OCT-Leakage.

Automated Analysis of Retina Extracellular Space using Optical Coherence Tomography.

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Disclosures

- Alimera Sciences - C
- Allergan - C S
- Bayer - C
- Gene Signal - C
- Novartis - C S
- Pfizer - C S
- Precision Ocular - C
- Retmarker, SA - C
- Roche - C
- Sanofi-Aventis – C
- Vifor Pharma - C
- Zeiss Meditec - C S

Open extracellular space in the retina

- **Smelser et al. (1965) > 20% extracellular space (retina)**
- **Paul Henkind and colleagues (1980):**

“the intercellular space in the retina is available for diffusion of even particulate matter”

Brain extracellular space: +/- 20%

Similar situation in the retina

Smelser et al. The Structure of the Eye. Stuttgart; 1965: 109.
Van Harreveld et al J. Cell Biol.1965; 25: 117.
Henkind et al. The blood-retinal barriers. 1980 Cunha-Vaz, Plenum Press.

Brightman and Reese. J. Cell Biol. 1969; 40: 668-677.
Kuffler. Proc. R. Soc. Lond.B.1967; 168:1-21.

Optical Reflectivity Measurements

Control - Healthy population:

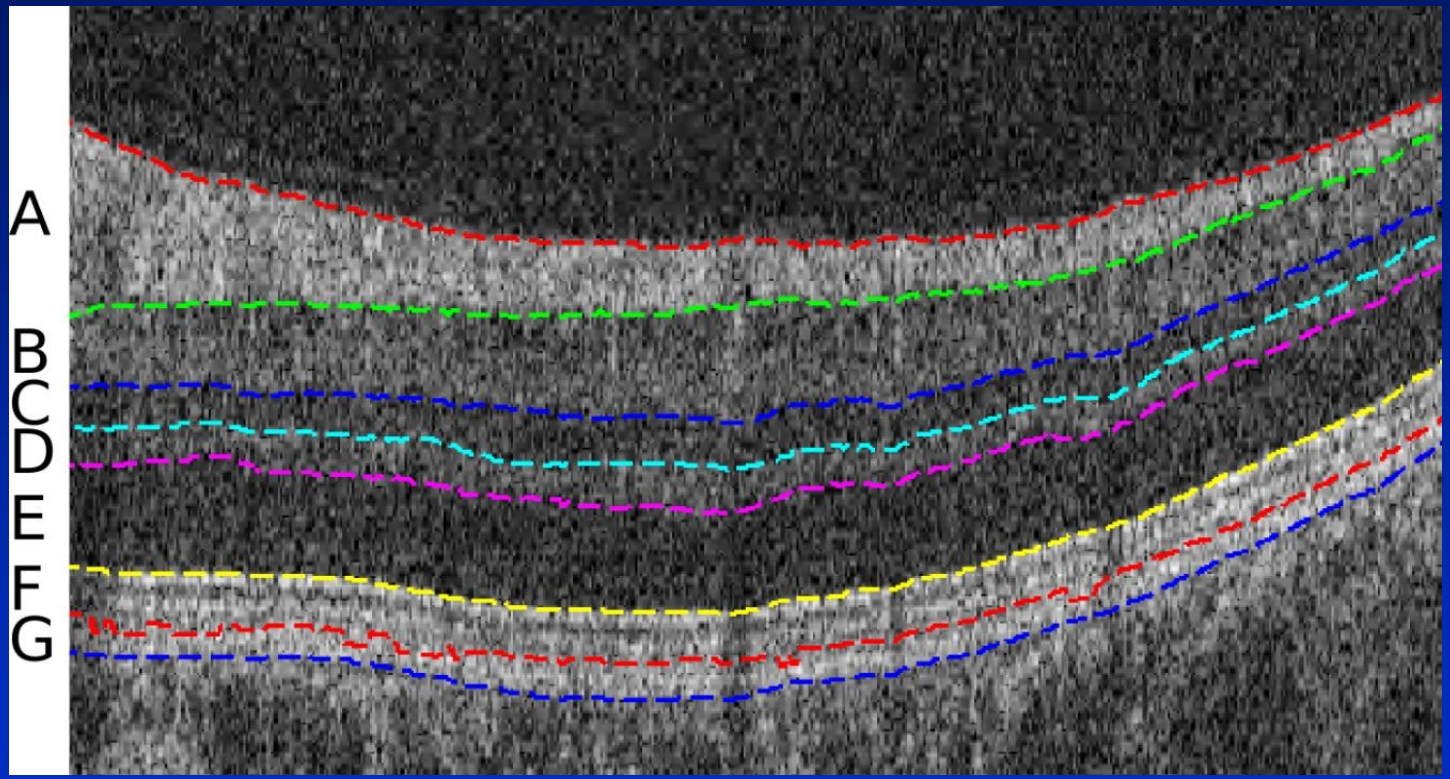
25 eyes from 25 patients

39-55 yrs (m±sd: 45.6±5.54)

