Ospedale Garibaldi-Nesima Catania
U.O.C. Oftalmologia
Direttore F.F.: Dott. Antonio Marino

Dawn of a New Era in Imaging

We make it visible

Performance e successi degli OCT/Angio-OCT

Studio Oculistico
In Oculis Salus
dott. A. Lucente

www.amedeolucente.it

Foreword: 25 Years of Optical Coherence Tomography

by:James Fujimoto and David Huang

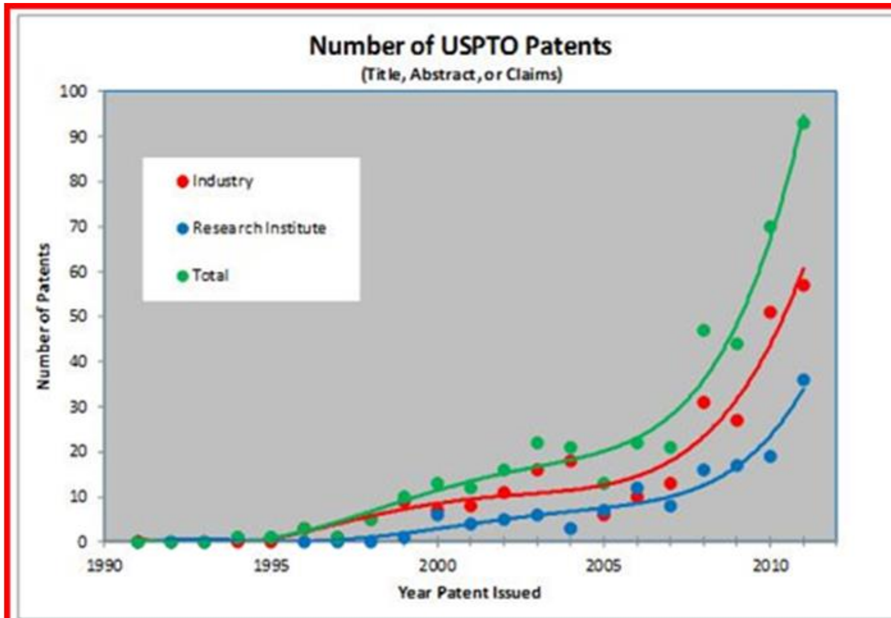
$1B\$ = 10^{9} \neq 1B€ = 10^{12}$

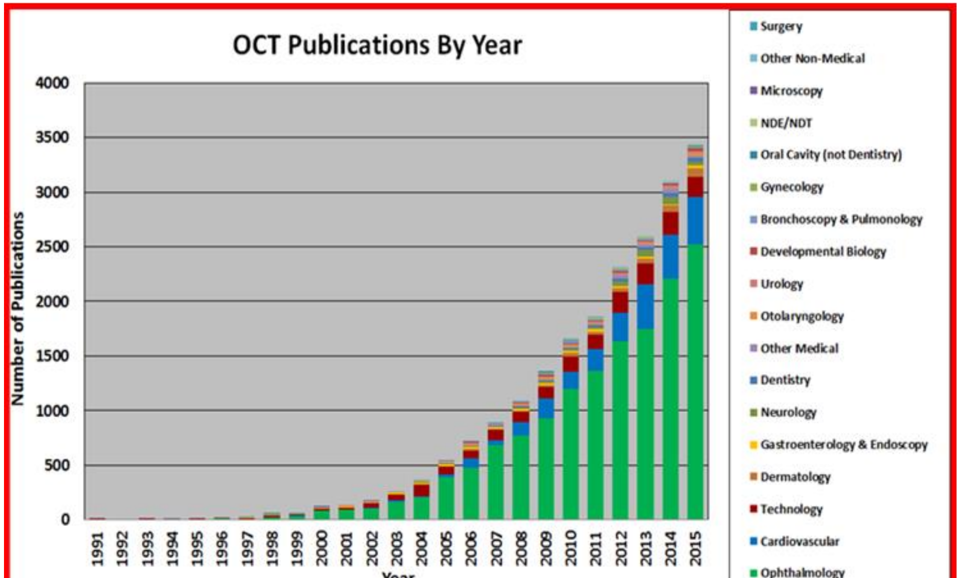
Scale metriche ≠ dal 1974

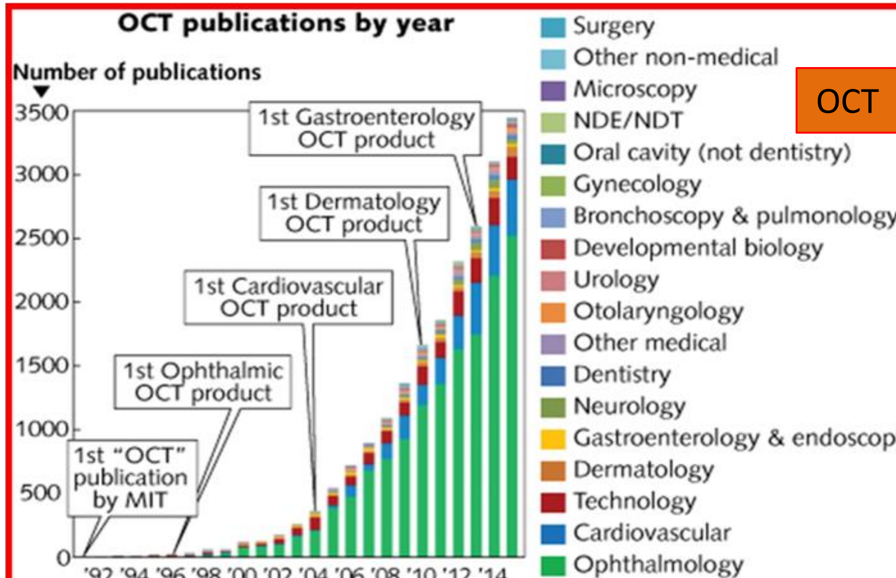
The market is just over $1B in 2012, and it is expected to grow by 18–30% per year for the foreseeable future

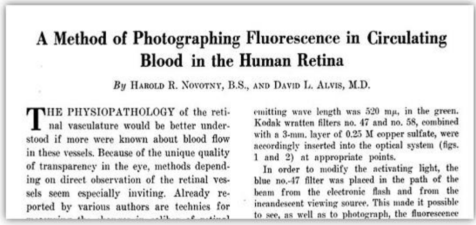
±50.000 OCT/AngioOCT

±250.000 Ophthalmologists









A Method of Photographing Fluorescence in Circulating Blood in the Human Retina

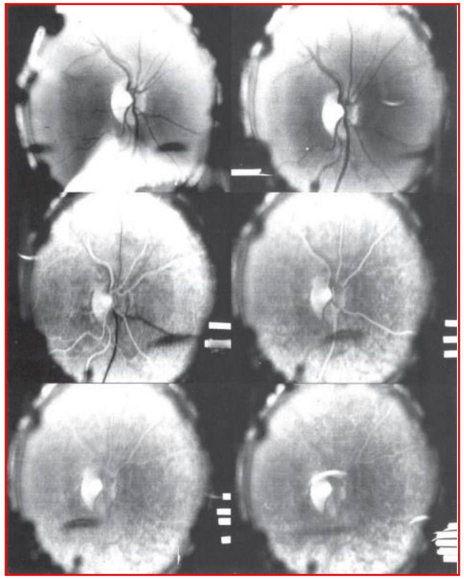
By Harold R. Novotny, B.S., and David L. Alvis, M.D.

THE PHYSIOPATHOLOGY of the retinal vasculature would be better understood if more were known about blood flow in these vessels. Because of the unique quality of transparency in the eye, methods depending on direct observation of the retinal vessels seem especially inviting. Already reported by various authors are technics for

emitting wave length was 520 mμ, in the green. Kodak wratten filters no. 47 and no. 58, combined with a 3-mm. layer of 0.25 M copper sulfate, were accordingly inserted into the optical system (figs. 1 and 2) at appropriate points.

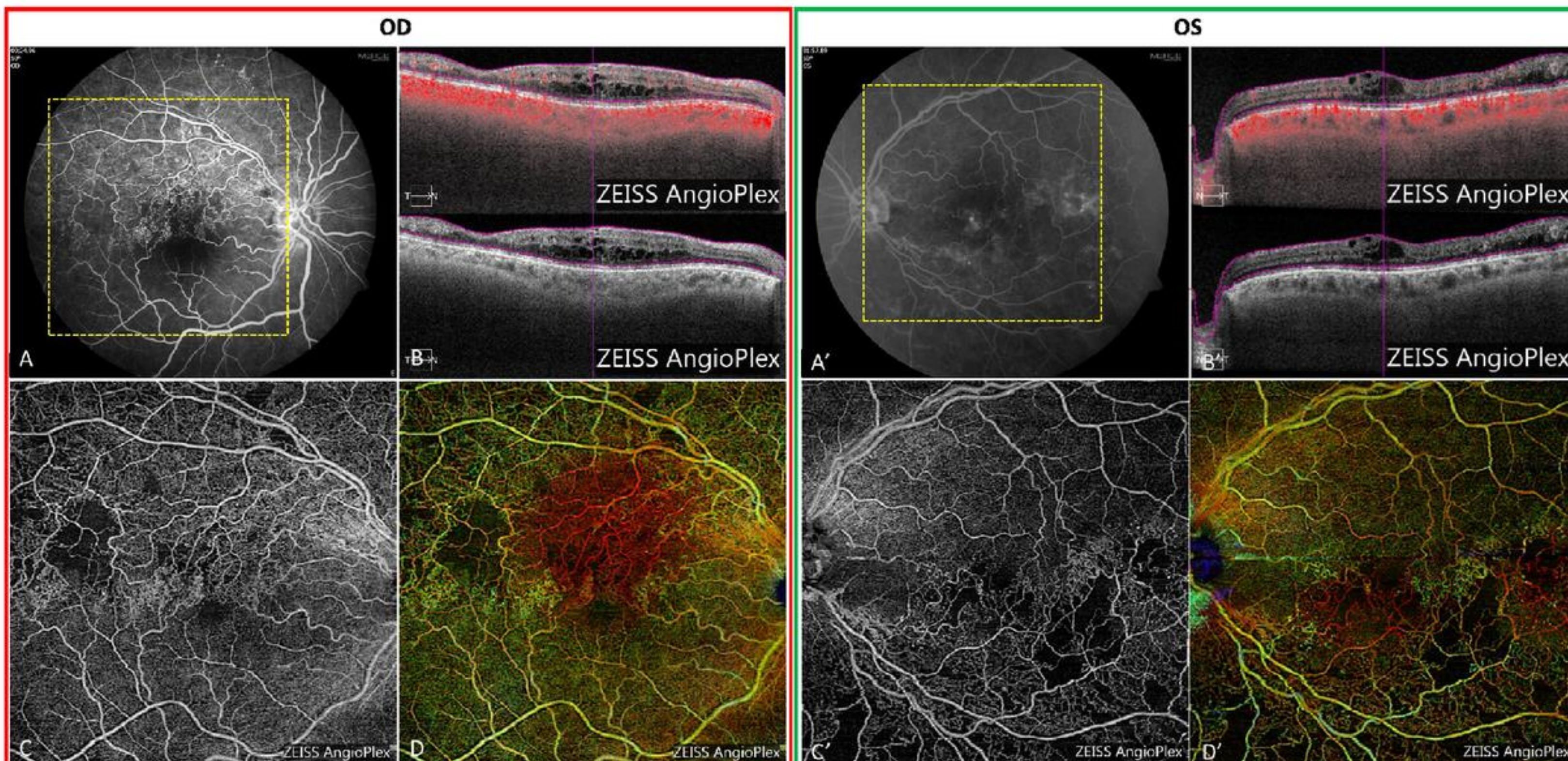
In order to modify the activating light, the blue no.-47 filter was placed in the path of the beam from the electronic flash and from the incandescent viewing source. This made it possible to see, as well as to photograph, the fluorescence

