Erasmus MC
Universitair Medisch Centrum Rotterdam

21st CardioVascular Summit
TCTAP 2016
April 26-29, 2016
Coex, Seoul, Korea

OCT&Pressure Wire-Guided Comprehensive Assessment for Coronary Artery Disease

Vulnerability Assessment Using OCT

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Disclosure

The institution Erasmus Medical Center receives research support from St. Jude Medical & consultancy fees from Boston Scientific.

Plaque Prone to Rupture

Inflamed, thin-cap fibroatheroma (TCFA)

- Lipid-rich, atheromatous core
- Thin fibrous cap, with
- Macrophage and lymphocyte infiltration
- Decreased SMC content
- Expansive remodeling

OCT Assessment of Vulnerability

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- OCT can visualize different plaque components: in vitro

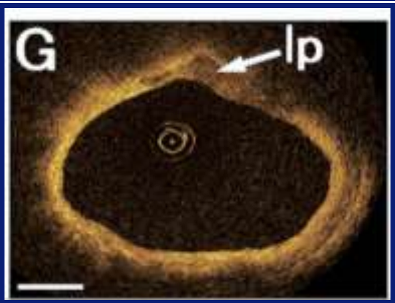
	Sens.	Spec.
Fibrous	71-79%	97-98%
Fibro-calcific	95-96%	97%
Lipid-rich	90-94%	90-92%

Overall agreement k = 0.83 to 0.84

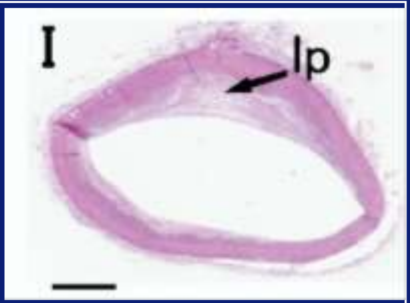
Yabushita et al. Circulation.2002:106:1640-1645.

OCT Assessment of Vulnerability

- OCT can visualize lipid rich-plaque.



OCT



Histology

modified from Kume et al. Am J Cardiol 2006;97:1172–117

OCT Assessment of Vulnerability

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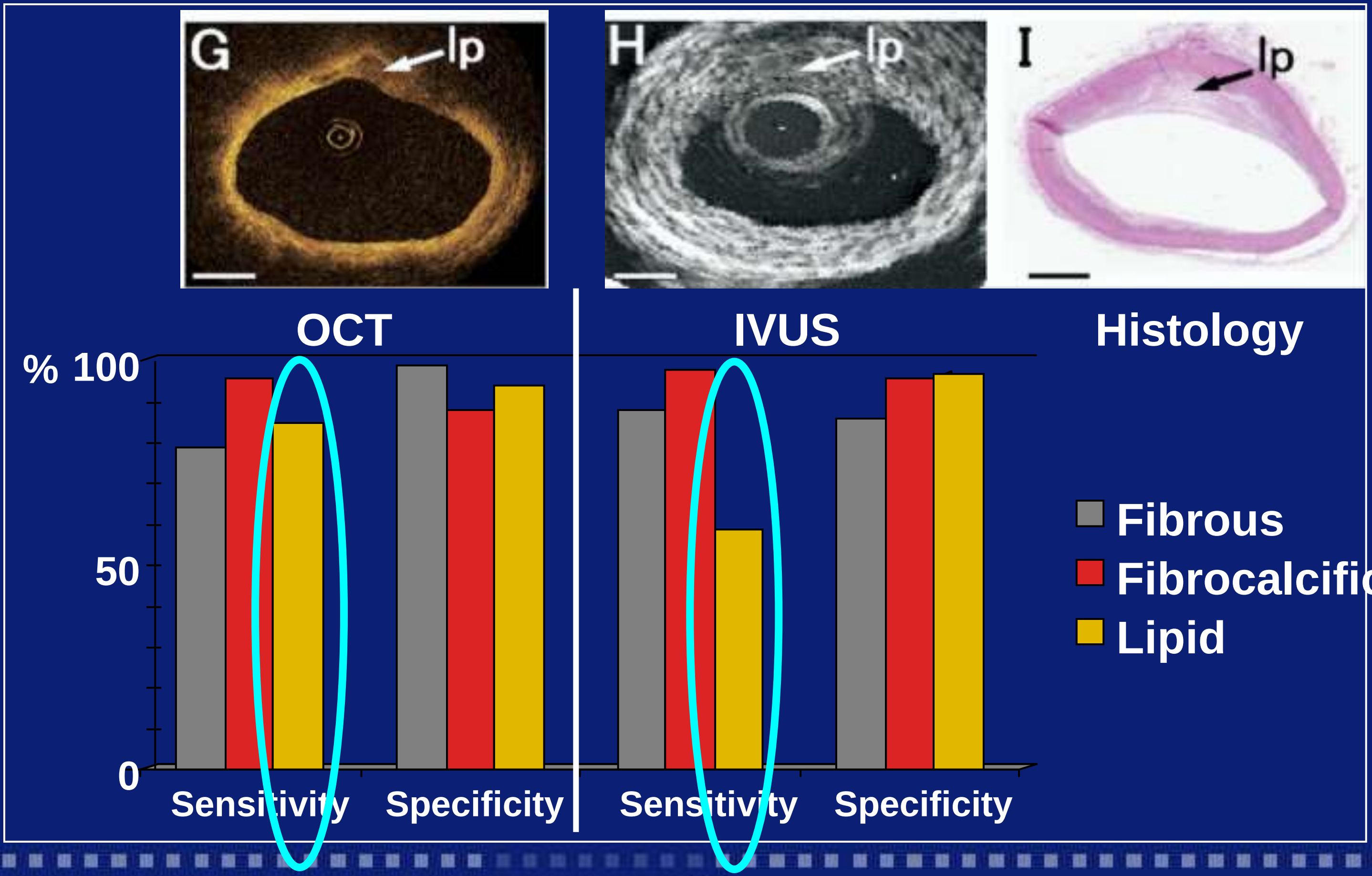
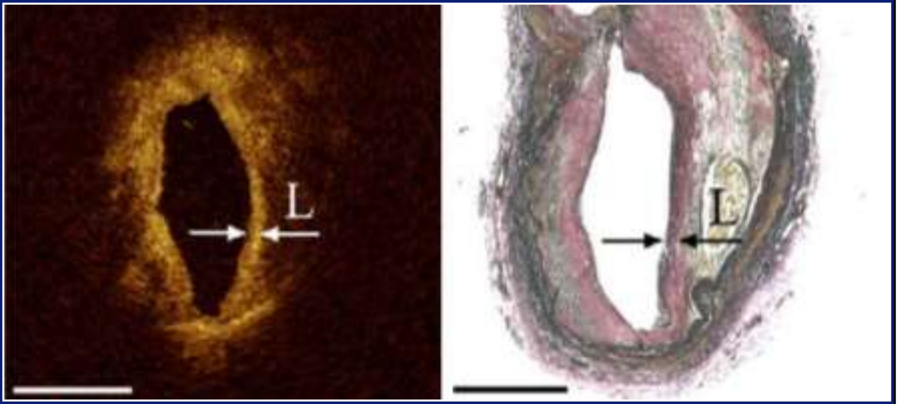


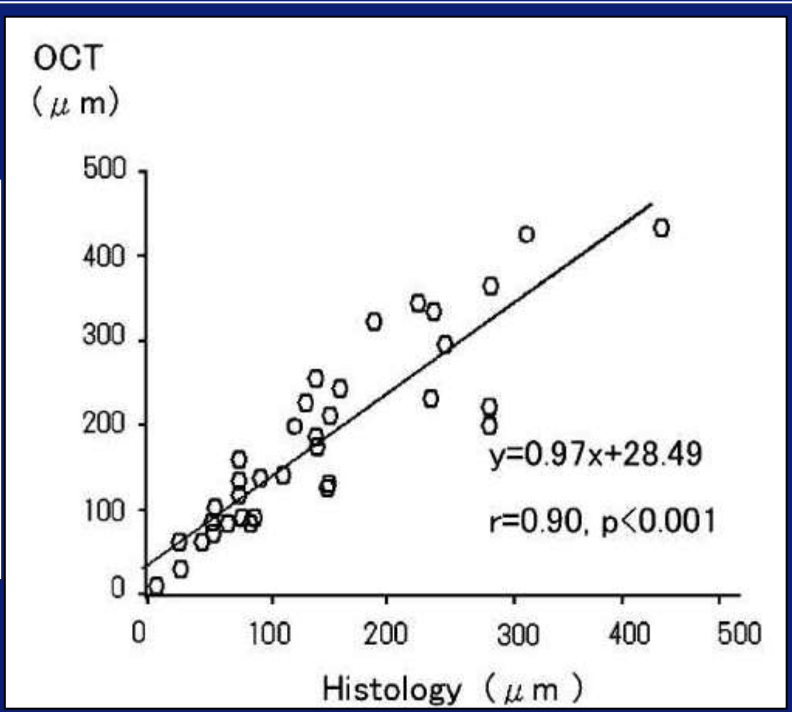
modified from Kume et al. Am J Cardiol 2006;97:1172–117

OCT Assessment of Vulnerability

- OCT can visualize lipid rich-plaque.
- OCT can visualize the thickness of a fibrous cap.

n= 102 Human coronaries





Kume et al. Am Heart J

OCT Assessment of Vulnerability

- OCT can visualize lipid rich-plaque.
- OCT can quantify the thickness of a fibrous cap (automated).

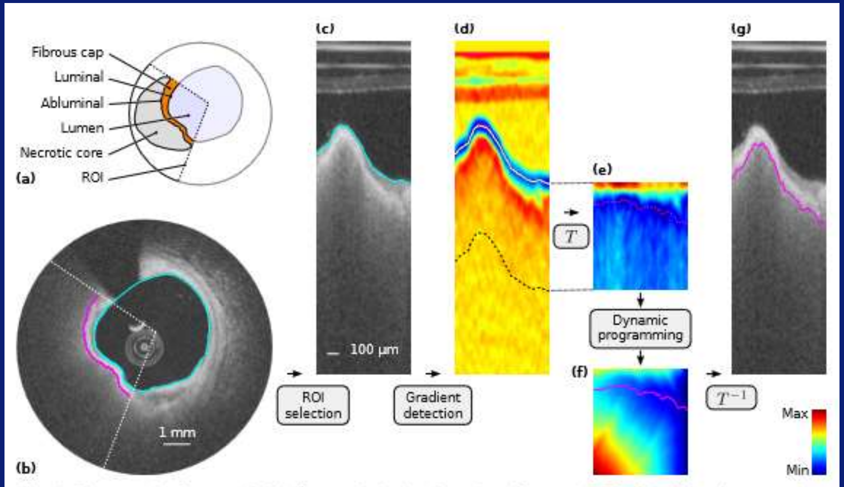
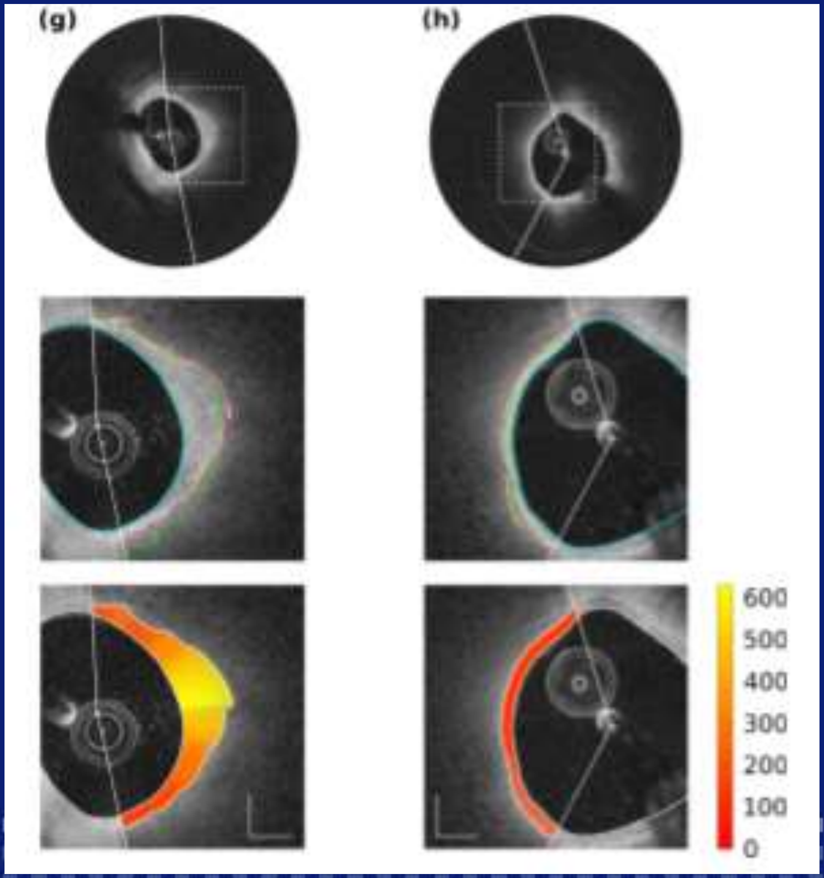


Fig. 1 Segmentation framework. (a) Cartoon depicting the region of interest (ROI, dashed lines) encompassing the fibrous cap. (b) OCT image of an *in vivo* human coronary artery, in Cartesian coordinates, with the resulting luminal (cyan line) and abluminal (magenta line) segmentation contours. (c) ROI in polar coordinates, with the luminal contour (cyan line). (d) Gradient image I_G. (e) Transformed cost image $\mathcal{C}_T$. (f) Cumulated cost $\mathbf{C}$, with the optimal path (magenta line). (g) Resulting abluminal segmentation contour.



Fully automated **segmentation of fibrous cap thickness**

Zahnd G et al. presented at MICCAI 2014

OCT Assessment of Vulnerability

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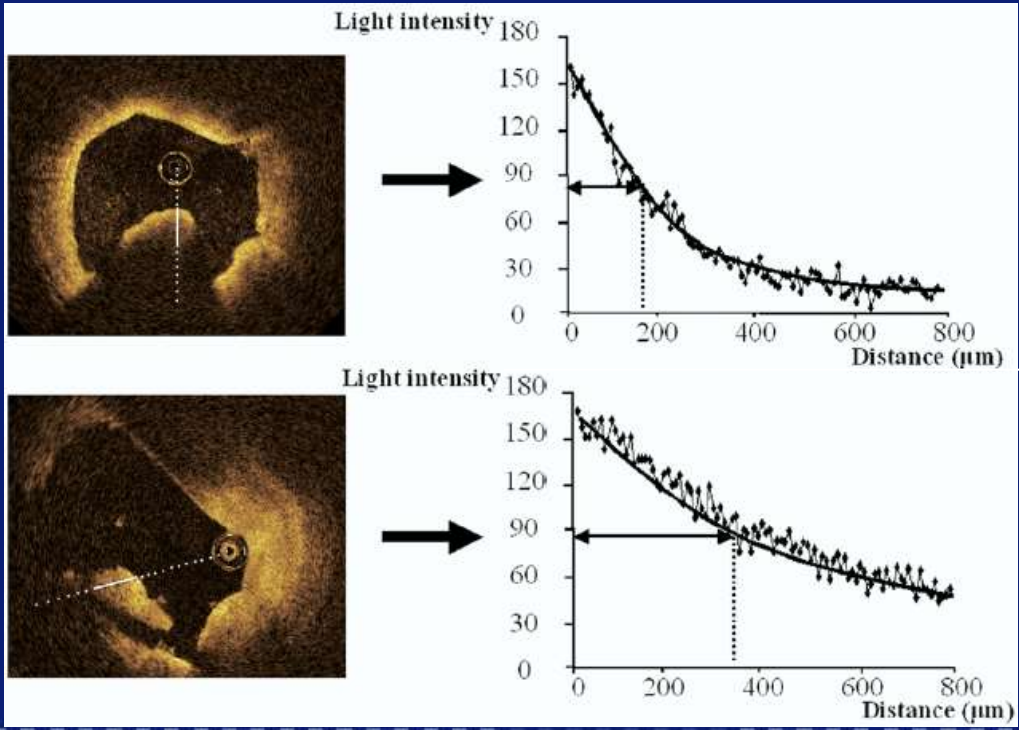
- OCT can visualize lipid rich-plaque.
- OCT can visualize a thin fibrous cap.
- **OCT can differentiate thrombus.**



Kume at al. Am J Cardiol 2006;97:1713–171

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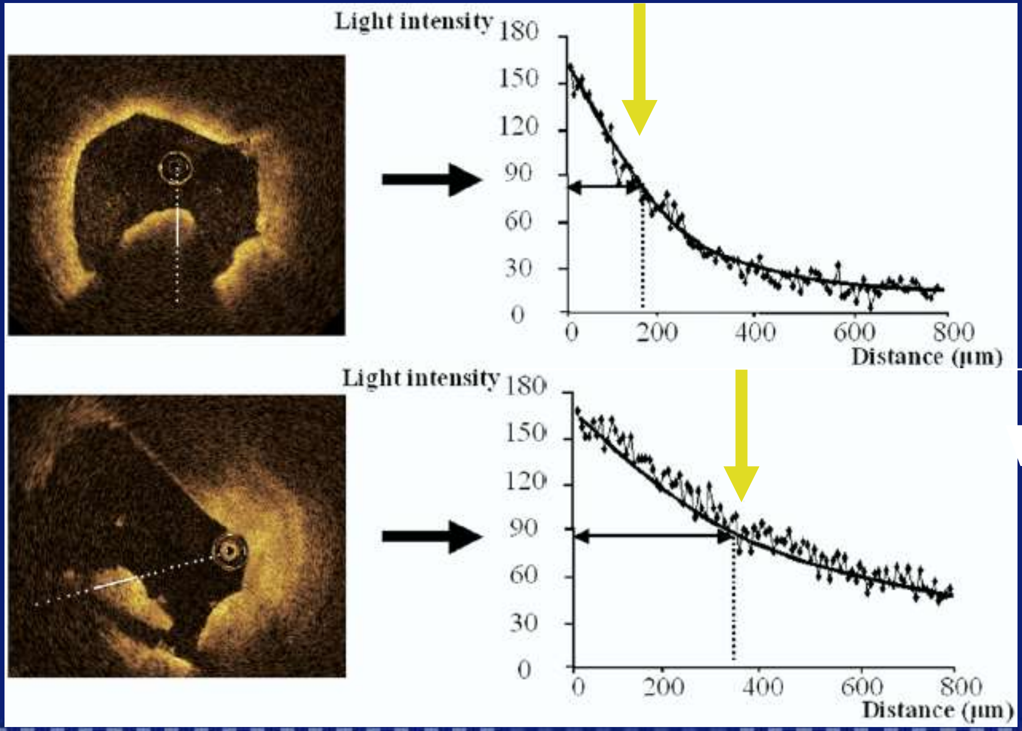

	peak intensity	½ width (μm)
red	130±18	183±42
white	145±34	324±50
P-value	0.12	0.0001

Ku Kume at al. Am J Cardiol 2006;97:1713–171

OCT Assessment of Vulnerability

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- OCT can visualize lipid rich-plaque.
- OCT can visualize a thin fibrous cap.
- OCT can differentiate thrombus.
- **OCT can diagnose thin cap fibroatheroma (TCFA)**

	TCFA (n=30)	Non-TCFA (n=47)	P value
IVUS findings			
Reference site			
EEM CSA, mm^2	14.7±6.2	12.6±3.9	0.064
Lumen CSA, mm^2	6.4±3.0	5.4±1.9	0.094
Plaque plus media CSA, mm^2	8.3±3.8	7.2±2.5	0.108
Lesion site			
EEM CSA, mm^2	15.3±6.1	13.4±4.2	0.110
Lumen CSA, mm^2	4.4±2.2	4.0±1.6	0.332
Plaque plus media CSA, mm^2	10.9±4.3	9.4±3.2	0.086
Plaque burden, %	71±7	70±7	0.636
Remodeling index	1.06±0.11	1.08±0.15	0.463
Positive remodeling, n (%)	15 (50%)	29 (62%)	0.157
OCT findings			
TCFA detected by OCT	27 (90%)		
Thickness of the fibrous cap, μm	46±32		

Kume at al.XXX 2009. In press.

