Exporing the Ocular surface from the basics to the more sophisticated

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des QUINZE-VINGTS

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15-20
HÔPITAL NATIONAL DE LA VISION
PARIS

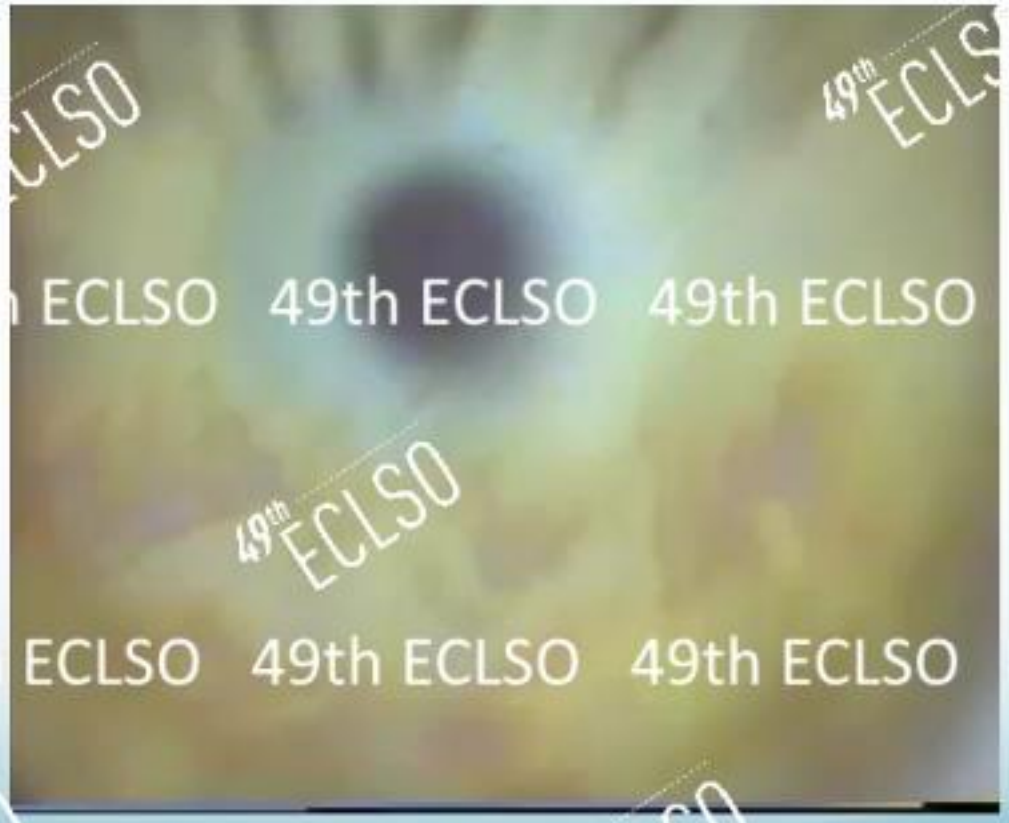
EuDES

Financial disclosure:

- Consultant for Abbvie, Alcon, Horus Pharma, Oculis, Santen, Théa

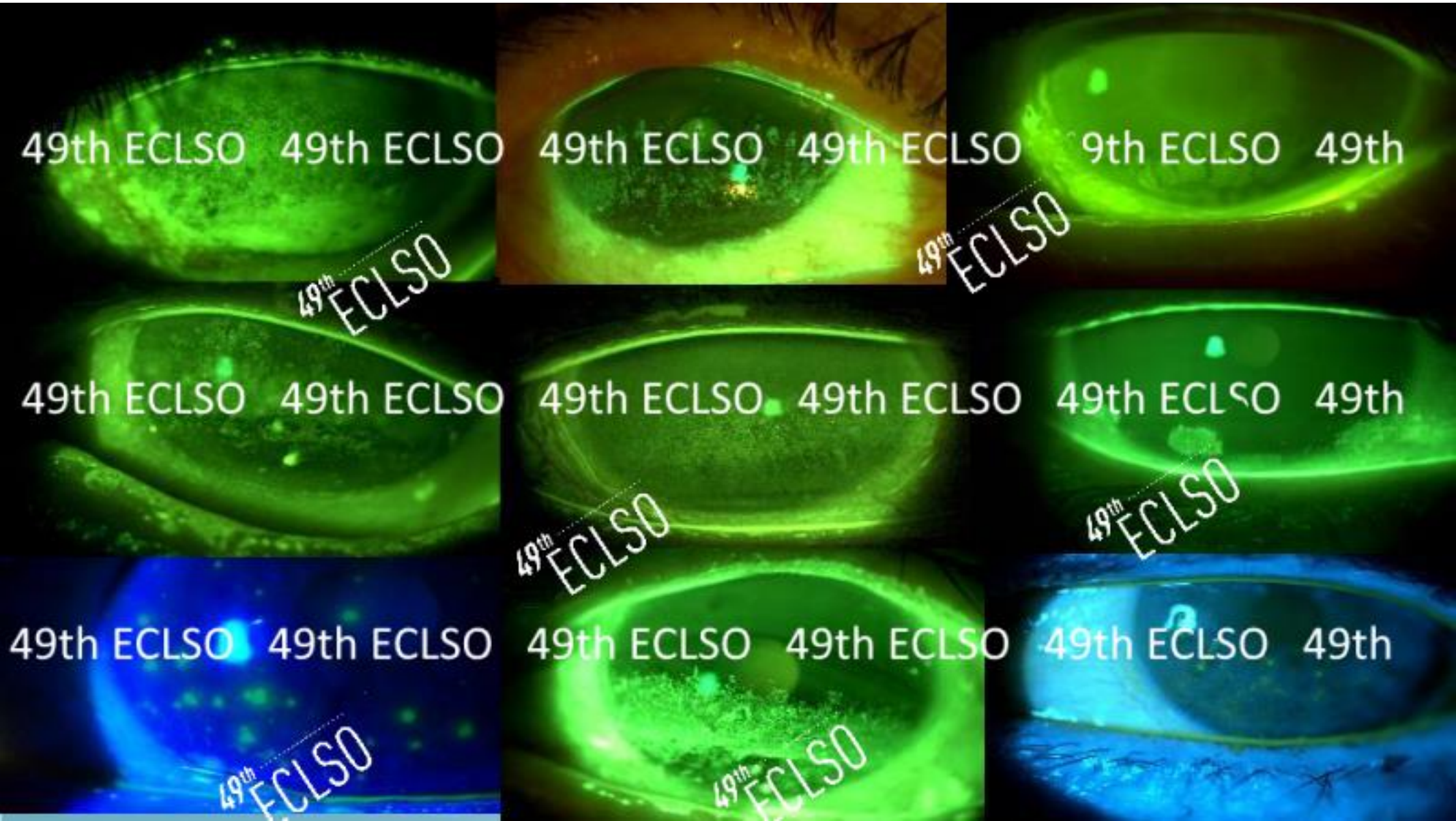
- No conflict of interest in this presentation

Many techniques have been developed to investigate the Tear Film and Ocular Surface



Courtesy Jean-Pierre Guillon

1- The basics: a single eyedrop of fluorescein may bring major information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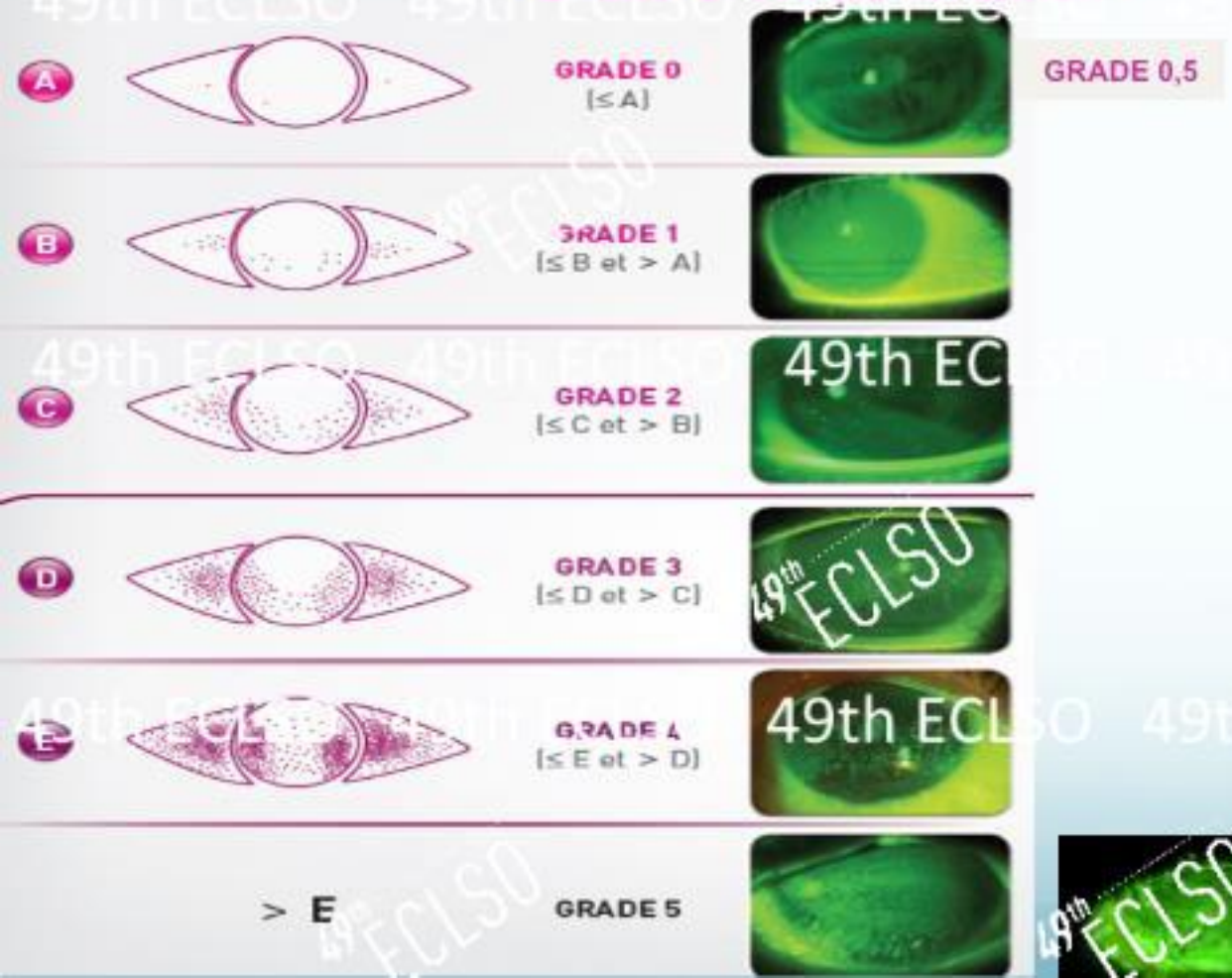
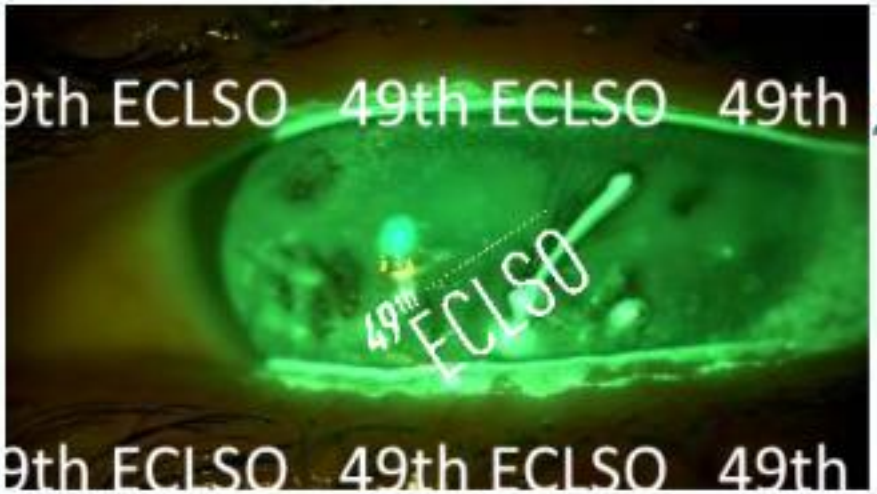
Scoring Severity: the Oxford Scale

Grade 0: No punctuation



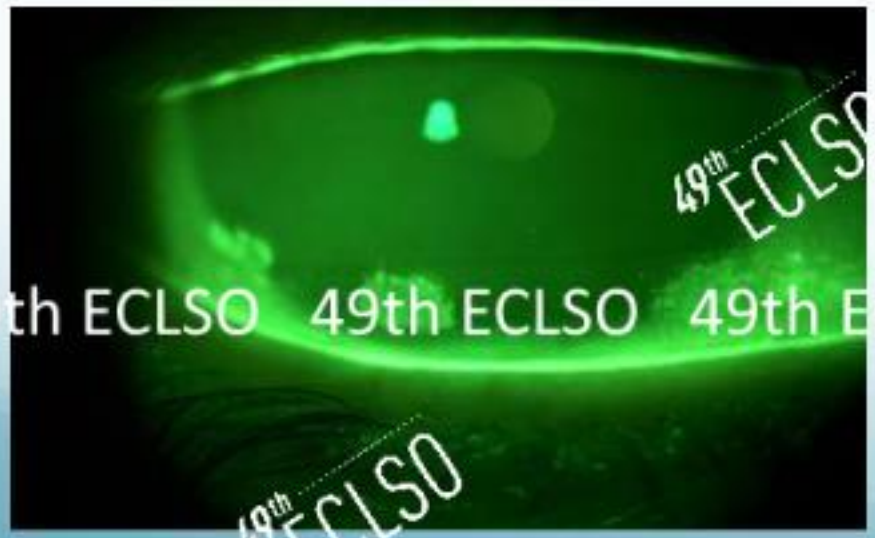
GRADE 0,5

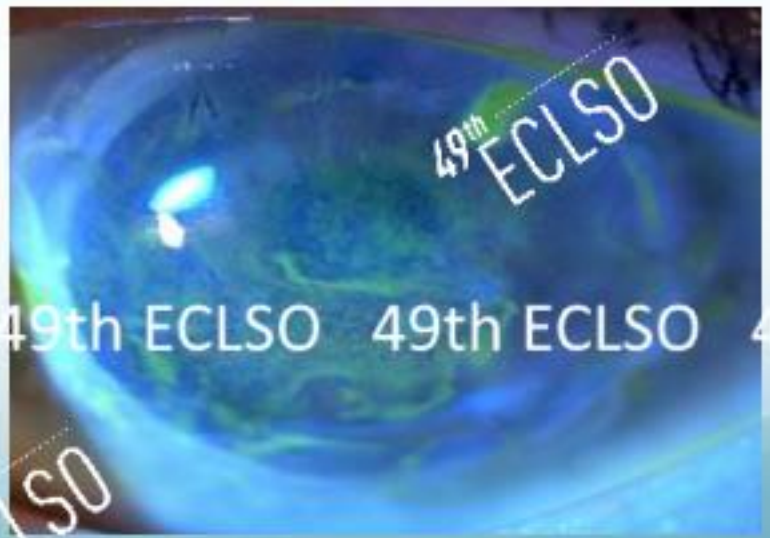
logarithmic scale
Bron et al. 2003

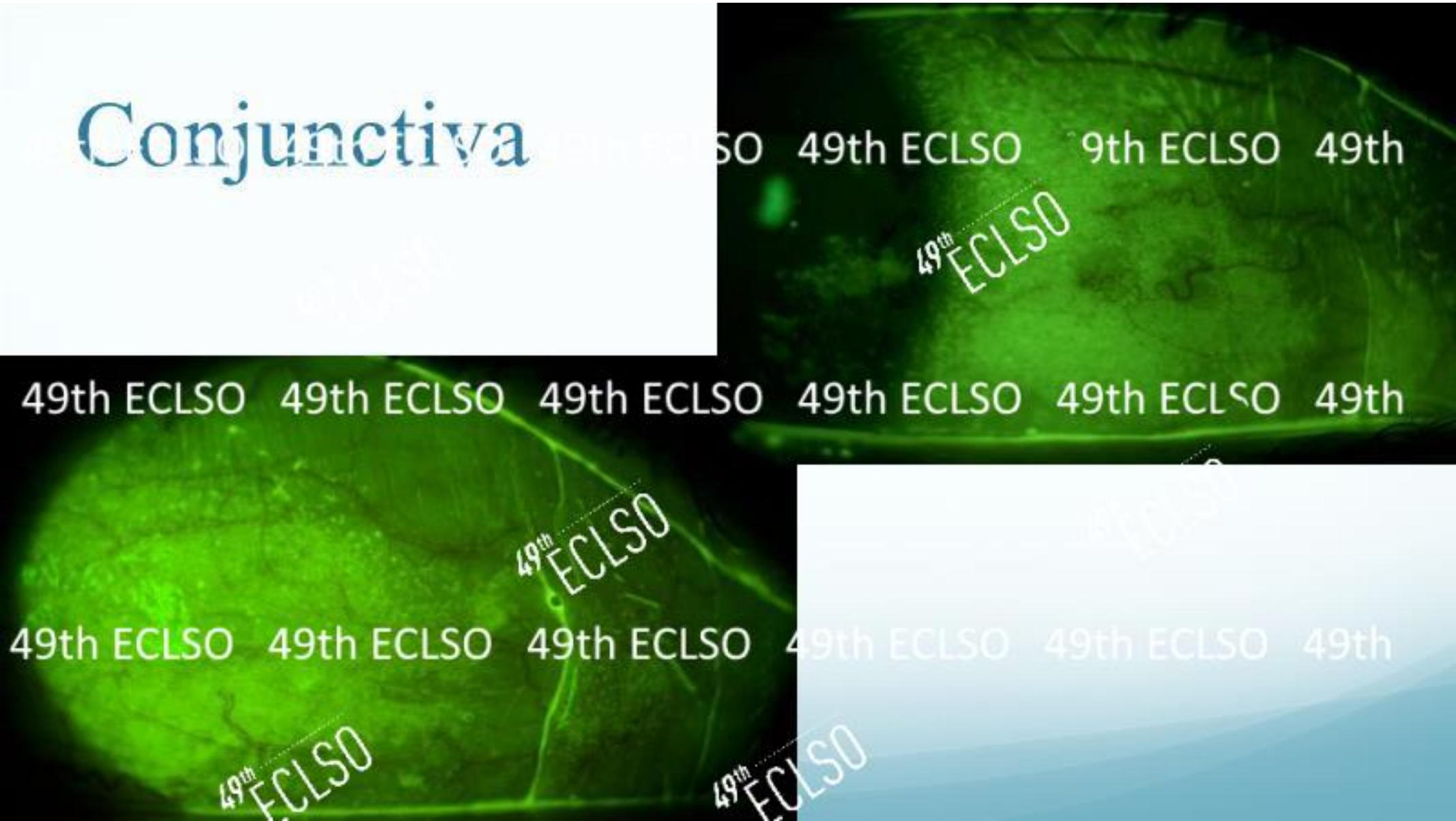


Additional signs of severity:

- filaments
- confluence
- conjunctivalization



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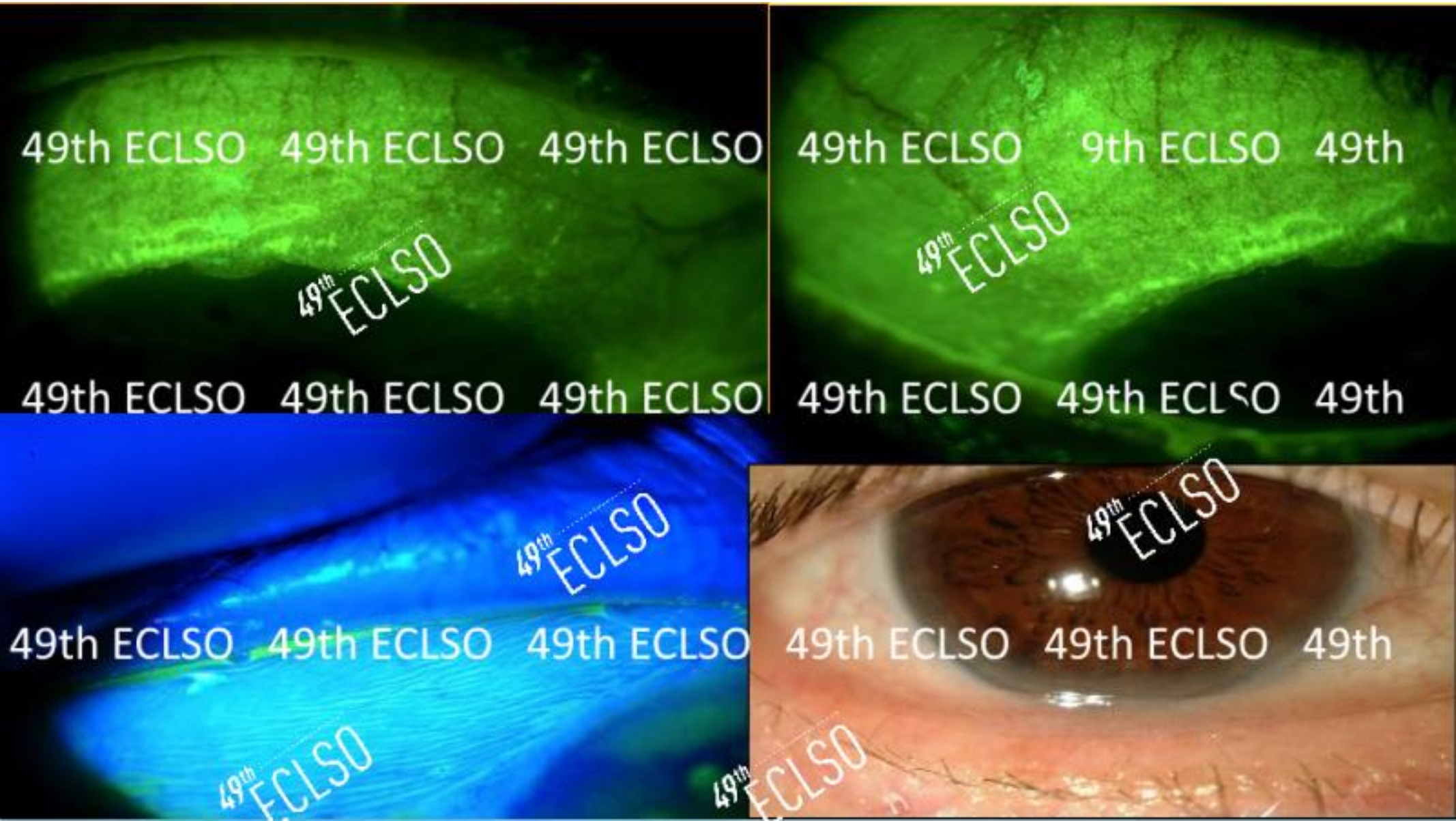
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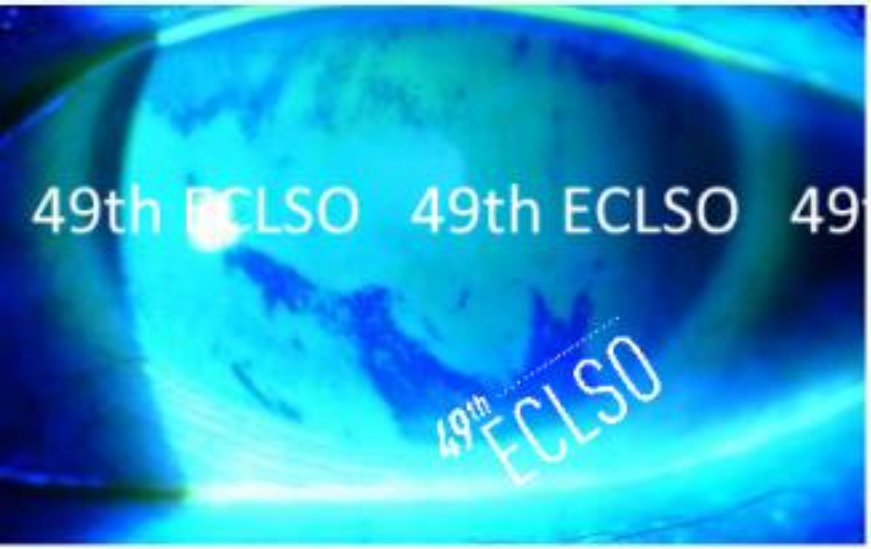
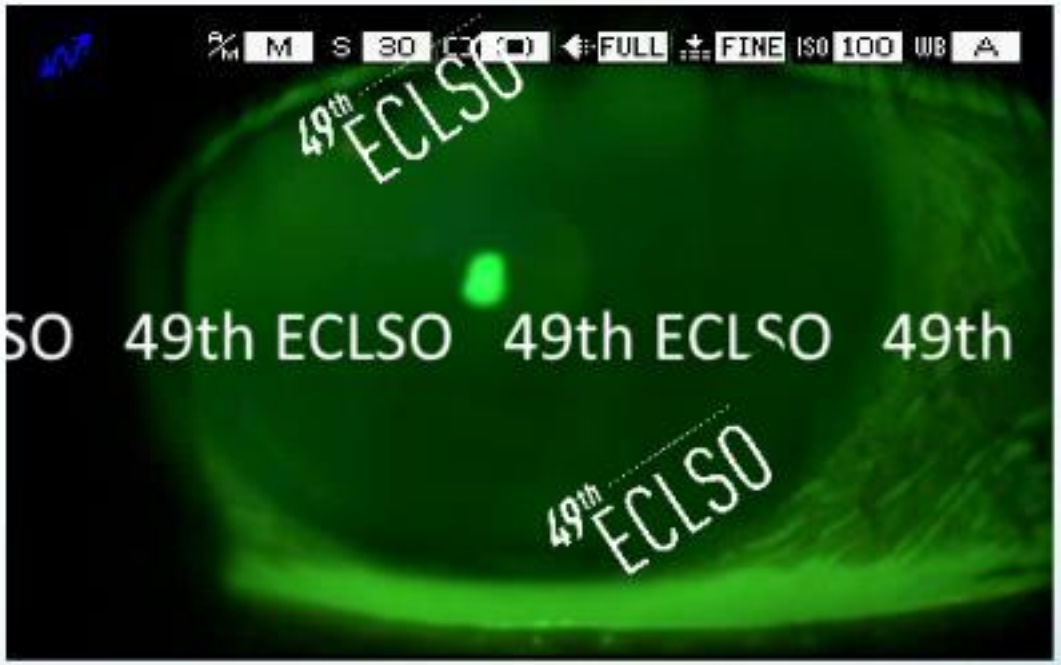
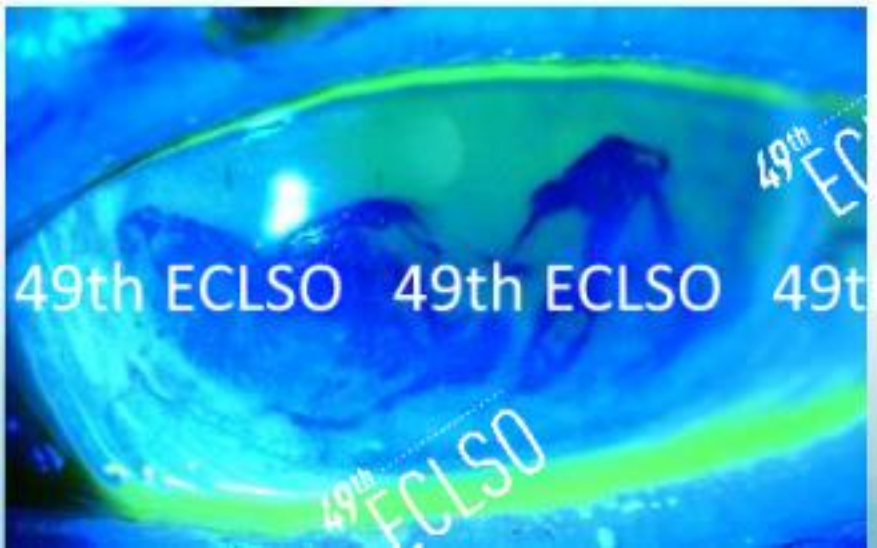


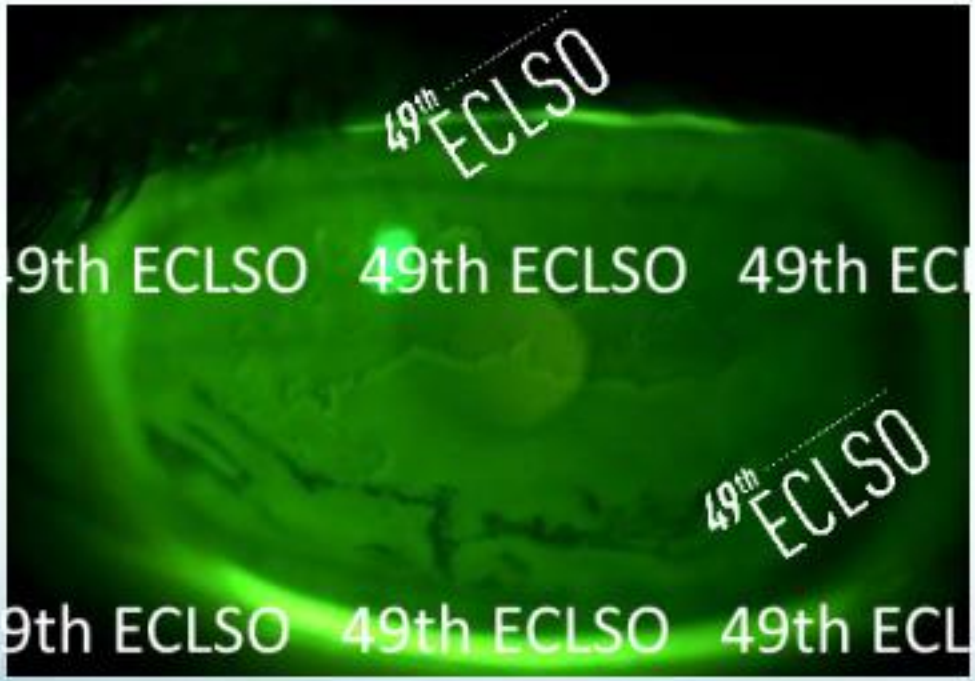
The Tear Film

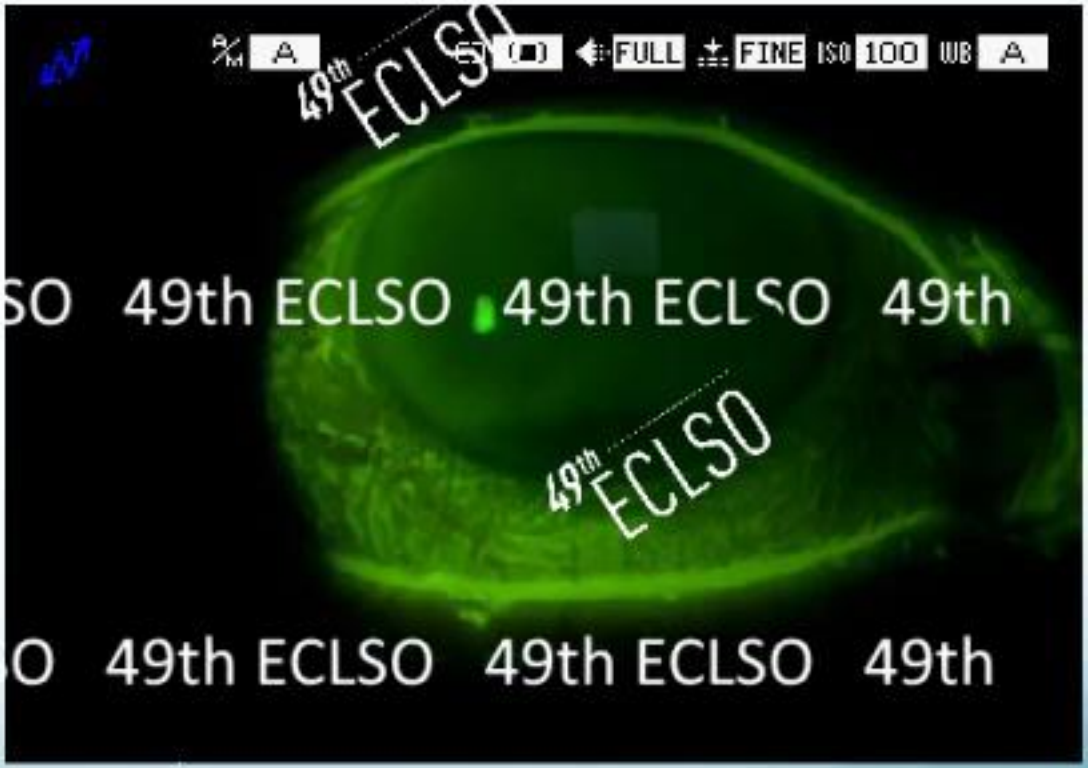




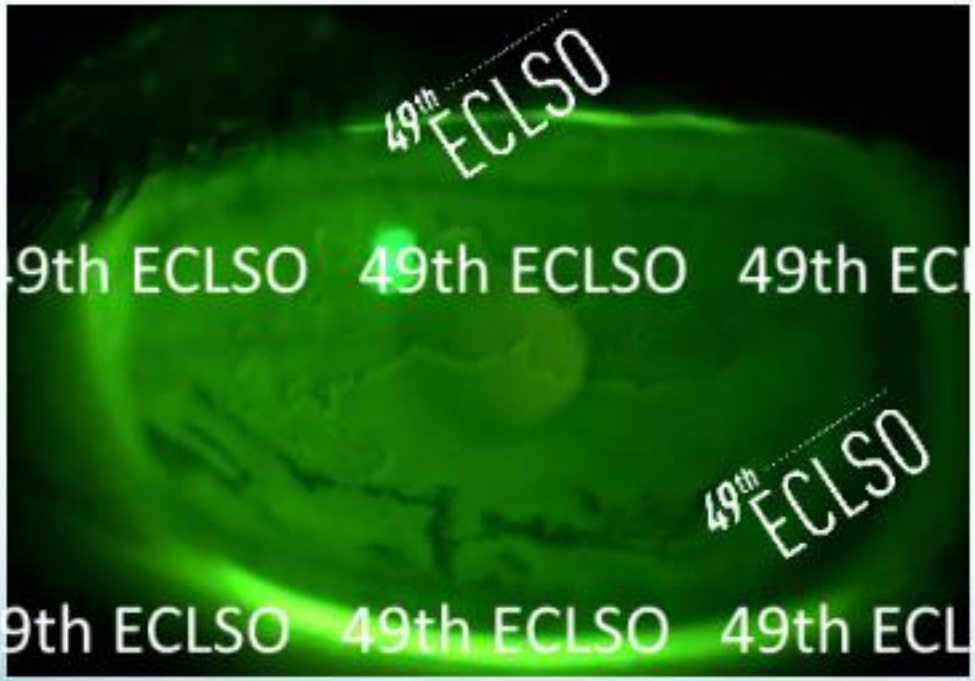
Tear Instability:
Evaporative, lipid-deficiency?
Mucin-deficiency?

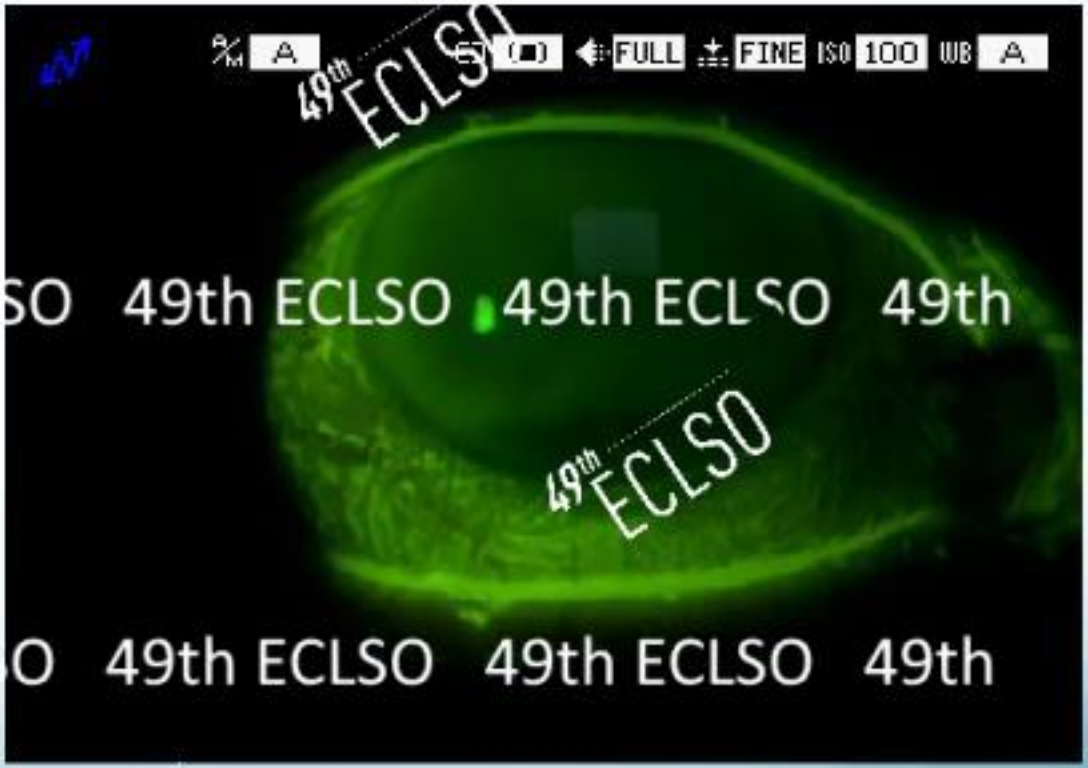
Intricated mechanisms





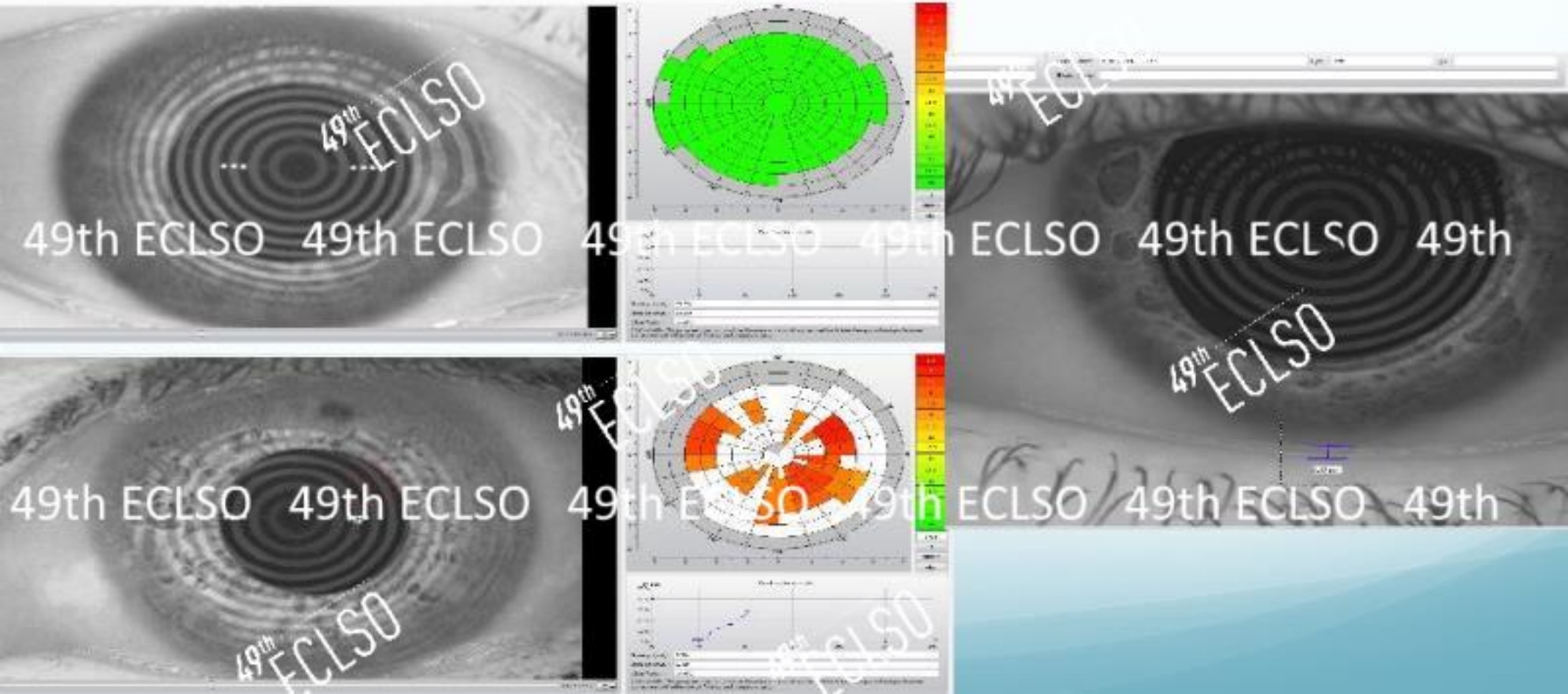
Intricated mechanisms





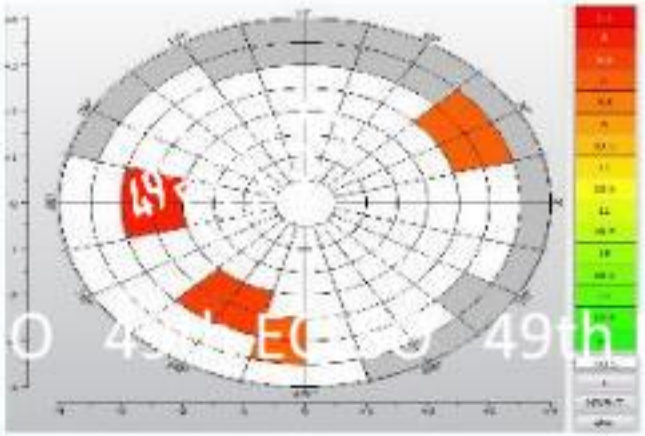
2- Biological and Functional (bio)markers

