

Dynamic Changes of Non-Culprit Coronary Lesions Over Time Under Standard of Care Therapy



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DISCLOSURE

No conflict of interest.

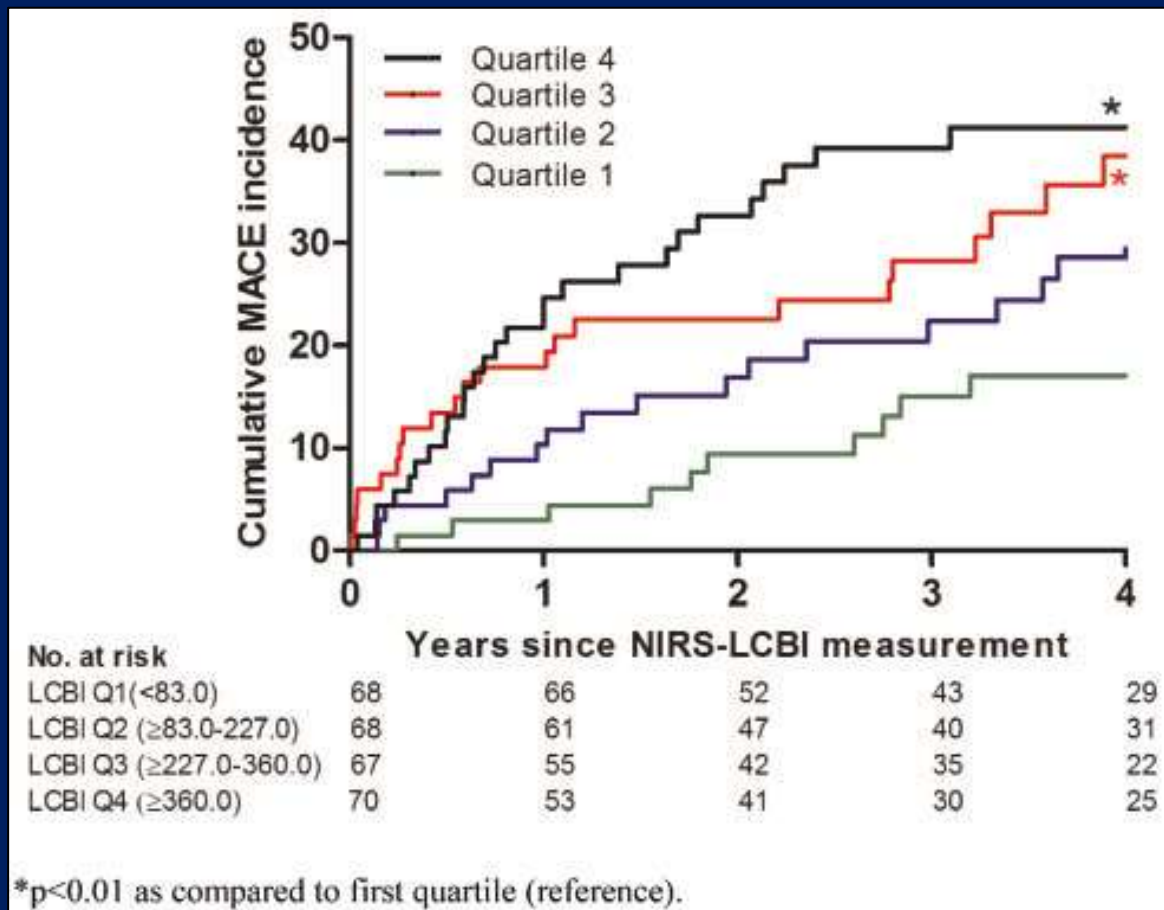
BACKGROUND

Progression of coronary artery disease is poorly understood.

Clinical studies show an association of plaque composition and subsequent clinical events in patients, suggesting plaque composition as a risk marker for vulnerable patients: VIVA, PROSPECT, ATHEROREMO

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Progression of coronary artery disease is poorly understood.



Plaque composition in **non culprit arteries** is associated with MACE (4y FUP)

Impact of lipid content (LCBI) on the risk of MACE, stratified by LCBI quartiles

LCBI
(Lipid Core Burden Index)

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Clinical studies show an association of plaque composition and subsequent clinical events in patients, suggesting plaque composition as a risk marker for vulnerable patients: VIVA, PROSPECT, ATHEROREMO

Little is known, however, on the **change of plaques over time.**

**To evaluate changes in plaque morphology
of non-culprit lesions over time
using a qualitative and quantitative approach.**

METHODS - PATIENTS

N=119 Pts

**The Thoraxcenter OCT database was screened
for patients undergoing serial OCT examinations
of the same vessel with an interval >3 months**

METHODS - OCT

OCT Acquisition

Fourier-Domain Systems: Lightlab C7; SJM Optis; Terumo Lunawave
Automated pullback. 20mm/sec
Flush: Visipaque 3ml/sec

ROI selection and matching

Serial OCT pullbacks were **matched** to each other using multiple **landmarks** and **synchronized by an automated algorithm** (QCU-CMS, LKEB, Leiden, NL) for corresponding frames and co-registered display.

