Erasmus MC
Universitair Medisch Centrum Rotterdam

Diagnosis and Treatment of Vulnerable Plaque: What Is New in 2015?

What to Do with Functionally Insignificant Vulnerable Plaque?

E. Regar

prepared with J. van der Sijde & A. Karanasos

Thoraxcenter

Erasmus Medical Center

Rotterdam, NL

20th CARDIOVASCULAR SUMMIT
TCTAP 2015

What to Do with Functionally Insignificant Vulnerable Plaque?

Erasmus MC

TREAT IT !

Vulnerable Plaque can Cause Life-Threatening Event

HOW?

What to Do with Functionally Insignificant Vulnerable Plaque?

Current Paradigm (2015)

Functionally significant plaque	Functionally insignificant plaque
⇩	⇩
PCI CABG	Medical therapy “Prevention”

What to Do with Functionally Insignificant Vulnerable Plaque?

Current Paradigm (2015)

Functionally significant plaque

↓

PCI
CABG

Functionally insignificant plaque

↓

Medical therapy
"Prevention"

Medical Therapy
Side-effects

Nitrates
Headache
Hypotension
Syncope
Relfex tachycardia

B-blockers
Fatigue, depression
Bradycardia
Heart block
Bronchospasm
Peripheral vasoconstriction

Aspirin
GI pain, ulceration, bleeding
Rash
Renal damage

Statins
Muscle ache
Hepatotoxicity
Myopathy
Constipation

ACEi
Hypotension
Headache
Cough
Renal damage

CCBs (HR lowering)
Bradycardia
Heart conduction defect
Low ejection fraction
Constipation

CCBs (DHP)
Headache
Ankle swelling
Fatigue
Flushing
Reflex tachycardia

Medical Therapy
Adherence

- Poor adherence
- Adherence is not greatly influenced by the class of drug prescribed

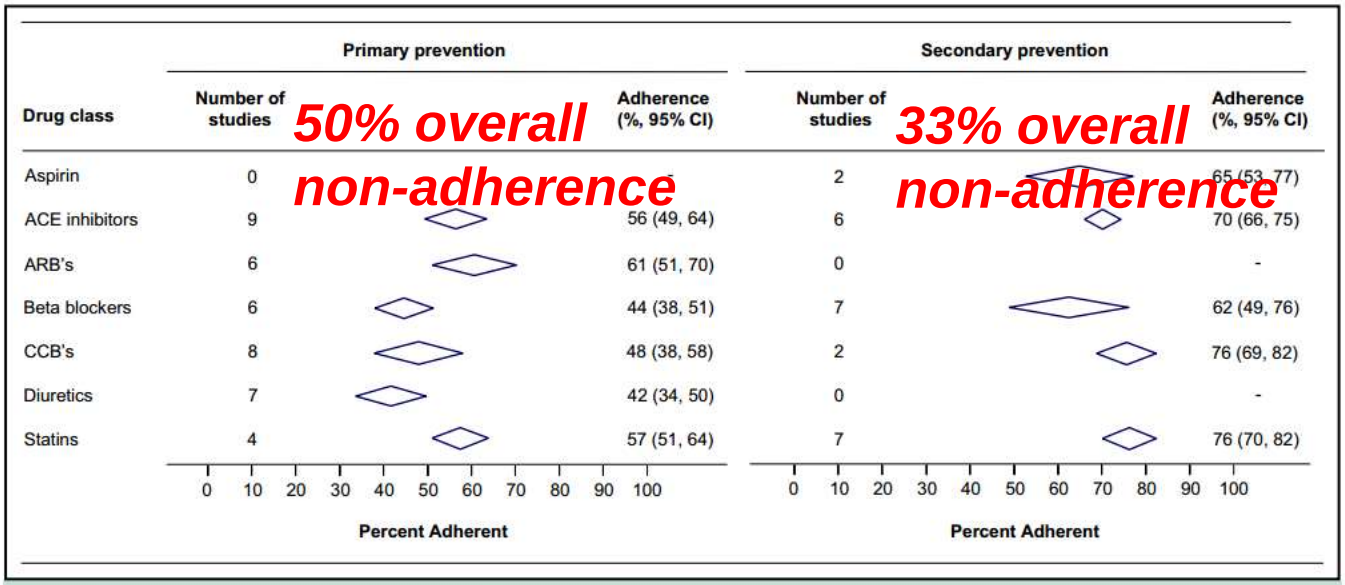


Figure 2 Percent adherence according to drug class and use in primary and secondary prevention. CI = confidence interval; ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; CCB = calcium channel blocker.

Naderi SH et al. Am J Med. 2012.

Medical Therapy
How Many Pills?

- 40 year old man
- Life expectancy of 80 years:

  5 pills a day

  x 365 days a year

  x 40 years

  = 73,000 pills.

73,000 pills x 1 gram = 73 kg of pills

Medical Therapy
How Many Pills?

- 40 year old man
- Life expectancy of 80 years:

  5 pills a day

  x 365 days a year

  x 40 years

  = 73,000 pills.

73,000 pills x 1 gram = 73 kg of pills

TO PREVENT THIS ???

Courtesy ms. ASA Autar, Dr. HMM van Beusekom

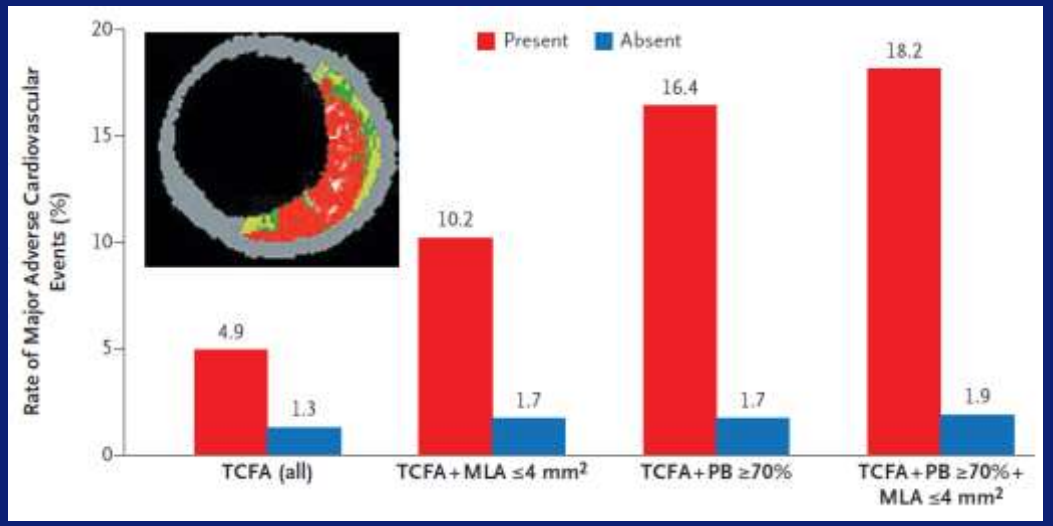
Medical Therapy
Are There Therapeutic Gaps?

Medical Therapy
Are There Therapeutic Gaps?

Non-culprit TCFA in pts with ACS have an increased risk of events despite optimal medical therapy:

Medical Therapy
Are There Therapeutic Gaps?

Non-culprit TCFA in pts with ACS have an increased risk of events despite optimal medical therapy:



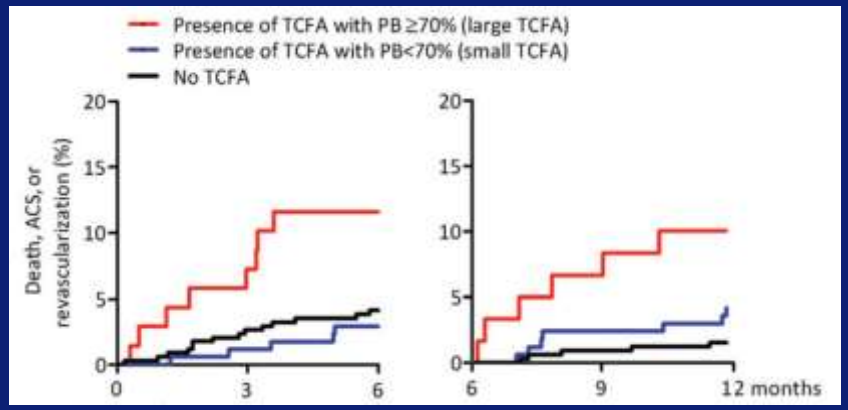
VH-TCFA morphology
Plaque burden > 70%
MLA < 4.0mm

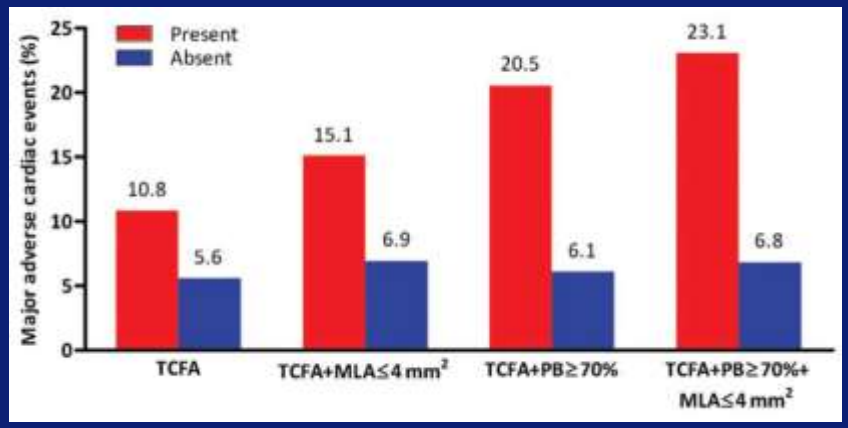
PROSPECT study

Stone et al. N Eng J Med 2011

Medical Therapy
Are There Therapeutic Gaps?