Image shows at the Fovea:
2.0 x 2.0 mm (A)
3.0 x 3.0 mm (B)
6.0 x 6.0 mm (C)
8.0 x 8.0 mm (D)
12 x 12 mm 12 x 16 mm
Images at the Optic Nerve:
3.0 x 3.0 mm (E)
6.0 x 6.0 mm (F)
8.0 x 8.0 mm

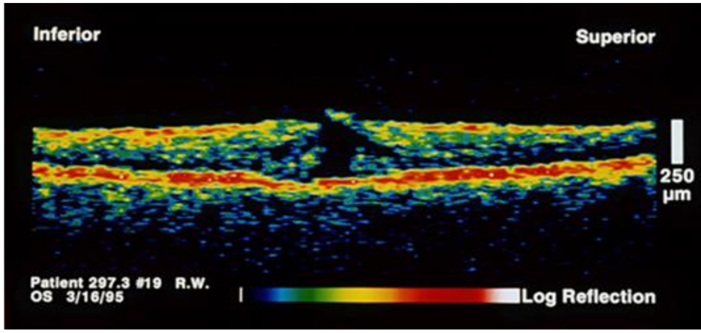
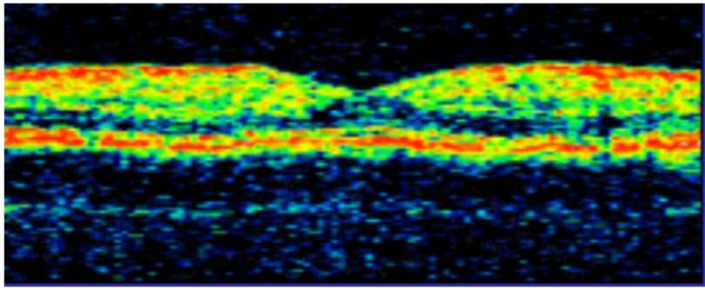
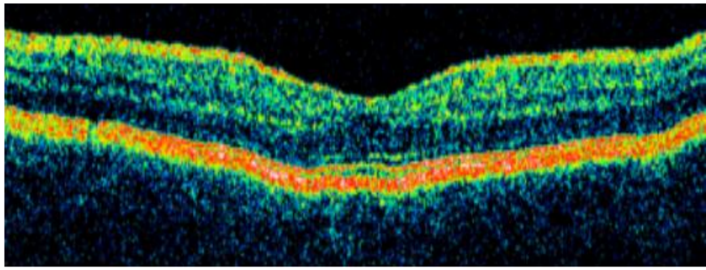
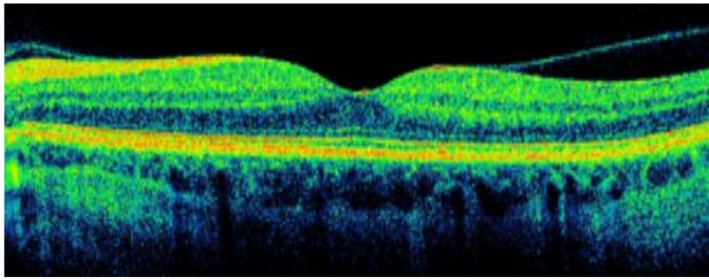


H. Novotny and D. Alvis; Circulation 1961

The first fluorescein angiogram taken in November 1959, of the right eye of David Alvis with Harold R. Novotny



50000 OCT
250000 Ophthalmologists

Model Image	Year	Single line Scan	Scans Sec	Resolution (microns)	B Scan
	OCT 1995 200/99	100 A-scans x 500 points	100	20	
	OCT2 2000 400/2002	100 A-scans x 500 points	100	20	
	OCT3 Stratus 2002 6000/2006	512 A-scans x1024 points	500	10	
	Cirrus HD-OCT 2007 10000/2012	4096 A-scans x 1024 points	27,000	5	

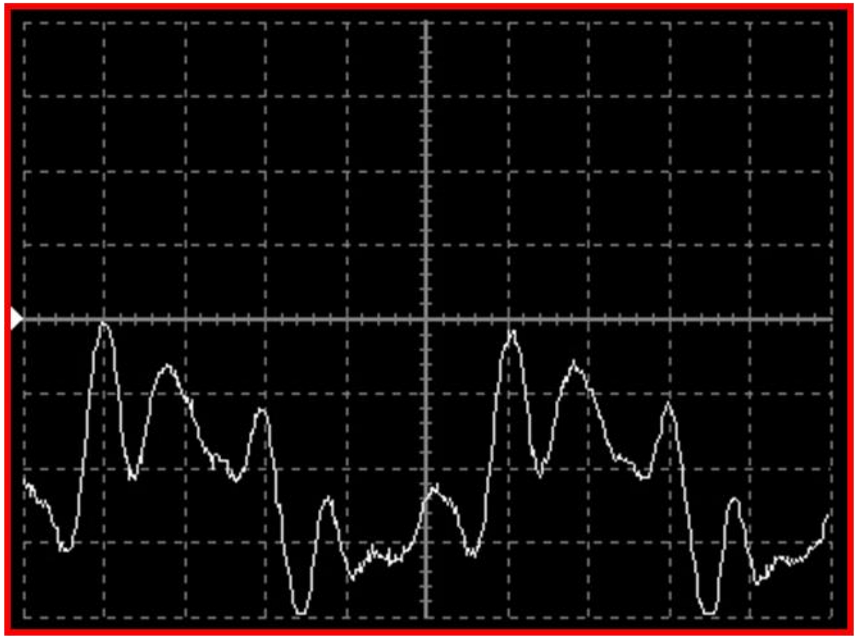
Dawn of a New Era in Imaging

x(t) vs X(f)

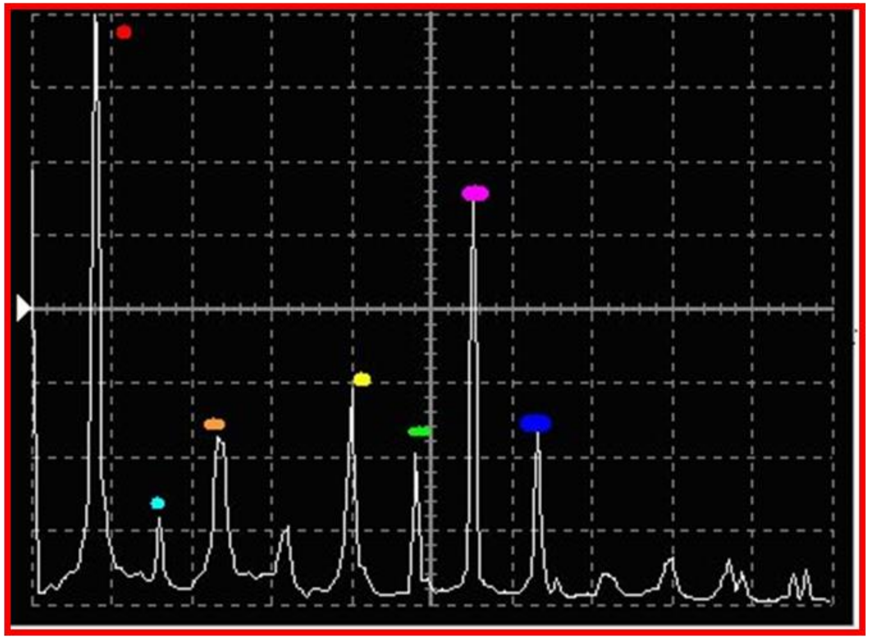
$$X(f) = \int_{-\infty}^{+\infty} x(t) \cdot e^{-j 2\pi f t} dt$$

$$x(t) = \int_{-\infty}^{+\infty} X(f) \cdot e^{+j 2\pi f t} df$$

Trasformata e Antitrasformata di Fourier

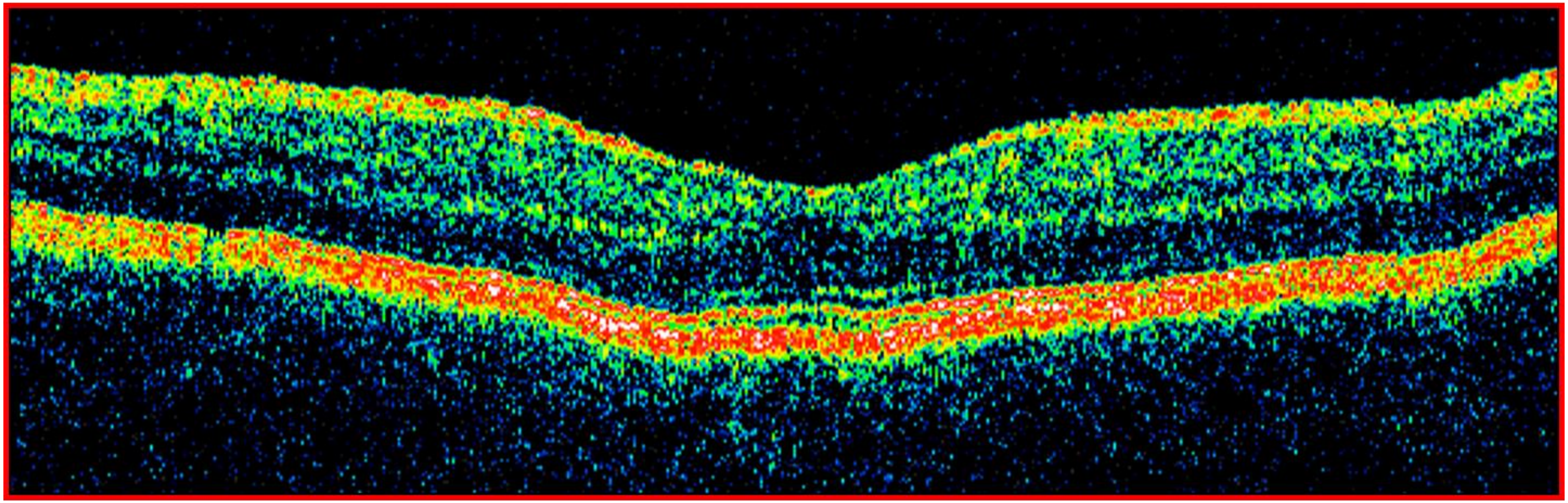


Nota musicale «la» di un clarinetto registrata tramite oscilloscopio nel dominio del tempo ***x(t)***

