The Future of Coronary Imaging and Coronary Physiology

Patrick W. Serruys

Imperial College, London, United Kingdom

Taku Asano

Academic Medical Center, Amsterdam, The Netherlands

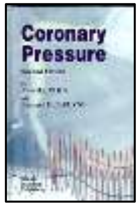
Yoshinobu Onuma

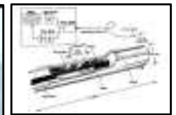
Erasmus Medical center, Rotterdam, The Netherlands

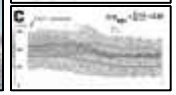
Tuesday, May 1,2018 10:45 - 11:00
Coronary theater, Level 1

Erasmus MC
Universitair Medisch Centrum Rotterdam

Part 1:
Future of physiology







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Velocity wire
Flow-velocity validation

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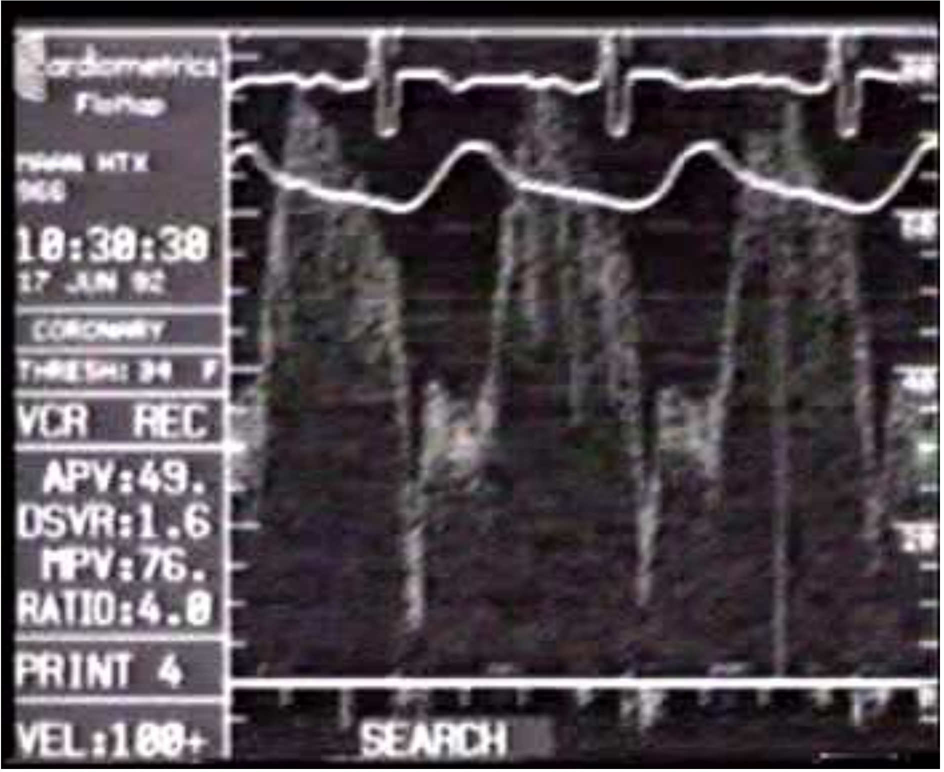
- 1993 P.W. Serruys (Double-wire Pressure-velocity)
- 1993 Håkan Emanuelsson, P.W. Serruys (SFR)
- 1993 Carlo Di Mario, P.W. Serruys (Hyperemic Index)
- 2004 M. Siebes, J.J Piek (Single wire Pressure-velocity)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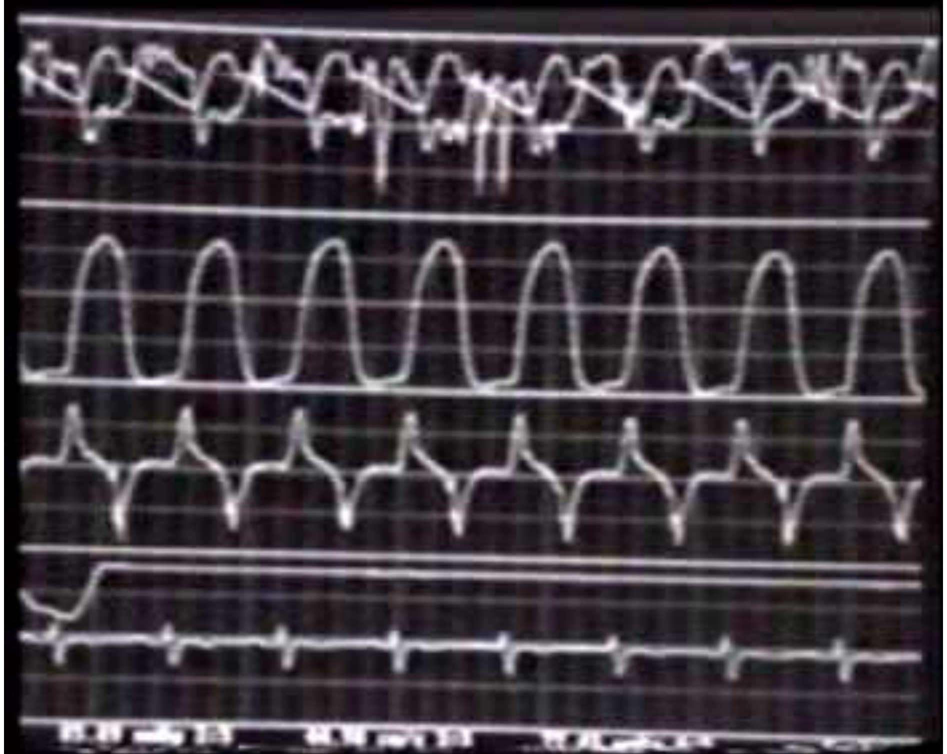