Non-culprit TCFA in pts with ACS have an increased risk of events despite optimal medical therapy:





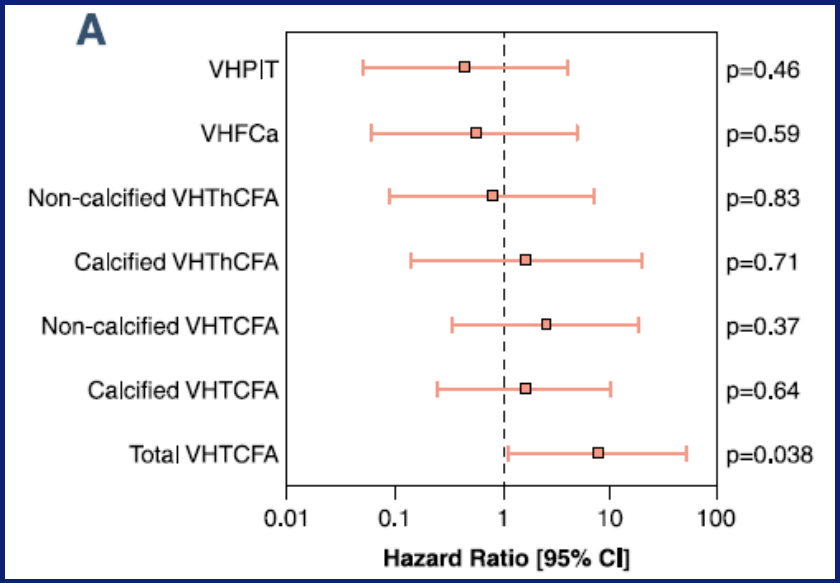
VH-TCFA morphology
Plaque burden > 70%
MLA < 4.0mm

ATHEROREMO study

Cheng et al. Eur Heart J 2014

Medical Therapy
Are There Therapeutic Gaps?

Non-culprit TCFA in pts with ACS have an increased risk of events despite optimal medical therapy:



VH-TCFA morphology
Plaque burden > 70%
MLA < 4.0mm

VIVA study

Calvert et al. JACC Img 2011

"Prophylactic" PCI
Is There Potential Benefit?

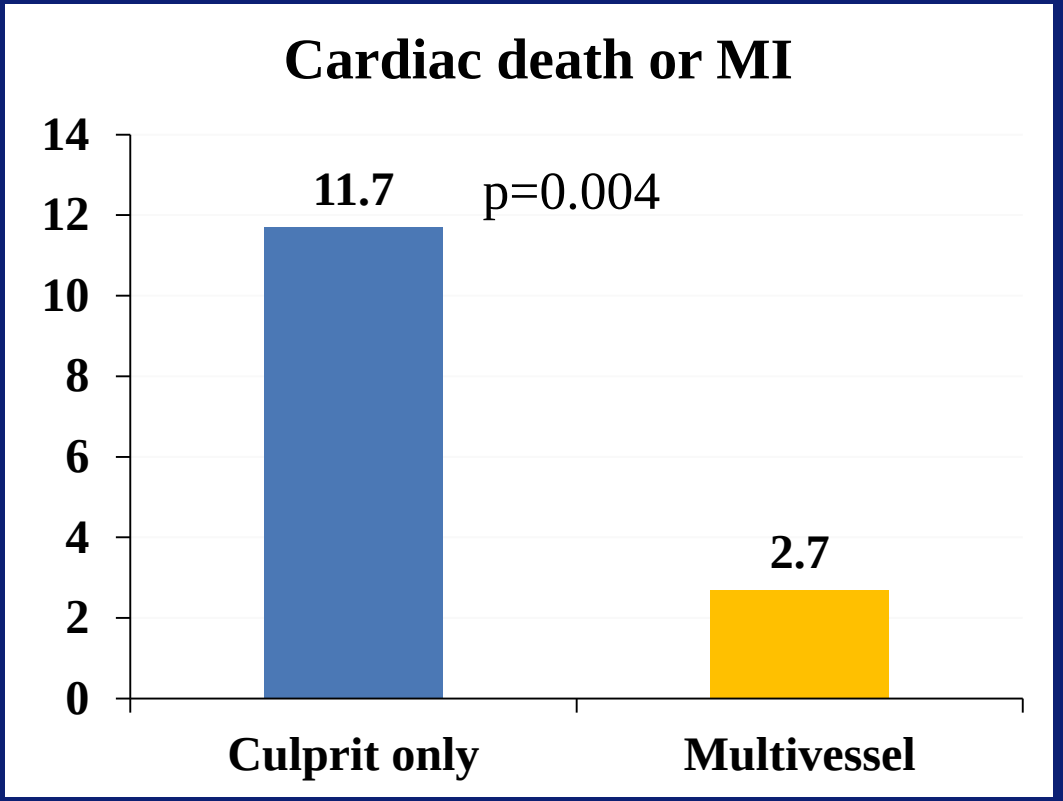
Erasmus MC

"Prophylactic" PCI
Is There Potential Benefit?

PRAMI study

Treatment of non-culprit lesions of MI could potentially improve prognosis!

In patients with STEMI and multivessel coronary disease, PCI of non-culprit reduced primary outcome, but also hard events



Wald et al. N Eng J Med 2013

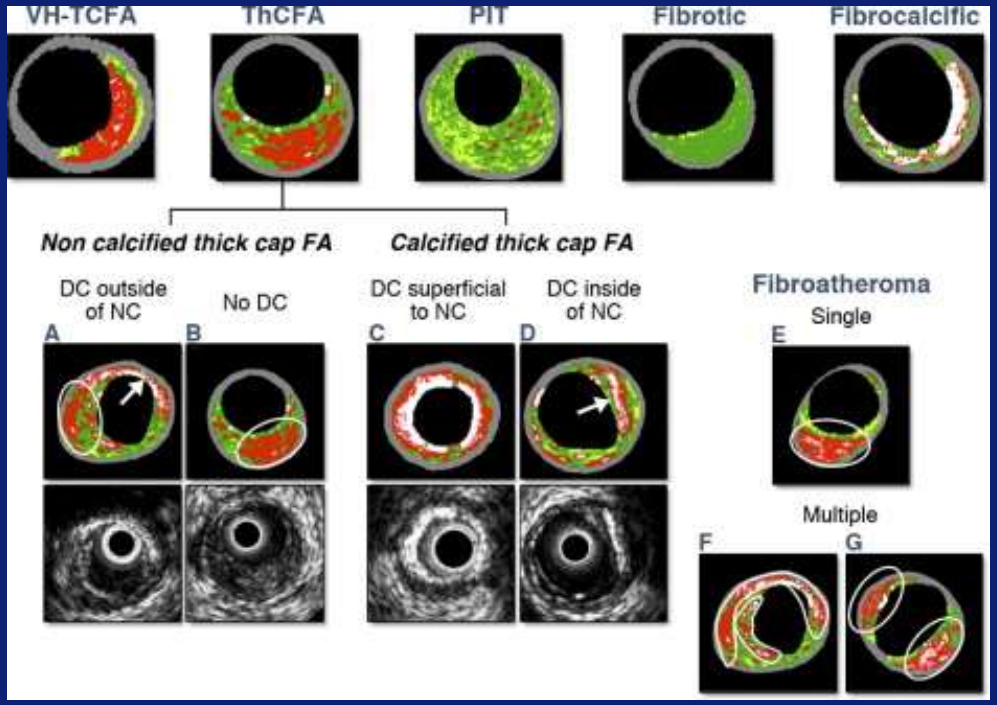
"Prophylactic" PCI: The Prerequisites
Can we Diagnose Vulnerable Plaque?

"Prophylactic" PCI: The Prerequisites
Can we Diagnose Vulnerable Plaque?

"Vulnerable plaque" caused by a TCFA can be identified with modern technology:

"Prophylactic" PCI: The Prerequisites
Can we Diagnose Vulnerable Plaque?

"Vulnerable plaque" caused by a TCFA can be identified with modern technology: IVUS VH



Maehara et al. JACC Img 2012

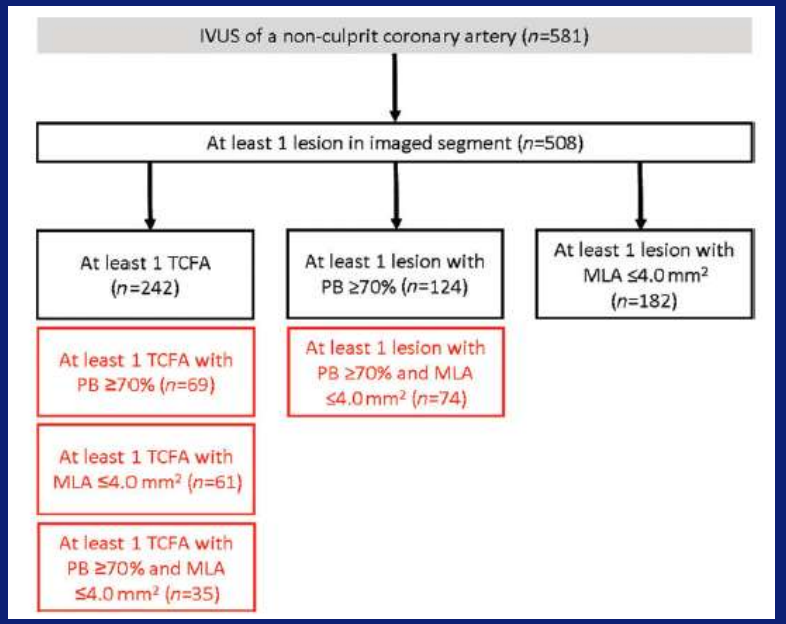
"Prophylactic" PCI: The Prerequisites
Can we Diagnose Vulnerable Plaque?

