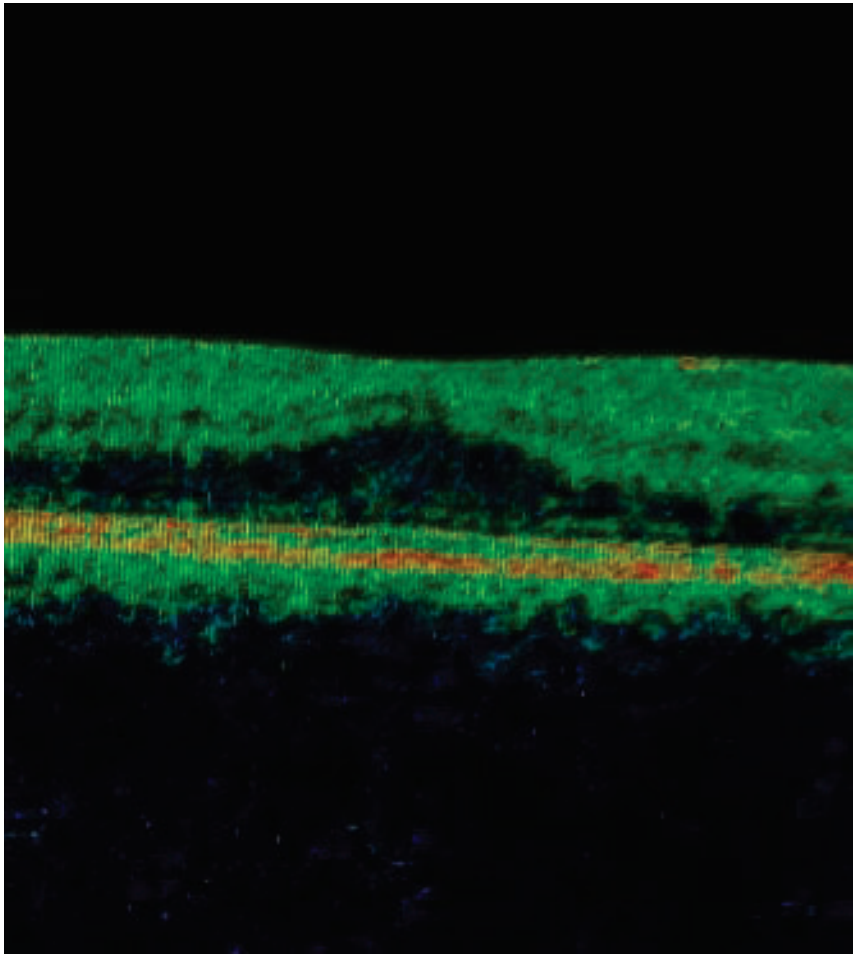
IGF-1 in retinopathy of prematurity, a CNS neurovascular disease, Liefl et al, *Early Hum Dev*. 2016 November; 102: 13-19

- Is ROP a risk factor, or can it be associated or a predictor of NVI?

OCT

- Pathological persistence of inner retinal layers in fovea and increased foveal thickness
- ROP with anatomical and visual classification does not correlate with VA outcomes later

IGF-1 in retinopathy of prematurity, a CNS neurovascular disease, Liefl et al, *Early Hum Dev*. 2016 November; 102: 13-19



Macula OCT of 10 yo with ROP treated and CVI

Is the visual impairment ocular, brain based, or combined?

And how do we measure it?

Early Human Development (2008) 84, 277–280

available at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/earlhumdev

Application of a neonatal assessment of visual function in a population of low risk full-term newborn

Daniela Ricci [a,b,*,1], Domenico M.M. Romeo [c,1], Francesca Serrao [d], Laura Cesarini [a], Francesca Gallini [d], Francesco Cota [d], Daniela Leone [a], Antonio A. Zuppa [d], Costantino Romagnoli [d], Frances Cowan [b], Eugenio Mercuri [a,b]

- 124 low risk term babies
- 38-41 weeks gestational age
- 48 ± 8 hours
- 50 infants examined also at 72 ± 8 hours
- 110 (89%) babies completed the assessment

How early is early?
Daniela Ricci MD.

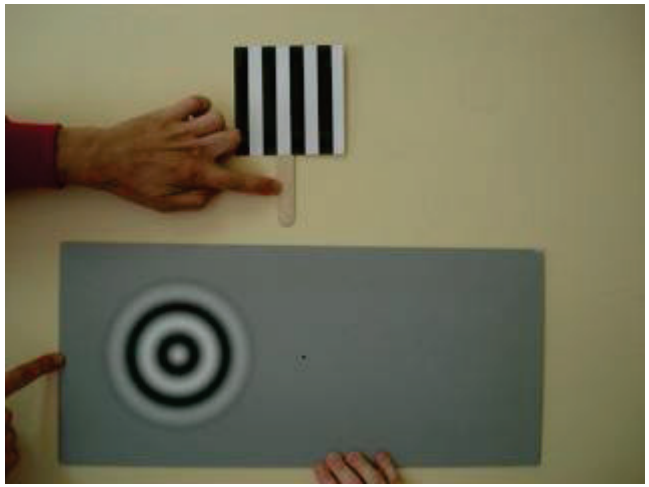
- Fixing and tracking

Already present in preterm babies

at 30-32 weeks of gestational age

Maturation:

- 30-32 : fix and track for a brief arc
- 35-36: track for a horizontal and a vertical arc
- 38: track in a circle



Early Hum Dev. 2010 Jan;86(1):29-33. Epub 2010 Jan 6, Ricci, D et al
Early assessment of visual function in preterm infants: how early is early?

Neonatal assessment of visual function: ideally

MARIANI FOUNDATION PROJECT

- Structured protocol
- Assessing several aspects of visual function
- Short
- Easy even for people not used to visual function
- Requiring small equipment
- Easy to use in difficult settings (NICU-incubator) – easy to clean
- Reliable

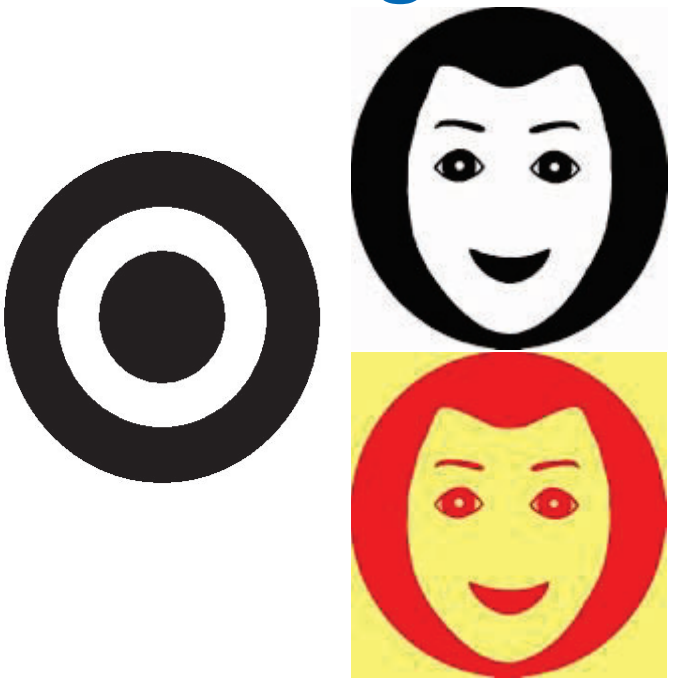
MARIANI FOUNDATION PROJECT

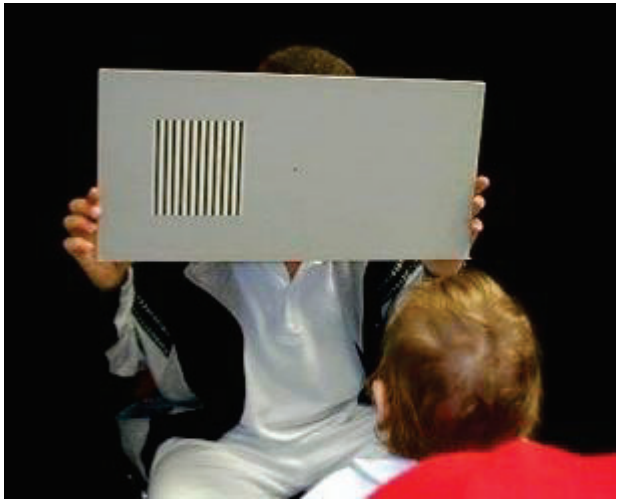
Development of an Italian network for early visual function: diagnosis, follow up and research

Aim of this project is to create an Italian pediatric visual function network in order to:

- agree on a library of protocols to be used according to the different etiology or involvement of visual function, for diagnosis, follow up and plans of intervention in infants with isolated CVI or with concomitant ocular involvement
- provide training for large maternity centers with excellent standards of neonatal care but less experienced in visual assessment
- establish common elements for the creation of a dataset that will facilitate data collection and sharing
- identify normal and abnormal development of visual function in relation to specific patterns of brain lesions

Neonatal visual assessment: targets





Early Human Development (2008) 84, 107–113

available at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/earlhumdev

Early assessment of visual function in full term newborns

Daniela Ricci [a,b], Laura Cesarini [a], Michela Groppo [c], Agnese De Carli [c], Francesca Gallini [d], Francesca Serrao [d], Monica Fumagalli [c], Frances Cowan [b], Luca A. Ramenghi [c], Shirley Anker [e], Eugenio Mercuri [a,b,*], Fabio Mosca [c]

Table 2 Final proforma with instruction

1	*Spontaneous ocular motility*: note spontaneous ocular movements before presenting a target		Mainly conjugated		Occasional strabismus		Occasional/ lateral nystagmus		Intermittent Strabismus		Nystagmus		Continuous Strabismus		Nystagmus	
					R	L	R	L	R	L	R	L	R	L	R	L
2	*Ocular movements with a target*: note ocular movements while presenting the target		Mainly conjugated		Occasional strabismus		Occasional/ lateral nystagmus		Intermittent Strabismus		Nystagmus		Continuous Strabismus		Nystagmus	
					R	L	R	L	R	L	R	L	R	L	R	L
3	*Fixation*: with the target in front of the infant at 25 cm, note the ability of the infant to fix on the target		Stable (>3 s)		Unstable (<3 s)				Absent							
	Tracking — black/white target															
	Tracking: note the infant's eye movement in response to the target movements															
4	*Horizontal*: with the target at 25 cm and starting in the midline move it slowly to both left and right	↔	Complete		Incomplete				Brief				Absent			
			R	L	R		L		R		L					
5	*Vertical*: with the target at 25 cm, and starting in the midline move it slowly upwards and downwards	↕	Complete		Incomplete				Brief				Absent			
			U	D	U		D		U		D					
6	*Arc*: with the target at 25 cm, move it slowly tracing an arc		Complete		Incomplete				Brief				Absent			
			R	L	R		L		R		L					
	Colour/discrimination/attention															
7	*Tracking coloured stimulus*: note the infant's eye movement in response to the target movements, starting from the midline towards lateral		Present		Absent											
8	*Stripes discrimination*: note the infant's ability to fixate on a series of targets of decreasing stripe widths held at a distance of 38 cm starting with the widest stripe; note the narrowest stripe width on which the infant fixates		Last card identified.....													
9	*Attention at distance*: after eliciting central fixation move the target slowly away and a few cm laterally from the infant and note the maximal distance at which focusing is maintained		Cm.....													