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Patient-level analysis: The complete baseline ROI per patient

Segment-level analysis: Baseline ROI was divided in 5mm sub-segments

METHODS - Assessment of Plaque Composition & Morphometry

Assessment of plaque composition: Visual

Plaque composition was diagnosed according to established criteria (1) and reported in a hierarchical manner.

Hierarchical plaque characterization

- a. Thin-cap fibroatheroma (TCFA): Max necrotic core arc $>90^\circ$ & fibrous cap thickness $\leq 65\mu\text{m}$.
- b. Fibroatheroma: Max necrotic core arc $>90^\circ$ & fibrous cap thickness $>65\mu\text{m}$.
- c. Fibrocalcific: Max calcium arc $>90^\circ$, with maximum necrotic core arc $\leq 90^\circ$.
- d. Fibrous: Max necrotic core arc $\leq 90^\circ$ and maximum calcium arc $\leq 90^\circ$.

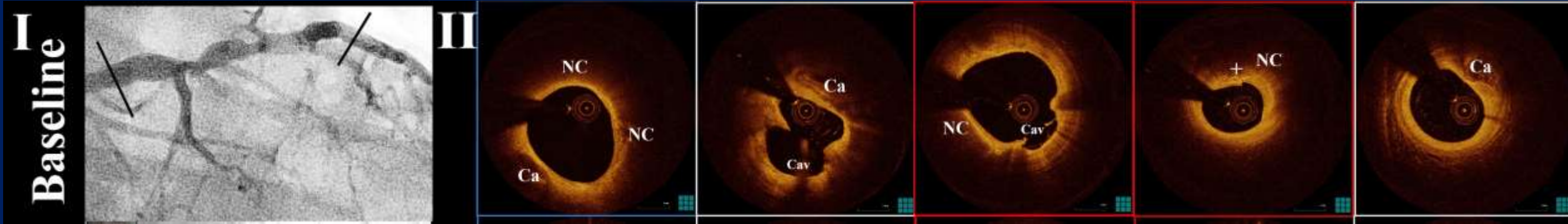
Assessment of plaque composition: Attenuation analysis

Values of tissue attenuation (2) for the entire perimeter of each cross-section for the entire studied segment were graphically plotted in a longitudinal attenuation map of the vessel.

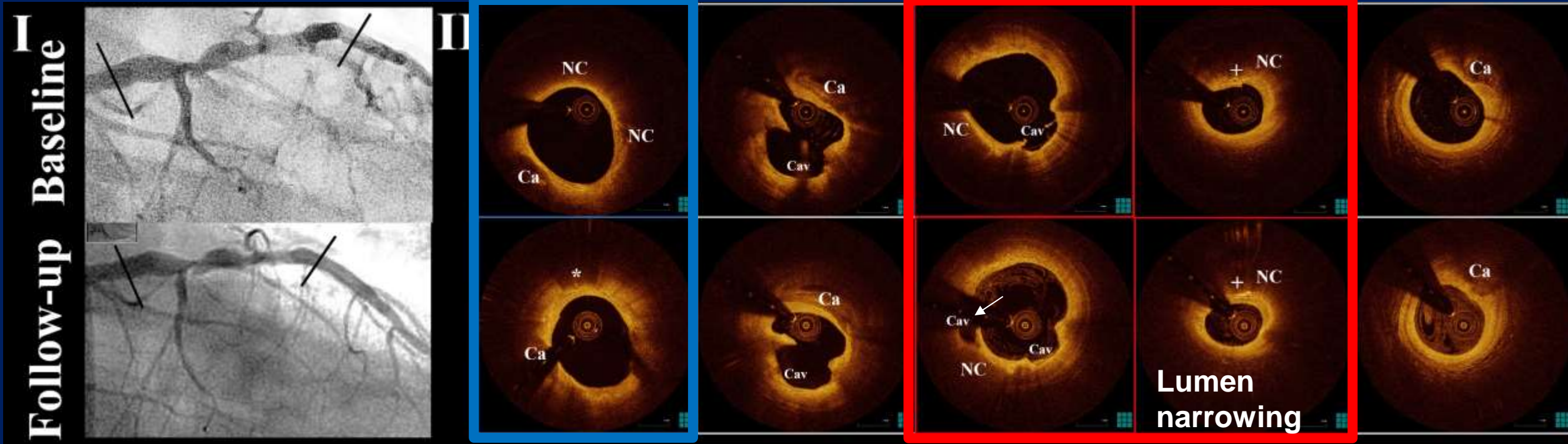
RESULTS – Changes in Clinical Syndrome Over Time*

Clinical Presentation n=72	Baseline	FUP (6.2 months)
Stable angina	40.3 %	16.7 %
Unstable angina	15.3 %	5.6 %
STEMI	38.9 %	---
NSTEMI	4.2 %	1.4 %
Asymptomatic	1.4 %	76.4 %