OCT Assessment of Vulnerability

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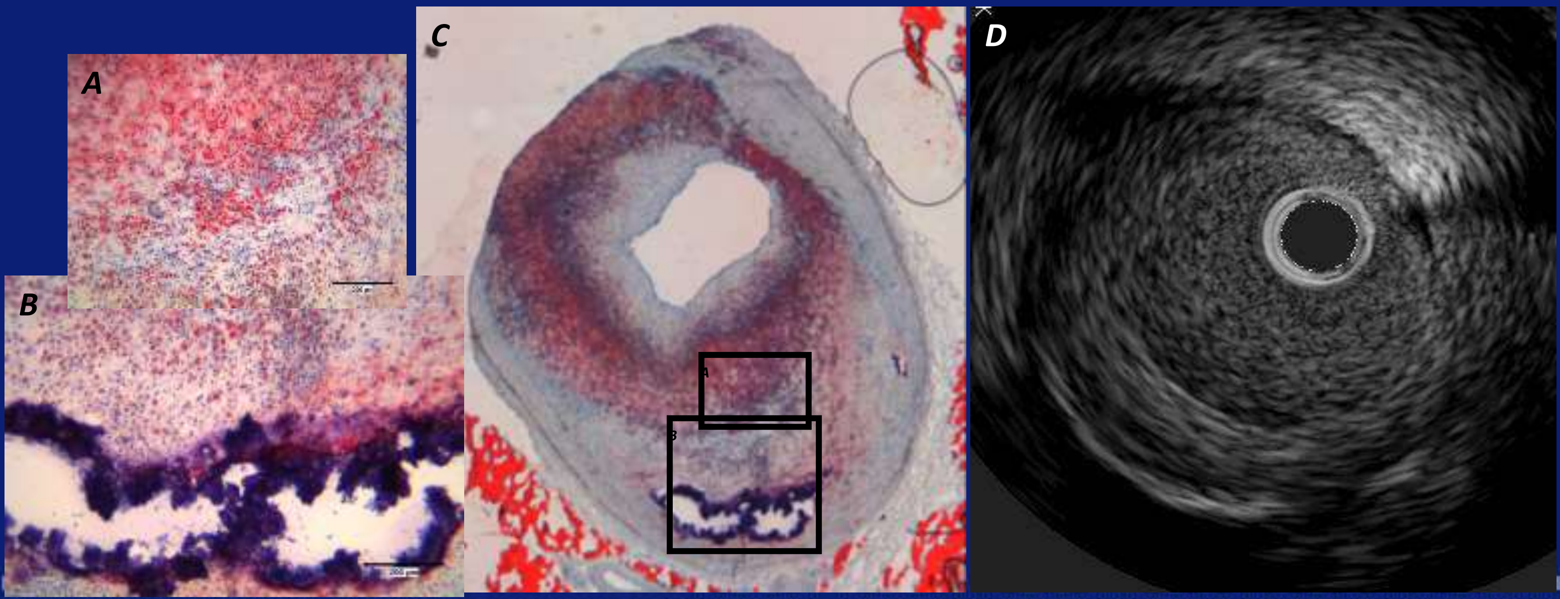
90%

Kume at al. 2009

OCT Assessment of Vulnerability

- *OCT can visualize lipid rich-plaque.*
- *OCT can visualize a thin fibrous cap.*
- *OCT can differentiate thrombus.*
- *OCT can diagnose thin cap fibroatheroma (TCFA)*
- ***OCT can visualize plaque changes over time***



Van Ditzhuijzen, Regar et al. Netherlands Heart J, 2011.

OCT Assessment of Vulnerability

Erasmus MC

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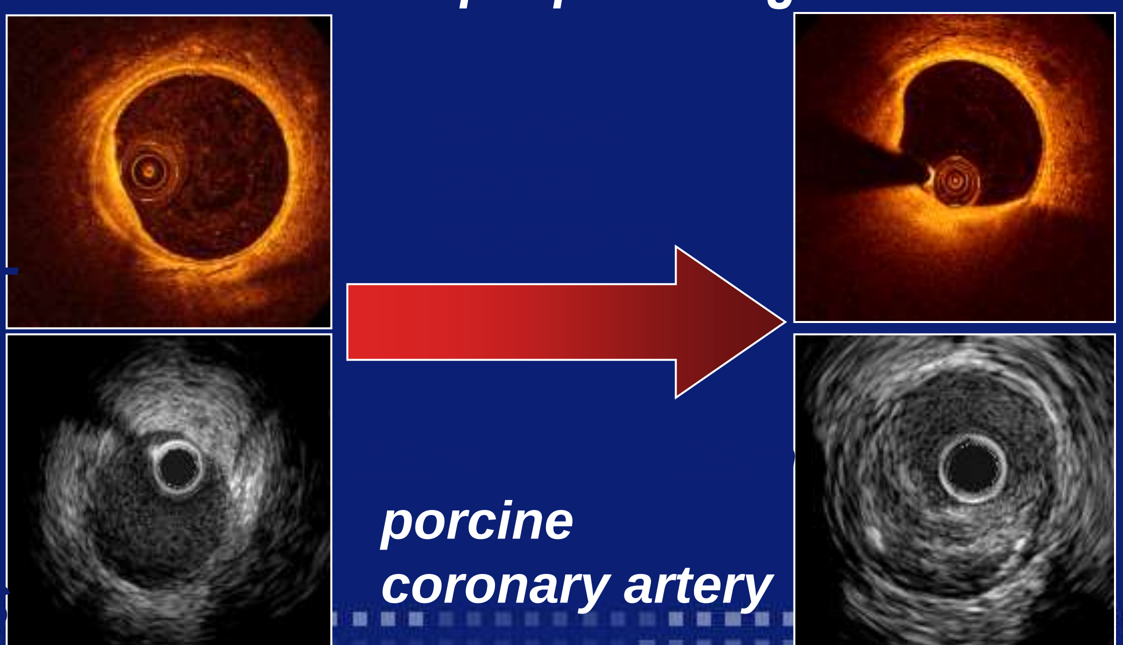


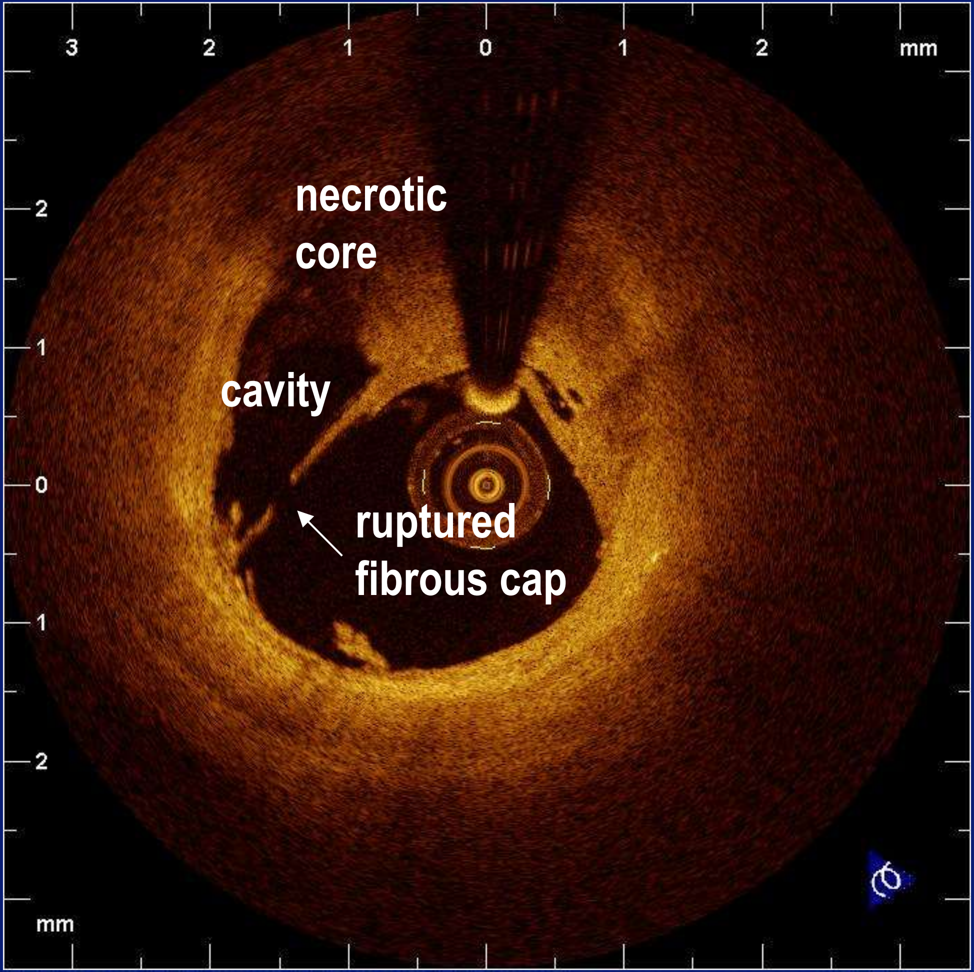
Van Ditzhuijzen, Regar et al. Netherlands Heart J, 2011.

OCT Assessment of Vulnerability

Erasmus MC

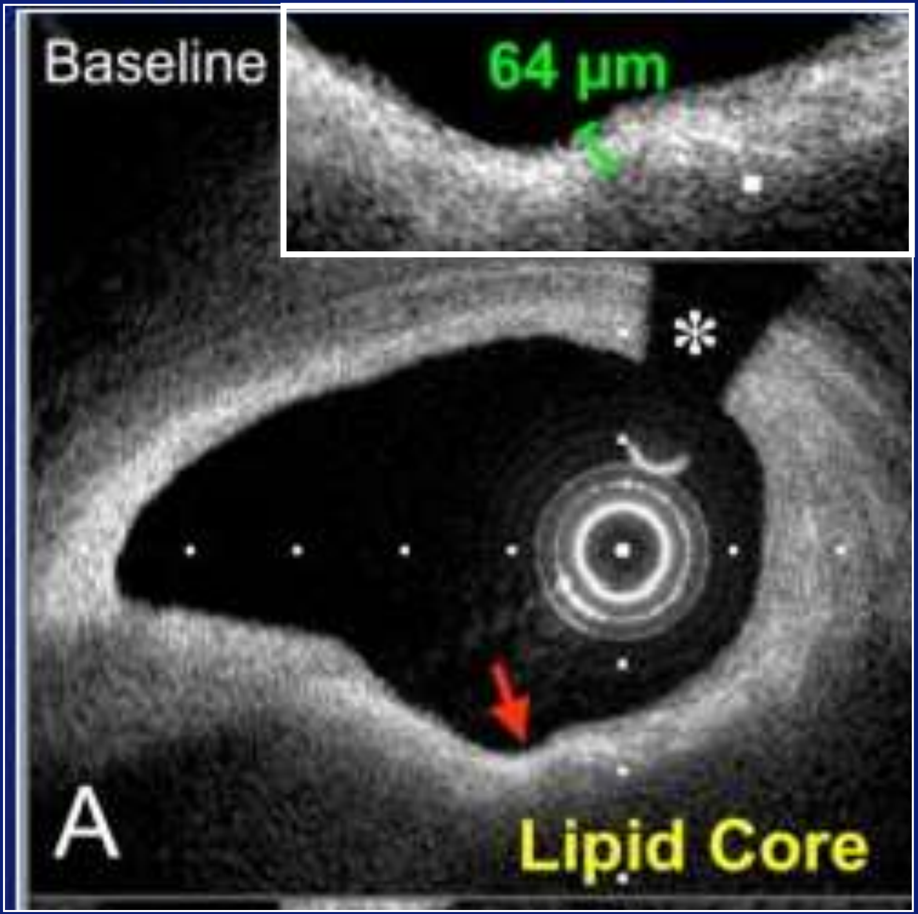
- *OCT can visualize lipid rich-plaque.*
- *OCT can visualize a thin fibrous cap.*
- *OCT can differentiate thrombus.*
- *OCT can diagnose thin cap fibroatheroma (TCFA)*
- *OCT can visualize plaque rupture & thrombosis in vivo*