Response to correction of refractive errors and hypoaccommodation in children with congenital Zika syndrome

Liana O. Ventura, MD, PhD,[a,b] Linda Lawrence, MD,[c] Camila V. Ventura, MD,[a,b] Gordon N. Dutton, MD, FRCOphth,[d] Polyana Marinho, MD,[a] Priscila F. Ferro, MD,[a] Adriana L. Gois, MD,[a,b] Natalia C. Dias, MD,[a] Larissa Ventura, MD,[a] Cynthia A. Moore, MD,[e] and Lea Hyvärinen, MD[f]

(J AAPOS 2017;21:480-484)

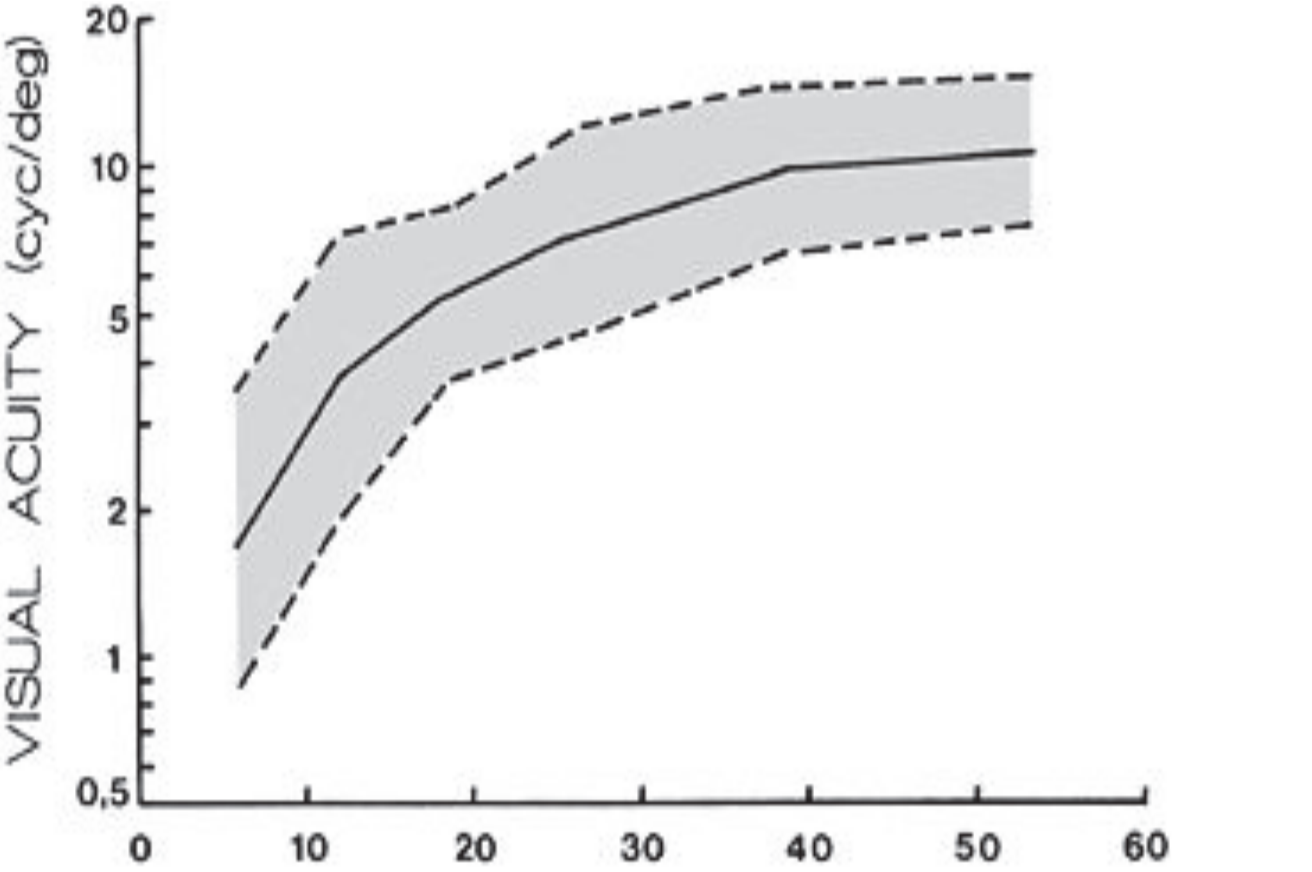
PURPOSE To describe the immediate response to correction of refractive errors and hypoaccommodation in children with congenital Zika syndrome (CZS).

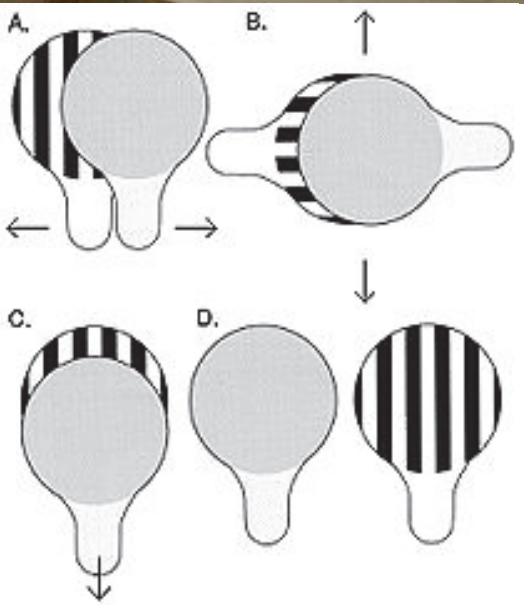
METHODS Children born between May and December 2015 with a confirmed diagnosis of CZS and enrolled in a multidisciplinary early intervention program were included in this study. All children received a comprehensive ophthalmic examination, including dynamic retinoscopy and cycloplegic refraction. Children were prescribed their full correction if they met the criteria for refractive error, and additional plus 3.00 overcorrection for strabismus, accommodative dysfunction, and/or low vision. Monocular and binocular visual responses to Lea Grating Test at 30 cm, with and without eyeglasses, were measured on day 1 of glasses wear.

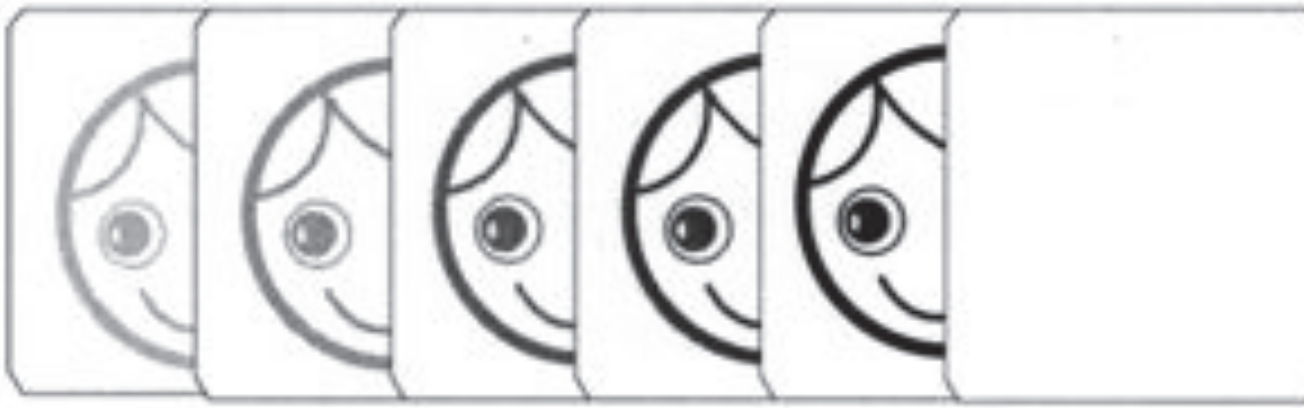
RESULTS A total of 60 children were evaluated (mean age at evaluation, 11.5 ± 1.1 months; range, 9.0-16.0 months). Lea Grating Test responses were abnormal in all children prior to spectacle correction. Hypoaccommodation was present in 17 of 21 children (81%). Overcorrection was prescribed for all children. Visual responses were subnormal even with glasses use; however, immediate improvement in binocular vision was found in 37 children (62%) and in 74 of 119 eyes (62.2%). For the monocular visual improvement, 27 of 115 eyes (23.5%) had structural abnormalities, and 44 of 115 eyes (38.3%) were structurally normal. There was a statistical difference between the cycloplegic refraction of the children in August and in November, including emmetropia ($P = 0.001$), hyperopia ($P = 0.000$), myopia ($P = 0.007$), and astigmatism ($P = 0.004$).

CONCLUSIONS Eyeglasses can improve visual acuity in children with CZS. Significant changes in their refractive status over time requires periodic updates. (J AAPOS 2017;21:480-484)


Hiding Heidi
Low Contrast Test


VISUAL ACUITY (cyc/deg)
20
10
5
2
1
0,5
0
10
20
30
40
50
60


A.
B.
C.
D.



Evaluation: Visual Developmental Milestones

Table 1. Visual development milestone of children with congenital Zika syndrome (n = 119) and healthy controls (n = 85)

Visual milestone	CZS group (n = 119)	Control group (n = 85)	*P* value[a]
8 Weeks: eye contact, n (%)	91/104 (87.5)	79/79 (100.0)	<0.001
3 months			
Social smile	57/106 (53.8)	78/80 (97.5)	<0.001
Regards hands	27/107 (25.2)	79/80 (98.8)	<0.001
5-6 months			
Goal directed reach	29/107 (27.1)	79/80 (98.8)	<0.001
Moves to reach	27/107 (25.2)	78/79 (98.7)	<0.001
Hands to the midline	15/107 (14.0)	78/79 (98.7)	<0.001
7-10 months			
Regard to facial features[b]	26/96 (27.1)	64/68 (94.1)	<0.001
11-12 months[c]			
Reach for a dangling object	1/2 (50.0)	3/3 (100.0)	NA

CZS, congenital Zika syndrome; *NA*, not applicable.
[a]Pearson's χ^2 test.
[b]Does not apply to age for 6 patients in study group and 9 patients in control group.
[c]Does not apply to age for 116 patients in study group and 73 in control group.

- From Deborah Chen PhD kanlovkids.org and

Dr. Lea personal correspondence, AAO.org

J AAPOS. 2017 Aug;21(4):295-299.e2. doi: 10.1016/j.jaapos.2017, Visual impairment in children with congenital Zika syndrome.,Ventura LO et al