PLAQUE MORPHOLOGY Over Time - INTENSITY MAP



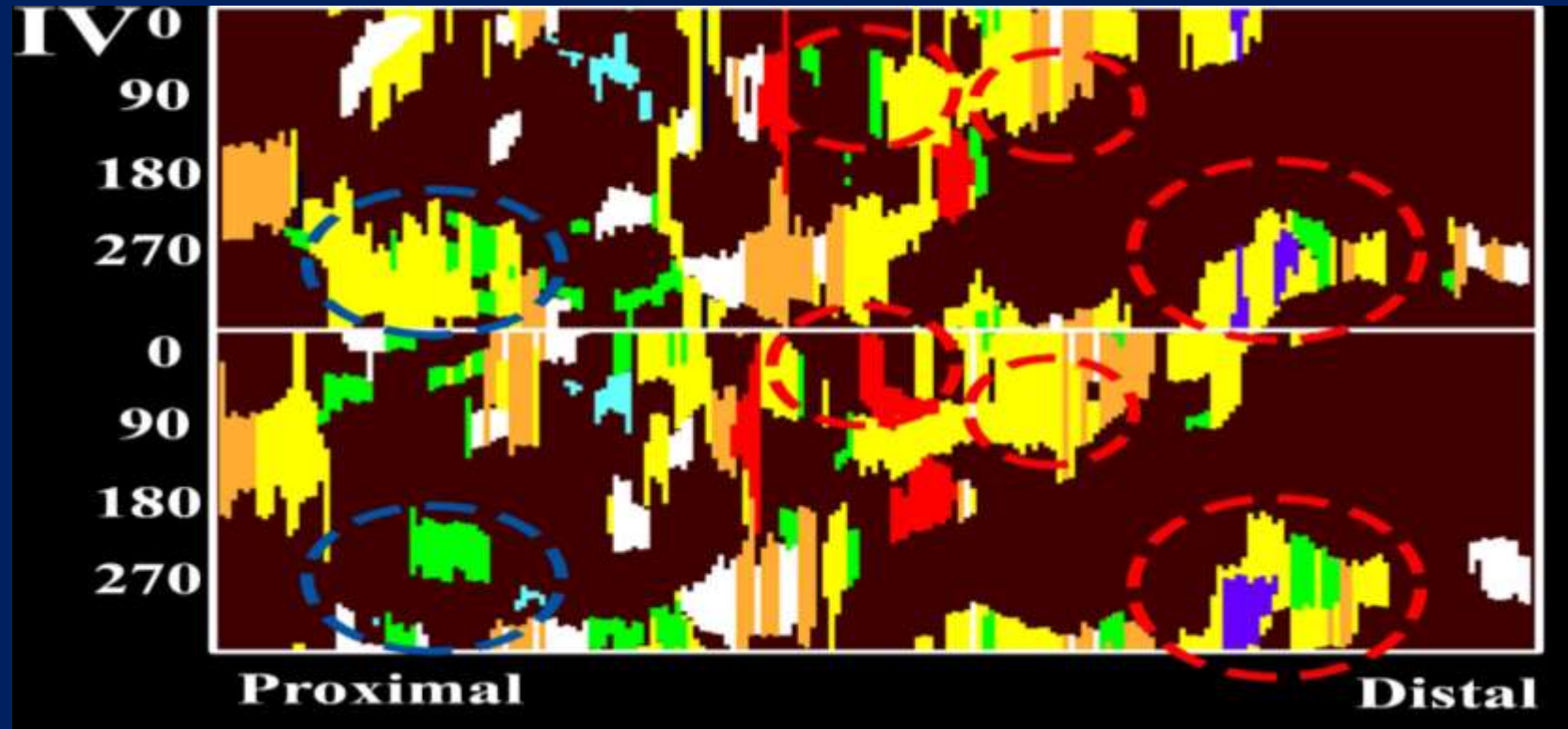
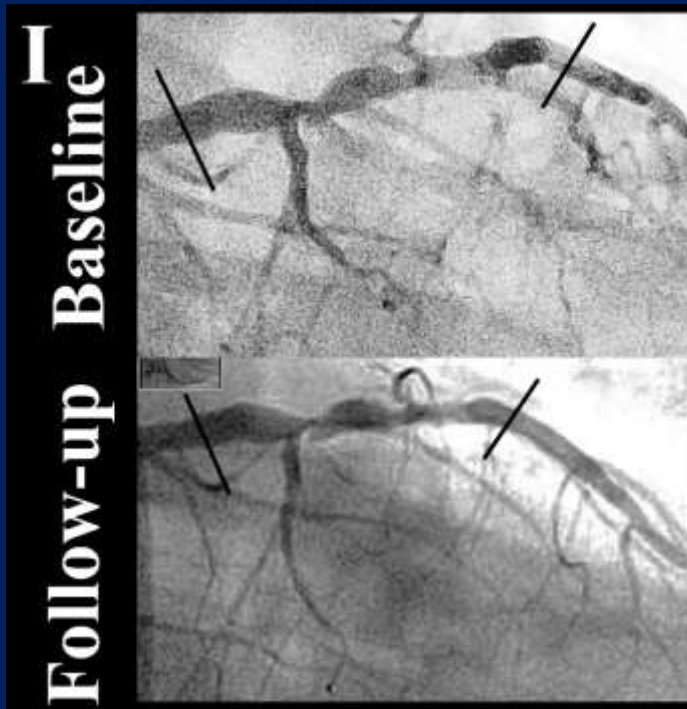
PLAQUE MORPHOLOGY Over Time - INTENSITY MAP



