

# Longitudinal changes of microvascular perfusion and neurodegeneration in early type 2 diabetic retinal disease

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# Financial disclosures

none



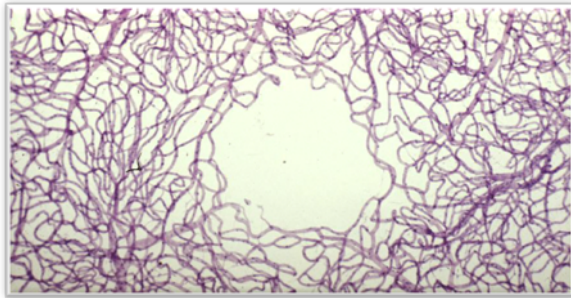
# Take-Home Messages

- Subclinical signs of parafoveal capillary dysfunction and inner retinal neurodegeneration/outer retinal thinning appear in parallel and are highly progressive even in the earliest stages of type 2 diabetic retinal disease
- Superficial vascular complex vessel density and ganglion cell/inner plexiform layer thickness seem to be particularly vulnerable in diabetic eyes with earliest DR stages
- Potentially related to incipient disintegration of the neurovascular unit
- Further studies needed to investigate these parameters as biomarkers for the microvasculopathic and the neuropathic component of diabetic retinal disease

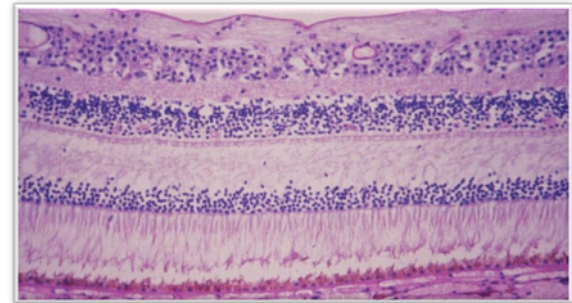


# Subclinical Signs of Diabetic Retinal Disease

**Impairment of microvascular architecture  
and perfusion (→ OCT-A)**



**Retinal neurodegeneration  
(→ neurosensory layer thinning in OCT)**



Source of images: <https://www.atlasophthalmology.net/atlas/>; <https://www.oxymap.com/>



**How will retinal microvascular and neurodegenerative signs change over a 2-year observational period in patients with type 2 diabetes and no or early DR?**



# Study Purpose

to monitor parafoveally and peripapillary subclinical changes in

- retinal capillary perfusion
- retinal layer thickness

in patients with type 2 diabetes and early diabetic retinal disease over two years



# Methods



# Study Population

**Adult patients with type II diabetes**

→ diabetes duration  $\geq 6$  years

## **Exclusion criteria:**

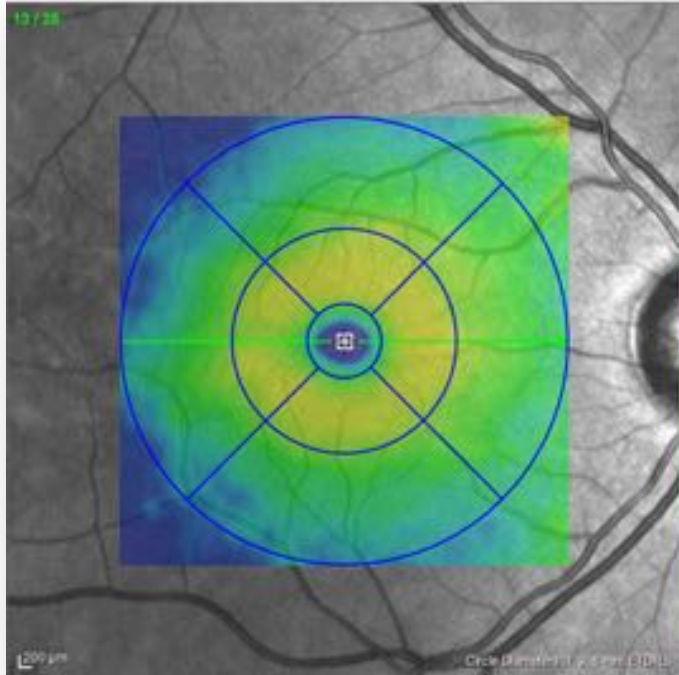
- Other ocular diseases (e.g. glaucoma, retinal detachment, macular hole, age-related macular degeneration, retinal vascular occlusion, macular dystrophies), media opacities, active intraocular inflammation, previous laser therapy or intraocular surgery in the last three months.
- Previous cardiovascular events
- HbA1c  $> 8\%$