Case Studies

BW 540, 23 wk. GA
post bevacizumab, age 1year old

Delayed visual maturation, expected because of extreme prematurity

High risk for CVI

Close developmental follow-up

Treatment Options: Primary Prevention

- Decrease preterm birth
- Modify or treat risk factors

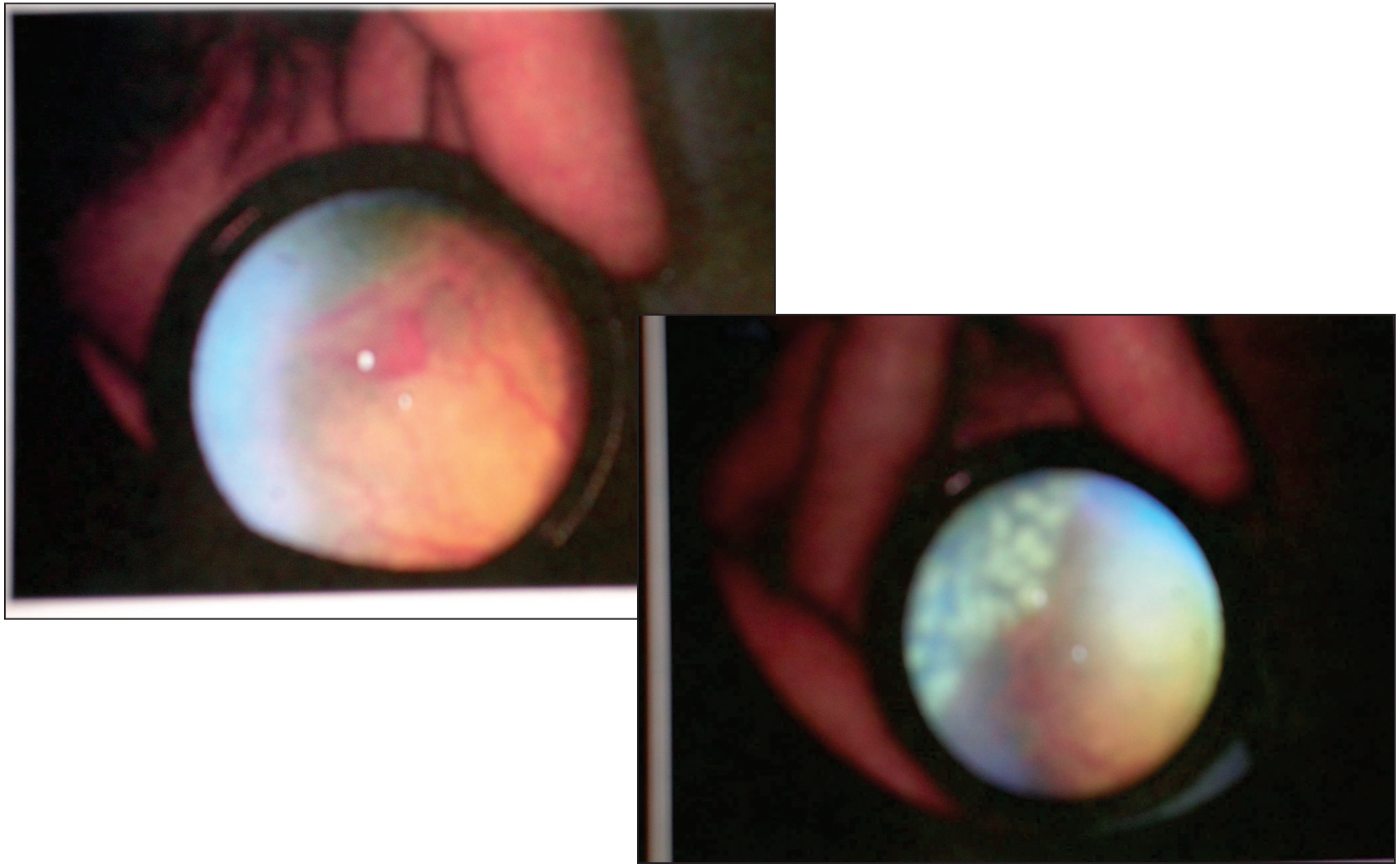
Current Treatment Options

- Retinal ablation
  - Laser photocoagulation of retina
  - Cryotherapy
- Intravitreal Anti-VEGF injections
  - Avastin
  - Lucentis

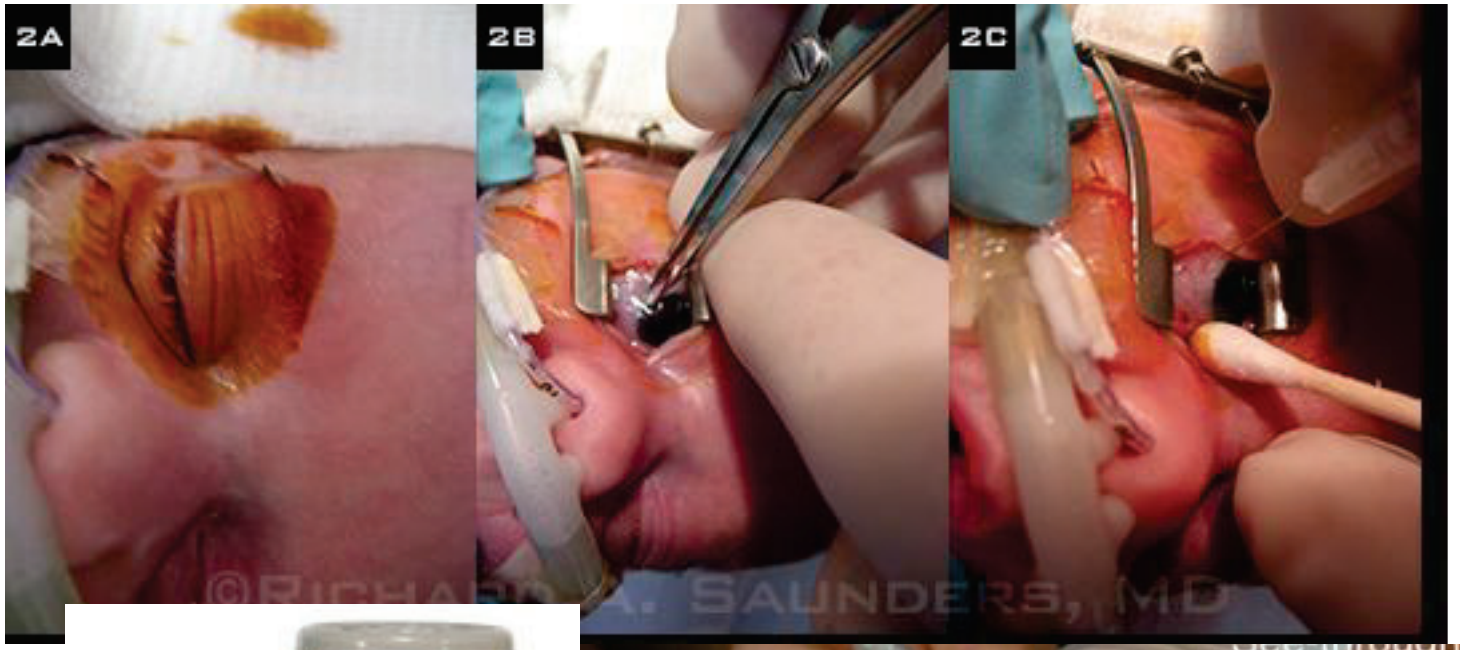
When a baby needs treatment for ROP

- Consider treating in OR or neonatal ICU
- Arrange Pediatric anesthesiologist/neonatologist for sedation
- Presence of treating physician (pediatric ophthalmologist or retina specialist)
- Informed Consent from parents
- Treatments: diode laser machine or intravitreal injection Avastin/Lucentis

Treatment: ROP laser photocoagulation




LVPE


2A
2B
2C


100 mg
25 mg/mL
AVASTIN
(bevacizumab)
For Intravenous Use
400 mg
25 mg/mL
AVASTIN
(bevacizumab)
For Intravenous Use

Treatment: Intravitreal anti-VEGF injection

- Anti-VEGF medicines have not been approved by the FDA to treat children, so its use is called off-label
- Current recommendations (2013):
  - Consideration may be given to treatment of infants with zone I, stage 3+ ROP with intravitreal injection of Avastin (bevacizumab)
  - Detailed informed consent as there remains unanswered questions involving dosage, timing, safety, visual outcomes and other long-term effects
  - Monitor weekly until the retina is fully vascularized

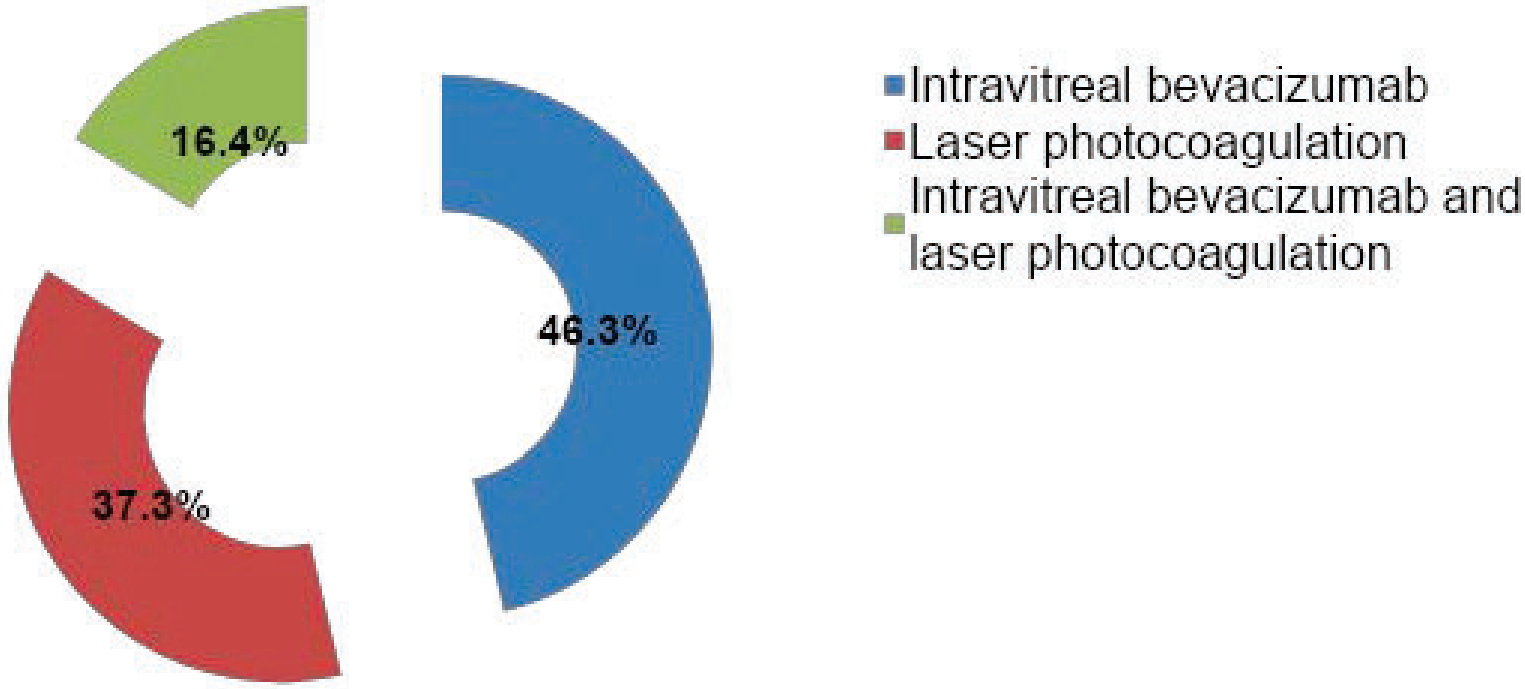
http://pediatrics.aappublications.org/content/131/1/189.full.html

Clinical Trials: Intravitreal anti-VEGF Injection

- Beat ROP Study: Established the role of anti-VEGF (Avastin) in the treatment of ROP
- Pediatric Eye Disease Investigators Group (PEDIG) has an undergoing clinical trials with Avastin to study the least dose required in treating ROP
- Novartis pharmaceutical has an undergoing clinical trial with Lucentis in treating ROP

Helen A. Mintz-Hittner, et al. Efficacy of Intravitreal Bevacizumab for Stage 3+ Retinopathy of Prematurity. BEAT-ROP Cooperative Group* The New England Journal of Medicine 2011