Optical Reflectivity Ratios/Optical Reflectivity Maps

Full scan and 7 retinal layers

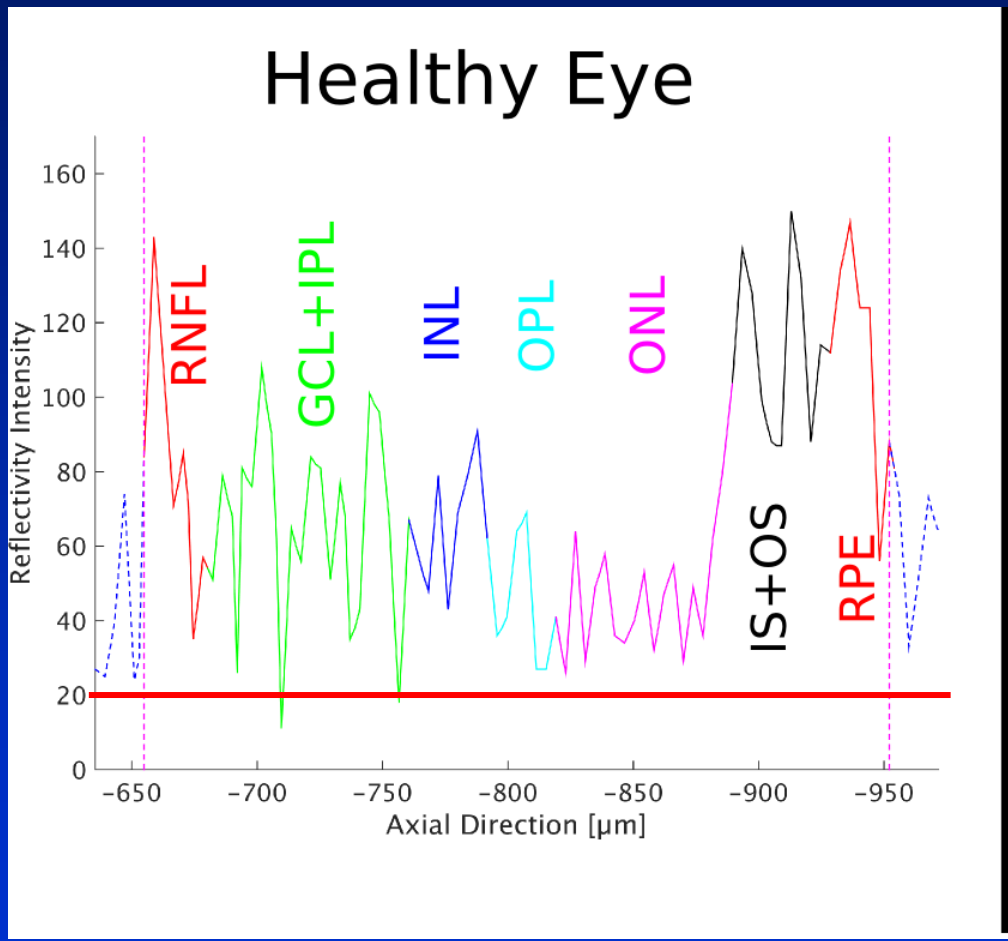
Segmentation algorithm implemented to automatically identify 8 retinal interfaces

