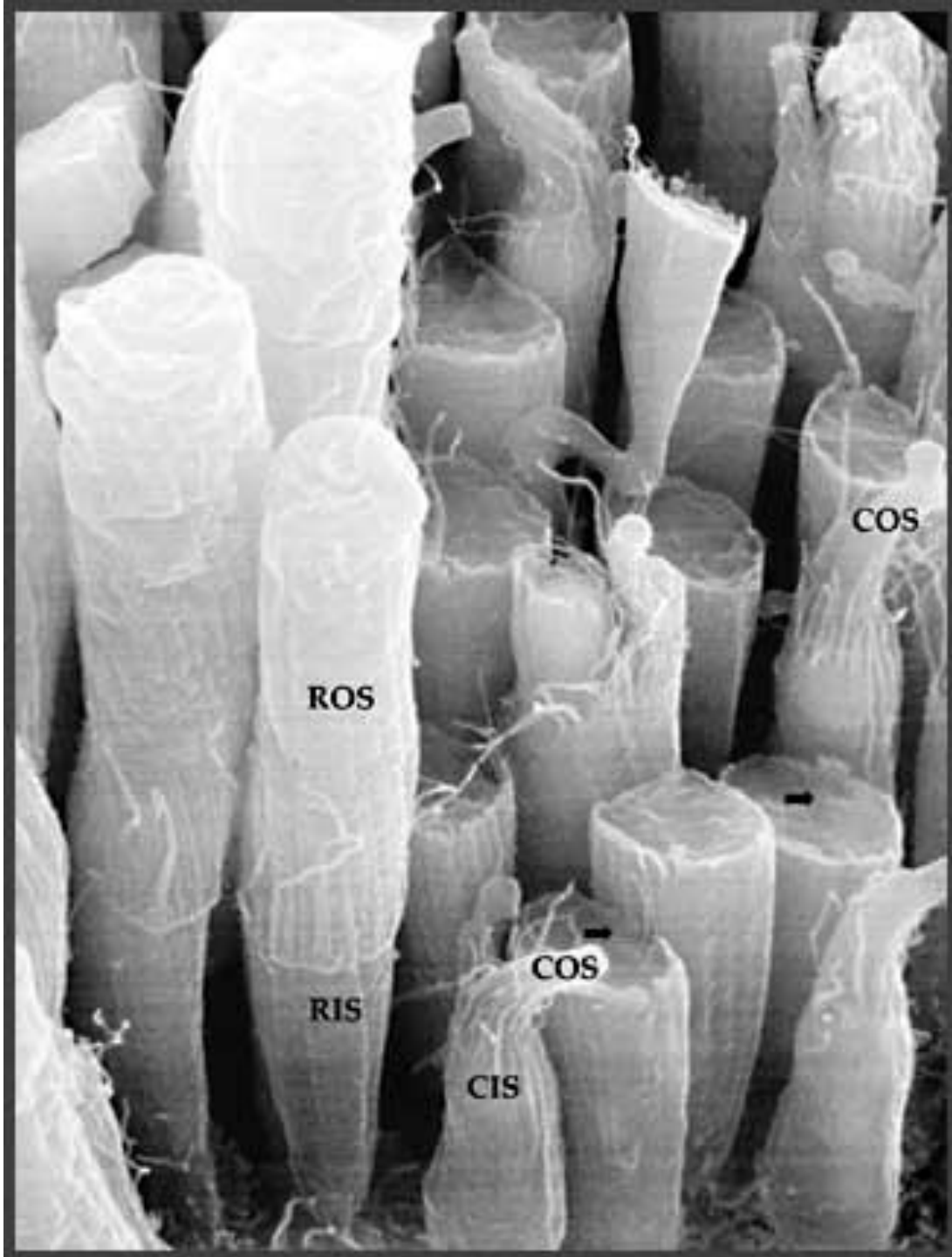
Växjö
17 september 2015

Att förstå och att utreda synnedsättning

ÖGONKLINIKEN
Skånes universitetssjukhus

Vesna Ponjavic



Vi är allt bättre på att:

- upptäcka synskada
- förstå bakomliggande orsaker till synnedsättning
- behandla och bota ögonsjukdomar

Sjukvården

Syncentraler

Optiker

Forskare

Prevalens blindhet och måttlig och svår synnedsättning i världen 1990 – 2010

Rupert Bourne, et al. *Br J Ophthalmology* 2014; 98: 629-638

Minskning under 20 år:

Blindhet	50%
Måttlig och svår synnedsättning	38%

”Höginkomstländer”:
USA, Västeuropa, Australien, Japan.

SVERIGE?

Region Skåne?

Minskning under 5 år (2009 – 2013)

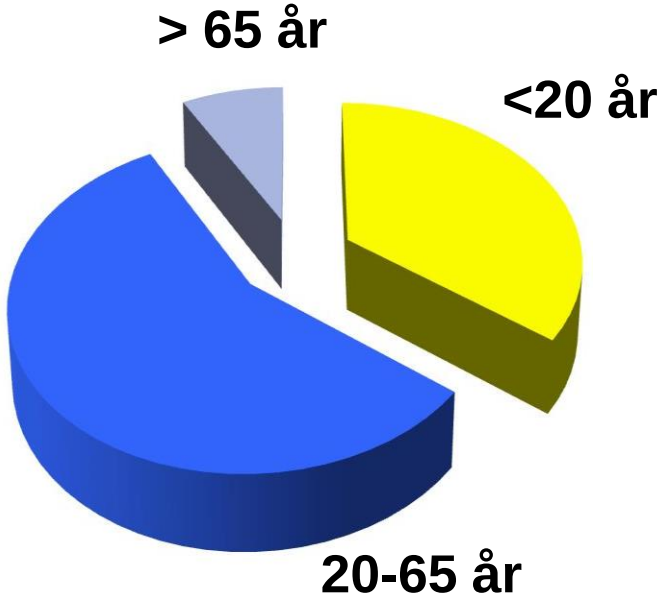
Blindhet / grav synnedsättning

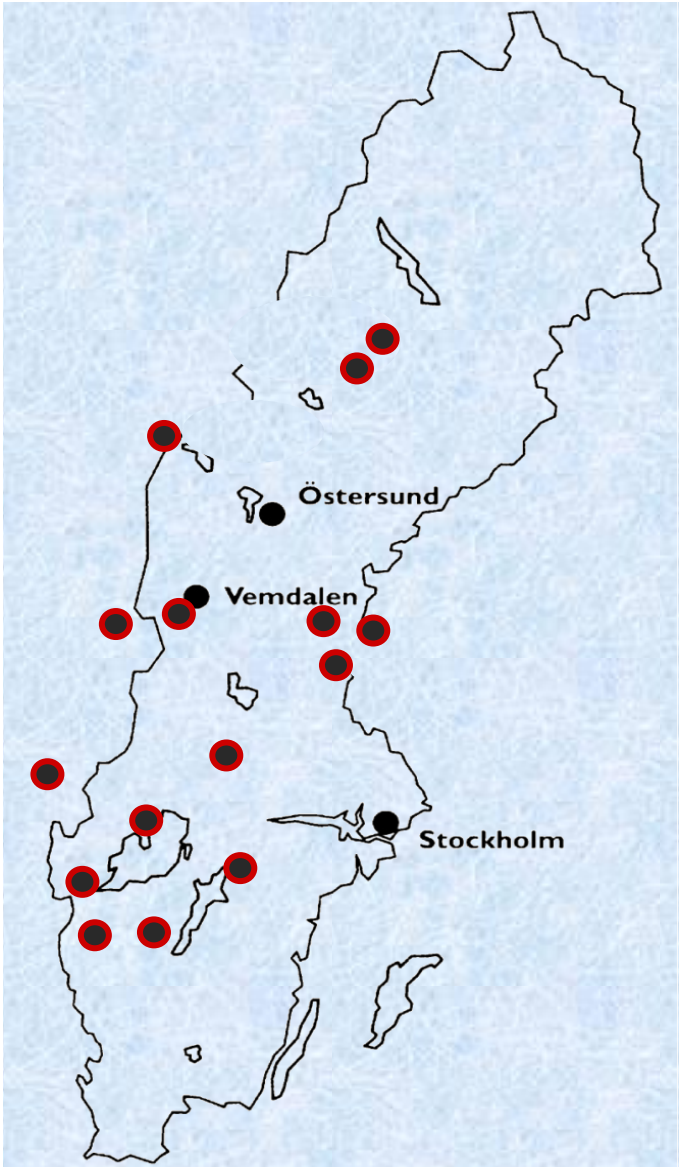
	Vuxna	*Barn/ungdom*
2009	181	15
2013	137	5

Aniela Meincke
Enhetschef, Habilitering &Hjälpmedel
Region Skåne, Synenheten för vuxna

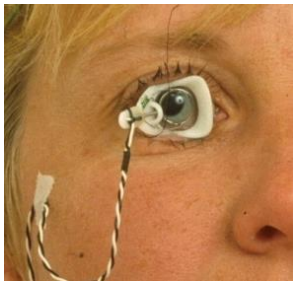
RP REGISTRET I LUND

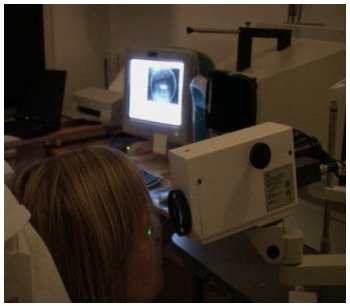
Sedan 1990 har vi undersökt 4000 patienter på Ögonmottagningen i Lund.

