# Widefield and Ultra-Widefield in Ophthalmology



Dawn of a New Era in Imaging We make it visible



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Prima fotografia del fondo oculare e della rudimentale Fundus Camera attribuita dalla maggior parte della letteratura a W.T. Jackman e J.D. Webster, nel 1886 pubblicata sul "Philadephya Photografer"

Lucien Hove 1848/1928, US Hermann von Helmholtz 1821/1894, Cancelliere della Fisica, Germany



Amedeo Lucente: Evoluzione della fotografia retinica e Imaging Widefield, Oftalmologia Domani Anno IX - 2018





ZEISS

#### **Reflex free RETINAL CAMERA after** NORDENSON

N instrument of simple construction which can be used in any hospital or private office without special training in photographic technique. To obtain a satisfactory record of fundus condition is a matter of minutes only.

Price \$768 f.o.b. N.Y.

CARL ZEISS, Inc., 485 Fifth Ave., New York Pacific Coast Branch: 728 South Hill Street, Los Angeles, Calif.

Reflex free Retinal Camera Zeiss after Nordenson, Price \$ 768 f.o.b. N.Y.







FF Retinal Camera Zeiss after Nordenson Year 1930 **Price \$ 768 f.o.b. N.Y.** (free on board, New York)

1 \$ 1930 = 76,5 \$ 768 \$ x 76,5 \$ ~ 58.752 \$

FoV ≥ 50°Widefield ImagingFoV ≥ 100°Ultra-Widefield Imaging

ISO 10940 International Organization for Standardization









FoV 133° x 133° (out of ISO) occhio emmetrope. One shot; lunghezza misurabile estremo/estremo SI/NT ~ 27 mm



FoV 200° wide by 200° tall (out of ISO) occhio emmetrope. Four shots montaggio automatico; lunghezza misurabile estremo/estremo ~ 41 mm





Diametro antero-posteriore	~ 24 mm
Circonferenza ~ 2 π r = 2 x 3,14 x 12	~ 75,36 mm
Corpo Ciliare	~ 6 mm
Bianco /bianco	~ 12 mm
Arco corneale sotteso a 12 mm	
~ 1/6 circonferenza (75,36: 6= 12,56)	~ 12,56 mm
Ora serrata/ora serrata ~ 12,56 + (6x2)	~ 24,56 mm
Ora serrata/ora serrata internamente	
75,36–[12,56 + (6 + 6)]	~ 50,8 mm
Angolo goniometrico settore circolare	
<b>~24,56</b> mm (75,36 : 360 = 24,56 : x; x ~ 117,32)	~ 117,32°
Fotografia con FoV di 180°	
copre un'emicirconferenza (75,36/2)	~ 37,68 mm
Area retinica sfera con raggio 12 mm	
$= 4 \pi r^2 = 4 \times 3,14 \times 12^2$	~ 1808 mm²
Area dell'emisfera = ½ di 1808 mm²	~ 904 mm²

Testut, Zaccheo, Bonnet, Orzalesi, le dimensioni del bulbo oculare umano sono: diametro trasverso 23,5 mm diametro verticale 23 mm diametro antero-posteriore 25-26 mm Forma ricalca un ellissoide triassiale



# >>>Clinical Cases.....

.....Enter the New Era of Retinal Care by Zeiss

































#### 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 reti- and vasculature would be better under- stool if more were known about blood flow in these vessels. Because of the unique quality of transparency in the eye, methods depend- ing on direct observation of the retinal ves- sels seem especially inviting. Already re- ported by various authors are technics for	entiting a wave length wave 500 mp, in the grows Kohak wratten bleves no A7 and no 56, embines with a 3-am, hyrer of 0.25 M copper sulfato, war- neordinely invested in to the optical hysten (fig- 1 and 2) at appropriate points. In order to modify the articular julied, in bleven from the electronic flash and from th- inomoders beckering source. This make it possible to see, as well as to pholograph, the flavores
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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





Model Image	Year Units Installed	Single line Scan	Scans Sec	Resolutio (microns)	n B Scan
	OCT 1995 200/99	100 A-scans x 500 points	100	20	Inferior Superior Superior 250 pm Patient 297.3 e19 R.W. OS 3/16/95
	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	4096 A-scans x 1024 points	27,000	5	