"Vulnerable plaque" caused by a TCFA can be identified with modern technology: IVUS VH

ATHEROREMO study

11.8%

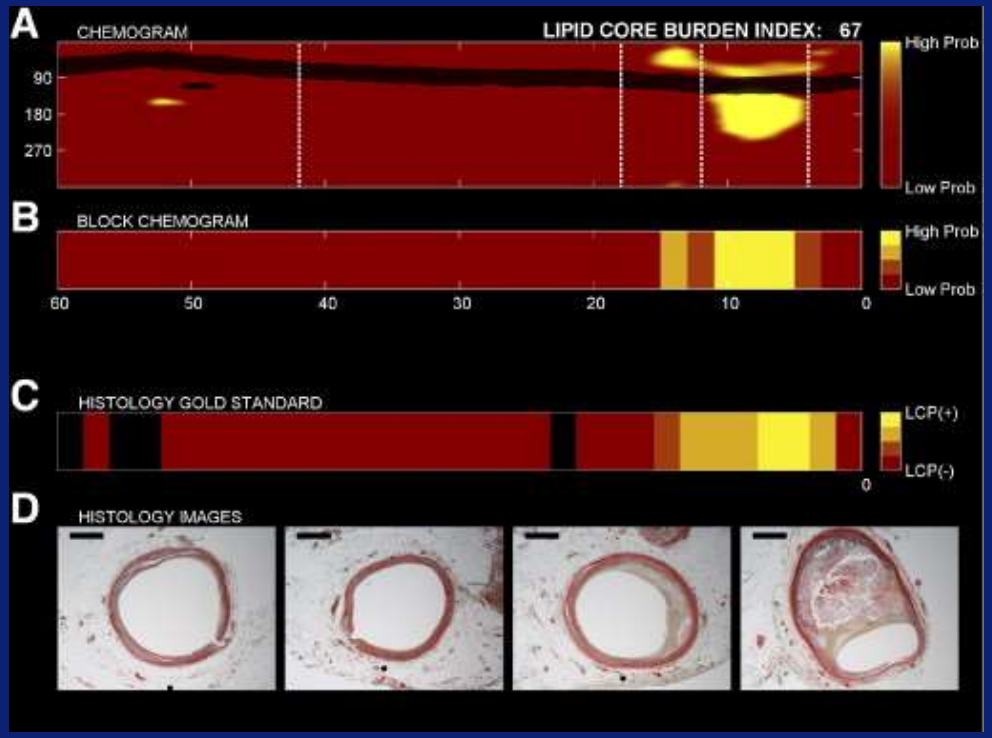
prevalence of VH-TCFA with high plaque burden per artery



Cheng et al. Eur Heart J 2014

"Prophylactic" PCI: The Prerequisites
Can we Diagnose Vulnerable Plaque?

"Vulnerable plaque" caused by a TCFA can be identified with modern technology: NIR



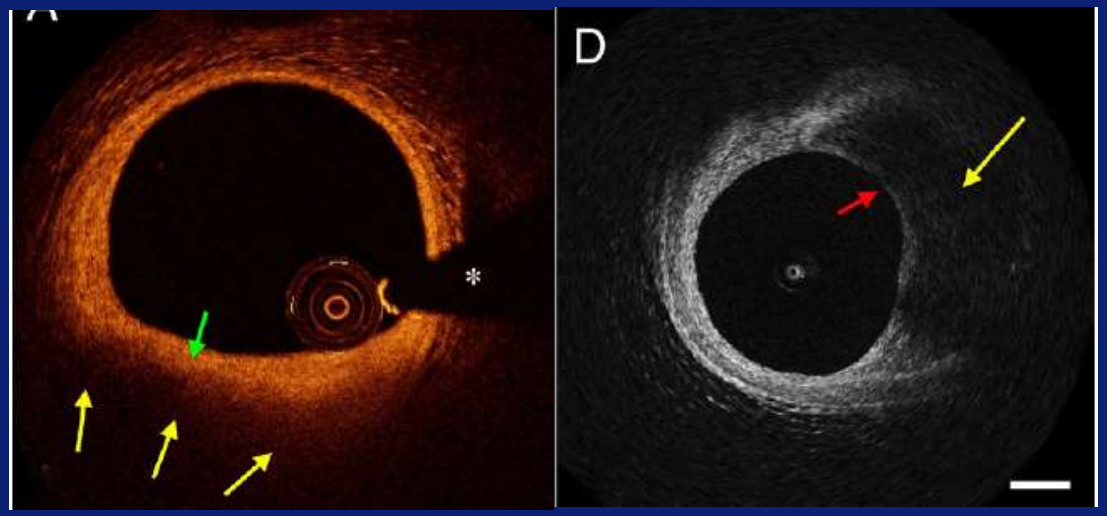
Gardner et al. JACC Img 2008

"Prophylactic" PCI: The Prerequisites
Can we Diagnose Vulnerable Plaque?

Erasmus MC

"Vulnerable plaque" caused by a TCFA can be identified with modern technology: OCT

Evidence level: High



Fibroatheroma with poorly defined borders and a cap

Fibroatheroma with thin fibrous cap

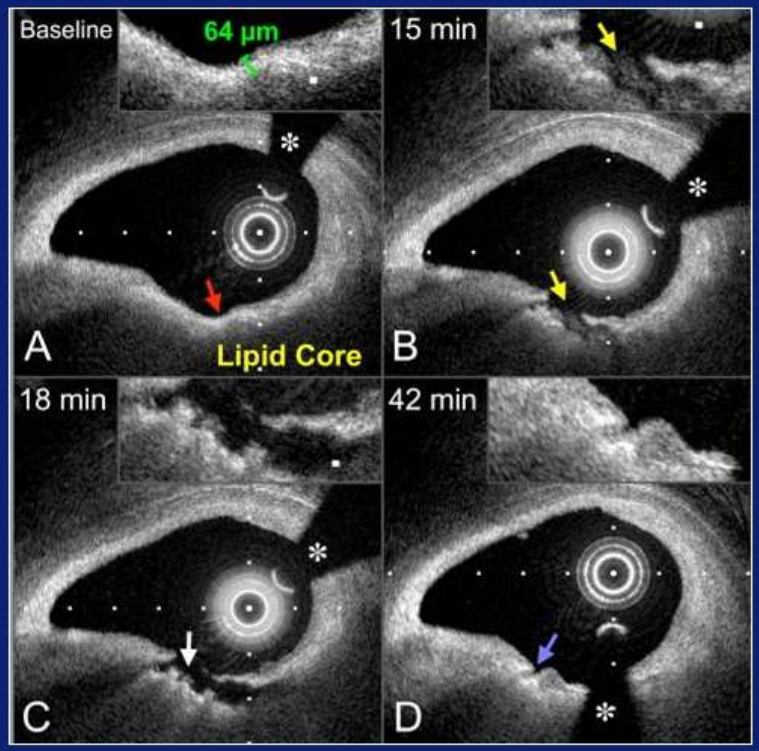
The International Working Group
For Intracoronary OCT Standardization And Validation

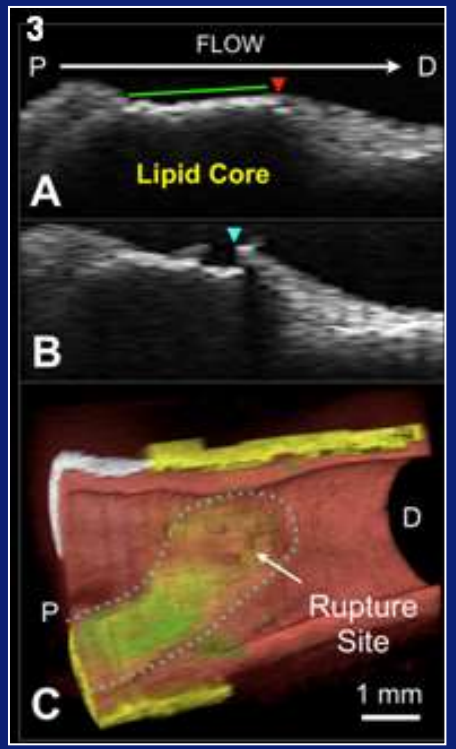
Tearney, Regar, Akasaka et al J Am Coll Cardiol. 2012

"Prophylactic" PCI: The Prerequisites
Can we Diagnose Vulnerable Plaque?

Erasmus MC

"Vulnerable plaque" caused by a TCFA can be identified with modern technology: OCT





Gonzalo N et al. JACC Imaging 2011

"Prophylactic" PCI: The Prerequisites

Can we Predict Prognosis of Vulnerable Plaque?

Erasmus MC

"Prophylactic" PCI: The Prerequisites

Can we Predict Prognosis of Vulnerable Plaque?