**2-Year Follow-Up**





# Spectral-Domain OCT

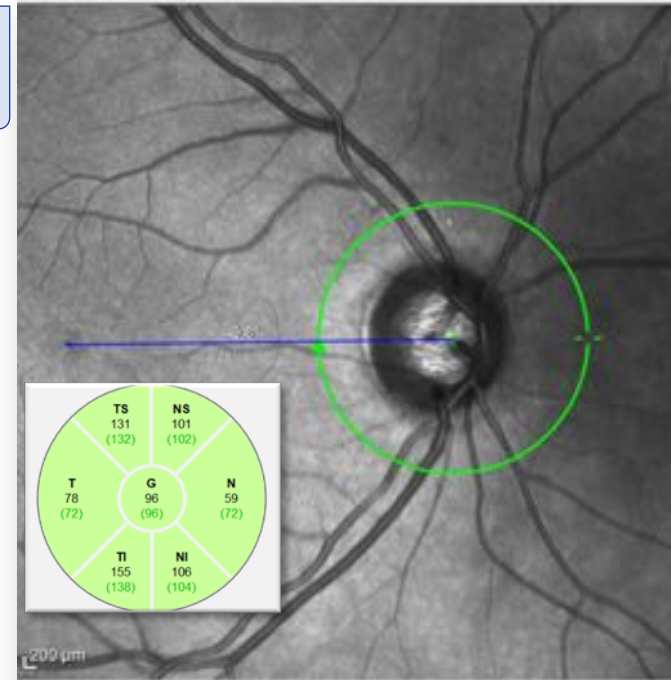


**Spectralis OCT**  
Heidelberg Engineering, Germany  
Software 1.10.2.0

→ RNFL  
GCL  
IPL  
INL  
OPL  
ONL  
RPE  
IRL  
PR

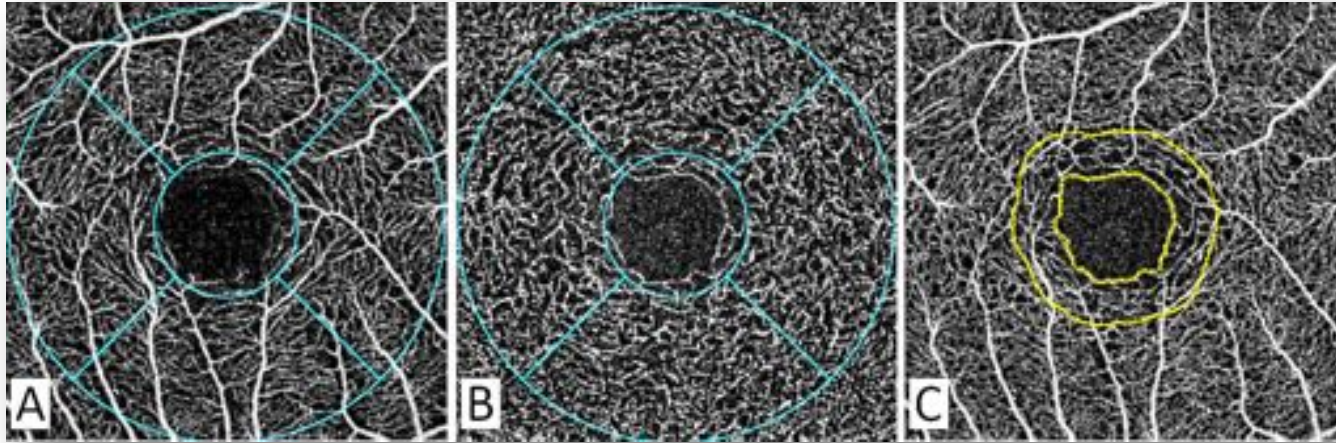
pRNFL ←

- **Macular** volume scans (25 B-scans)
- Full 6-mm ETDRS grid



- 12° (~ 3.6 mm) circular scan centered on **optic disc**

# OCT-Angiography



RTVue-XR Avanti

Optovue, USA

Angiovue Software v2017.1.0.155

→ 6 x 6 mm volume scans  
centered on the fovea

1. **Parafoveal vessel density (VD)** in the “**superficial vascular complex**” (*Panel A*) / “**deep vascular complex**” (*Panel B*)  
in a parafoveal 3-mm diameter ring excluding central 1 mm of fovea
2. **Foveal avascular zone (FAZ) area** (mm<sup>2</sup>) in the “retinal slab” (*Panel C*)
3. **FAZ perimeter** (mm) in the “retinal slab” (*Panel C*)
4. **FAZ acircularity index** in the “retinal slab” (*Panel C*)

# Results



# Baseline Characteristics

59 patients, 21 female  
117 eyes (58 left)

**Age**, mean  $\pm$  SD in years

57  $\pm$  10

**Diabetes duration**, mean  $\pm$  SD in years

11  $\pm$  10

**Hemoglobin A1c**, mean  $\pm$  SD in %

7.2  $\pm$  0.7

**Insulin therapy**, n (%)

25 (42)

**History of hypertension**, n (%)

41 (70)

**History of dyslipidemia**, n (%)

36 (61)

**ETDRS BCVA**, mean  $\pm$  SD in letters (Snellen equivalent)

88  $\pm$  6 (20/25 – 20/15)

**Pseudophakia**

pseudophakic, 1 eye, n (%)