## Foreword: 25 Years of Optical Coherence Tomography

by:James Fujimoto and David Huang

1st "OCT" 500 publication

by MIT

'92 '94 '96 '98 '00 '02 '04 '06 '08 '10 '12 '14



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





Gastroenterology & endoscopy

Dermatology

Cardiovascular

Ophthalmology

Technology





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

### - 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)



#### Dawn of a New Era in Imaging

x(t) vs X(f)



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

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

#### Trasformata e Antitrasformata di Fourier



Nota musicale «la» di un clarinetto scomposta in sotto-onde nel dominio delle frequenze 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.





#### Strati della retina e della coroide

Si può osservare, dall'alto in basso, lo strato delle fibre del nervo ottico con la limitante interna formata da fibrille di cellule di Müller.

 Strato delle cellule ganglionari, i cui assoni formano lo strato delle fibre ottiche.

 Plessiforme interna, dove si connettono le cellule
bipolari e ganglionari. Vi sono strutture orizzontali formate in parte da fibrille delle cellule di Müller.

- Strato nucleare interno delle cellule bipolari.

 Strato plessiforme esterno, dove si connettono fotorecettori e cellule bipolari. Sono presenti anche strutture orizzontali delle cellule orizzontali e fibrille delle cellule di Müller.

Strato dei nuclei dei fotorecettori.

La membrana della limitante esterna, formata da fibrille provenienti dalle fibre di Müller, forma una rete che circonda coni e bastoncelli.

Giunzione segmento interno e segmento esterno dei fotorecettori.

- Segmento esterno dei coni e dei bastoncelli.
- Giunzione fra estremità esterna dei coni e dei bastoncelli e fibrille delle cellule epiteliali.
- Corpo delle cellule epiteliali.
- Membrana di Bruch e coriocapillare.
- Strato di Sattler dei piccoli vasi della coroide.
- Strato di Haller dei grandi vasi della coroide.
- Interfaccia fra coroide e sclera.

Sclera.

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) EPR-Bruch

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 EPR in questa posizione



## 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**





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).

## **Perfusion Density and Vessel Density**


## AngioPlex & Analysis Layer

# • 10 slab +

Retina Depth Encoded Retina VRI Vitreo-Retinal Interface Superficial Retinal Layer Deep Retinal Layer Avascular Sub RPE Choroid RPE-RPE fit ORCC Outer Retina to Choriocapillaris



#### **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	AT 22	
	Superficial: Red Deep: Green Avascular: Blue	S D A ZEISS AngioPlex.	T N ZEISS AngioPlex
Retina	Inner Boundary: ILM Outer Boundary: RPE = RPEfit - 70μm	Etis AndoPer	T N ZEISS AngioPlex



## **AngioPlex Analysis Layer Presets: VRI and Superficial**





## **AngioPlex Analysis Layer Presets: Deep and Avascular**







## **AngioPlex Analysis Layer Presets: Choriocapillaris and Choroid**

## <u>- Choriocapillaris not used</u>



Inner Boundary CCIB=RPE+29µm

Outer Boundary CCOB = RPE+49µm



### - Choroid



Inner Boundary ChIB = RPEfit + 64µm

Outer Boundary ChOB = RPEfit + 115µm -





## **Useful to visualize CNV & Wet AMD**

ORCC: Outer Retina to Choriocapillaris visualize classic CNV or occult

**RPE to RPE fit: visualize CNV** 

Sub-RPE: visualize CNV







Blood flow of the ONH is supplied by two main sources 1

- Central retinal artery (CRA), which supplies the superficial RNFL layer of the ONH
- Posterior ciliary artery (PCA) circulation

Blood flow to the RNFL is supplied by the microcirculation coming from the retinal radial peripapillary capillaries (RPC) OCTA can visualize the RPC network but traditional fluorescein angiography cannot <sup>2</sup> OCTA for GLAUCOMA: It has been reported that optic disc perfusion may be useful in the evaluation of glaucoma and glaucoma progression <sub>3,4</sub>