*Reduction in necrotic core

LAD in a pt presenting with new anginal symptoms 20 months after PCI of the LCx

PLAQUE MORPHOLOGY Over Time - PLAQUE SPREAD OUT MAP

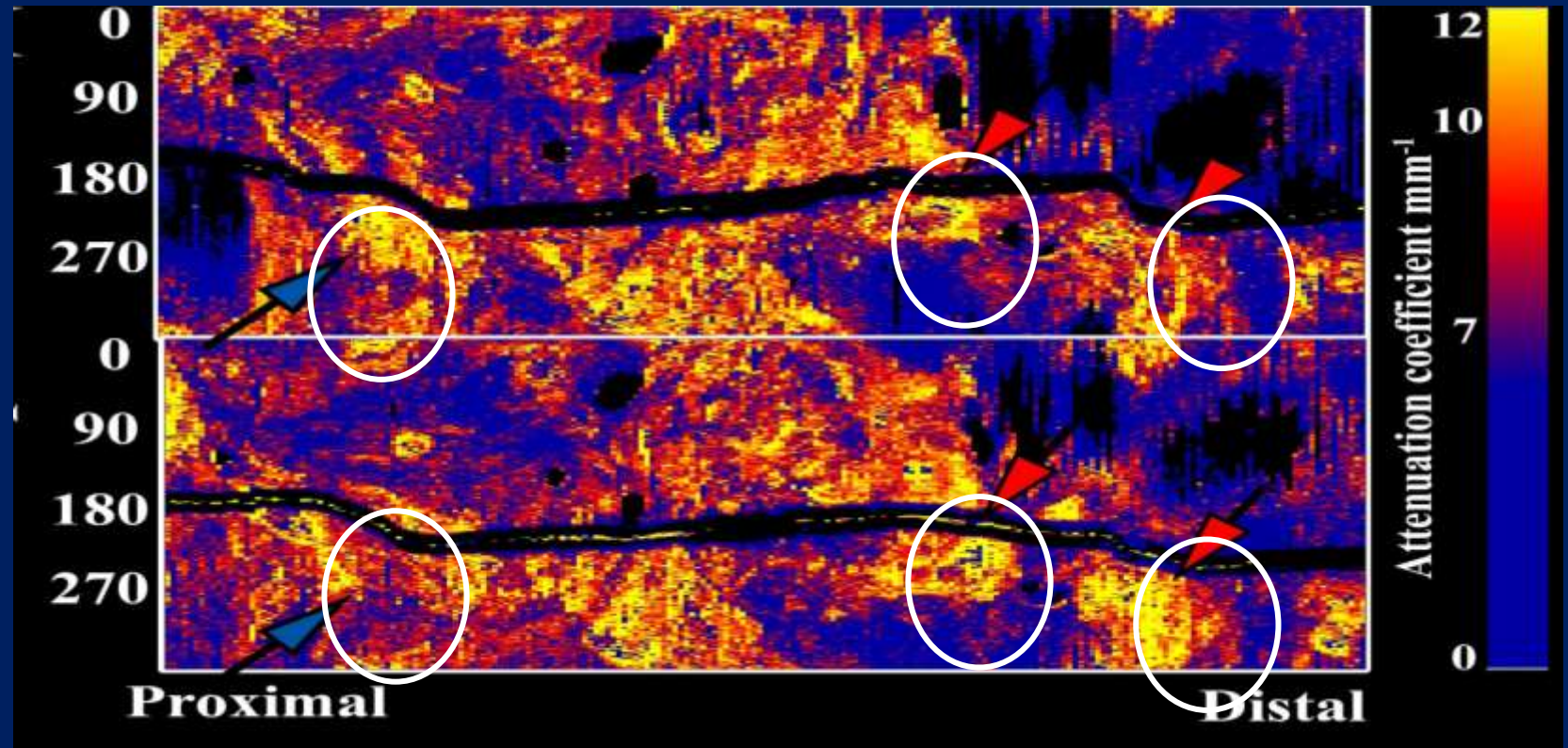
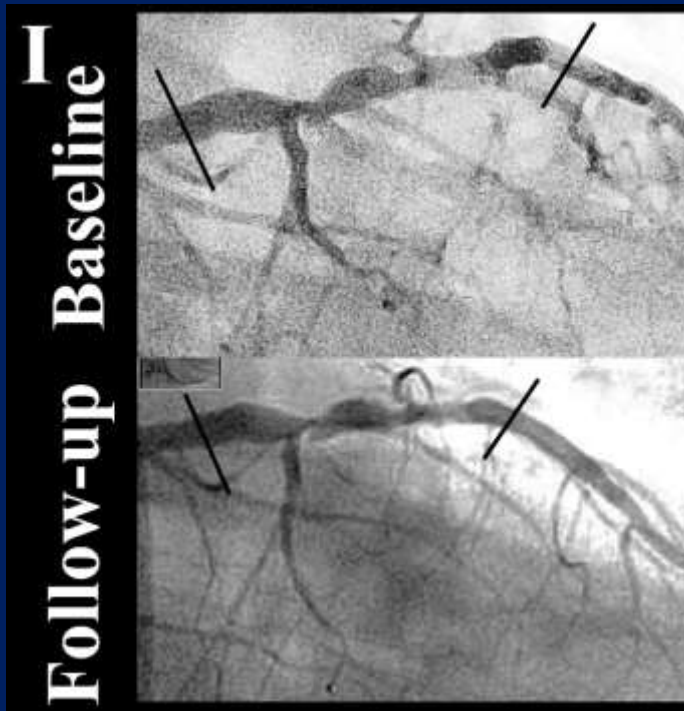