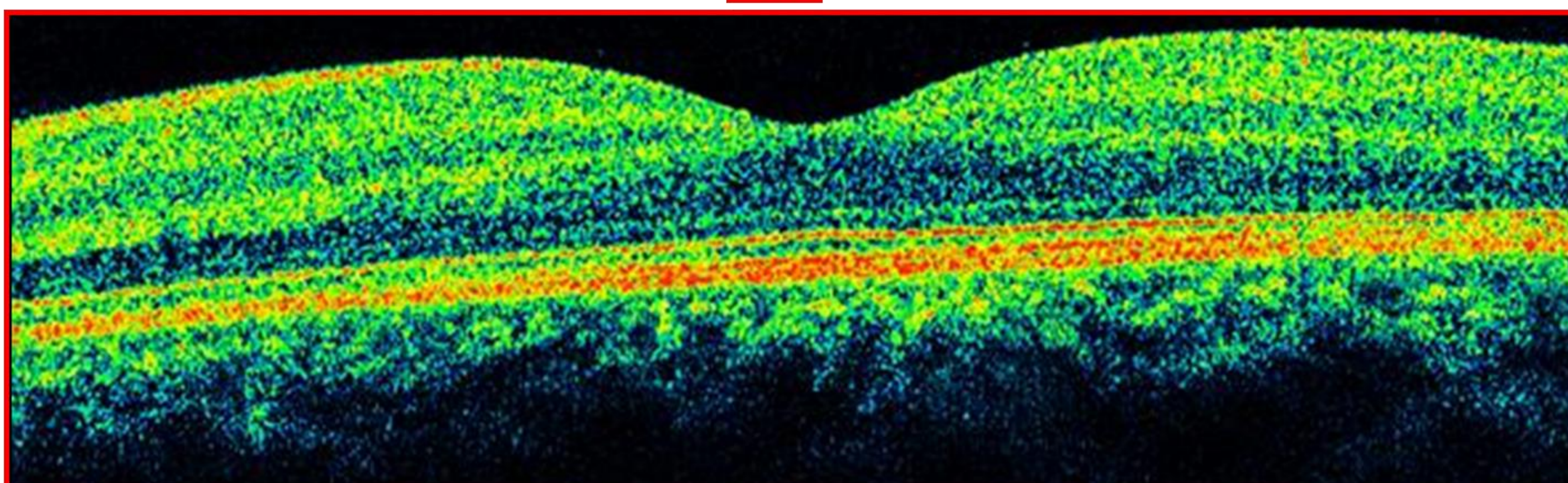


Nota musicale «la» di un clarinetto scomposta in sotto-onde nel dominio delle frequenze ***X(f)***

$x(t)$

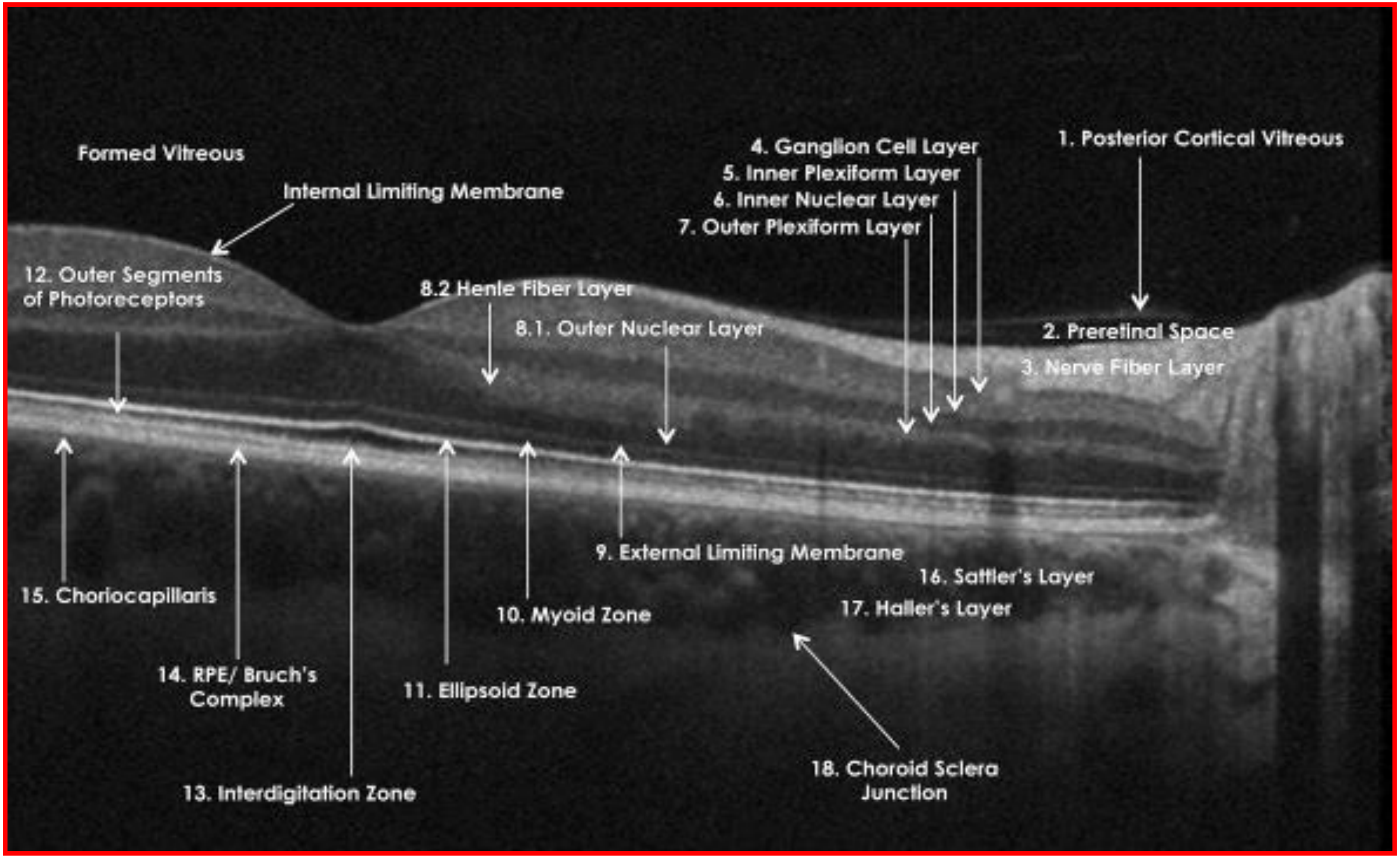


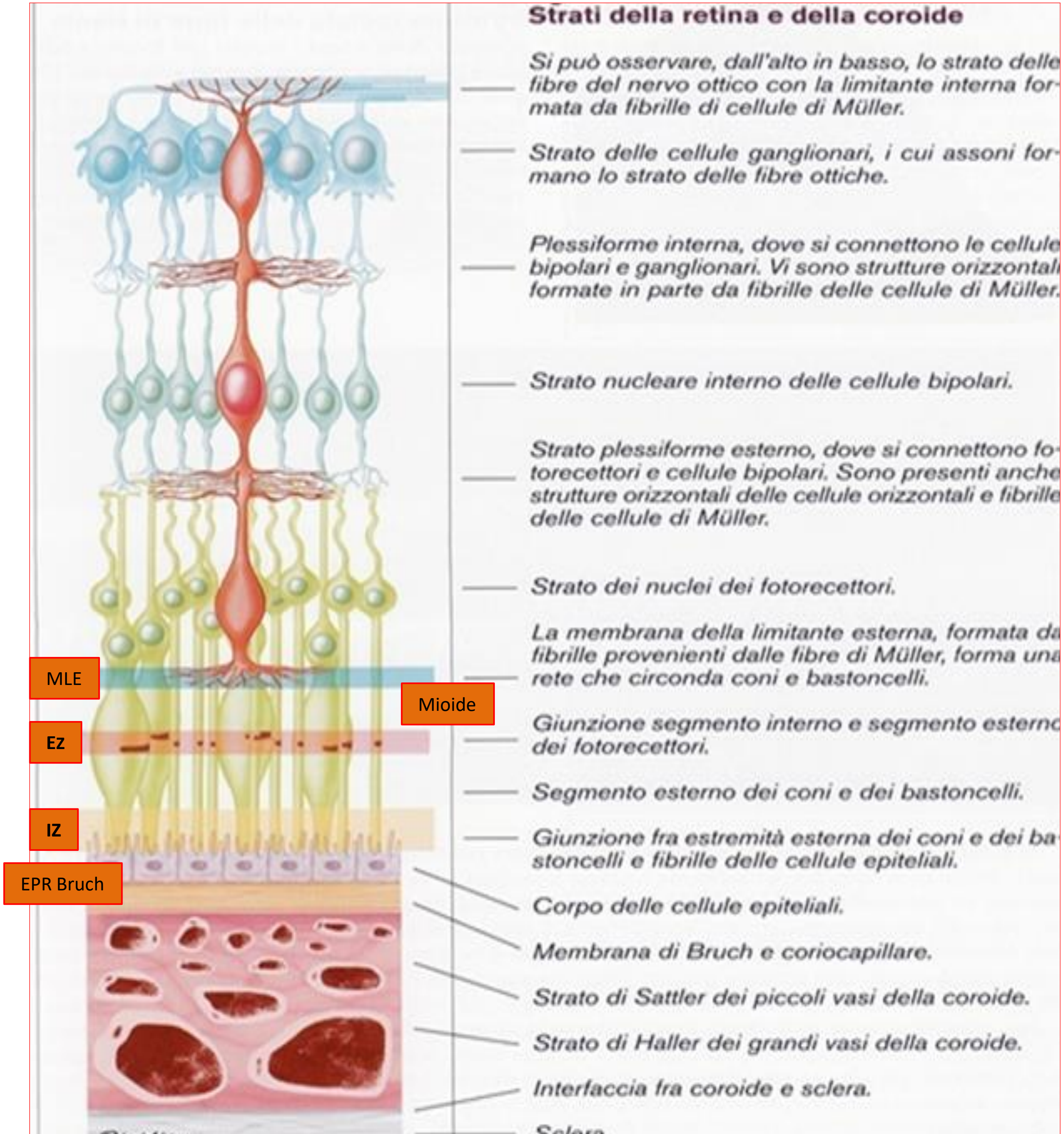
$X(f)$



International Nomenclature OCT (INOCT) 2014

By: Staurenghi G, Sadda S, Chakravarthy U, Spaide RF; International Nomenclature for Optical Coherence Tomography (IN•OCT) Panel.