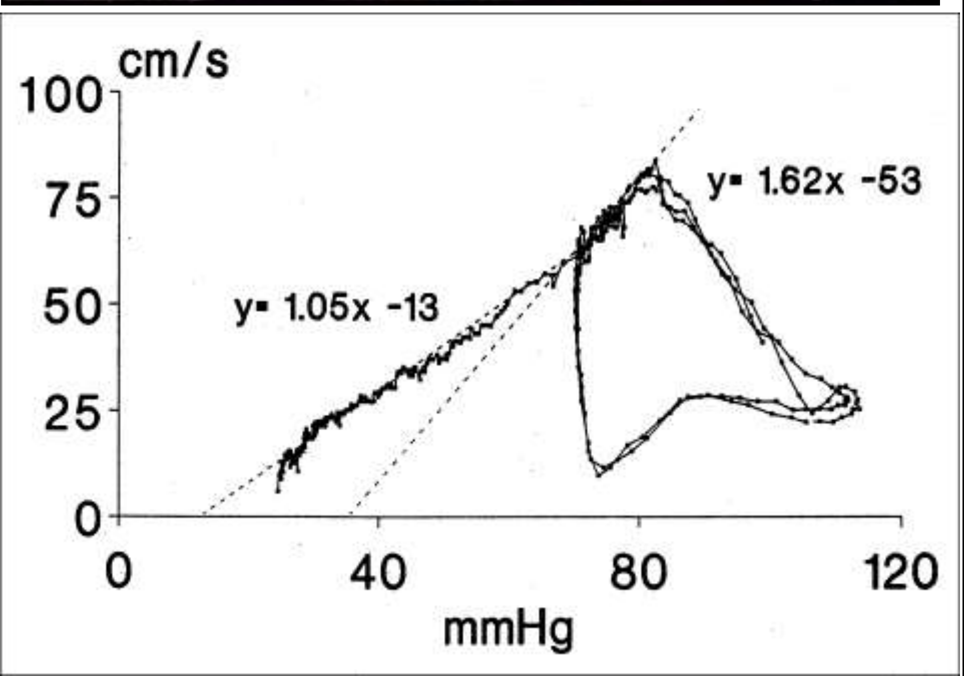
cm/s
100
75
50
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0
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