Plaque spread-out maps with color-coded tissues

Blue circle: Reduction

Red circle: Progressions

PLAQUE MORPHOLOGY Over Time - ATTENUATION MAP



Attenuation spread-out maps showing the longitudinal distribution of maximum attenuation coefficient values along the entire segment

Blue arrow: Reduction

Red arrow: Progressions

RESULTS – Changes in Plaque Over Time*

PATIENT LEVEL	Baseline	Follow-up	p-value ⁺	SEGMENT LEVEL	Baseline	Follow-up	p-value ⁺
Minimal lumen area, mm ²	5.24 ± 2.86	5.28 ± 2.93	0.76	Minimal lumen area, mm ²	7.07 ± 3.75	6.86 ± 3.73	0.018
Mean lumen area, mm ²	8.22 ± 3.63	7.87 ± 3.68	0.049	Mean lumen area, mm ²	8.15 ± 4.14	7.92 ± 3.98	0.005
Plaque morphology n(%)			0.81	Plaque morphology n(%)			0.84
Fibroatheroma	30(41.7)	34(47.2)		Fibroatheroma	105(40.9)	110(42.8)	
Fibrocalcific	0	0		Fibrocalcific	1(0.4)	0	
Fibrous	16(22.2)	16(22.2)		Fibrous	118(45.9)	123(47.9)	
TCFA	26(36.1)	22(30.6)		TCFA	33(12.8)	24(9.3)	
Mean necrotic core arc, (°)	99.9 ± 35.6	96.7 ± 35.4	0.21	Mean necrotic core arc, (°)	96.7 ± 43.0	94.8 ± 39.1	0.48
Max necrotic core arc, (°)	170.9 ± 67.4	174.1 ± 79.7	0.67	Max necrotic core arc, (°)	133.7 ± 65.0	135.4 ± 71.0	0.81
RNCI, %	15.24 ± 10.46	15.18 ± 10.76	0.91	RNCI, %	15.33 ± 15.07	15.15 ± 14.27	0.76
Mean calcium arc, (°)	72.1 ± 51.0	62.0 ± 42.8	0.25	Mean calcium arc, (°)	76.9 ± 59.9	82.5 ± 56.4	0.59
Max calcium arc, (°)	100.7 ± 83.8	90.6 ± 82.9	0.31	Max calcium arc, (°)	98.4 ± 83.9	108.6 ± 89.5	0.34
RCI, %	1.87 ± 6.03	1.85 ± 6.75	0.92	RCI, %	1.59 ± 6.11	1.79 ± 7.03	0.38
Minimum cap thickness, μm	88 ± 53	91 ± 65	0.68	Minimum cap thickness, μm	120 ± 75	134 ± 81	0.019
Average cap thickness, μm	183 ± 62	209 ± 67	0.01	Average cap thickness, μm	184 ± 80	206 ± 83	0.002
IPA6, mm ⁻¹	480.71 ± 144.97	464.36 ± 152.76	0.48	IPA6, mm ⁻¹	472.77 ± 179.94	444.52 ± 185.86	0.036
IPA11, mm ⁻¹	52.40 ± 41.00	44.73 ± 36.23	0.049	IPA11, mm ⁻¹	49.46 ± 52.42	42.72 ± 45.74	0.022

* *under standard of care therapy*

RESULTS – Changes in Plaque Morphometry Over Time*

PATIENT LEVEL	Baseline	Follow-up	p-value ⁺
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PATIENT LEVEL, n=72

 **Mean lumen area, mm²**
8.2±3.6 7.8±3.6 0.049

 **Ave cap thickness (mm)**
183±62 209±67 0.01

 **IPA¹¹**
52±41 44±36 0.049




SEGMENT LEVEL	Baseline	Follow-up	p-value ⁺
Minimal lumen area, mm ²	7.07 ± 3.75	6.86 ± 3.73	0.018
Mean lumen area, mm ²	8.15 ± 4.14	7.92 ± 3.98	0.005
Plaque morphology n(%)			0.84
Fibroatheroma	105(40.9)	110(42.8)	
Fibrocalcific	1(0.4)	0	
Fibrous	118(45.9)	123(47.9)	
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RESULTS – Changes in Plaque Morphometry Over Time*