1 (1.7)

pseudophakic, both eyes, n (%)

5 (6.5)



# Presence & Progression of DR Stage

## Baseline:

no DR in **105 eyes (89.7%)**

mild NPDR in **6 eyes (5.1%)**

moderate NPDR in **6 eyes (5.1%)**

## Progression of DR after 2 years:

no DR to mild NPDR in **10 eyes (8.5%)**

mild to moderate NPDR in **3 eyes (2.6%)**



# Baseline OCT(A) Parameters - Macula

OCTA parameters (Para)fovea



Optical coherence tomography angiography metrics			
SVC VD, %	51.00 ± 5.77		
DVC VD, %	52.57 ± 4.11		
FAZ area, mm <sup>2</sup>	0.245 ± 0.115		
FAZ perimeter, mm	1.853 ± 0.465		
FAZ AI	1.080 ± 0.032		
Retinal layer thicknesses*			
	CSF	Inner ETDRS Ring	Outer ETDRS Ring
RT	275 ± 21	339 ± 14	297 ± 14
RNFL	13 ± 2	22 ± 2	36 ± 5
GCL	15 ± 5	51 ± 5	37 ± 5
IPL	22 ± 4	42 ± 3	30 ± 3
INL	20 ± 6	40 ± 4	32 ± 3
OPL	26 ± 6	32 ± 3	28 ± 2
ONL	92 ± 10	69 ± 6	55 ± 6
RPE	17 ± 3	16 ± 2	14 ± 1
IRL	186 ± 22	256 ± 13	218 ± 13
PR	89 ± 5	83 ± 3	80 ± 2
pRNFL	101 ± 8		

(Neuro)retinal layer thicknesses  
Macula



# OCTA Parameters – Macula

**Statistically significant REDUCTION of VD in SVC** ( $-1.425 \pm 0.290\%/year$ ,  $p < 0.0001$ )

**but NOT in VD of DVC** ( $-0.392 \pm 0.211\%/year$ ,  $p = 0.0643$ )

## 2 Years Later

**Statistically significant INCREASE of FAZ area** ( $+0.008 \pm 0.002\text{mm}^2/year$ ,  $p < 0.0001$ )  
**perimeter** ( $+0.036 \pm 0.010\text{mm}/year$ ,  $p = 0.006$ )  
**acircularity index** ( $+0.005 \pm 0.002/year$ ,  $p = 0.0280$ )