Symptomatic Plaque Rupture: STEMI



Regar et al. Herz 2011

Asymptomatic Witnessed Plaque Rupture



Gonzalo, Regar et al. JACC Imaging. 2011

Asymptomatic Witnessed Plaque Rupture

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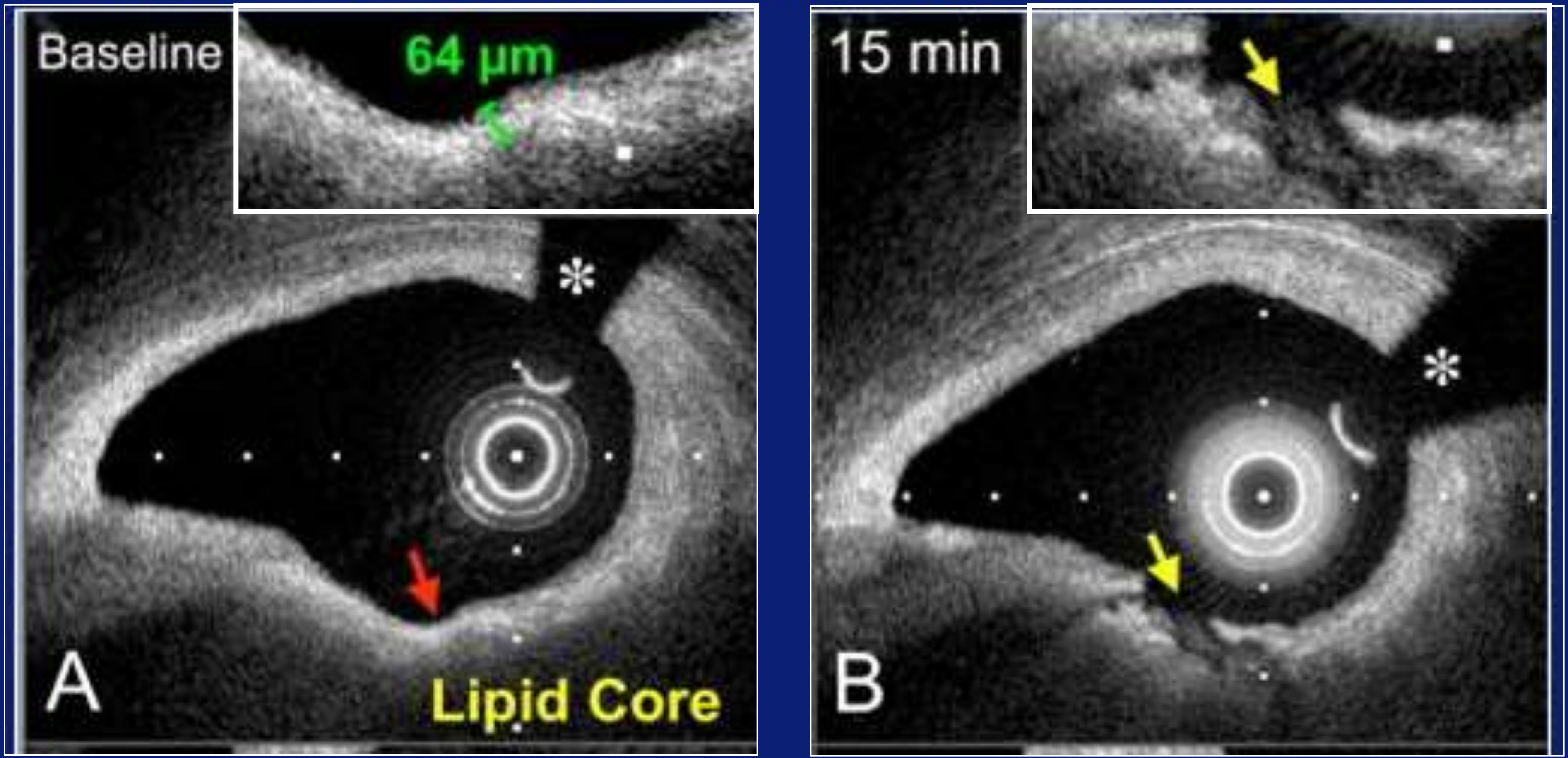
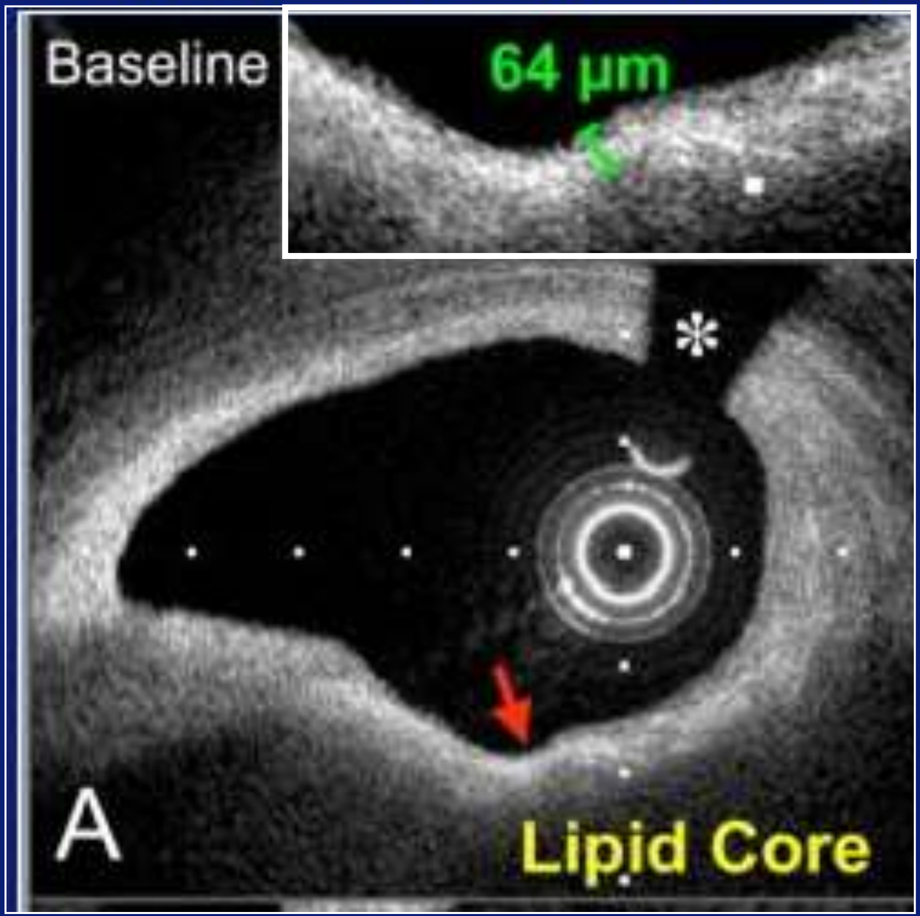
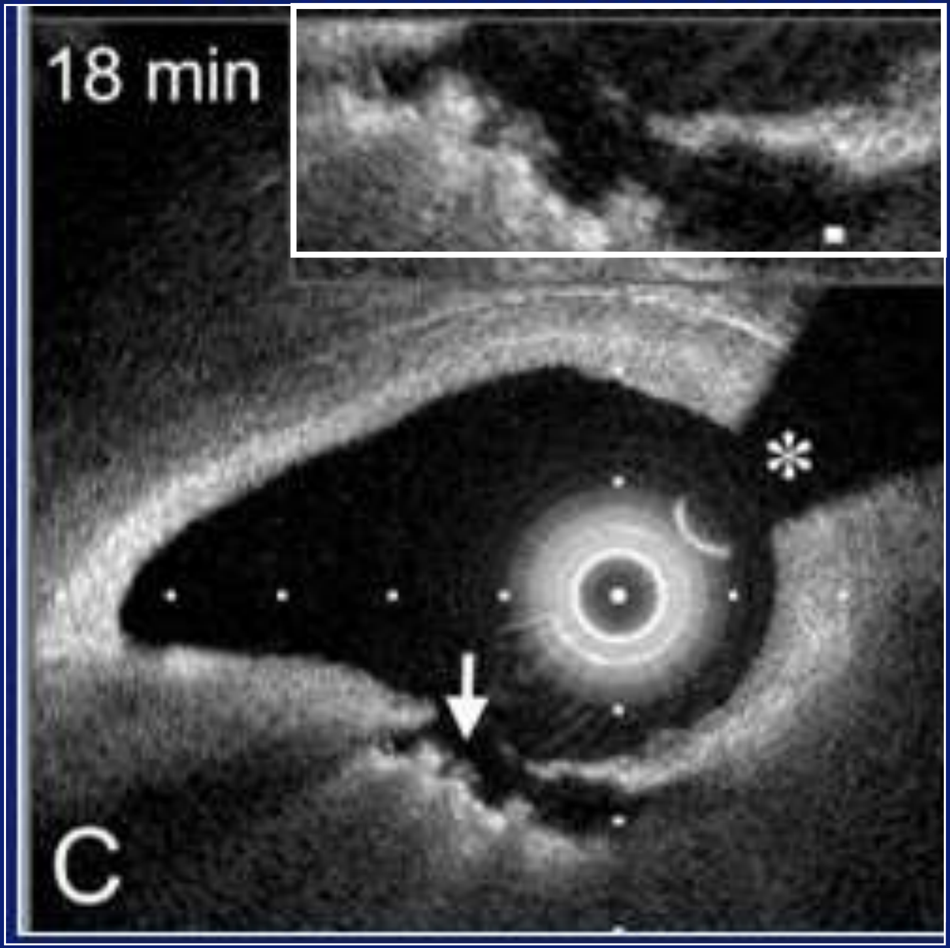


Plaque rupture

Gonzalo, Regar et al. JACC Imaging. 2011

Asymptomatic Witnessed Plaque Rupture

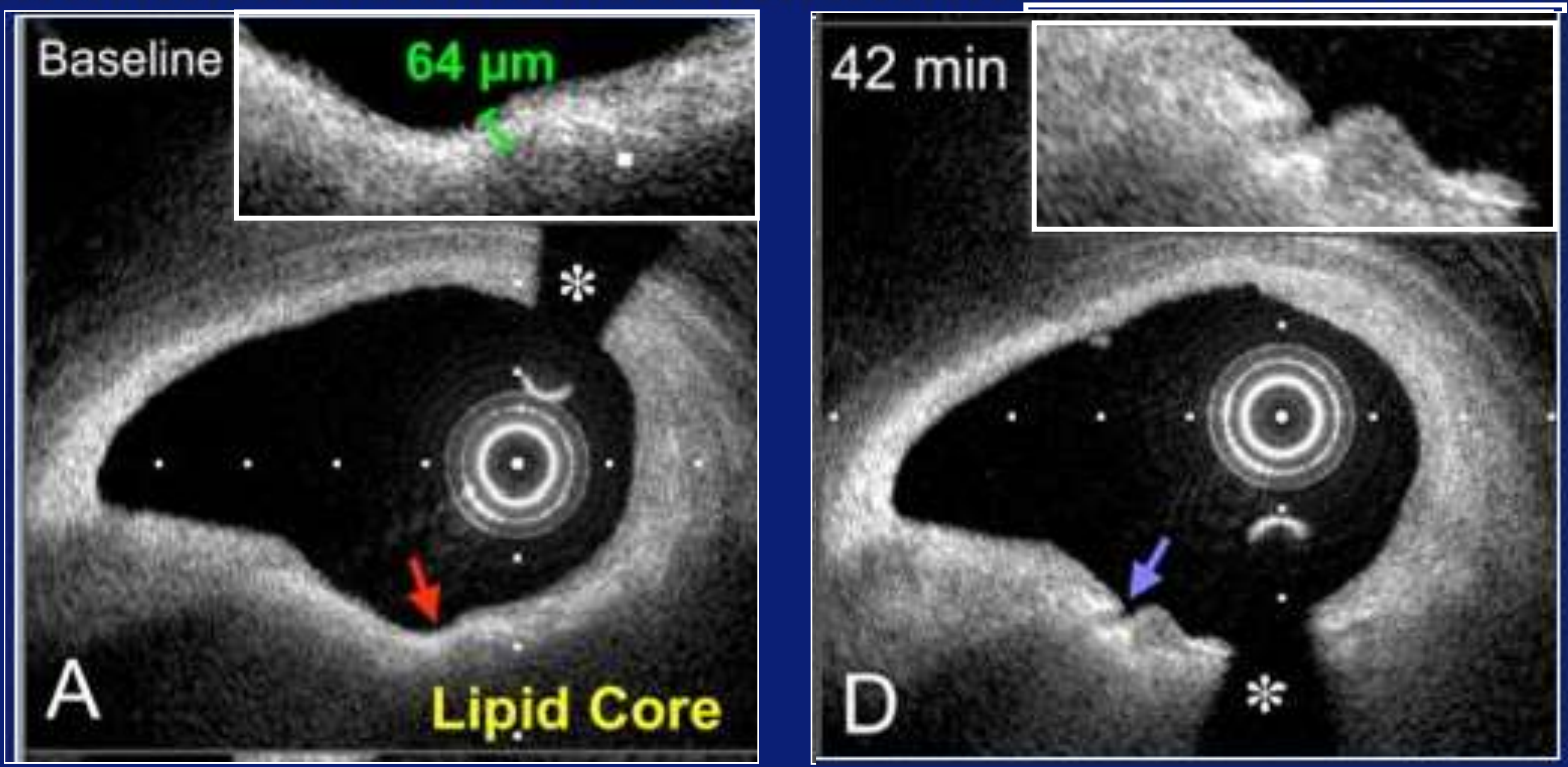




Empty cavity

Gonzalo, Regar et al. JACC Imaging. 2011

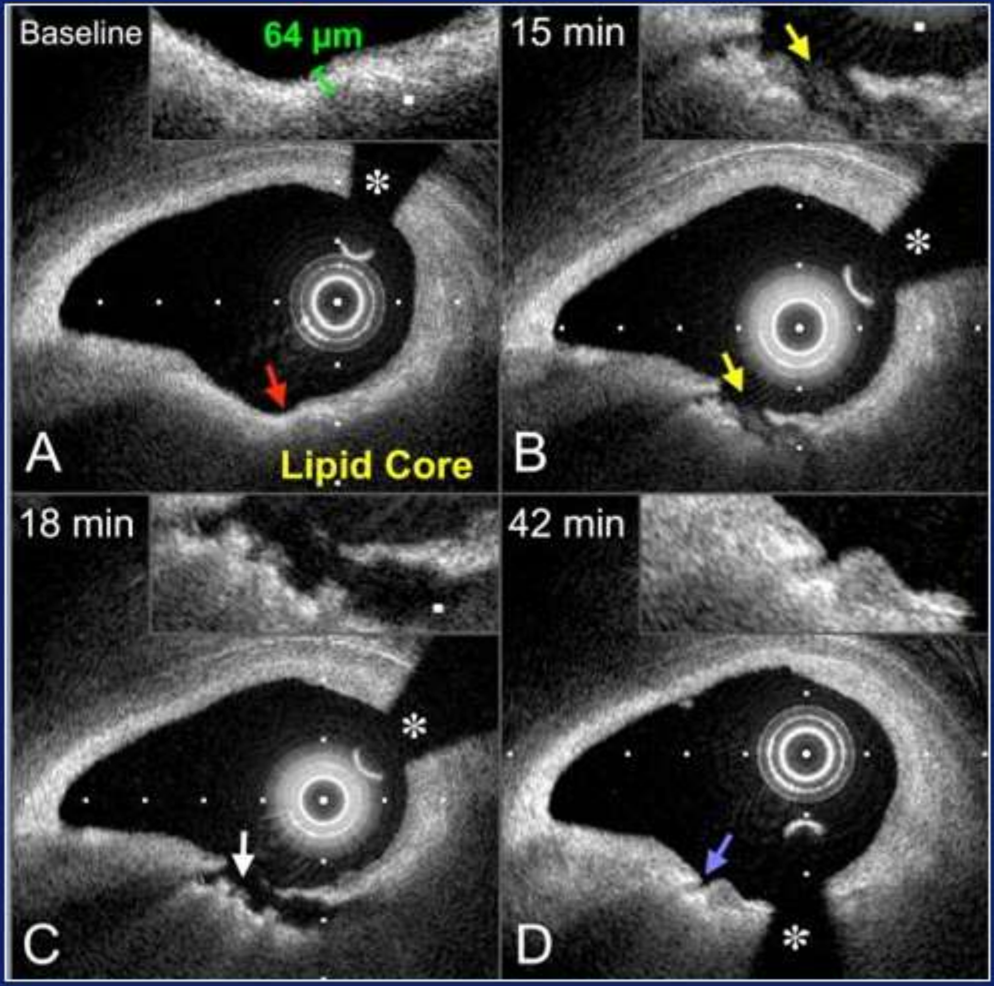
Asymptomatic Witnessed Plaque Rupture

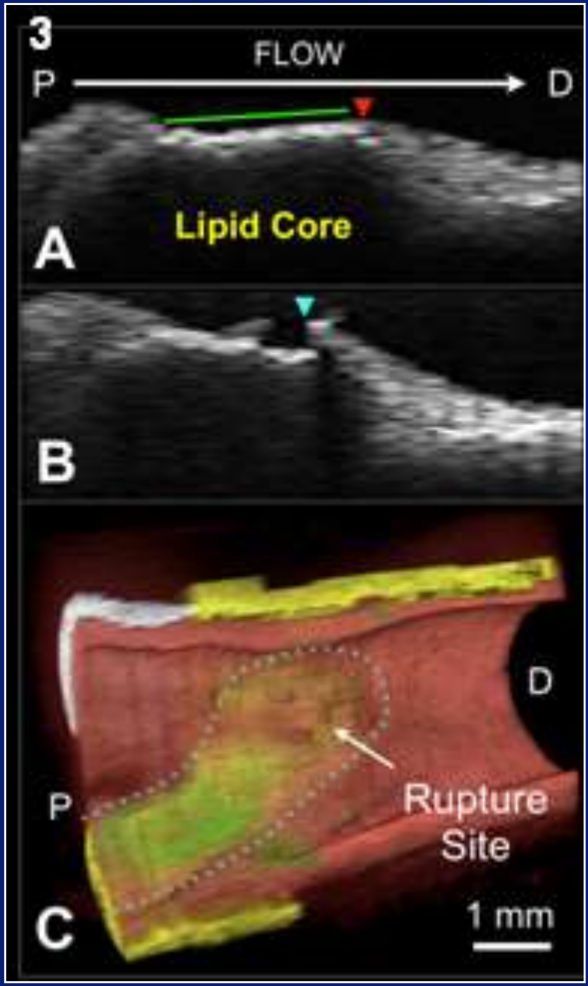


Thrombus, filling rupture defect

Gonzalo, Regar et al. JACC Imaging. 2011

Asymptomatic Witnessed Plaque Rupture





Gonzalo N et al. JACC Imaging 2011

Symptomatic Witnessed Plaque Rupture Periprocedural

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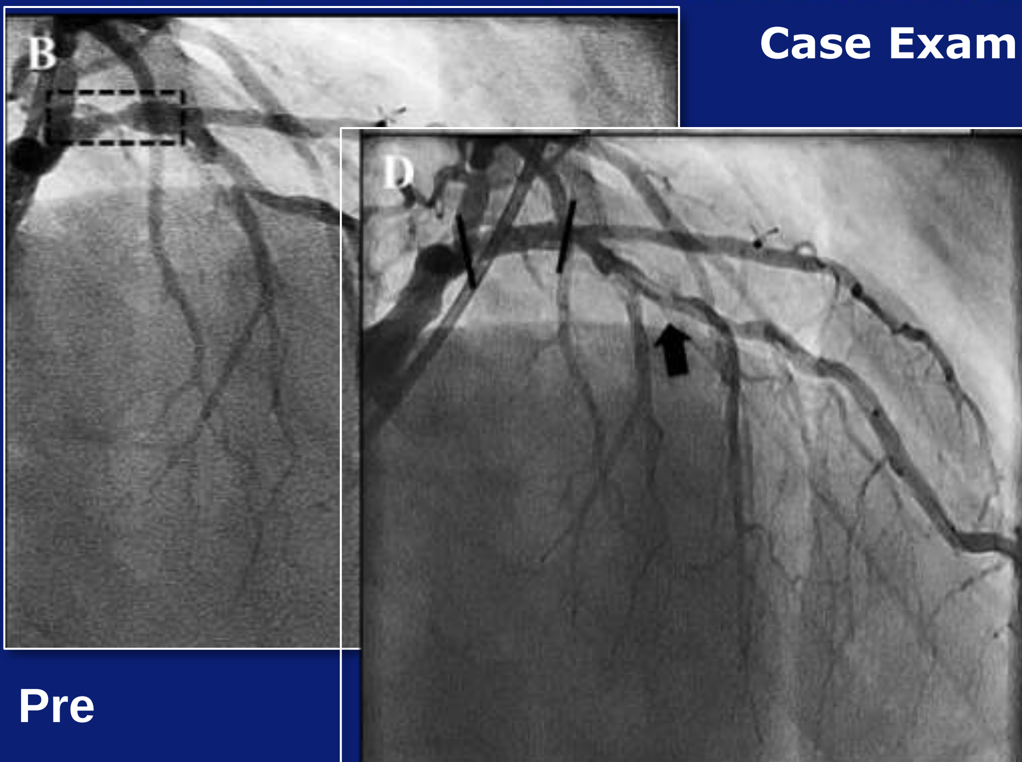
Case Example: 64y, male, stable angina CCS 3