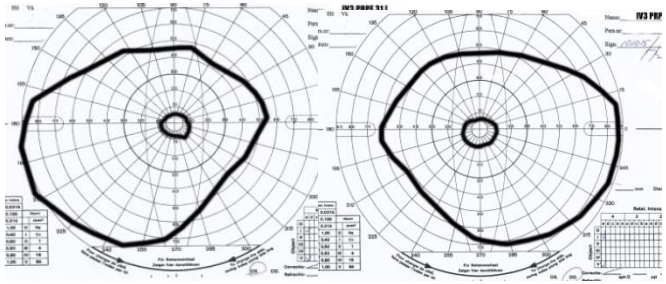


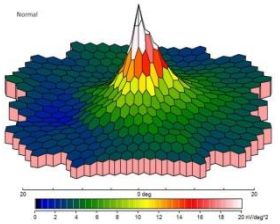


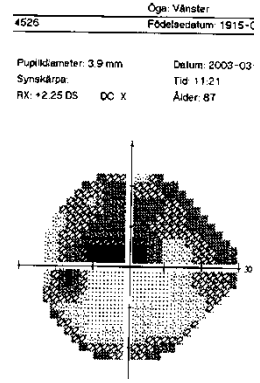
En dag på ERG mottagningen i Lund

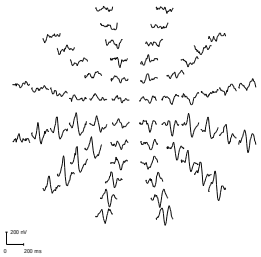


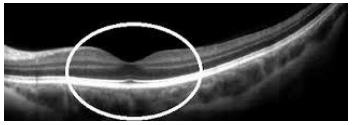


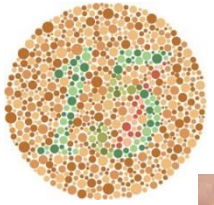


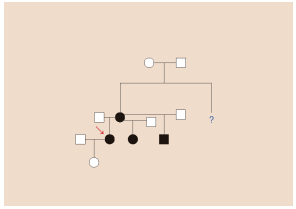


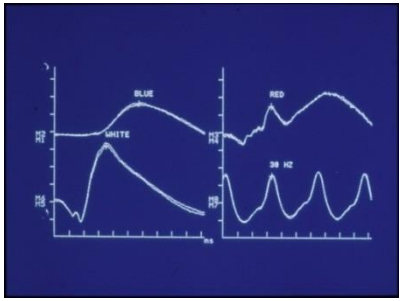












SYNSKÄRPA

Snellen/KM

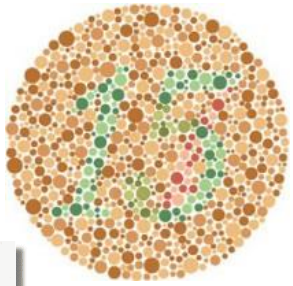
EDTRS

Närsyn LIX

Sloan low contrast visual acuity chart

FÄRGSINNE

Boström-Kugelberg →



Ishihara →

Farnsworth D-15 →

Anomaloskop →

SST = Sahlgren saturation test →

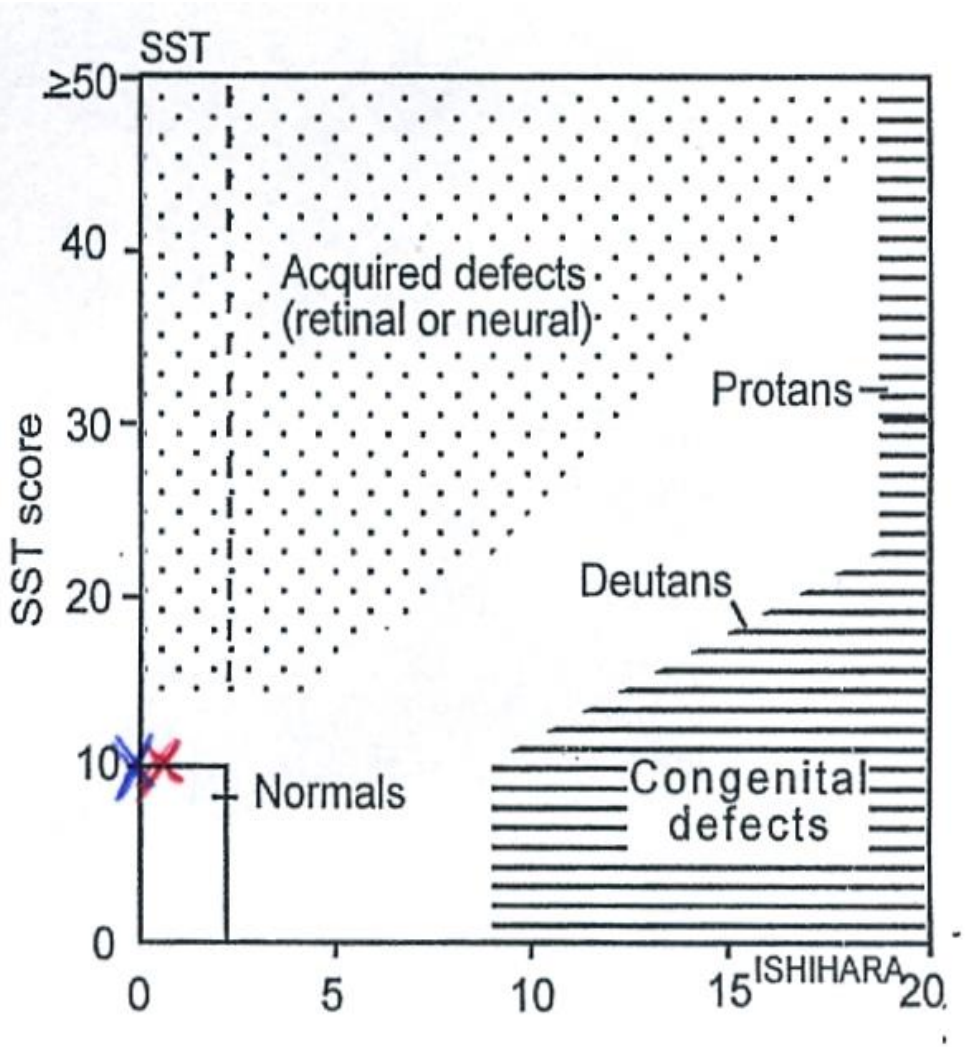
FÄRGSINNE

Y-axel

SST poäng

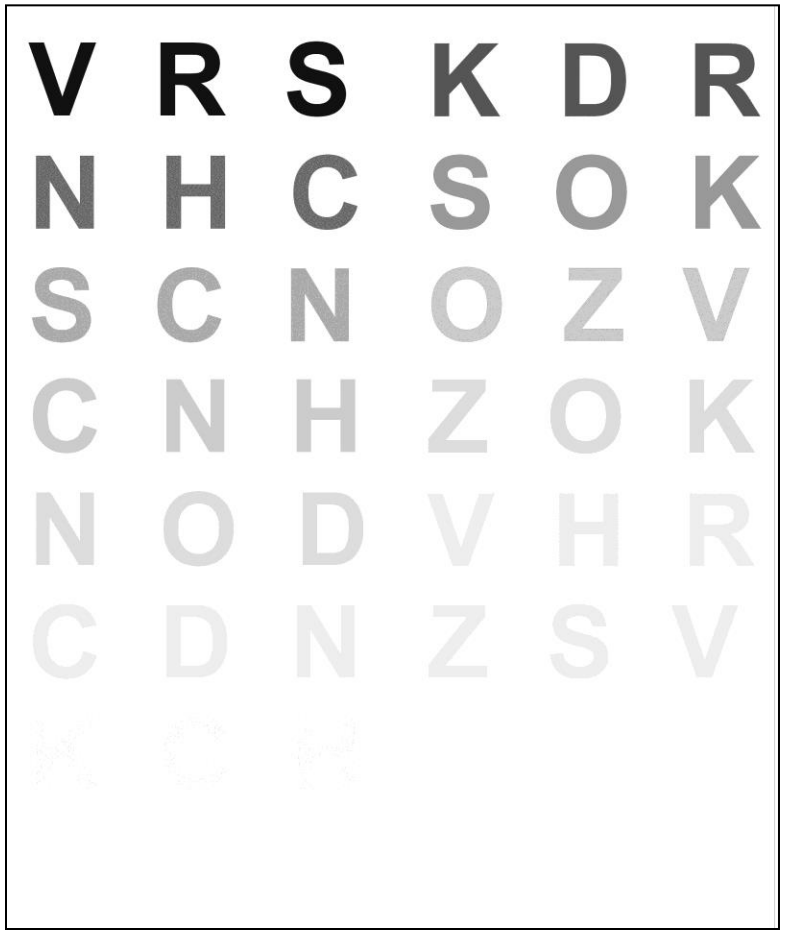
X-axel

Antal FEL på Ishihara

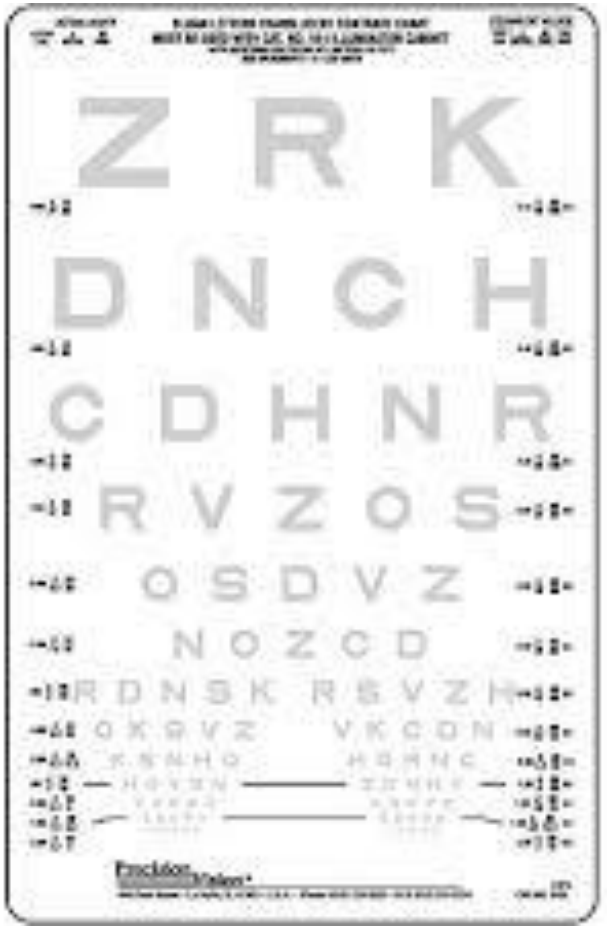


KONTRAST

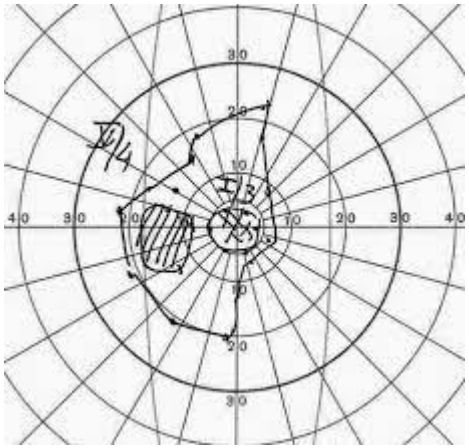
Pelli Robson

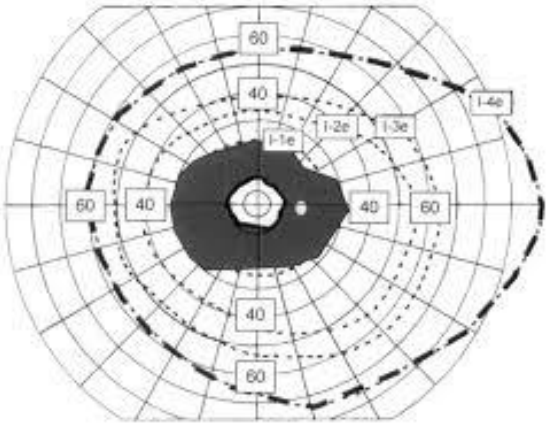


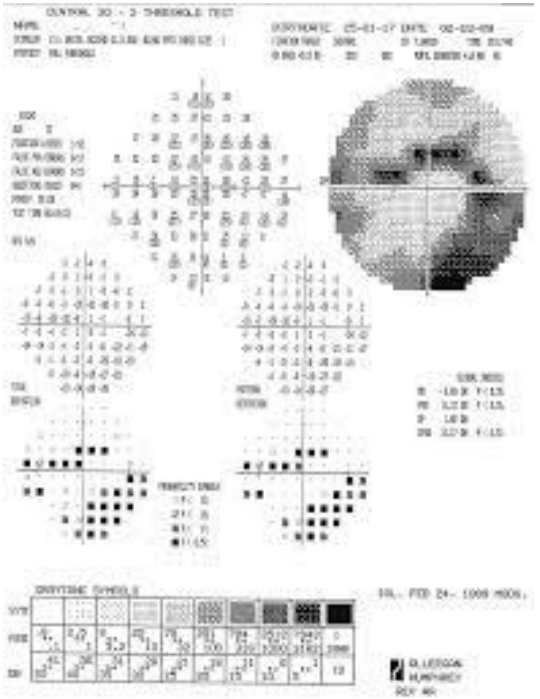
Sloan

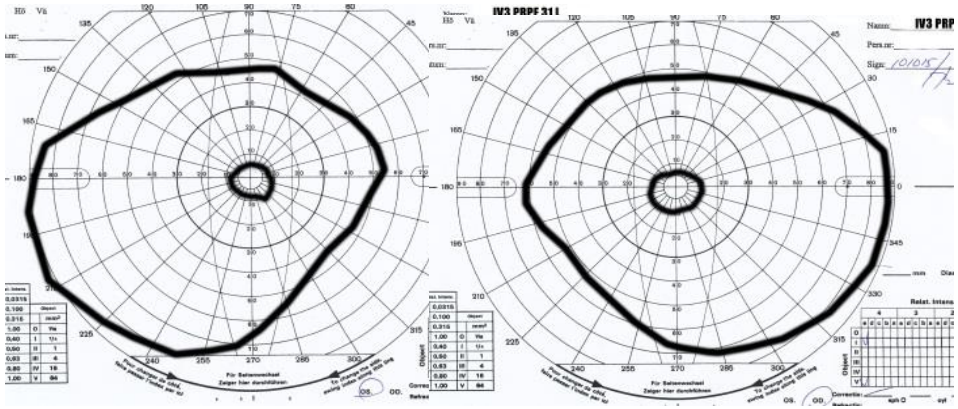