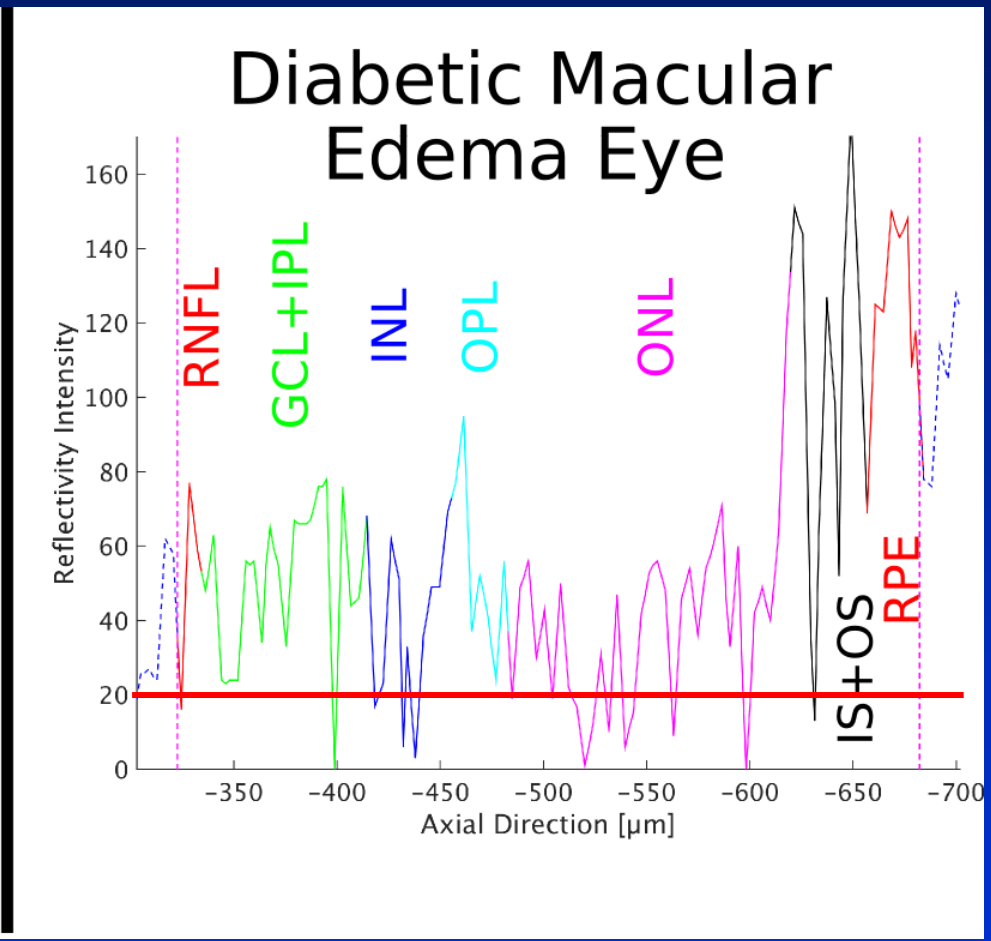


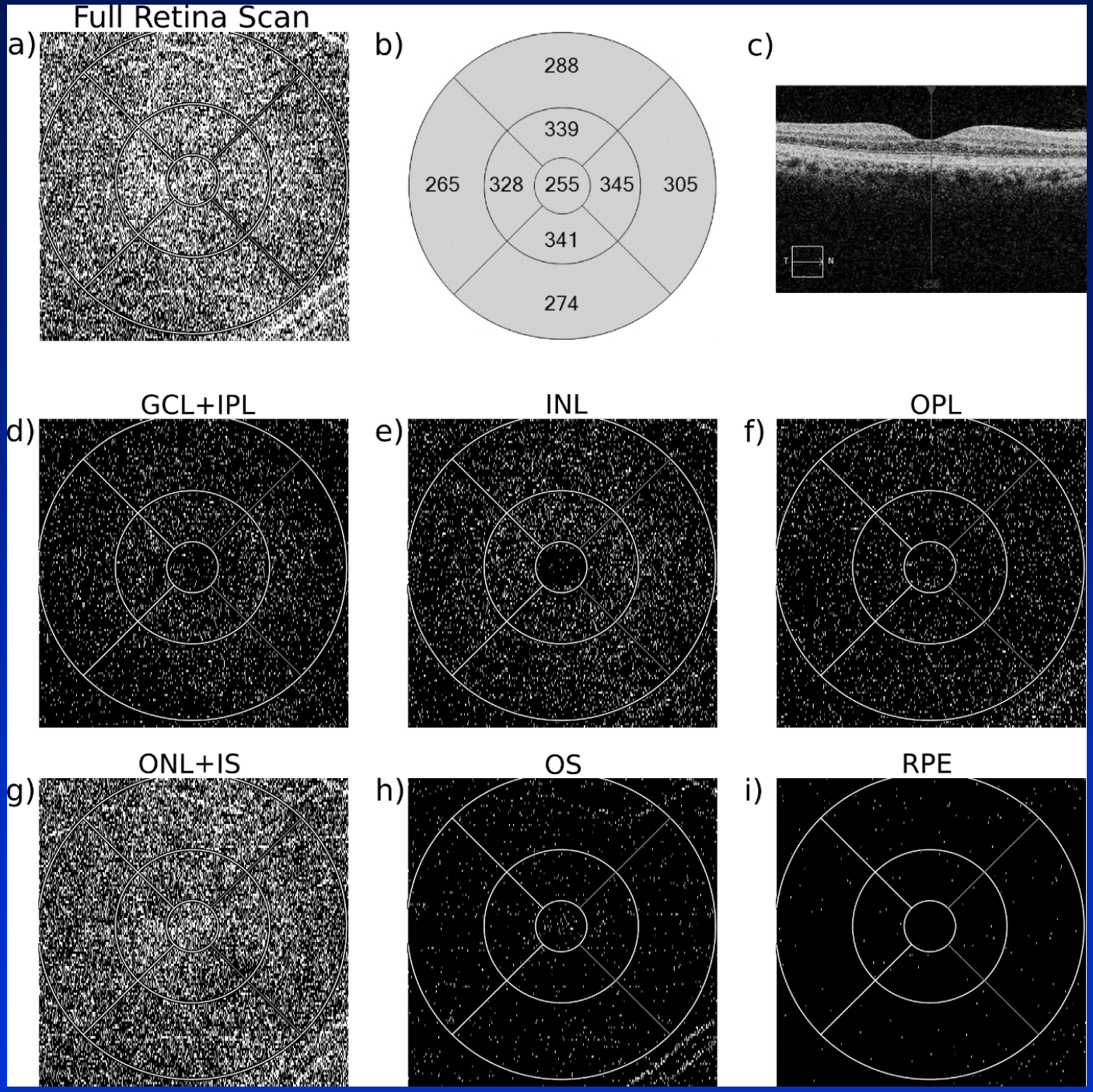
A) RNFL; B) GCL+IPL; C) INL; D) OPL;

E) ONL+IS; F) OS; G) RPE.