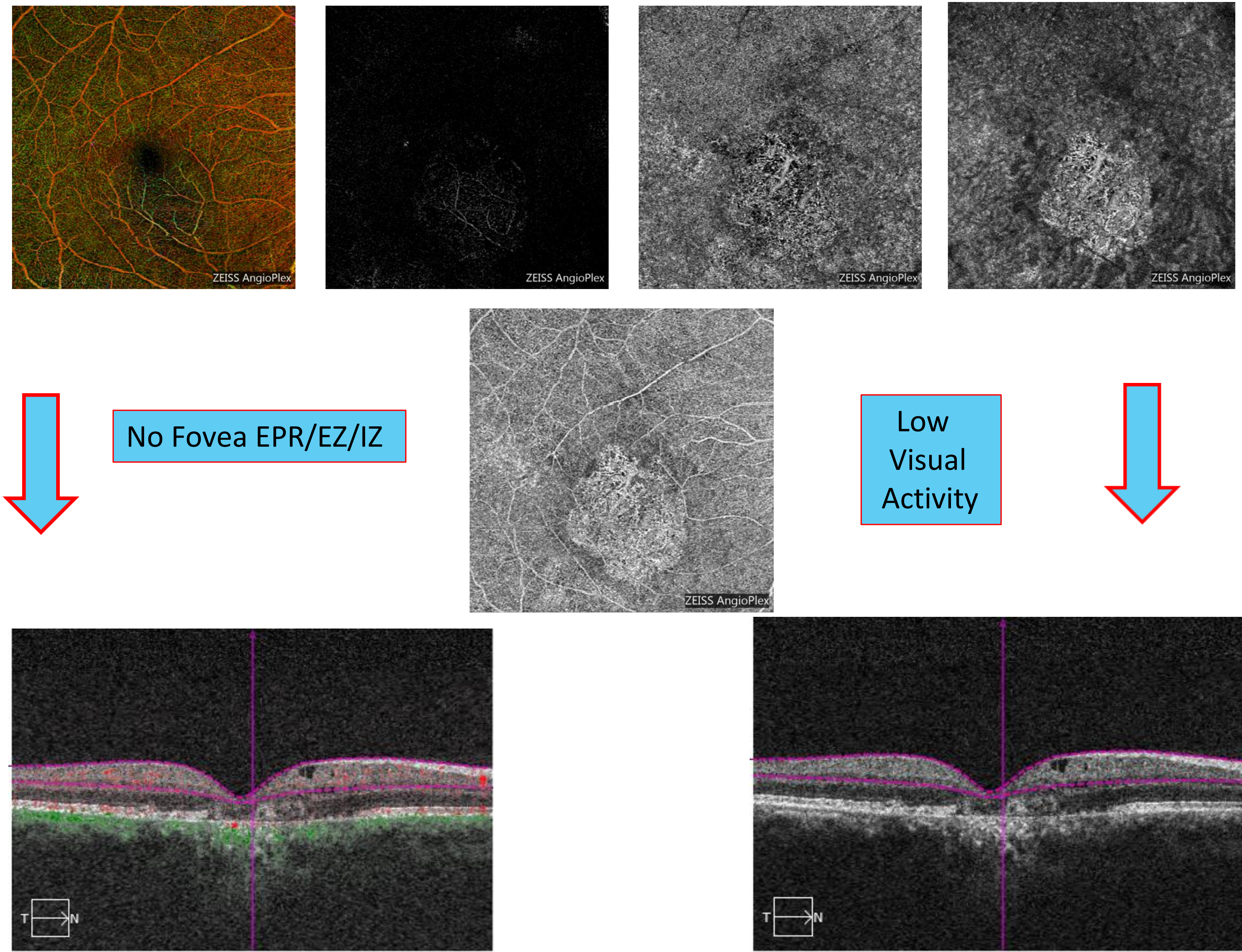


1) La membrana limitante esterna **(ELM)** si trova al confine tra i corpi cellulari (nuclei) e i segmenti interni dei fotorecettori e comprende gruppi di complessi giunzionali tra le cellule Müller e i fotorecettori.

2) La Zona Ellissoidale (**EZ)**, precedentemente indicata come giunzione del segmento interno /segmento esterno del fotorecettore **(IS /OS),** è ora pensata per essere formata principalmente dai mitocondri all'interno dello strato ellissoidale della porzione esterna dei segmenti interni di i fotorecettori. In una fovea normale, la distanza dalla linea EZ all'ELM è inferiore a quella dalla linea EZ all'EPR

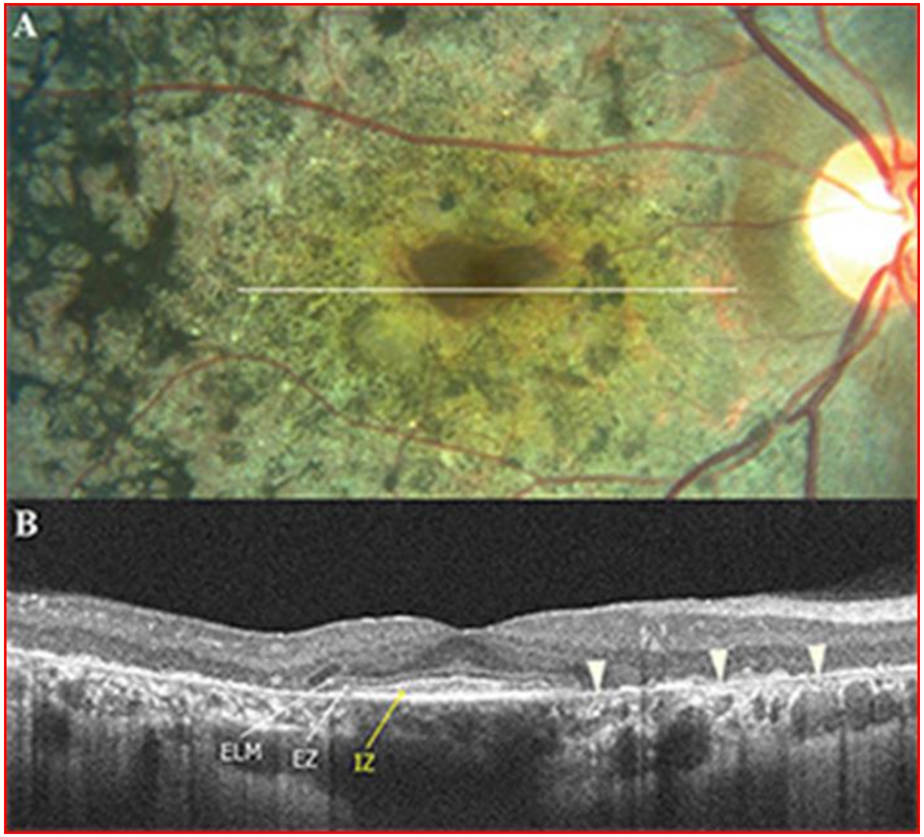
3) La Zona di Interdigitazione **(IZ)** corrisponde al cilindro di contatto rappresentato dagli apici delle celle EPR che racchiudono parte dei segmenti esterni del cono. Questo strato era precedentemente indicato come punte del segmento esterno del cono **(COST)** o punte del segmento esterno dello stelo **(ROST),** e non è sempre distinguibile dal livello RPE sottostante, anche nei soggetti normali.

4) La banda epiteliale del pigmento retinico è formata dall'EPR e dalla membrana di Bruch (indistinguibili l'una dall'altra in uno stato normale utilizzando gli attuali sistemi SD-OCT). Nella fovea, questa banda è più spessa, il che indica che le strutture coroidali possono anche contribuire all'iper-riflettività della banda RPE in questa posizione


ZEISS AngioPlex
ZEISS AngioPlex
ZEISS AngioPlex
ZEISS AngioPlex
No Fovea EPR/EZ/IZ
ZEISS AngioPlex
Low Visual Activity
T
N
T
N

However, OCT of retinal degenerative diseases over time has demonstrated that ELM, EZ and IZ lengths are highly correlated with each other, and disorganization seems to occur in a stepwise order: **first at the IZ**, followed by the EZ and finally the ELM line

The ELM zone has been reported as the first structure to recover after macular hole closure, and its recovery has been considered a sign of intact photoreceptor cell bodies and Müller cells



"Outer Retinal Layers as Predictors of Vision Loss" by **Marco A. Bonini Filho et al.** Published 15 April 2015

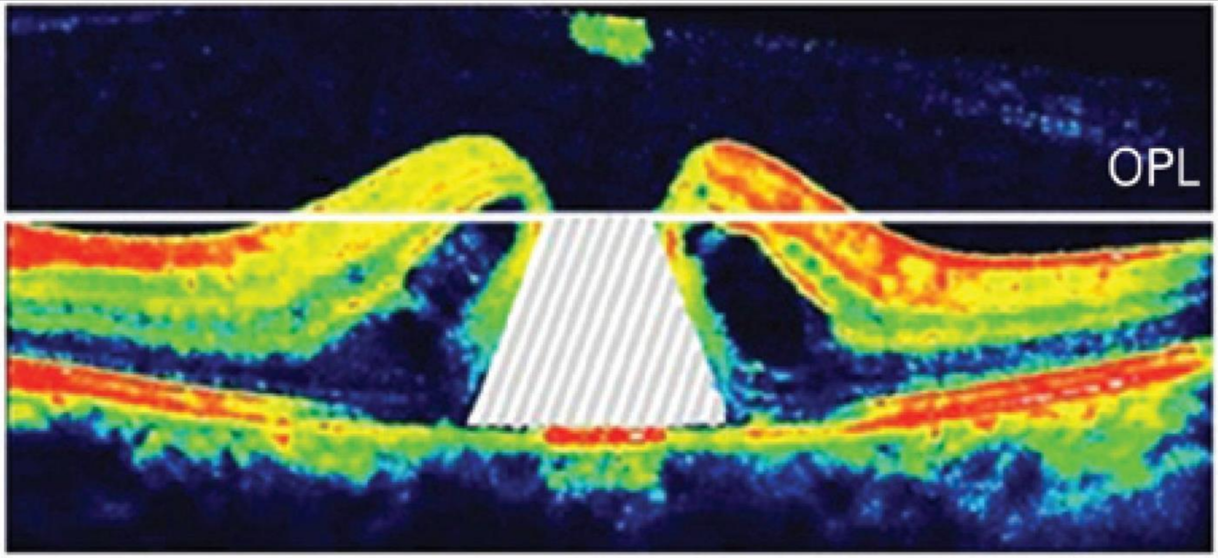
A relationship between the pre-treatment status of the ELM and post-treatment visual outcomes has been described for epiretinal membranes, age-related macular degeneration and diabetic macular edema.

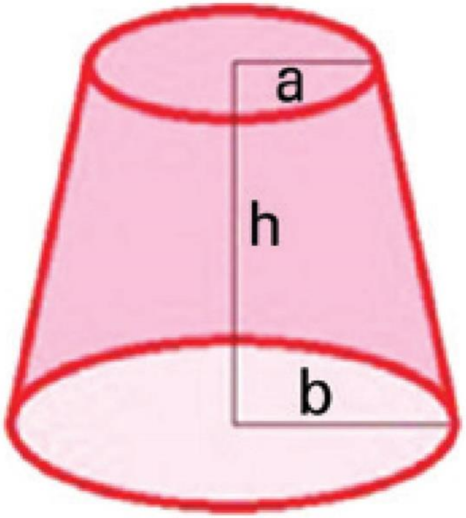
Right eye of a 38-year-old woman diagnosed with retinitis pigmentosa. Best-corrected visual acuity was 20/30.

A) The color photo showed typical pigment retinal epithelium atrophic abnormalities sparing the central macula.

B) Spectral-domain optical coherence tomography showed that there was an extensive perifoveal region where outer retina layers (stars) were absent and the RPE was irregular or absent (arrowheads). However, the outer retinal bands were preserved in the foveal region, which correlated with the relatively normal visual acuity. Arrows indicate the end points of the **ELM, EZ and IZ, respectively**.