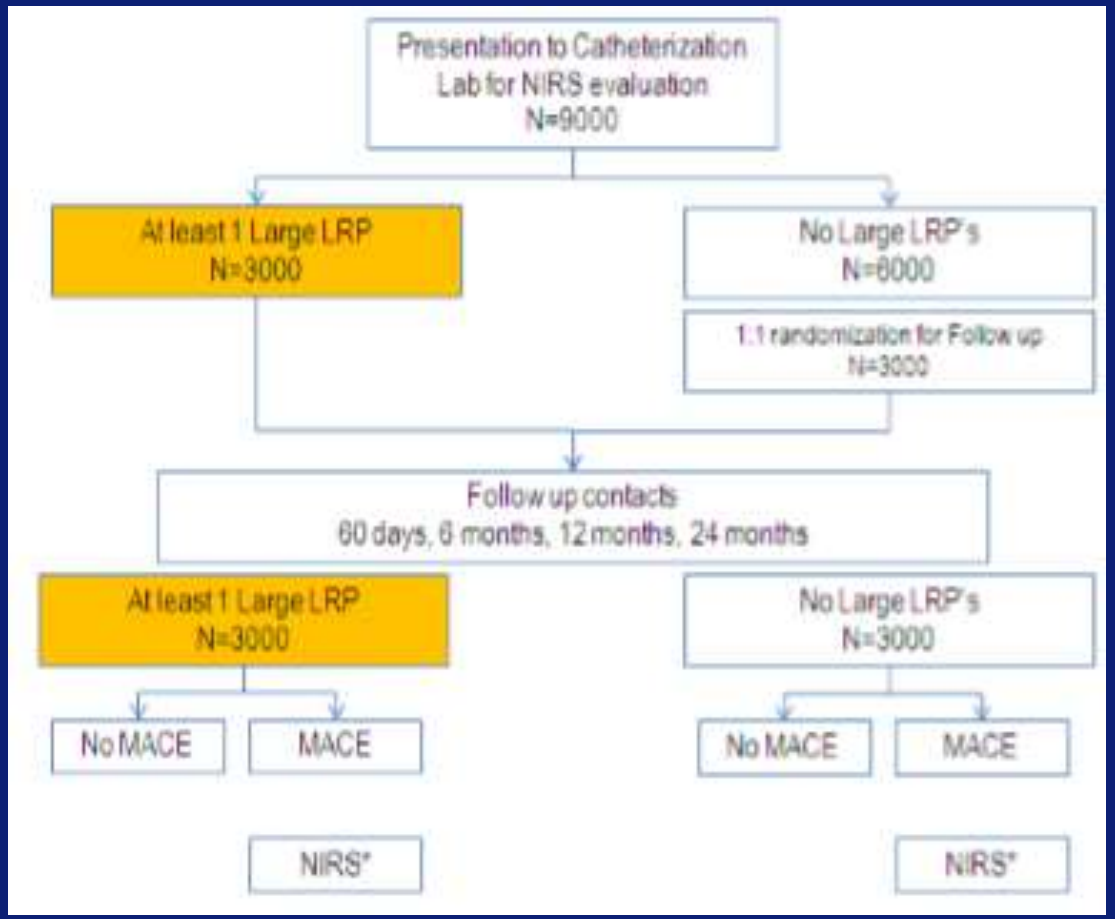
Erasmus MC

NIRS:
Prognostic Value ?

Lipid-Rich-Plaque (LRP) Registry

N=9000 pts
FUP: 2 years

PI: R. Waksman



"Prophylactic" PCI: The Prerequisites
Do we Have a Local Treatment Concept?

Erasmus MC

"Prophylactic" PCI: The Prerequisites
Do we Have a Local Treatment Concept?

Erasmus MC

Plaque composition and architecture can be modified.

ABSORB A Trial: BVS

2006 - Pre

2006 - Final

2007 - FUP 6m

2012 – FUP 5y

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 64, NO. 22, 2014
© 2014 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION ISSN 0735-1097/$36.00
PUBLISHED BY ELSEVIER INC. http://dx.doi.org/10.1016/j.jacc.2014.09.021

OCT Assessment of the Long-Term Vascular Healing Response 5 Years After Everolimus-Eluting Bioresorbable Vascular Scaffold

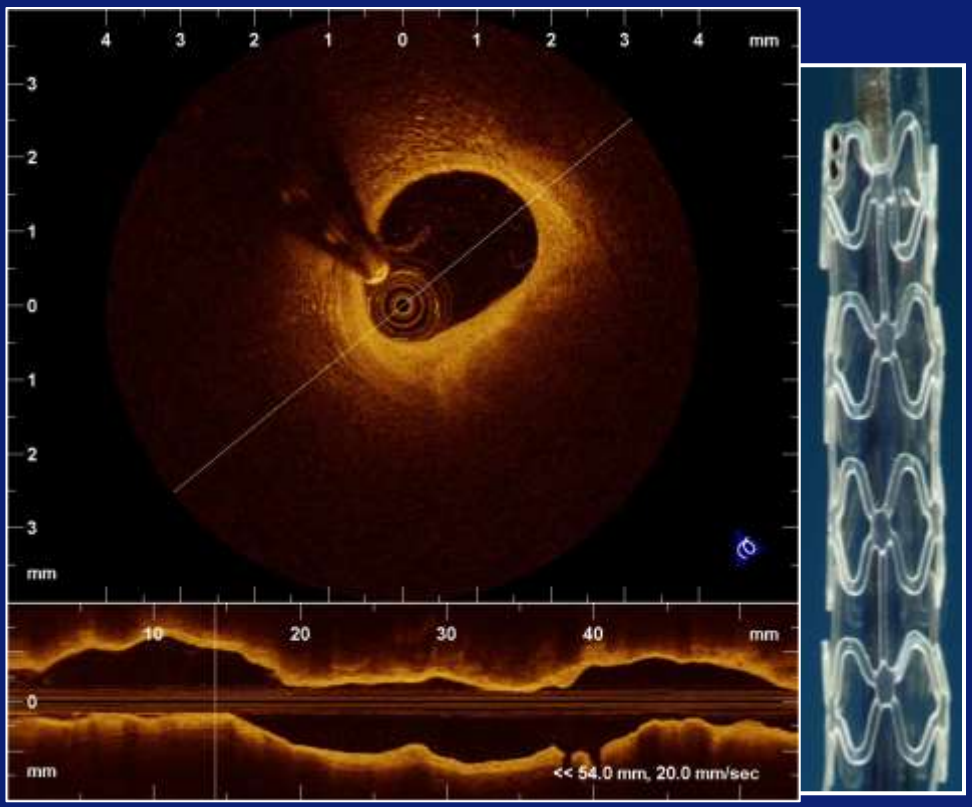
Antonios Karanasos, MD,* Gihan Simsek, MD,* Muthukarrupan Gnanadesigan, MSc,†
Nienke S. van Ditzhuijzen, MSc,* Raphael Freire, MD,* Jouke Dijkstra, PhD,‡ Shengxian Tu, PhD,‡
Nicolas Van Mieghem, MD,* Gijs van Soest, PhD,‡ Peter de Jaegere, MD, PhD,* Patrick W. Serruys, MD, PhD,*
Felix Zijlstra, MD, PhD,* Robert-Jan van Geuns, MD, PhD,* Evelyn Regar, MD, PhD*

Karanasos A et al. JACC 2014

"Prophylactic" PCI: The Prerequisites
Do we Have a Local Treatment Concept?

Erasmus MC

Plaque composition and architecture can be modified.



2006 - Pre

2006 - Final

2007 - FUP 6m

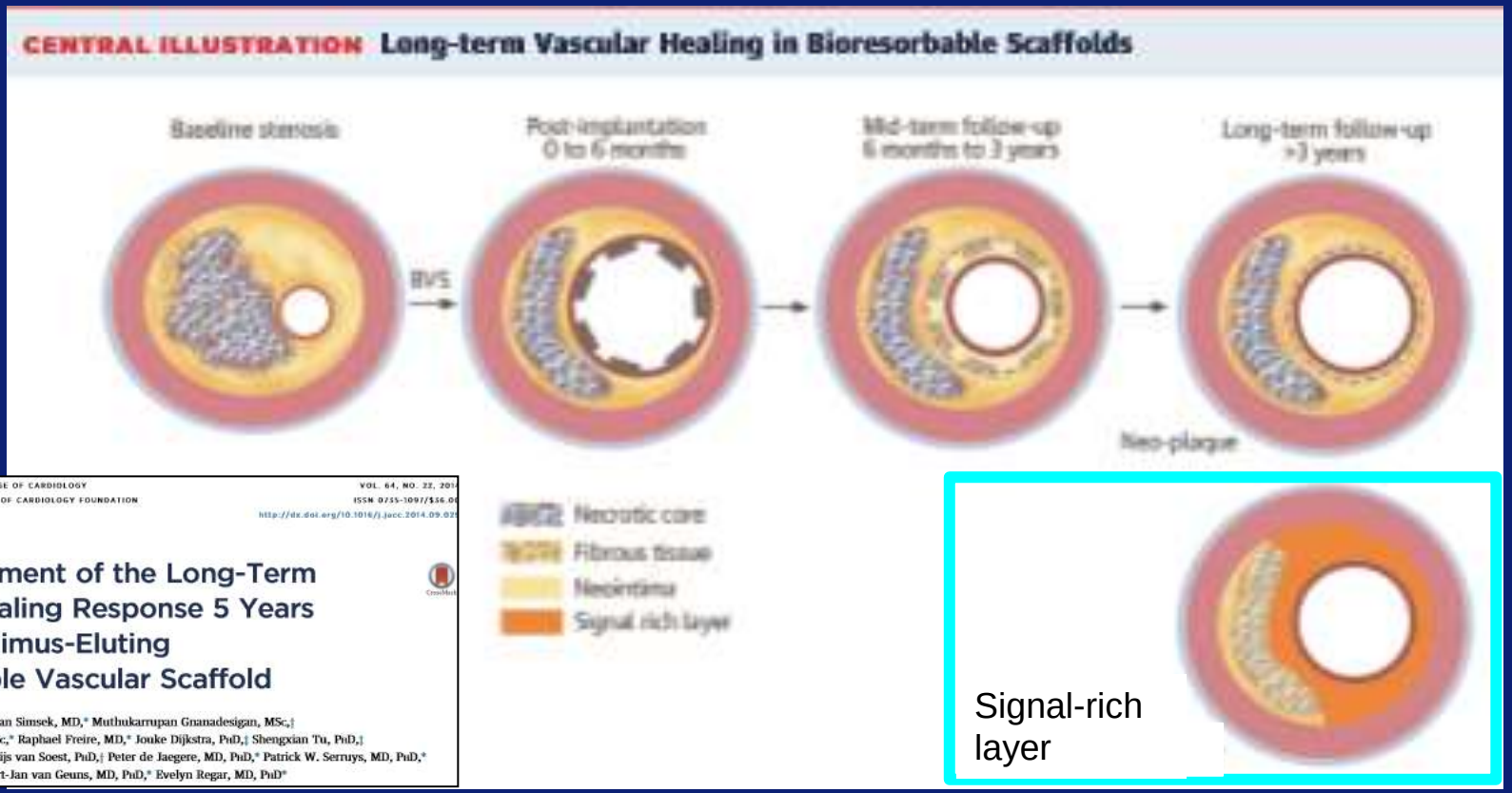
2012 – FUP 5y

Karanasos A et al. JACC 2014

"Prophylactic" PCI: The Prerequisites
Do we Have a Local Treatment Concept?