Cirrus SD-OCT A-Scan optical reflectivity profiles



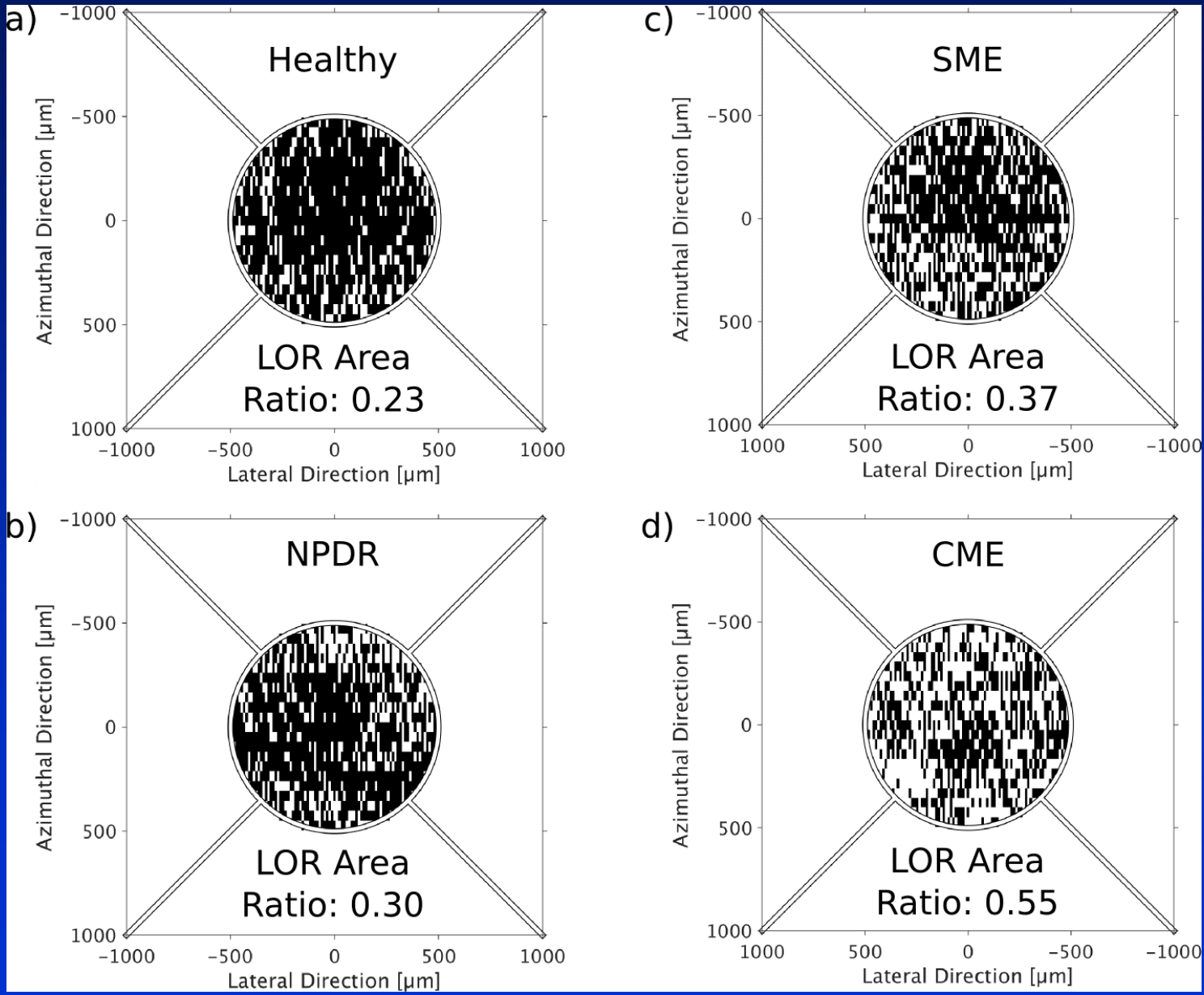




OCT-Leakage LOR maps of a healthy subject

Healthy vs. NPDR (no edema, subclinical and clinical edema)

LOR maps for the INL at the Central Subfield



Diabetic eyes/patients: 38 (subclinical and clinical macular edema)