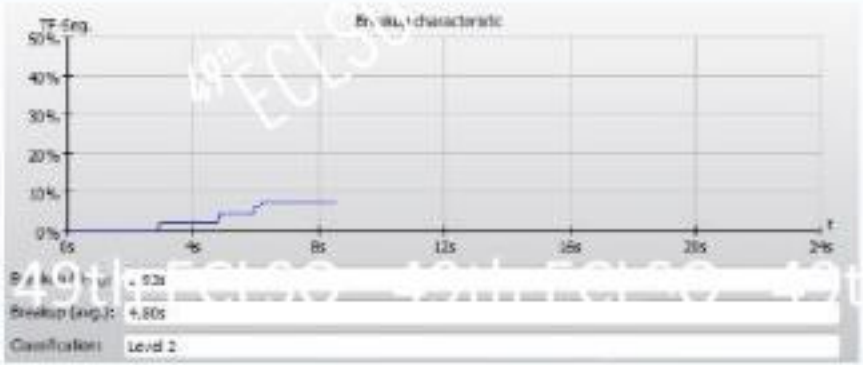
KERATOGRAPH 5 (Oculus): NIKBUT and Tear Meniscus Height



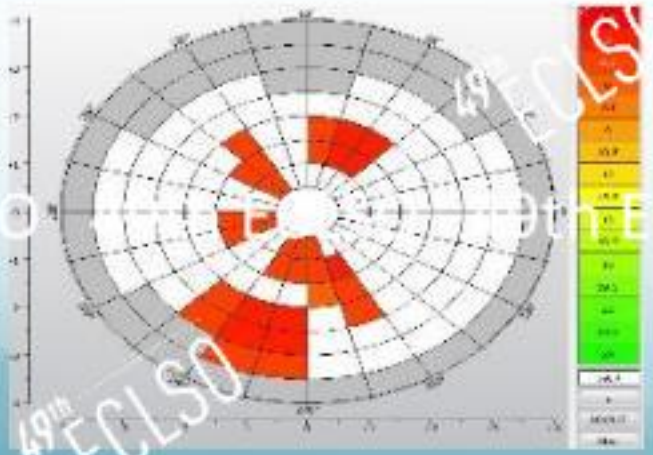
KERATOGRAPH 5: dynamics

OD

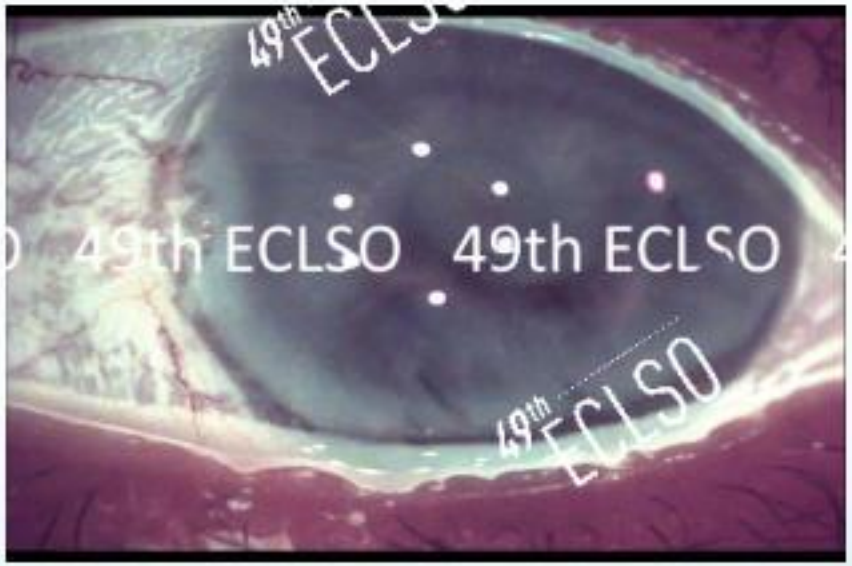




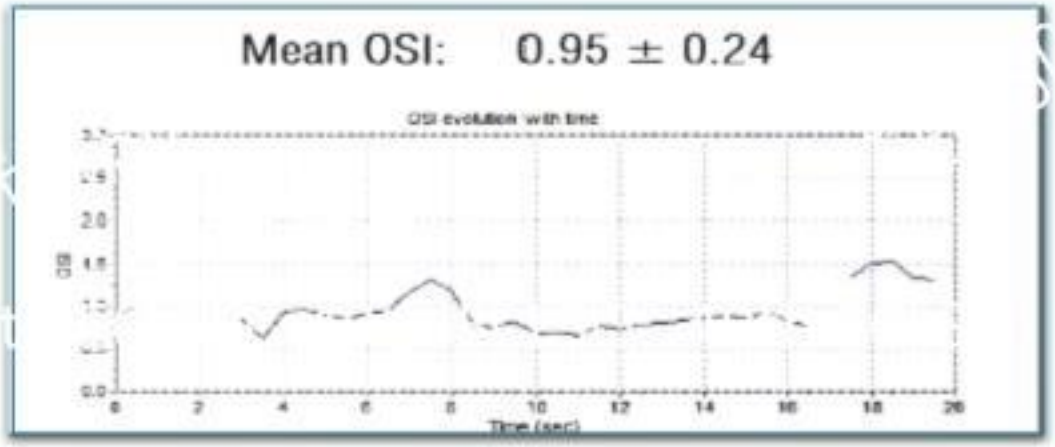
OS

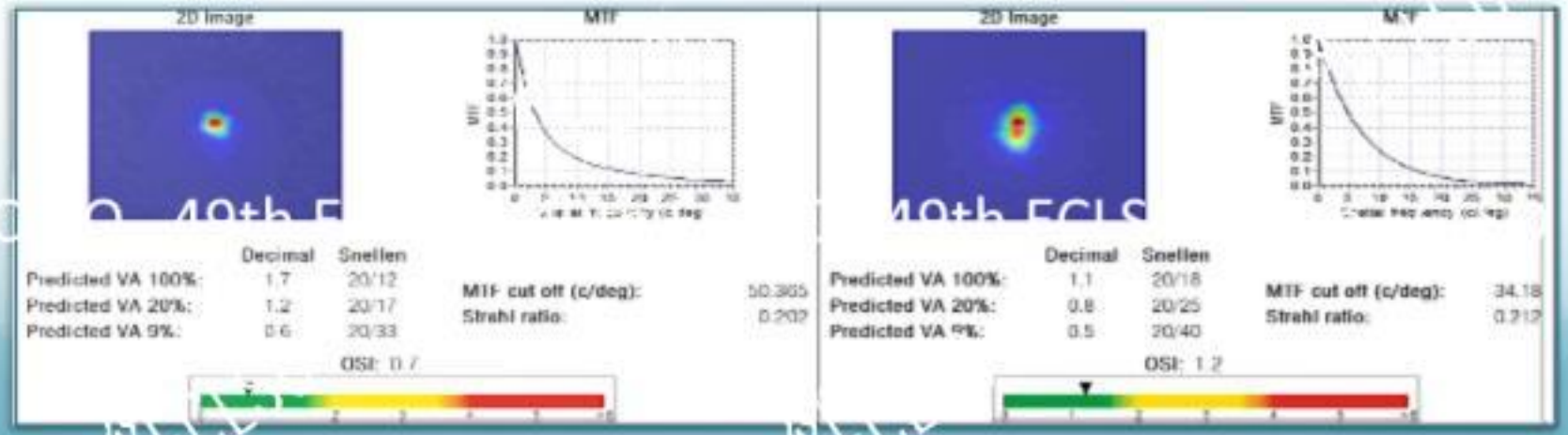


Various tear disruption types (Yokoi et al.)

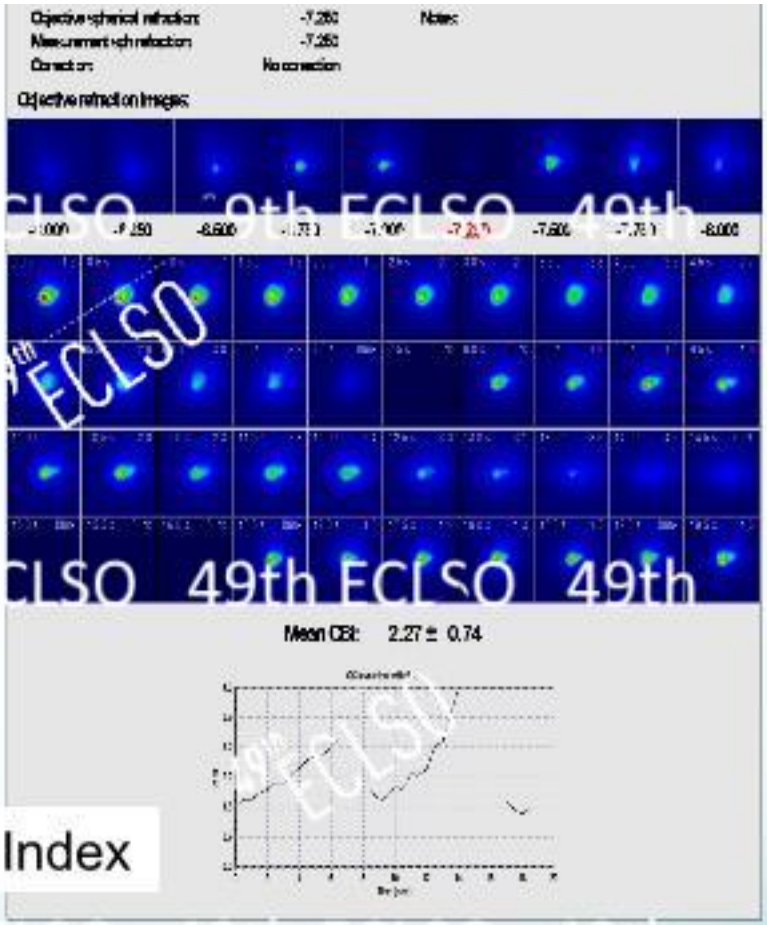


OQAS (Visiometrics S.L.): AN ANALYSIS OF VISUAL FUNCTION





OSD AND VISUAL QUALITY



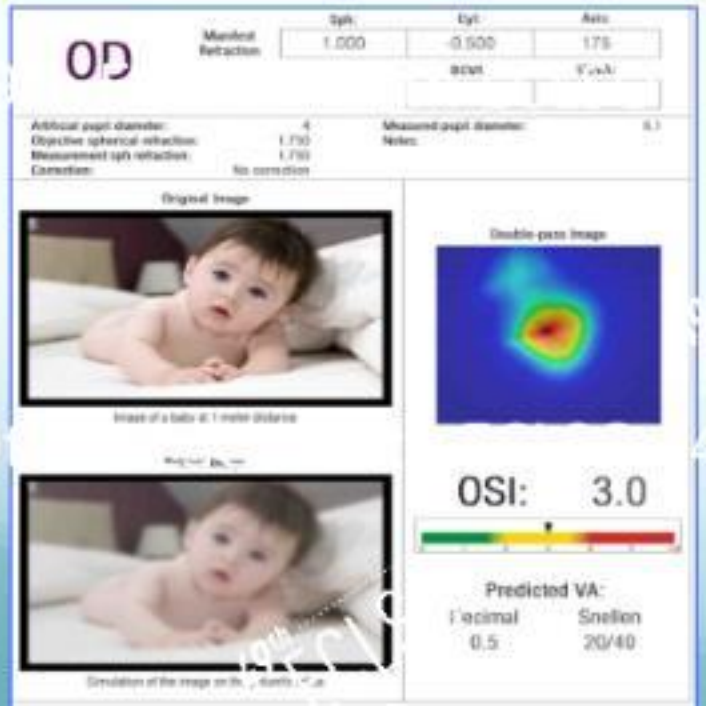
tvst

https://doi.org/10.1167/tvst.7.4.5

Article

Impact of Dry Eye Disease on Vision Quality: An Optical Quality Analysis System Study

Antoine Herbaut[1], Hong Liang[2], Christine Rabut[2], Liem Trinh[1], Karima Kessal[2,3], Christophe Baudouin[1–4], and Antoine Labbé[1–4]



OSI: Optical Scattering Index

Table 3. Correlations Between the OSI and OSI SD with the Different Clinical Tests

	OSDI Score	BUT	Oxford	Van Bijsterveld	Schirmer	Age	Sex	OSI SD
OSI								
r	0.17*	−0.21*	0.31*	0.33*	−0.19*	0.36*	0.01	0.71*
P	0.038*	0.013*	0.0002*	0.0001*	0.025*	<0.0001*	0.91	<0.0001*
OSI SD								
r	0.12	−0.18*	0.18*	0.25*	−0.11	0.13	−0.07	
P	0.15	0.038*	0.032*	0.003*	0.192	0.126	0.43	

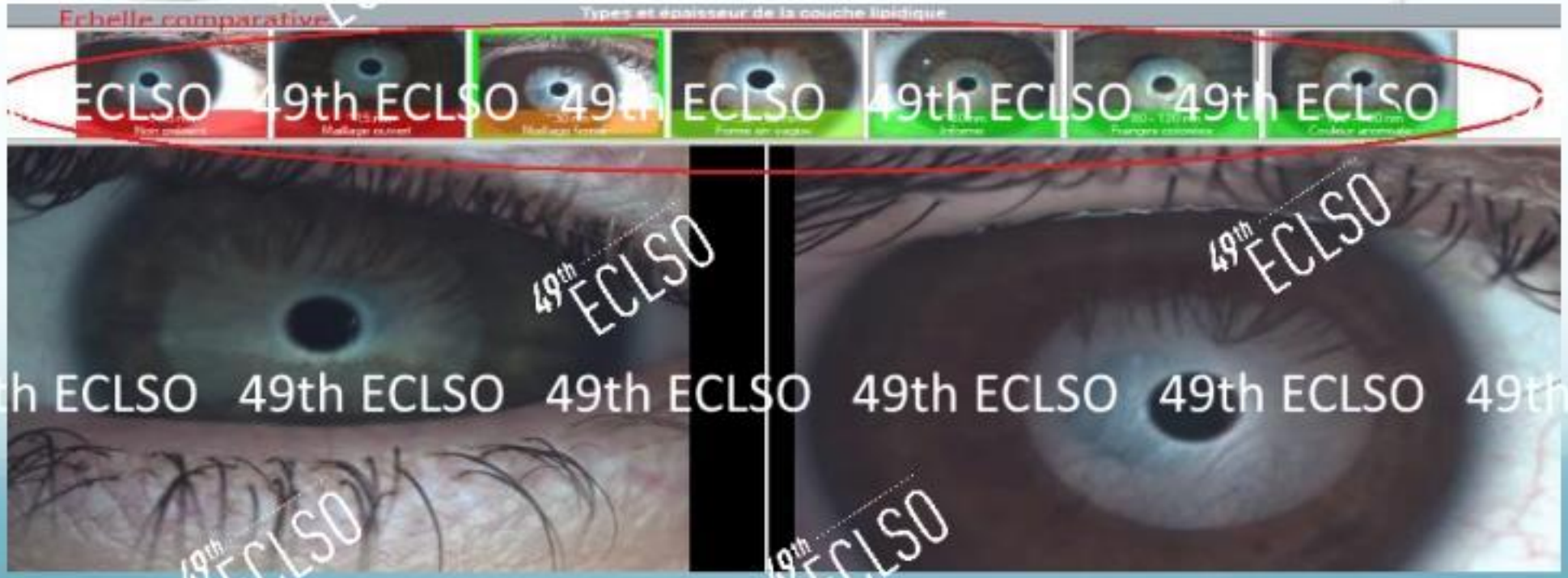
* Signifies correlations between parameters.

Interferometry

- Tearscope (Keeler)
- Lipiview (J&J)
- Lacrydiag (Quantel)

Interferometry

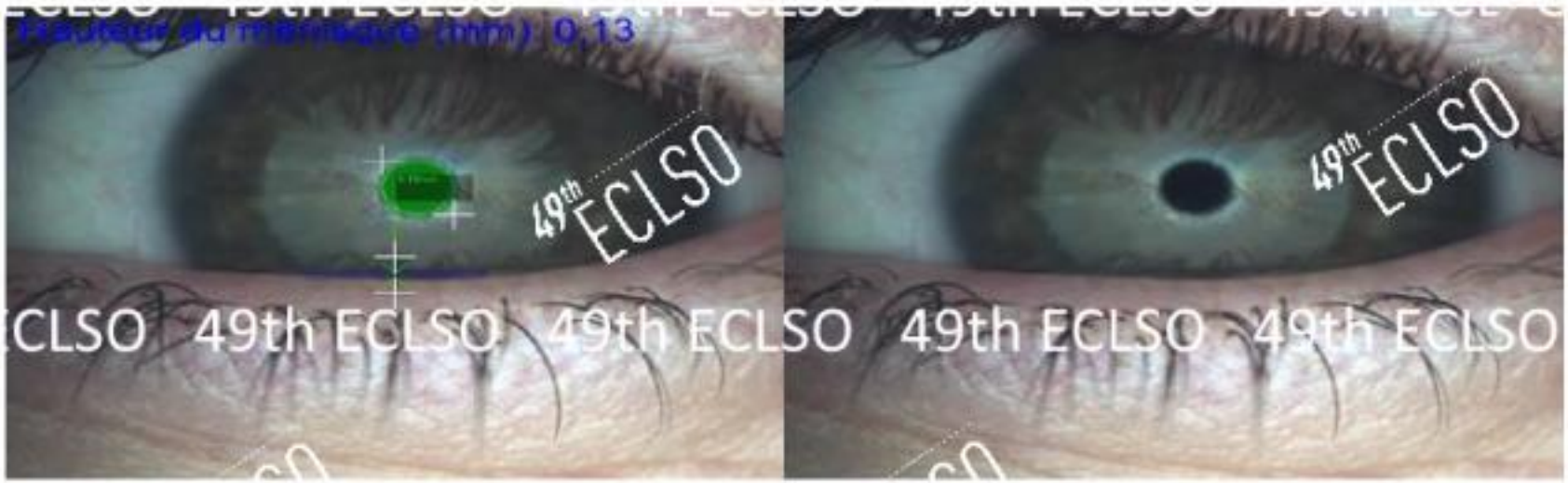
Lacrydiag ® (Quantel)