PATIENT LEVEL	Baseline	Follow-up	p-value [†]
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PATIENT LEVEL, n=72

 Mean lumen area, mm ²	8.2±3.6	7.8±3.6	0.049
 Ave cap thickness (mm)	183±62	209±67	0.01
 IPA ¹¹	52±41	44±36	0.049

SEGMENT LEVEL	Baseline	Follow-up	p-value [†]
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SEGMENT LEVEL, n=256

 Mean lumen area, mm ²	8.1±4.1	7.9±3.9	0.005
 Min lumen area, mm ²	7.0±4.1	6.8±3.7	0.018
 Ave cap thickness (mm)	184±80	206±83	0.019
 Min cap thickness (mm)	120±75	134±81	0.002
 IPA ¹¹	49±52	42±45	0.022
 IPA ⁶	472 ±179	444±185	0.022

* under standard of care therapy

RESULTS – Changes in Plaque Morphology Over Time*

PATIENT LEVEL	Baseline	Follow-up	p-value [†]	SEGMENT LEVEL	Baseline	Follow-up	p-value [†]
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* *under standard of care therapy*

RESULTS – Changes in Plaque Morphology Over Time*

PATIENT LEVEL	Baseline	Follow-up	p-value*
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PATIENT LEVEL, n=72

• Fibroatheroma	41.7%	47.2%	ns
• Fibrocalcific	0%	0%	ns
• Fibrous	22.2%	22.2%	ns
• TCFA	36.1%	30.6%	ns

SEGMENT LEVEL	Baseline	Follow-up	p-value*
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SEGMENT LEVEL, n=256

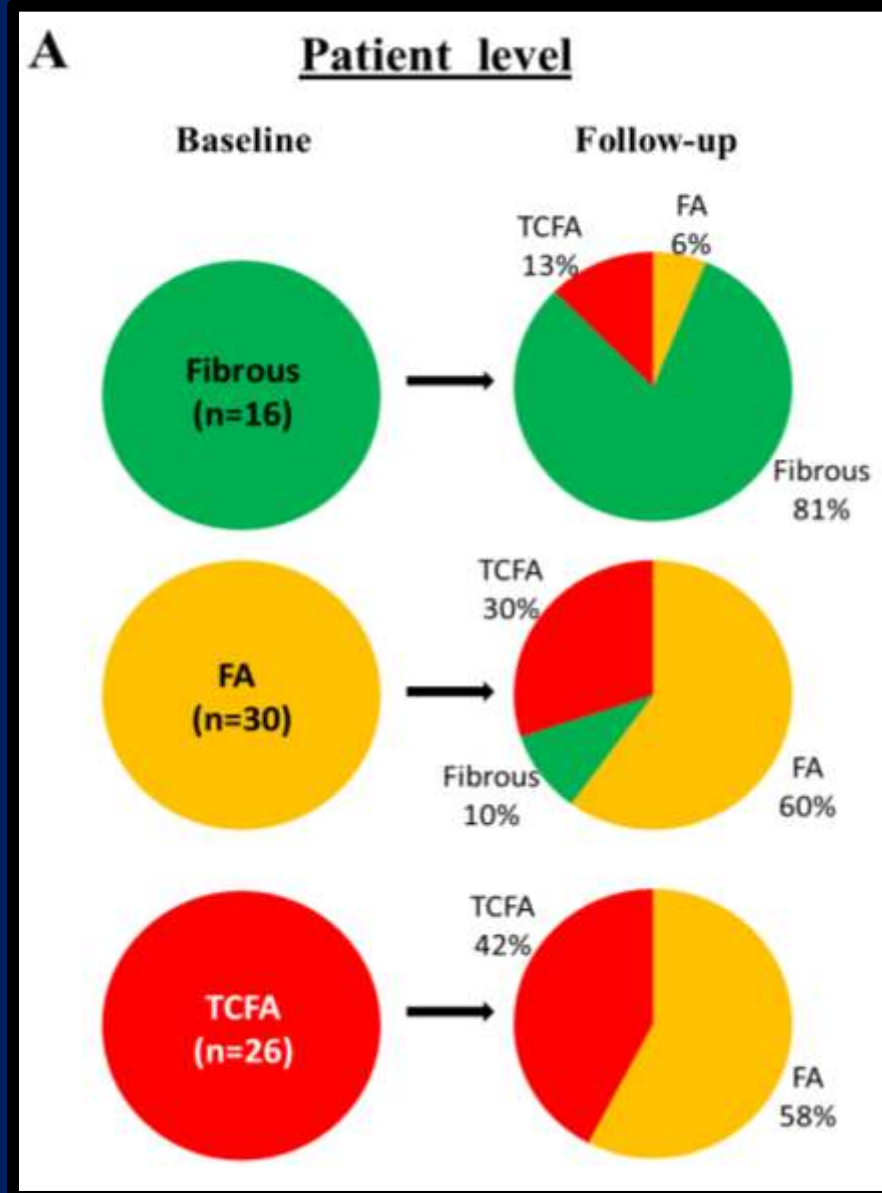
• Fibroatheroma	40.9%	42.8%	ns
• Fibrocalcific	1%	0%	ns
• Fibrous	45.9%	47.9%	ns
• TCFA	12.8%	9.3%	ns