2
+
2
≠
4





$$V = \frac{\pi}{3} h \left(a^2 + ab + b^2\right)$$

Calculation of the macular hole volume (MHV; mm³) according to the formula that gives the volume of a truncated cone

by: Taylan Ozturk et al. Arq. Bras. Oftalmol. vol.79 no.3 **São Paulo May./June 2016**

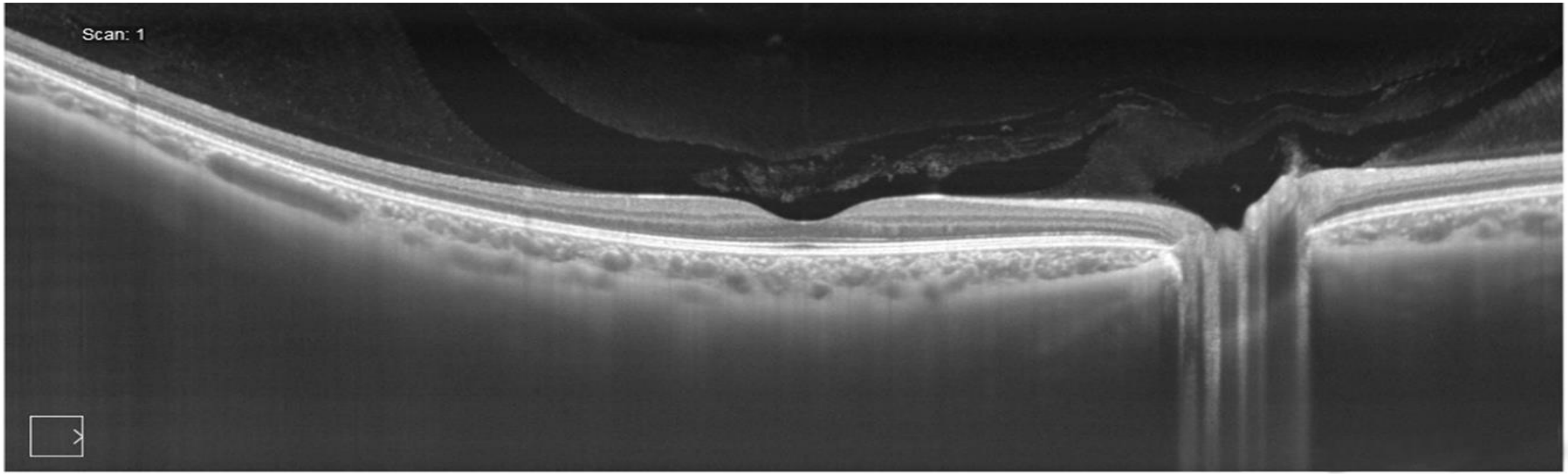
No statistical correlations were found between MHV and postoperative BCVA ($p=0.588$) and between MHV and disease recurrence ($p=0.544$). A weak negative correlation existed between MHV and final CMT (Central Macular Thickness) scores ($p=0.04$, $r=-0.383$).

Pre Retinal: Qualitative OCT Assessment
Intra-Retinal: Qualitative OCT Assessment
Sub-retinal/RPE: Qualitative OCT Assessment

- Pre-retinal membrane
- Epi-retinal membrane
- Vitreo-retinal strands
- Vitreo-retinal traction
- Syneresis
- Pre-retinal neovascular membrane NVE
- Pre-papillary neovascular membrane NVD

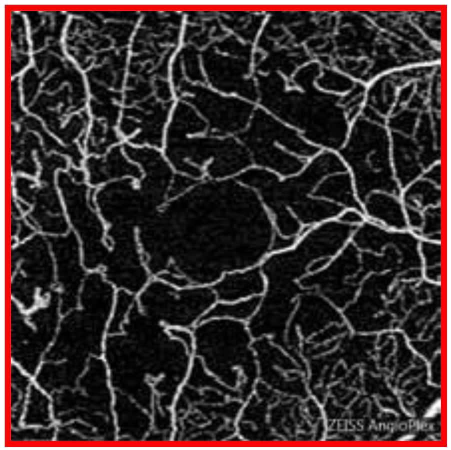
Diffuse intra-retinal oedema
Cystoid macular oedema
Hard exudate
Scar tissue
Atrophic degeneration
Neovascularization

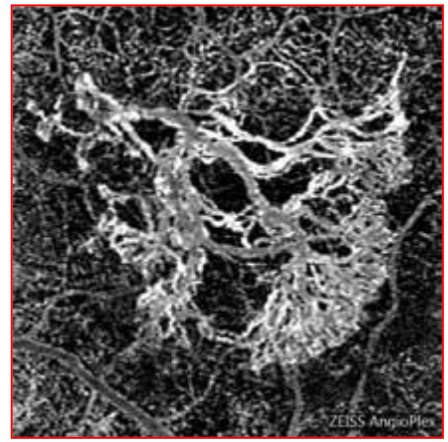
Choroidal neovascularization
RPE detachment
Drusen
Sub-retinal fibrosis
Scar tissue
RPE atrophy

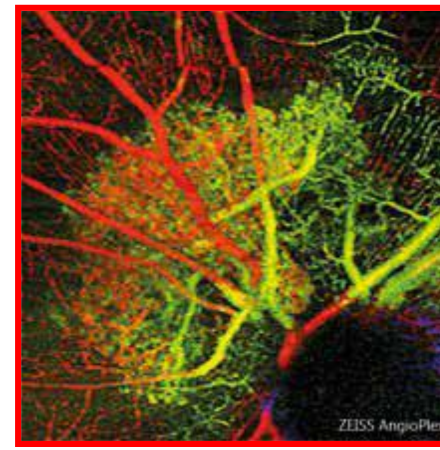


HD-Spotlight fino a 16 mm altamente dettagliato scansione B by SS-OCT Plex Elite Zeiss

Dal segnale tomografico al segnale decorrelato: l'imaging vascolare nelle malattie neuroretiniche







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=

- 55,9% Zeiss **OCT**
- 35,6% Heidelberg By Mark Hillen
- 6,4% Topcon
- 2,1% Nidek

Mark Hillen. Benchmarking OCT. The Ophthalmologist, February 2016, #27

- **Zeiss →AngioPlex Cirrus 5000**
- Optovue→RTvue Avanti AngioVue
- Topcon→DRI OCT Triton
- Heidelberg→Spectralis con modulo OCT2
- Nidek→RS-3000 Advance OCT Angio-Scan
- Canon →OCT-HS100 Angio-eXpertcon modulo AX (Gruppo Haag-Streit)

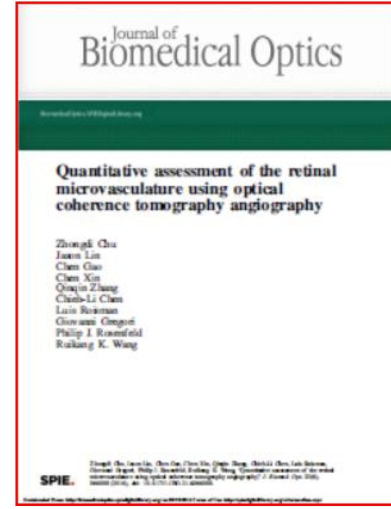
- **HD-Cirrus Zeiss68.000 A-Scan/Sec →OMAGc (Optical Microangiography complex)**
- RTvue Avanti Optovue70.000A-Scan/Sec →SSADA (Split Spectrum Amplitude Decorrelation Angiography)
- SS OCT DRI OCT Topcon100.000A-Scan/Sec →OCTARA (OCT Angiography Ratio Analysis)
- Spectralis Heidelberg70.000 A-Scan/Sec →Full SADA (Spectrum Amplitude Decorrelation Algorithm)

vessel area density
vessel skeleton density
vessel diameter index
vessel perimeter index
vessel complexity index

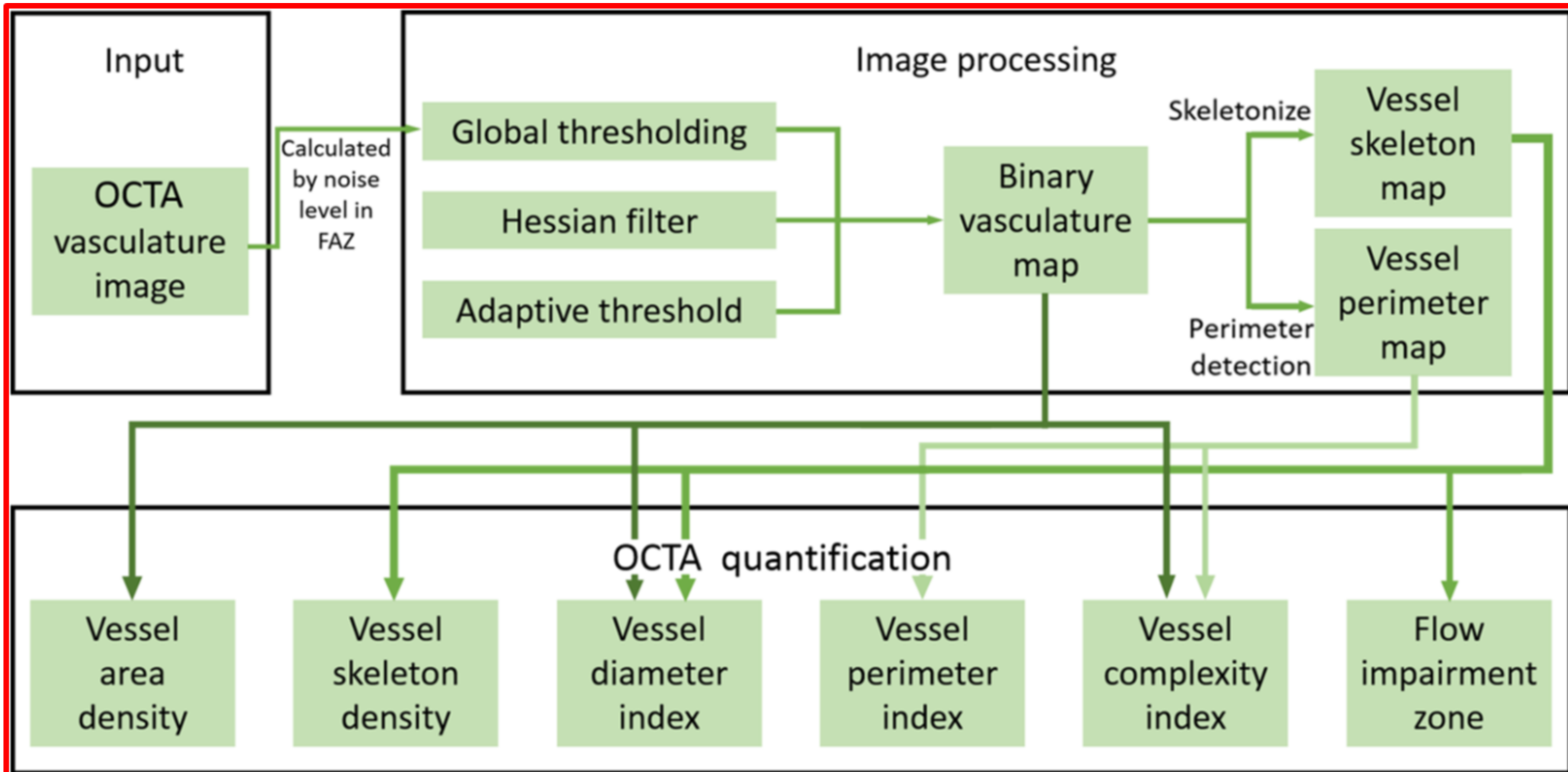
Overview of the quantitative OMAG algorithm