Pre

Direct stenting
3.5mm/12mm;18atm

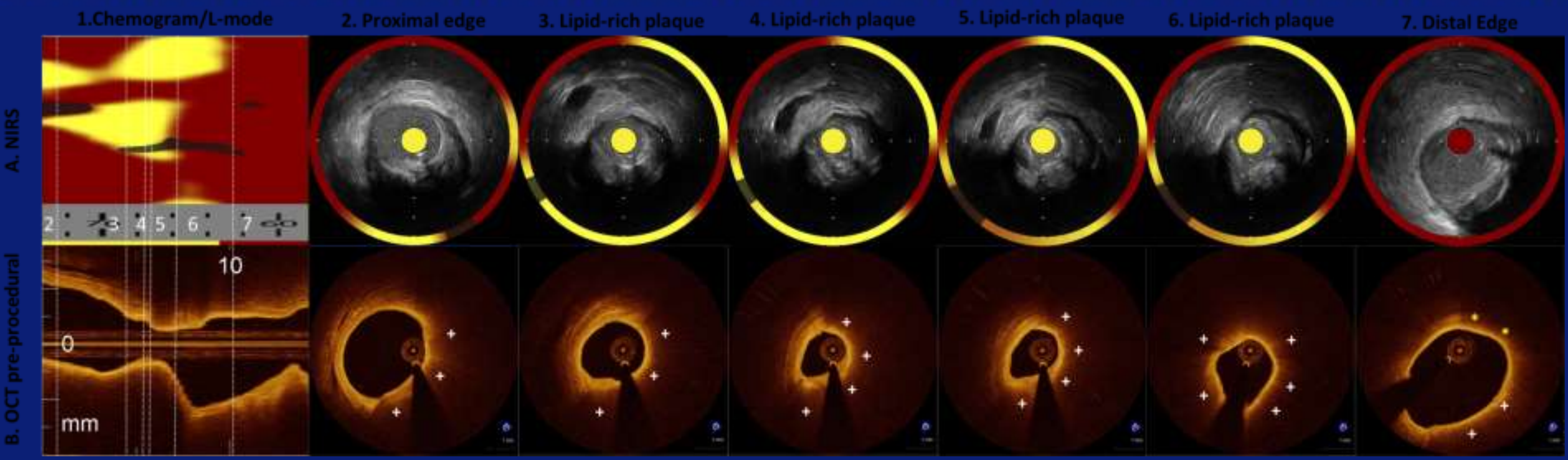
Vasospasm, haziness, slow flow

Postdilation
4.0mm/8mm;18atm

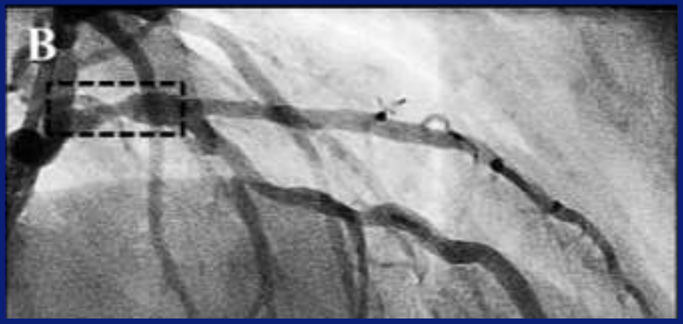
Post PCI: Troponin *53ng/L*

(ULN: 13ng/L)

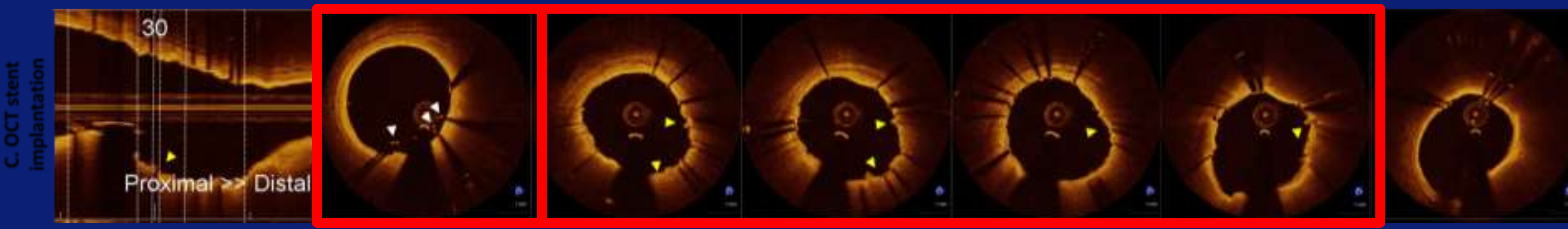
Symptomatic Witnessed Plaque Rupture Periprocedural



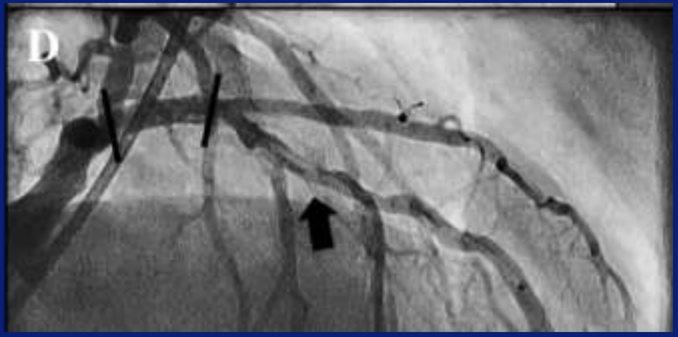
Pre-intervention imaging: lipid-rich culprit lesion



Symptomatic Witnessed Plaque Rupture Periprocedural

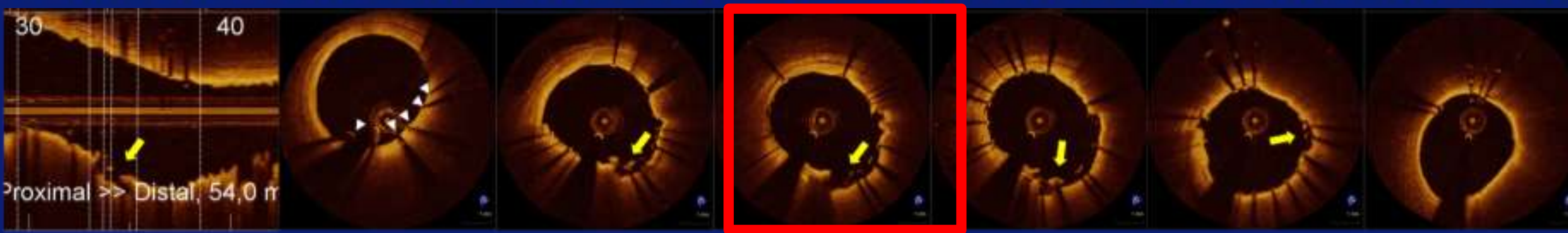


Post stent: Strut malapposition proximal
Tissue protrusion within stent

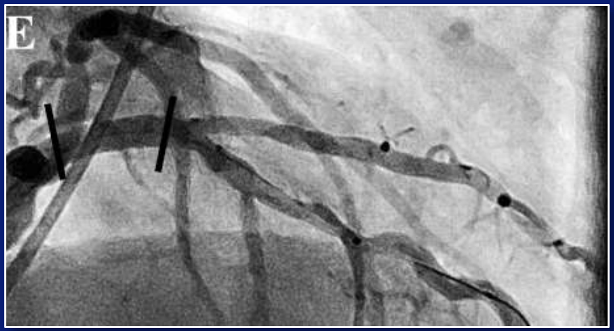


Symptomatic Witnessed Plaque Rupture Periprocedural

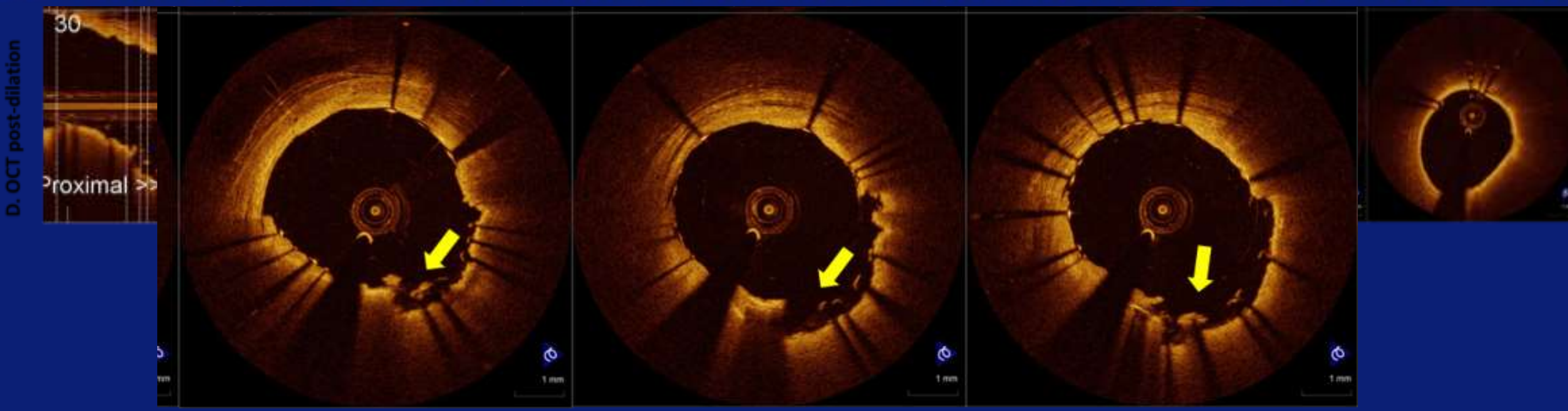
D. OCT post-dilation



Postdilation: Disruption of lipid-rich plaque



Symptomatic Witnessed Plaque Rupture Periprocedural



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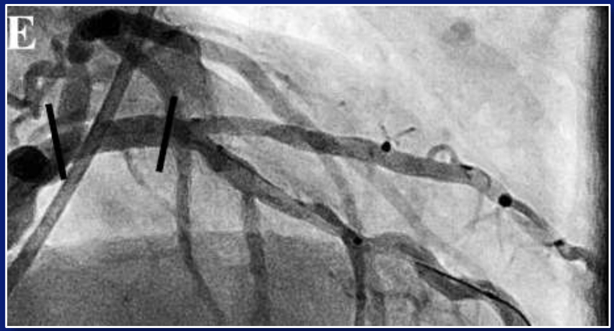

Symptomatic Witnessed Plaque Rupture Periprocedural

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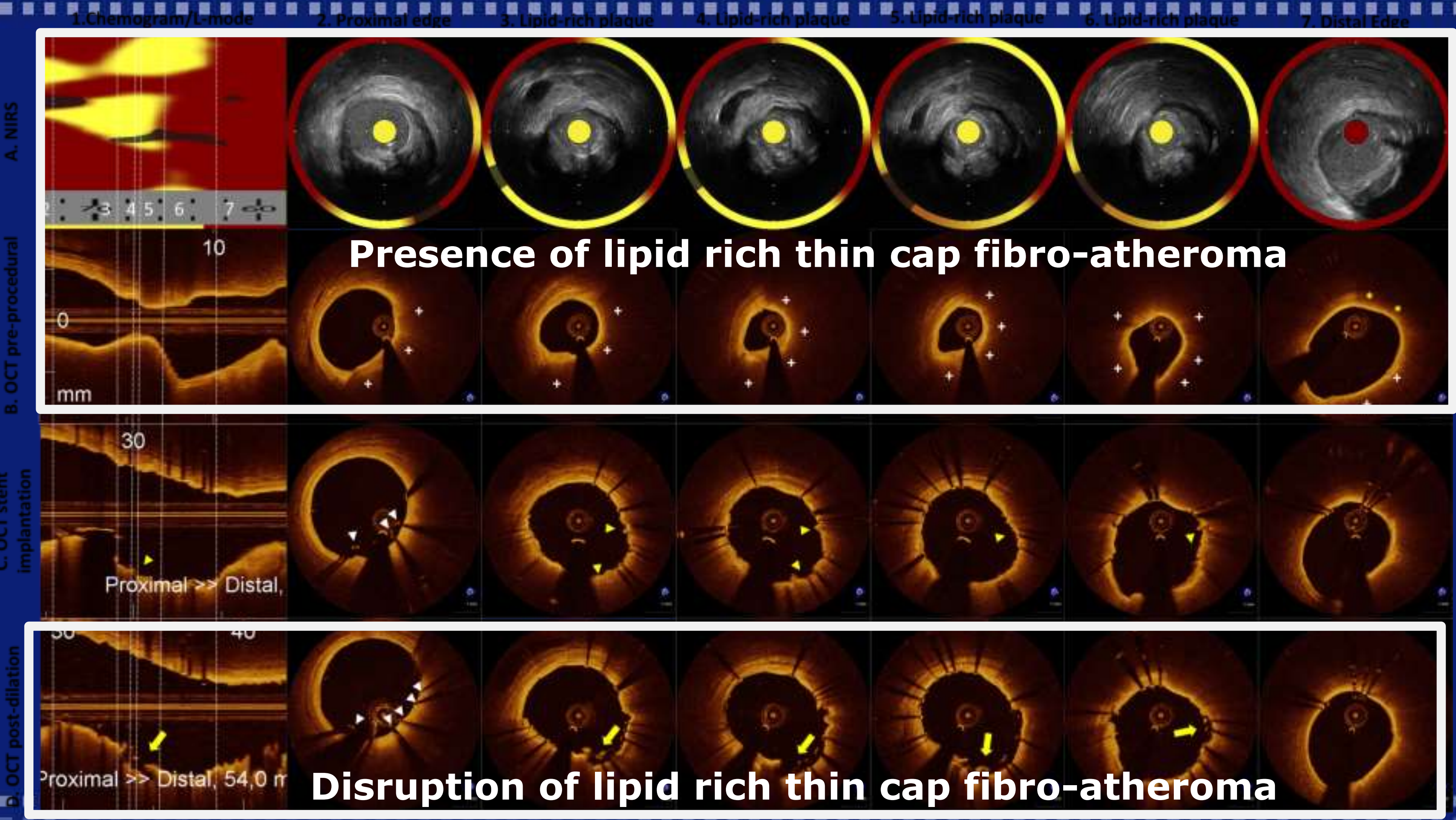

OCT Assessment of Vulnerability

Plaque Prone to Rupture

Inflamed, thin-cap fibroatheroma (TCFA)

- ✓ Lipid-rich, atheromatous core
- ✓ Thin fibrous cap, with
- ✓ Macrophage and lymphocyte infiltration

OCT Assessment of Vulnerability

- **OCT can visualize the pathologic substrate in patients**

OCT Assessment of Vulnerability

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- OCT can visualize the pathologic substrate in patients
- Standardization of nomenclature & definitions of IV OCT findings

Consensus Standards for Acquisition, Measurement, and Reporting of Intravascular Optical Coherence Tomography Studies

A Report From the International Working Group for Intravascular Optical Coherence Tomography Standardization and Validation

Guillermo J. Tearney, MD, PHD, *Writing Committee Co-Chair,**
Evelyn Regar, MD, PHD, *Writing Committee Co-Chair,*† Takashi Akasaka, MD, *Writing Committee Co-Chair,*‡
Tom Adriaenssens, MD, Peter Barlis, MD, Hiram G. Bezerra, MD, Brett Bouma, PHD,
Nico Bruining, PHD, Jin-man Cho, MD, PHD, Saqib Chowdhary, PHD, Marco A. Costa, MD, PHD,
Ranil de Silva, MD, PHD, Jouke Dijkstra, PHD, Carlo Di Mario, MD, PHD, Darius Dudeck, MD, PHD,
Erlin Falk, MD, PHD, Marc D. Feldman, MD, Peter Fitzgerald, MD, Hector Garcia, MD,
Nieves Gonzalo, MD, Juan F. Granada, MD, Giulio Guagliumi, MD, Niels R. Holm, MD,
Yasuhiro Honda, MD, Fumiaki Ikeno, MD, Masanori Kawasaki, MD, Janusz Kochman, MD, PHD,
Lukasz Koltowski, MD, Takashi Kubo, MD, PHD, Teruyoshi Kume, MD, Hiroyuki Kyono, MD,
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Akiko Maehara, MD, Olivia Manfrini, MD, Gary S. Mintz, MD, Kyiouchi Mizuno, MD,
Marie-angèle Morel, MD, Seemantini Nadkarni, PHD, Hiroyuki Okura, MD, Hiromasa Otake, MD,
Arkadiusz Pietrasik, MD, Francesco Prati, MD, Lorenz Räber, MD, Maria D. Radu, MD,
Johannes Rieber, MD, Maria Riga, MD, Andrew Rollins, PHD, Mireille Rosenberg, PHD, Vasile Sirbu, MD,
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Eliot Siegel, MD, Shinjo Sonada, MD, Melissa Suter, PHD, Shigeho Takarada, MD, PHD,
Atsushi Tanaka, MD, PHD, Mitsuyasu Terashima, MD, Thim Troels, MD, PHD, Shiro Uemura, MD, PHD,
Giovanni J. Ughi, PHD, Heleen M.M. van Beusekom, PHD, Antonius F.W. van der Steen, PHD,
Gerrit-Ann van Es, PHD, Gijs van Soest, PHD, Renu Virmani, MD, Sergio Waxman, MD,
Neil J. Weissman, MD, Giora Weisz, MD

Boston, Massachusetts; Rotterdam, the Netherlands; and Wakayama, Japan

J Am Coll Cardiol 2012; 59(12):1058–72

OCT Assessment of Vulnerability
Standardization of Nomenclature & Definitions

Fibroatheroma (A)