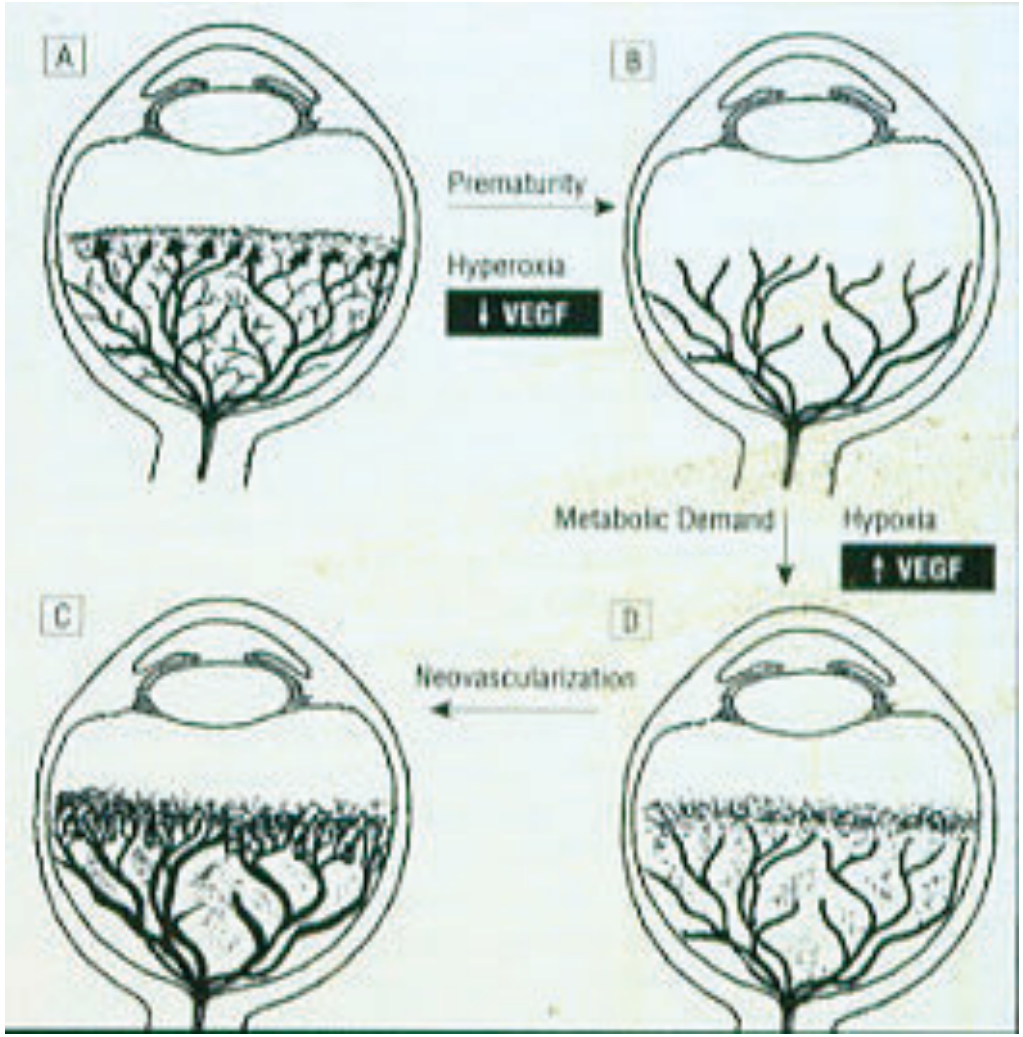
Web-Survey: For infants with type 1 ROP, nearly 50% physicians prefers Avastin as primary monotherapy



Courtesy: Swati Agarwal-Sinha, MD

Anti-VEGF treatment for ROP

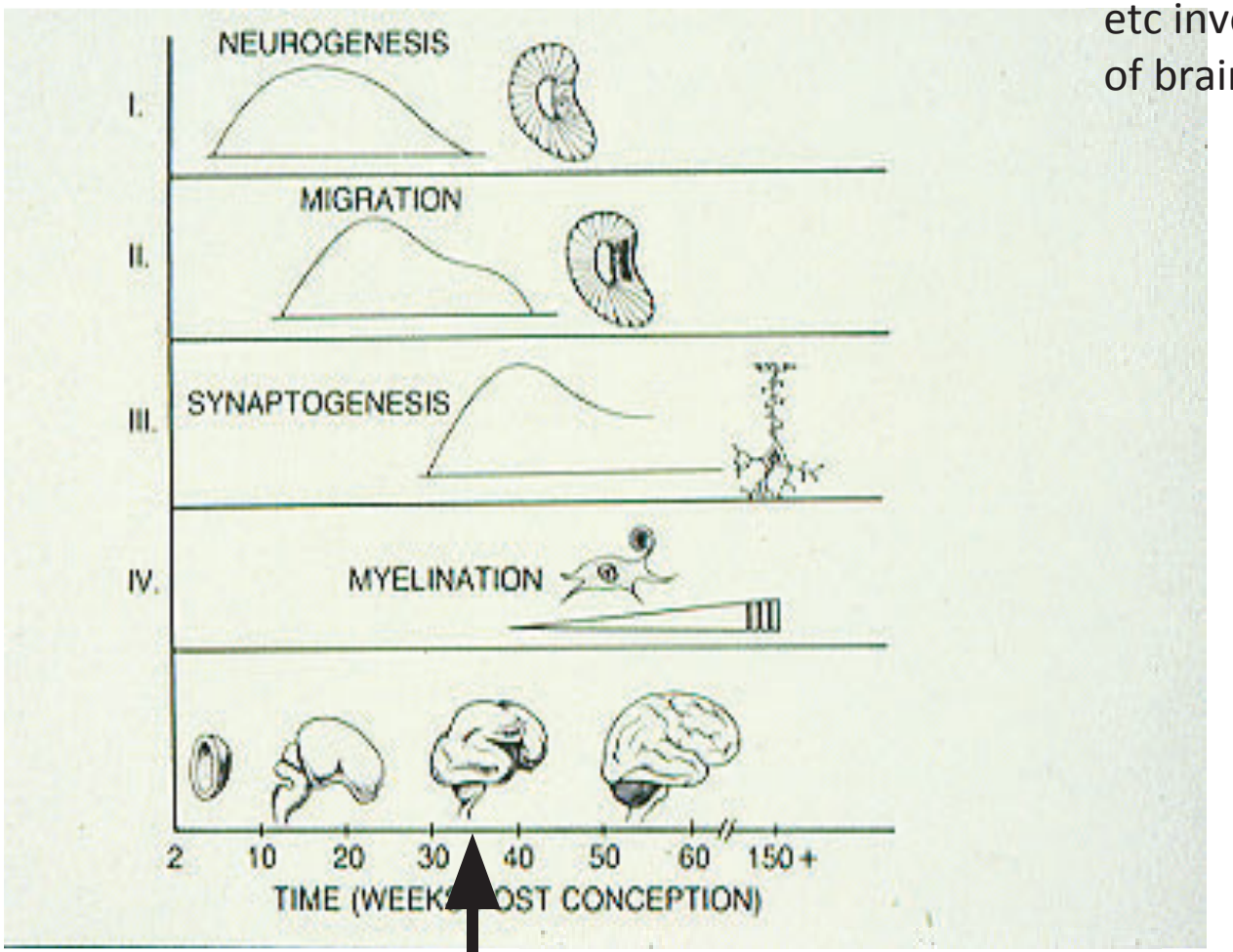
- There are a number of angiogenic factors reported to be involved in mouse oxygen induced retinopathy (OIR) models
- Vascular endothelial growth factor (VEGF) is one of the factors involved in the pathogenesis of ROP



Courtesy G Gole

Angiogenesis

Angiogenesis is also involved in neurogenesis, synaptogenesis, etc involved in the development of brain, besides ROP