Erasmus MC

Plaque composition and architecture can be modified.



JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 64, NO. 22, 2014
© 2014 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION ISSN 0735-1097/$36.00
PUBLISHED BY ELSEVIER INC. http://dx.doi.org/10.1016/j.jacc.2014.09.025

OCT Assessment of the Long-Term Vascular Healing Response 5 Years After Everolimus-Eluting Bioresorbable Vascular Scaffold

Antonios Karanasos, MD,* Gihan Simsek, MD,* Muthukarrupan Gnanadesigan, MSc,†
Nienke S. van Ditzhuijzen, MSc,* Raphael Freire, MD,* Jouke Dijkstra, PhD,‡ Shengxian Tu, PhD,‡
Nicolas Van Mieghem, MD,* Gijs van Soest, PhD,‖ Peter de Jaegere, MD, PhD,* Patrick W. Serruys, MD, PhD,*
Felix Zijlstra, MD, PhD,* Robert-Jan van Geuns, MD, PhD,* Evelyn Regar, MD, PhD*

Karanasos A et al. JACC 2014

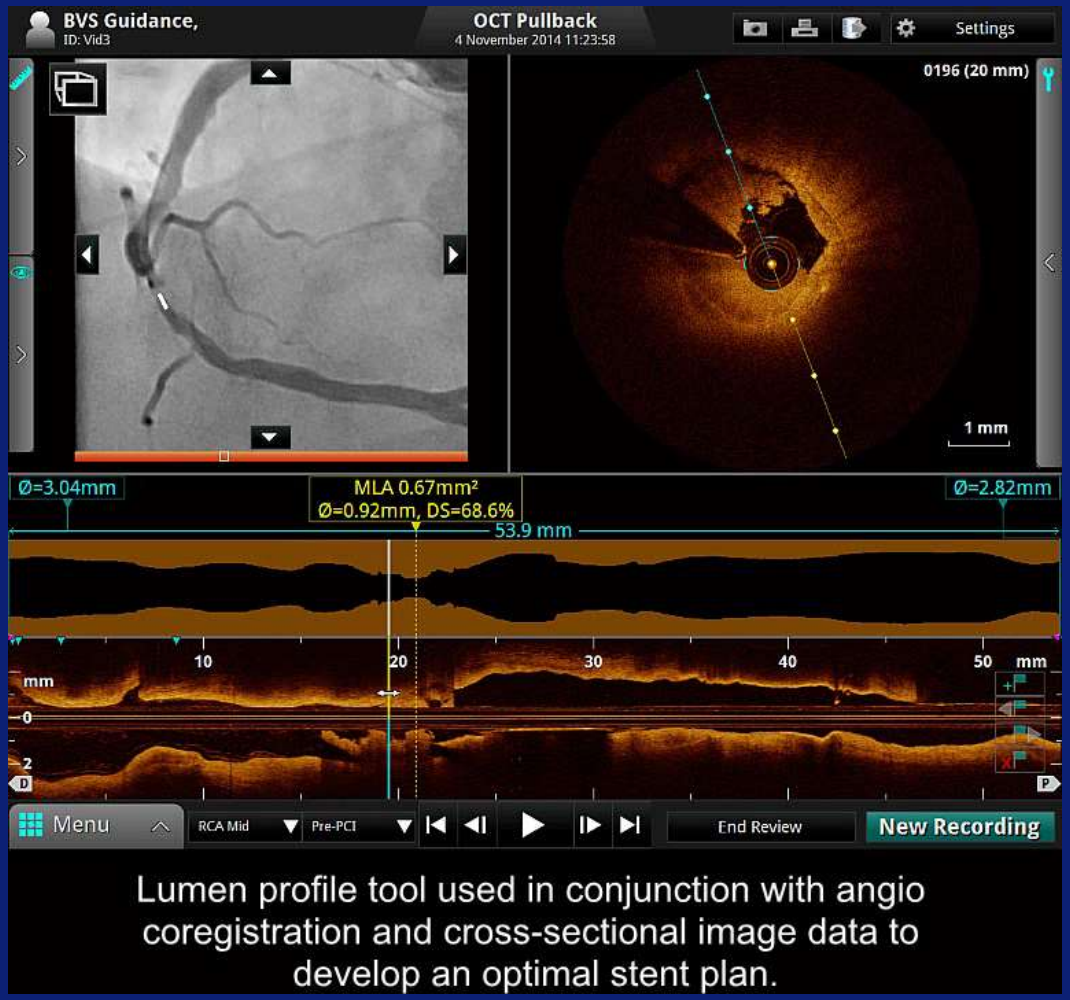
"Prophylactic" PCI: The Prerequisites

How Can we Localize The Non-Significant Lesion?

"Prophylactic" PCI: The Prerequisites

How Can we Localize The Non-Significant Lesion?

Angio-Co-registration



Lumen profile tool used in conjunction with angio coregistration and cross-sectional image data to develop an optimal stent plan.

St Jude, Optis i

What To Do With Functionally Insignificant Plaque?
We are Making Progress ...

In 2015,

We have instruments for routine clinical use in our hands, that can identify thin cap fibroatheroma/ vulnerable plaques.

Large scale observational studies are ongoing and will provide insights into the prognostic value of such findings.

Large scale interventional studies are ongoing and will provide insights into treatment effects.

Prospect II & Prospect Absorb

PI: David Erlinge

What To Do With Functionally Insignificant Plaque?
The Interesting Questions …

Benefit of stent/scaffold

Risk of TCFA treatment

Culprit TFCA have a higher risk for periprocedural MI & worse outcome

RR ~ 10

Goldstein J at el. Circ Cardiovasc Interv 2011

Lee et al. Circ Cardiovasc Interv 2011

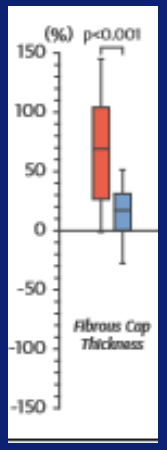
What To Do With Functionally Insignificant Plaque?
The Interesting Questions …

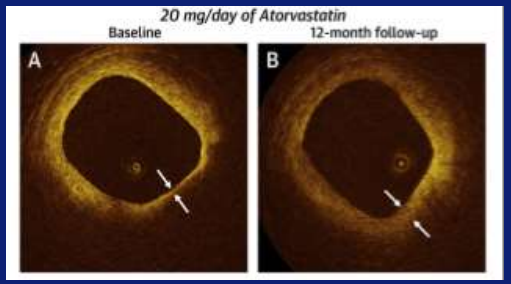
Erasmus MC

Benefit of stent/scaffold

Intensified Statin Therapy

EASY-FIT Trial:
50% Increase in TCFA cap thickness over 24m





Atorvastatin 20mg
Atorvastatin 5mg

Komukai et al. JACC 2014

What To Do With Functionally Insignificant Plaque?

The Interesting Questions …

… an avenue to personalized medicine?

Personalized Medicine: Hope or Hype?

By: Leslie Pray, Ph.D. © 2008 Nature Education

Citation: Pray, L. (2008) Personalized medicine: Hope or hype? *Nature Education* 1(1):72

Hippocrates used a person's physique and the seasons to personalize treatments for his patients. The modern scientific industry hopes to use your DNA.

REVIEW

Frontiers in cardiovascular medicine

Personalized medicine: hope or hype?

Keyan Salari[1], Hugh Watkins[2], and Euan A. Ashley[3]*

[1]Department of Genetics, Stanford University School of Medicine, Stanford, CA, USA; [2]Department of Cardiovascular Medicine, University of Oxford, Oxford, UK; and [3]Center for Inherited Cardiovascular Disease, Division of Cardiovascular Medicine, Stanford University School of Medicine, Falk Cardiovascular Research Building, 300 Pasteur Drive, Stanford, CA 94305, USA

Received 21 April 2011; revised 21 March 2012; accepted 3 April 2012; online publish-ahead-of-print 1 June 2012

Perspectives

Gray JA. The Lancet 2013

The Art of Medicine

The shift to personalised and population medicine

What To Do With Functionally Insignificant Plaque?

Even better Diagnosis of Vulnerability ? ...