*

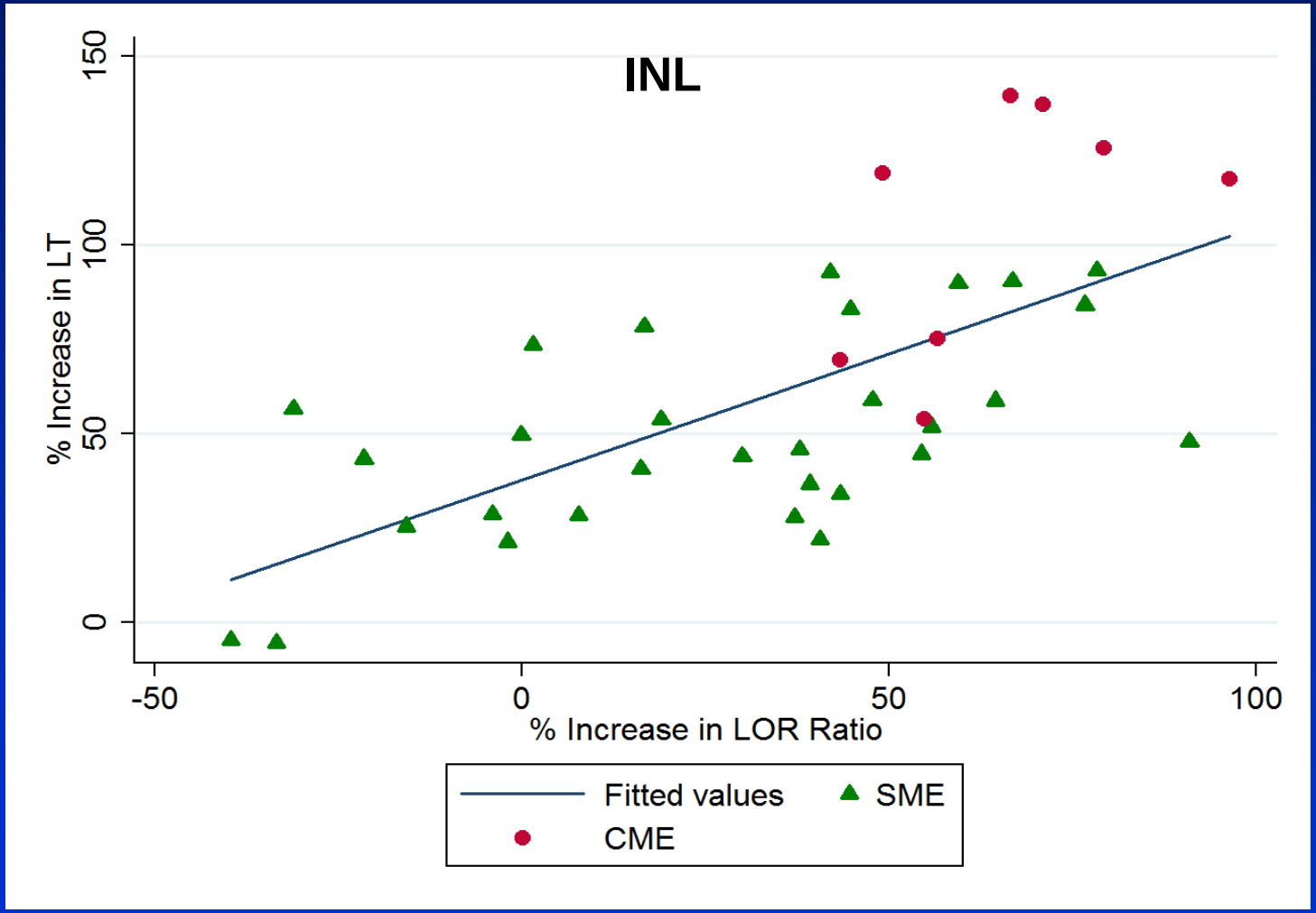
% Increase in SD-OCT LOR area ratios vs. % Increase in layer thickness

CSF					
Layer		SME N=30		CME N=8	
		% Increase LOR Ratio	% Increase Layer Thickness	% Increase LOR Ratio	% Increase Layer Thickness
RNFL	Avg.	-17.47	1.51	3.02	44.11
	S. Dev.	38.15	48.15	25.90	69.54
GCL+IPL	Avg.	2.68	15.35	30.78	39.60
	S. Dev.	27.80	16.66	17.43	18.34
INL	Avg.	27.43	49.94	64.68	104.73
	S. Dev.	35.31	26.97	17.43	33.27
OPL	Avg.	7.11	29.20	24.13	47.29
	S. Dev.	27.02	24.78	25.80	27.34
ONL	Avg.	0.68	8.73	1.20	11.23
	S. Dev.	2.70	8.03	1.90	10.77
OS+IS	Avg.	-18.28	-3.22	2.71	-1.82
	S. Dev.	35.72	11.45	57.32	3.69
RPE	Avg.	14.00	-2.03	23.38	-4.07
	S. Dev.	58.69	10.41	40.03	9.53