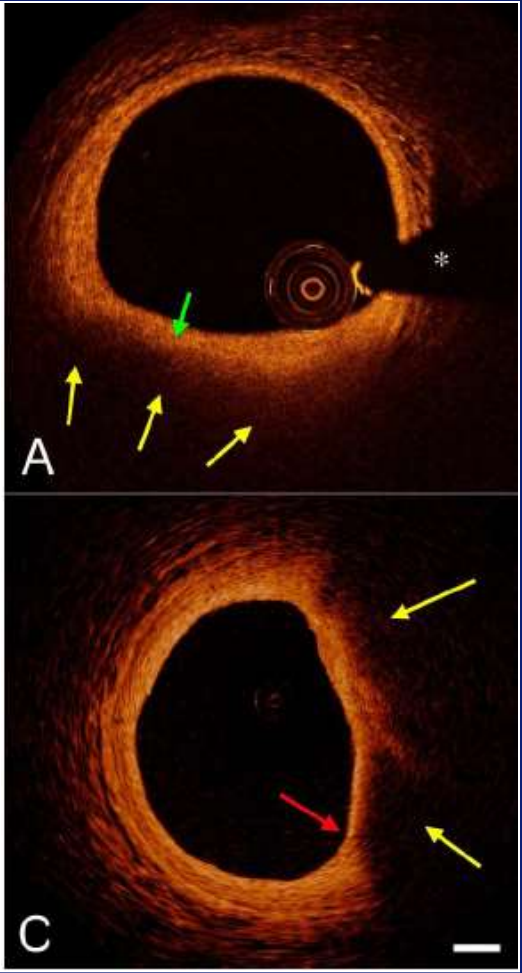
lesion with an OCT-delineated fibrous cap and a lipid pool

OCT thin cap fibroatheroma (C)

an OCT-delineated necrotic core with an overlying fibrous cap where the min. thickness is less than a predetermined threshold

Fibrous cap

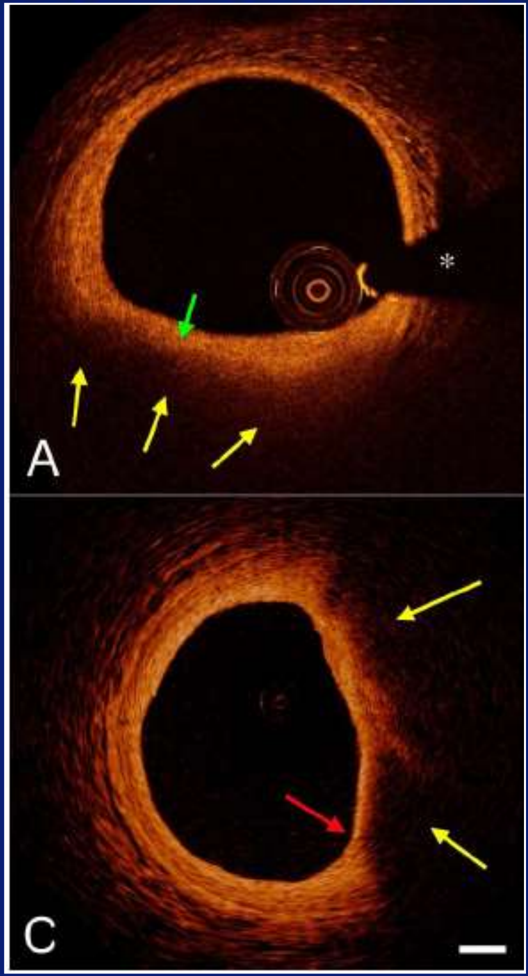
is a tissue layer, which is often signal-rich, overlying a lipid pool, necrotic core, or calcium.



International Working Group on OCT Standardization and Validation; JACC. 2012

OCT Assessment of Vulnerability

Is this good enough?



OCT Pifalls

Moderate positive predictive value!

Accuracy of OCT, Grayscale IVUS, and Their Combination for the Diagnosis of Coronary TCFA

An Ex Vivo Validation Study

Kenichi Fujii, MD,* Hiroyuki Hao, MD,† Masahiko Shibuya, MD,* Takahiro Imanaka, MD,* Masashi Fukunaga, MD,* Kojiro Miki, MD,* Hiroto Tamaru, MD,* Hisashi Sawada, MD,* Yoshiro Naito, MD,* Mitsumasa Ohyanagi, MD,‡ Seiichi Hirota, MD,† Tohru Masuyama, MD*

Fuji K et al. JACC Cardiovasc Img 2015 Apr;8(4):451-60

OCT Pifalls

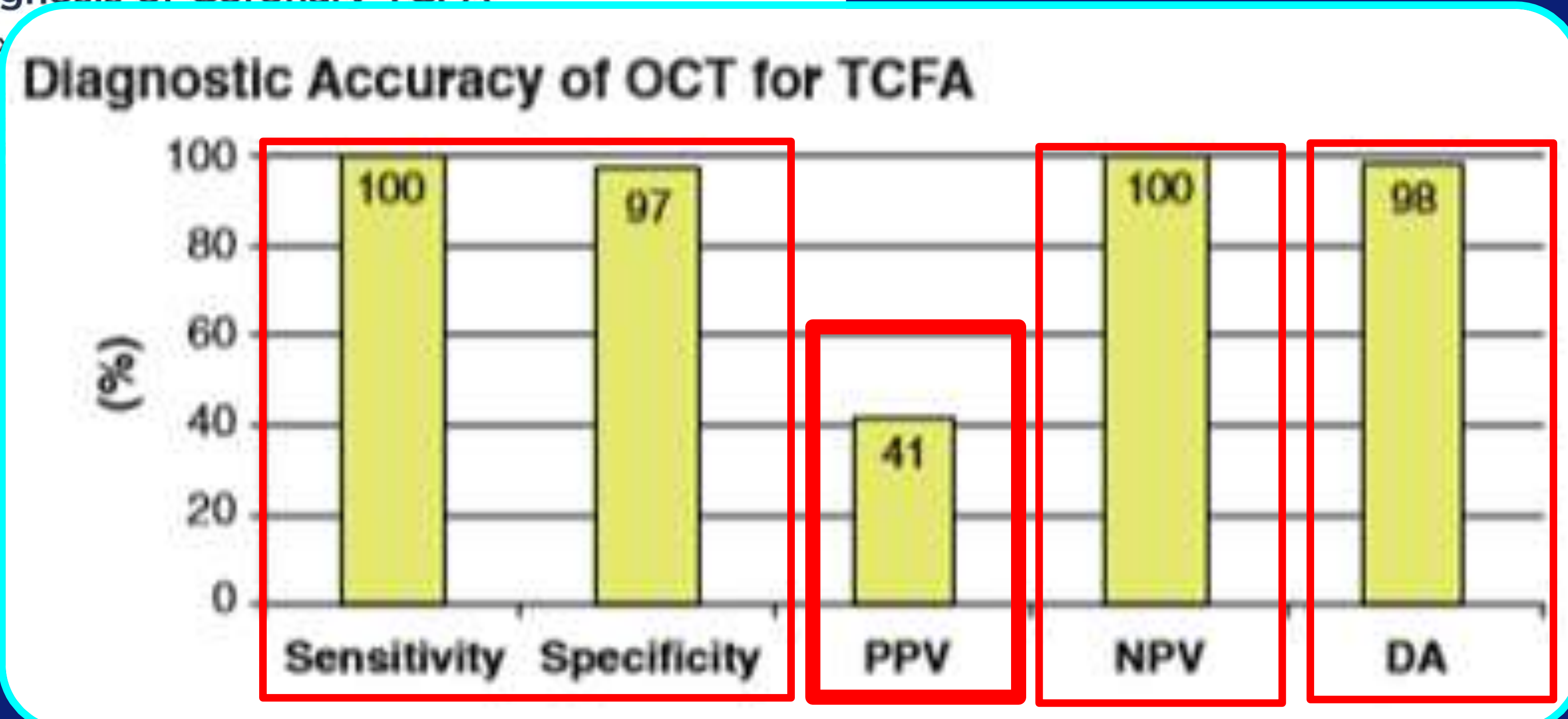
Moderate positive predictive value!

Erasmus MC

Accuracy of OCT, Grayscale IVUS, and Their Combination for the Diagnosis of Coronary TCFA

An E[...]

Kenichi [...]
Kojiro M[...]
Seiichi H[...]



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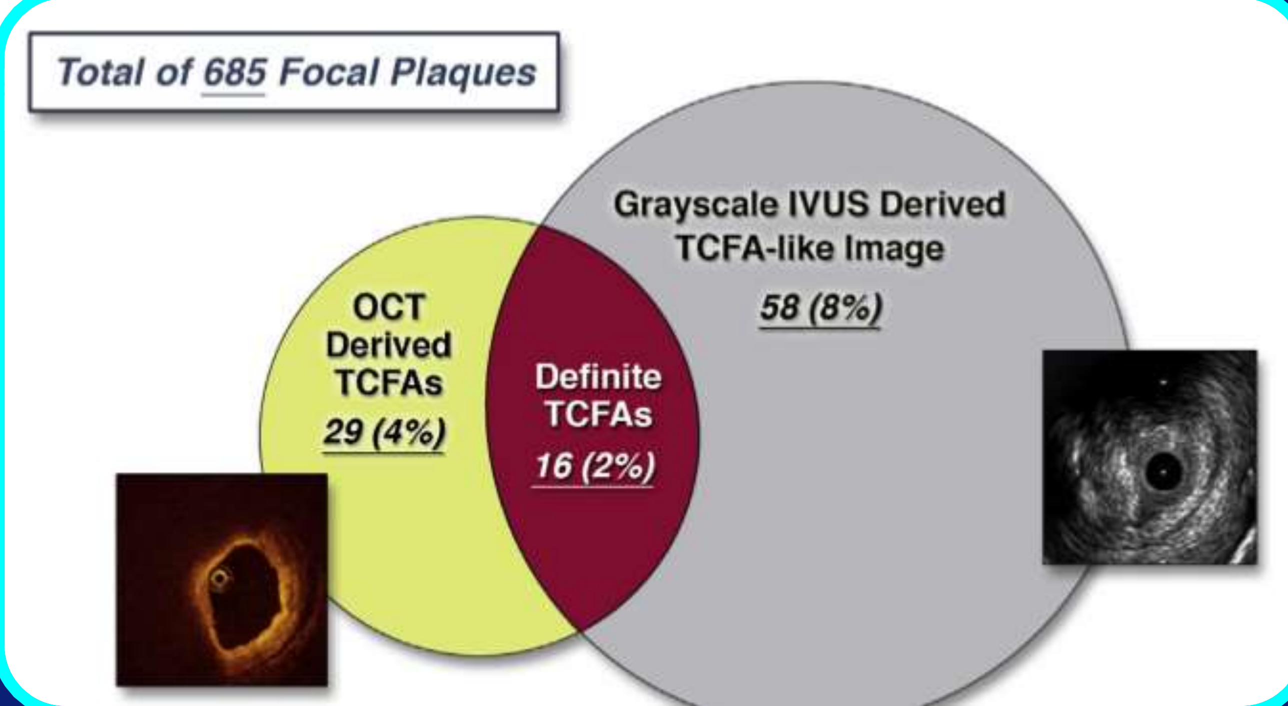


Fuji K et al. JACC Cardiovasc Img 2015 Apr;8(4):451-60

OCT Pitfalls

OCT TCFA - Comparison to Histologic Classification

OCT	**Fibrous tissue area**		
	Thick *160-910 µm*	**Medium-thin** *90-140 µm*	**Thin** *30-60 µm*
	38	**9**	**13**
Histo	*25 Thick fibrous cap* *8 Fibro-calcific* *5 Fibrous*		*11 Thin fibrous cap* *11 Fibro-calcific*

to 2 main limitations of OCT imaging. First, the penetration depth of OCT is limited to 1 to 2 mm, which does not allow the accurate detection of signal-poor areas possibly representing lipid pools or calcium behind fibrous tissue. This may generate false-positive fibrous plaques, false-negative fibrocalcific plaques, and false-negative thick-cap fibroatheromas. Second, OCT analysis often confuses the presence of lipid pools with that of calcium deposits, or vice versa. As

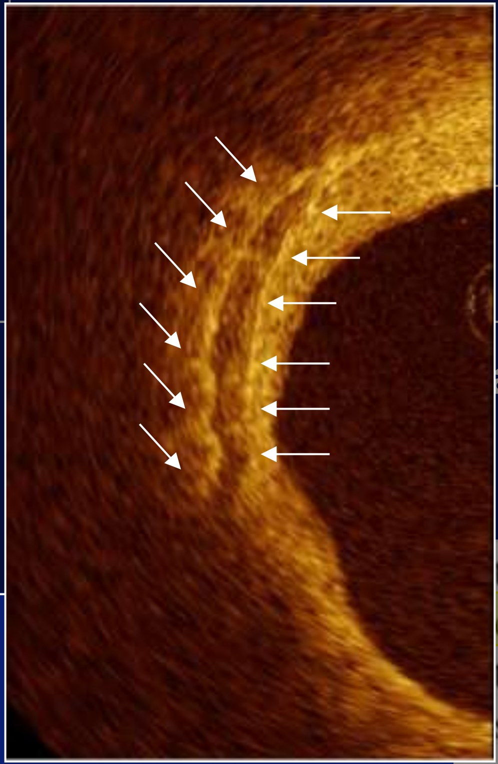
Manfrini et al: Am J Cardiol 2006;98:156-159)

OCT Pitfalls

Confusion of Lipid with Calcium

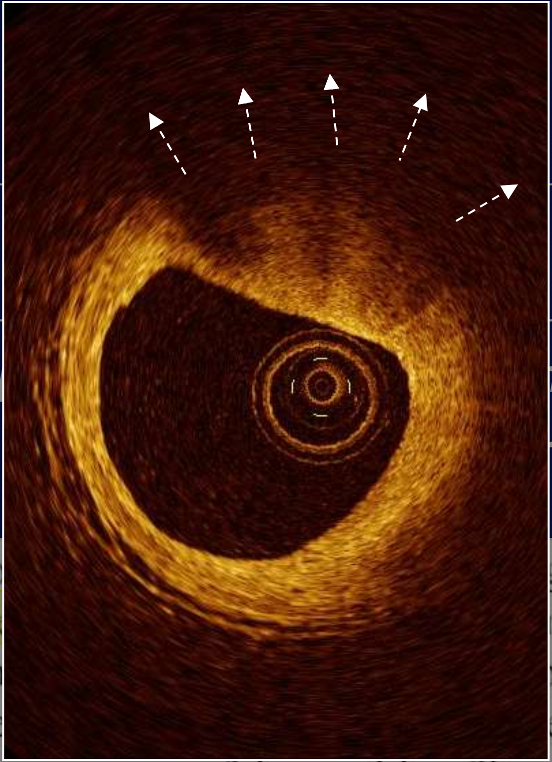
OCT		Thin *30-60 µm*
		13
Histo		...n fibrous cap ...o-calcific

Calcified lesion



Sharply delineated borders

Lipid-rich lesion



Diffuse borders

...ging. First, the penetration
...mm, which does not allow
...poor areas possibly repre-
...ehind fibrous tissue. This
...us plaques, false-negative
...gative thick-cap fibroathe-
romas. Second, OCT analysis often confuses the presence of
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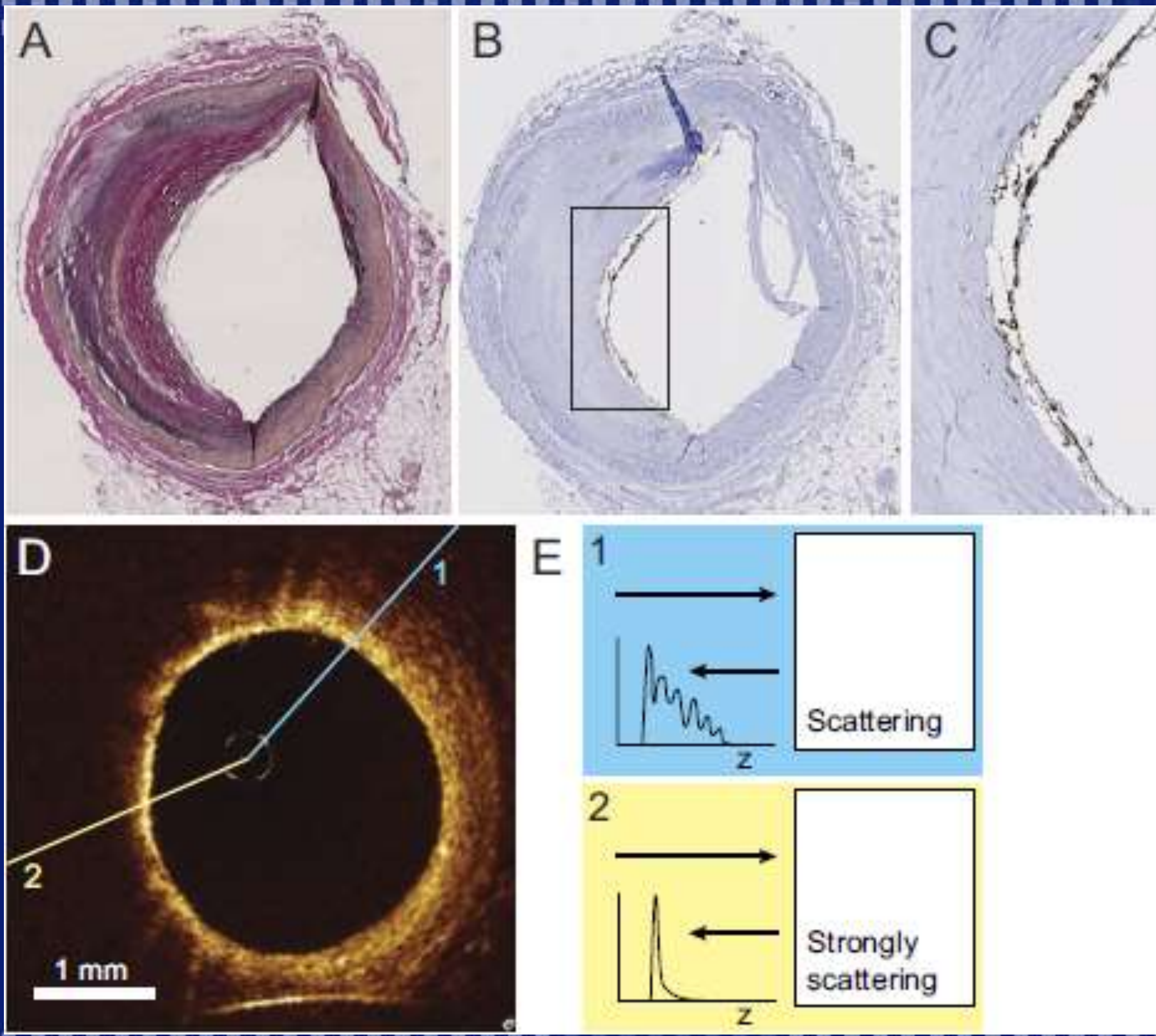
clinical examples

OCT Pitfalls

Artefacts: Macrophage scattering



The region of thickened intima appears as a TCFA

due to strong scattering & shadowing by macrophages.