OCT:

Future Directions Improved Quantification: Fibrous Cap

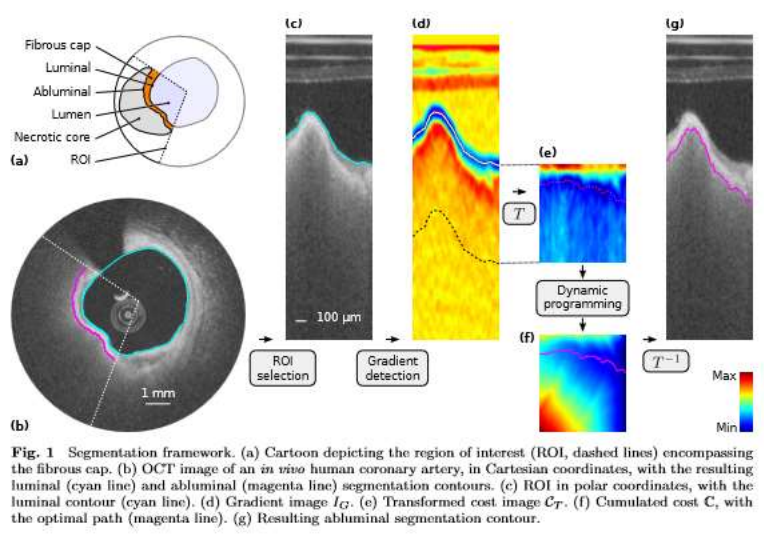
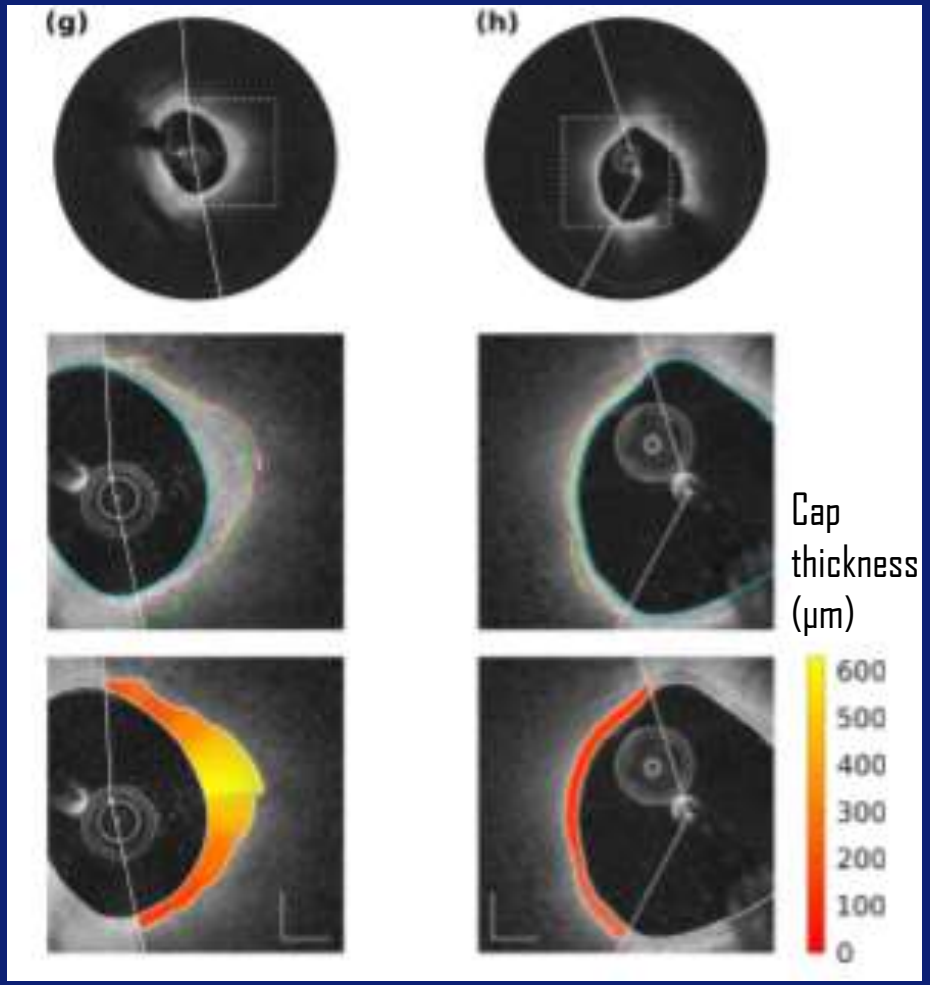


Fig. 1 Segmentation framework. (a) Cartoon depicting the region of interest (ROI, dashed lines) encompassing the fibrous cap. (b) OCT image of an *in vivo* human coronary artery, in Cartesian coordinates, with the resulting luminal (cyan line) and abluminal (magenta line) segmentation contours. (c) ROI 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.

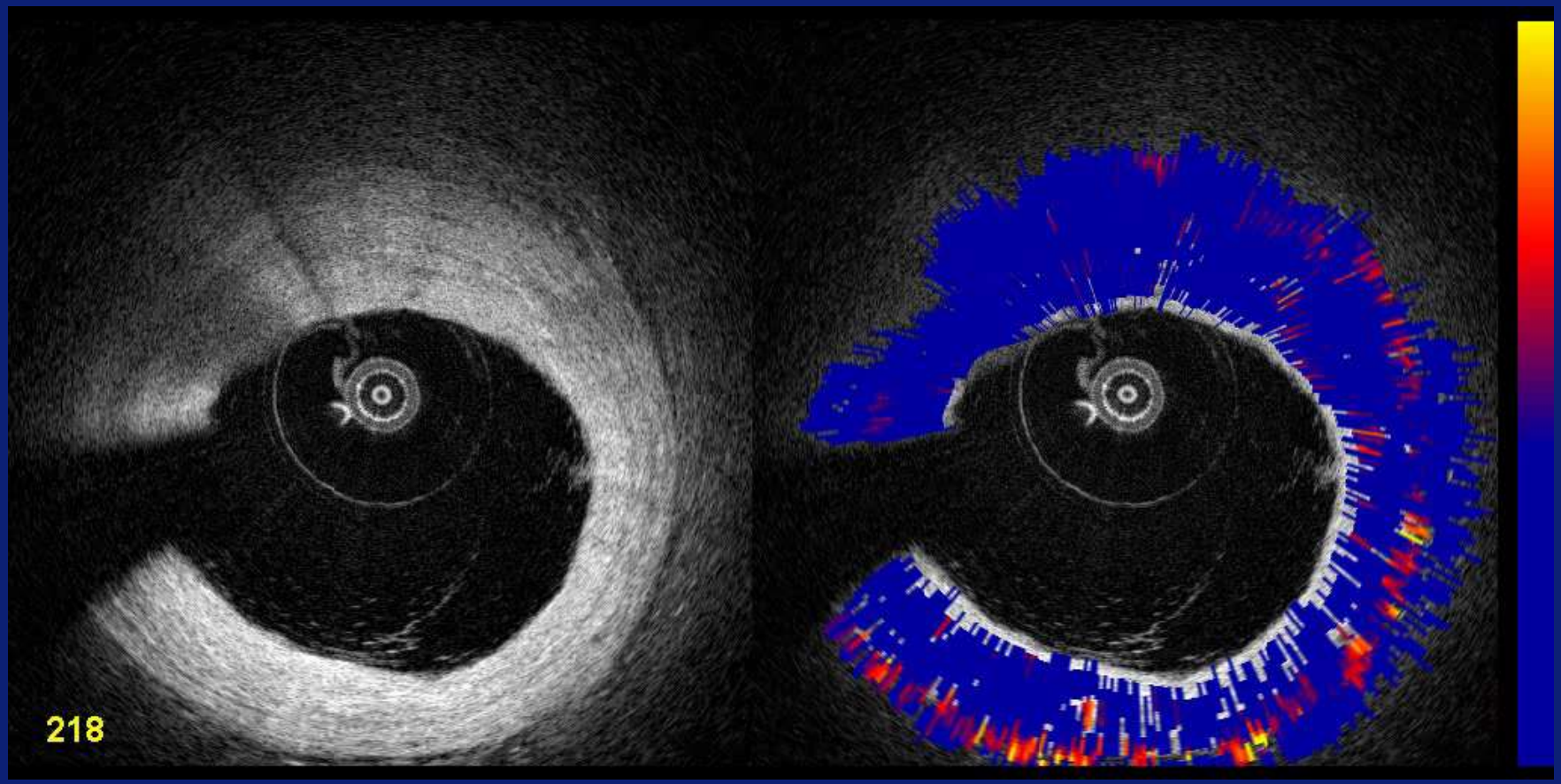


Fully automated segmentation of fibrous cap thickness

Zahnd G et al. presented at MICCAI 2014

OCT:

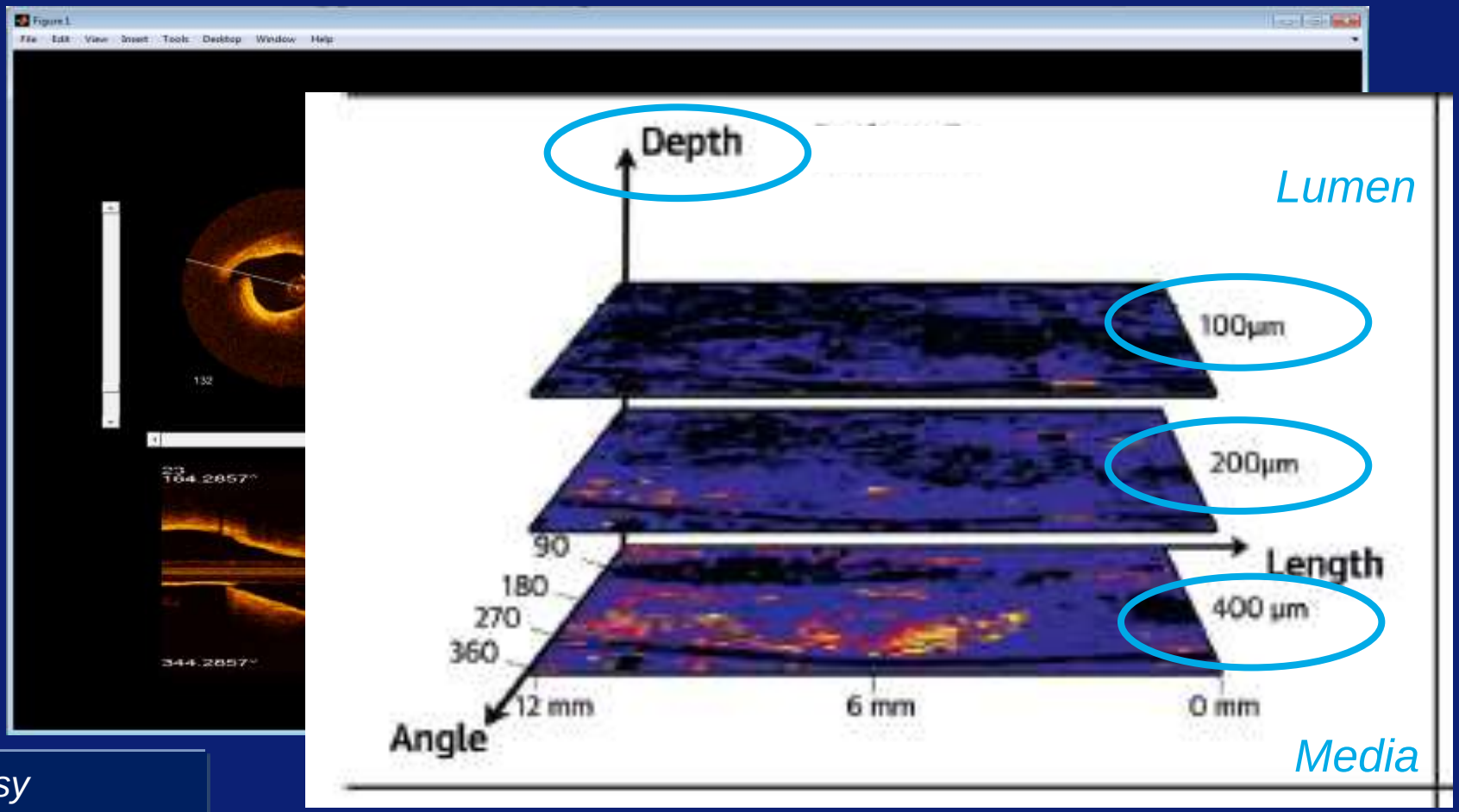
Future Directions Tissue Characterization: Optical Attenuation Imaging