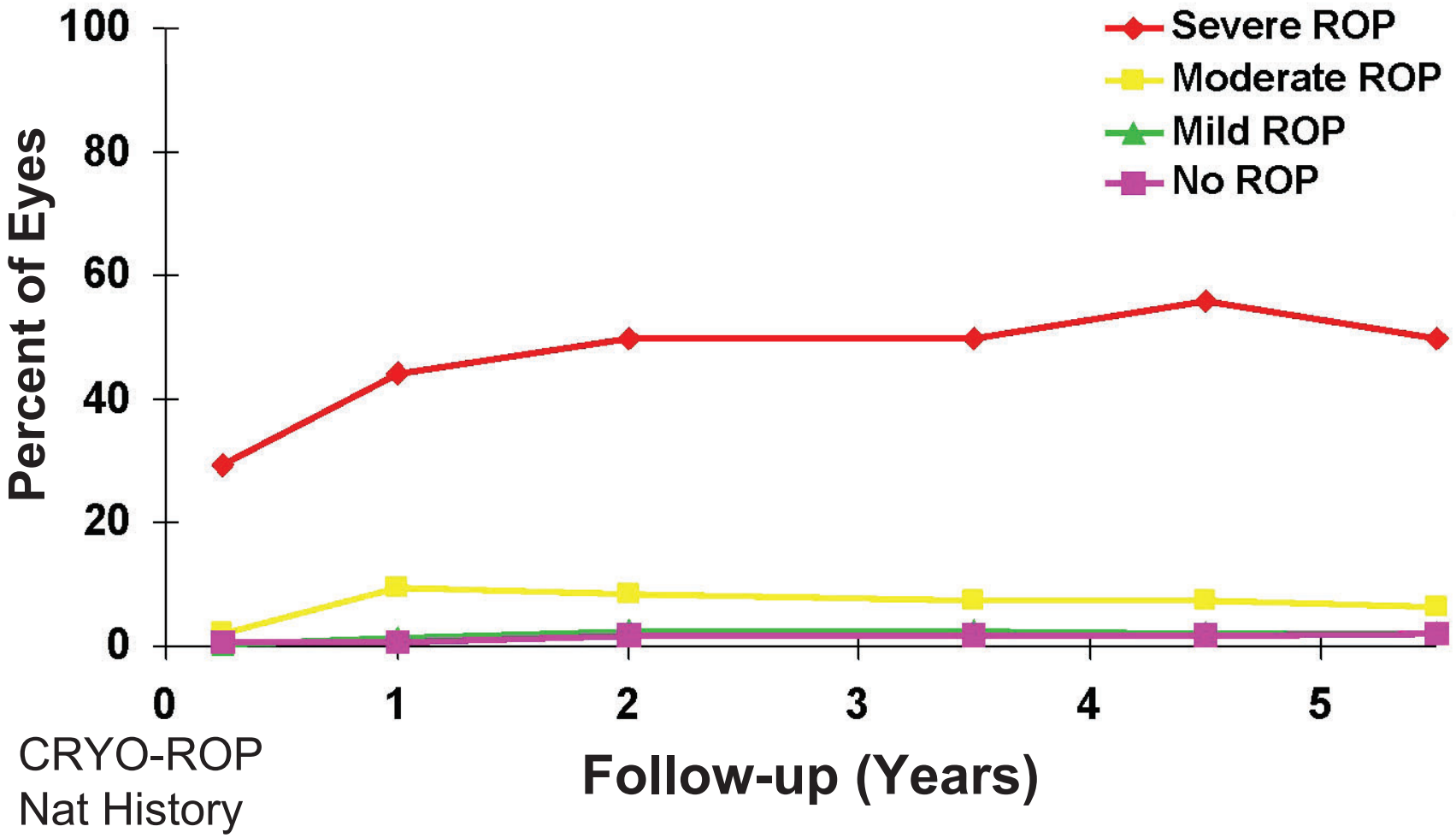
ROP most severe

Courtesy G Gole

Long term sequelae of ROP

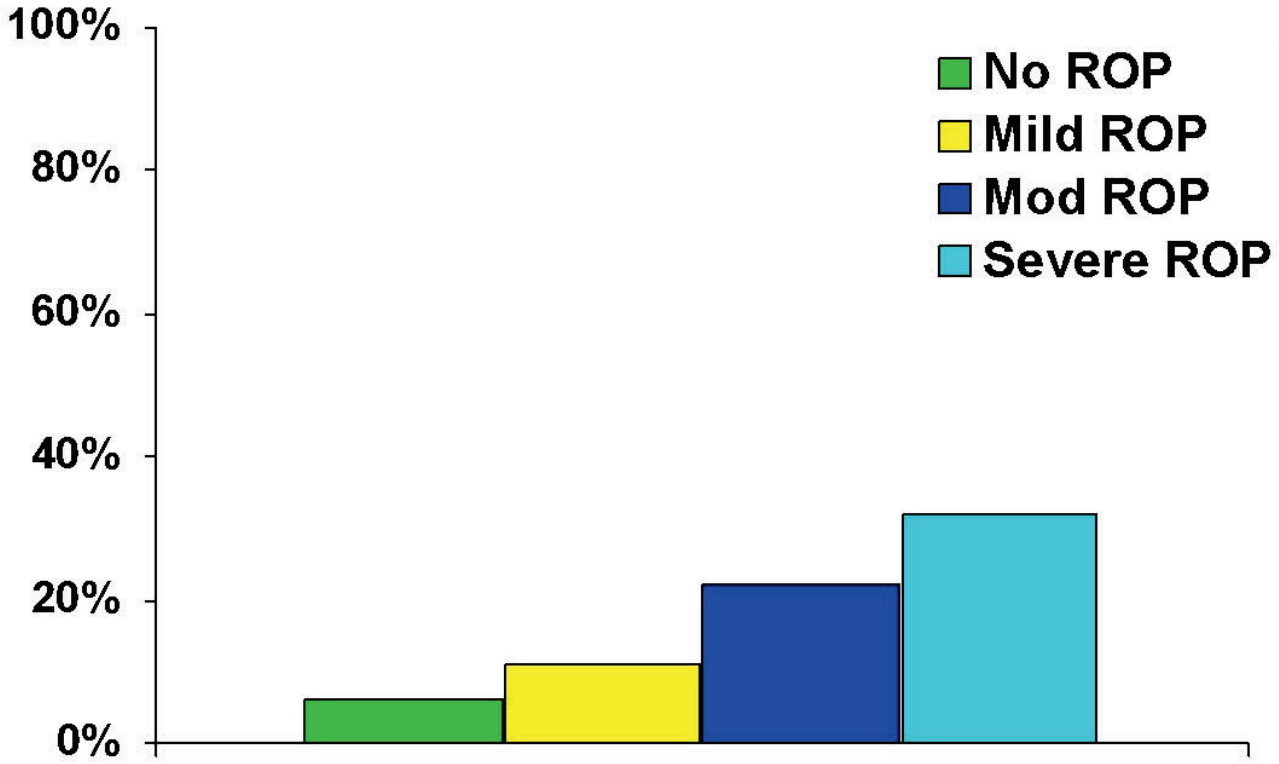
- Myopia (near-sightedness)- need for full time glasses to see at distance
  - Risk higher with Laser photocoagulation
- Anisometropia- leading to risk of lazy eye (amblyopia)
  - Risk higher with Laser photocoagulation
- Restriction of peripheral visual fields
  - Risk higher with Laser photocoagulation
- Macular dragging (compromising the central reading/ writing vision)
- Eccentric fixation causing misalignment of eyes (strabismus)
- Astigmatism (needing glasses full time)

Prevalence of high myopia in preterm Children (≥ 5.0D)



CRYO-ROP
Nat History

Strabismus in preterm children with BW <1251g



AT I YEAR EXAM

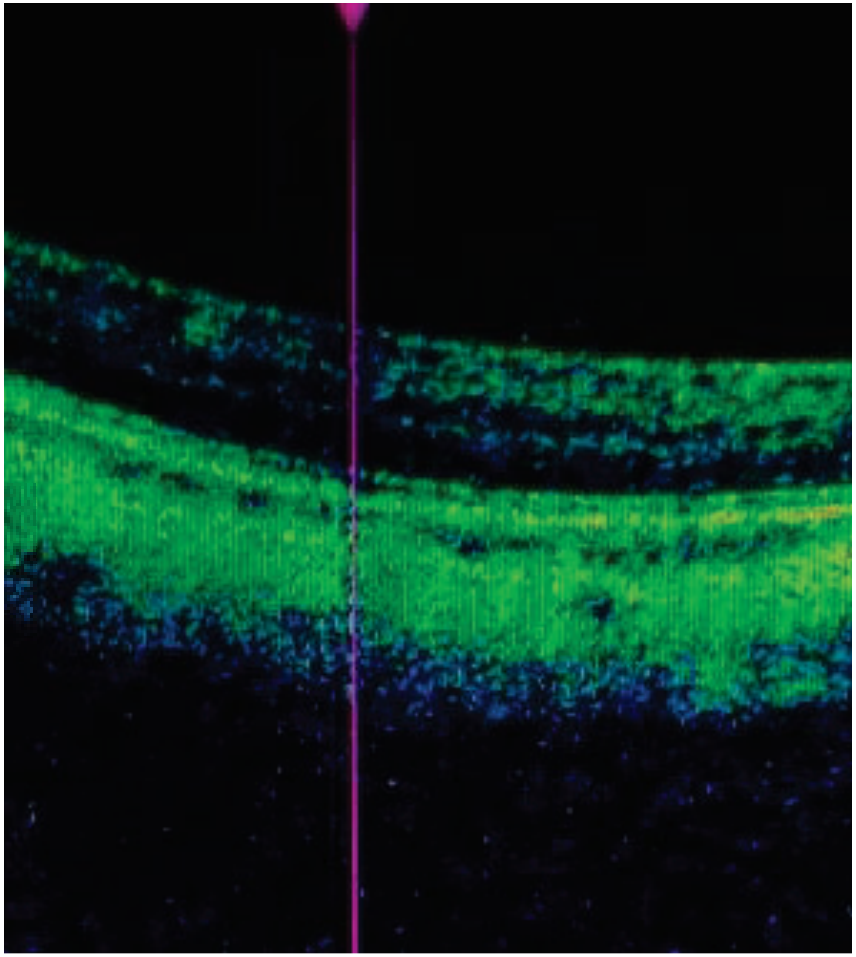
CRYO-ROP
Nat History

Retinopathy of prematurity
School age

- Delightful young lady
- 13 years
- Birth weight 520 gms, 1lb 2 oz, 24 weeks
- NICU course difficult, chest tube
- ROP diode laser ou
- Stage 5 OD NLP
- Stage 3 OS, threshold with extensive diode laser -15.50, macular dragging
- In regular classroom
- Parents have elected no contact sports

Retinopathy of Prematurity
School age

Interventions
Orientation and Mobility!!
Educational plan by TVI with IEP team



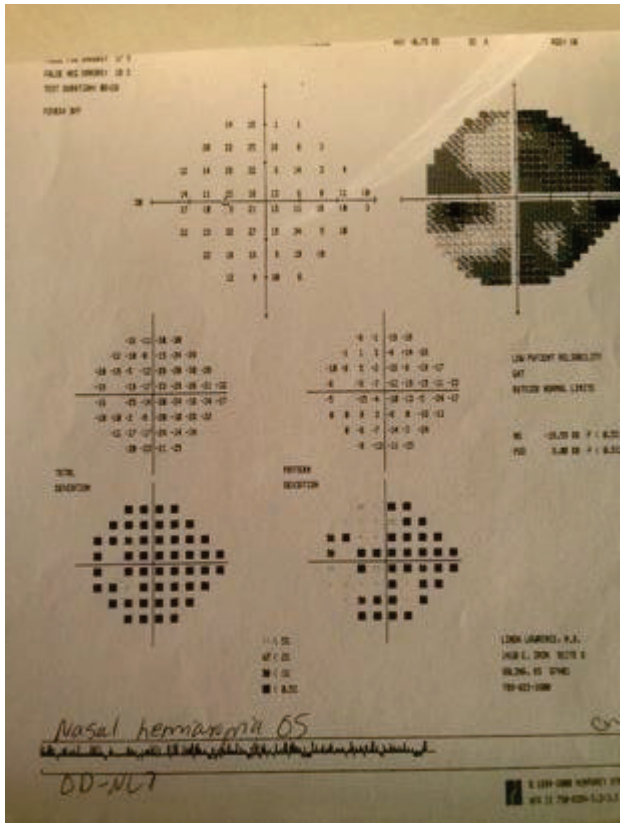
Macula OCT age 12 you

Retinopathy of prematurity
School age: Next steps?

1. Was dropped from services because she is 20/40!
2. Have consult with O&M
3. Learning media assessment
4. Clinical Low vision evaluation with OD or MD

To determine magnification needs

Able to do visual field !



Front of the Eye

Retinopathy of prematurity
School age challenges

- **Poor self esteem: teach to advocate for self**

- **Thick glasses further distorted vision**
- **Participated in refractive surgery trial**
- **Now -4.00, can read without glasses and functional vision and social interactions with peers improved**

Refractive Surgery in Children

- Ethical considerations

Past treatments

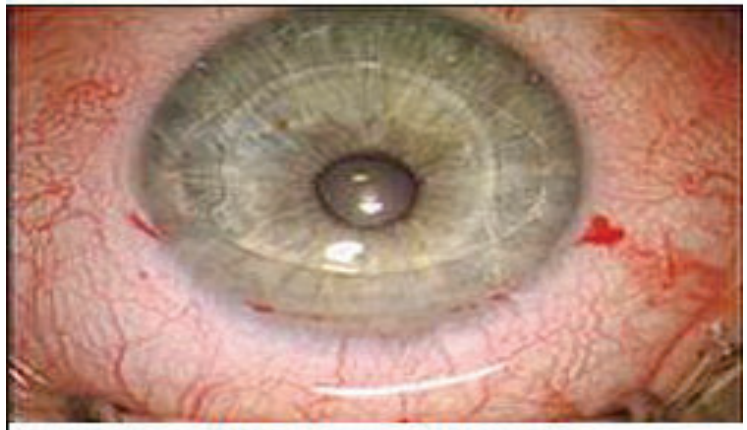
- Glasses
- Contact lenses
- Bifocals!

- Possibilities

- Phakic lens implant
- Lasik
- Secondary lens implants in aphakes

Pediatric Refractive Surgery

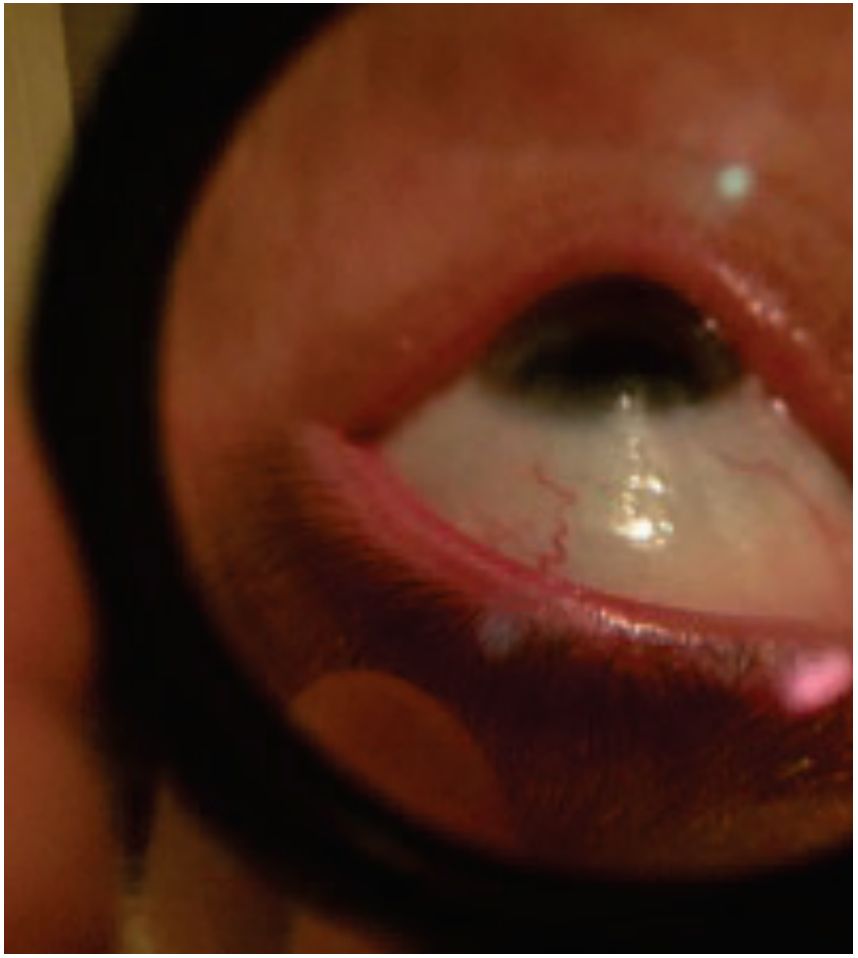
Lasik, PRK



Artisan IOL implanted in pediatric eye.