Flowchart

MATLAB
è un ambiente per il calcolo numerico e l'analisi statistica



by Zhongdi Chu et al. Journal of Biomedical Optics 21(6), 066008 (June 2016)



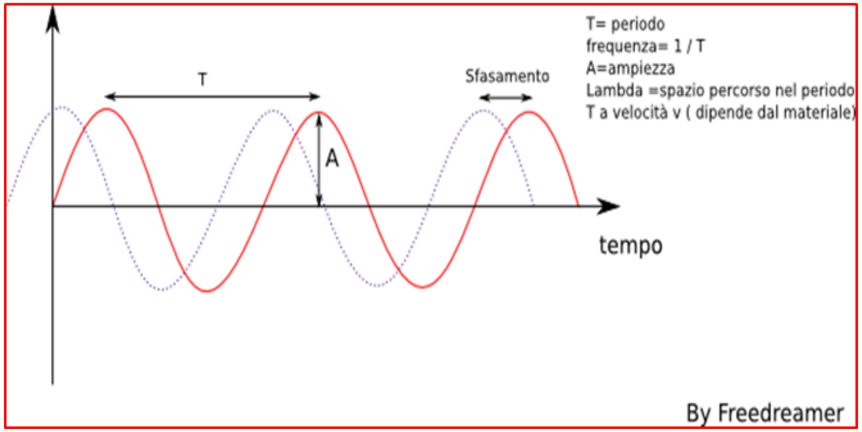
The algorithms used in OCTA

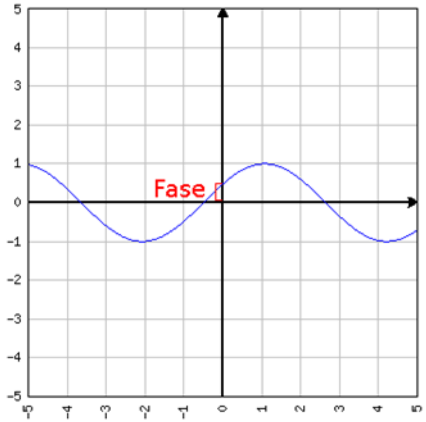
- Optical microangiography (OMAG),
- Split-spectrum amplitude decorrelation angiography (SSADA)
- OCT angiography ratio analysis (OCTARA)
- Speckle variance
- Phase variance
- Correlation mapping.

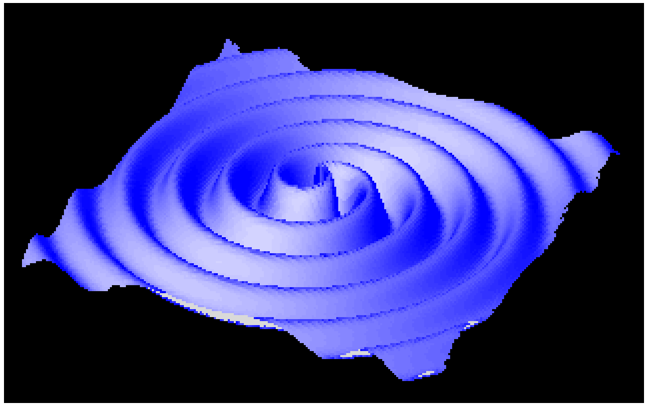
Zhang A, Zhang Q, Chen CL, Wang RK
Methods and algorithms for optical coherence tomography-based angiography: a review and comparison. J Biomed Opt. 2015 Oct;20(10):100901. doi: 10.1117/1.JBO.20.10.100901.

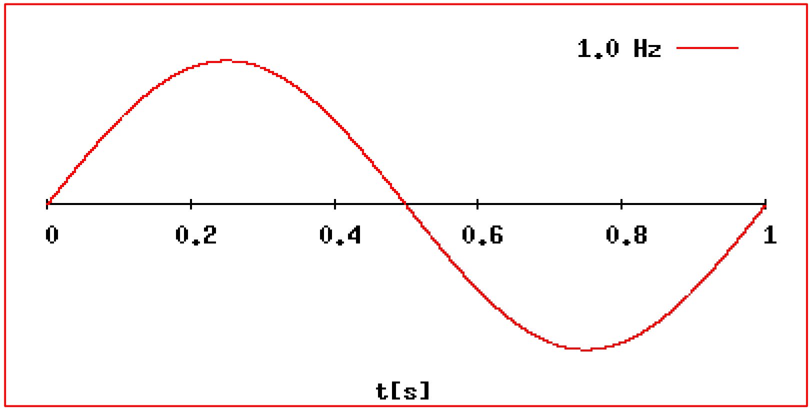
In a recent study, when algorithms including OMAG, speckle variance, phase variance, SSADA and correlation mapping were compared, ***it was found that OMAG****, as the method utilising complex OCT signals to contrast retinal blood flow* ***provided the best visual result for the of retinal microvascular networks concerning image contrast and vessel connectivity****.*

What is a wave? «energy propagated through matter» A. Einstein







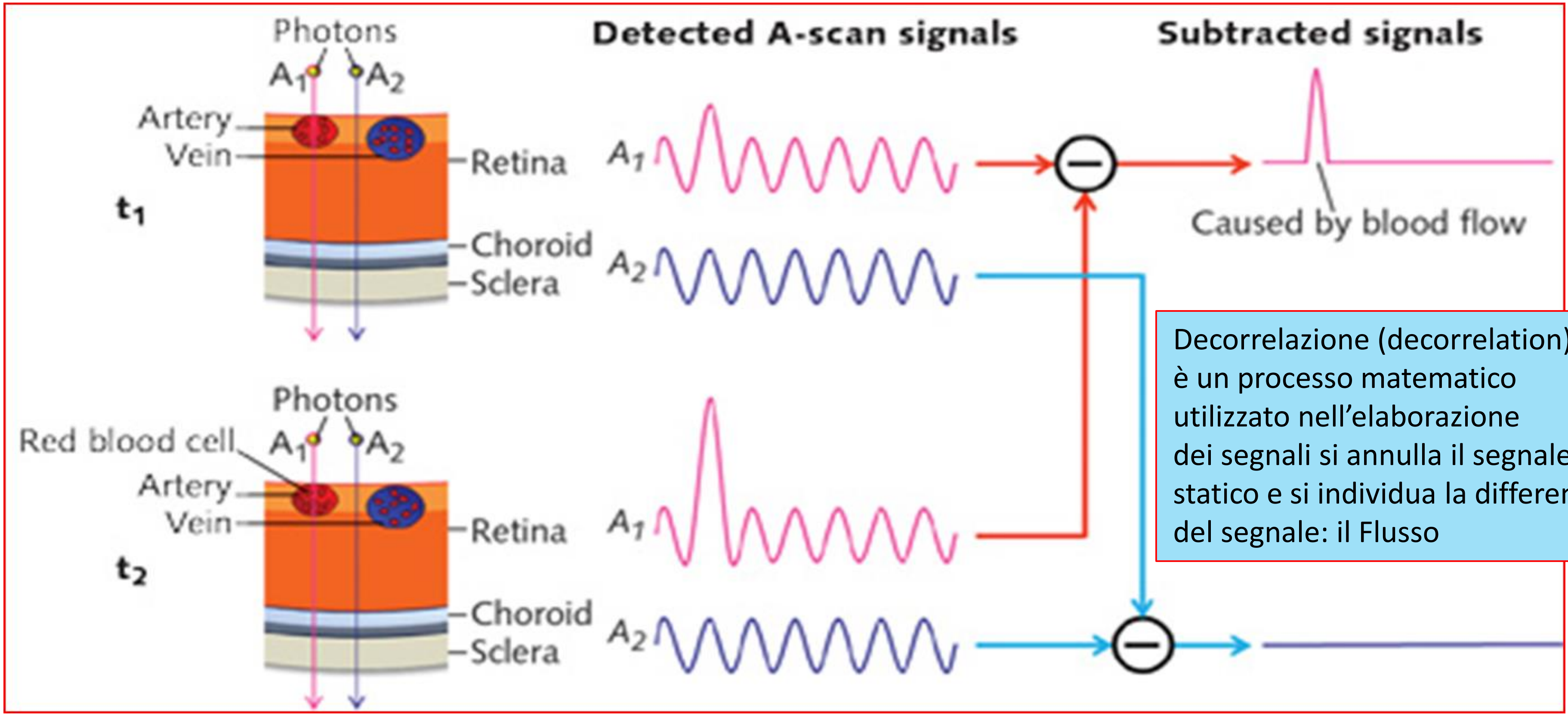


a)Angiografia dyeless basata sull'ampiezza del segnale OCT

b) Angiografia dyeless basata sulla fase del segnale OCT

c) Angiografia dyeless basata sull'ampiezza e sulla fase del segnale OCT (complex signal)

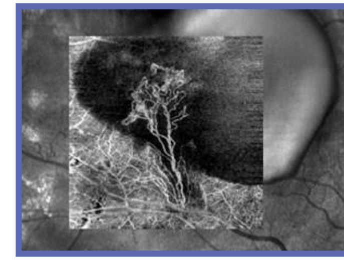
How OCTA Works → decorrelation



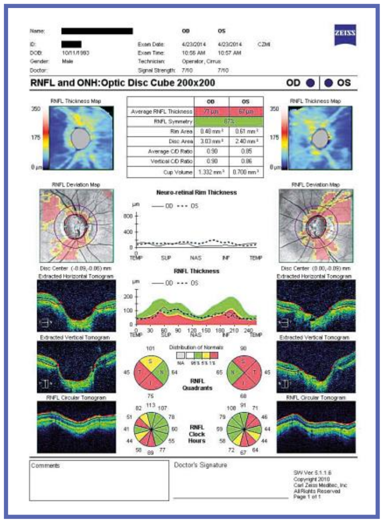
Decorrelazione (decorrelation): è un processo matematico utilizzato nell'elaborazione dei segnali si annulla il segnale statico e si individua la differenza del segnale: il Flusso

As moving blood cells pass through vessels, they generate changes in OCT signals. Based on this concept, a blood flow signal can be extracted by subtracting the OCT signals from the same location but at different time points (red path). The OCT signals will be different at these locations, while OCT signals from surrounding retinal tissues will remain steady (blue path).