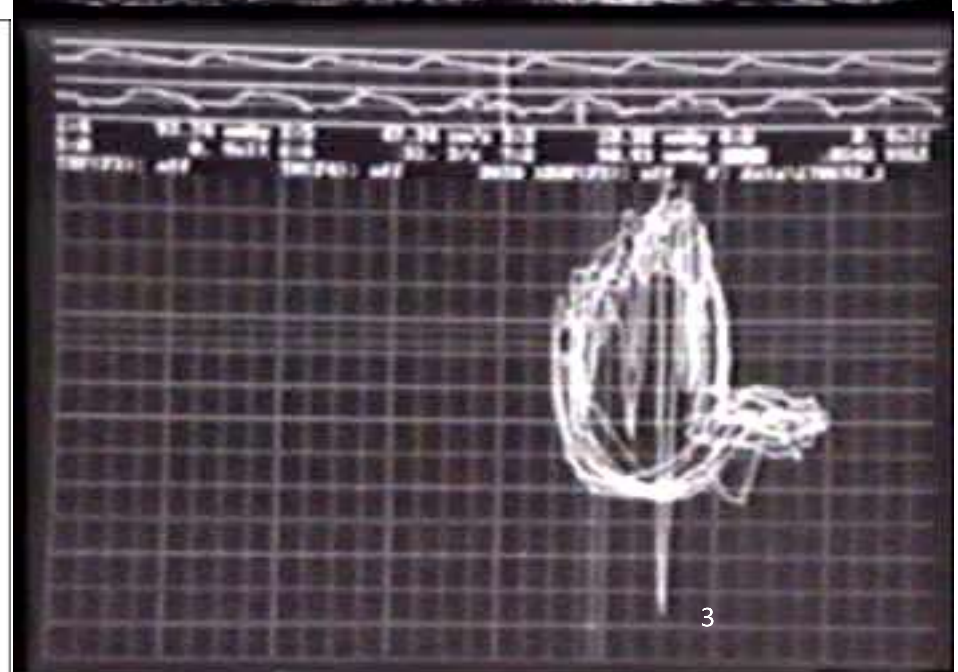
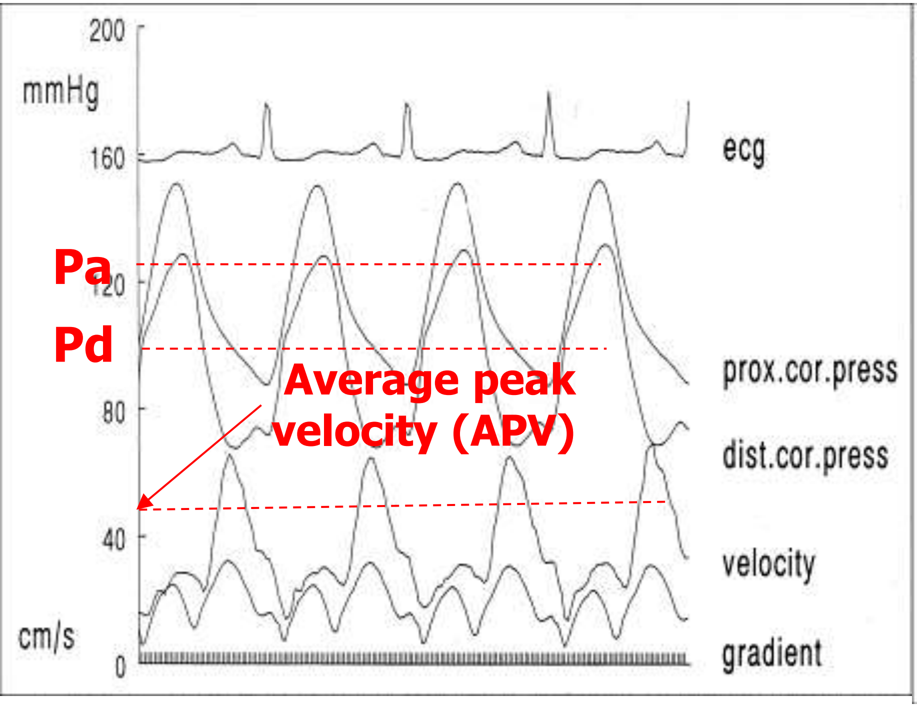
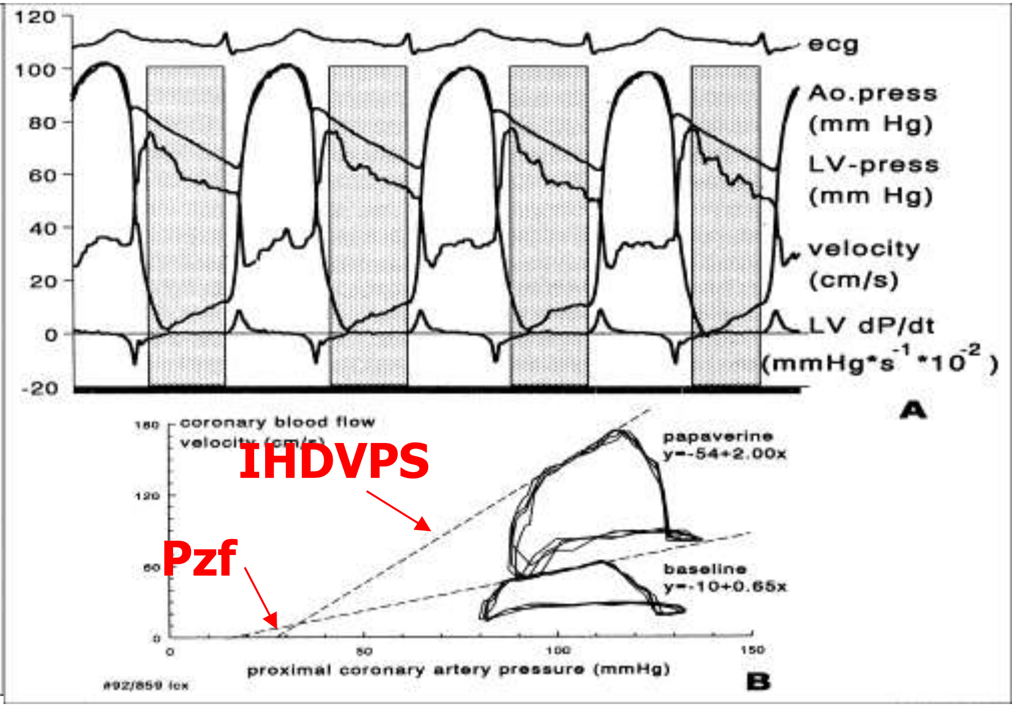
40
80
120
mmHg
y= 1.62x -53
y= 1.05x -13