 Hayreh SS. Blood supply of the optic nerve head and its role in optic atrophy, glaucoma, and oedema of the optic disc. Br J Ophthalmol 1969;53:721-748.
Spaide RF, Klancnik JM, Cooney MJ. Retinal Vascular Layers Imaged by Fluorescein Angiography and Optical Coherence

- Tomography Angiography. JAMA Ophthalmol 2015;133:45-50.
- 3. Chen CL, Bojikian KD, Gupta D, Wen JC, Zhang Q, Xin C, Kono R, Mudumbai RC, Johnstone MA, Chen PP, Wang, RK, "Optic nerve head perfusion in normal eyes and eyes with glaucoma using optical coherence tomography-based microangiography," Quant Imaging Med Surg, 2016 Apr;6(2):125-133
- 4. Chen CL, Zhang A, Bojikian KD, Wen, JC, Zhang, Q, Xin, C, Mudumbai, RC, Johnstone, MA, Chen, PP, Wang, RK, "Peripapillary Retinal Nerve Fiber Layer Vascular Microcirculation in Glaucoma using Optical Coherence Tomography–based Microangiography," Invest Ophthalmol Vis Sci. 2016 Jul;57(9):OCT475–OCT485



Relationship between **visual field loss** and **RGC numbers.** A normal visual field in a healthy individual has approximately **1 million RGCs**. At a **mean deviation of -2 dB**, which equates to an **early field defect**, **RGC number** has decreased by around **350,000 cells**. At **-10 dB**, a field defect that can result **in functional impairment** and **quality of life decline**, **RGC number** has **decreased** by **a further 250,000 cells from the RGC number at -2 dB** 

by Felipe Medeiros The Ophthalmologist; May 2017





#### ONH Angiography Analysis: ONH Angiography 4.5 mm x 4.5 mm

P = Perfusion = Area perfusa/area totale F = Fux Index = Lunghezza vasi/area totale

Reference: Top ILM Botton RNFL







## >>>Clinical Cases.....

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Example of retinal layer segmentation. Two retinal boundaries were segmented: inner limiting membrane (ILM) (the yellow line), retinal pigment epithelium (RPE) (the red line outside the optic disc) and anterior surface of lamina cribrosa (LC) (the same red line within the optic disc). (A,B) Structural and blood flow cross-sectional image superimposed with segmented retinal boundaries. by: Chieh-Li Chen et al.

## **AngioPlex Metrix for ONH**

Normal

Glaucoma

Advanced Glaucoma









1. Hayreh SS. Blood supply of the optic nerve head and its role in optic atrophy, glaucoma, and oedema of the optic disc. Br J Ophthalmol 1969;53:721-748.

2. Spaide RF, Klancnik JM, Cooney MJ. Retinal Vascular Layers Imaged by Fluorescein Angiography and Optical Coherence Tomography Angiography. JAMA Ophthalmol 2015;133:45-50.

3. Chen CL, Bojikian KD, Gupta D, Wen JC, Zhang Q, Xin C, Kono R, Mudumbai RC, Johnstone MA, Chen PP, Wang, RK, "Optic nerve head perfusion in normal eyes and eyes with glaucoma using optical coherence tomography-based microangiography," Quant Imaging Med Surg, 2016 Apr;6(2):125-133

4. Chen CL, Zhang A, Bojikian KD, Wen, JC, Zhang, Q, Xin, C, Mudumbai, RC, Johnstone, MA, Chen, PP, Wang, RK, "Peripapillary Retinal Nerve Fiber Layer Vascular Microcirculation in Glaucoma using Optical Coherence Tomography–based Microangiography," Invest Ophthalmol Vis Sci. 2016 Jul;57(9):OCT475–OCT485

## Stress /Strain and IOP and finite elements

## SLO 78 aa Glaucoma peripapillare





Uno studio biomeccanico del danno strutturale e sulla deformabilità sclerale (Strain) è condotto da anni da Claude Burgoyne (Portland Oregon, USA). Da oltre un decennio Burgoyne studia gli effetti della IOP sulla sclera e, in particolar modo, sulla regione peripapillare

Bruno L., Fazio M. A., Poggialini A., Lucente A. Identificazione dei Meccanismi di Danneggiamento dei Tessuti dell'Occhio Mediante Analisi Numeriche e Sperimentali. Atti del convegno "9° Congresso Internaz. SOI 2011. Massimo A. Fazio, Rafael Grytz, L. Bruno, Michael J. A. Girard, Stuart Gardiner, Christopher A. Girkin, J. Crawford Downs. Regional Variations in Mechanical Strain in the Posterior Human Sclera. Investigative Ophthalmology & Visual Science, August 2012, Vol. 53, No. 9.

