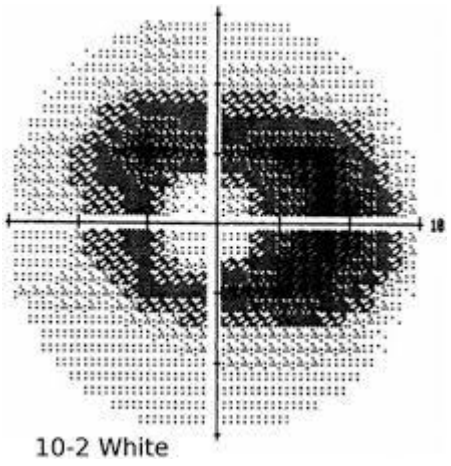
SYNFÄLT

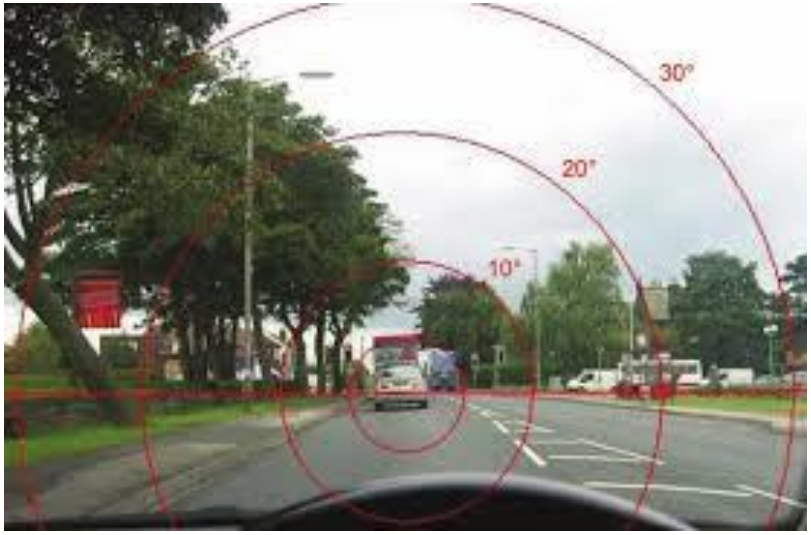


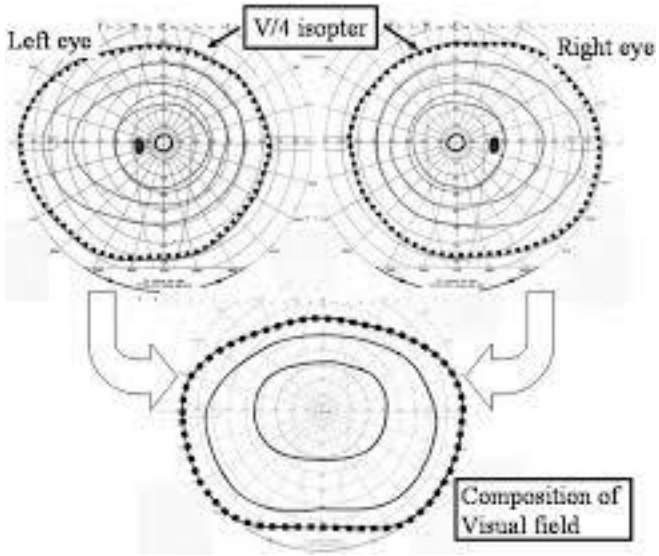


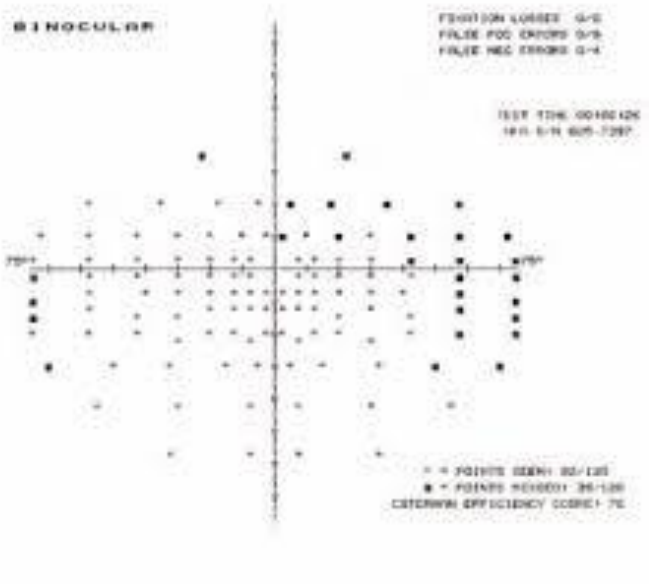






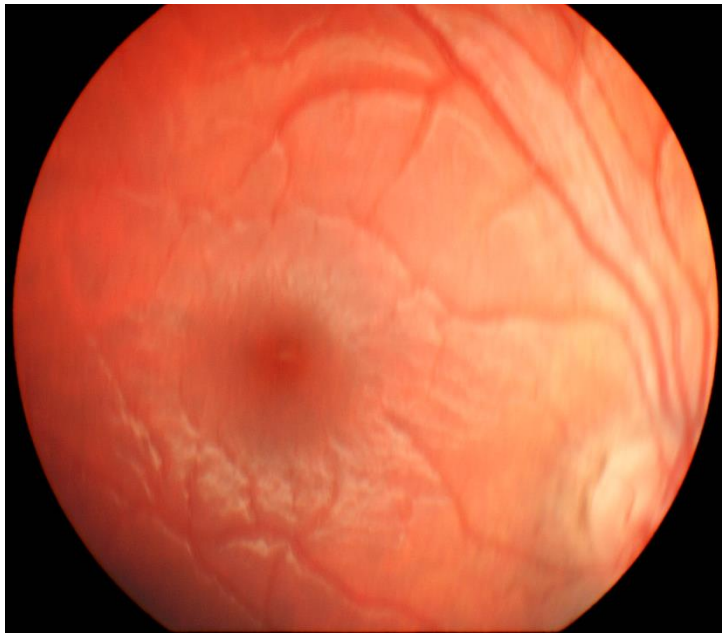

30°
20°
10°


Left eye
V/4 isopter
Right eye
Composition of
Visual field

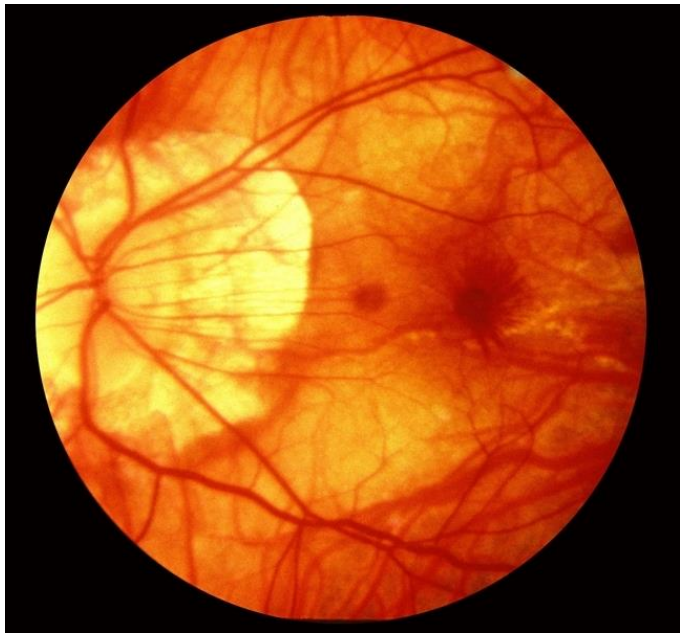

BINOCULAR

ÖGONBOTTEN BEDÖMNING

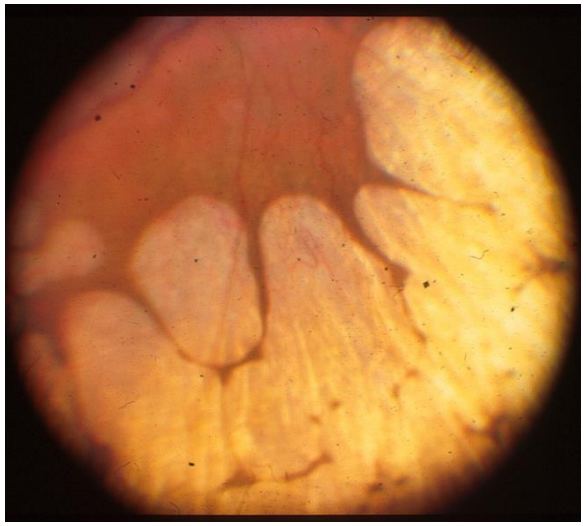
Retinal degeneration, barn 5 år

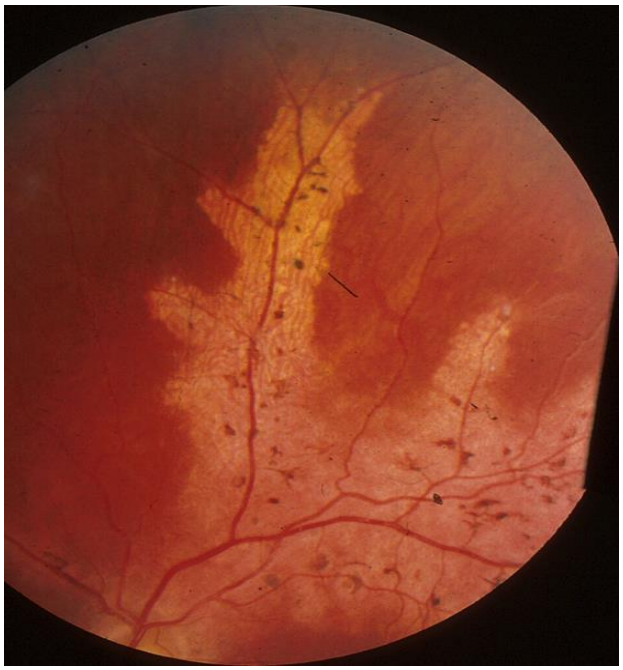


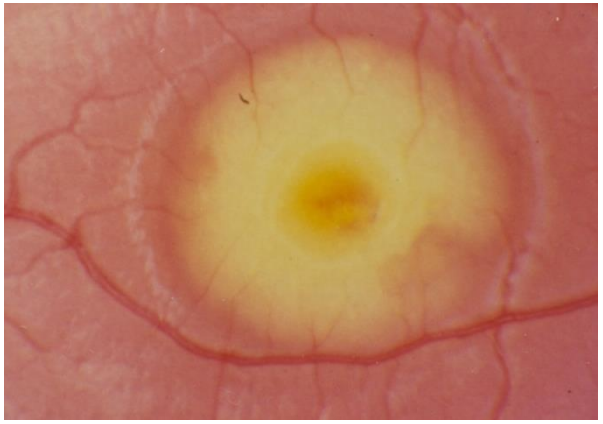
Höggradig myopi, vuxen

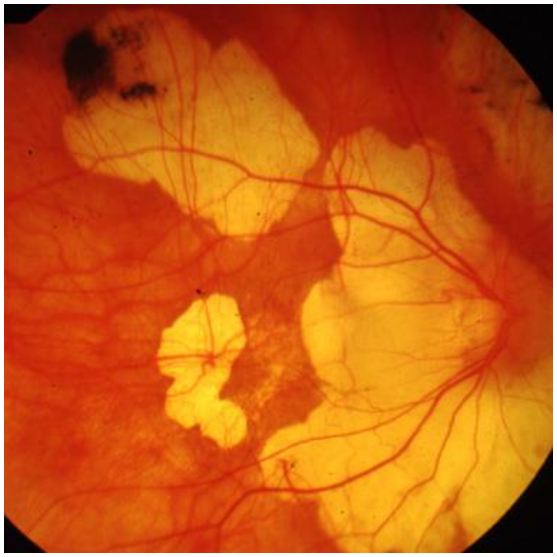


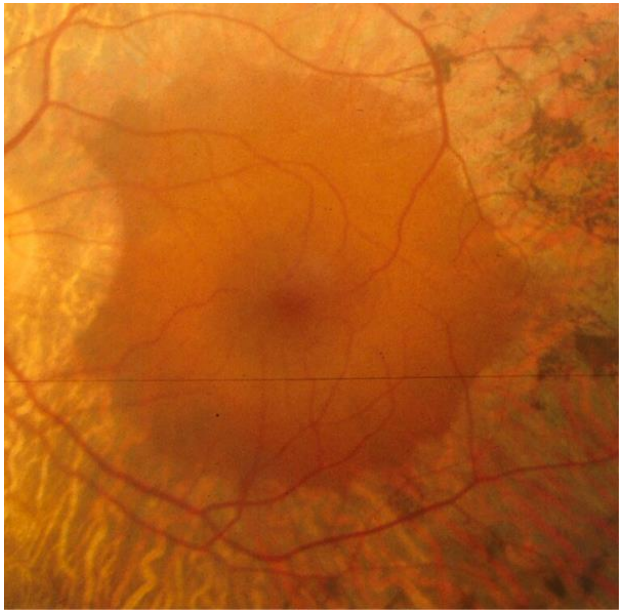
Patologi i ögonbotten
≠
synnedsättning

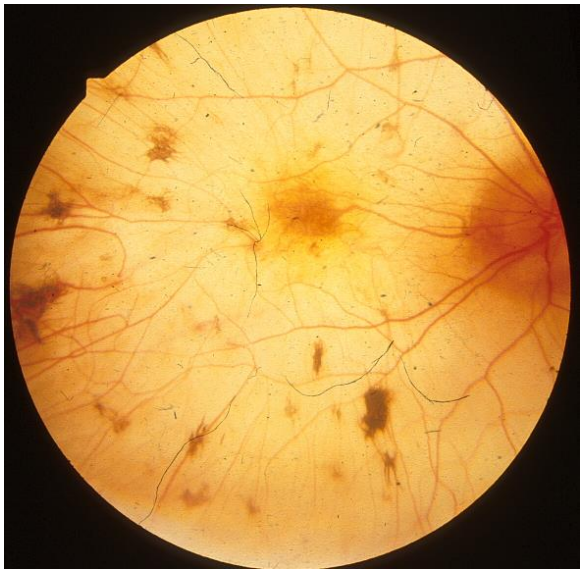




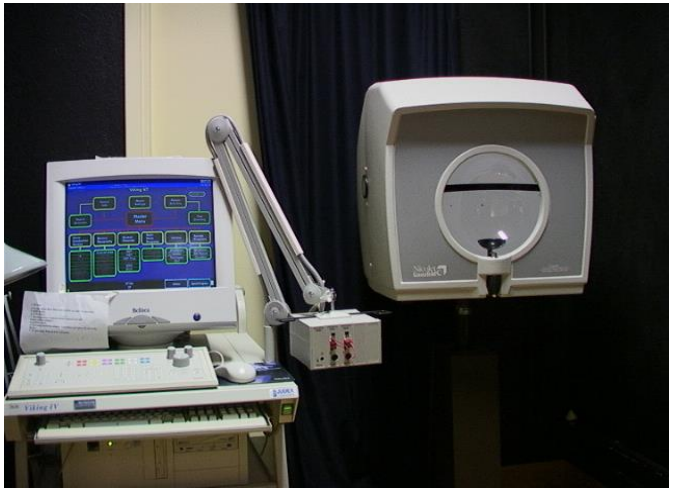


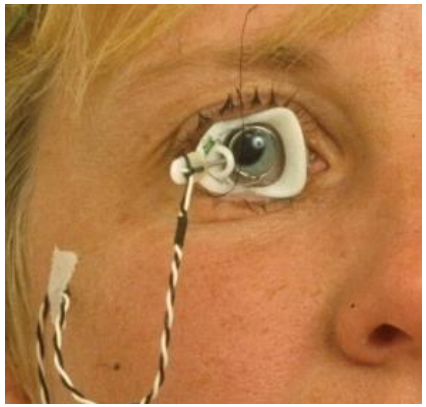


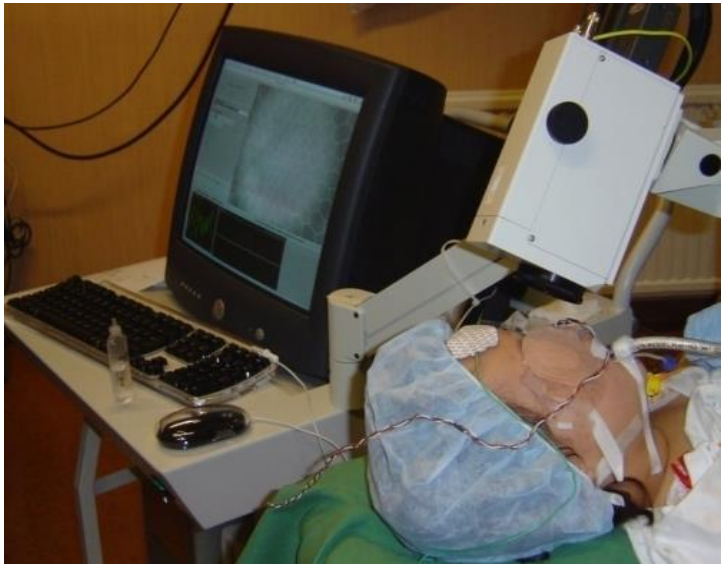


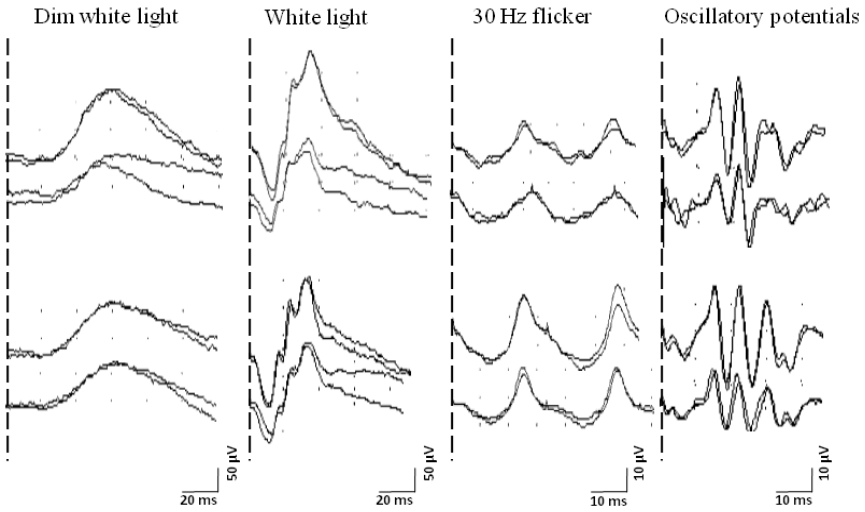


RETINAL FUNKTION

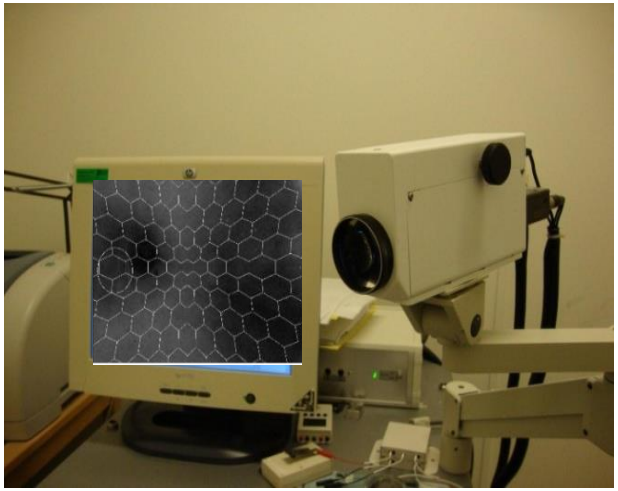


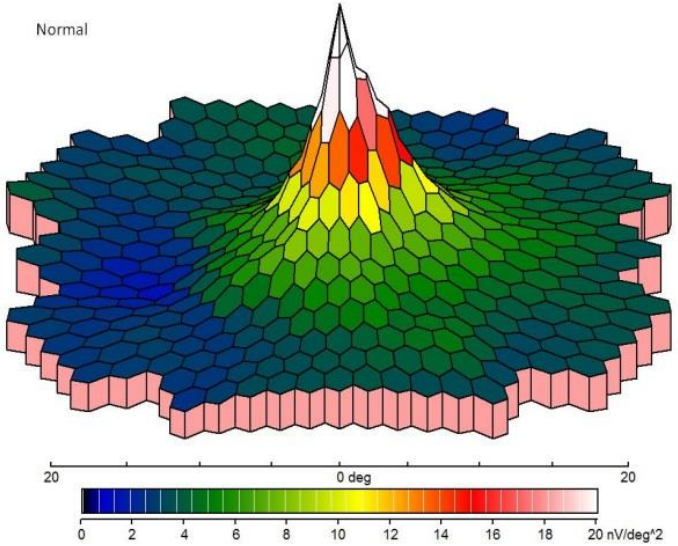


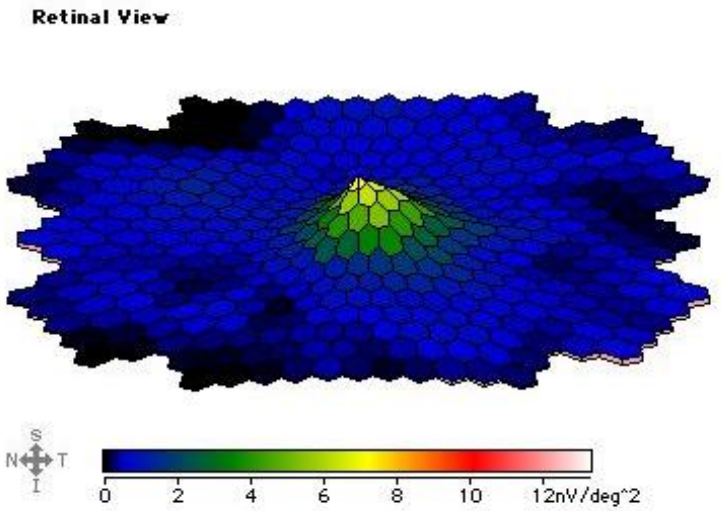