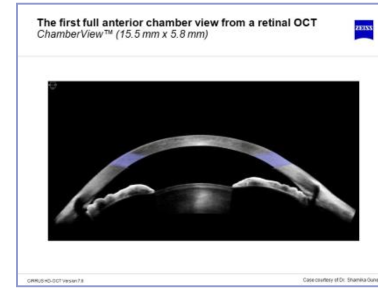
by CHIEH-LI CHEN 11/13/2015 Bio Optics World

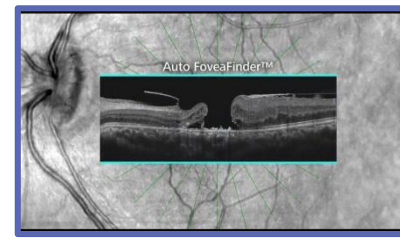


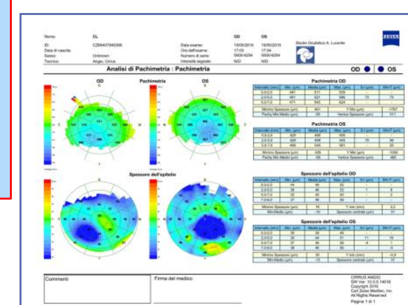
INDEX Angio Plex Cirrus

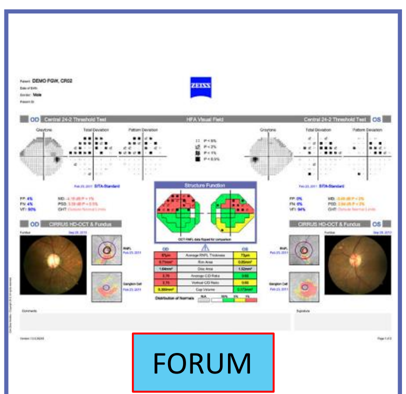


AngioPlex™ OCT
Angiography En face
Analysis Advanced RPE Analysis
Macular Thickness Analysis
Macular Change Analysis
HD 1 line
HD 21 Line
RNFL and ONH Analysis
ONH/RNFL Guided Progression Analysis™ (GPA™)
Ganglion Cell Analysis
GCA Guided Progression Analysis (GPA)
PanoMap™ Analysis
Anterior ChamberAnalysis
Wide Angle-to-Angle
Analysis Pachymetry **(epithelial and stromal thickness maps)**
Analysis HD Cornea
HD Angle
HFA–CIRRUS Structure-Function Report









Perfusion Density and Vessel Density

$$Perfusion\ Density = \frac{Area\ Perfusa\ [mm^2]}{Area\ Totale\ [mm^2]}$$

$$Vessel\ Density\ [mm^{-1}] = \frac{Lunghezza\ Vasi\ [mm]}{Area\ Totale\ [mm^2]}$$

The VD was defined as the percentage of signal-positive pixels/area of interest

The flow index is defined as the average decorrelation values in the segmented area

The Vessel Density is defined as the percentage area occupied by vessels the segmented area

$$\frac{\int_A D \cdot V dA}{\int_A dA}$$

If not (*V*=1, if vessel; *V*=0,

$$\frac{\int_A V dA}{\int_A dA}$$

If not (*V*=1, if vessel; *V*=0,

Numero di pubblicazione WO2014040070 A1
Tipo di pubblicazione Richiesta
Numero domanda PCT/US2013/059047
Data di pubblicazione 13 mar 2014
Data di registrazione 10 set 2013
Data di priorità 10 set 2012
Pubblicato anche come CA2883402A1, Altri 5 »
Inventori David Huang, Yali Jia, Jason Tokayer, Ou Tan
Candidato Oregon Health & Science University
Esporta citazione BiBTeX, EndNote, RefMan
Citazioni di brevetti (5), Con riferimenti in (1), Classificazioni (15), Eventi legali (4)

Flusso Vessel Density

			Precedente	Corrente
Nome:				
ID:	CZMI1545286560	Data esame:	08/06/2016	26/04/2017
Data di nascita:		Ora dell'esame:	09:22	16:06
Sesso:	Unknown	Numero di serie:	5000-6254	5000-6254
Tecnico:	Angio, Cirrus	Intensità segnale:	8/10	8/10

Studio Oculistico A. Lucente

ZEISS

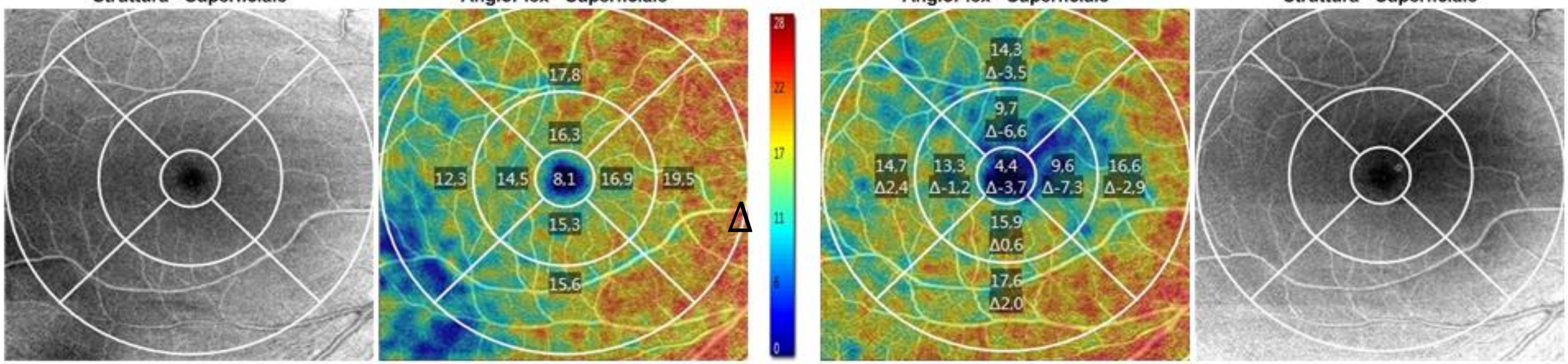
Analisi angiografica della variazione : Angiography 6x6 mm

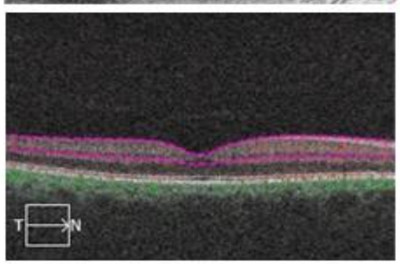
OD ● ○ OS

Esame 1 (scansione precedente)
08/06/2016 09:22:45
Segnale (8/10)

Segnale (8/10)
Esame 2 (scansione selezionata)
26/04/2017 16:06:15

Struttura - Superficiale | AngioPlex - Superficiale | AngioPlex - Superficiale | Struttura - Superficiale





Parte sup.: ILM Parte inf.: IPL
Monitorato durante la scansione

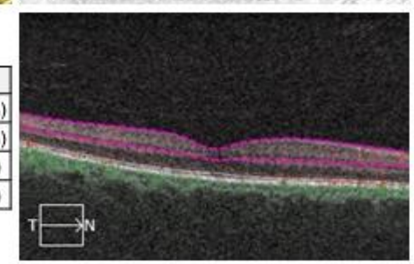
Sovrapposizioni
Struttura - Nessuno
AngioPlex - Vaso Mappa

Angiometria
ETDRS - Vaso

Regione	Esame 1	Esame 2	Differenza
Centrale	8,1 mm⁻¹	4,4 mm⁻¹	-3,7 mm⁻¹ (-46%)
Interna	15,8 mm⁻¹	12,1 mm⁻¹	-3,7 mm⁻¹ (-23%)
Esterna	16,3 mm⁻¹	15,8 mm⁻¹	-0,5 mm⁻¹ (-3%)
Completo	16,0 mm⁻¹	14,7 mm⁻¹	-1,3 mm⁻¹ (-8%)

FAZ

	Esame 1	Esame 2	Differenza
Area	0,21 mm²	0,40 mm²	0,19 mm² (90%)
Perimetro	2,02 mm	3,60 mm	1,58 mm (78%)
Circolarità	0,66	0,39	-0,27 (-41%)



Parte sup.: ILM Parte inf.: IPL
Monitorato durante la scansione

Commenti

Firma del medico

CIRRUS ANGIO
SW Ver: 10.0.0.14618

Pagina 1 di 1

AngioPlex Metrix™for HD-Cirrus 5000

- **Density measure (ETDRS, central, inner, full)**

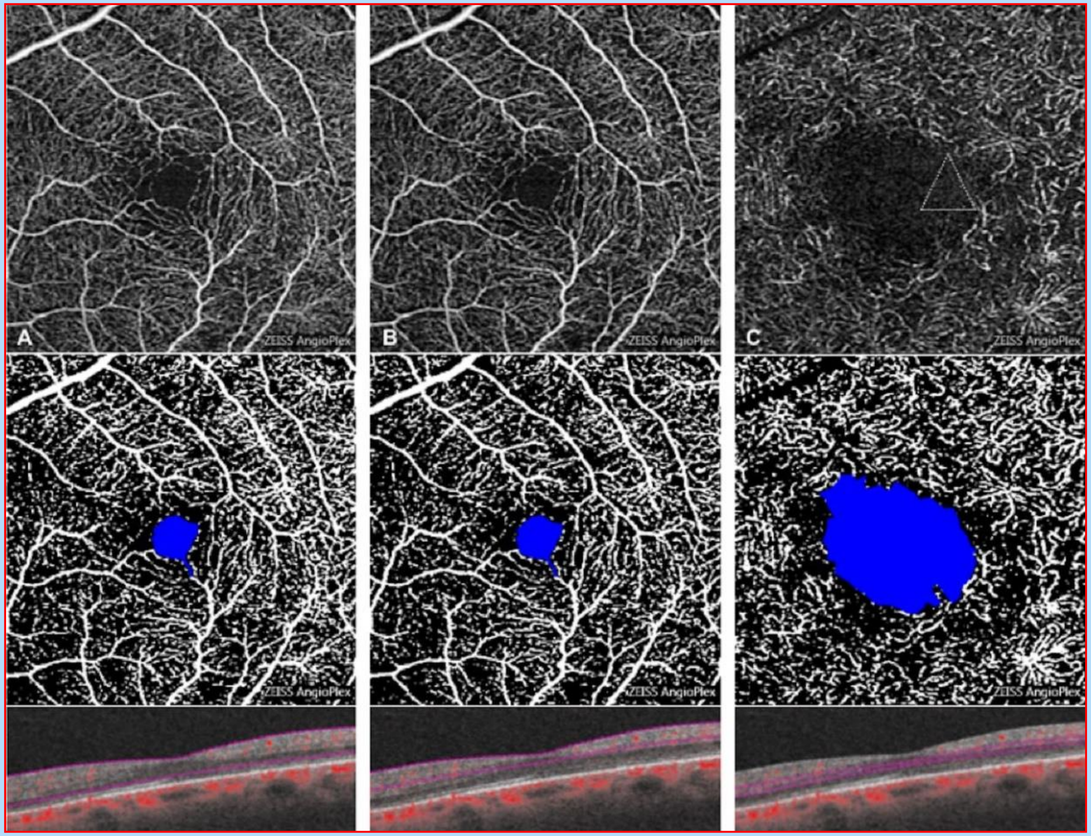
densità dei vasi/Vessel Density
densità di perfusione/Flow Index