Tear Meniscus

Note:
- Hauteur du ménisque (mm): 0,13

OS



Hauteur du ménisque lacrymal (mm): 0,13mm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MEIBOGRAPHY (Keratograph 5, Lipiview, Lacrydiag)
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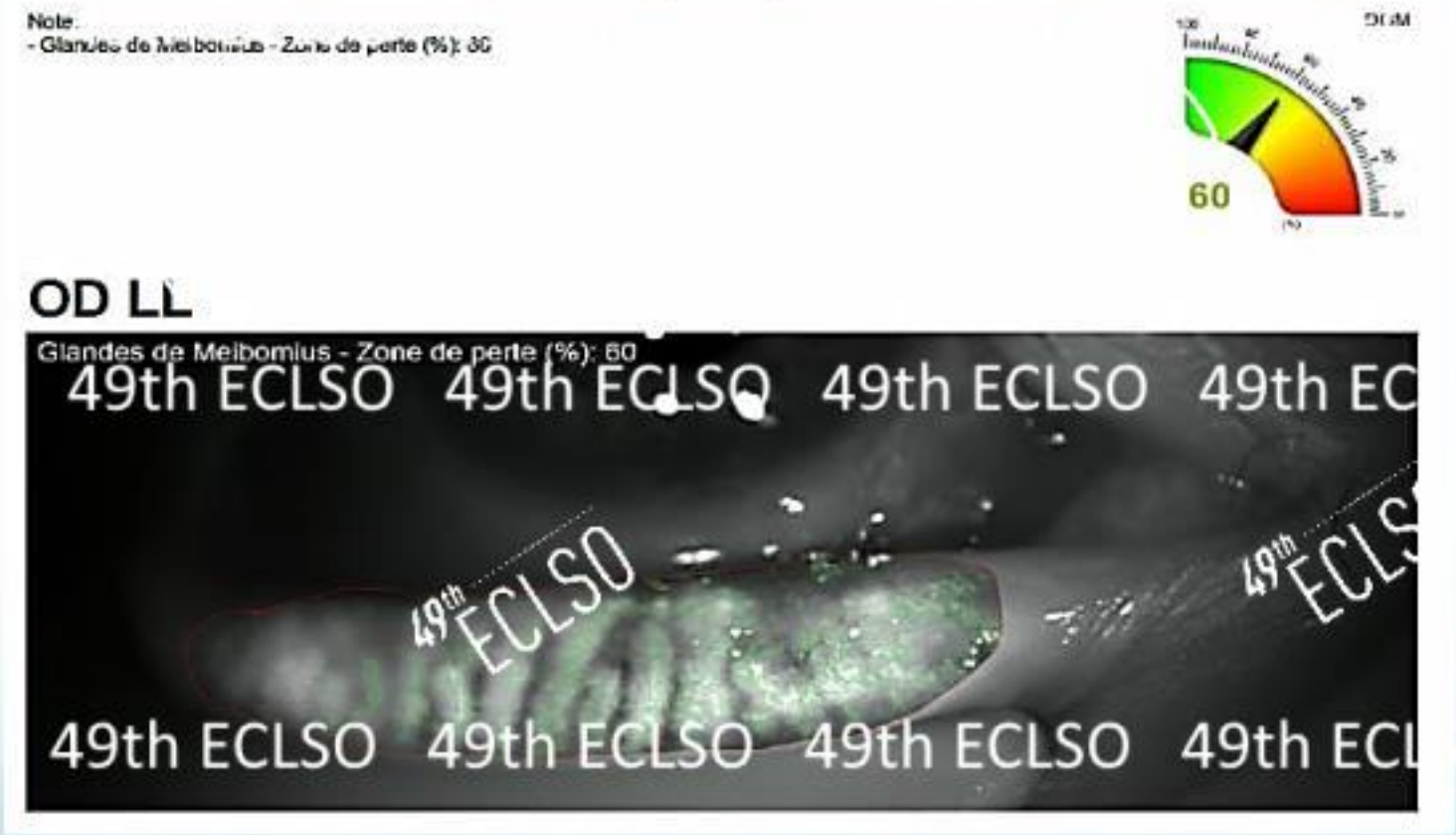
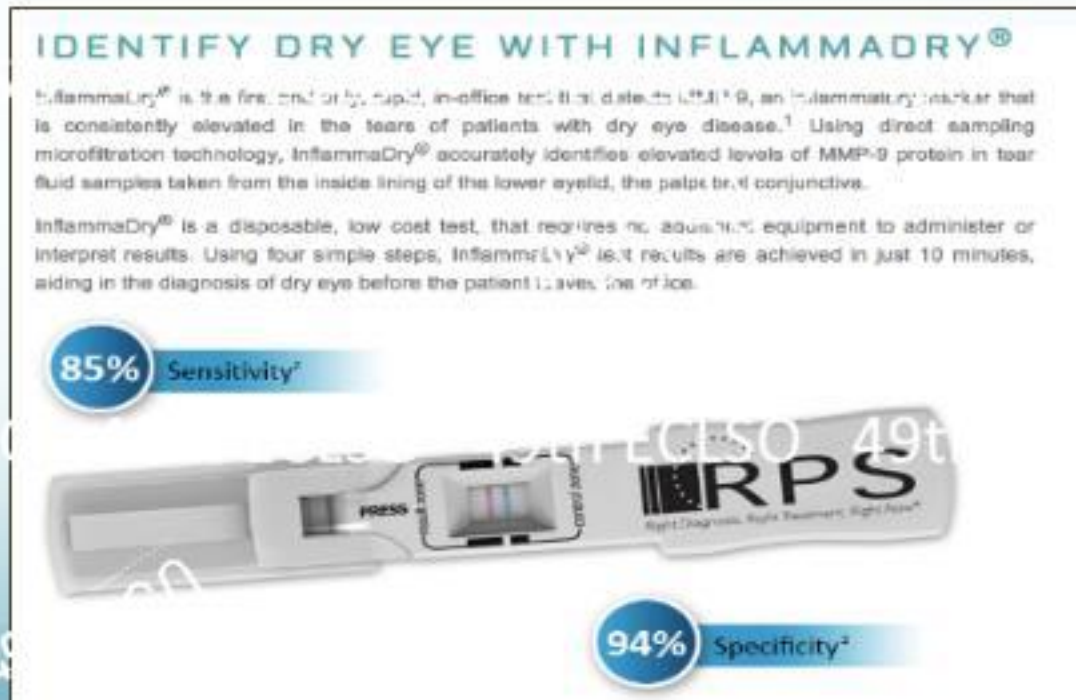
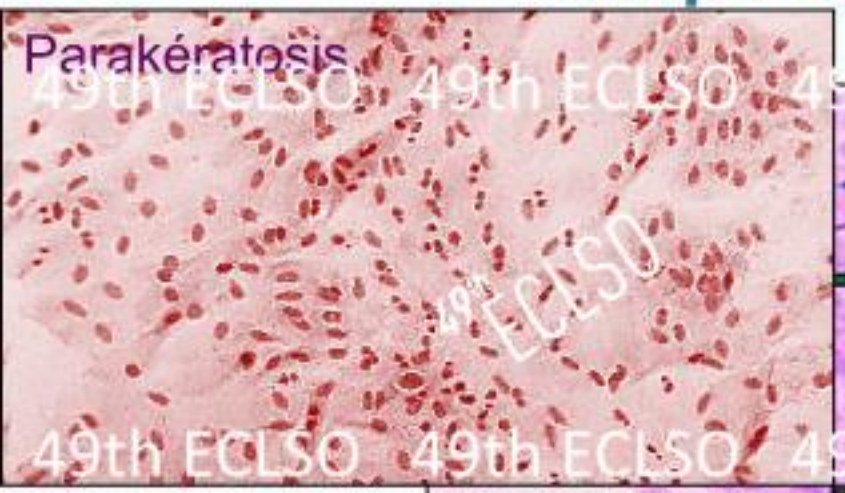
Meibography (Lacrydiag®)

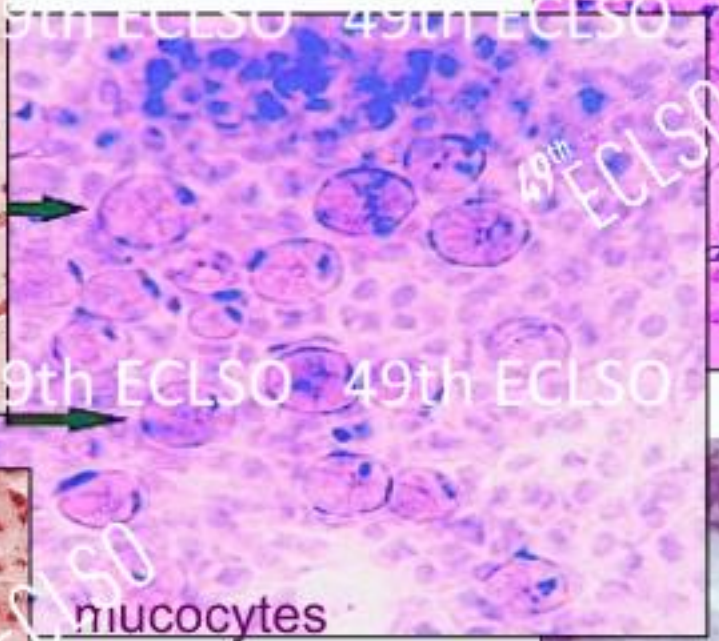


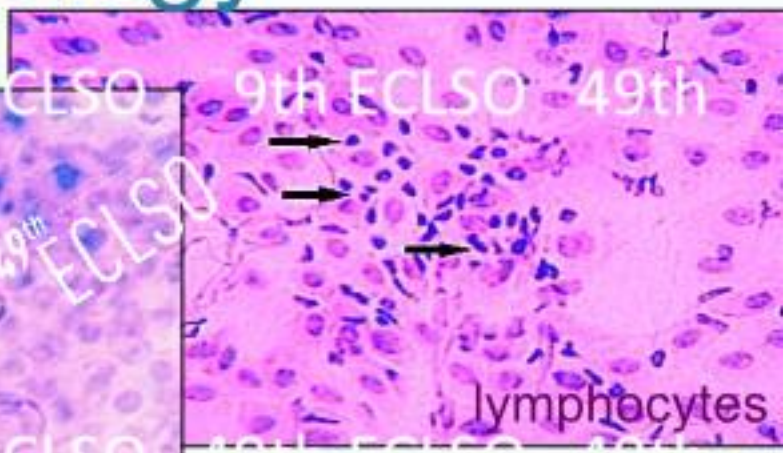
Tear osmolarity and MMP9 correlate to inflammation and severe DED

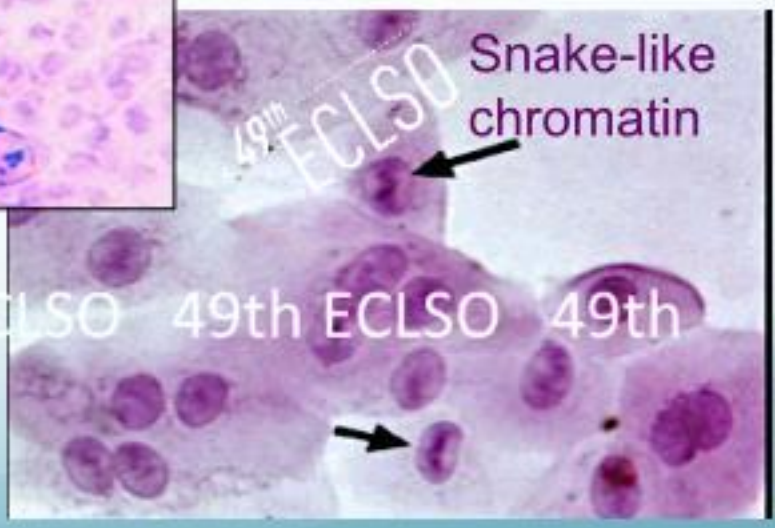


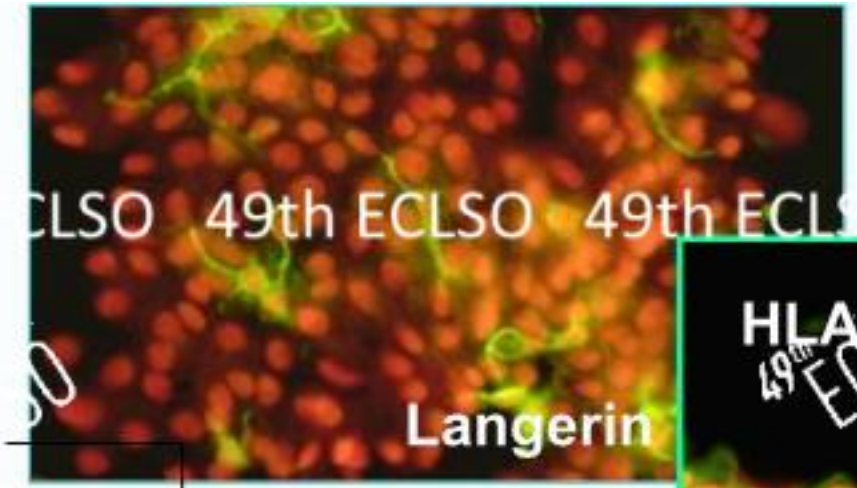
Impression Cytology

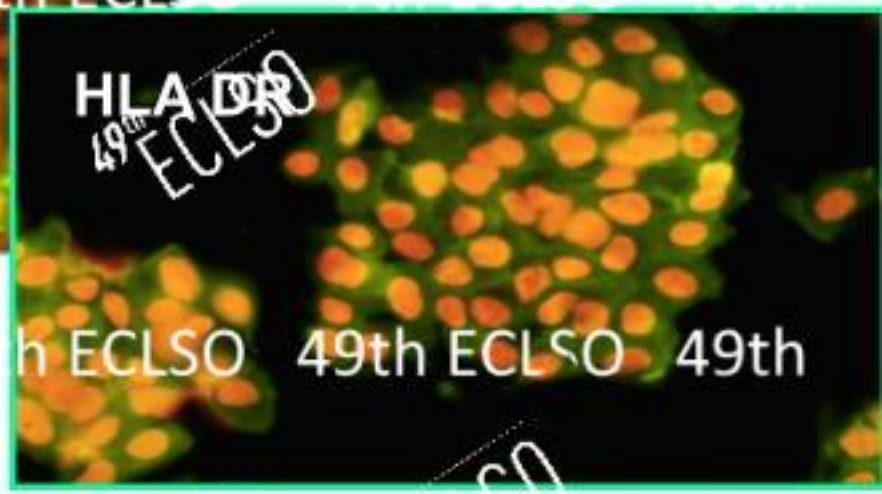


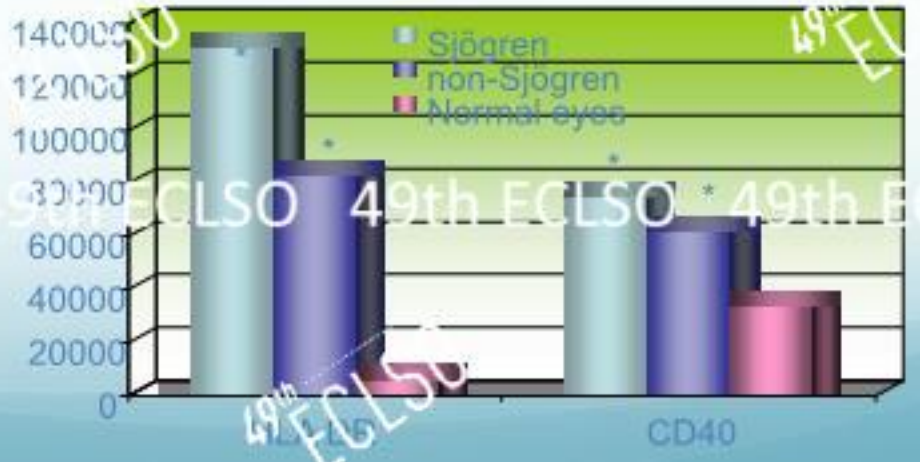




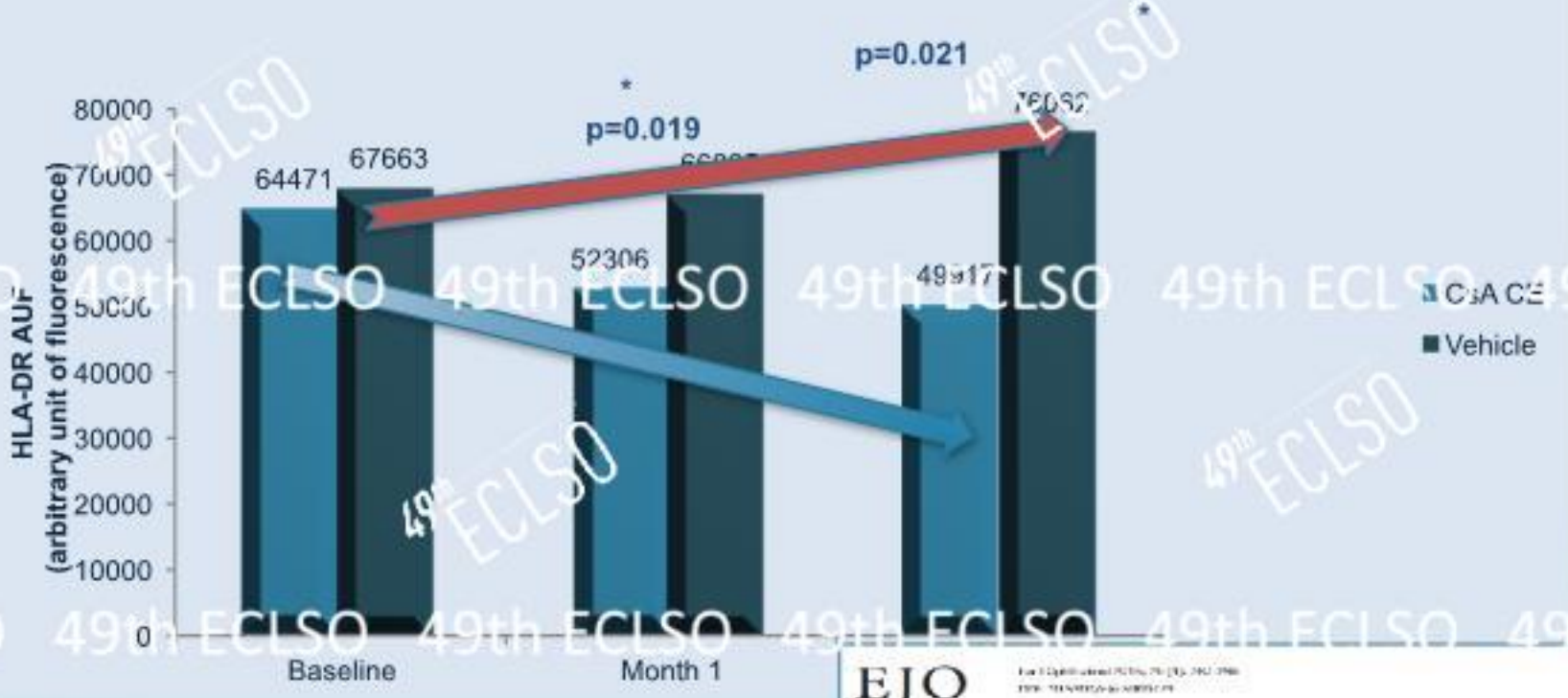



Langerin


HLA DR


140000
120000
100000
80000
60000
40000
20000
0
Sjögren
non-Sjögren
Normal eyes
CD40

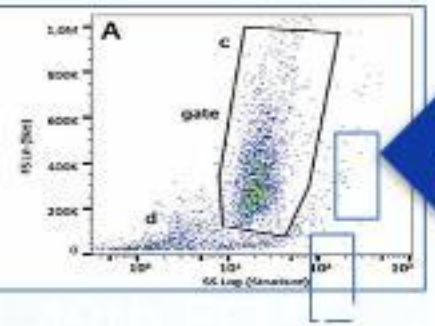
0.1% Topical cyclosporine (Ikervis®) Showed Statistically Significant Improvement in HLA DR

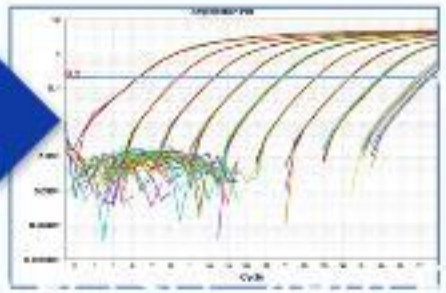


EJO

ORIGINAL ARTICLE

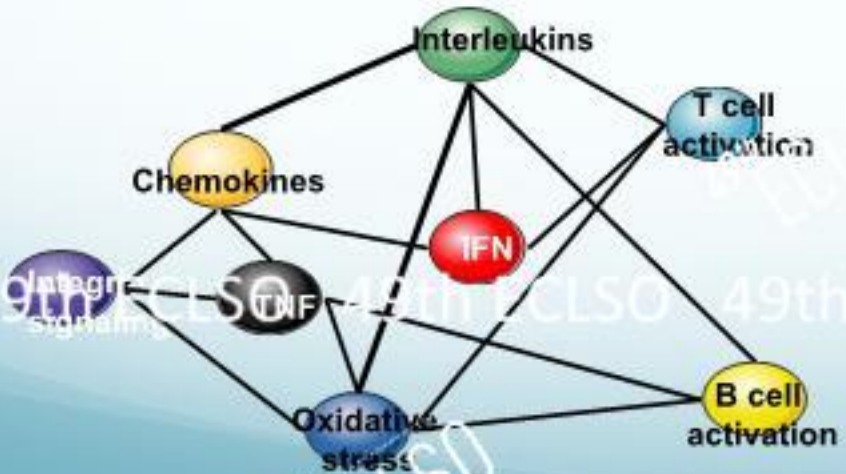
Efficacy and safety of 0.1% cyclosporine A cationic emulsion in the treatment of severe dry eye disease: a multicenter randomized trial





The « omics » offer unlimited potential markers

Proteomics
Transcriptomics
Lipidomics
Metabolomics
Microbiomics



nanoString TECHNOLOGIES

HLA DR correlates with many inflammatory markers

Genes	Gene name	HLA-DRA	
		R	p
(A) OF THE 200 DETECTED GENES, 21 TARGETS DISPLAY A HIGH CORRELATION (R > 0.8) WITH BOTH HLA-DR TRA[illegible]			
HLA-DRB1	Major histocompatibility complex, class II, DR alpha	0.90	***
[illegible]	[illegible]		***
IFN AND ISGs			
IRF1	IFN regulatory factor 1	0.88	***
IFI44	Interferon-induced protein 44	0.84	***
HSH2D	Hematopoietic SH2 domain containing	0.83	***
MX1	Myxovirus (influenza virus) resistance 1	0.85	***
OAS2	2'-5'-oligoadenylate synthetase 2	0.82	***
Toll-Like Receptors and Related Factors			
TLR2	Toll-like receptor 2	0.82	***
TLR3	Toll-like receptor 3	0.82	***
MYD88	Myeloid differentiation primary response gene (88)	0.80	***
TNF Superfamily			
[illegible]	CD40 molecule	[illegible]	***
[illegible]	TNF receptor-associated factor 2	0.80	***
TRADD	TNFRSF1A-associated via death domain	0.81	***
Enzymes			
RIPK2	Receptor-interacting serine-threonine kinase 2	0.84	***
Chemokines/cytokines			
CCL22	Chemokine (C-C motif) ligand 22	0.80	***
IL15	Interleukin 15	0.80	***
Complement and CRP			
C2	Complement component 2	0.88	***
CFB	Complement factor B	0.83	***
STAT			
STAT1	Signal transducer and activator of transcription 1	0.89	***
[illegible]	[illegible]	[illegible]	***
STAT3	Signal transducer and activator of transcription 3	[illegible]	***
MAPK			
MAPK8	Mitogen-activated protein kinase 8	0.82	***
MAPKAPK2	Mitogen-activated protein kinase-activated protein kinase 2	0.81	***