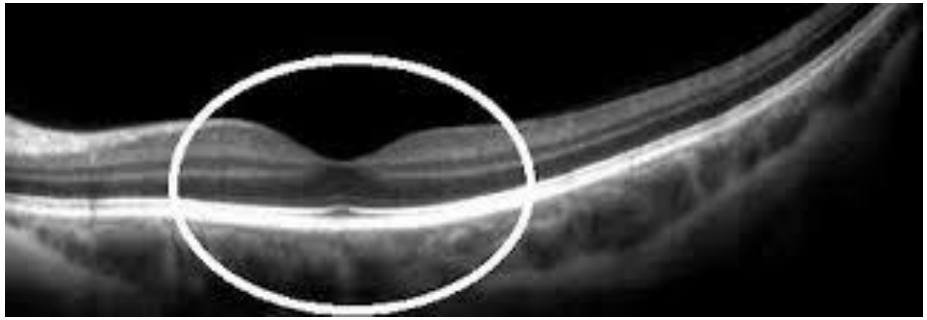
MAKULA FUNKTION

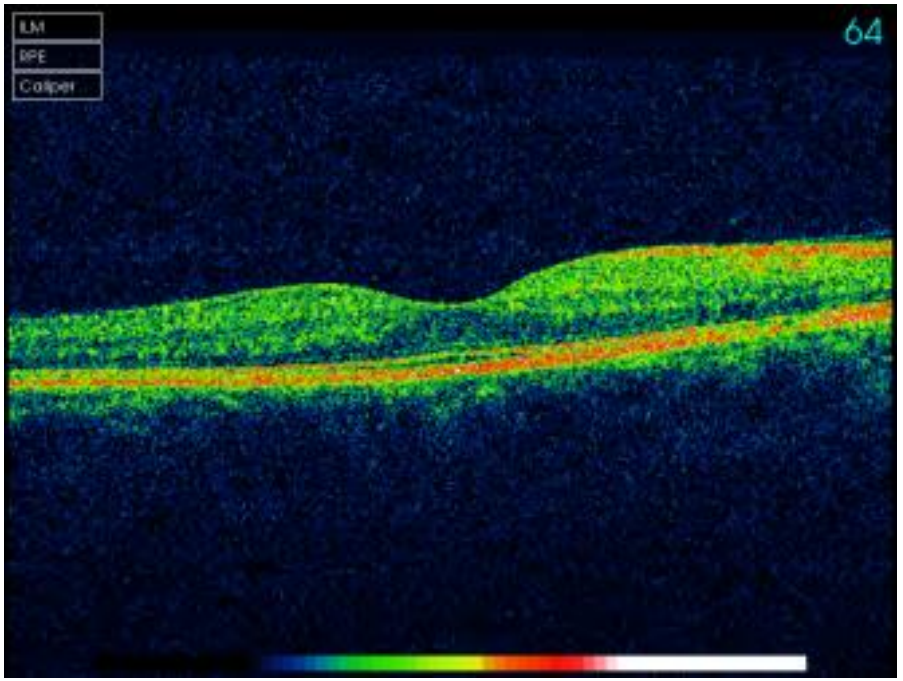


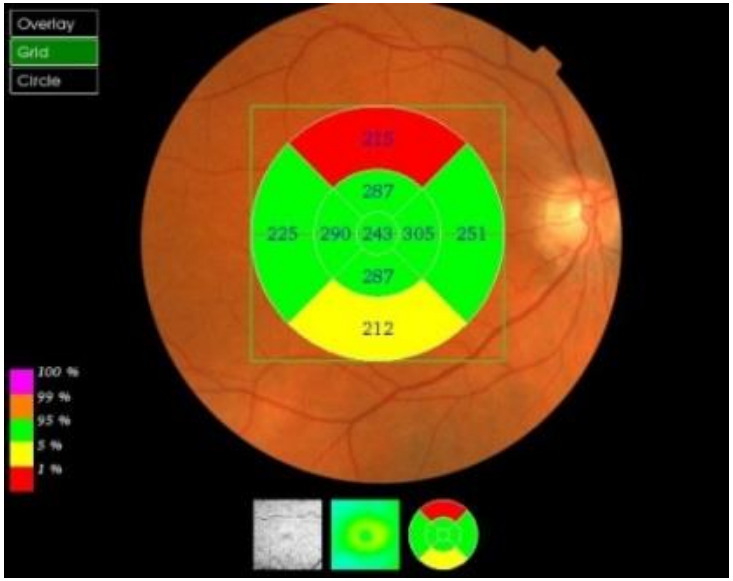


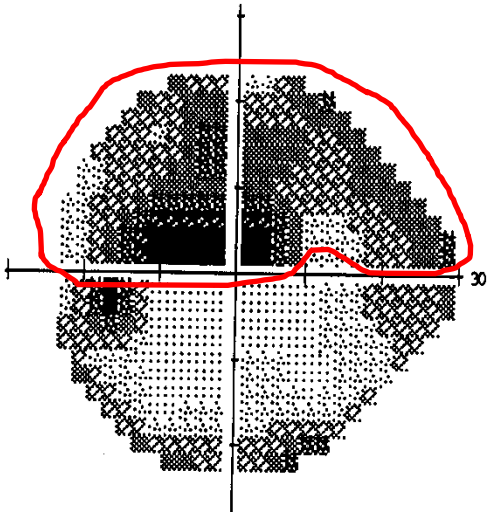


RETINAL STRUKTUR





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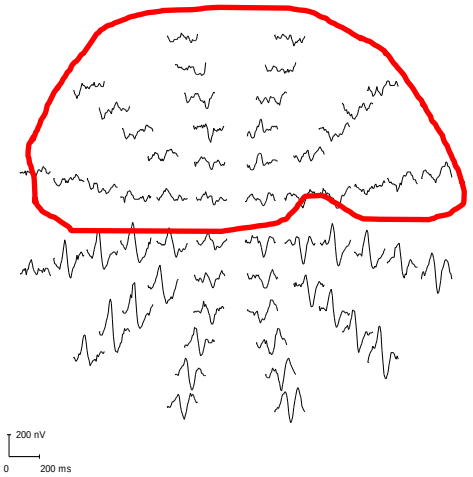
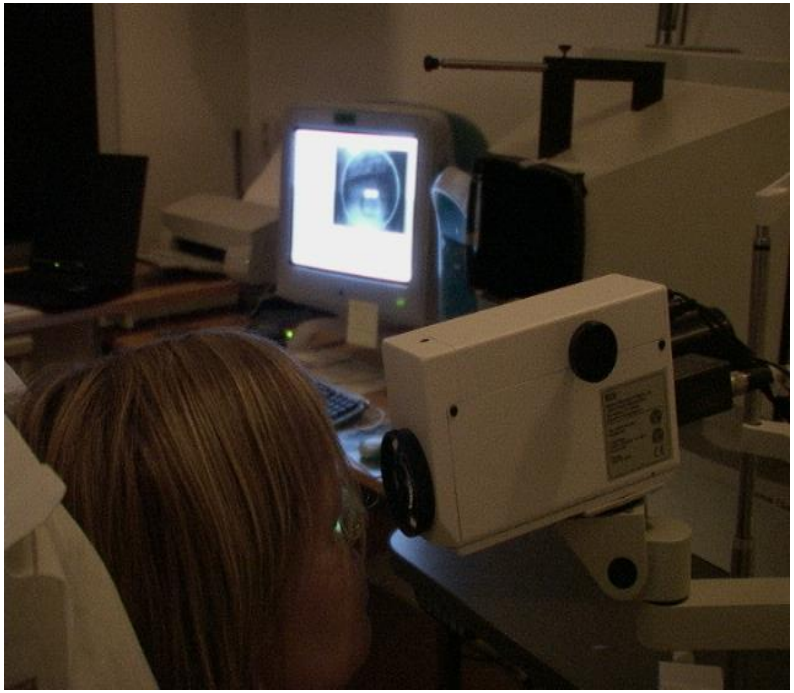
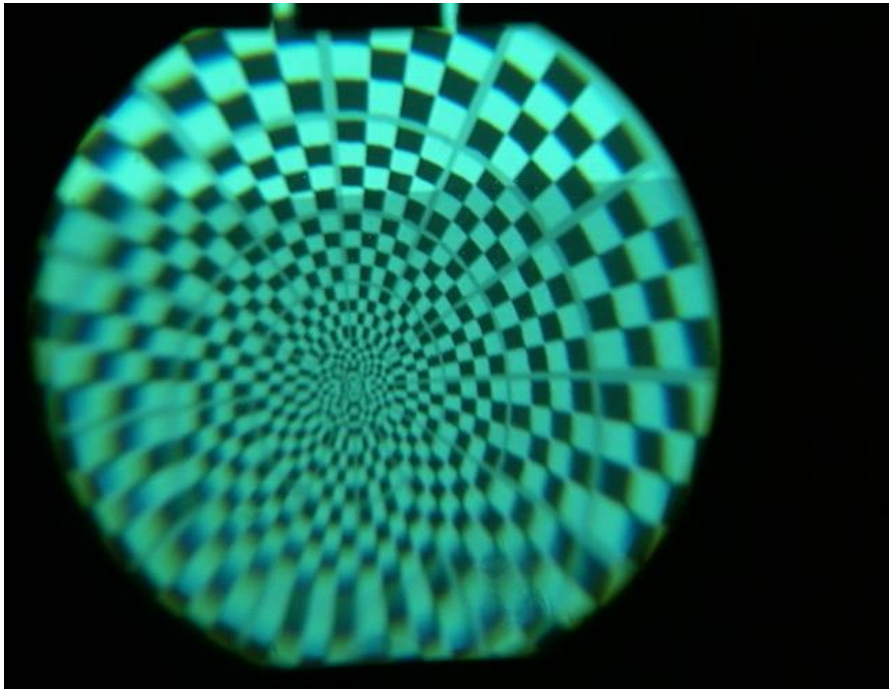

200 nV
0
200 ms





Full-fälts ERG normalt?

↓

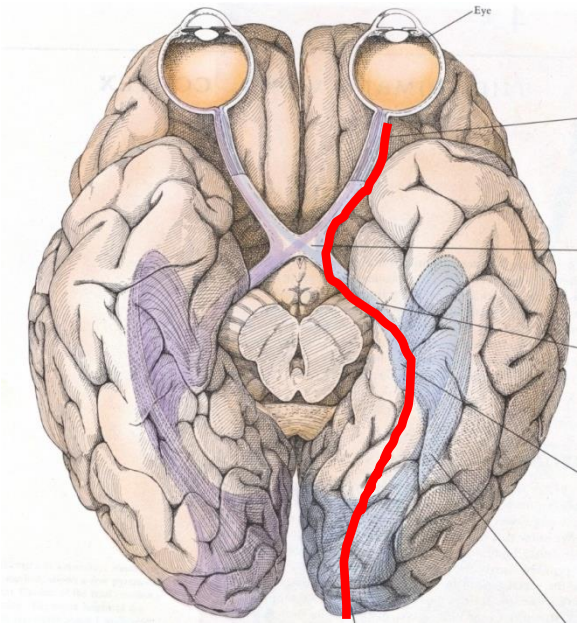
Multikokalt ERG normalt?

↓

Multifokalt VEP?

↓

DIAGNOS



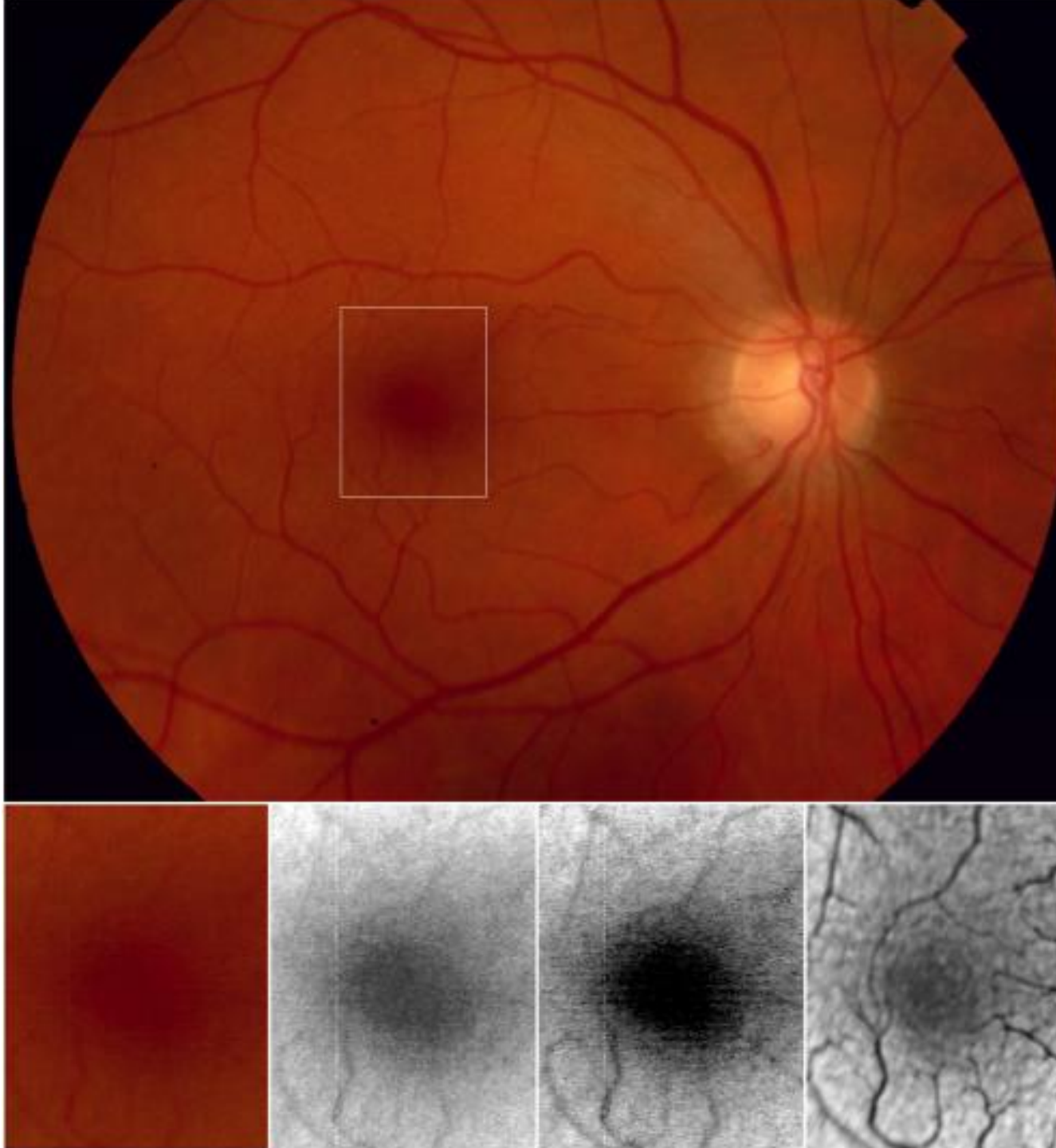
RETINAL STRUKTUR

DCAO =

Dual-conjugate
adaptive optics

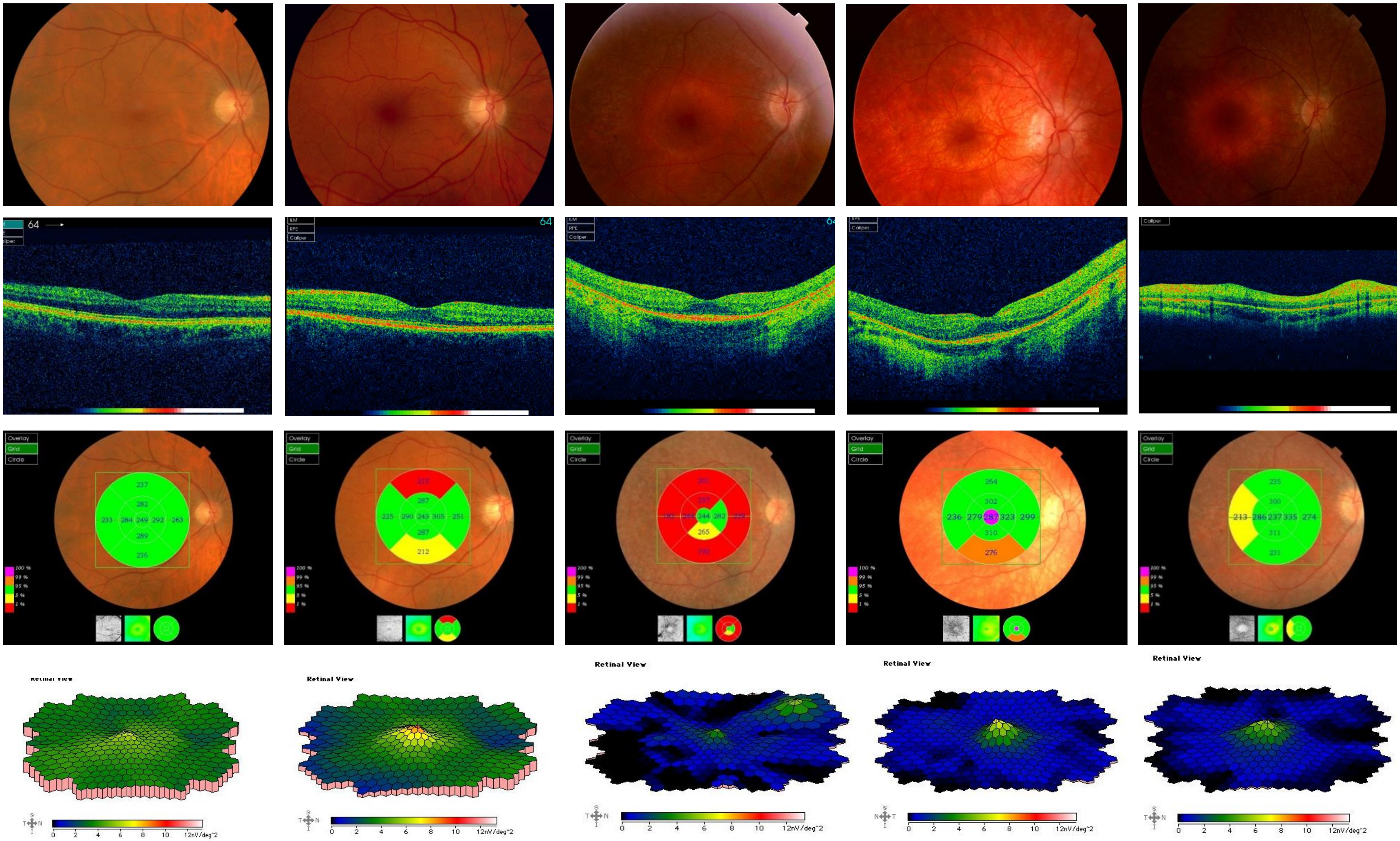
Zoran Popovic
Jörgen Thaung

Göteborgs universitet



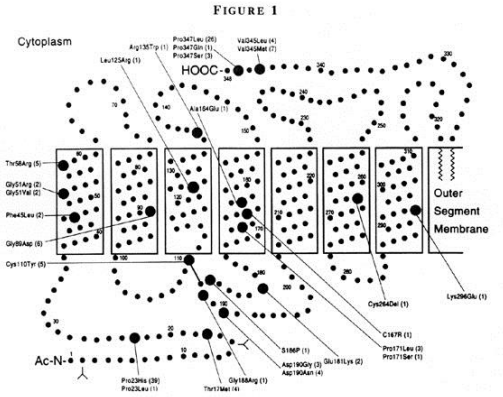
Family B

I 2 | II 1 | III 1 | III 2 | III 3



RP REGISTRET

- genotyp
- mutationer



RPGRIP
RLBP1
OPA1
RPGR ORF15
RP2
Cone alpha-SU of PDE B
CNGB3 B
CNGA3 B
Red-green (hybrid)
Bestropin
RS1
Rhodopsin
RETGC-1
RPGR A
CLN3
CHM (Rab escort p)