8 mm x 8 mm



**FM** RD Angio OD 01/2018





Name: ID: DOB: Gender: Technician:	Sierosa CZMI220218430 12/11/1965 Male Operator, Cirrus	Exam Date: Exam Time: Serial Number: Signal Strength:	OD 03/10/2018 15:47 5000-6254 6/10	CZMI	ZEISS
	Angiography	Analysis : Angiography 3x	3 mm		OD 🌒 🔿 OS
Retina Depth	Encoded Retina	AngioPlex - Avaso	sular	Structure - Av	ascular
RPE-RPI	E Fit ORCC	TIN Slice: 104 Top: OPL+111µ	Bottom: RPEFit+41µ		Tracked during scan
Comments	ysis Edited: 03/10/2018 15:55	Doctor's Signature			CIRRUS ANGIO SW Ver: 11.0.0.29946 Copyright 2018 Carl Zeiss Meditec, Inc All Rights Reserved Page 1 of 1

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## **CNV Classification based on location by Gass and Freund**

• Type 1: below EPR or Sub-EPR Occulta (Jung and Freund AJO 2014)

Forma più comune, placca ICG, **anti-vegf** + polipoide, net tra EPR e Bruch, **wider than type 2**, **avascular zone usually not involved** 

• Type 2: above EPR or Sub-Retinal Classica, i net penetrano il complesso coroide-Bruch-EPR e proliferano nello spazio sottoretinico al di sopra dell'EPR, + miopia patologica, coroidite multifocale, anti-vegf - smaller than type 1, Very heterogeneous shapes avascular zone always involved.

• **Type 3: intraretinal RAP** o anastomosi retino-coroideali (RCA) 15% of patients with neovascular age-related macular degeneration, bilateral disease, presence of pigment epithelial detachments, and reticular pseudodrusen, introduced by Freund in 2008 in vivo imaging does not allow us to conclusively rule out **preexisting Type 1** neovascularization or even early RCA; intraretinal anastomosis from the **deep plexus going toward the RPE**. YANNUZZI PROPOSED THREE VARIANTS

• Type 4: mixed 1-2 initially located below the EPR Type 1, NV spread out into the outer retina Type 1

• **Filamentous (pachychoroid)NVs** by Warrow DJ. Retina. 2013; **Type 1** (sub-retinal pigment epithelium) associated with choroidal thickening that includes pachychoroid pigment epitheliopathy, central serous chorioretinopathy, and polypoidal choroidal vasculopathy

• **Myopic CNVS**  $\pm$  10%  $\geq$  6 D, 26 mm axial length start **above the EPR Type 2** and penetrate into avascular zone, usually small size, even if they can get to be much bigger

#### Residual flow in fibrosis

OCT-A Sensitivity = 81.8%, Specificity = 100%





















AngioPlex Montage See more with wide-field OCT angiography (up to 50 degrees) Comparable to most traditional fundus cameras



Montage 5 images 8x8mmm with AngioPlex Cirrus Zeiss 5000







Stude Countro

Montage 6 images 6x6mm with AngioPlex Cirrus Zeiss 5000



Ultra-widefield OCTA (~20-mm width, 10-mm height,7-mm depth) 200-kHz Swept-Source OCT System. (by Simon S. Gao et al.)



"Any sufficiently advanced technology is indistinguishable from magic." Arthur C. Clarke (1917/2008) was one of the most important and influential figures in 20th century science fiction.






## Widefield and Ultra-Widefield in Ophthalmology



## Thank you for your kind attention!



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