*Spearman's rank-order correlation test was carried out, p < 0.001***.*

frontiers in Immunology

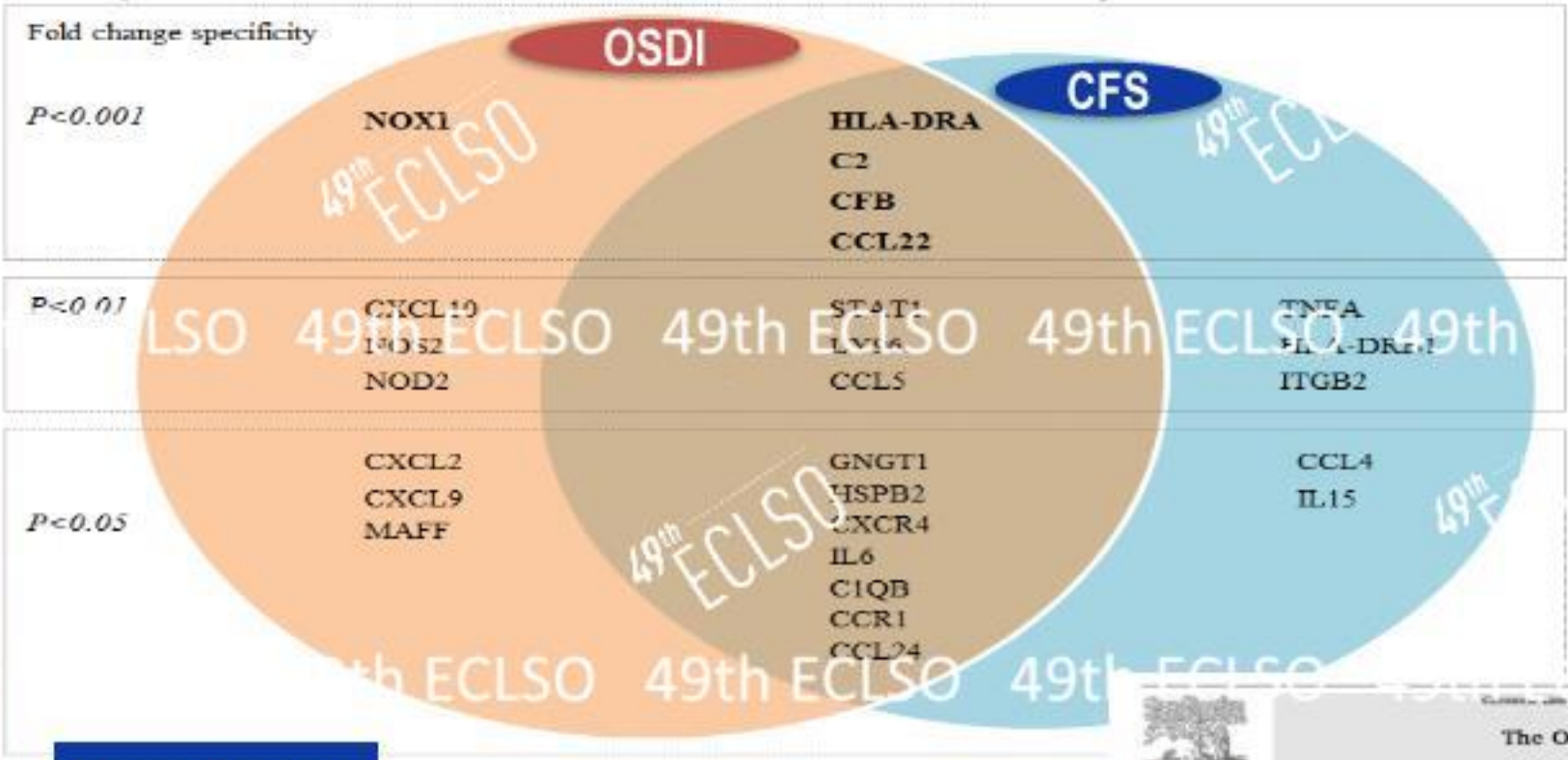
ORIGINAL RESEARCH
published: 15 October 2018
doi: 10.3389/fimmu.2018.02271

Conjunctival Inflammatory Gene Expression Profiling in Dry Eye Disease: Correlations With HLA-DRA and HLA-DRB1

Distribution of selected targets in Sjogren patients

26 targets correlated with either OSDI or CFS

14 targets correlated with both OSDI & CFS



Venn diagram

The Ocular Surface

Original Research

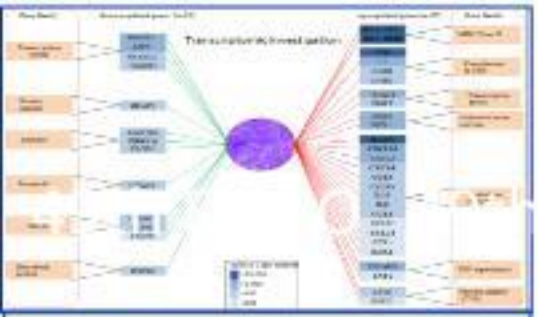
Correlation of clinical symptoms and signs with conjunctival gene expression in primary Sjögren syndrome dry eye patients

H. Liang, K. Kessal, G. Rabut, P. Daull, J.S. Garrigue, S. Melik Parsadaniantz, M. Doeguier, C. Baudouin, F. Brignole-Baudouin

What could we do with biomarkers?

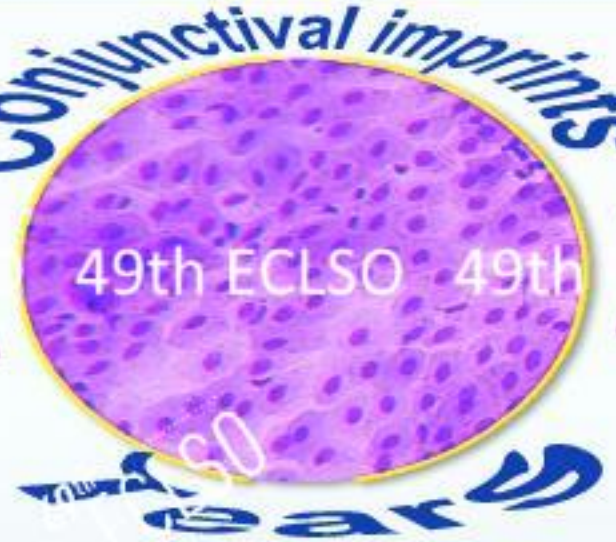
- Dry Eye vs. Allergy
- Allergic vs. Irritative
- IgE-dependent vs non IgE-dépendent
- Severe vs. Not severe
- Autoimmune vs. Inflammatory
- MGD vs. Hyposecretory
- Mucin-deficient vs. Lipid-deficient
- Infectious vs. Inflammatory
- Bacterial vs. Non bacterial
- Early vs. Evoluted
- Treatment efficient vs. Poorly efficient vs. Toxic
- And so many other…

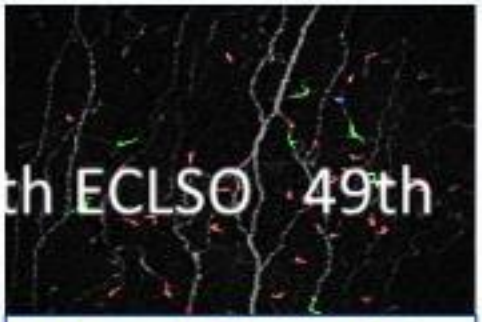
New tools of investigation



Molecular signature classification

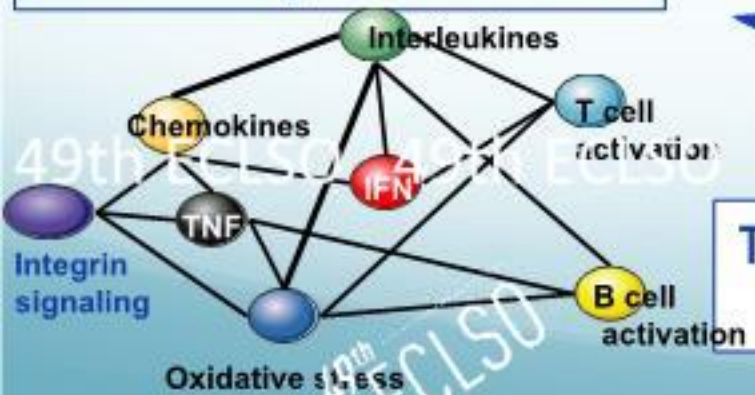
Flow cytometric quantification of proteins & receptors





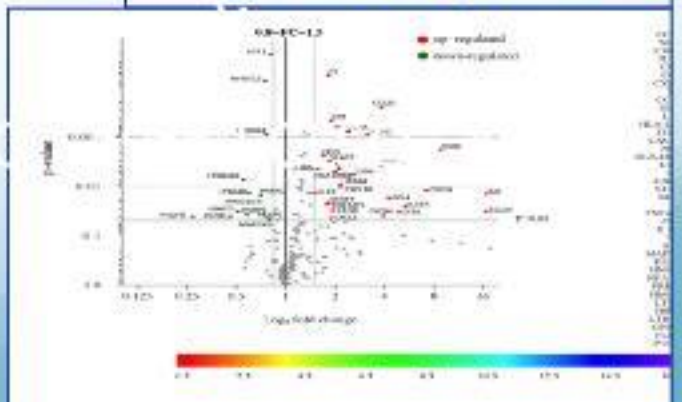
Correlations with clinical and paraclinical findings

Inflammatory interactome



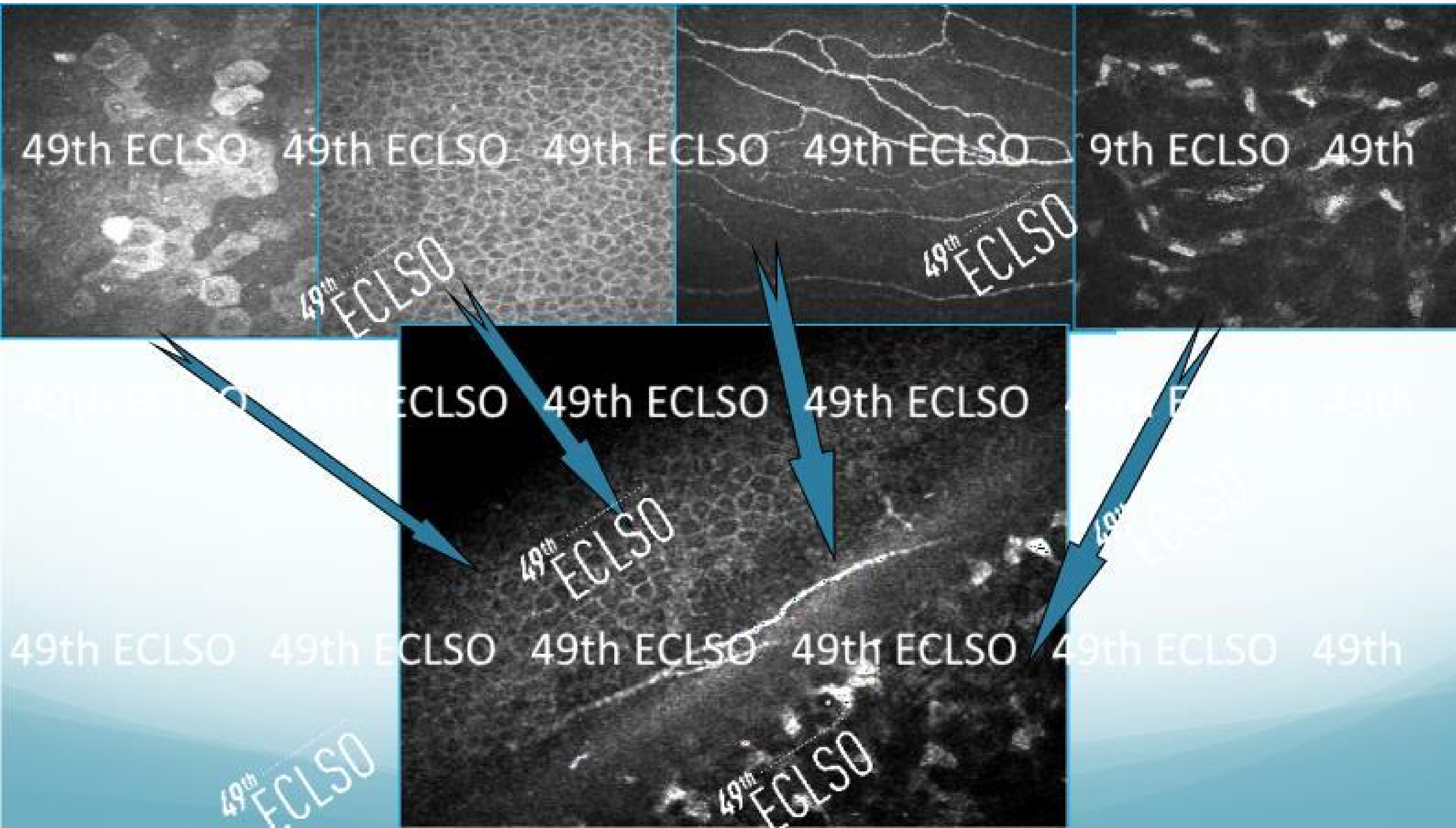
Transcriptomic investigation
miRNA investigation

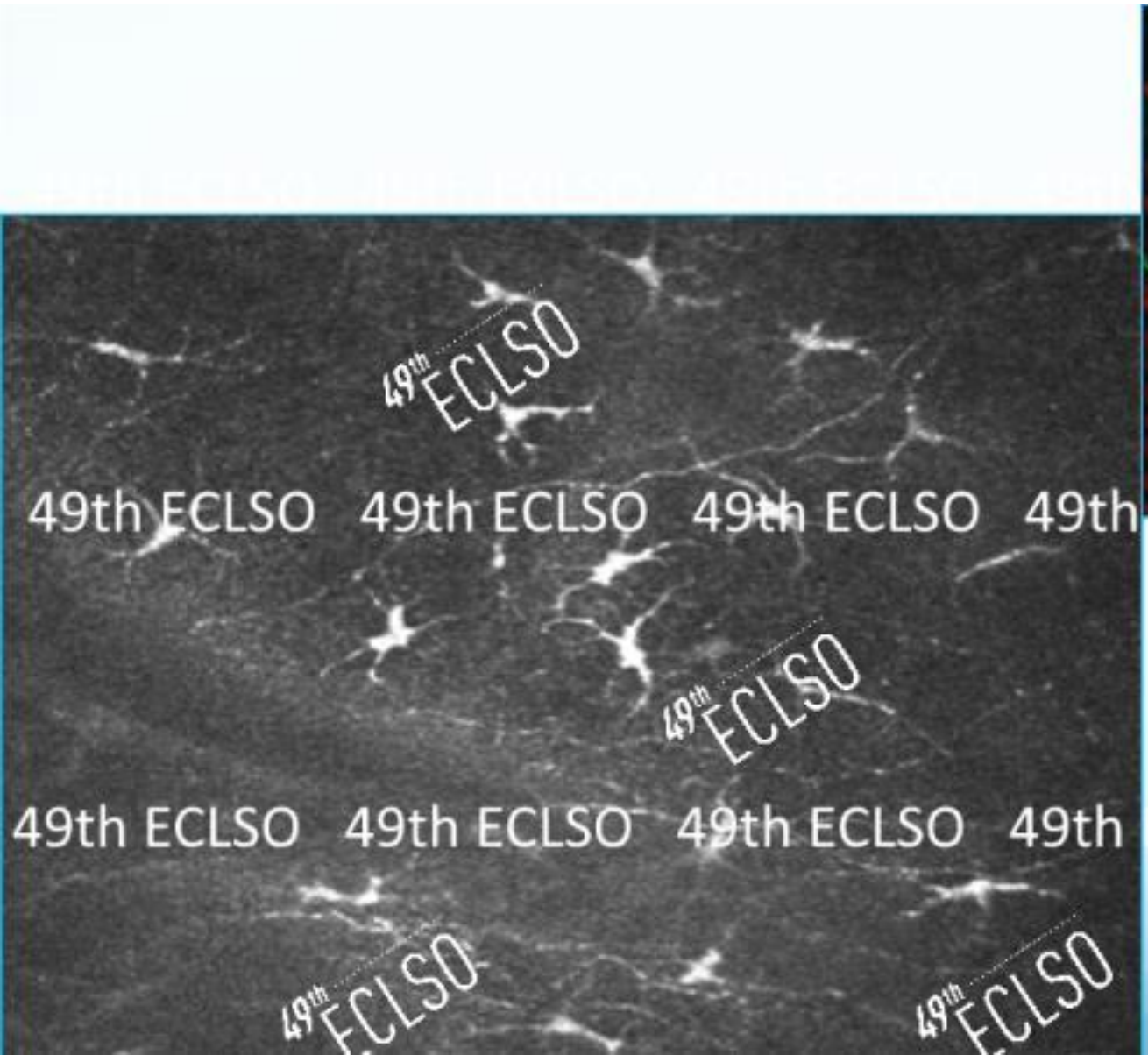
Differentially expressed genes



Imaging techniques: In Vivo Confocal Microscopy

Images taken with the HRT Rostock Cornea Module (Heidelberg Engineering)