Phakic lens implants

Keratoconus



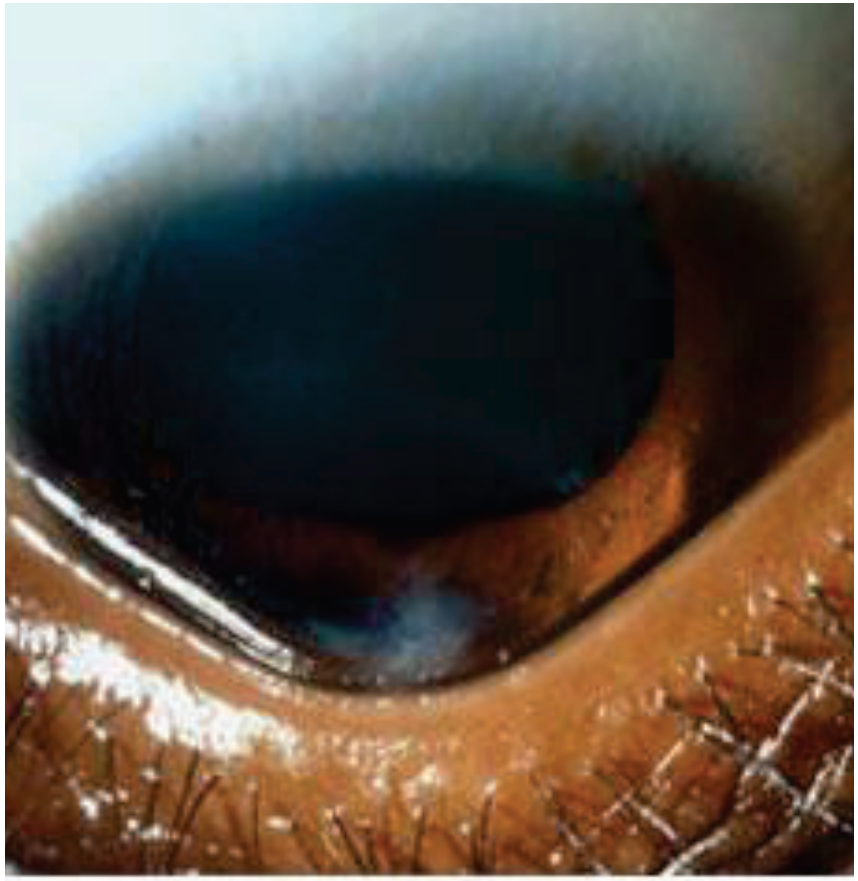
What is keratoconus?

- A condition in which the cornea begins to thin and bulge in a cone shape
- Symptoms develop around puberty
- More common in Down syndrome (71%)

Past treatments

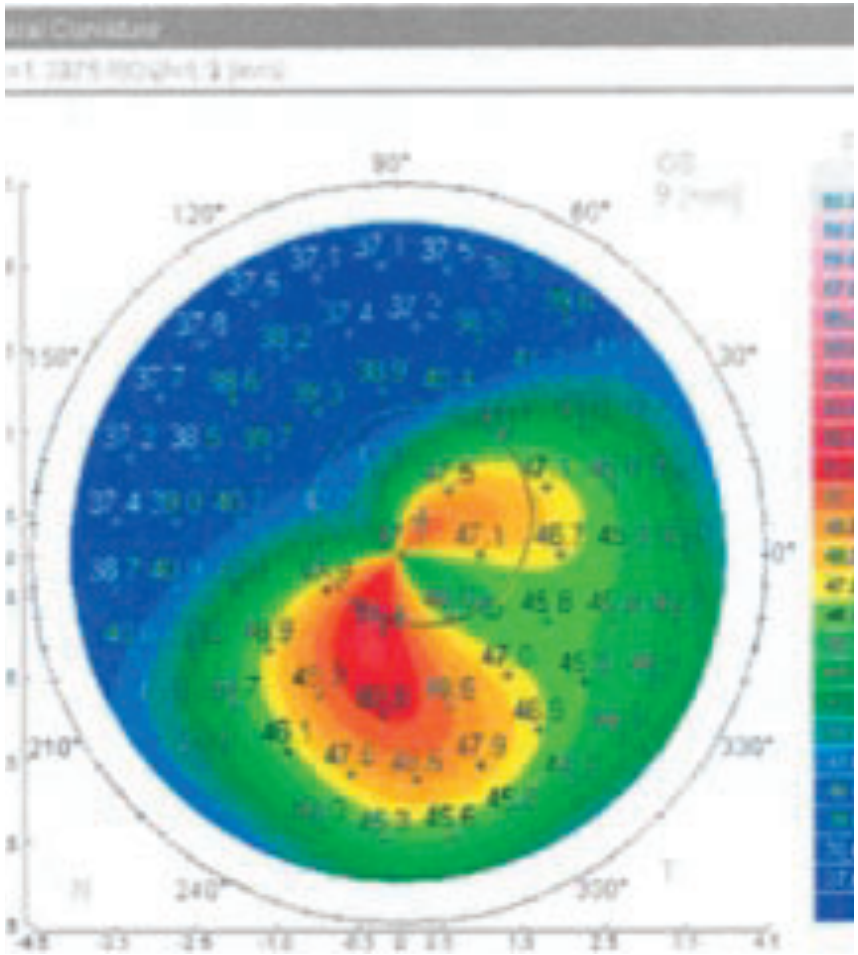
- Glasses
- Contact lenses
- Corneal transplant

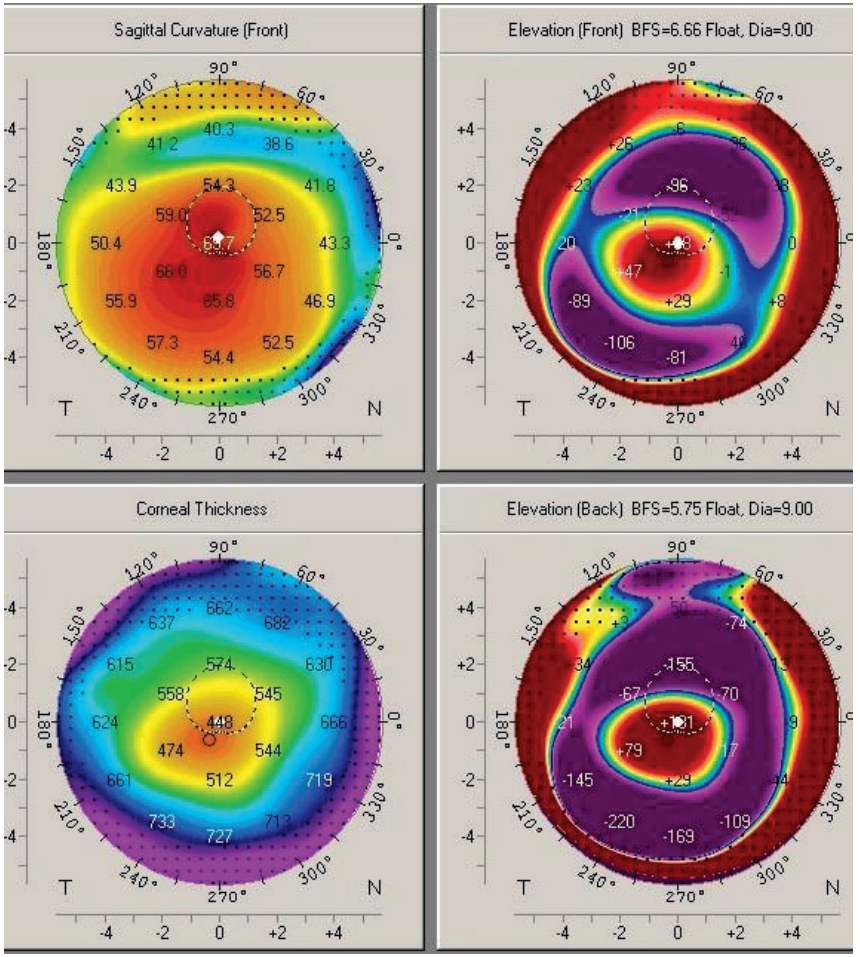
Keratoconus



ig. 1 keratoconus

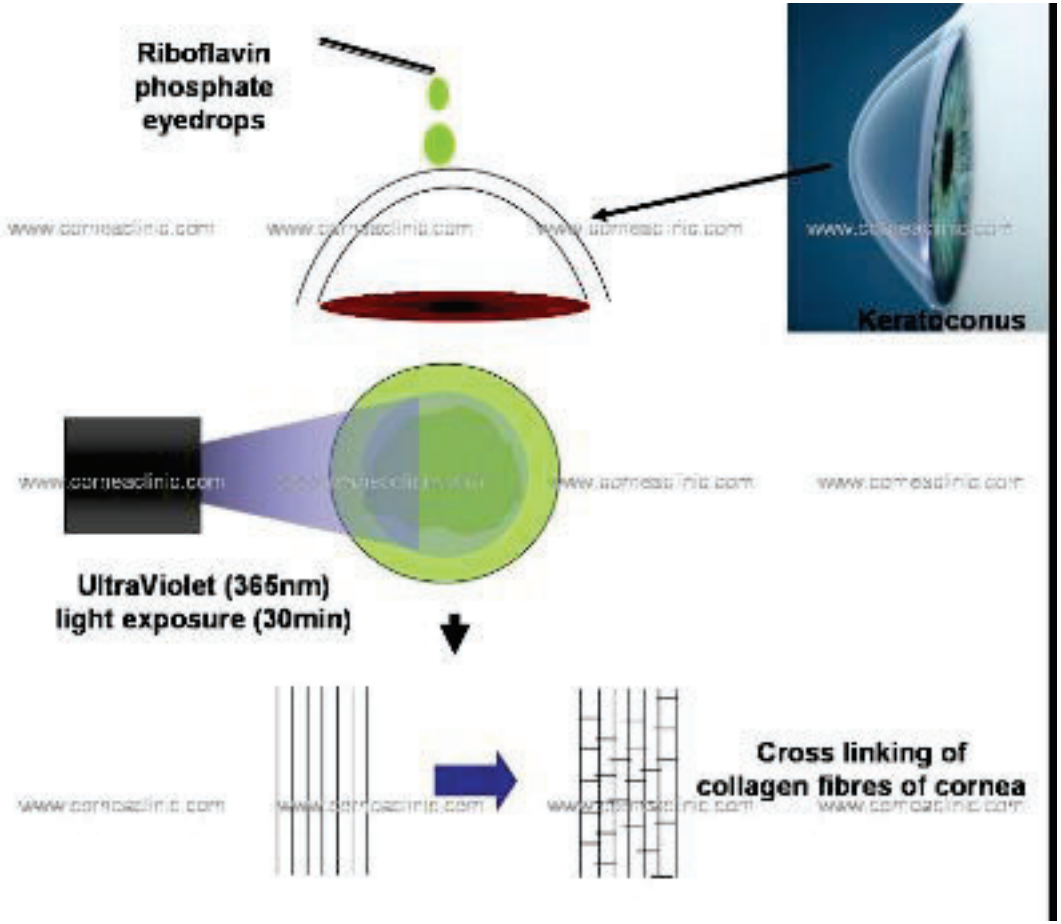
- Degenerative
- Type of corneal ectasia or dystrophy
- 1/2000
- Sporadic or inherited (10%) AD or AR
- Comorbidities: Down syndrome, atopy, Marfan's, Lebers congenital amaurosis




Sagittal Curvature (Front)
Elevation (Front) BFS=6.66 Float, Dia=9.00
Corneal Thickness
Elevation (Back) BFS=5.75 Float, Dia=9.00

Corneal cross linking (CXL)

- Combination of vit B2 drops and ultraviolet light applied to corneal over controlled length of time
- Procedure takes about an hour
- In children general anesthesia


Riboflavin
phosphate
eyedrops
Keratoconus
UltraViolet (365nm)
light exposure (30min)
Cross linking of
collagen fibres of cornea

Corneal Crosslinking

- Now FDA approved
- Careful evaluation
- Doesn’t cure, stabilizes

Why do infants wear glasses and how to talk to parents.