Peripherin/RDS
Ataxin-7
KLHL7
IMPDH1
BBS2
BBS7
BBS10
AILP1
CEP 290
GUCY2D
CRB1
RPE65
PRPF8
PRPF31
PDE6B
PDE6A

MYO7A (USH1B)
CDH23-USH1D
Usherin-USH2A
PCDH15-USH1F
RP1
CERKL
RGR
RDS
PNR/NR2E3
ABCC6
ALMS
NYX
ABCA4
DDP-1
Kearn Sayre(mtDNA)
LHON (mtDNA)

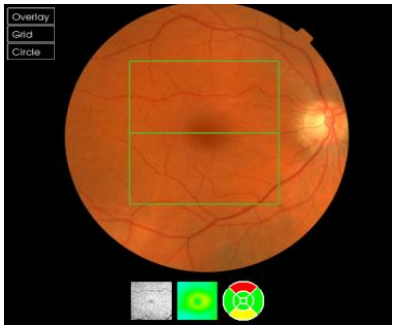
Patient II 1 in Family B with mutations in the *RHO135/GUCY2D* genes

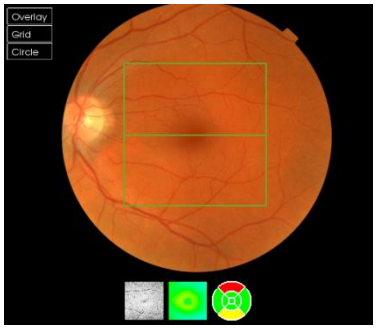
adRP PRPF31

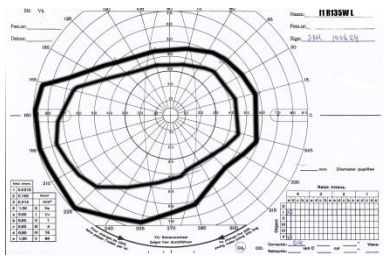
Visus:

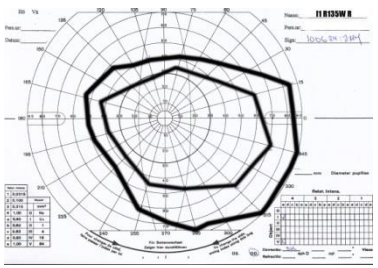
OD 0.9

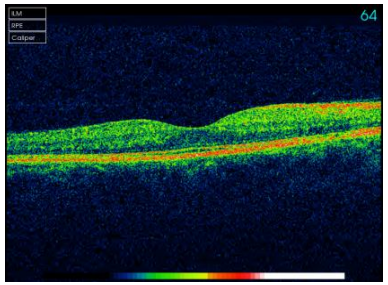
OS 0.7

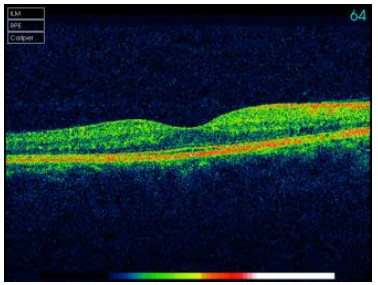


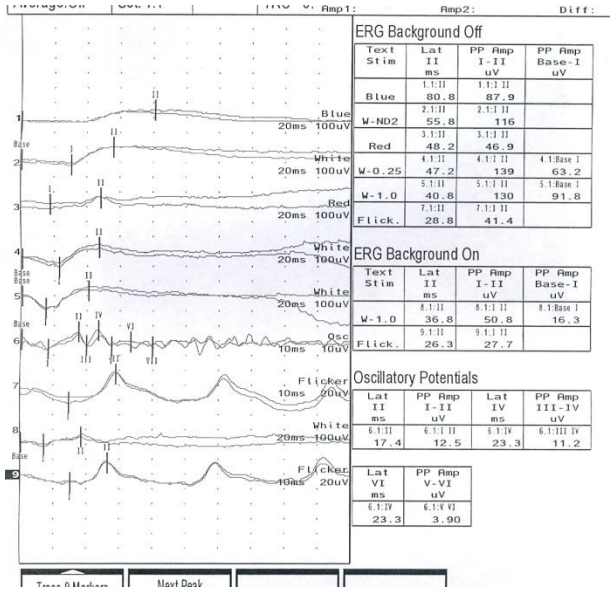


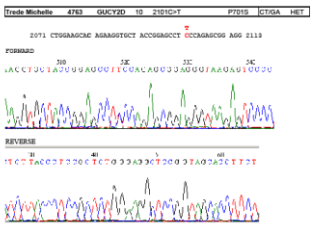


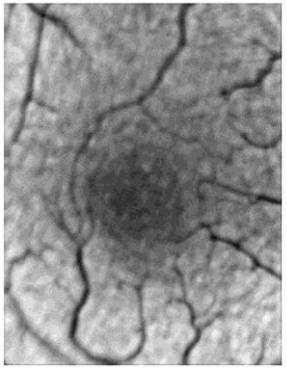


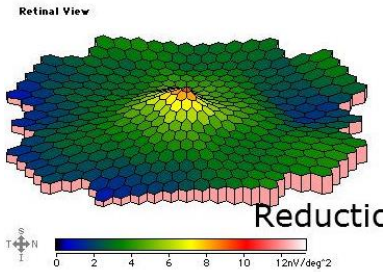


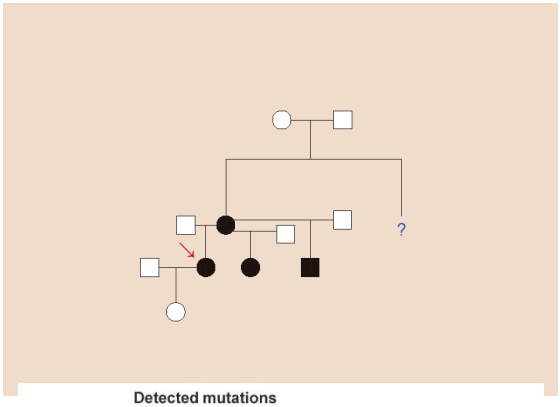












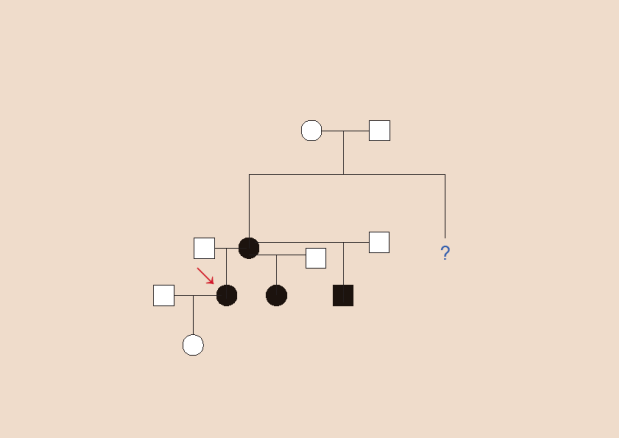
Detected mutations

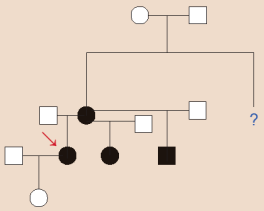
	Gene	Exon	Nucleotide change	Amino acid change	Genotyping results	Zygosity	Type of variation	Verified by sequencing
310-2167	RHO	2	403C>T	R135W	CT/GA	HET	Mut	
1120-4763	RHO	2	403C>T	R135W	CT/GA	HET	Mut	
0130-0914	RHO	2	403C>T	R135W	CT/GA	HET	Mut	

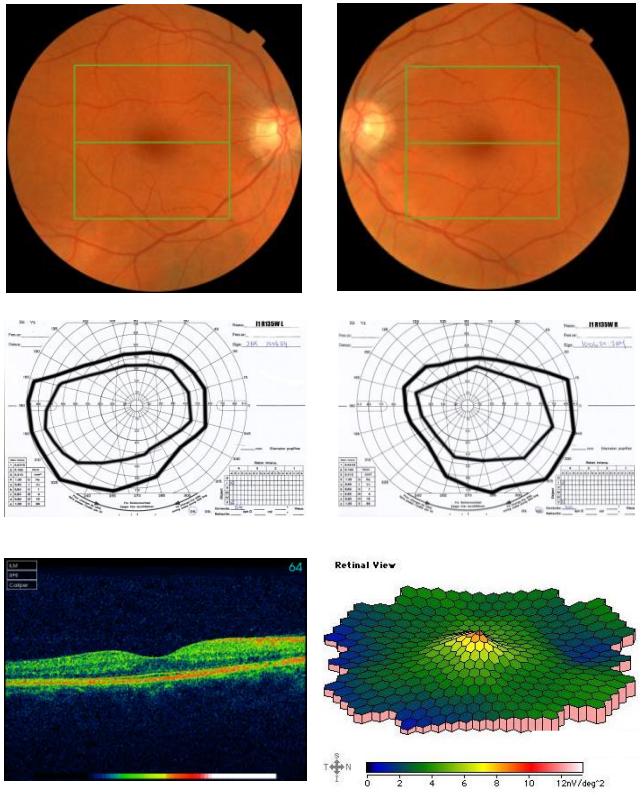
SNP - single nucleotide polymorphism
MUT - mutation that leads to amino acid substitution

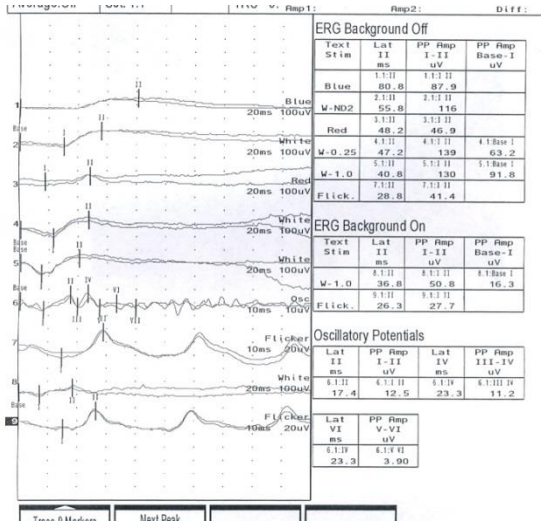
En dag på ERG mottagningen i Lund

Läkarundersökning
Sjukhistoria
Hereditet, släktskap, stamtavla
Samtal om synproblem
Information, diagnos, prognos, körkort, genetisk rådgivning
Behandling
Kurator
Syncentral
Ingen tidsbegränsning
Remiss svar









Patient med a d RP och mutations in the *RHO(R135W)* genen

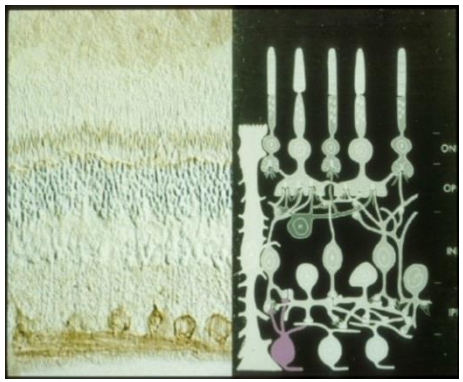
KLINISK FORSKNING

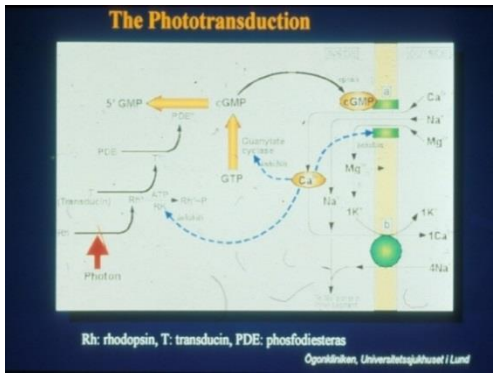
RP fenotyp – genotyp

Metodutveckling

Läkemedelstoxicitet

Vad händer egentligen i retina?





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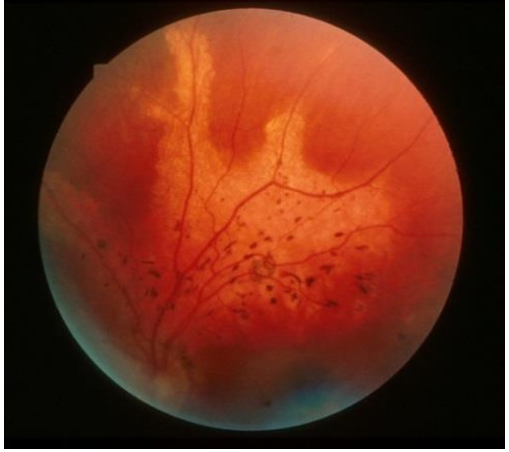
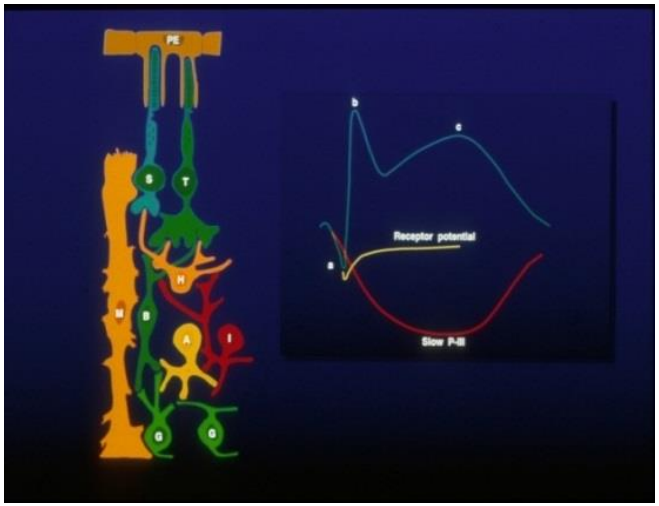
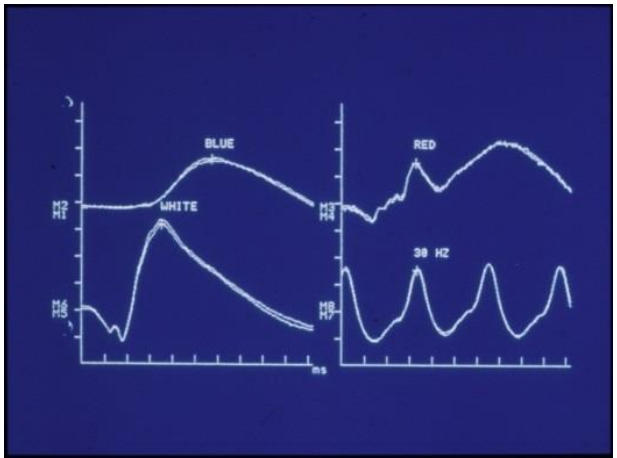
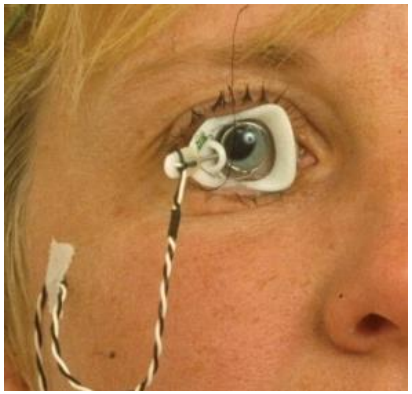
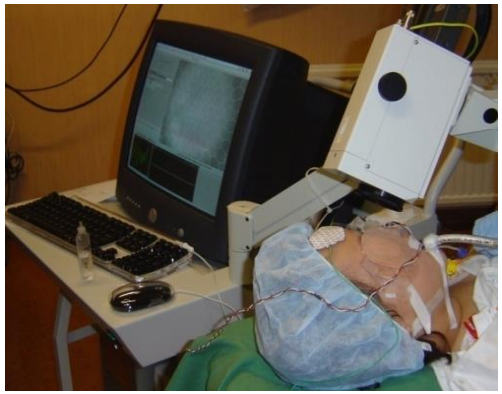