# Change of (neuro-)retinal layer thicknesses over 2-year Follow-Up Period

	ETDRS grid area	Estimated change/year*	p-value		ETDRS grid area	Estimated change/year*	p-value
RT	CSF	-0.949 ± 0.408	<b>0.0205</b>	OPL	CSF	+0.129 ± 0.170	0.4492
	inner ring	-0.232 ± 0.207	0.2617		inner ring	-0.515 ± 0.121	<b>&lt;0.0001</b>
	outer ring	-0.735 ± 0.388	0.0591		outer ring	-0.408 ± 0.059	<b>&lt;0.0001</b>
	inner+outer ring	-0.971 ± 0.468	<b>0.0387</b>		inner+outer ring	-0.921 ± 0.161	<b>&lt;0.0001</b>
RNFL	CSF	-0.104 ± 0.070	0.1363	ONL	CSF	+0.010 ± 0.279	0.9711
	inner ring	+0.099 ± 0.072	0.1745		inner ring	+0.121 ± 0.167	0.4681
	outer ring	+0.101 ± 0.121	0.4027		outer ring	-0.131 ± 0.139	0.3448
	inner+outer ring	+0.204 ± 0.175	0.2435		inner+outer ring	-0.011 ± 0.277	0.9692
GCL	CSF	-0.230 ± 0.090	<b>0.0105</b>	RPE	CSF	-0.210 ± 0.089	<b>0.0187</b>
	inner ring	-0.210 ± 0.064	<b>0.0012</b>		inner ring	-0.217 ± 0.052	<b>&lt;0.0001</b>
	outer ring	-0.324 ± 0.155	<b>0.0372</b>		outer ring	-0.166 ± 0.043	<b>0.0001</b>
	inner+outer ring	-0.539 ± 0.150	<b>0.0004</b>		inner+outer ring	-0.385 ± 0.084	<b>&lt;0.0001</b>
IPL	CSF	-0.460 ± 0.083	<b>&lt;0.0001</b>	IRL	CSF	-0.467 ± 0.414	0.2595
	inner ring	-0.196 ± 0.049	<b>0.0001</b>		inner ring	-1.078 ± 0.608	0.0767
	outer ring	-0.163 ± 0.114	0.1524		outer ring	-1.381 ± 0.639	<b>0.0313</b>
	inner+outer ring	-0.361 ± 0.127	<b>0.0045</b>		inner+outer ring	-1.078 ± 0.608	0.0767
INL	CSF	-0.036 ± 0.394	0.9263	PR	CSF	-0.472 ± 0.133	<b>0.004</b>
	inner ring	+0.161 ± 0.536	0.7642		inner ring	-0.190 ± 0.082	<b>0.0210</b>
	outer ring	-0.195 ± 0.480	0.6854		outer ring	-0.133 ± 0.067	<b>0.0484</b>
	inner+outer ring	-0.035 ± 0.1010	0.9556		inner+outer ring	-0.325 ± 0.139	<b>0.0201</b>
				pRNFL		+0.02 ± 0.15	0.9169

- study not powered to investigate subclinical microvascular or neurodegenerative parameters as predictors for future DR progression



# Conclusions

## Subclinical alterations in parafoveal capillary perfusion

- profound decrease in parafoveal VD in the SVC
- finding supports previous results suggesting that SVC integrity is considerably impaired in early, pre-clinical DR, while DVC seems to become affected in more advanced disease stages

## Change in retinal layer thicknesses

- trend towards decreasing total thickness in this cohort of patients without diabetic macular edema and with early stages of DR
- rapid decline in GCL and IPL thickness in the inner retina
- RNFL did not statistically significantly decrease in either the macular or the peripapillary region

# Thanks for your attention