Response to correction of refractive errors and hypoaccommodation in children with congenital Zika syndrome

Liana O. Ventura, MD, PhD,[a,b] Linda Lawrence, MD,[c] Camila V. Ventura, MD,[a,b] Gordon N. Dutton, MD, FRCOphth,[d] Polyana Marinho, MD,[a] Priscila F. Ferro, MD,[a] Adriana L. Gois, MD,[a,b] Natalia C. Dias, MD,[a] Larissa Ventura, MD,[a] Cynthia A. Moore, MD,[e] and Lea Hyvärinen, MD[f]

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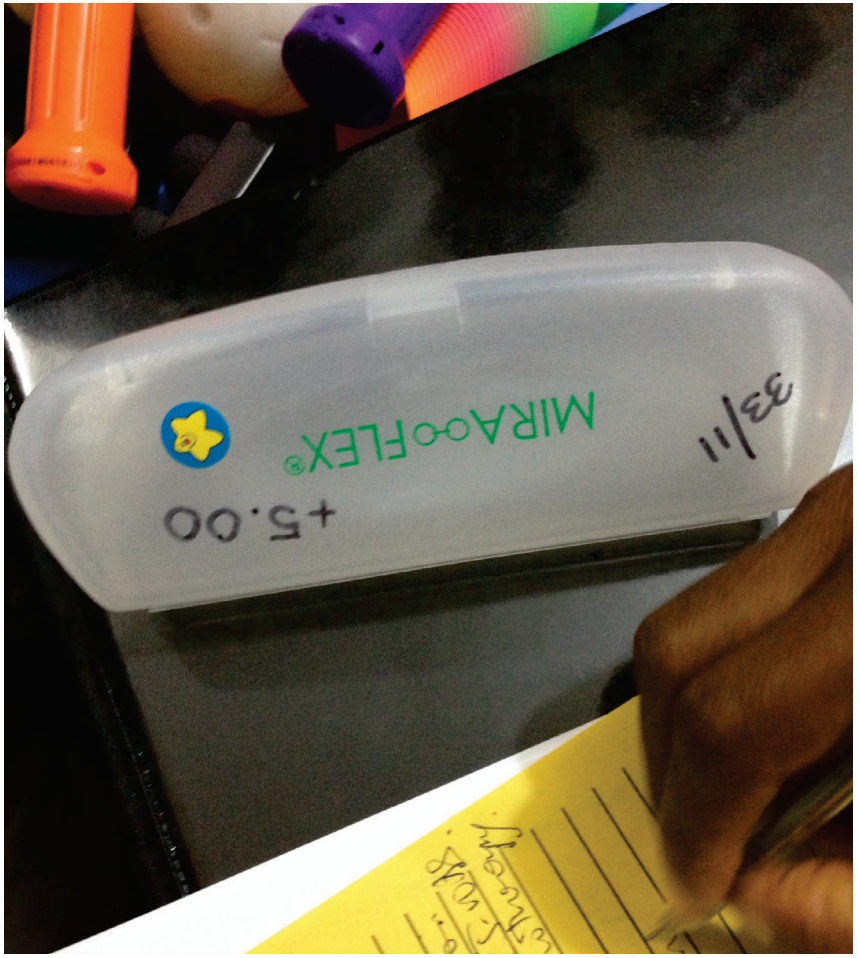
CONCLUSIONS Eyeglasses can improve visual acuity in children with CZS. Significant changes in their refractive status over time requires periodic updates. (J AAPOS 2017;21:480-484)

Lack of Accommodation
measure it!



Glasses??

- Do a refraction and think about it!
- Dynamic retinoscopy….

Prior to dilation with correction

- Cycloplegic refraction
- Children with Low Vision deserve it!

Cycloplegic refraction with appropriate prescription of glasses

- Make sure child is comfortable and supported
- Document difference in child's behaviors
- Trial set may be helpful
- Individualize for child's needs

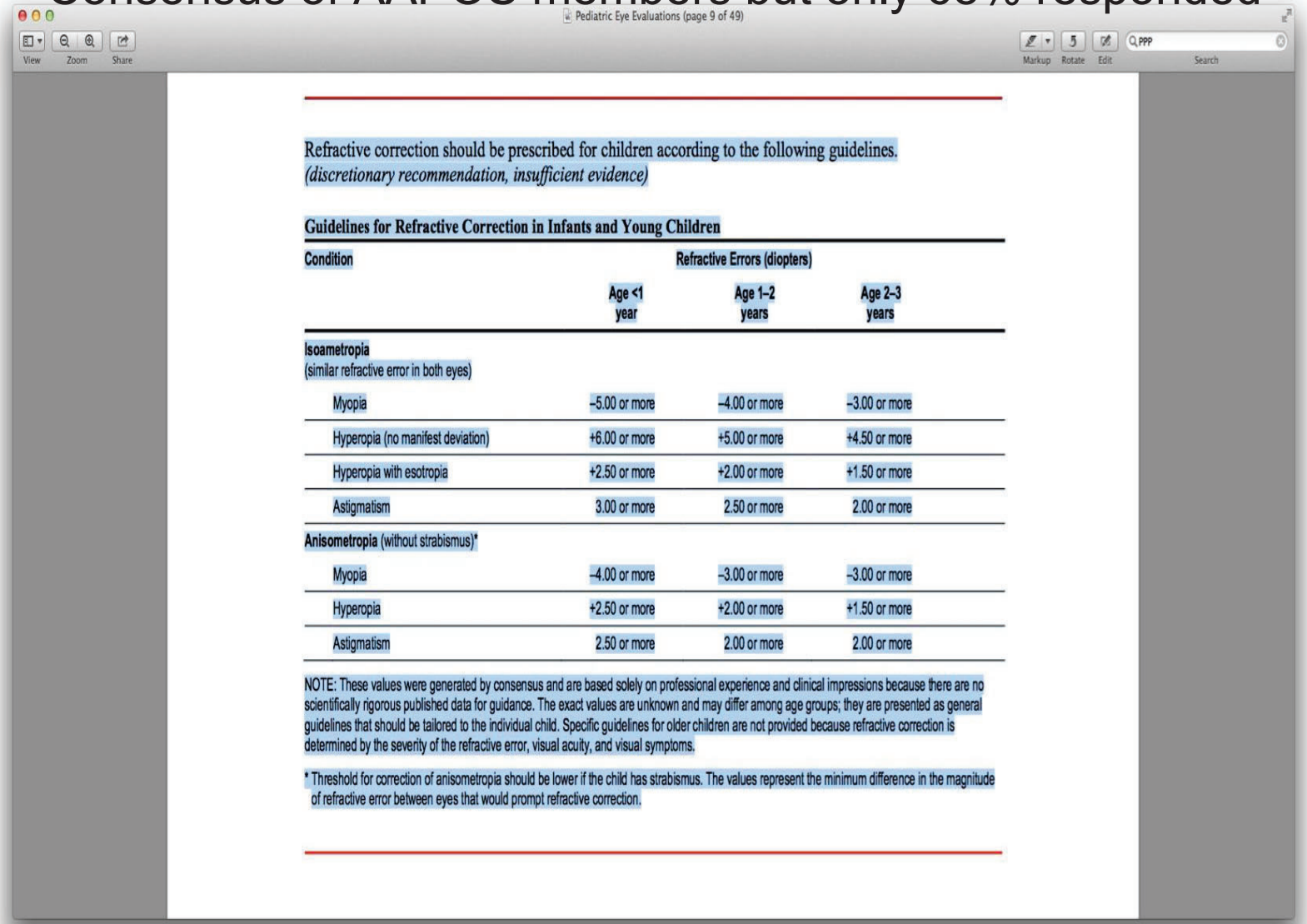
Significant refractive errors

What is a significant refractive error?

Who made the rules?

1998

Consensus of AAPOS members but only 68% responded



Refractive correction should be prescribed for children according to the following guidelines. *(discretionary recommendation, insufficient evidence)*

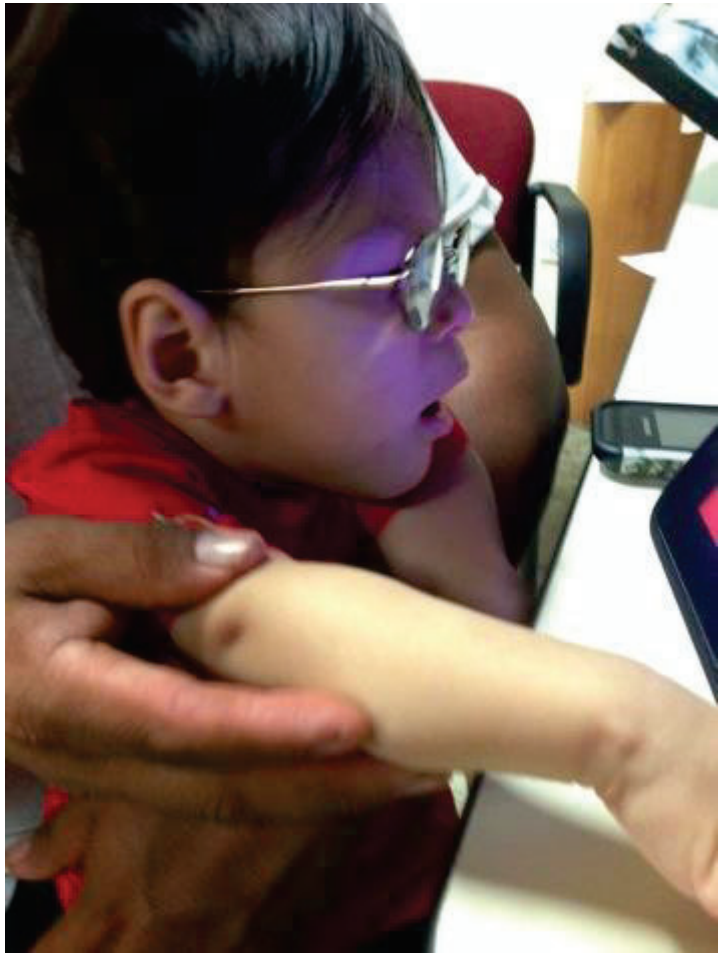
Guidelines for Refractive Correction in Infants and Young Children

Condition	Refractive Errors (diopters)		
	Age <1 year	Age 1–2 years	Age 2–3 years
Isoametropia (similar refractive error in both eyes)			
Myopia	–5.00 or more	–4.00 or more	–3.00 or more
Hyperopia (no manifest deviation)	+6.00 or more	+5.00 or more	+4.50 or more
Hyperopia with esotropia	+2.50 or more	+2.00 or more	+1.50 or more
Astigmatism	3.00 or more	2.50 or more	2.00 or more
Anisometropia (without strabismus)*			
Myopia	–4.00 or more	–3.00 or more	–3.00 or more
Hyperopia	+2.50 or more	+2.00 or more	+1.50 or more
Astigmatism	2.50 or more	2.00 or more	2.00 or more

NOTE: These values were generated by consensus and are based solely on professional experience and clinical impressions because there are no scientifically rigorous published data for guidance. The exact values are unknown and may differ among age groups; they are presented as general guidelines that should be tailored to the individual child. Specific guidelines for older children are not provided because refractive correction is determined by the severity of the refractive error, visual acuity, and visual symptoms.

* Threshold for correction of anisometropia should be lower if the child has strabismus. The values represent the minimum difference in the magnitude of refractive error between eyes that would prompt refractive correction.

Refraction



- Based on 1% cyclopentolate refraction • Full: anisometropia, astigmatism, myopia
- Hyperopia – Fully correct (primarily for ET)
- OR – Under-correct symmetrically*
- *no more than 1.50 D for most PEDIG studies

Proper fitting

Wrap around

poorly fitting cable temples on left and well fitting cables on right.