OCT Pifalls

Artefacts cause misclassification!

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Incidence of artefacts in clinical setting

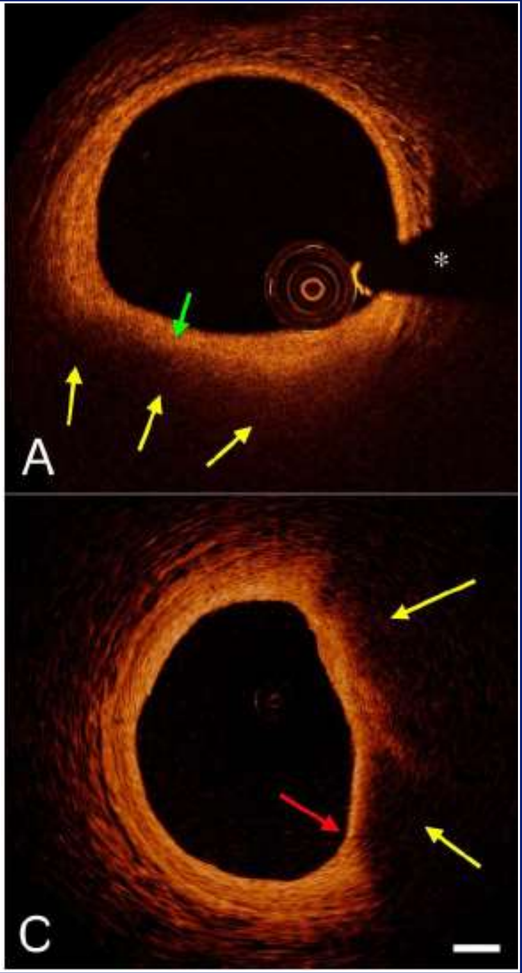
Category	# observations		
	Pullbacks	*Sections*	*Frames*
	Total 37		*Total 4597*
1: Superficial attenuation	16	26	94
2: Tangential signal dropout	15	27	145
3: Catheter shadowing	12	21	35
4: Axial PSF tail	0	0	0
5: Proximity brightening	12	17	313

Van Soest G et al, J Biomed Opt 2010

OCT Assessment of Vulnerability

Erasmus MC

Can we predict rupture?

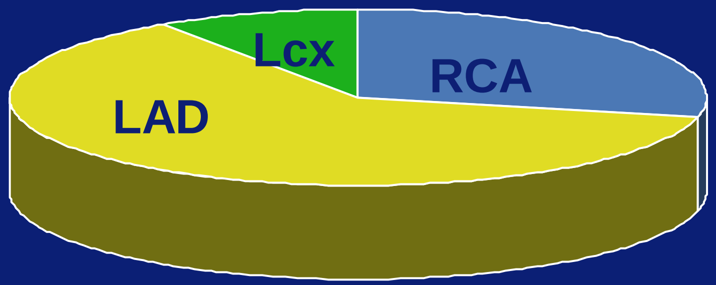


In-Vivo Fibrous Cap Detection Pilot: Patient Characteristics

n= 23 patients

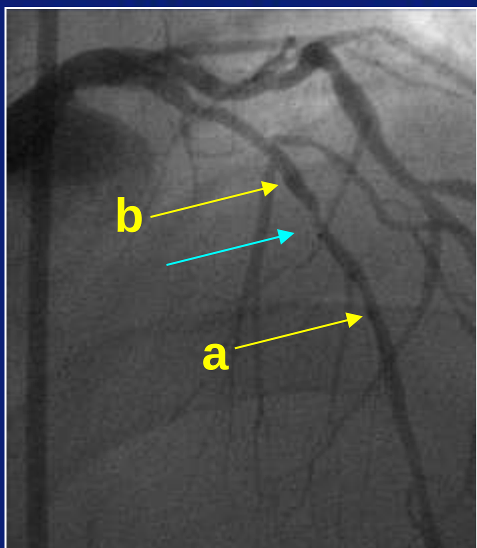
Age (yrs)	61±11
Male	18
Clinical presentation	
Silent ischemia	1
Stable angina	18
Unstable angina	4
Extent of CAD	
1 VD	14
2 VD	5
3 VD	4
Previous MI	6
Hypertension	13
Dyslipidemia	11
Current smoker	5
IDDM	2
Pos. family history	6

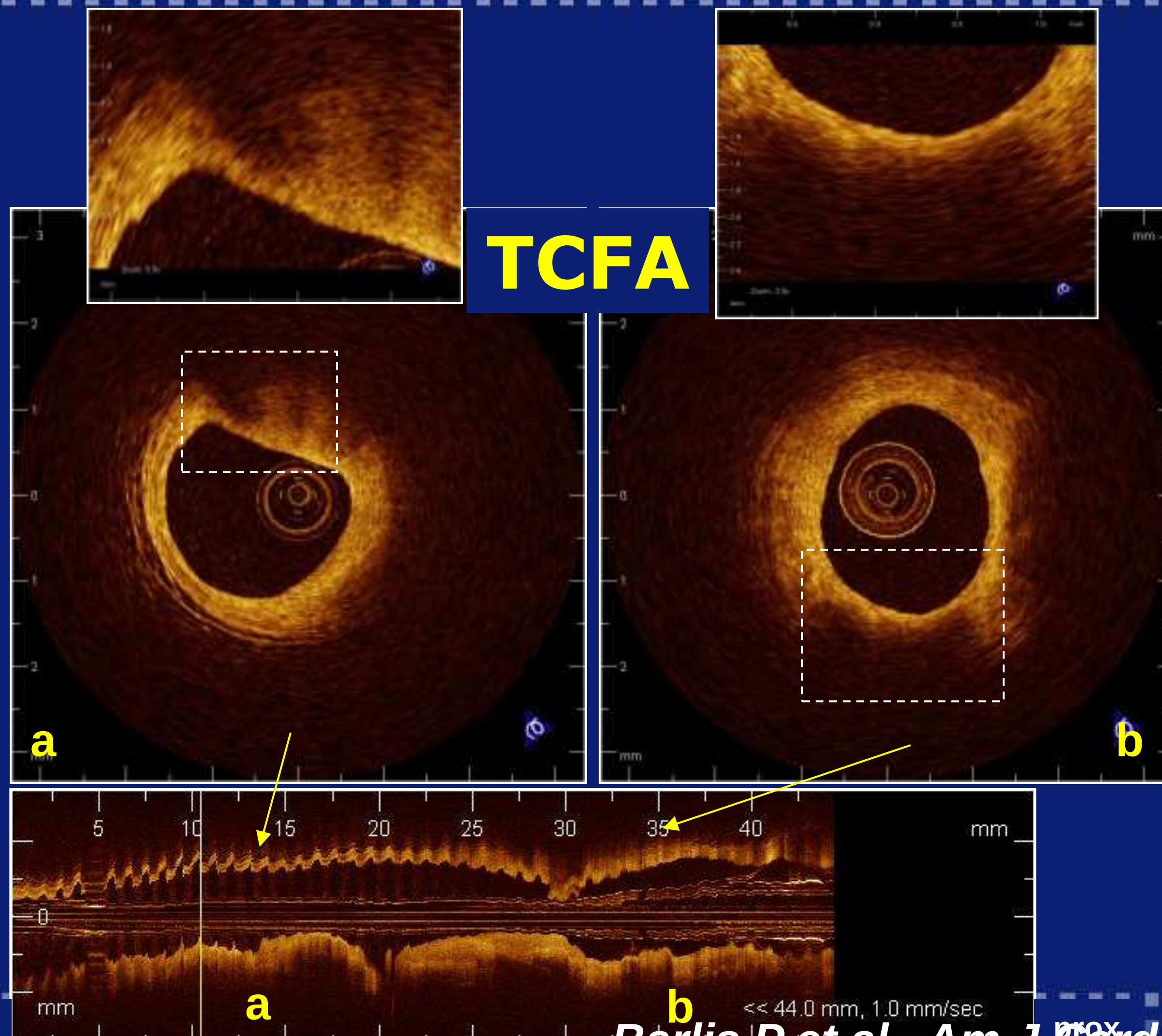
Target Vessel (%)



Barlis P et al . Am J Cardiol. 2008

In-Vivo Fibrous Cap Detection Pilot: Case Example: Non-Culprit Lesion





Barlis P et al . Am J Cardiol. 2008

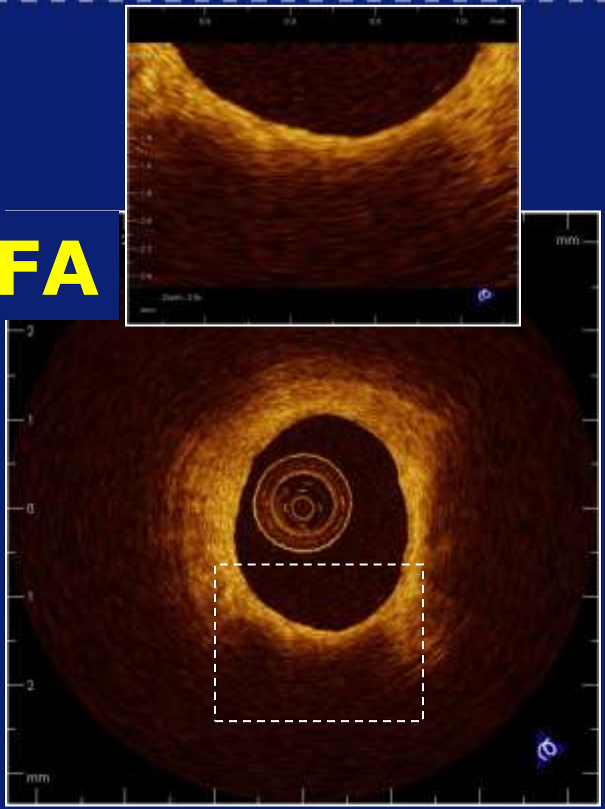
In-Vivo Fibrous Cap Detection Pilot: Case Example: Non-Culprit Lesion

n=7 (6 Pts)

↓

3 Pts: Unstable angina
2 Pts: ACS two weeks earlier
1 Pt: Stable angina

TCFA



Barlis P et al . Am J Cardiol. 2008

In-Vivo Fibrous Cap Detection Pilot: Case Example: Non-Culprit Lesion

Erasmus MC

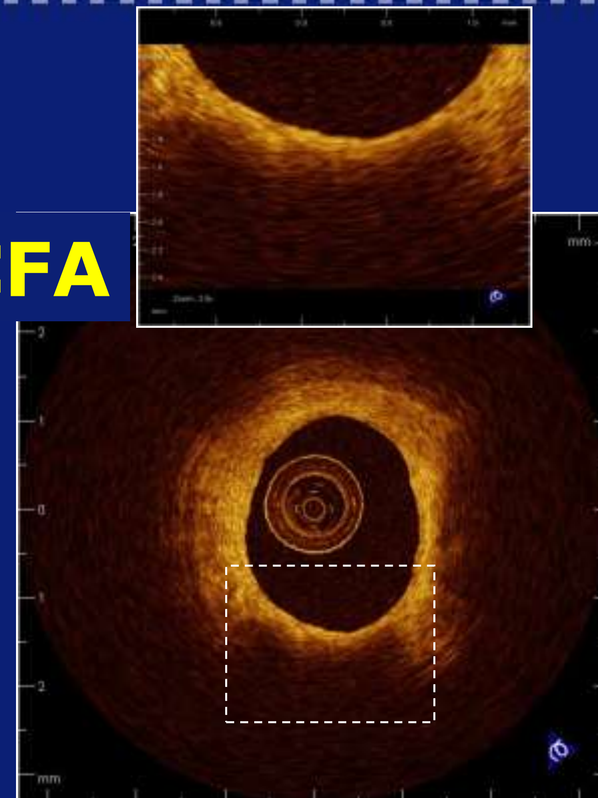
n=7 (6 Pts)

↓

Cap thickness: 0.19±0.05mm

Circumf. extent: 103 ±49º

TCFA



Barlis P et al . Am J Cardiol. 2008

Pilot Results: Clinical Outcome at 24 Months FUP

n=23

Erasmus MC

Remote from culprit
Cap thickness: 0.19±0.05mm
Circumferential extent: 103 ±49°

Thin Fibrous Cap 6 Pts

Death	0
Acute myocardial infarction	0
Revascularisation	1
Hospitalization	1
Angina status CCS I CCS II CCS III CCS IV	 *5* *1* *0* *0*

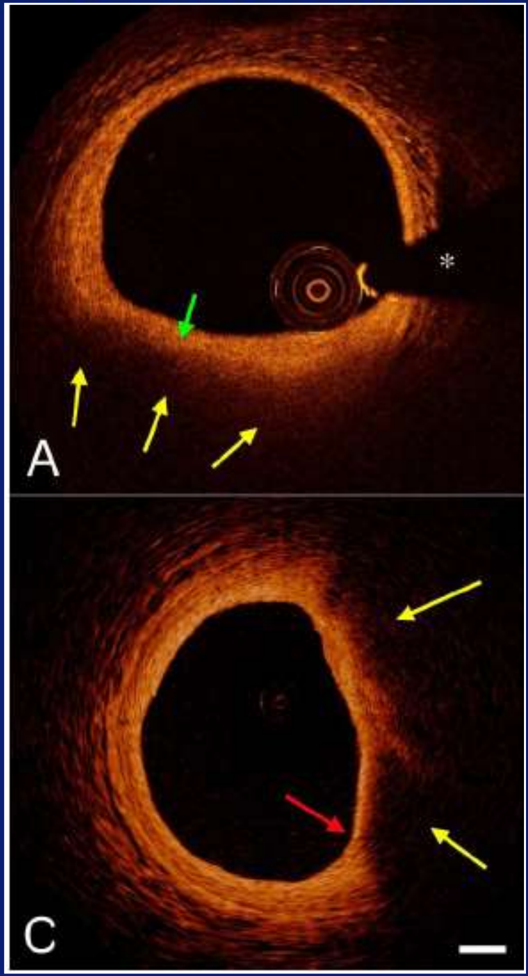
Repeat-PCI for in-stent restenosis

Uneventful hip endo-prosthesis

Barlis P et al . Am J Cardiol. 2008

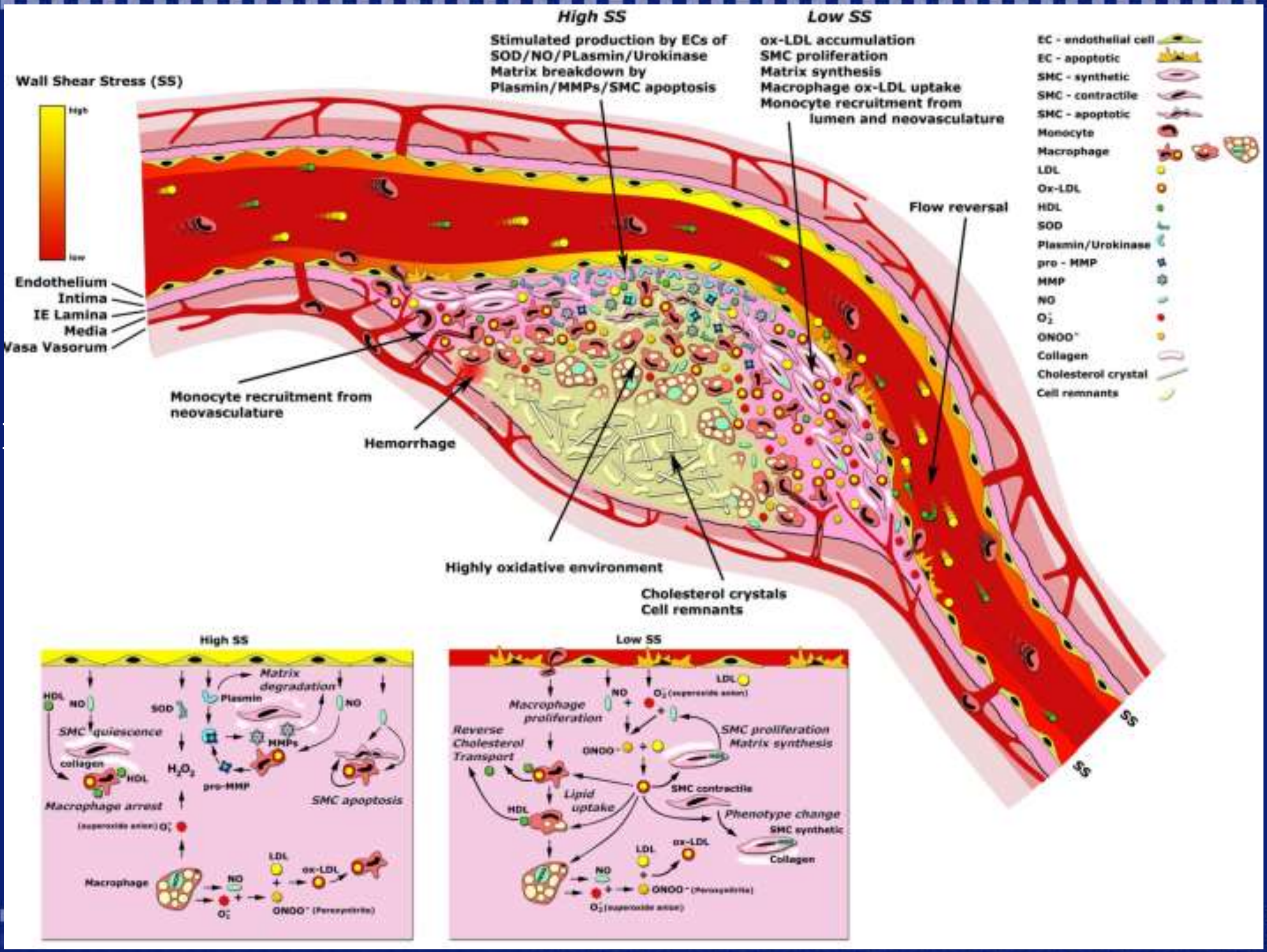
OCT Assessment of Vulnerability
From Morphology to Symptomatic Rupture
Is There a Missing Link?