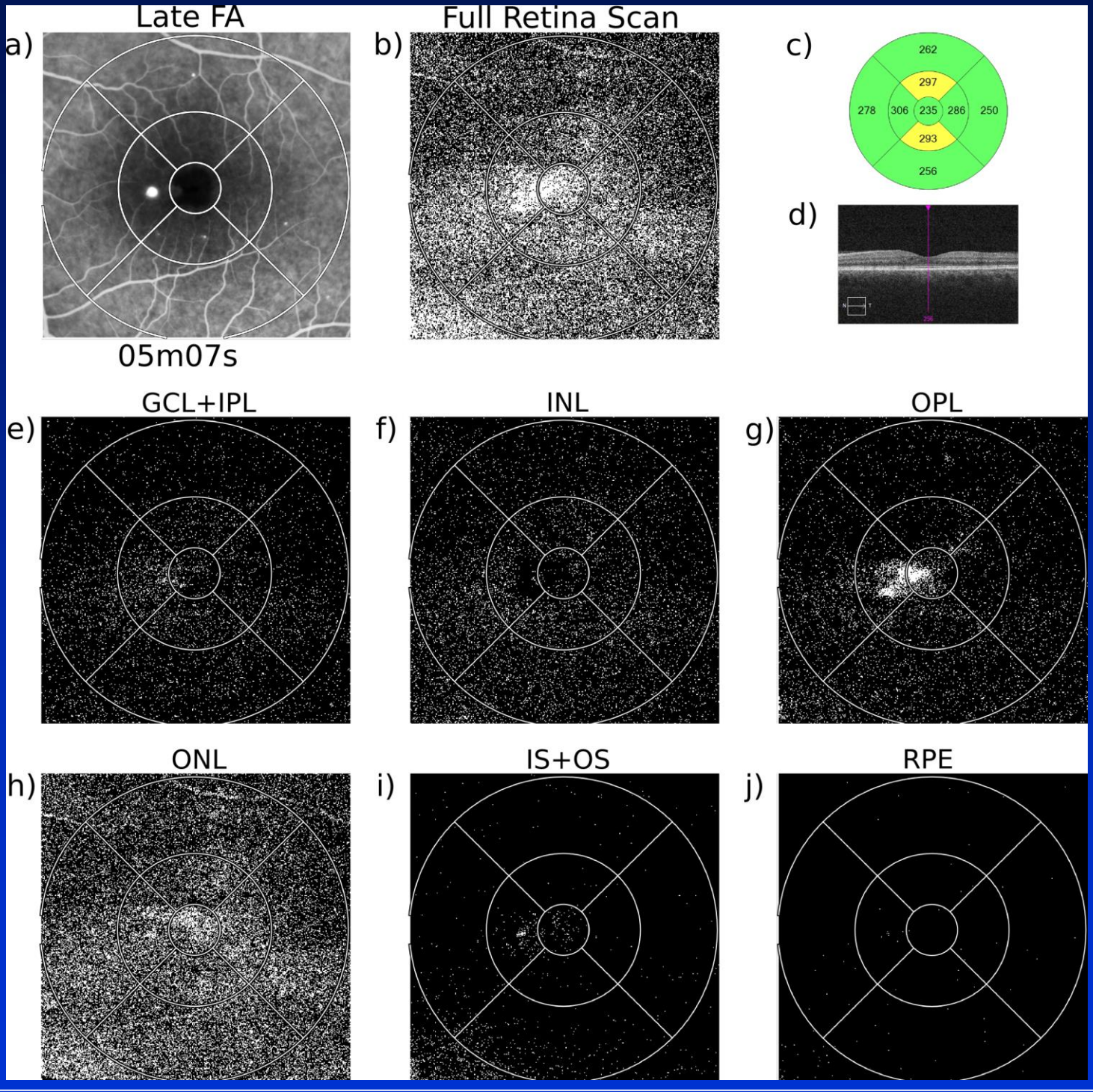
Demonstration of proof of concept

Diabetic eyes/patients: 38 (subclinical and clinical macular edema)

% Increase in SD-OCT LOR area ratios vs. % Increase in layer thickness



Spearman correlation coefficient = 0.71 (p<0.001) (Strong correlation)