Proper fitting

Smashes eye closed

Proper fitting

Accommodative Esotropia

- including prescription of bifocals as indicated

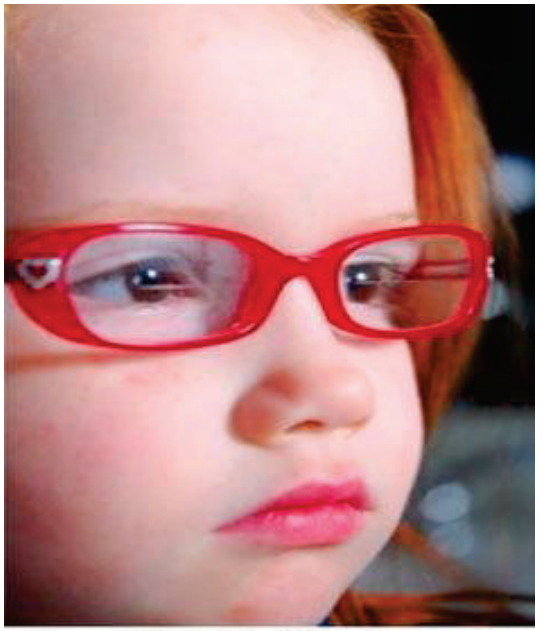


Figure 3: Well fitting bifocal.

Anisometropia/amblyopia

Bifocals in children with Down syndrome (BiDS) – visual acuity, accommodation and early literacy skills Krithika Nandakumar and Susan J. Leat School of Optometry, University of Waterloo, Ontario, Canada Acta Ophthalmol. 2010: 88: e196–e204

Although preliminary and longitudinal in nature, the current study gives evidence of **superior focusing, better near VA, improved literacy skills** over time and enhanced school performance as a result of bifocal prescription in children with DS.

The children adapt well to bifocal wear.

Bifocals should be considered in the clinical management of children and teenagers with DS.

More long-term studies are required to demonstrate whether long-term bifocal wear would improve absolute VA.

Dev Med Child Neurol. 2000 Oct;42(10):701-3.

Reduced accommodative function in dyskinetic cerebral palsy: a novel management strategy.

Ross LM1, Heron G, Mackie R, McWilliam R, Dutton GN

A 9-year-old boy with **dyskinetic cerebral palsy** secondary to neonatal encephalopathy is described. He presented with **blurring of near vision** which had begun to impact on his school work. Objective assessment of accommodation showed that very little was present, although convergence was almost normal. The near-vision symptoms were completely removed and reading dramatically improved with the provision of varifocal spectacles**. Varifocal** lenses provide an optimal correction for far, intermediate (i.e. for computer screens), and near distances (i.e. for reading). Managing this type of patient with varifocal spectacles has not been previously reported. It is clearly very important to prescribe an optimal spectacle correction to provide clear vision to optimize learning.

Other uses for glasses in children with low vision

1. magnification for low vision
2. “blinder” effect of thick frames for those with attention deficits
3. Protection from injury
4. Transition lenses or tints for photophobia
5. Individualize!

Questions the families need answers to :

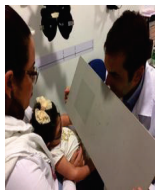
1. What are the glasses for?
2. Does the family and educational team understand when the glasses are to be worn?
3. What is the expected outcome of the glasses?
4. Do they promote visual, social, motor, communication skills?
5. How do we assess this outcome?
6. What are the family QOL issues?
7. What is the role for refractive surgery?

Basic Principals of eyeglass wear

Each child is unique.
The visual pathways are the sensory channel responsible for much of the information the infant/toddler receives.
Glasses are prescribed for a variety of optical, medical, and functional reasons.
Proper fitting of glasses enhances wear.
The reasons for the glasses prescription and wearing should be understood by parents, educators, and therapists to help facilitate their proper use and enhance development of vision as well as overall development.

Common Questions about Infant/Toddler Glasses

1. What are the glasses for?
2. Do the glasses promote social, motor, communication, or adaptive skill development?
3. What is the expected outcome and who accesses the outcome? (What can the child do better with the glasses wear that could not do before?)
4. When are the glasses to be worn and do parent's and team understand?
5. What are the hardships for the family and child and how do we overcome these?



Teller cards for acuity

Cycloplegic refraction

LEA GRATINGS

Trial Lenses

Why are glasses prescribed?

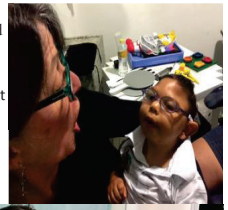
Rarely is vision considered as a contributing factor when developmental delay is suspected.
There is little consensus as to the best method of assessing vision in young children with neurological delay or disability, or the prescribing of eyeglasses.
I continue to be amazed at how refractive correction can improve function in children with developmental delay.

1. ***Significant refractive error***, with evaluation not only according to published consensus standards for typically developing babies, but for the individual baby's needs.

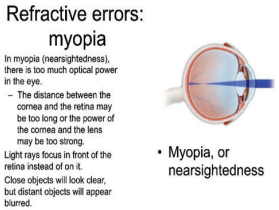
Myopia (nearsighted), Hyperopia (farsighted), anisometropia (different prescriptions in each eye) and astigmatism are common eye conditions that require glasses to help with prevention of amblyopia, and proper development of the visual system, as well as enhance the overall development of the child.

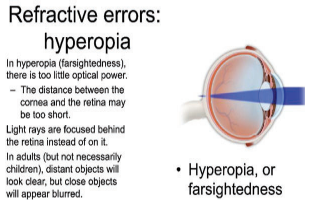
Aphakia may occur after lens removal for congenital cataracts in a baby.

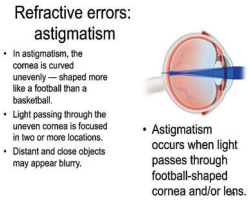
2. Prevent amblyopia from optical errors in eyes (very high myopia, high hyperopia, astigmatism that is significant or amblyogenic anisometropia



Baby with congenital Zika virus syndrome and microcephaly.
Much improved eye contact with overplussed glasses.(+3.00 more than cycloplegic refraction)
Worn for near, supervised tasks.





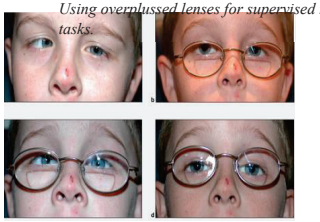


Toddler with myopia. Full time wear.
Notice the lens minimizes the face.

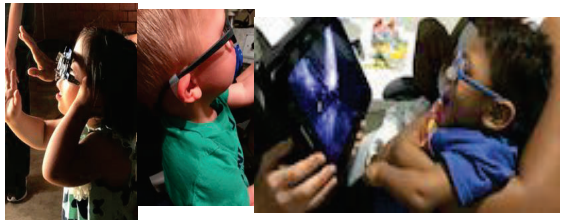
Poor focusing in baby with microcephaly in Africa.
Using overplussed lenses for supervised near tasks.

3. Lack of accommodation (focusing) measured by dynamic retinoscopy; The difficulty with accommodation may occur because of inadequate neurological direction, lack of motivation or attention to near target by child, seizure medication or medication (hyocine) used to decrease salivation can paralyze pupil and affect accommodation. This means that hyperopia which is typical in a child may not be compensated for: no focusing at near, no compensation for hyperopia, blurred or poor quality of image.

4. Correction of strabismus (eye turning). Typically would be accommodative esotropia), may occur earlier in children with neurodevelopmental disabilities, these are typically hyperopic children (plus prescription, or "farsighted")



Hyperopic glasses for strabismus with bifocal. Full time.
Notice how magnifies the face.



Fitting Tips for glasses

Comfort is important as well as function.

Temple Pieces

Proper fitting

Wrap around

Mom and optician figured out best fit for this child with different ear placement and head shape!

OTHER USES FOR GLASSES

1. Protection for children with low vision/blindness
2. Transition or tints for photophobia
3. Magnification for Low Vision
4. "Blinder effect" ??
5. All children are unique.

Baby with transition lenses.
Severe photophobia. (CZS)

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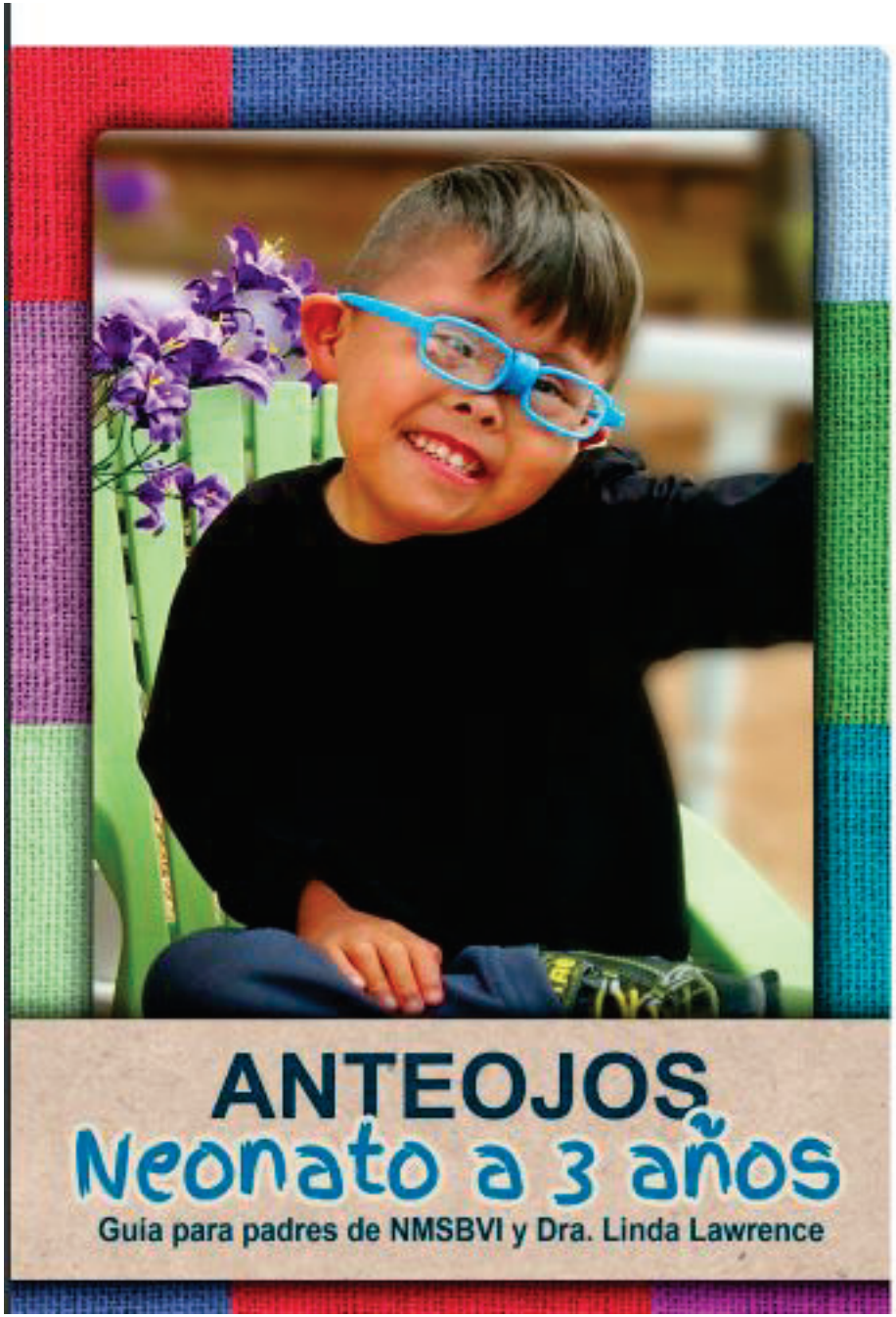
ANTEOJOS
Neonato a 3 años
Guía para padres de NMSBVI y Dra. Linda Lawrence