Courtesy Gijs van Soest, Biomedical Engineering, EMC

OCT:

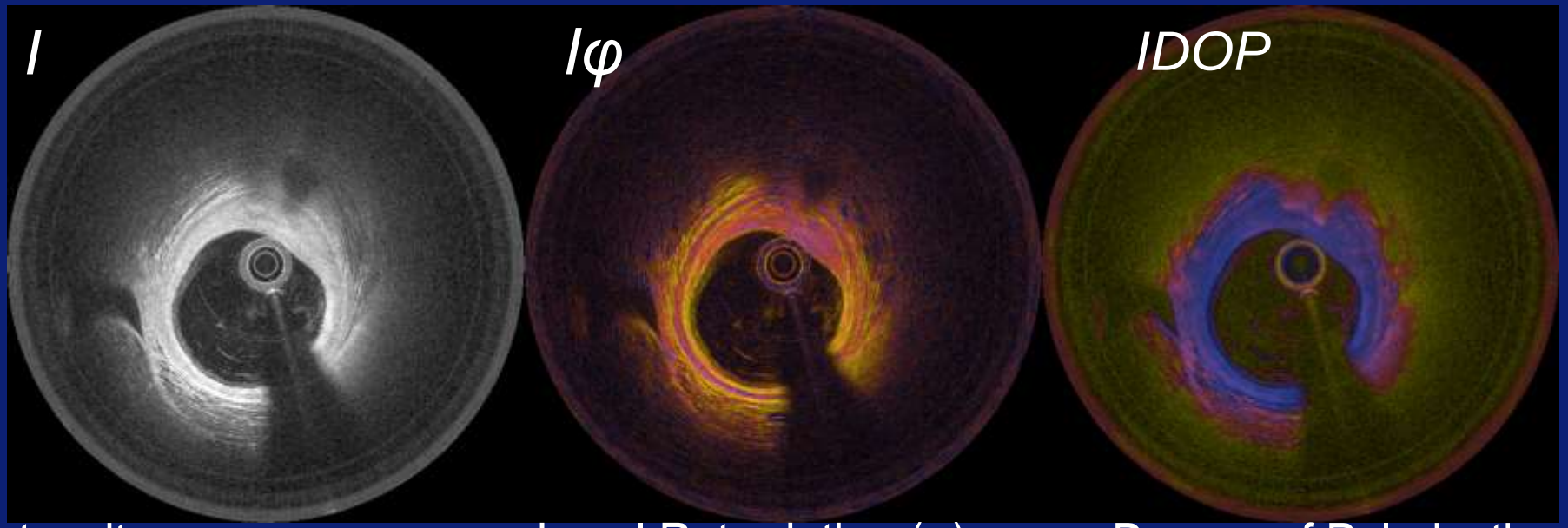
Future Directions Tissue Characterization: Optical Attenuation Imaging



Courtesy
M. Gnanadesigan
T. Kameyama

OCT:

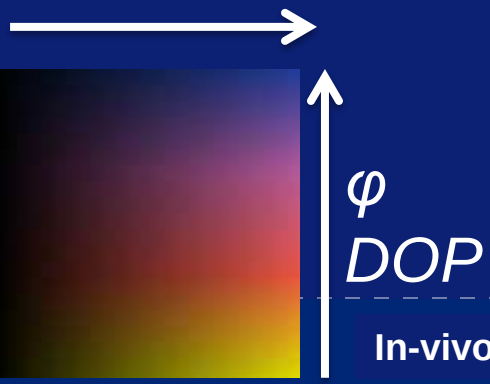
Future Directions Tissue Characterization: Polarization Sensitive Imaging



Intensity

Local Retardation (φ)

Degree of Polarization (DOP)



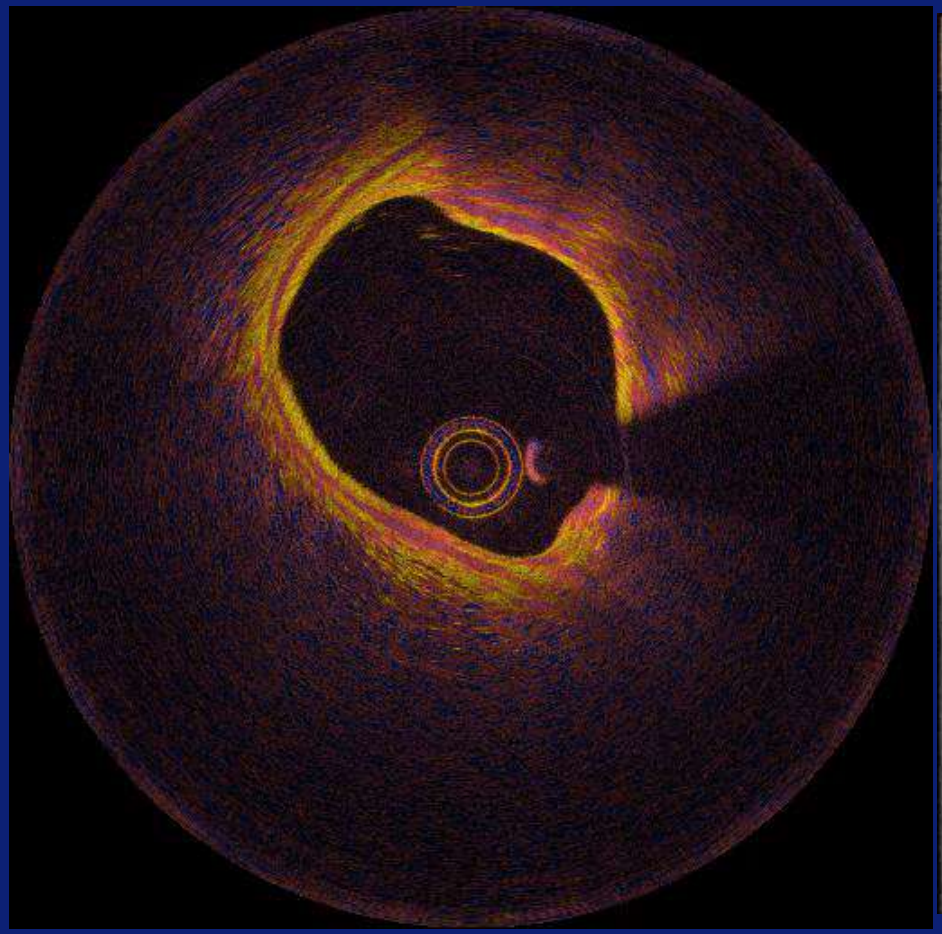
-Local retardation (high) reveals collagen

-DOP (low) hints at foam cells, lipid, macrophages

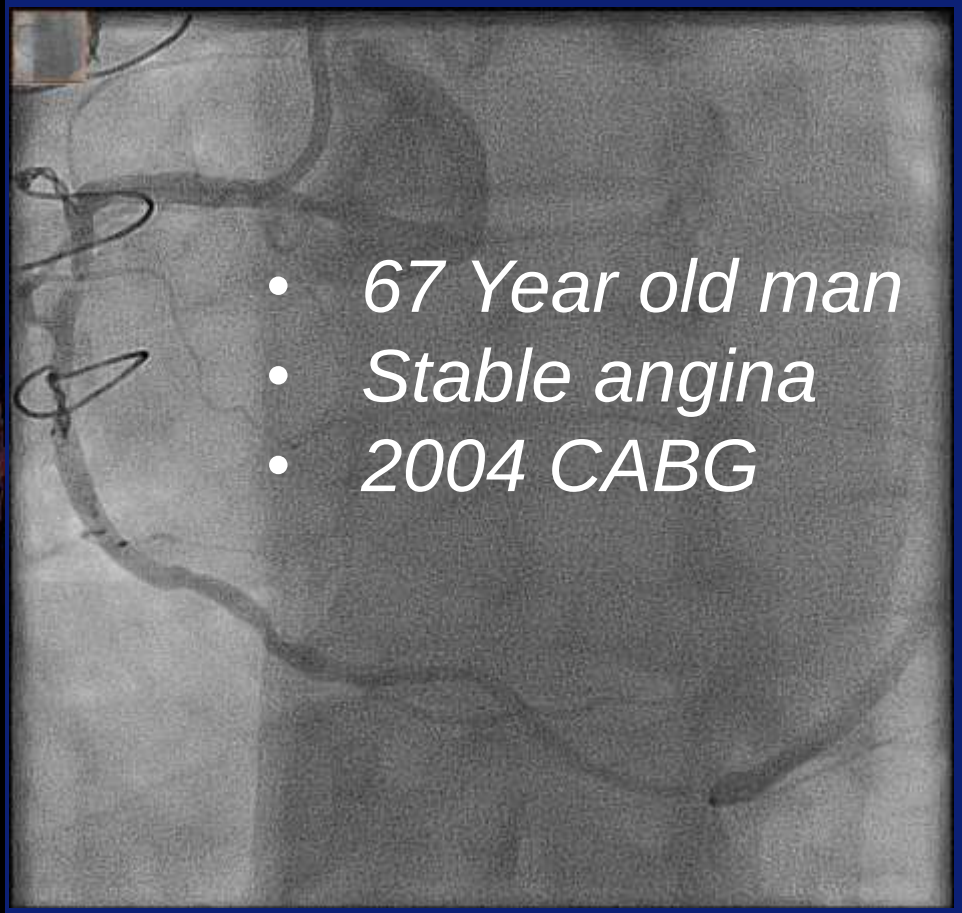
In-vivo human coronary; in cooperation with Villinger M, Bouma B, MGH Boston, USA