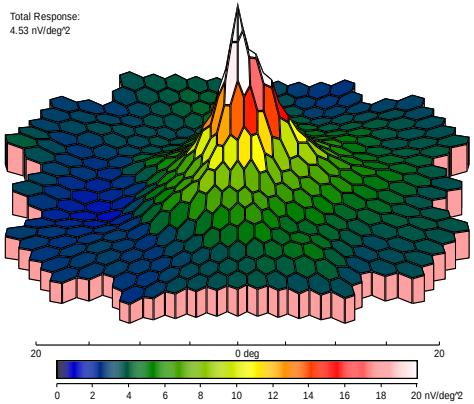




EXPERIMENTELL FORSKNING - från kliniken till labbet







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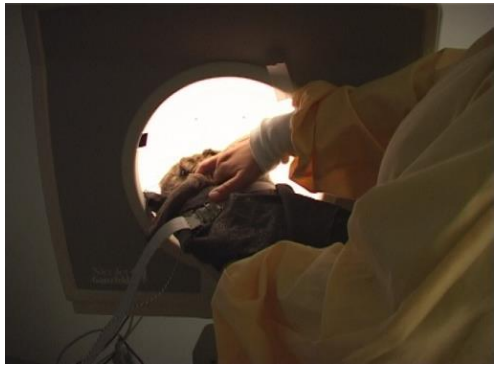
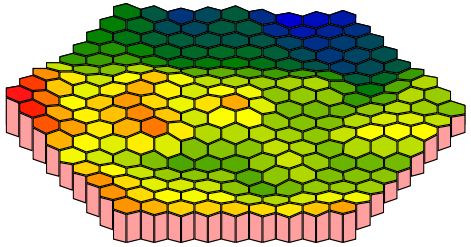
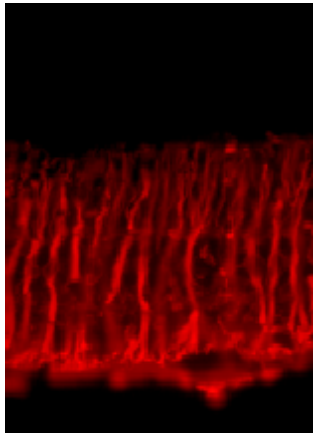
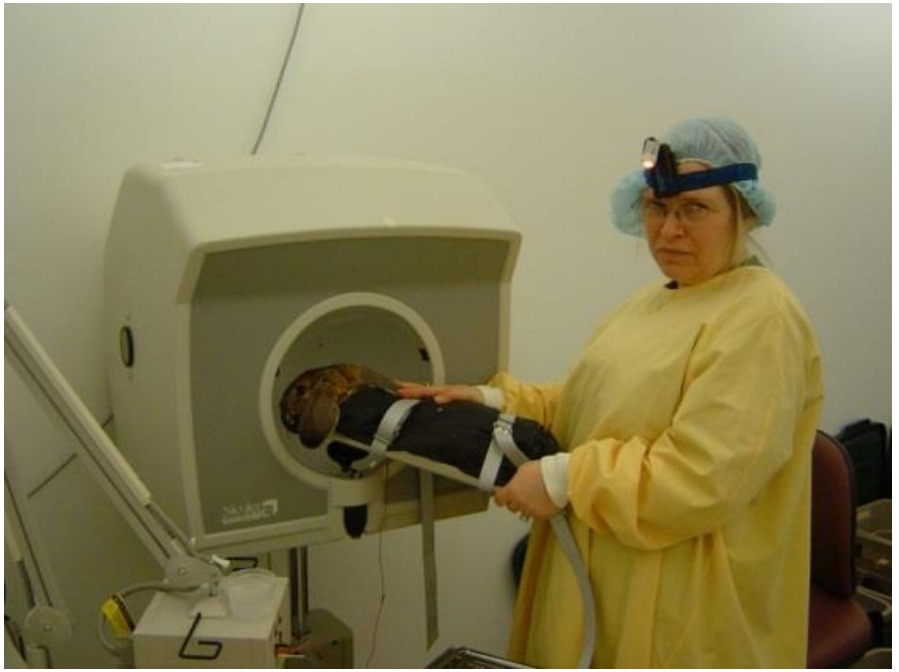
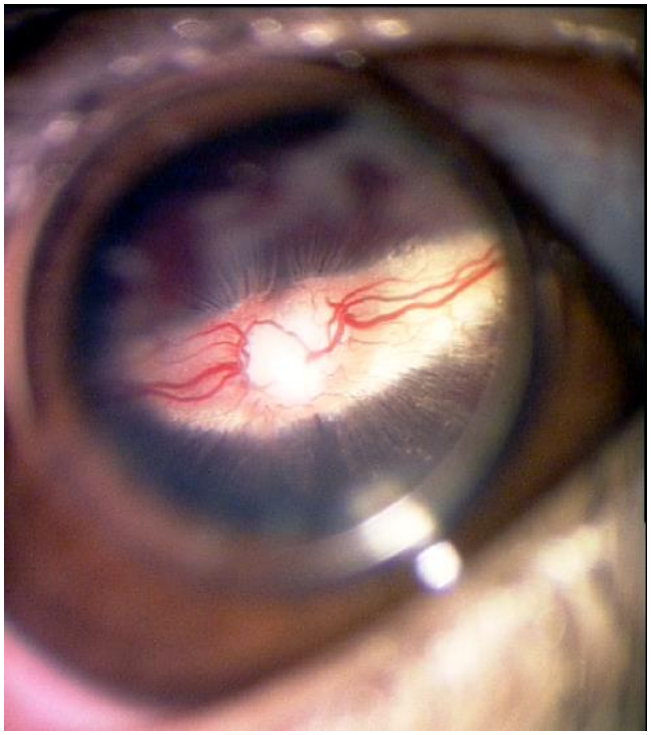


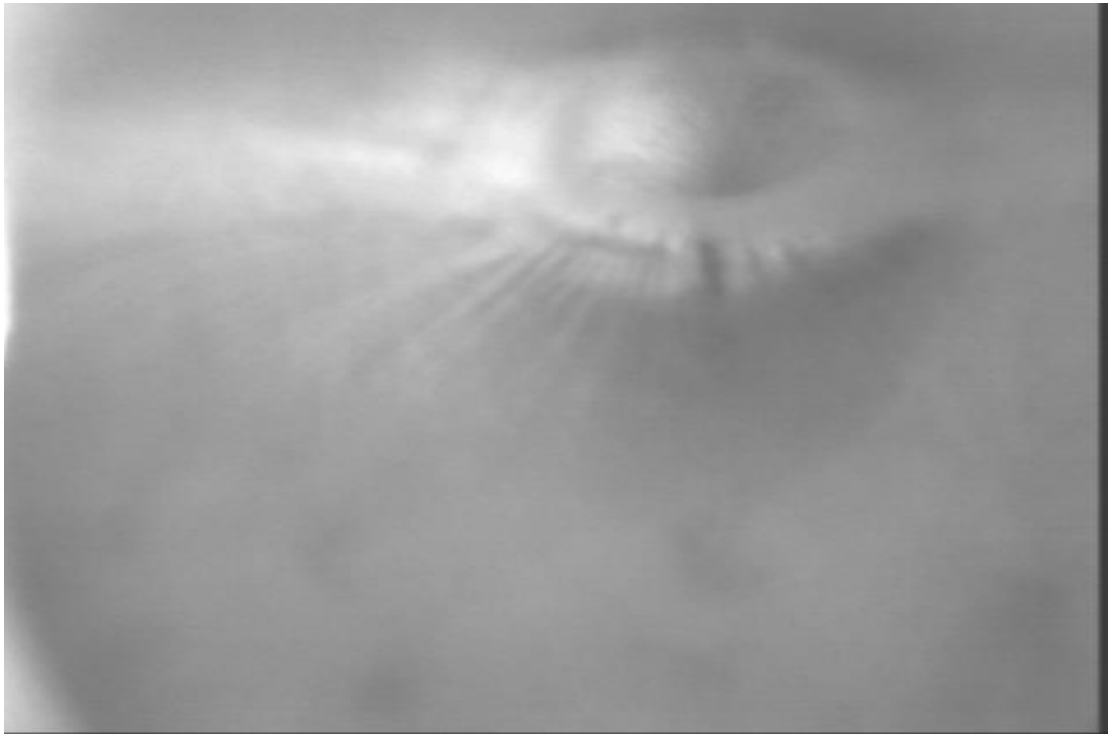


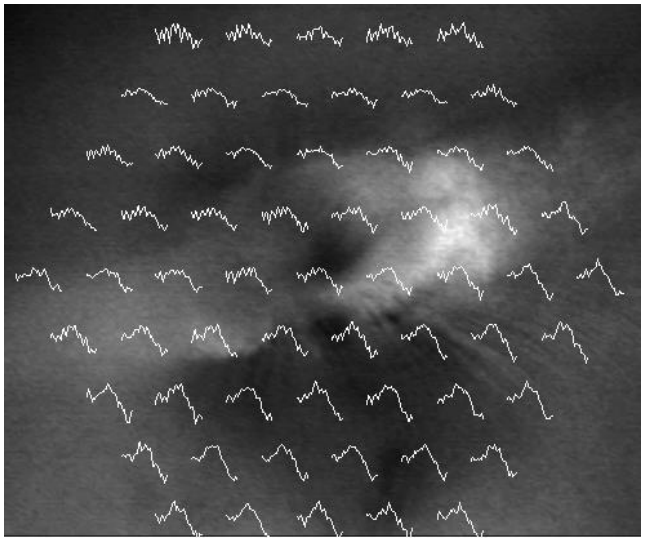


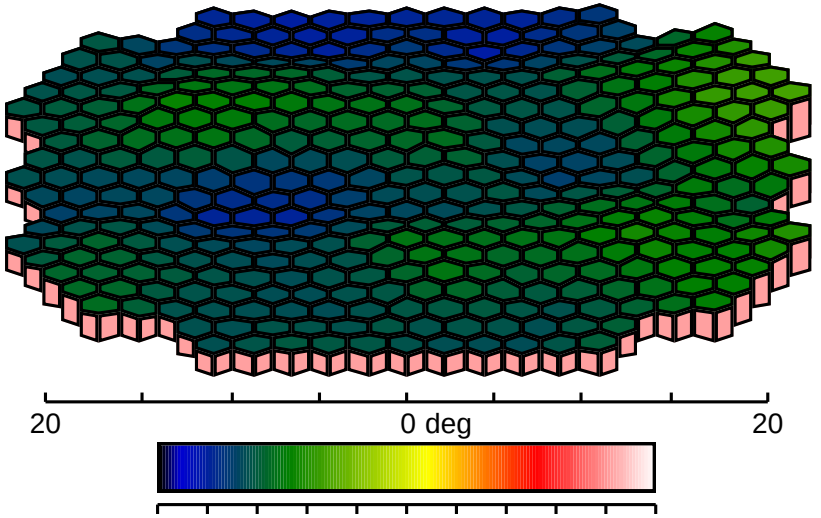
Full-field ERG In rabbit







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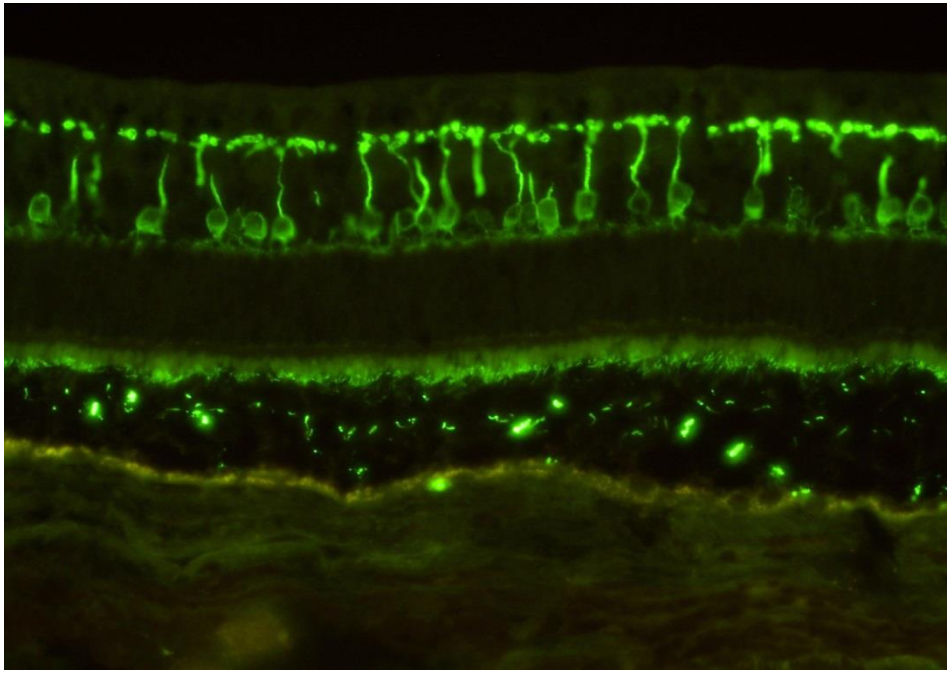

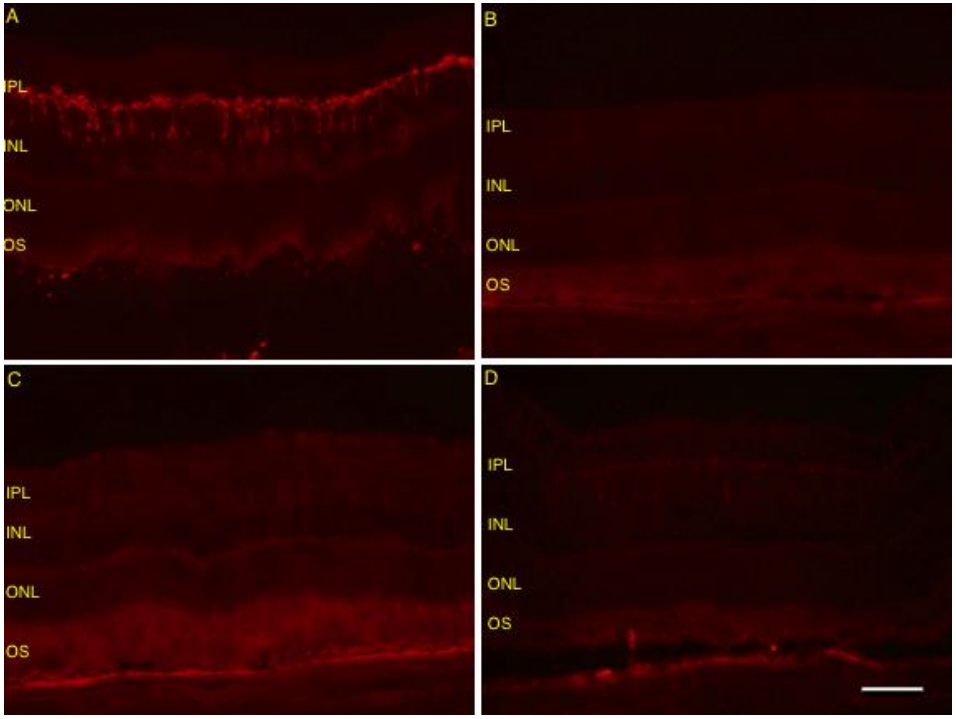
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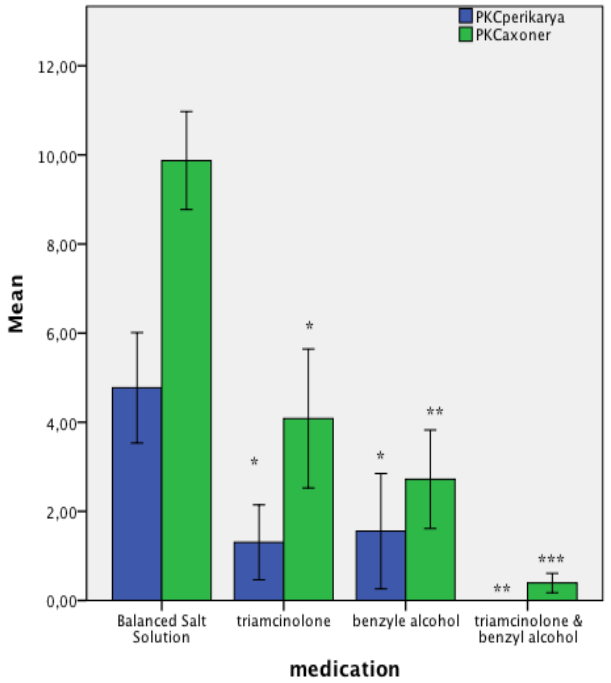
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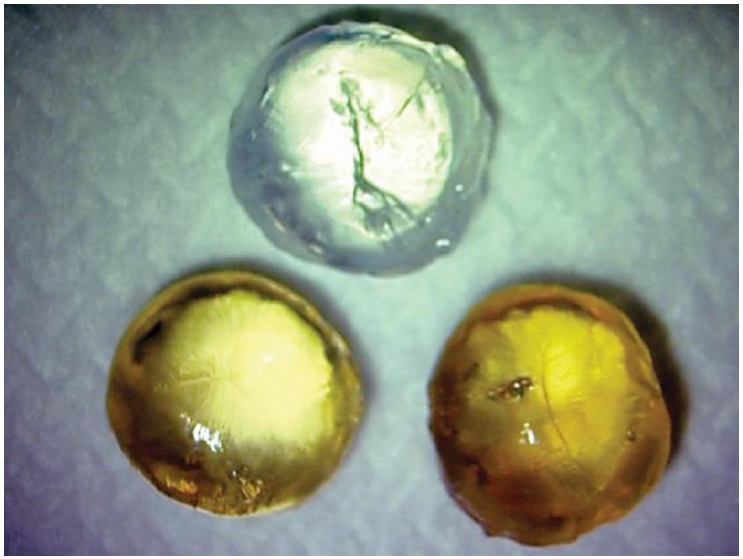