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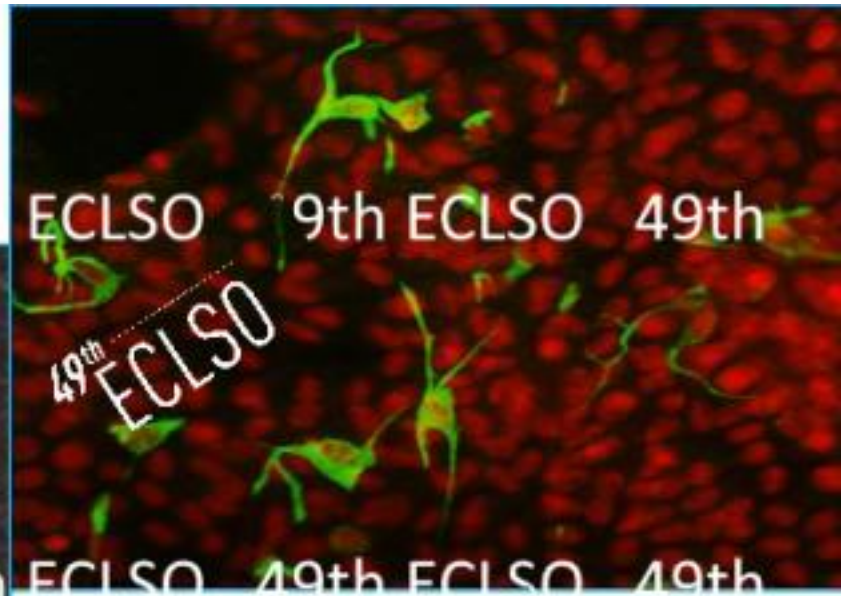
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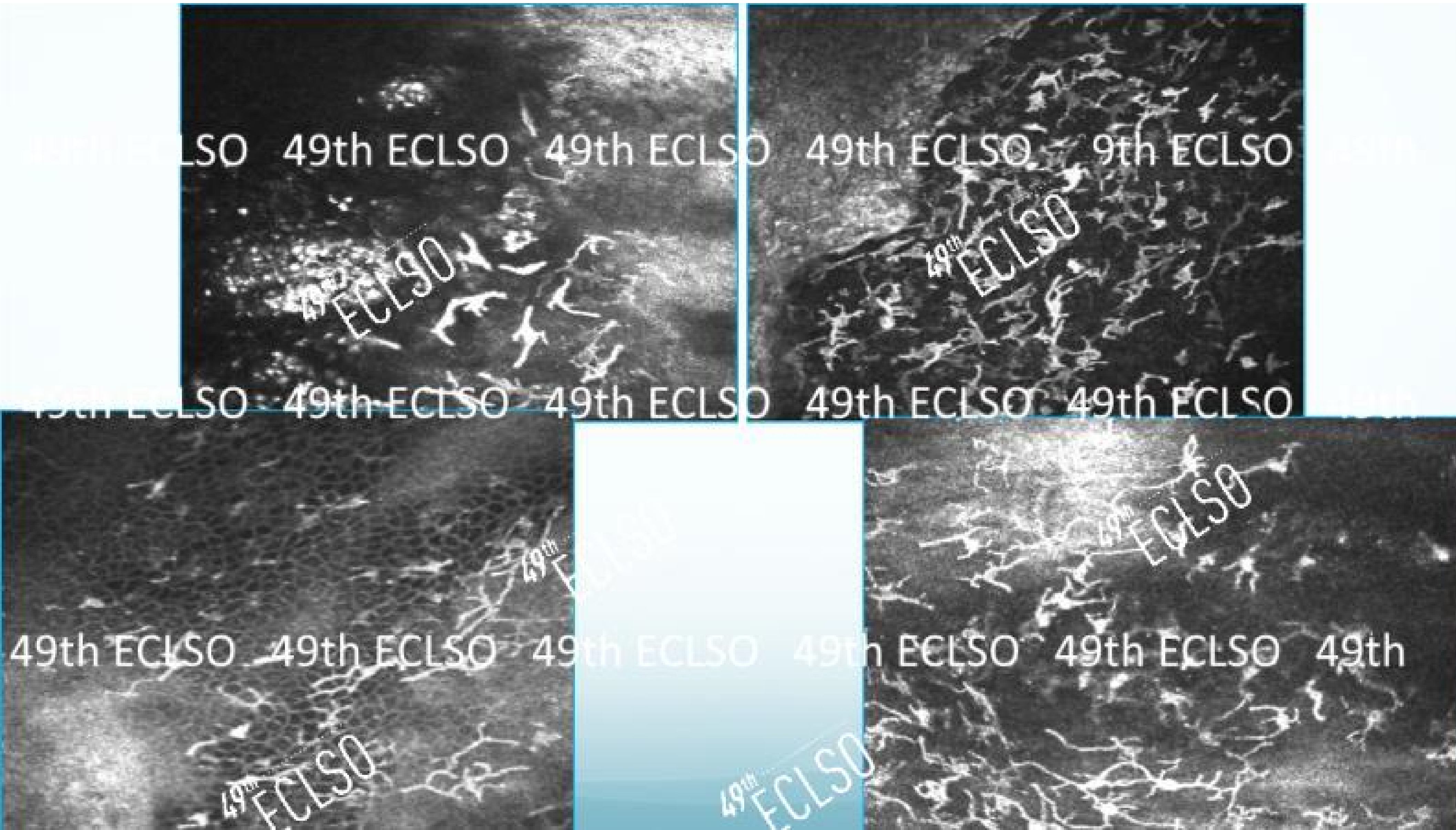
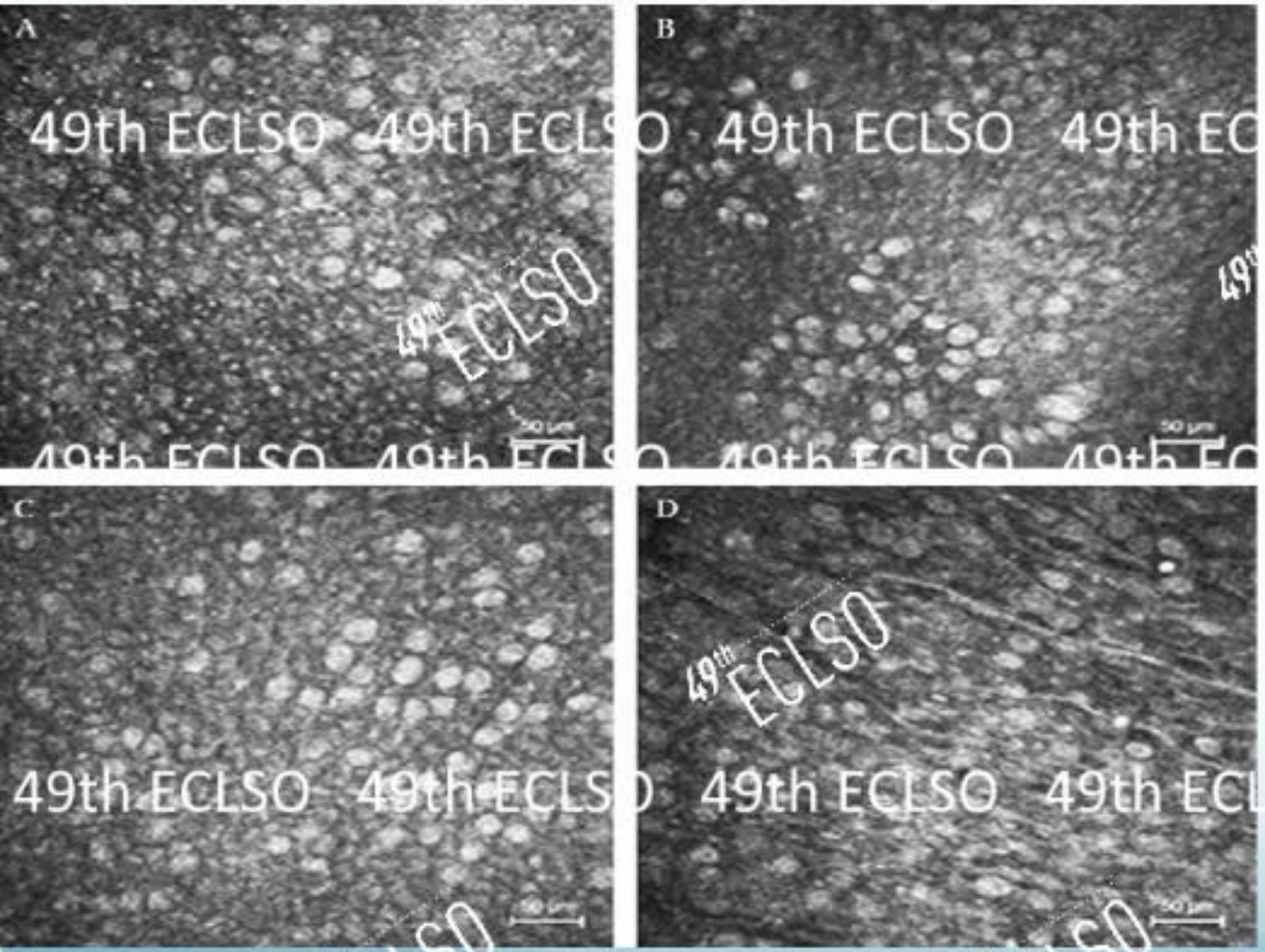
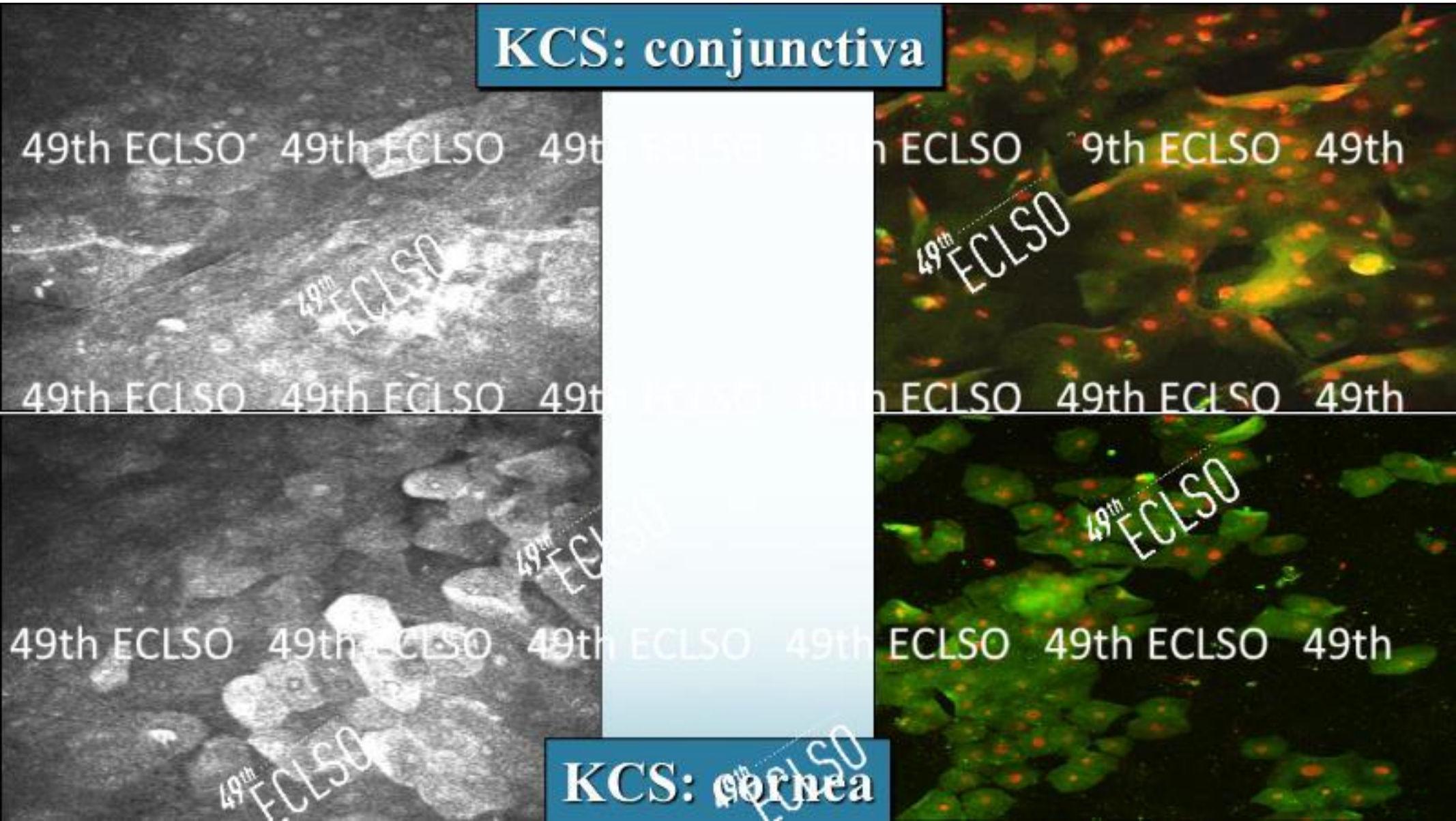
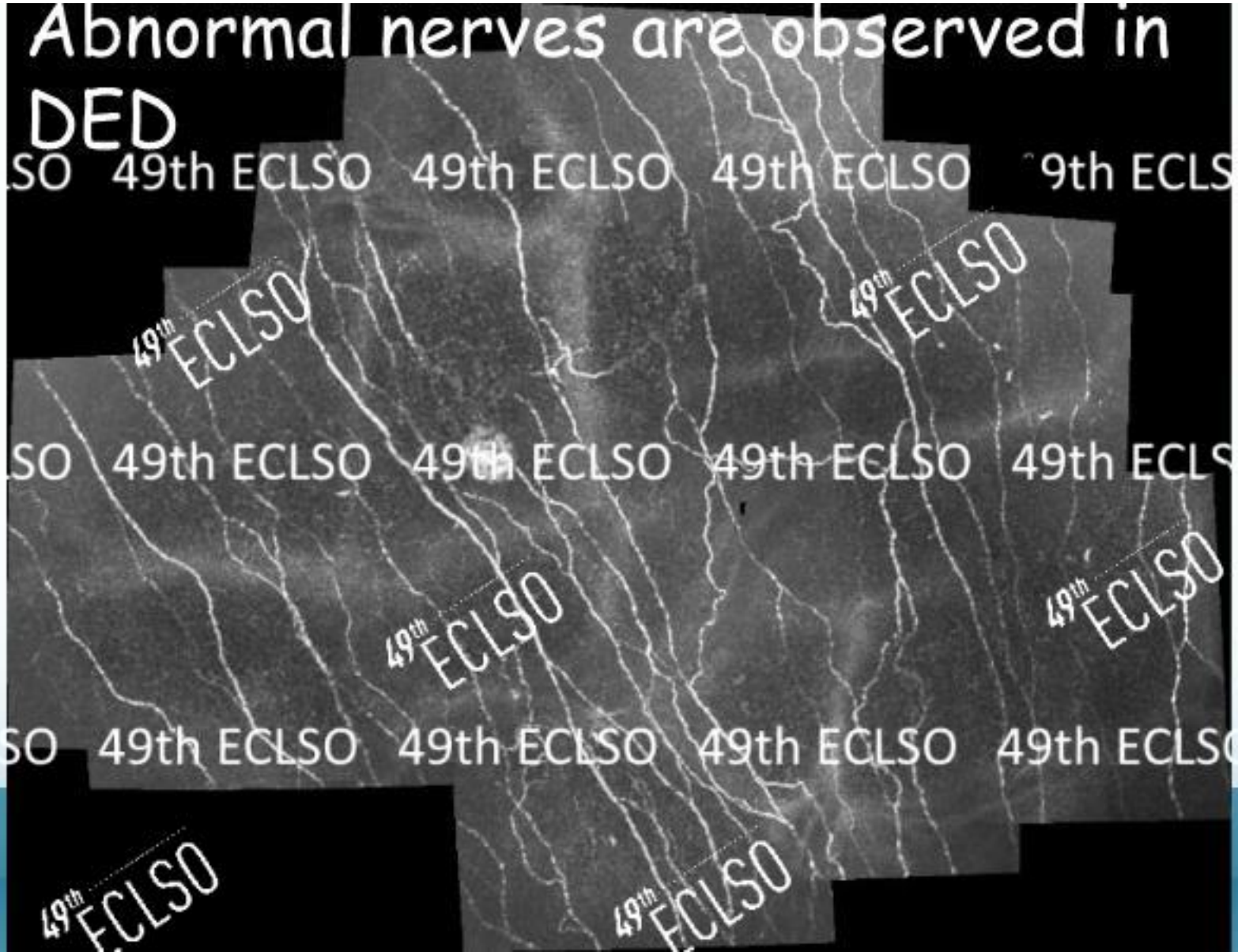




Goblet cells


KCS: conjunctiva
KCS: cornea
49th ECLSO


Abnormal nerves are observed in DED
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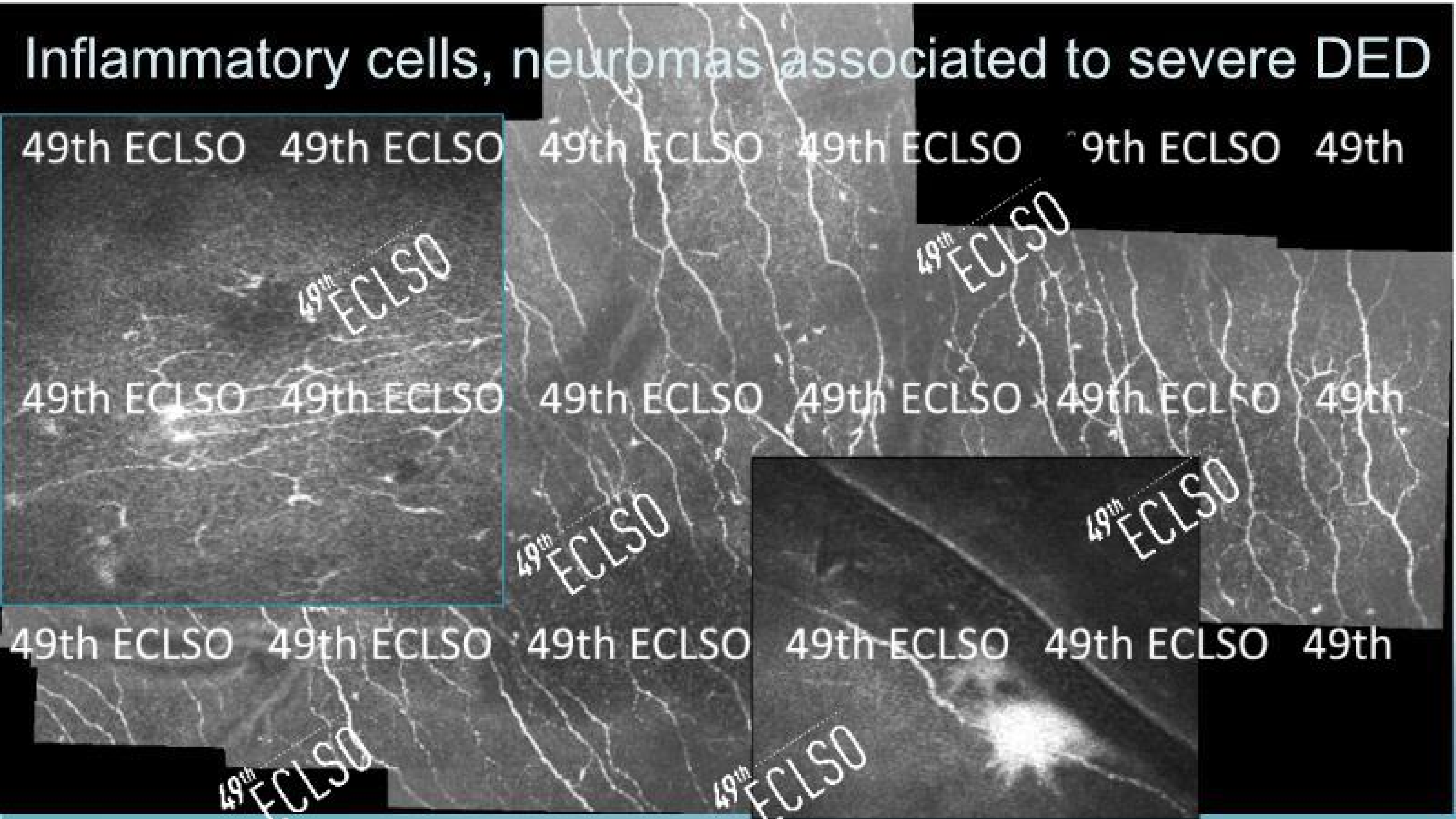
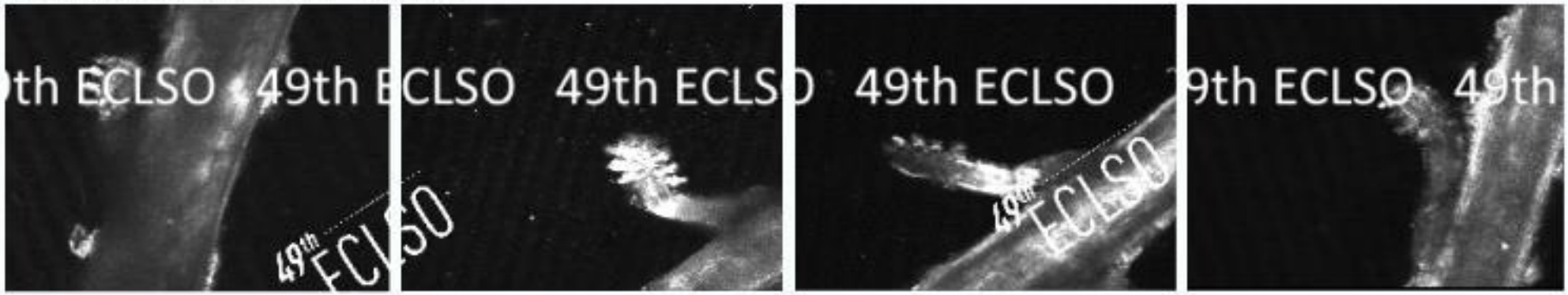
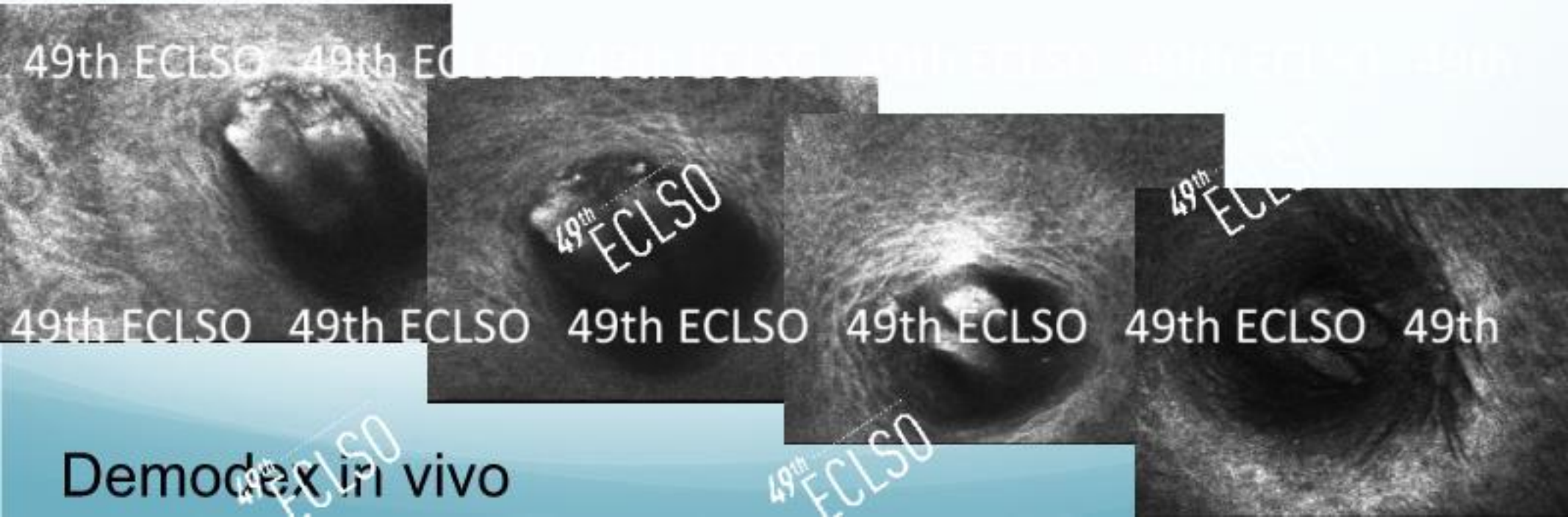
Inflammatory cells, neuromas associated to severe DED