OCT:

Future Directions Tissue Characterization: Polarization Sensitive Imaging



Local Retardation (φ)

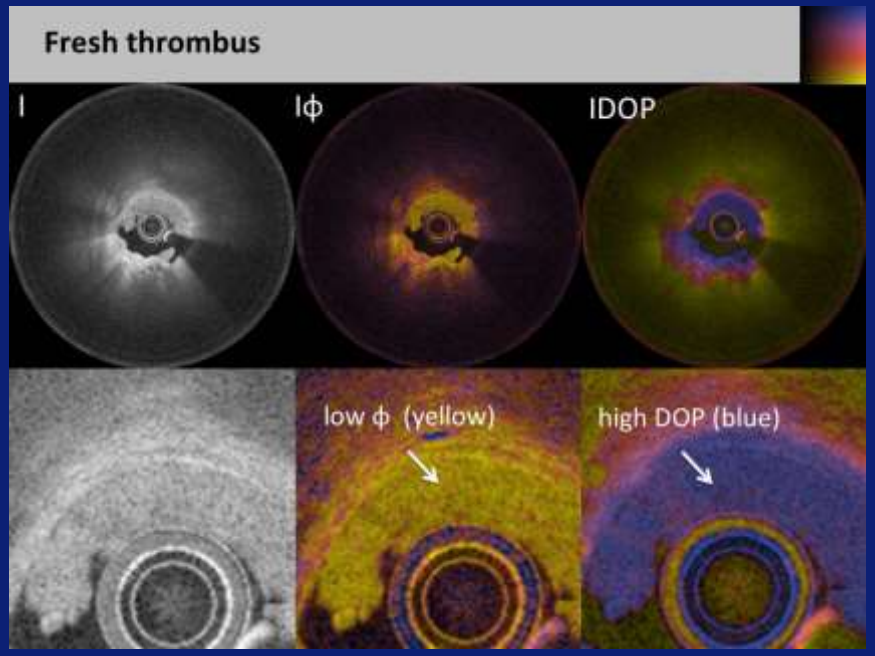


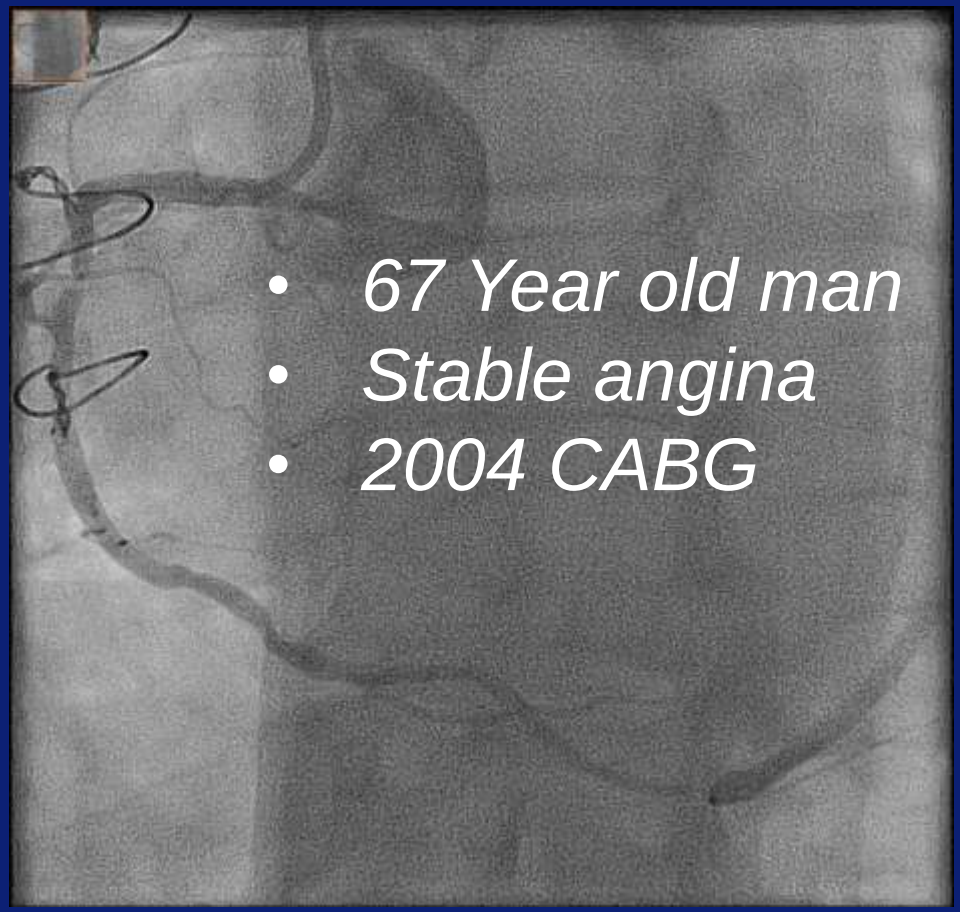
- *67 Year old man*
- *Stable angina*
- *2004 CABG*

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

OCT:

Future Directions Tissue Characterization: Polarization Sensitive Imaging



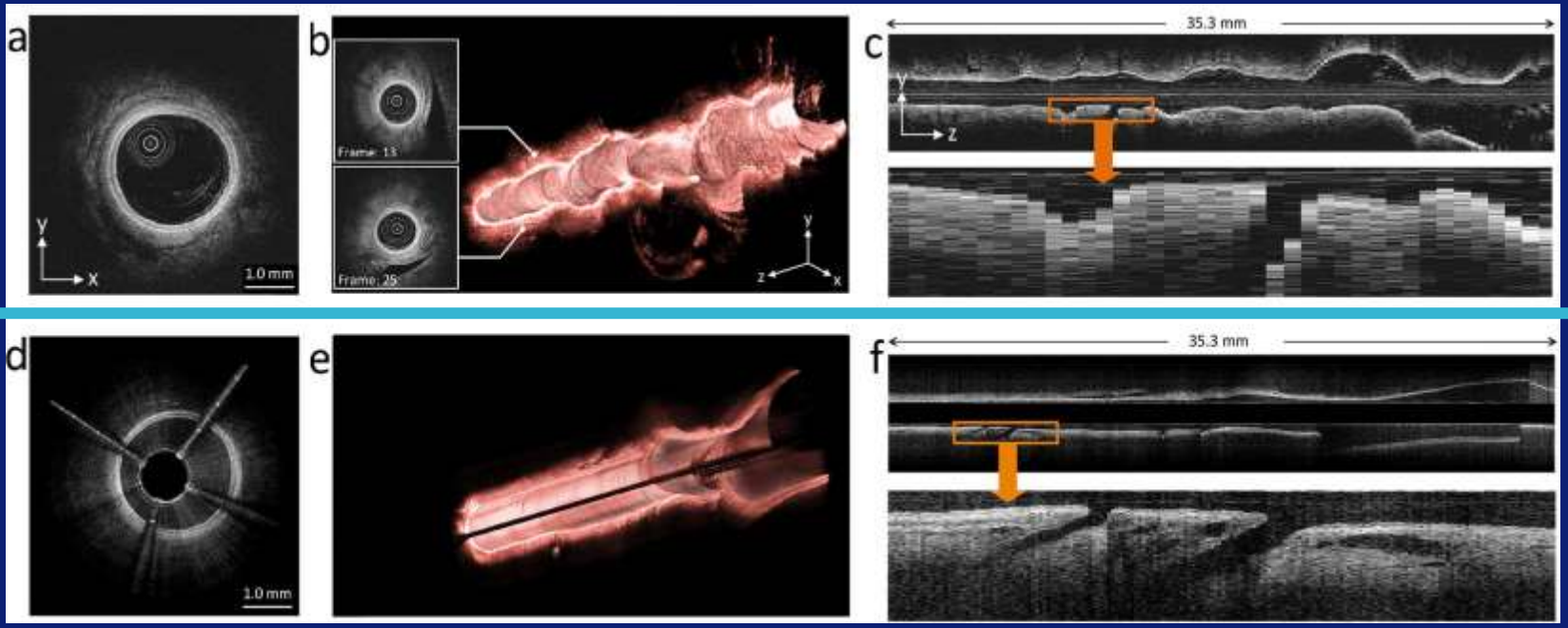


In-vivo human coronary; in cooperation with Villinger M, Bouma B, MGH Boston, USA

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).

Thank you for your attention!

PhD Students

A. Karanasos
J.M. Fam
B.C. Zhang
J. van der Sijde
N. van Ditzhuijsen

Interventional Cardiology

J. Ligthart
K. Witberg
R. Diletti
R.J. van Geuns
P. de Jaegere
N. van Mieghem
M. Valgimigli
F. Zijlstra

Experimental Cardiology

H. van Beusekom

Hemodynamics Laboratory

J. Wentzel
F. Gijsen

Bioengineering

G. van Soest
A.F.W. van der Steen

Imaging Group

N. Bruining
S. de Winter
K. Sihan