- **FAZ Parameters**

Area mm^2
Perimetro (mm)
Circolarità della FAZ

- **Angiography Change**

Vessel Density
Fow Index
FAZ

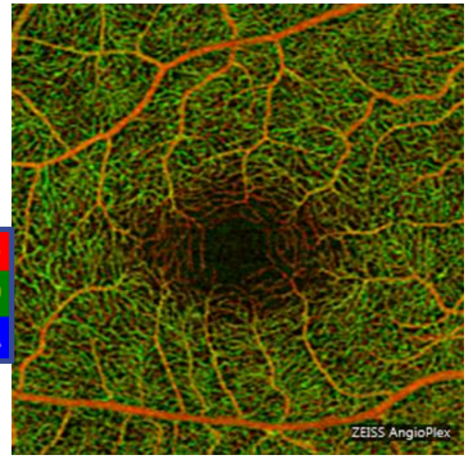
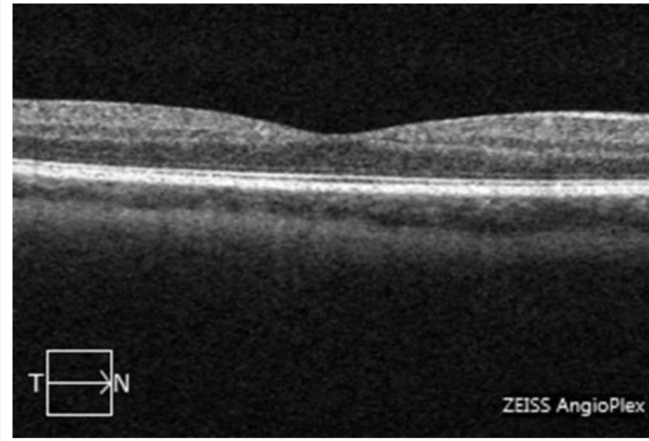
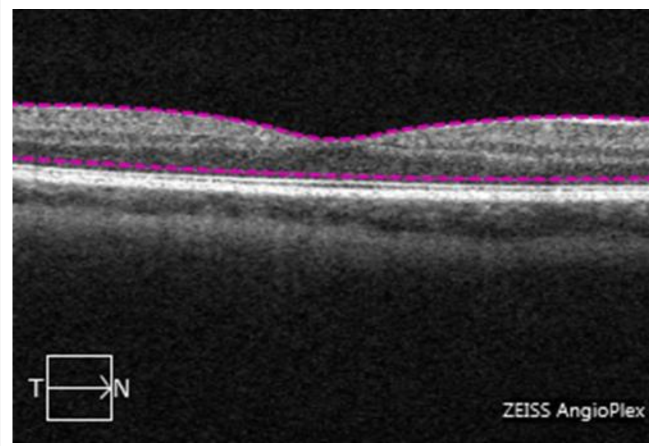


AngioPlex & Analysis Layer

- 9slab +

Retina Encoded
Retina
VRI Vitreo-Retinal Interface
Superficial Retinal Layer
Deep Retinal Layer
Avascular
Choriocapillaris
Choroid
Occhio intero

AngioPlex Analysis Layer Presets: Retina Depth Encoded and Retina

Layer Preset	Layer Boundaries	Example Image (Normal Eye)	B-scan with Layers
Retina Depth Encoded	Combination of: Superfical, Deep, and Avascular Layers Superficial: Red (S) Deep: Green (D) Avascular: Blue (A)		
Retina	Inner Boundary: ILM Outer Boundary: RPE = RPEfit - 70µm		

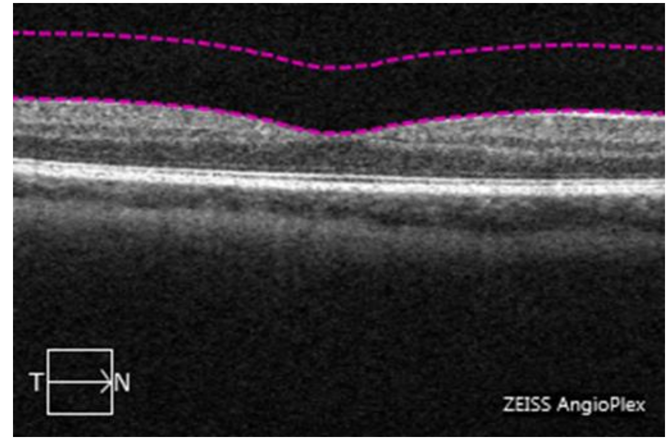
AngioPlex Analysis Layer Presets: VRI and Superficial

- VRI Vitreo-Retinal Interface

Inner Boundary

– 300µm

Outer Boundary ILM

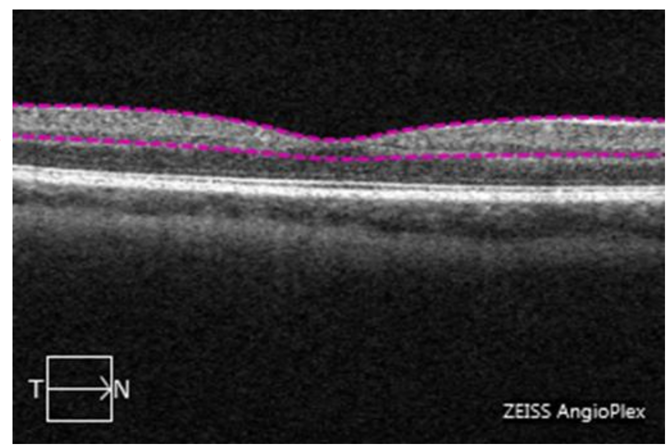


- Superficial Superficial Retinal Layer

Inner Boundary ILM

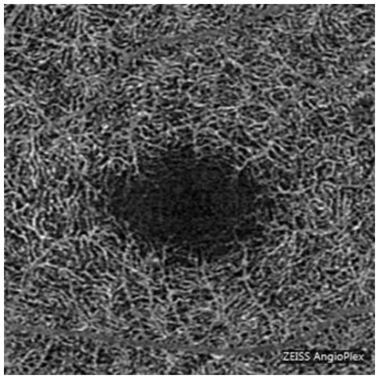
IPL=ILM+70%(OPL-ILM)

Outer Boundary IPL



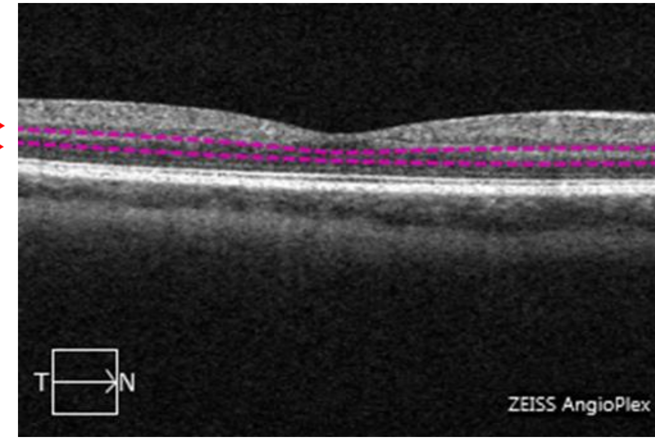
AngioPlex Analysis Layer Presets: Deep and Avascular

- Deep Deep Retinal Layer



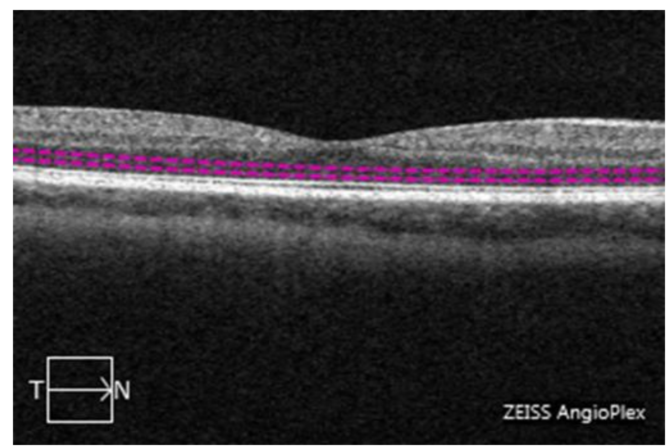
Inner Boundary IPL

Outer Boundary OPL=RPEfit–110µm



Inner Boundary OPL

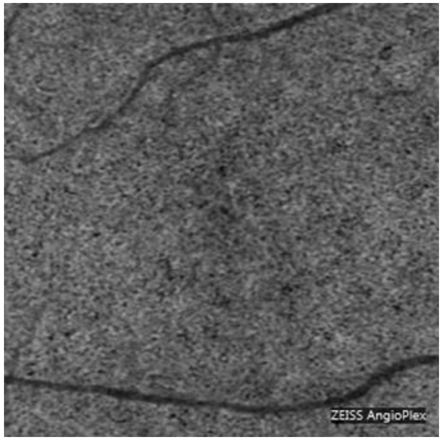
Outer Boundary IS/OS=RPEfit-70µm



- Avascular Avascular Retina

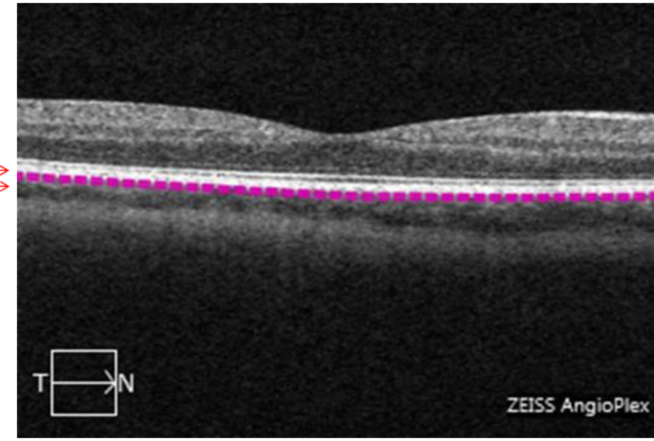
AngioPlex Analysis Layer Presets: Choriocapillaris and Choroid

- Choriocapillaris

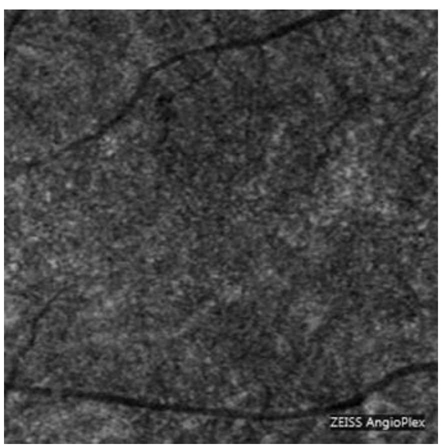


Inner Boundary CCIB=RPE+29µm

Outer Boundary CCOB = RPE+49µm

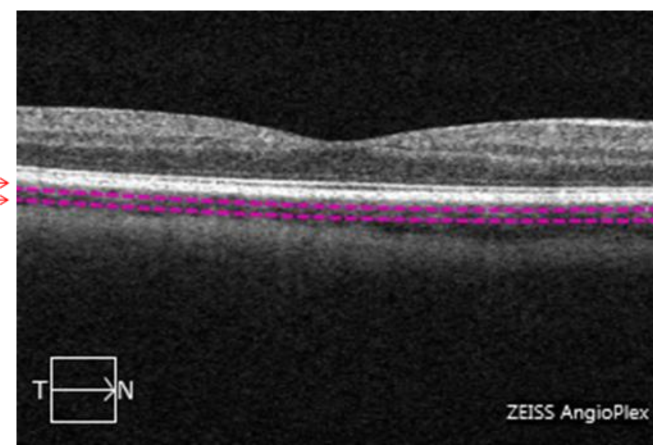


- Choroid



Inner Boundary ChIB = RPEfit + 64µm

Outer Boundary ChOB = RPEfit + 115µm



Thank you for your kind attention!

Angio-Plex Cirrus HD Zeiss Über Alles

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In Oculis Salus
dott. A. Lucente

www.amedeolucente.it