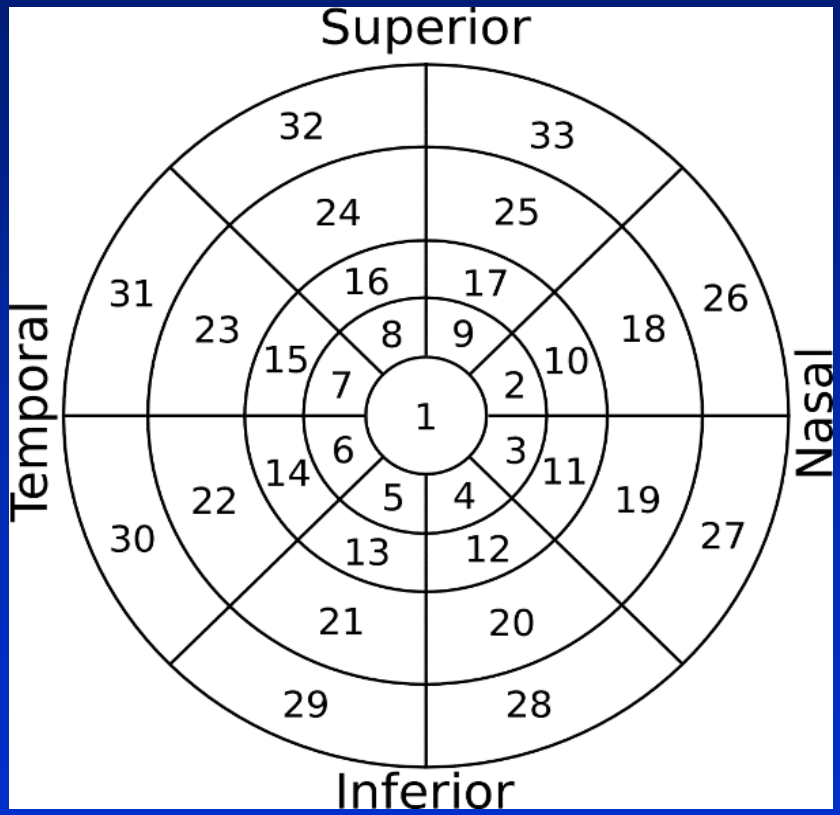


Identification of sites of Leakage

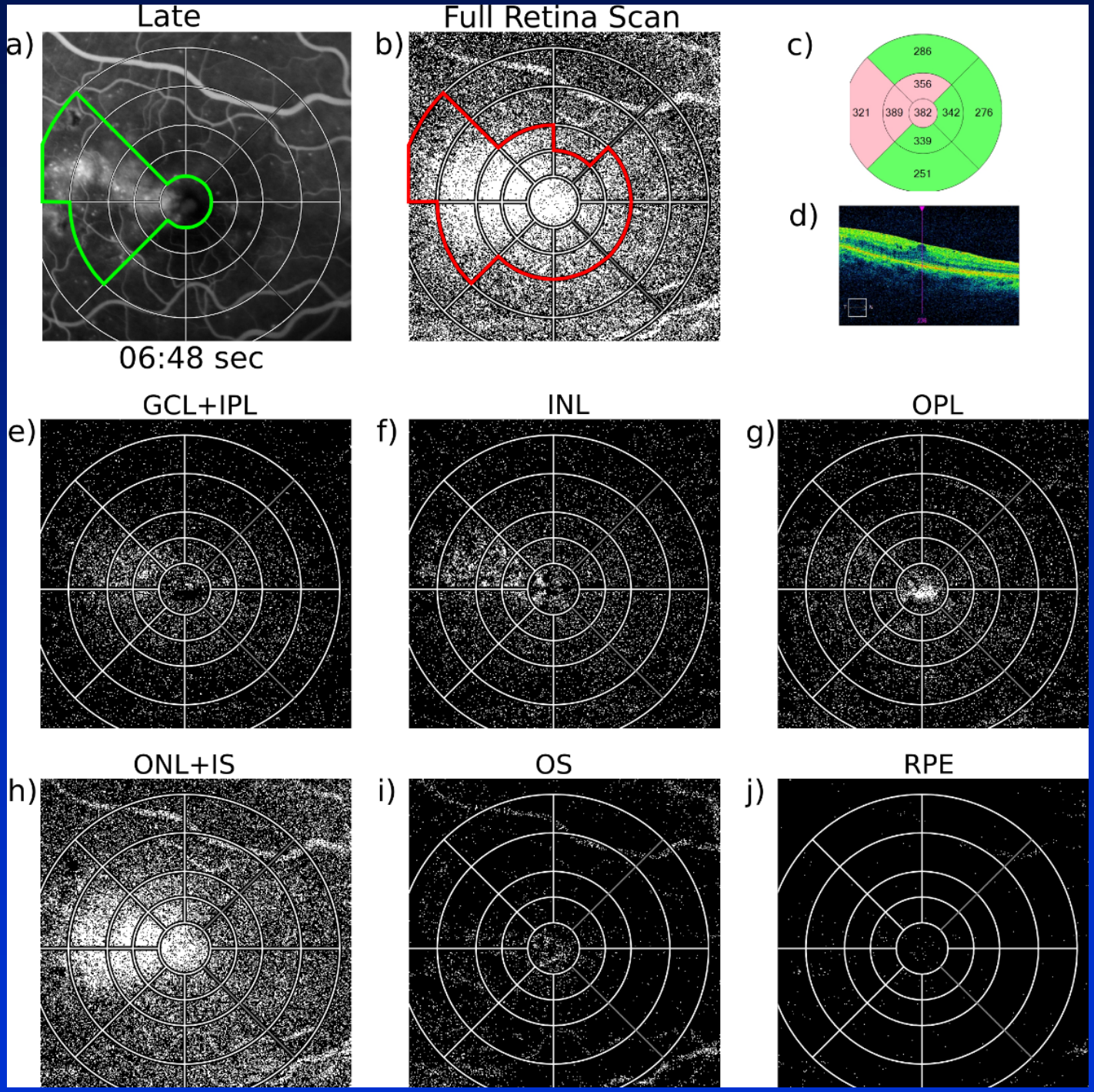
Eye with diabetic SME and minimal signs of fluorescein leakage on FA.