Hemodynamic parameters of PV analysis





Intracoronary Pressure and Flow Velocity with Sensor-Tip Guidewires: A New Methodologic Approach for Assessment of Coronary Hemodynamics Before and After Coronary Interventions

P.W. Serruys et al., Am J Cardiol 1993;71:41-53

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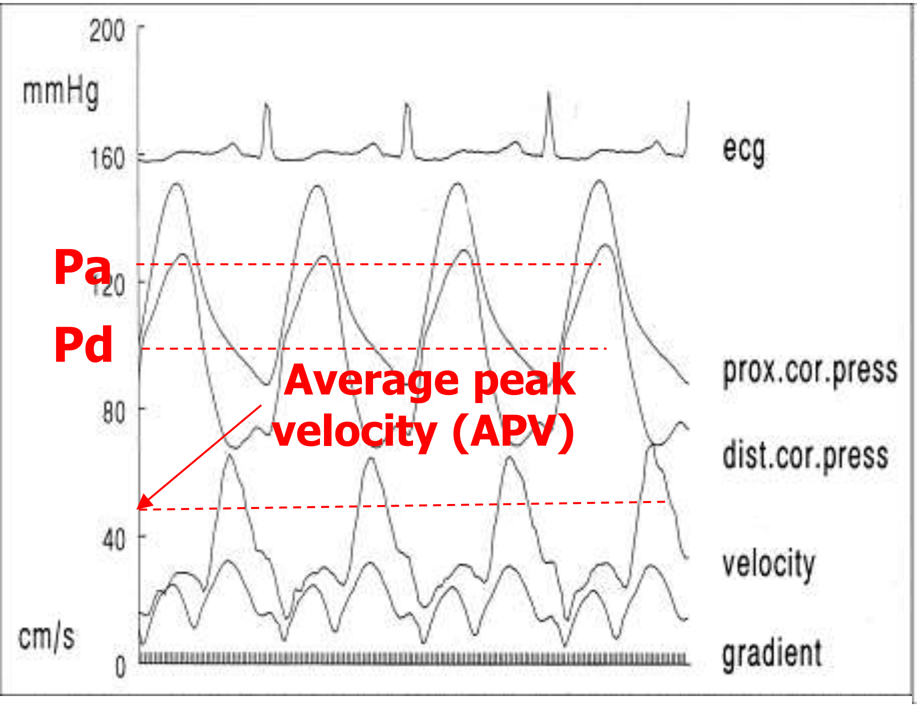
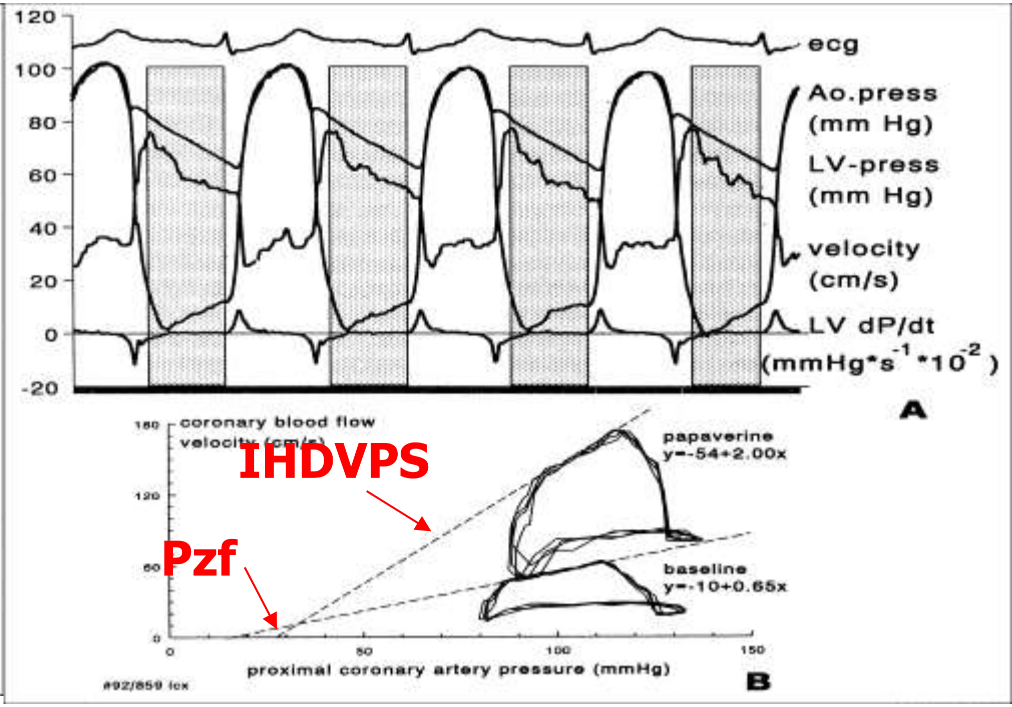




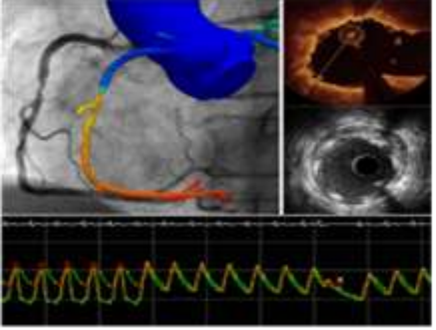
$$\textbf{FFR} = \frac{Pd\ (hyperemic)}{Pa\ (hyperemic)}$$

$$\textbf{Stenotic resistance (SR)} = \frac{Pa - Pd}{APV}$$

$$\textbf{CFR} = \frac{APV\ (hyperemic)}{APV\ (rest)}$$

(CFVR)