Demodex ex vivo

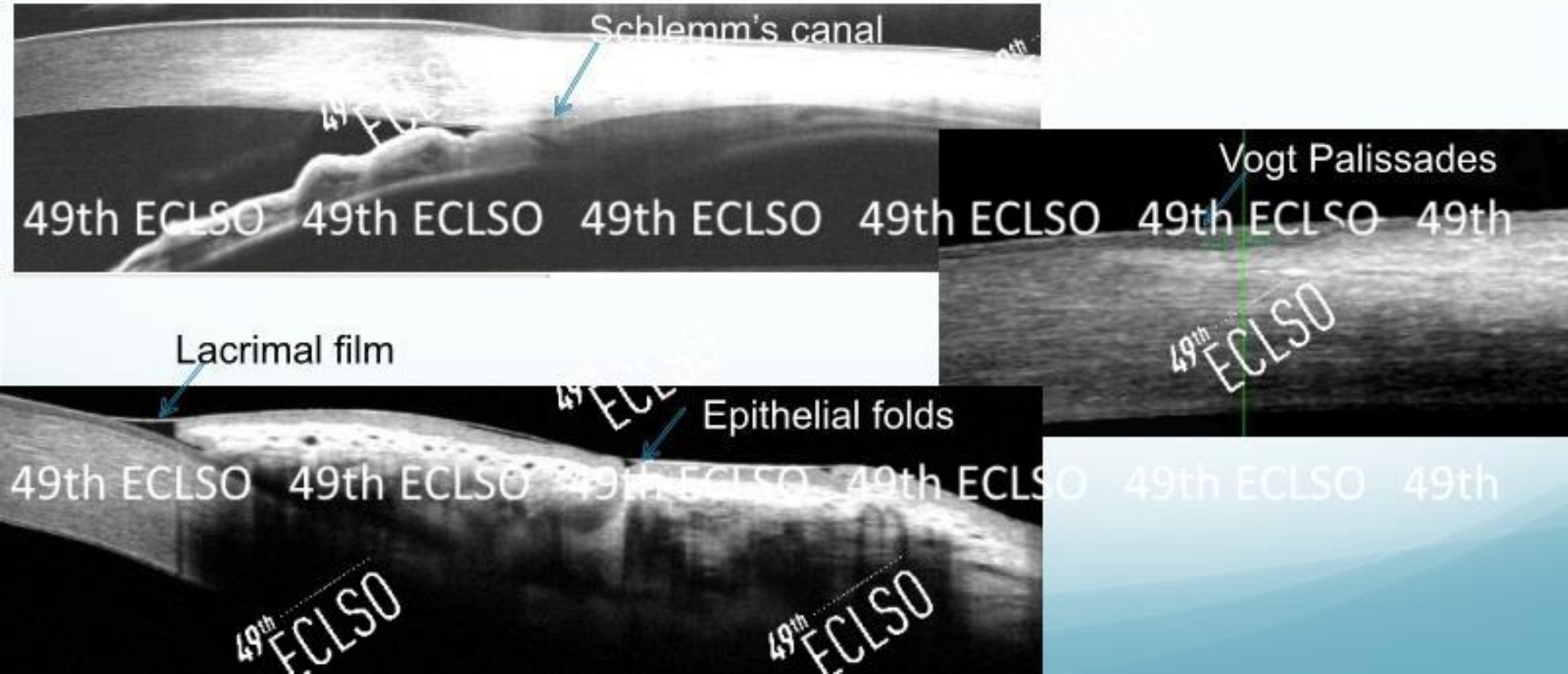


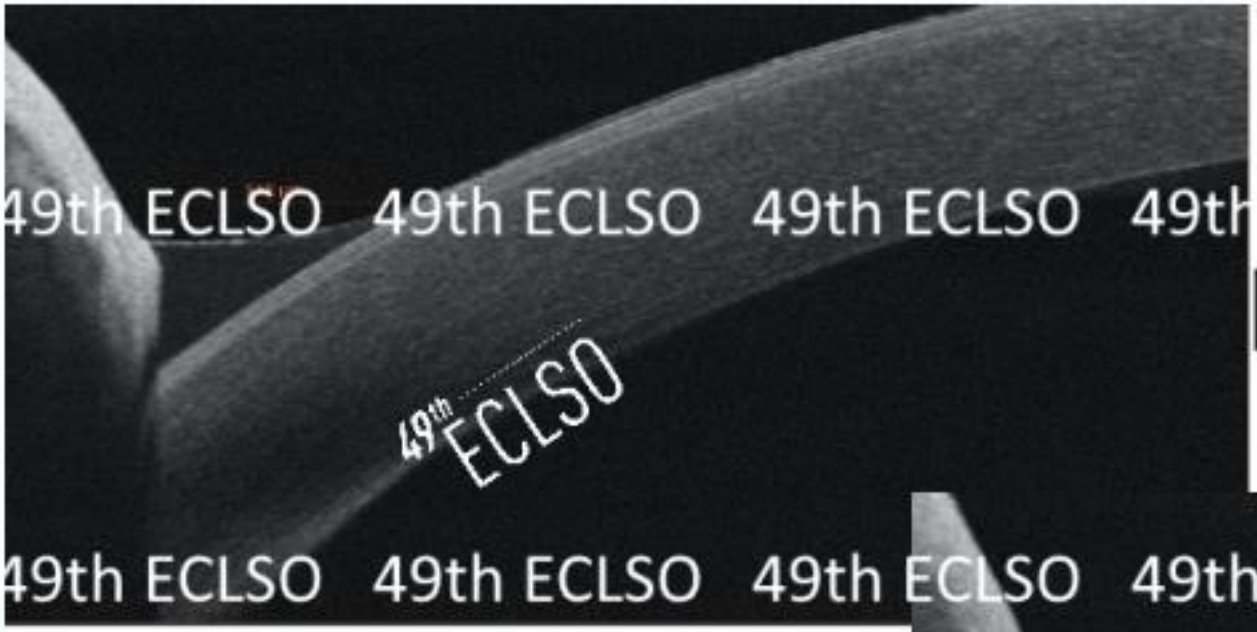


Demodex in vivo

What about OCT?

SD-OCT in anterior segment

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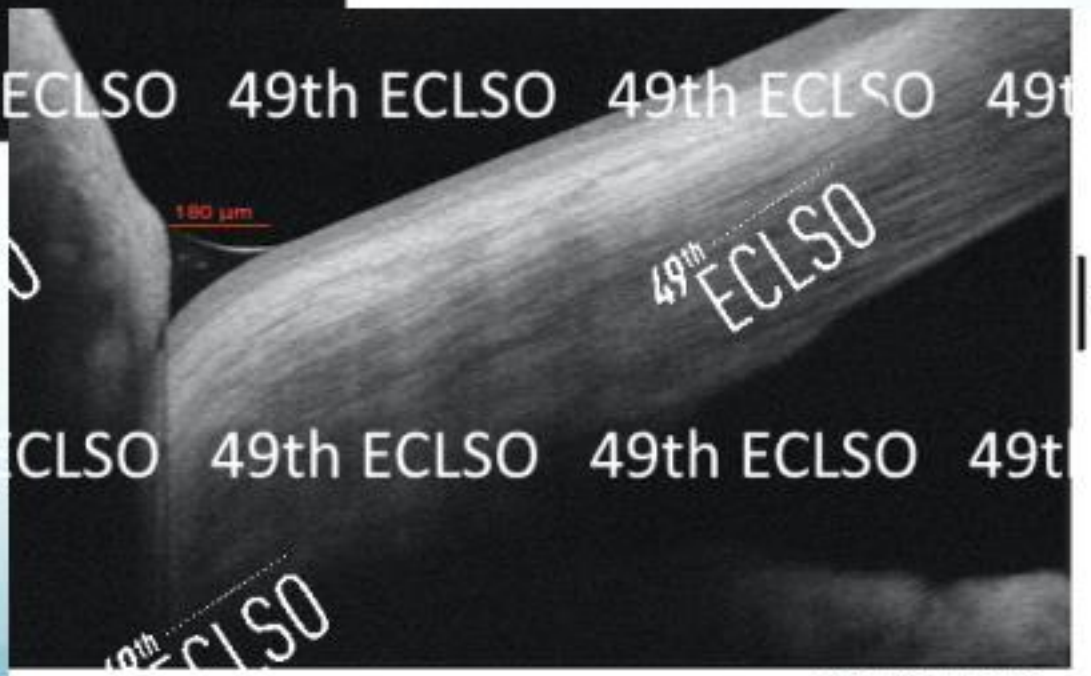
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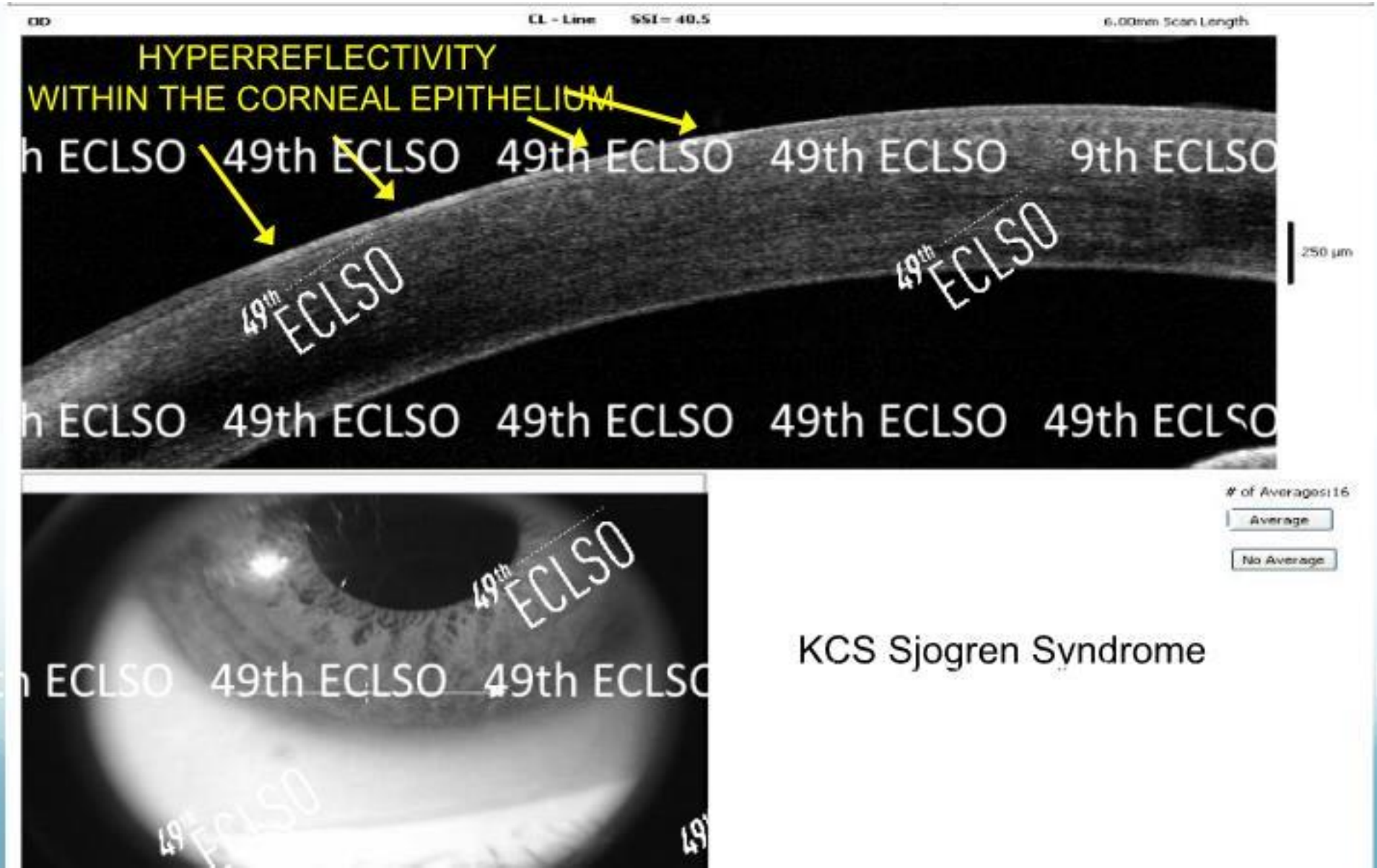
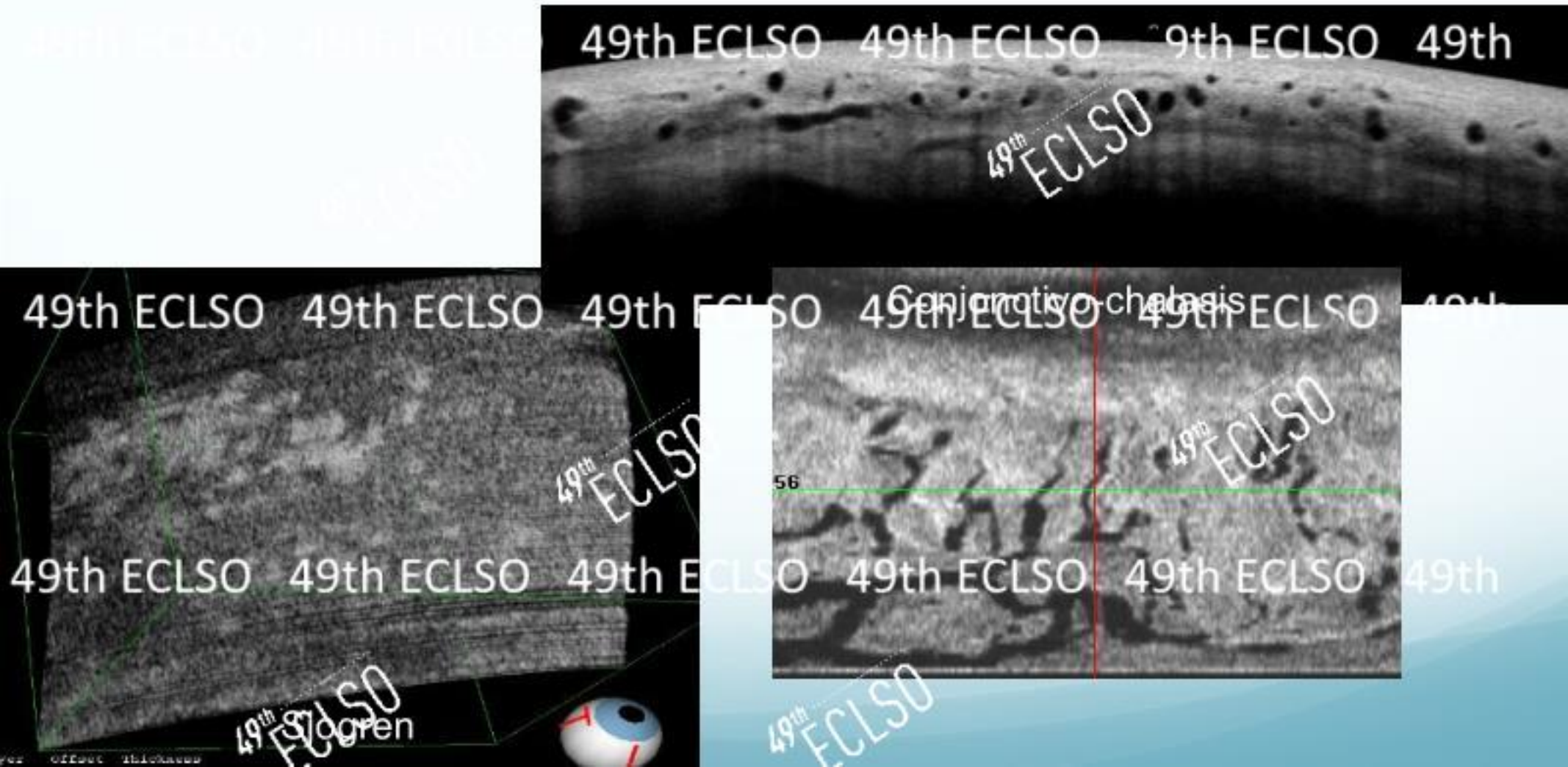
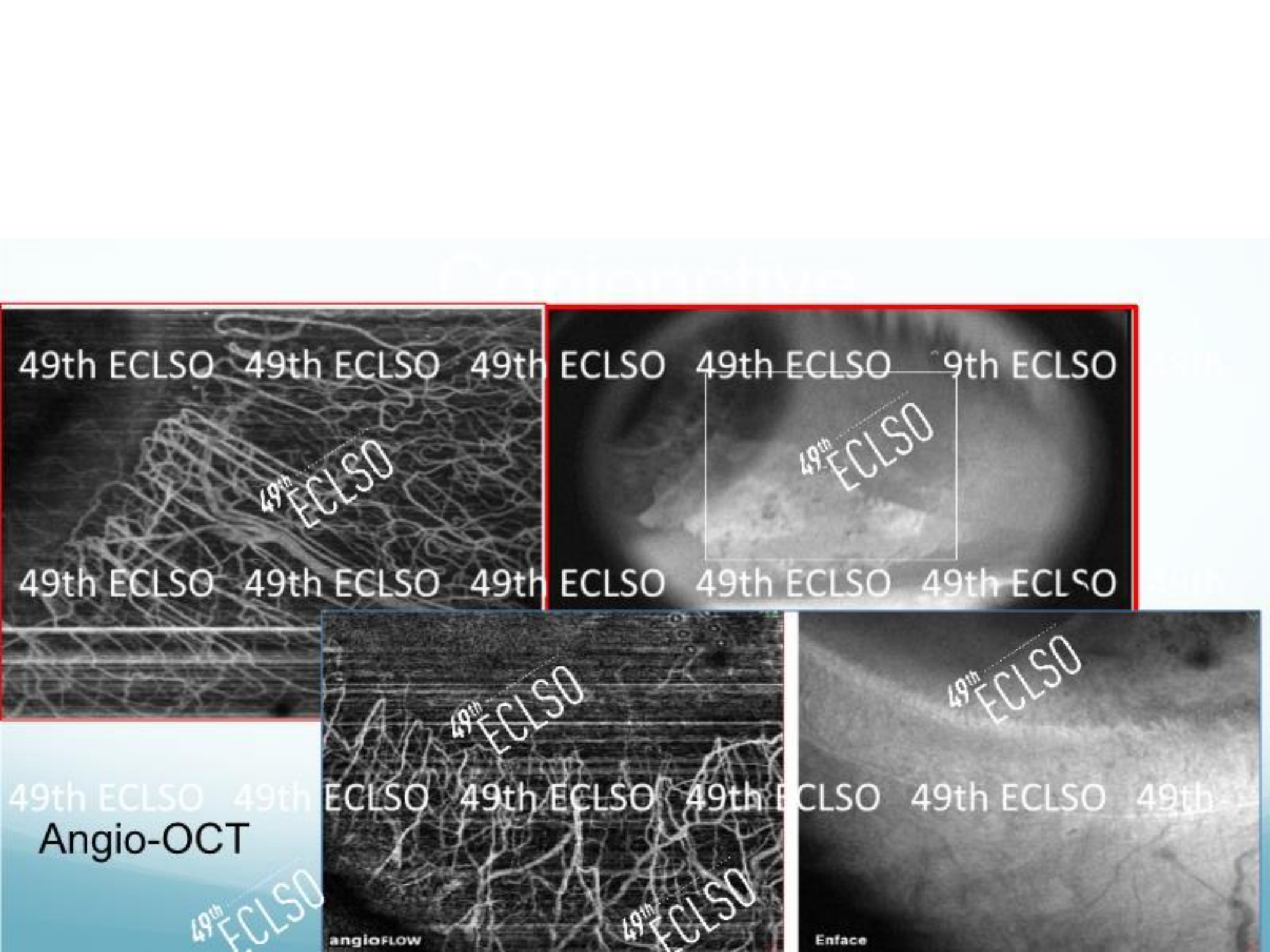
180 µm
49th ECLSO
49th ECLSO 49th ECLSO 49th ECLSO 49t
8.00mm Scan Length