Ärftliga näthinnesjukdomar (RP)

Ärftliga gulafläck sjukdomar

Läkemedelseffekter i ögat

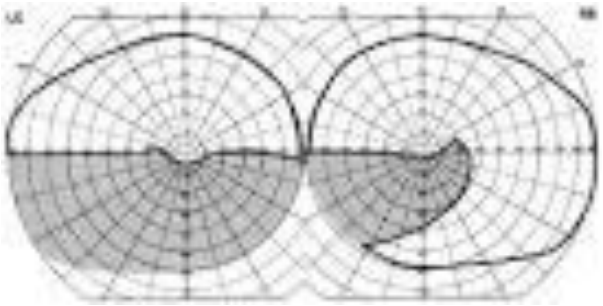
Åldersförändringar och diabetesförändringar i gula fläcken

Blodproppssjukdomar i ögat

Effekter av näthinnekirurgi i ögat

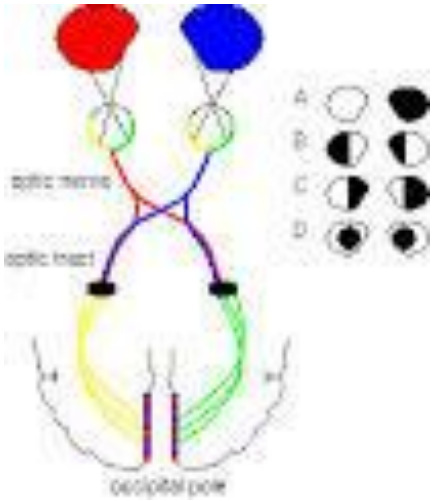
Synnervssjukdomar

Neurooftalmologi

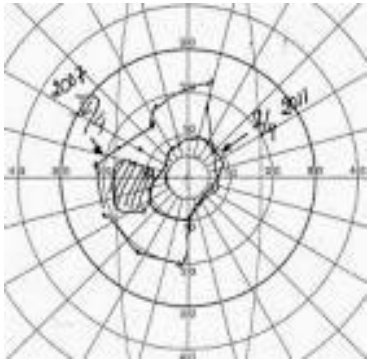


Synfältsdefekter

- Altitudinell synfältsdefekt (optikusinfarkt)
- Homonym hemianopsi (cerebral patologi)
- Koncentriska s f defekter (funktionell)



S ofta lågt, svårt att bedöma utan att karakterisera synfältsdefekten.

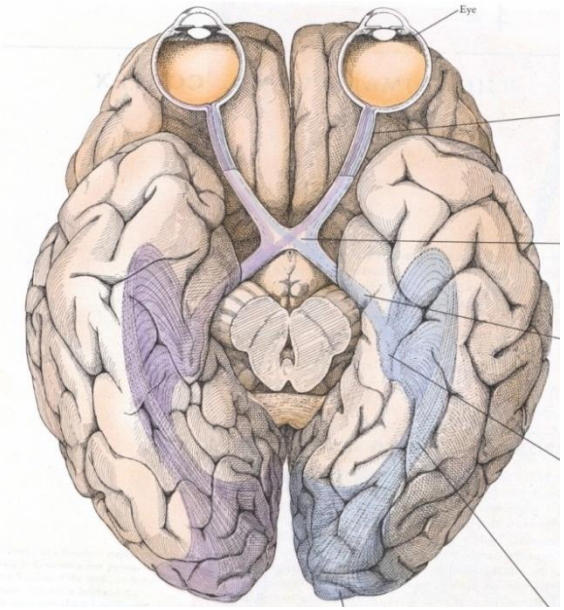


Neurokirurg

”Ögat är helt enkelt en utbuktning av hjärnan….”

Oftalmolog

”Hjärnan är helt enkelt en utbuktning av ögat….”



Endogena depressioner

- 25-50% av befolkningen drabbas av depression någon gång i livet
- Heterogen sjukdom, svår diagnos kliniskt
- Biomarkör saknas (MRT hjärna, CT-PET, EEG(Q), LORETA, genetics, proteomics-liquor, BDNF i serum, mm.)
- Nya behandlingar på gång, effekt redan inom några timmar, mätmetod behövs för evaluering av effekt och monitorering av behandling

Tidigare studier har visat påverkad synfunktion:

1. Kontrastseende ↓
2. Pattern ERG ↓
3. Full-fälts ERG ↓
4. EOG ↓
5. Färgseende (subj. försämring) ↓

20 pat med ”egentlig depression”
MDD – major depressive disorder

- S
- Lix
- BK
- Ishihara
- SST
- Kontrastseende
- SF
- mfVEP
- fERG
- mfERG
- OCT
- Fundusfoto
- Läkarbedömning

Finns det en biologisk markör för endogen depression?

Målsättningar

- Förbättra diagnostik
- Gradera sjukdom
- Utvärdera behandlingseffekt

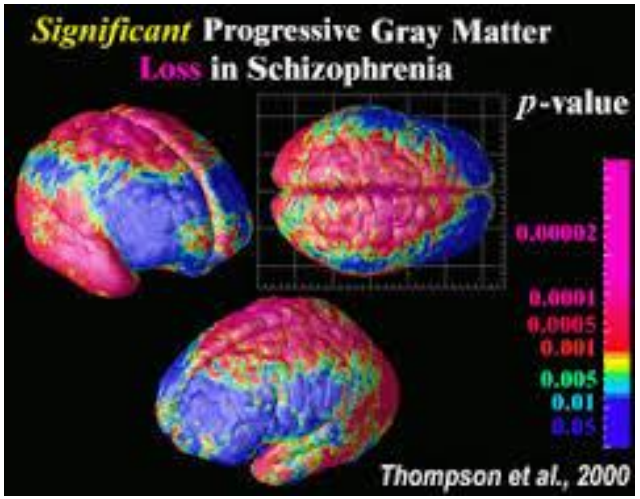
Fler psykiatriska diagnoser

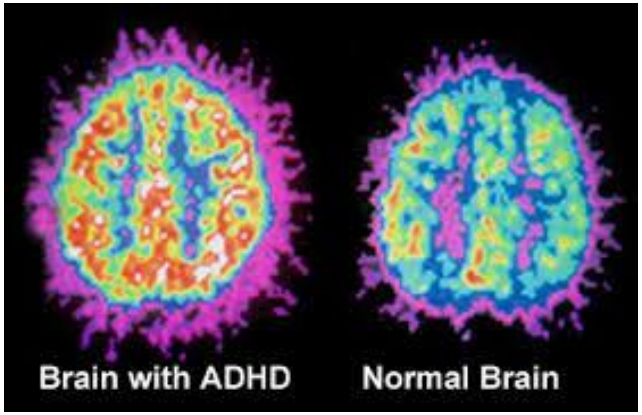
Schizofreni

ADHD

Autism

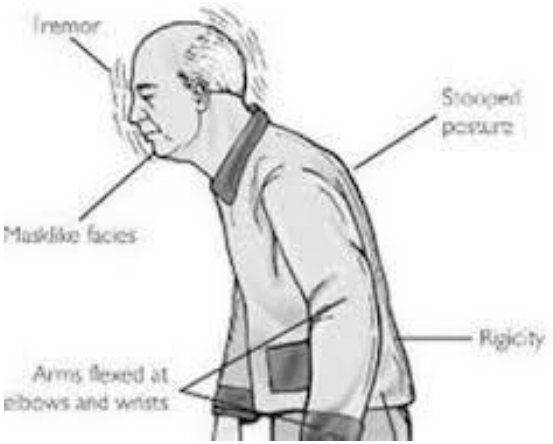
Beroende (droger, alkohol)





Neurodegeneration

- Parkinsons sjukdom
- Alzheimers sjukdom
- Multipel skleros



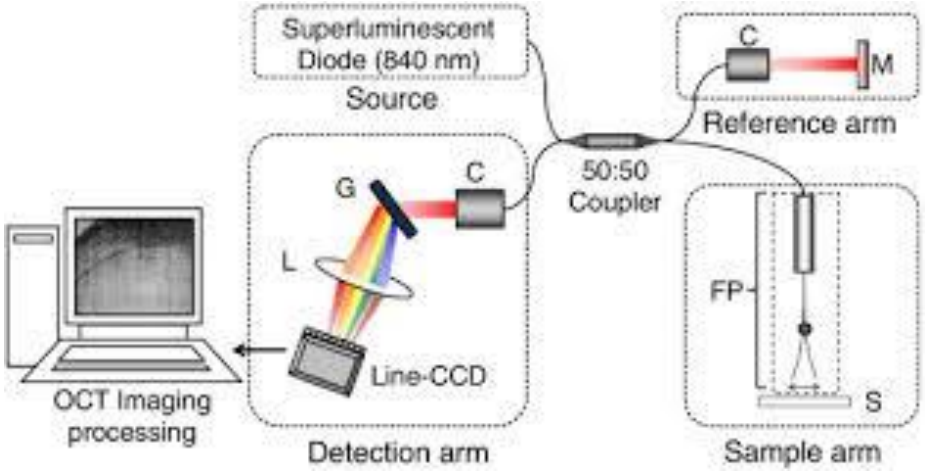
Parkinson	Alzheimer	Multipel skleros
OCT (RNFL ↓, fovea ↓)	OCT (RNFL ↓, fovea ↓)	OCT (RNFL ↓, fovea ↓)
p ERG	p ERG	p ERG
mf ERG	mf ERG	mf ERG
p VEP	p VEP	p VEP
Kontrastseende ↓	?	Kontrastseende ↓

OCT =

Optical coherence tomography

Tvärsnittsbilder (tomogram)

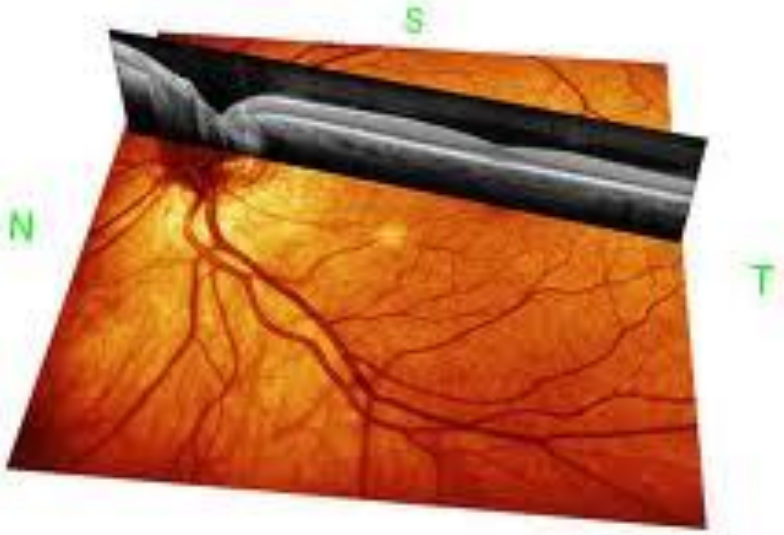
Analog till B-mode ultraljud

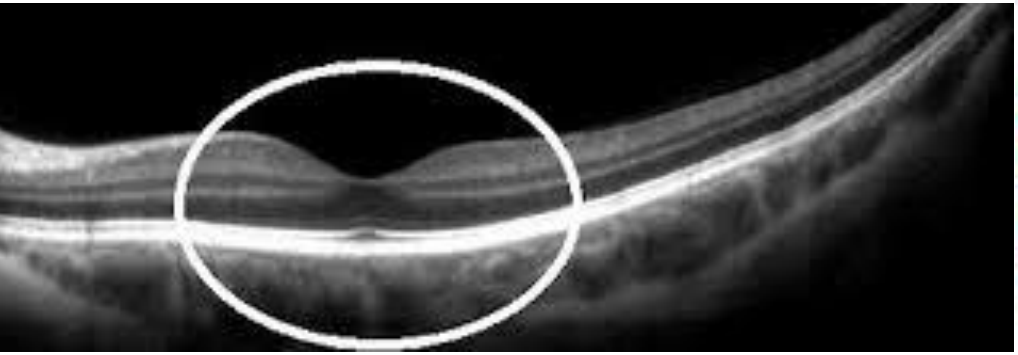


Kräver inte kontakt med vävnaden som vi undersöker = icke-invasiv

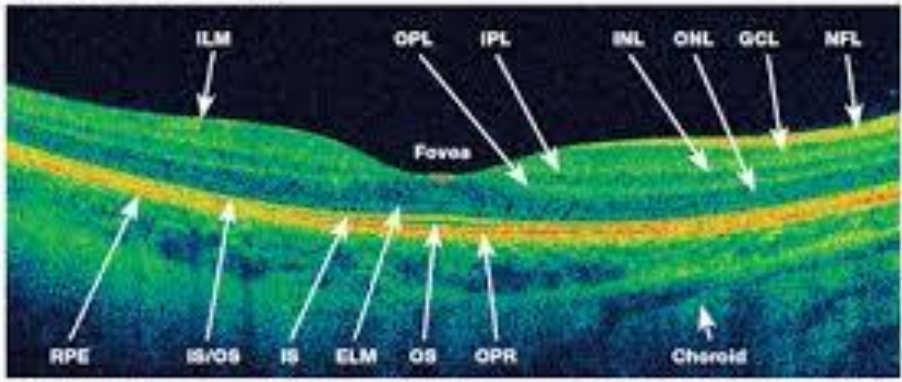
Teknologi
Low-coherence interferometry
Near-infrared ljusstråle (840 nm) riktas mot vävnaden

OCT mäter de reflekterade ljusstrålarna avseende magnitud och lokalisation.