Agreement between OCT-Leakage and FA in Diabetic Retinopathy

52 Eyes with DR (ETDRS 10-53)

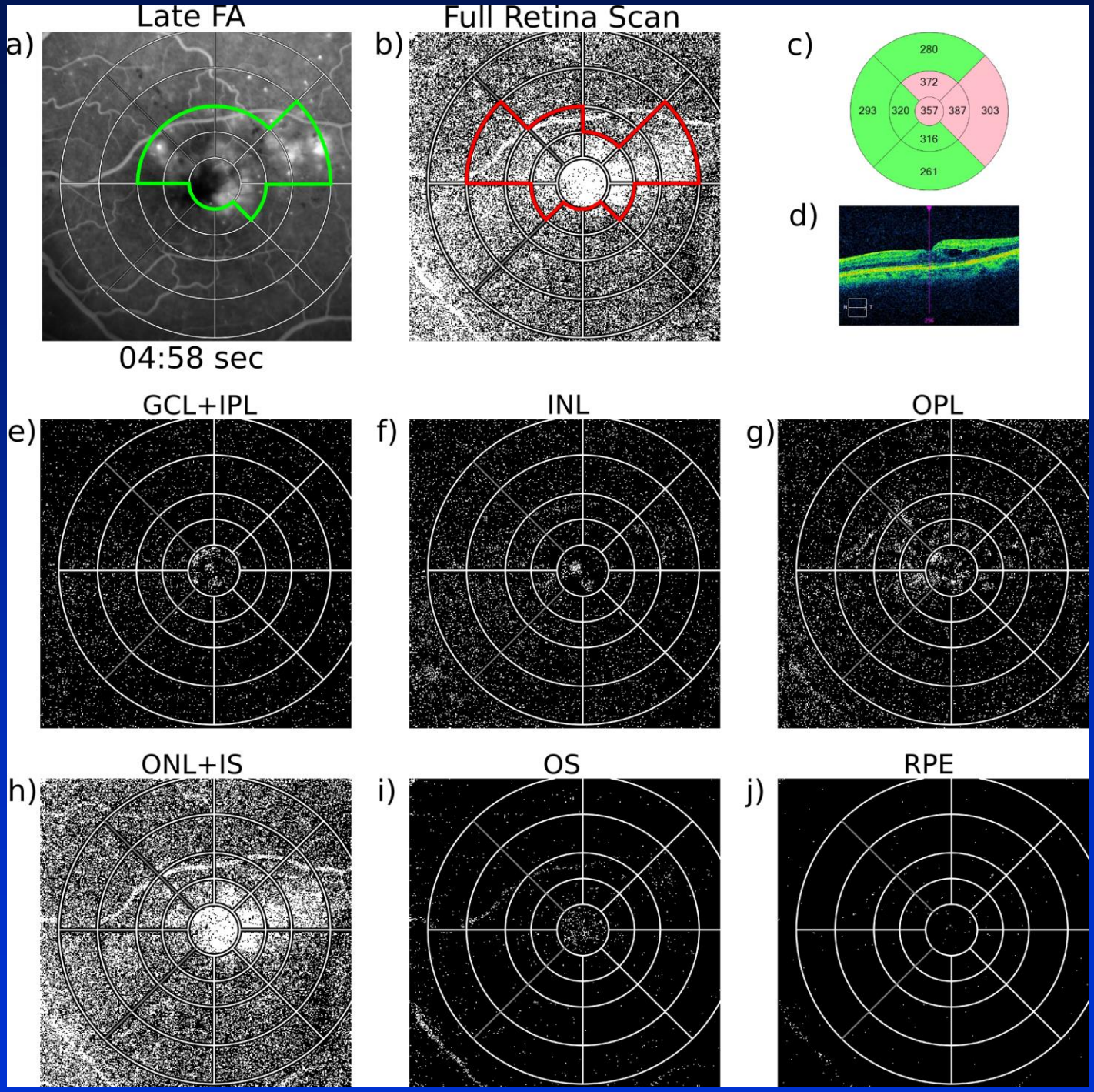


ETDRS grid covering the central subfield (section 1), the subdivided inner ring (sections 2 to 17) and outer ring (sections 18 to 33).



Identification of sites of Leakage

Eye of a subject with well-defined leakage on FA.



Identification of sites of Leakage

Eye of a subject with well-defined leakage on FA.

Agreement between OCT-Leakage and FA

FA leakage	LOR abnormalities	
	No	Yes
No (n=289)	218 (75.4%)	71 (24.6%)
Yes (n=74)	3 (4.1%)	71 (95.9%)

Sensitivity (95% CI)	Specificity (95% CI)	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)
95.9%	75.4%	50%	98.6%
(91.4-100.0)	(61.7-89.2)	(41.5-58.5)	(96.1-99.7)

CI= Confidence Interval

Conclusions

1. It is possible to reliably locate and quantify increases in the retinal extracellular space in diabetic patients. The changes in the retinal extracellular space correlate well with the occurrence and degree of retinal edema.

2. OCT-Leakage is able to identify the location of the increases of retinal extracellular space in the different layers of the retina.

3. OCT-Leakage based on the determination of LOR-ratios (Low optical reflectivity ratio) allows the identification of the main sites of leakage and the areas of leakage visible on late FA images.

4. OCT-Leakage location and quantification is able to complement OCT Microangiography.