RESULTS – Changes in Plaque Morphology Over Time*

PATIENT LEVEL	Baseline	Follow-up	p-value [†]	SEGMENT LEVEL	Baseline	Follow-up	p-value [†]
PATIENT LEVEL, n=72				SEGMENT LEVEL, n=256			
• Fibroatheroma	41.7%	47.2%	ns	• Fibroatheroma	40.9%	42.8%	ns
• Fibrocalcific	0%	0%	ns	• Fibrocalcific	1%	0%	ns
• Fibrous	22.2%	22.2%	ns	• Fibrous	45.9%	47.9%	ns
• TCFA	36.1%	30.6%	ns	• TCFA	12.8%	9.3%	ns

What is happening ?

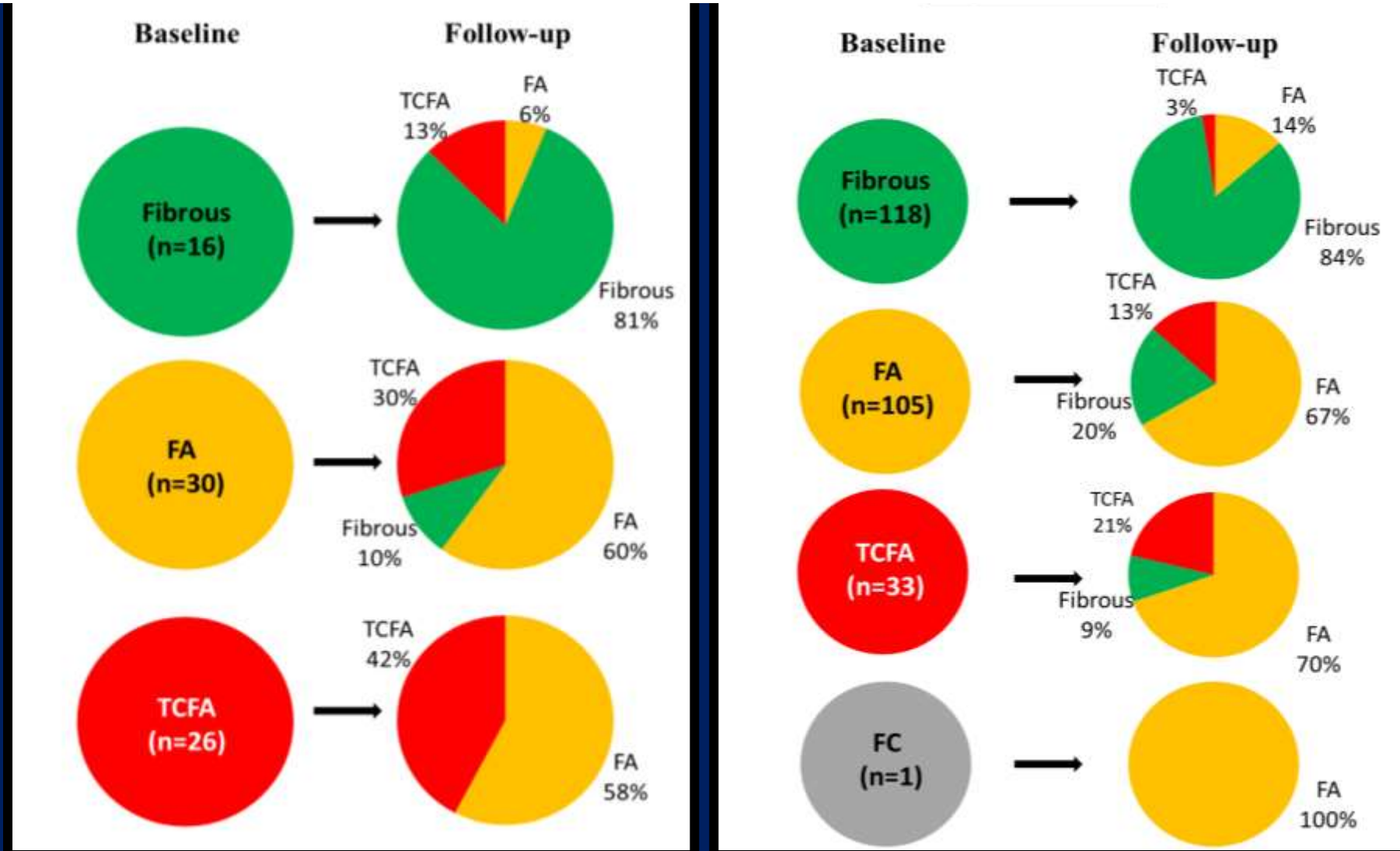
RESULTS – Changes in Plaque Morphology Over Time* Patient Level



	Baseline	FUP
FIBROUS	100%	81%
FIBRO-ATHEROMA	100%	60%
TCFA	100%	42%

RESULTS – Changes in Plaque Morphology Over Time* Patient Level

Plaque do not change uniformly in one direction (either favorable or unfavorable) !