Trigger?

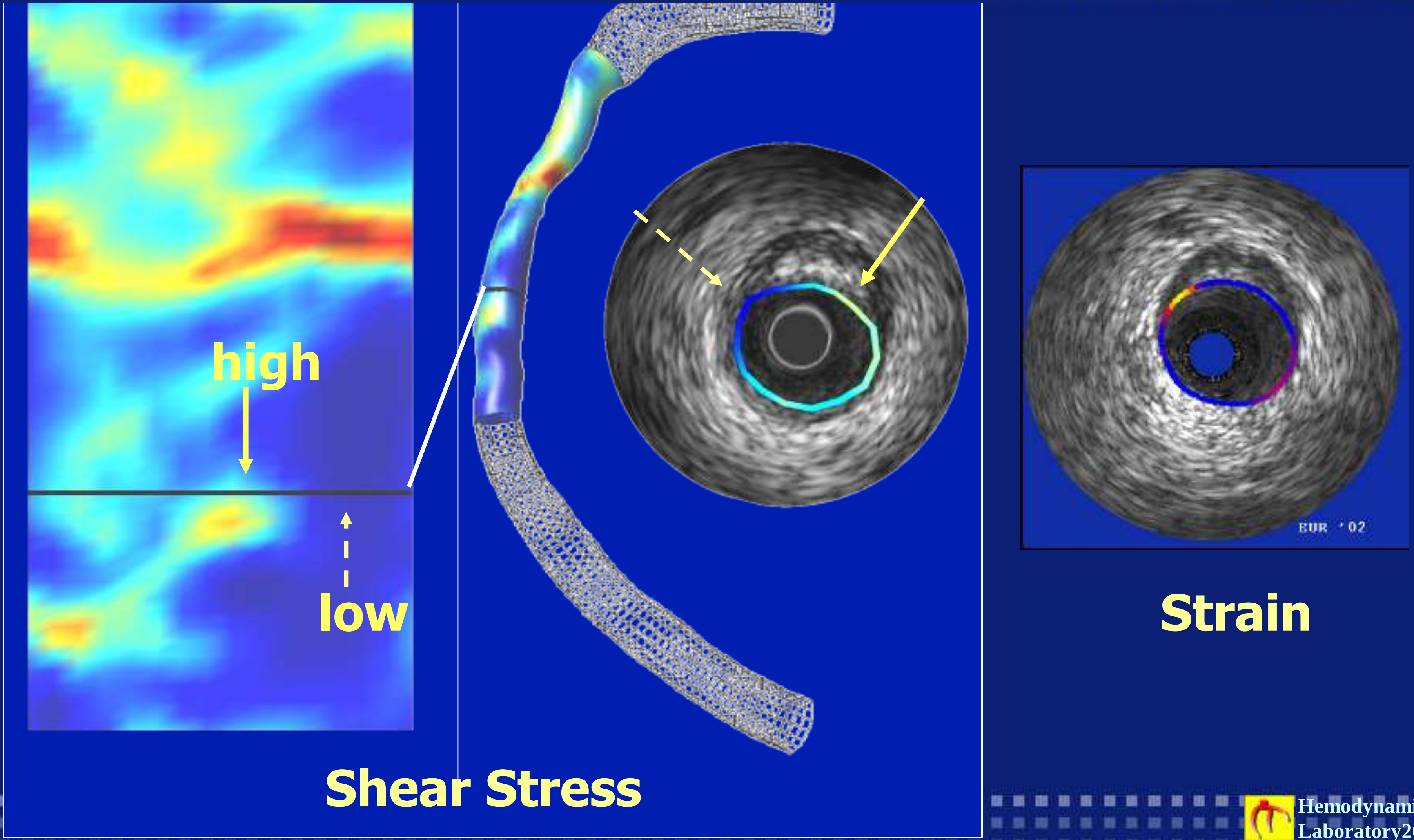


OCT Assessment of Vulnerability
From Morphology to Symptomatic Rupture
Is There a Missing Link?

Erasmus MC



OCT Assessment of Vulnerability
From Morphology to Symptomatic Rupture
Is There a Missing Link?



OCT Assessment of Vulnerability
From Morphology to Symptomatic Rupture
Is There a Missing Link?

Erasmus MC

Intra-plaque Hemorrhage

- Leaking from **vasa vasorum** or shoulders of plaque with extensive **angiogenesis**
- Fissure of fibrous cap

Virmani, et al
ATVB 2000; 20: 1262

OCT Assessment of Vulnerability

Erasmus MC

- OCT can visualize in vivo features for vulnerable plaque: TFCA (neovascularization, calcified nodule, thrombosis)

- High sensitivity, specificity, &negative predictive value
- Positive predictive value is moderate!

- Further validation needed!!
  - Diagnostic accuracy of plaque features
  - Interstudy/ inter-OCT system/ interobserver variablity

OCT:

Future Directions Tissue Characterization: Optical Attenuation Imaging

- *Imaging: C7XR, Visipaque flush 3ml/s*
- *Lumen segmentation*
- *Speckle filtering*
- *Analyze using single scattering model; window length > 200 µm*

$$\langle i_d(r) \rangle = I_0 \cdot T_{cath}(r) \cdot \hat{S}(r) \cdot \exp(-\mu_t r)$$

$T_{cath}(r)$: catheter axial PSF

$\hat{S}(r)$: roll-off correction

van Soest G et al, J. Biomed. Opt. 2010

OCT:
Future Directions

Tissue Characterization: Optical Attenuation Imaging

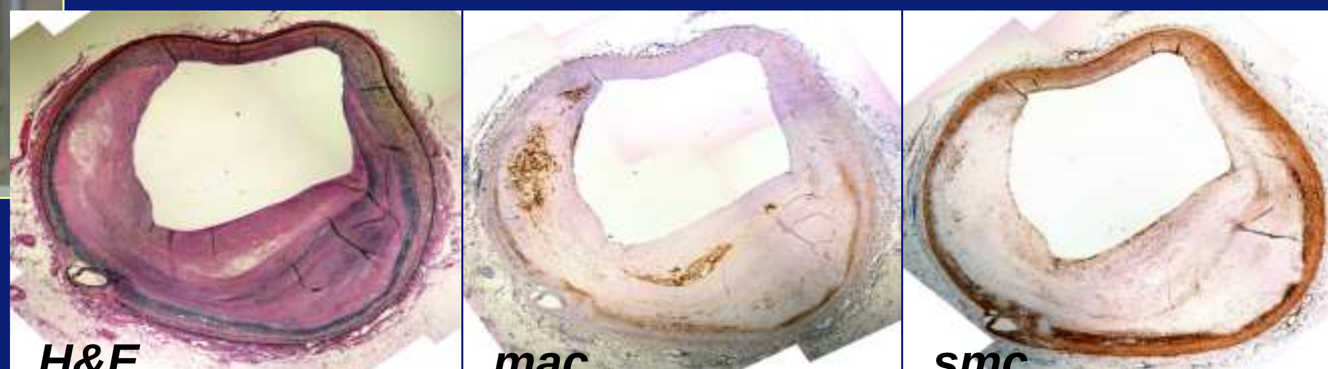
Relation between tissue type & attenuation coefficient

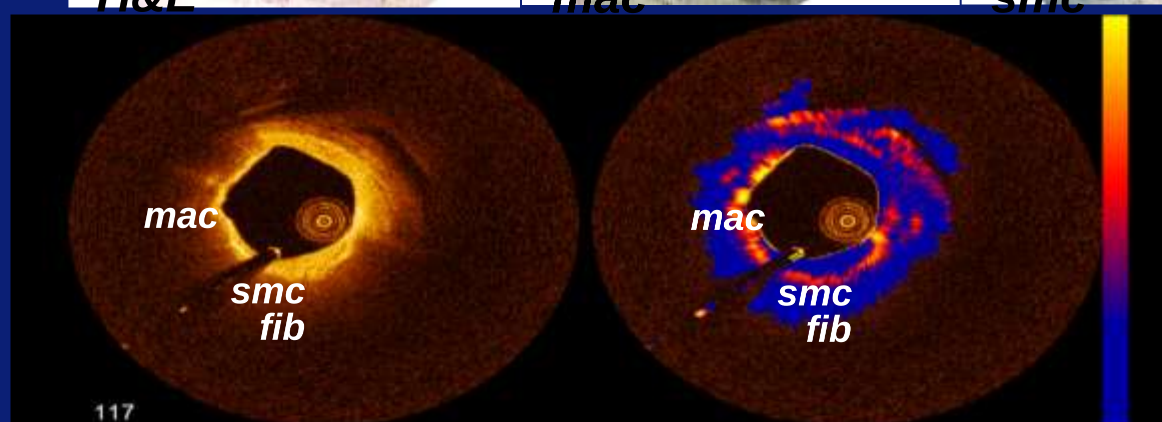
Fibrous	low
Calcium	low
Necrotic core	HIGH
Macrophages	very HIGH

van Soest G et al, J. Biomed. Opt. 2010

OCT:

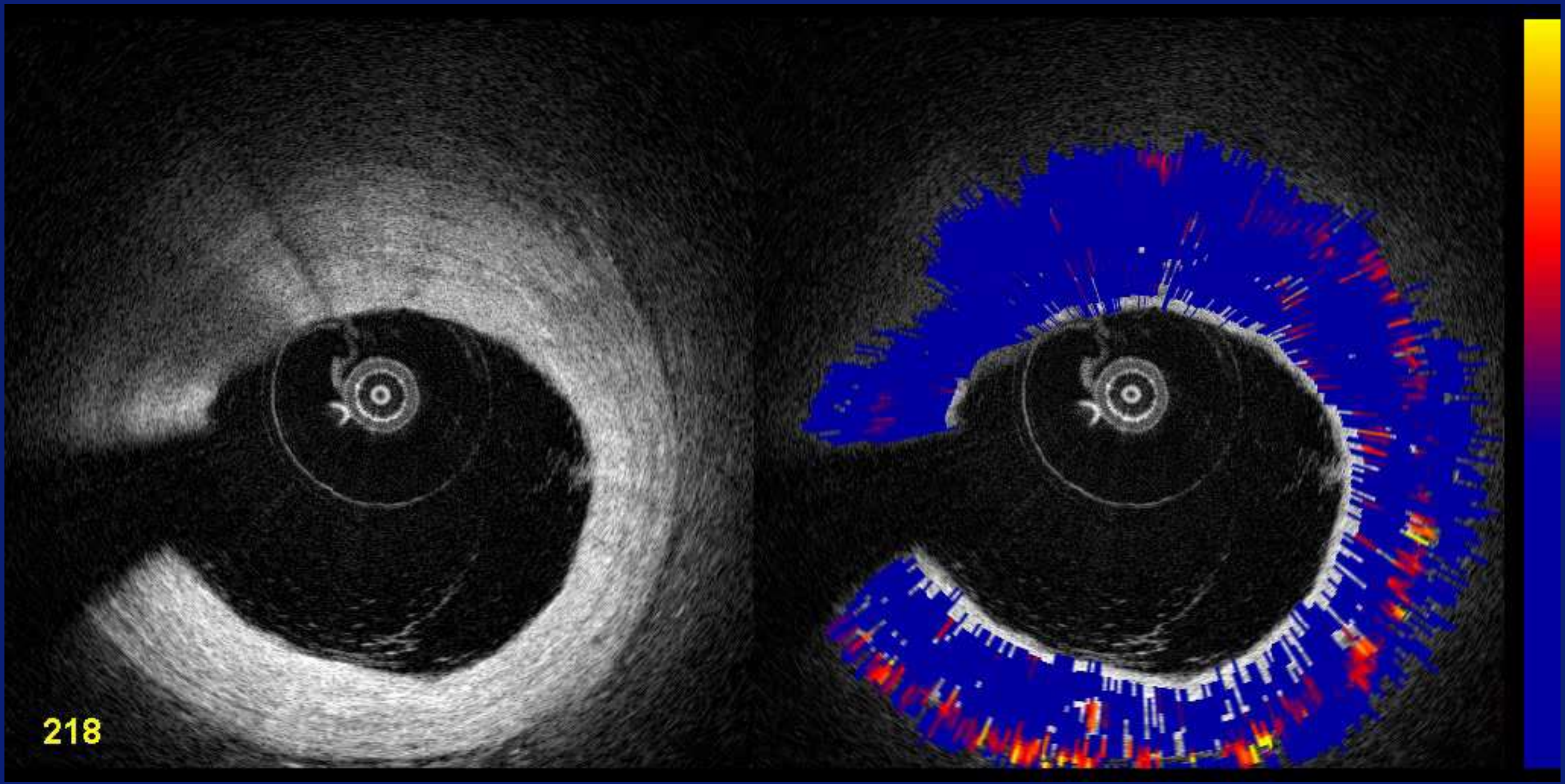
Future Directions Tissue Characterization: Optical Attenuation Imaging