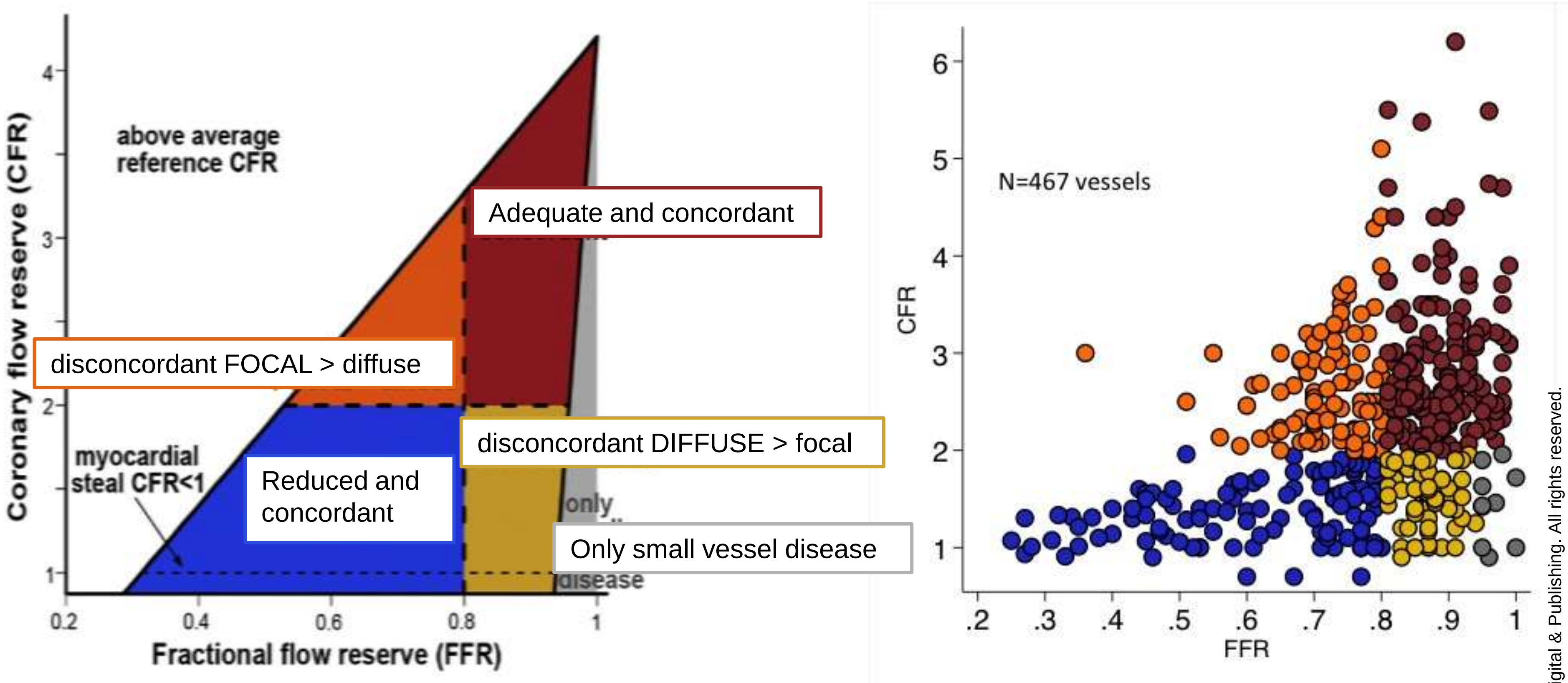
$$\textbf{Microvascular resistance (MR)} = \frac{Pd}{APV}$$



- SECOND EDITION -

CORONARY STENOSIS IMAGING, STRUCTURE AND PHYSIOLOGY

Edited by Javier Escaned and Patrick W. Serruys



Combined use of intracoronary pressure and flow to assess ischemic heart disease

Mauro Echavarría-Pinto, Tim P. van de Hoef, Hector M. Garcia-Garcia, Enrico Cerrato, Chris Broyd, Patrick W. Serruys, Jan J. Piek, Javier Escaned