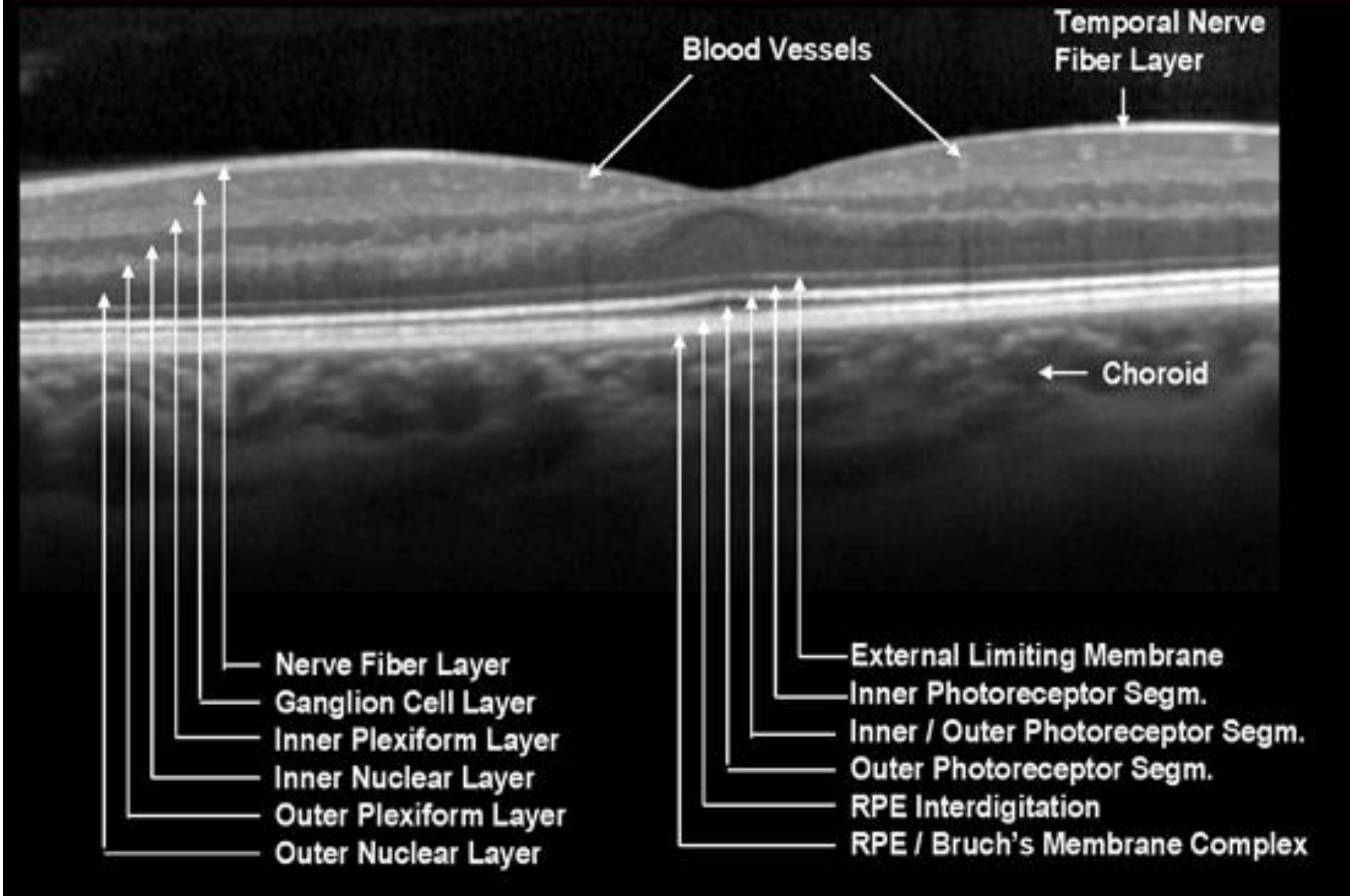


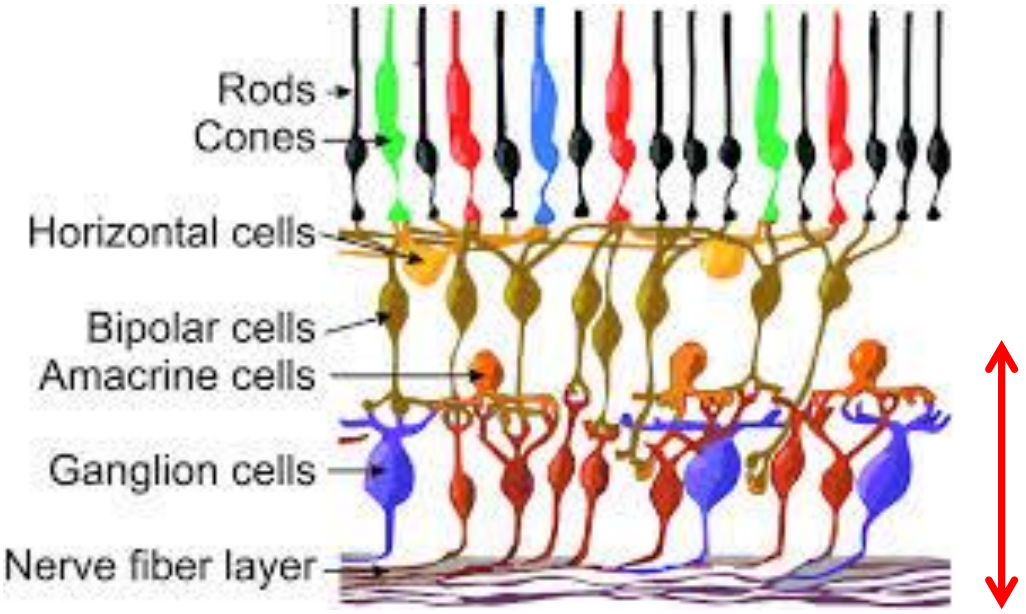
An HD-OCT scan of a healthy eye



NFL: Nerve fiber layer
ILM: Inner limiting membrane
GCL: Ganglion cell layer
IPL: Inner plexiform layer
INL: Inner nuclear layer
OPL: Outer plexiform layer
ONL: Outer nuclear layer
ELM: External limiting membrane
IS: Photoreceptor inner segment
OS: Photoreceptor outer segment
IS/OS: Interface between IS and OS
RPE: Retinal pigment epithelium
OPR: Outer photoreceptor/RPE complex

Retinal Labeled Layers (Image zoomed to ~15°)





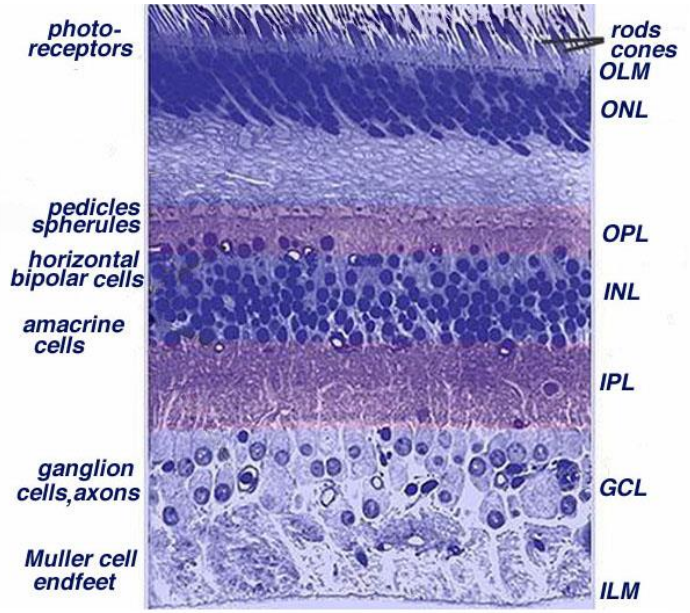
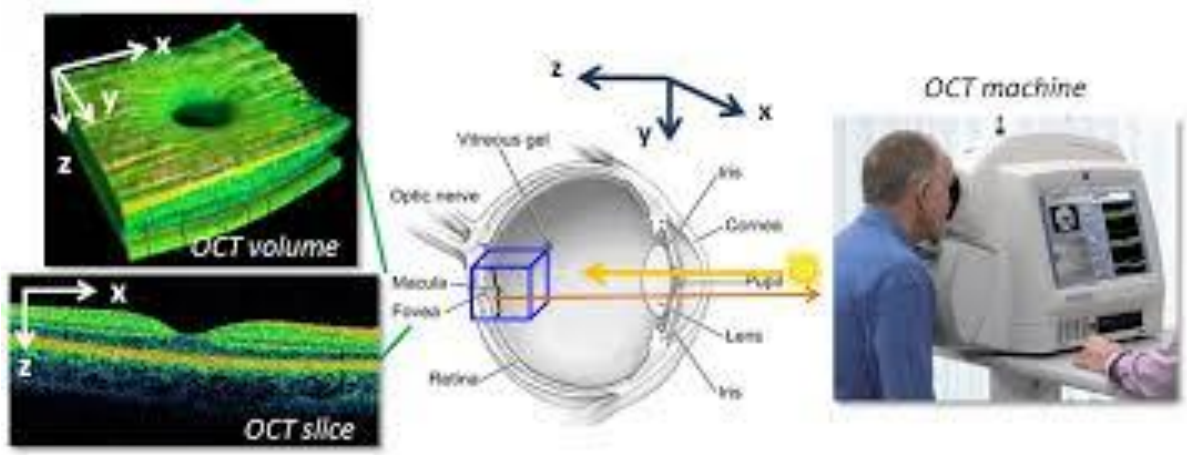


Fig. 3. Light micrograph of a vertical section through central human retina.

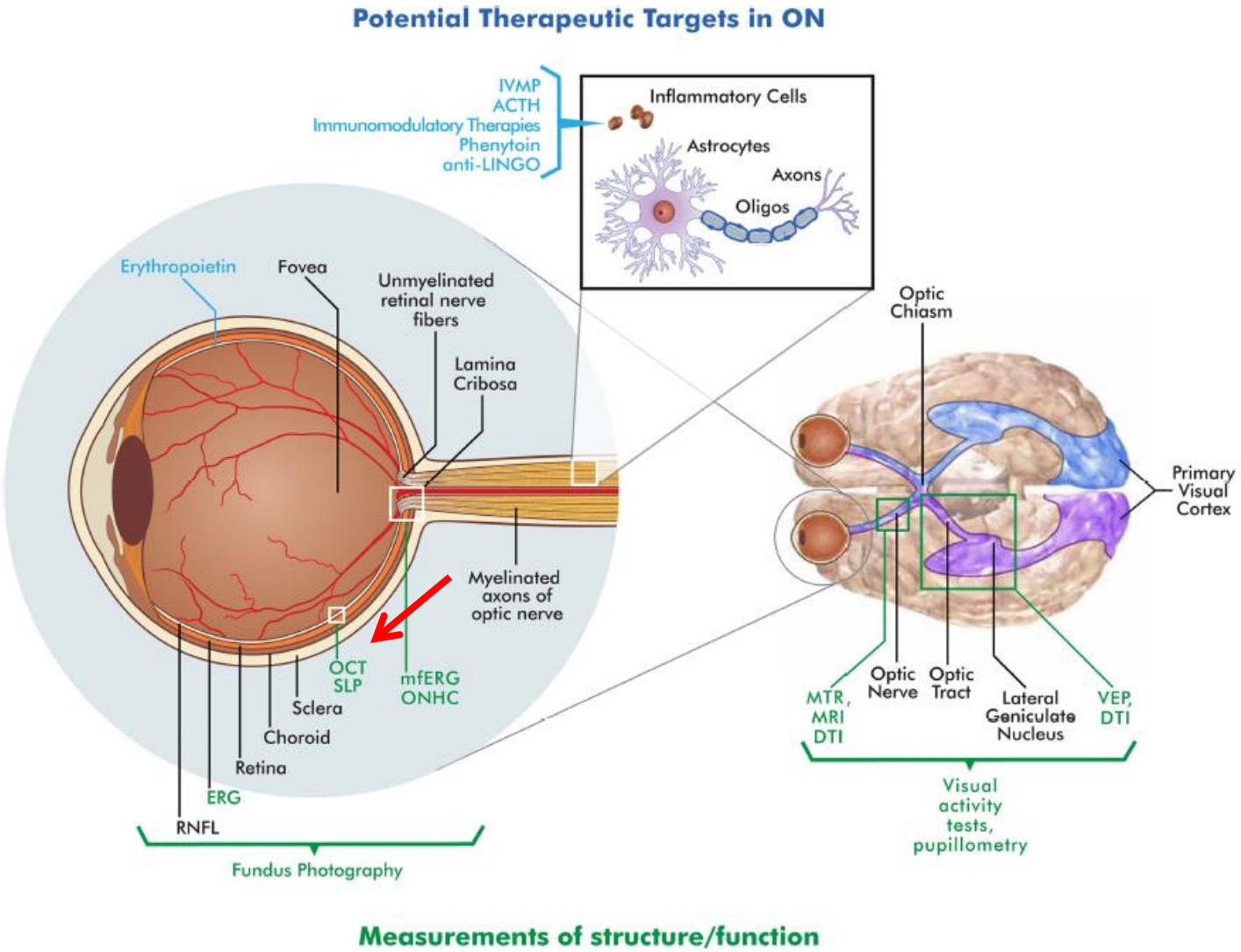
RNFL + GCL + IPL ett mått på neurodegeneration?

1. Cross scan
2. 7Line Raster Scan
3. Radial Scan
4. 5Line Cross Scan
5. 3D Macula Scan
6. 3D Vertical Scan
7. 3D Wide Scan
8. 7Line Raster vertical Scan
9. Line Scan

RNFL
GCL
GCL + IPL
Macula thickness
Macula volume



Bennett et al. *JNNP* 2015;86(7):709-808



Multipel skleros

Biological markers of prognostic value

MRI
- High resolution imaging
- Brain volumetry
- Magnetisation transfer imaging
- Magnetic resonance spectroscopy
- Cervical cord pattern
- Ultra-high-field MRI

OCB = Oligoclonal bands
- CSF IgG, IgM

Antimyelin Antibodies

Visual pathway (”MS VisualPath study)
- Visual acuity Sloan (HCVA and LCVA)
- Color vision HRR
- mf VEP
- Fundus imaging
- OCT (RNFL thickness and macular volume)

Ingen enskild biomarkör kan uppfylla målet – att ge en tidig prognos

”More complex bio marker panels or signatures…”

Kombination av flera olika biomarkörer?

Multipel skleros

Retinal imaging and funktion

- OCT (RNFL ↓ , fovea ↓) ✓
- mfERG ✓
- pERG
- mfVEP ✓
- pVEP

Kan OCT prediktera sjukdomsgrad vid MS?

Petra Nilsson	Neurologkliniken
Magnhild Sandberg	Neurologkliniken
Kasim Abul-Kasim	Bild och funktion

Alla patienter som kommer till neurologen med nydiagnos MS

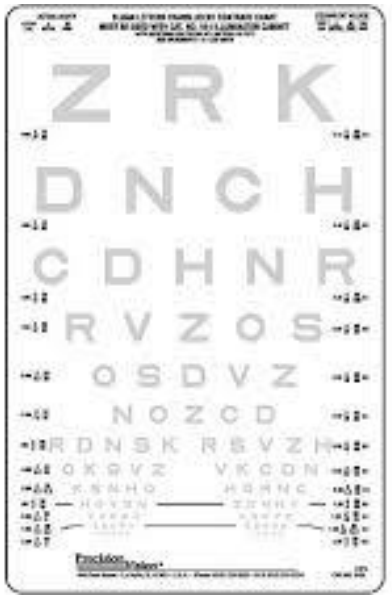
Neurologens dagvårdsavdelning?

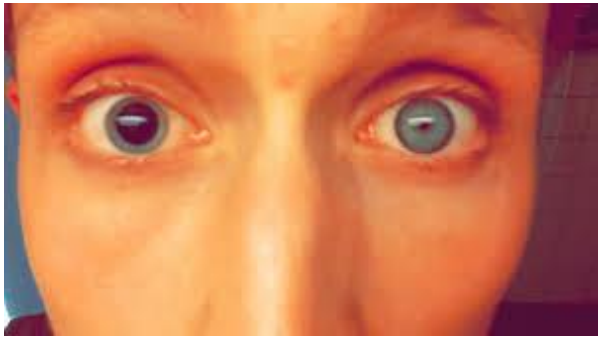
Samma dag, 30 min på ögonkliniken

Uppföljning – 3 mån, 1 år, och sedan årligen

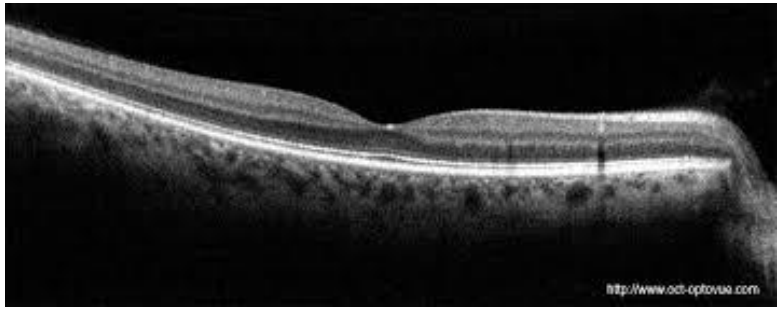
Synskärpa

Kontrast





Pupill dilatation endast 1 öga



OCT

OCT som biomarkör för neurodegeneration

PLANERING

1. Etisk ansökan ✓
2. Kontakta tillverkare och diskutera lämpligt protokoll ✓
3. Konsultera statistiker betr. powerberäkning och metoder
4. Inhandla Sloan kontrasttavla ✓
5. Skapa protokoll ✓
6. Startdatum

Att förstå neurodegeneration - framtiden

Kan OCT förbättra diagnostik av Parkinsons sjukdom?

Kan OCT förbättra diagnostik av Alzheimer sjukdom?

Kan synfunktion och elektrofysiologi ge information om biologiska processer i hjärnan?

Att förstå synnedsättning - framtiden

- Metodutveckling
- Forskning – klinisk och djurexperimentell
- Tänka ”bortom ögat”
- Delge resultat till patient, familj, ansvariga läkare och syncentraler
- Fortsätta en strävan mot att minska blindhet

Sten Andréasson

Ingmarie Holst

Boel Nilsson

Lena Mitkiewicz

Ulrika Kjellström

Lotta Gränse