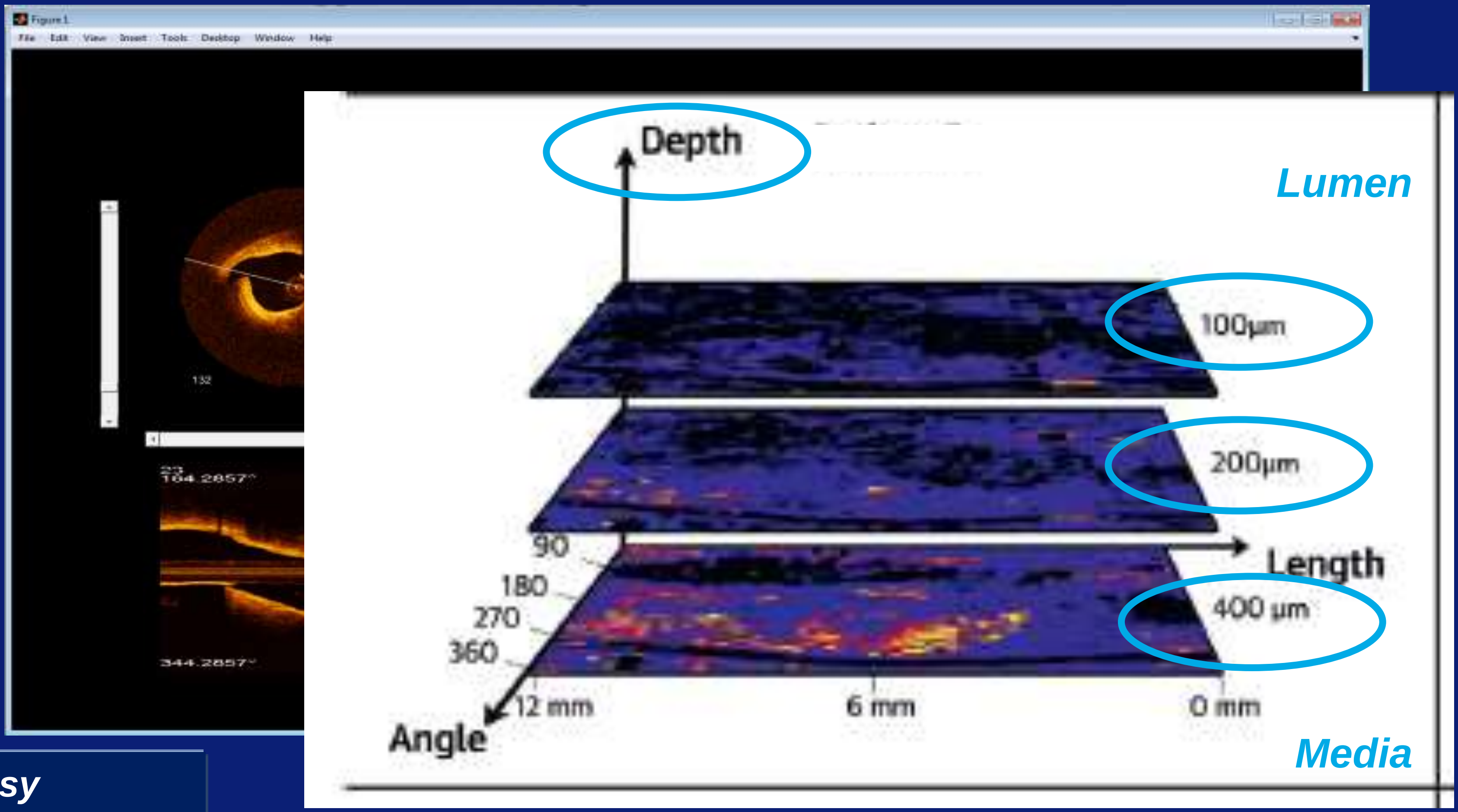
ex vivo pullback; Tom Johnson @ BHI

OCT:
Future Directions Tissue Characterization: Optical Attenuation Imaging



Courtesy Gijs van Soest, Biomedical Engineering, EMC

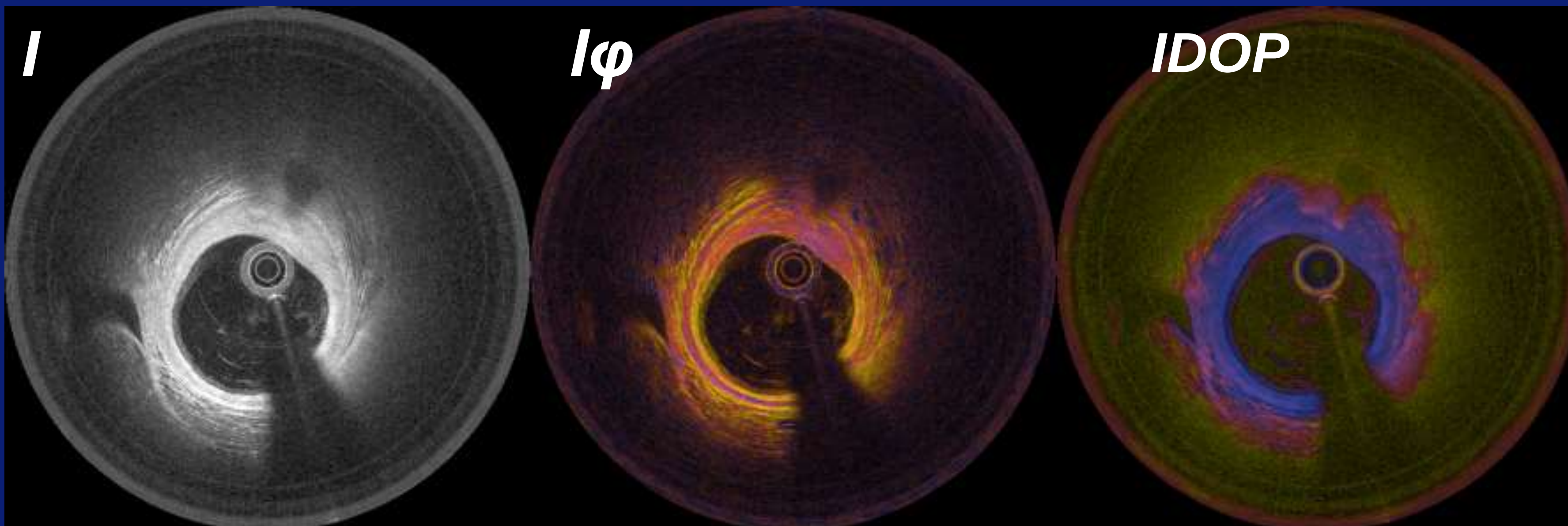
OCT:
Future Directions Tissue Characterization: Optical Attenuation Imaging



Courtesy
M. Gnanadesigan
T. Kameyama

OCT:

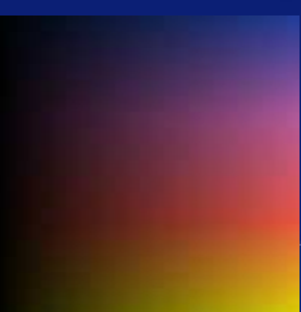
Future Directions Tissue Characterization: Polarization Sensitive Imaging



Intensity

Local Retardation (φ)

Degree of Polarization (DOP)



φ
DOP

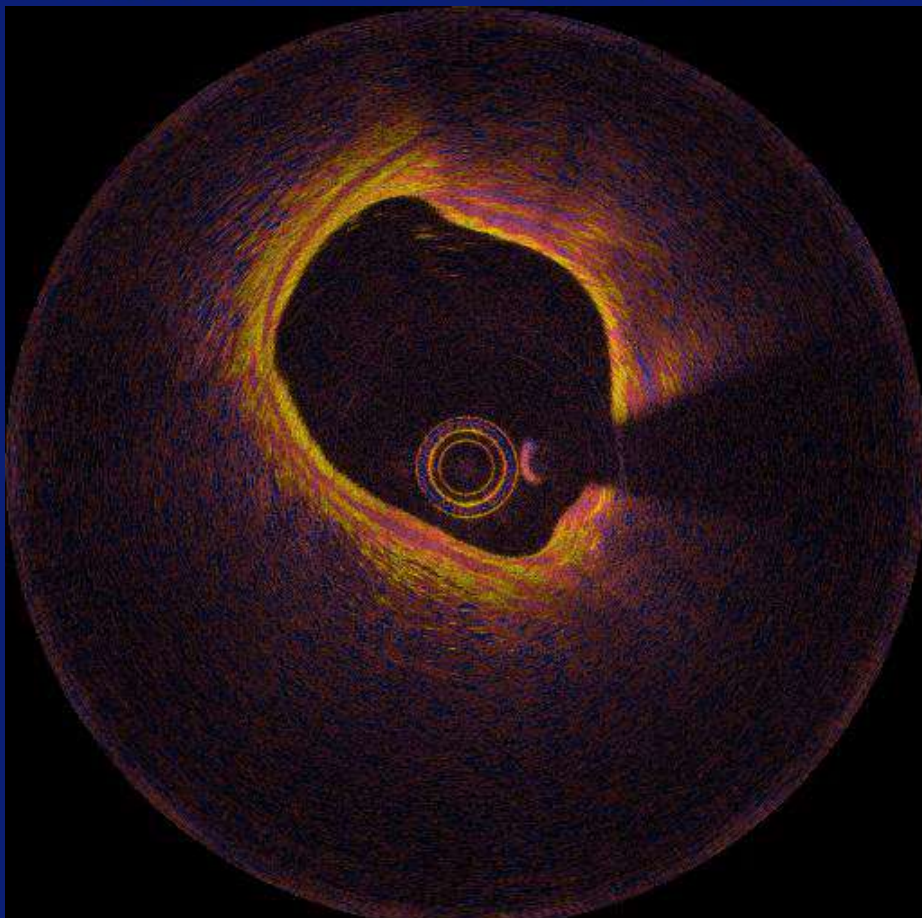
- -Local retardation (high) reveals collagen
- -DOP (low) hints at foam cells, lipid, macrophages

In-vivo human coronary; in cooperation with Villinger M, Bouma B, MGH Boston, USA

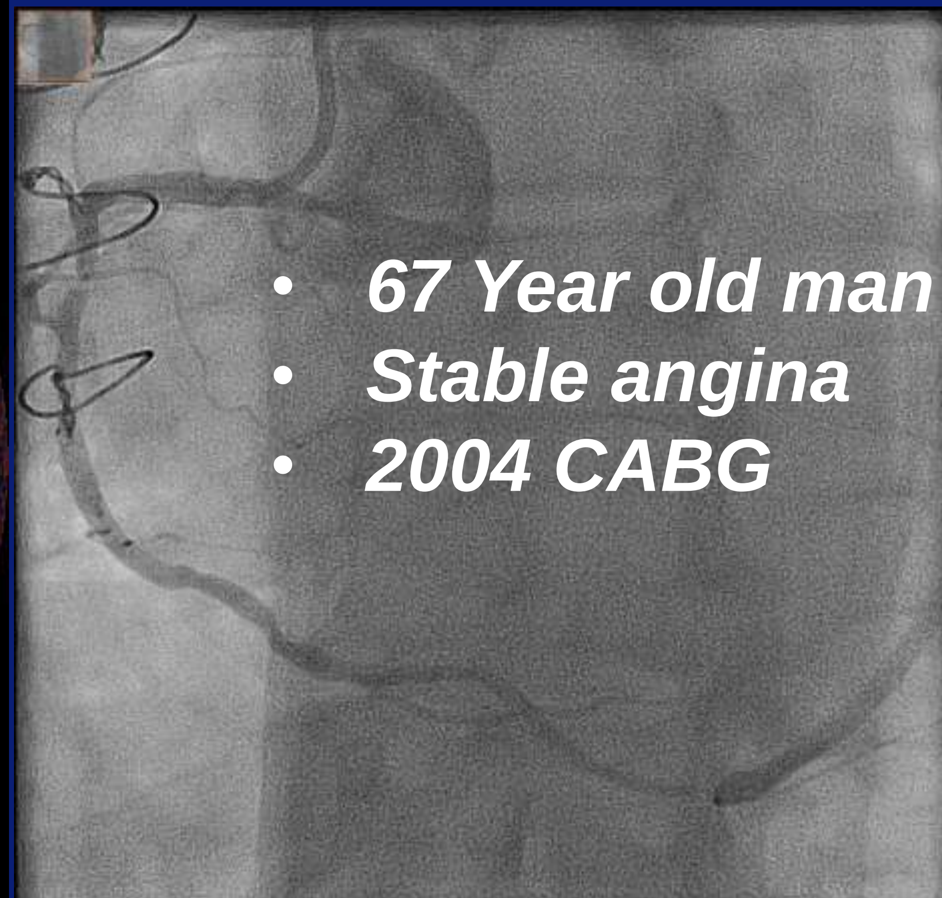
OCT:

Future Directions

Tissue Characterization: Polarization Sensitive Imaging



Local Retardation (φ)

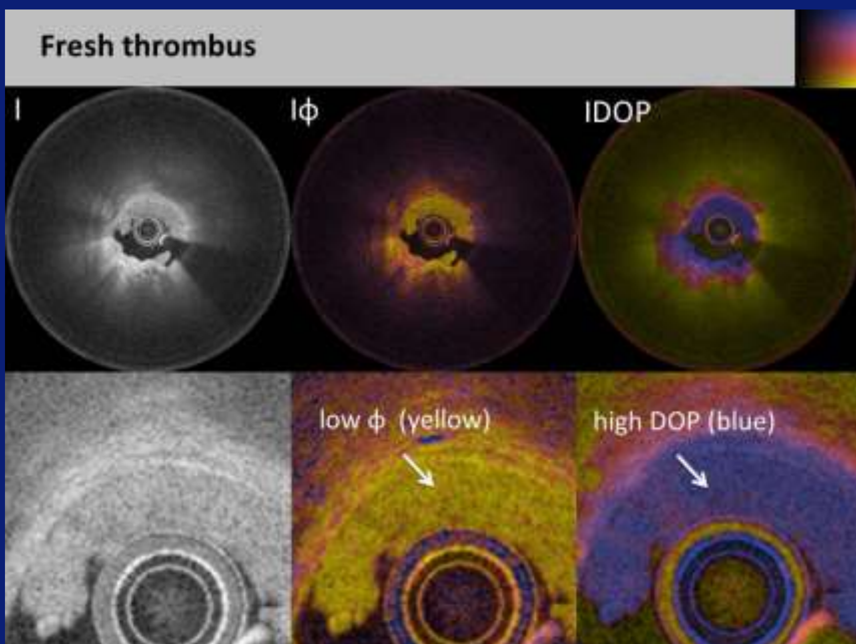


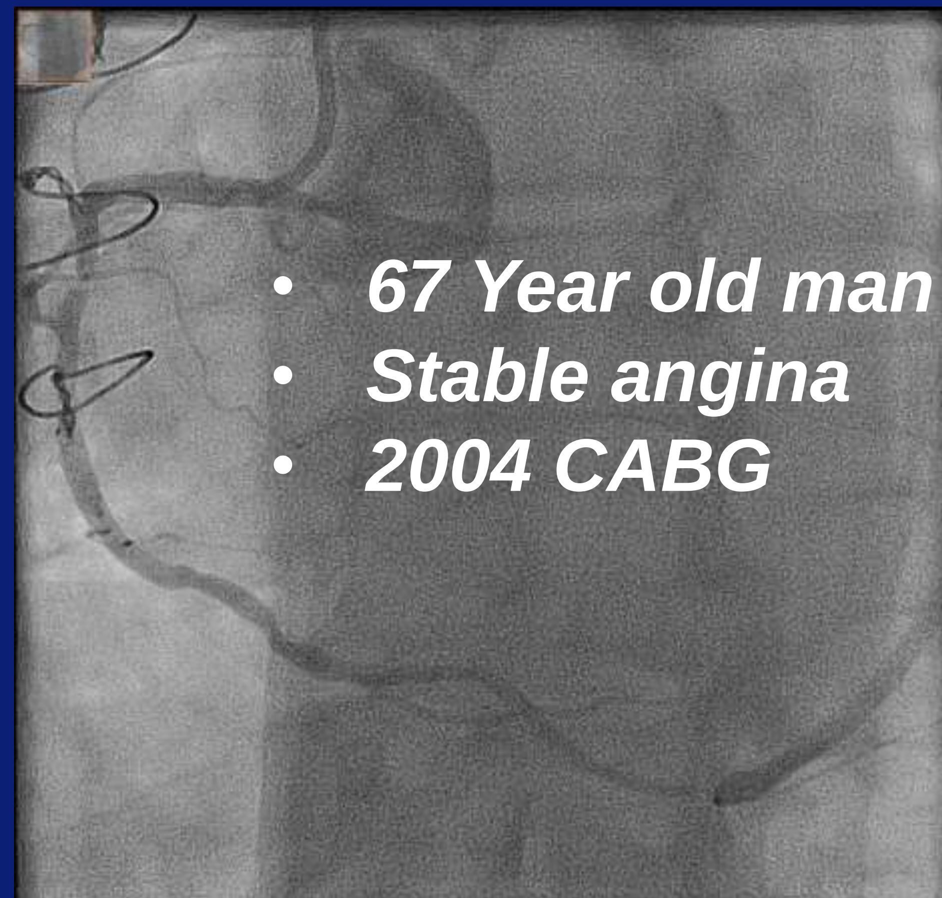
- *67 Year old man*
- *Stable angina*
- *2004 CABG*

In-vivo human coronary; in cooperation with Villinger M, Bouma B, MGH Boston, USA

OCT:

Future Directions Tissue Characterization: Polarization Sensitive Imaging





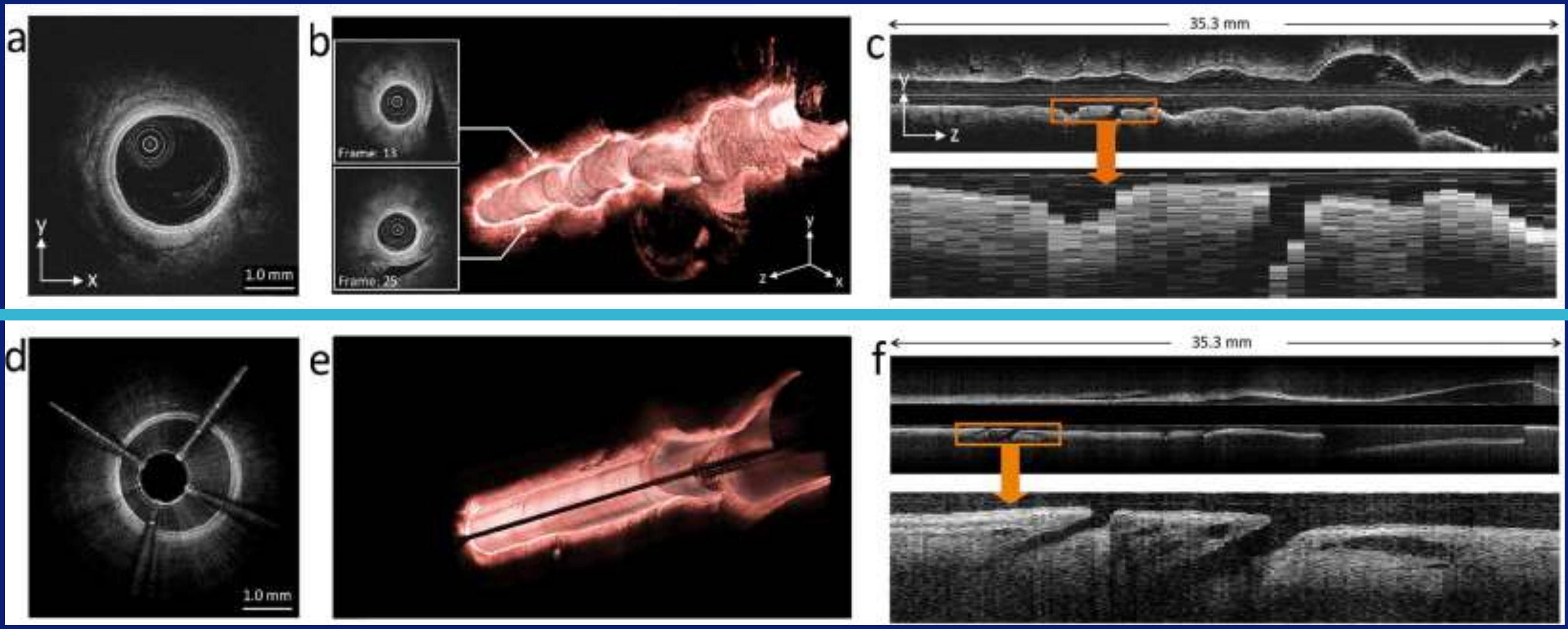
- *67 Year old man*
- *Stable angina*
- *2004 CABG*

In-vivo human coronary; in cooperation with Villinger M, Bouma B, MGH Boston, USA

OCT:

Future Directions Ultrafast "Heartbeat" OCT

Conventional OCT: 100 fps & 20 mm/s pullback speed (200 µm frame pitch).



Heartbeat OCT: 3200 fps & 100 mm/s pullback speed (31 µm frame pitch).

Wang T. van Soest G. presented at EuroPCR 2014

Wang T.. et al. Optics letters 38, 1715-1717 (2013).

OCT:

Future Directions Ultrafast "Heartbeat" OCT

Wang T. van Soest G. presented at EuroPCR 2014

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Thank you for your attention!

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