RESULTS – Changes in Plaque Morphology Over Time*

Hierarchical Plaque Morphology (%)	Patient Level
Favorable change	25.0
No change	58.3
Unfavorable change	16.7

RESULTS – Changes in Plaque Morphology Over Time*

Hierarchical Plaque Morphology (%)	Patient Level	Segment Level
Favorable change	25.0	18.3
No change	58.3	68.5
Unfavorable change	16.7	12.8

RESULTS – Changes in Plaque Morphology - Predictors

	Favorable Odds ratio (95% CI)	Unfavorable Odds ratio (95% CI)
Age (per year)	1.006(0.972-1.041)	1.003(0.962-1.046)
Male gender	1.485(0.498-4.431)	1.384(0.393-4.871)
Interval (per month)	0.955(0.897-1.018)	1.044(0.984-1.107)
MI at baseline	1.085(0.523-2.251)	1.096(0.467-2.574)
Hypertension	0.894(0.425-1.879)	1.121(0.481-2.615)
Diabetes	1.621(0.452-5.813)	1.039(0.199-5.431)
Dyslipidemia	0.638(0.303-1.346)	1.331(0.560-3.161)
Smoker	0.936(0.343-2.557)	0.787(0.253-2.452)

Patient characteristics



RESULTS – Changes in Plaque Morphology - Predictors

	Favorable Odds ratio (95% CI)	Unfavorable Odds ratio (95% CI)
Statin use	3.188(0.673-15.096)	1.043(0.289-3.762)
Total cholesterol	1.447(0.752-2.784)	0.940(0.555-1.590)
LAD	0.457(0.174-1.198)	6.609(0.810-53.913)
LCX	0.692(0.251-1.905)	3.383(0.372-30.747)
No stent in artery	1.452(0.418-5.046)	1.449(0.412-5.105)
Distal to stent	1.842(0.855-3.968)	0.662(0.273-1.611)
Proximal to stent	-	-

Rx, Cholesterol

Vessel

Location in artery



RESULTS – Changes in Plaque Morphology - Predictors

	Favorable	Unfavorable
	Odds ratio (95% CI)	Odds ratio (95% CI)
Family history of CAD	0.383(0.188-0.781)*	0.617(0.264-1.441)



Family history of CAD

OR 0.383

DYNAMIC CHANGES IN NON-CULPRIT CORONARY LESIONS

In pts with coronary artery disease under standard of care treatment
non-culprit plaques show

DYNAMIC CHANGES IN NON-CULPRIT CORONARY LESIONS

In pts with coronary artery disease under standard of care treatment non-culprit plaques show

- frequently a change in morphology over time

42% Patients

31% Segments

DYNAMIC CHANGES IN NON-CULPRIT CORONARY LESIONS

In pts with coronary artery disease under standard of care treatment non-culprit plaques show

- frequently a change in morphology over time
- **change** in morphology over time is **highly variable** within pts *and* segments

18.3% Stabilization

12.8% Destabilization

Segment analysis

DYNAMIC CHANGES IN NON-CULPRIT CORONARY LESIONS

In pts with coronary artery disease under standard of care treatment non-culprit plaques show

- frequently a change in morphology over time
- change in morphology over time is highly variable within pts *and* segments

This **effect is hidden when globally assessed** in the entire cohort, with the exception of cap thickness where modest thickening was observed

hierarchical plaque type analysis showed no change over time

DYNAMIC CHANGES IN NON-CULPRIT CORONARY LESIONS

*In pts with coronary artery disease under standard of care treatment
non-culprit plaques*

- *change in morphology over time frequently*
- *change in morphology over time is highly variable*

This effect is hidden when globally assessed in the entire cohort,
with the exception of cap thickness where modest thickening was observed

Prediction of plaque changes is poor.

OR 0.38 CAD
Family history
for favorable changes

Atheroremo IVUS study:

Genome-wide association study of plaque morphology

« We found **12 SNPS** in proximity of **8 genes** which were possibly associated with **plaque vulnerability** »



Title: The European Collaborative Project on Inflammation and Vascular Wall Remodeling in Atherosclerosis - Intravascular Ultrasound (ATHEROREMO-IVUS) Study.

Authors: Sanneke P.M. de Boer, M.D; Yael Baran, MSc; Hector M. Garcia-Garcia, Itamar Eskin, MSc; Mattie Lenzen, Marcus E. Kleber, Evelyn Regar, M.D, PhD; Peter J. de Jaegere, M.D, PhD; Jurgen M. Ligthart, Robert Jan van Geuns, M.D, PhD; Terho Lehtimäki, Reijo Laaksonen, PhD; Eric Boersma, PhD; Winfried März, M.D, PhD; Eran Halperin, PhD; Patrick W. Serruys, M.D, PhD; Wolfgang Koenig, M.D, PhD

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Thank you for your attention !