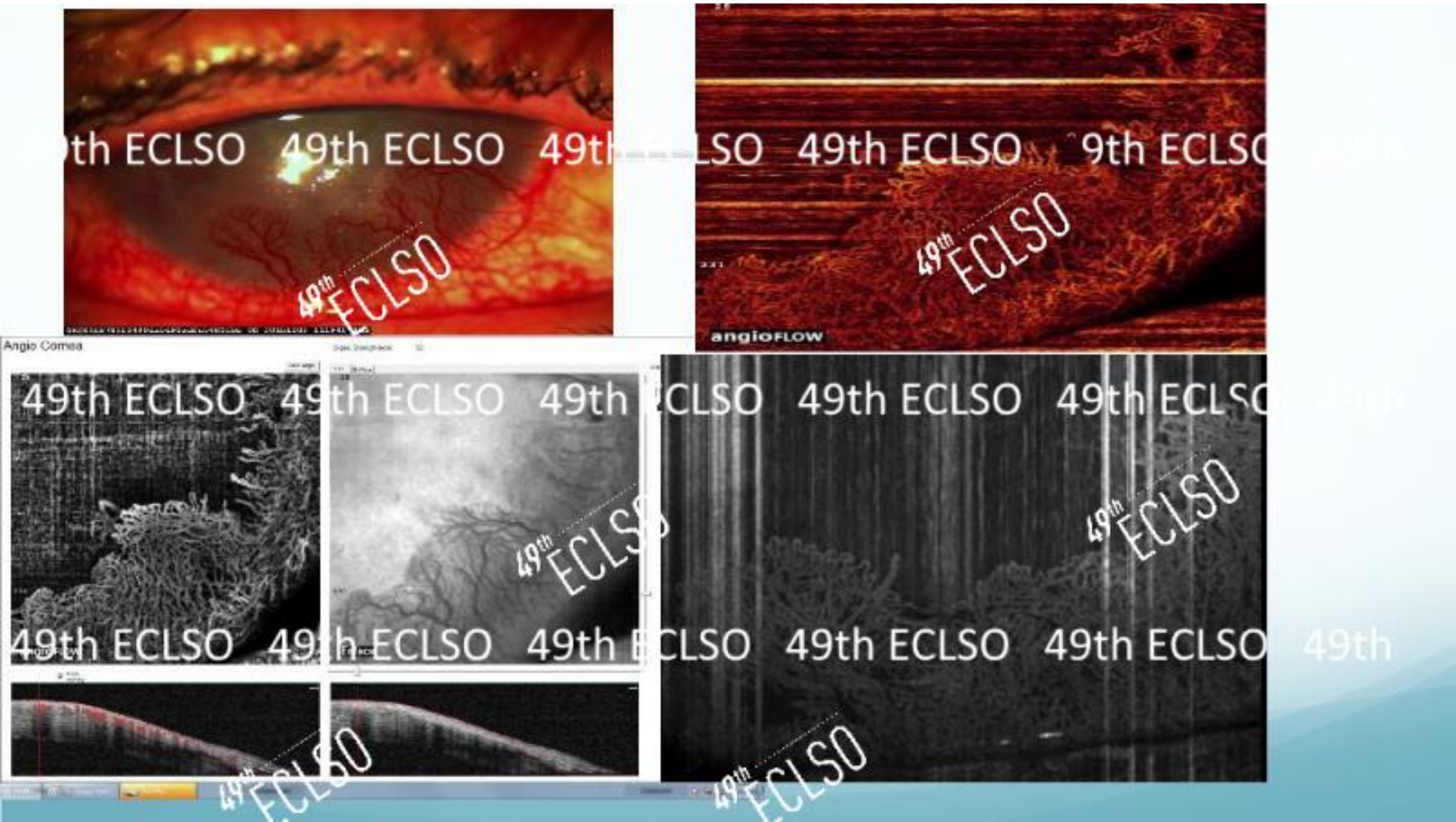


KCS Sjogren Syndrome

En-face OCT




49th ECLSO
Angio-OCT
angioFLOW
Enface


49th ECLSO
angioFLOW
Angio Cornea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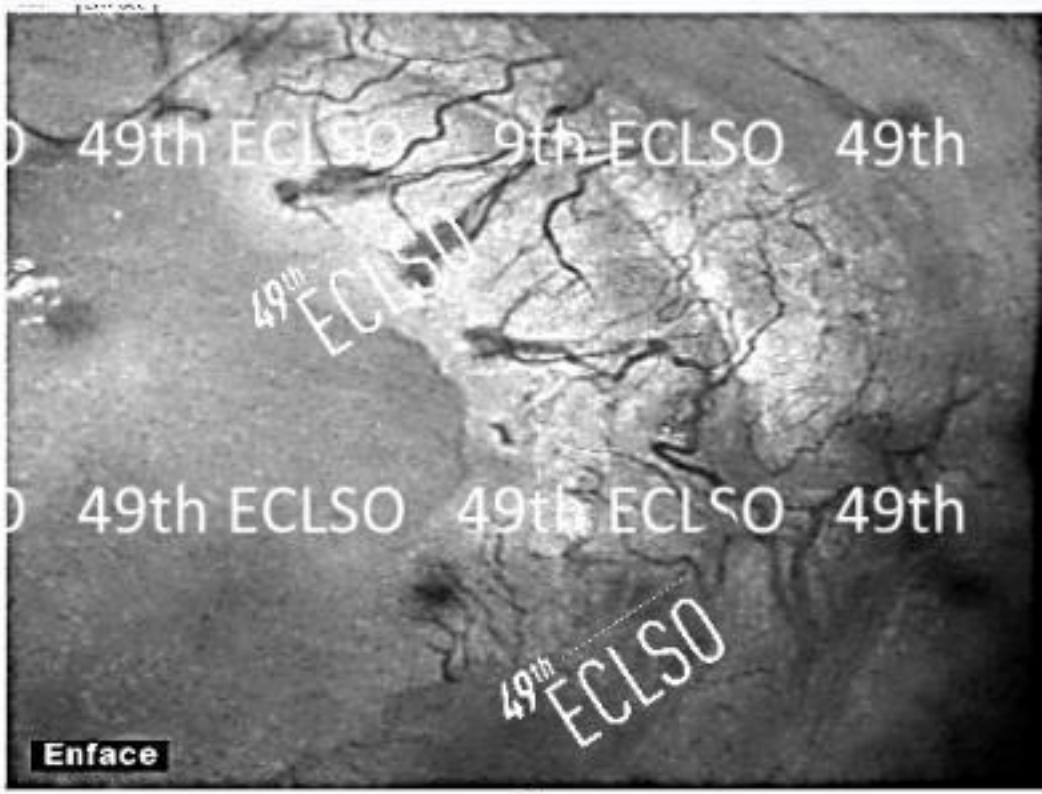
angioFLOW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49th ECLSO
Enface


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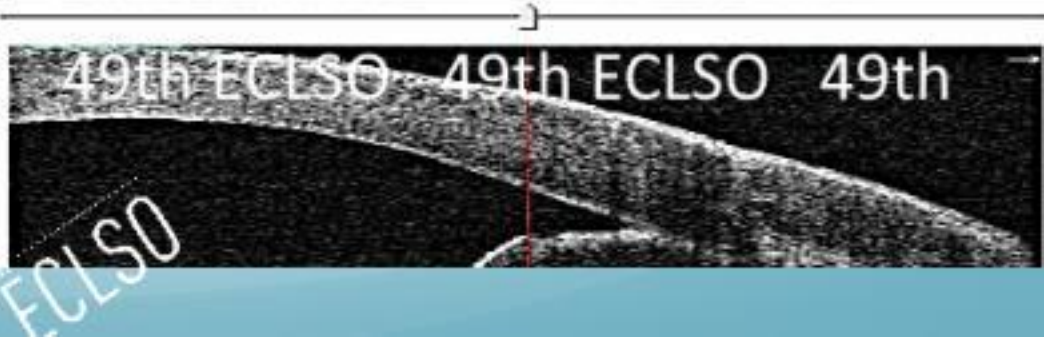
49th ECLSO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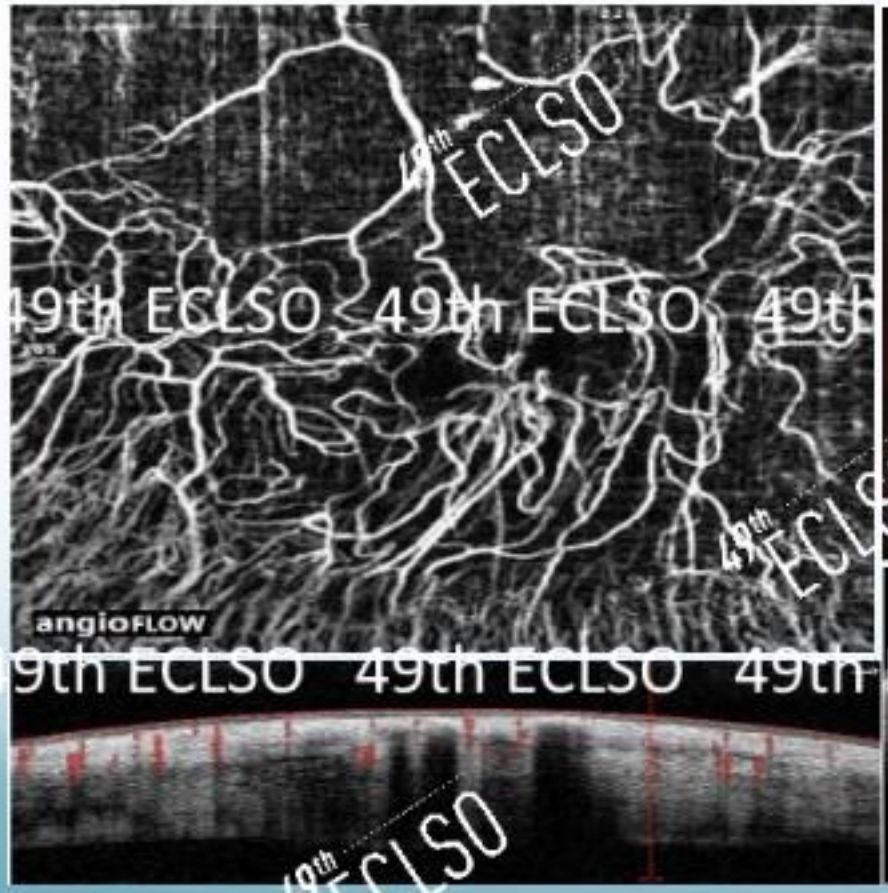
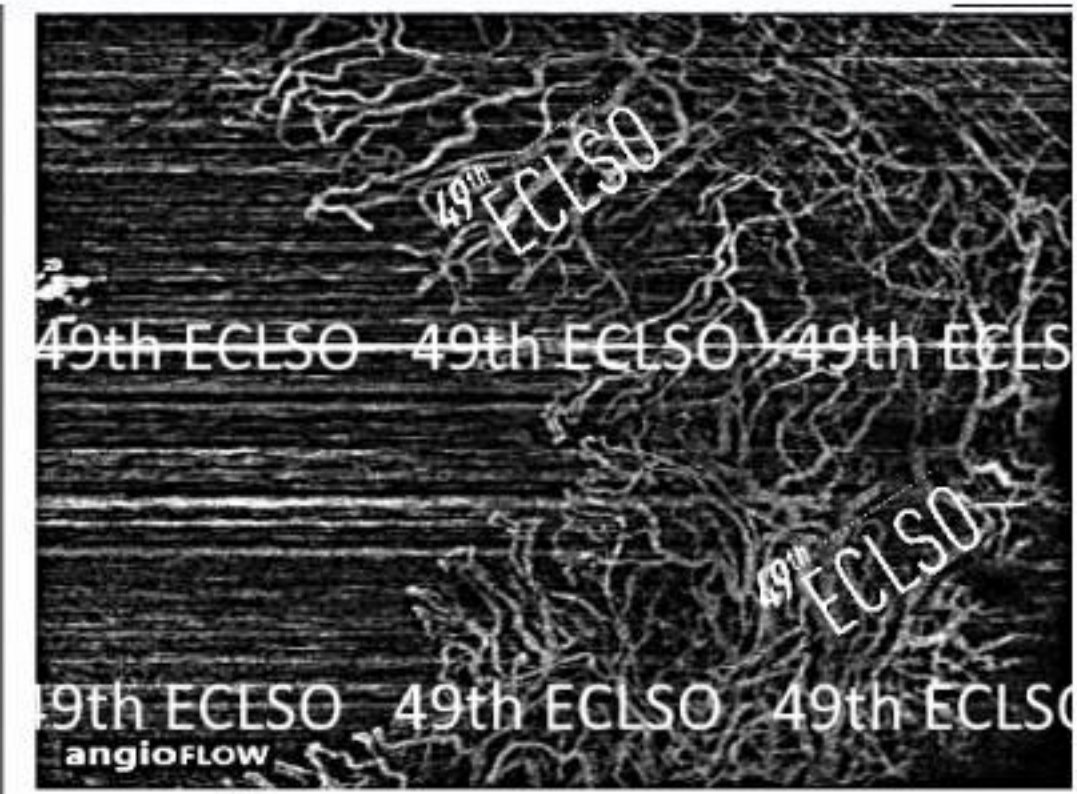
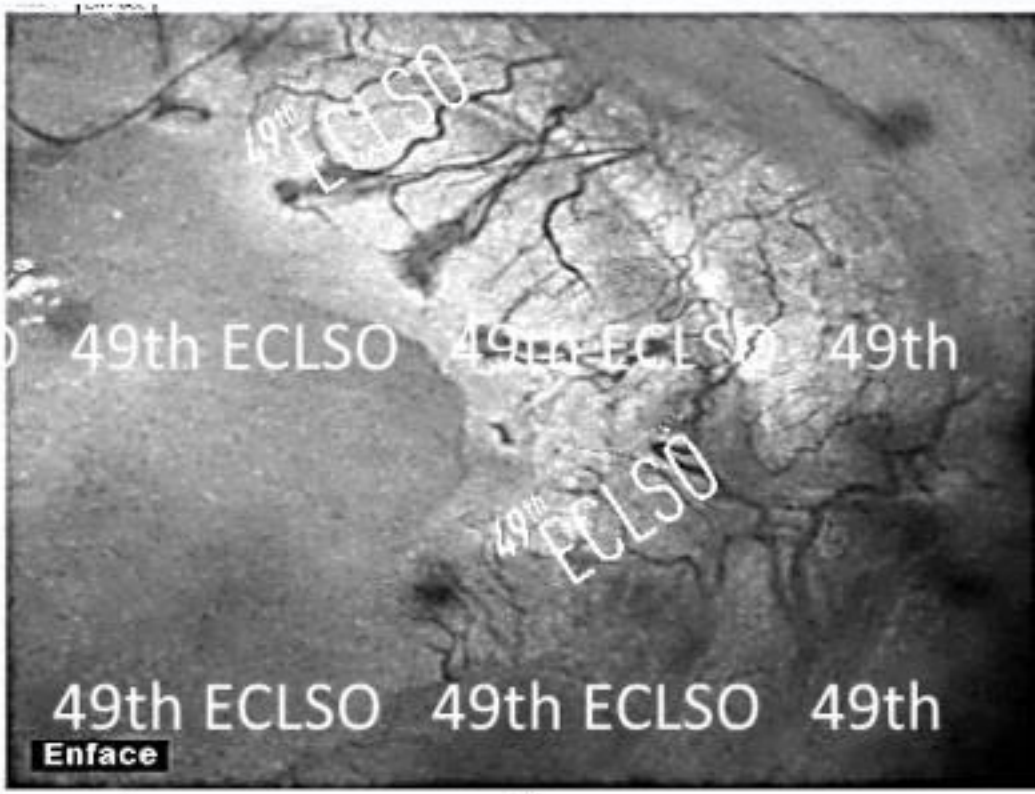
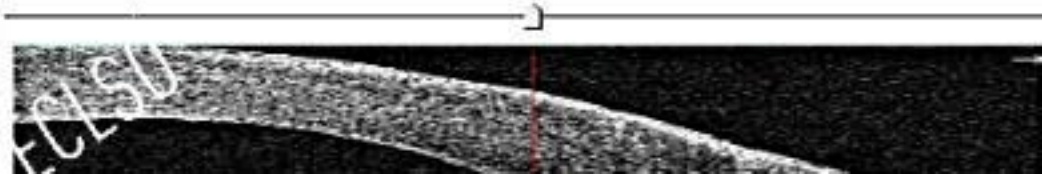
What are we really observing?



A second vascular network: Lymphatics





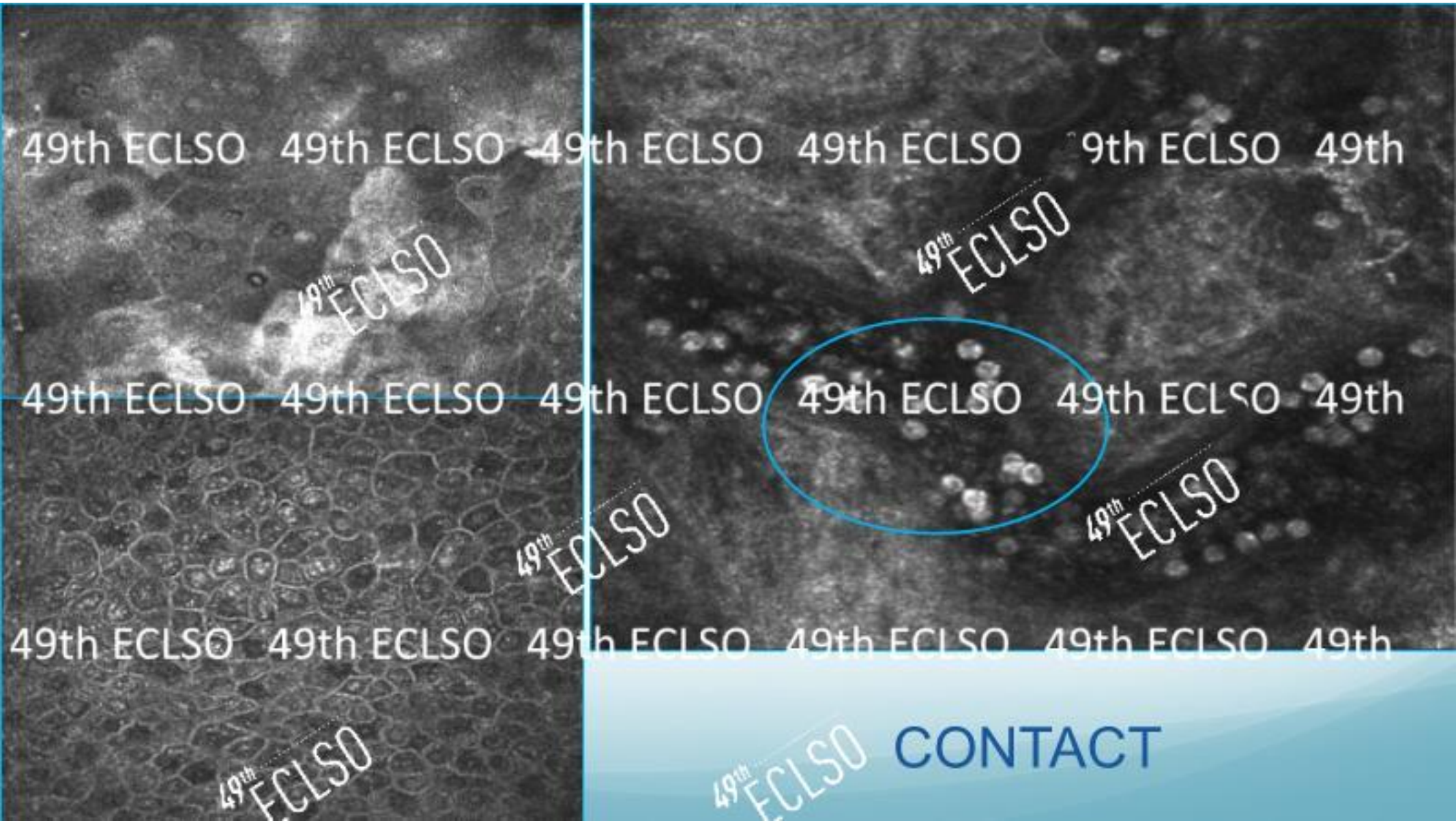


The future?

Reliable and predictive biomarkers for diagnosis, prognosis and therapeutic monitoring

Point-of-care technologies

Better resolutions of non-contact techniques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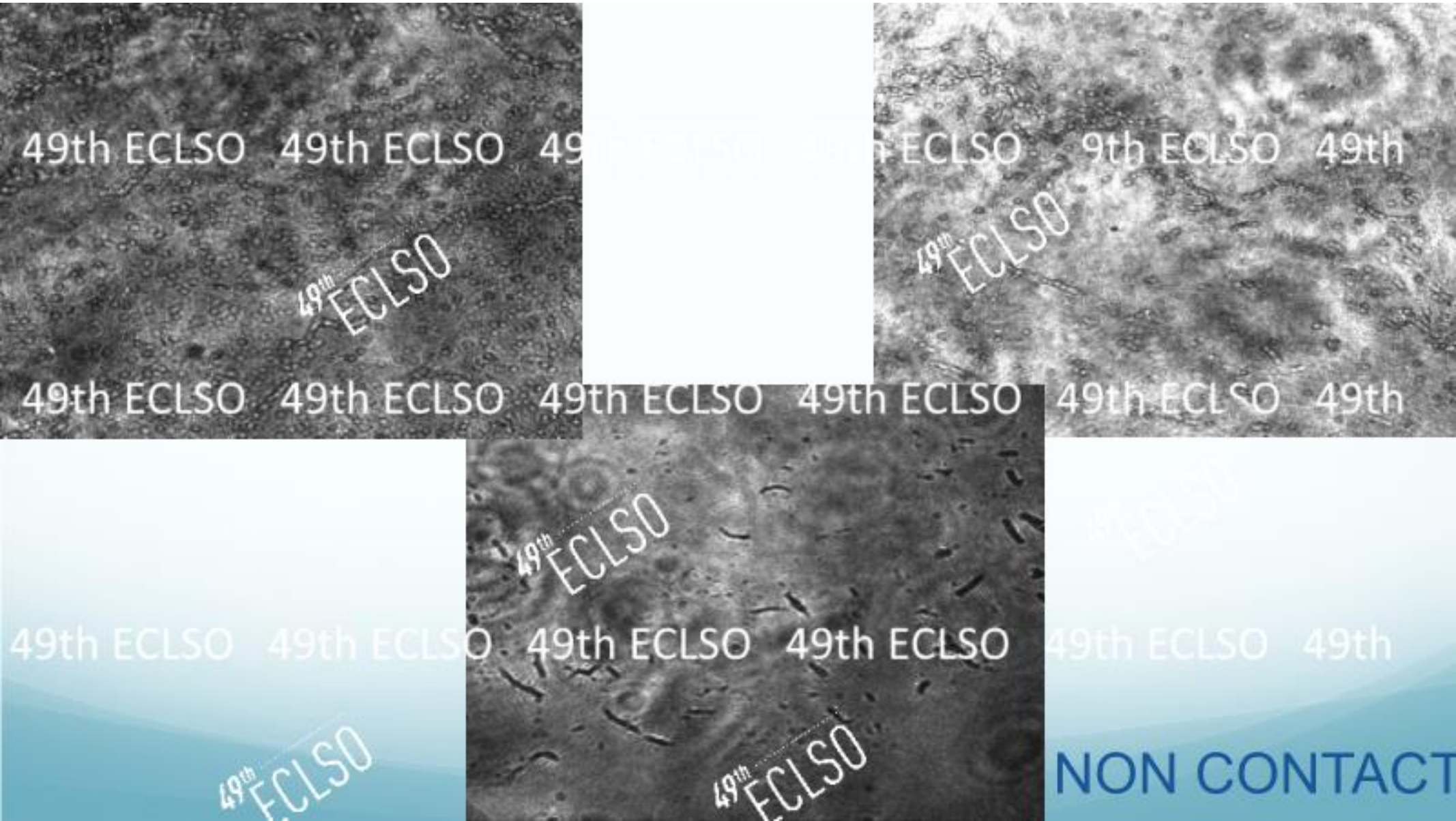
CONTACT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NON CONTACT

Thank you for your attention