Today we are still using these combined parameters (single pressure-velocity wire) to compare at 3 years Xience and ABSORB in an attempt to understand their different impact on physiology

Conventional indices:

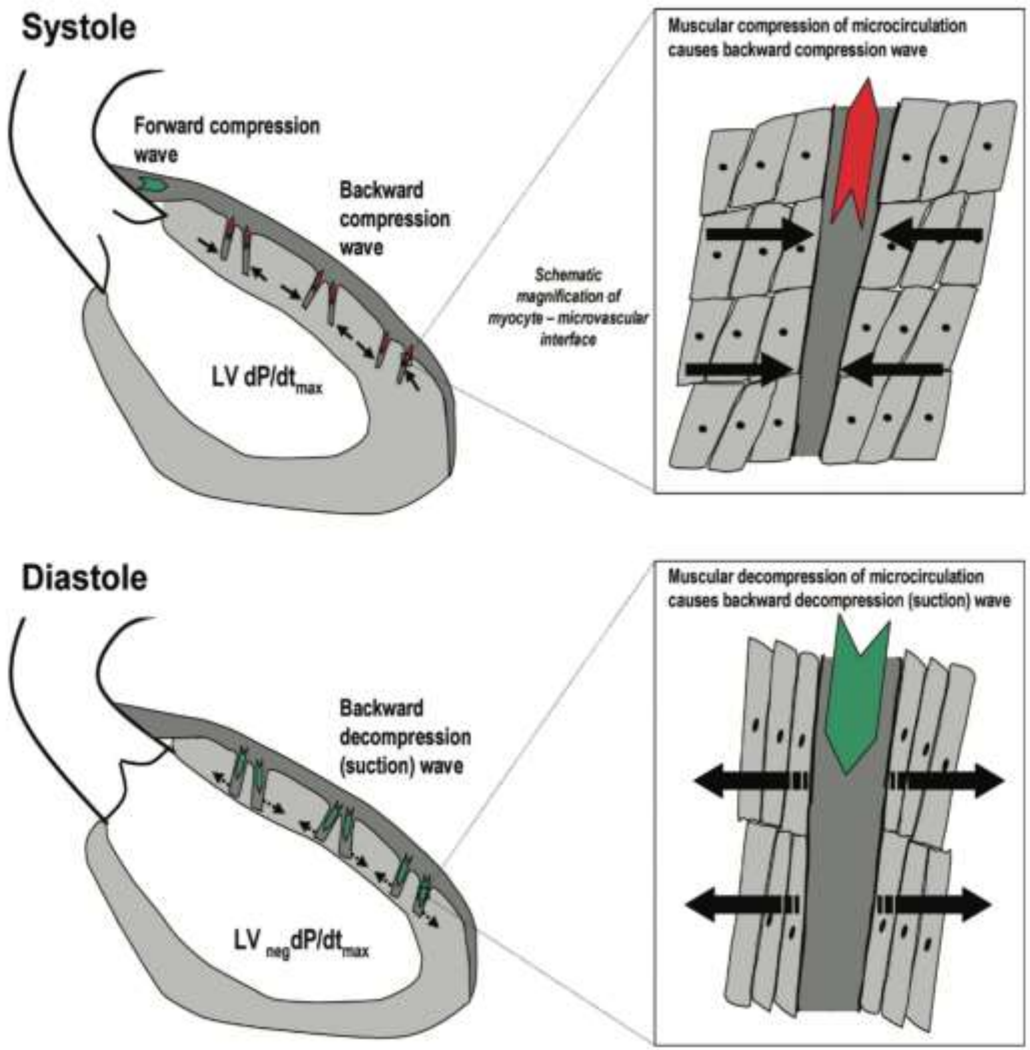
- FFR
- Coronary flow reserve (CFR)
- Hypereamic stenosis resistance (HSR)
- Hyperaemic microvascular resistance (HMR)

Indices derived from pressure-velocity loop analysis:

- Epicardial conductance (C_{epi})
- Microcirculatory conductance (C_{micro})

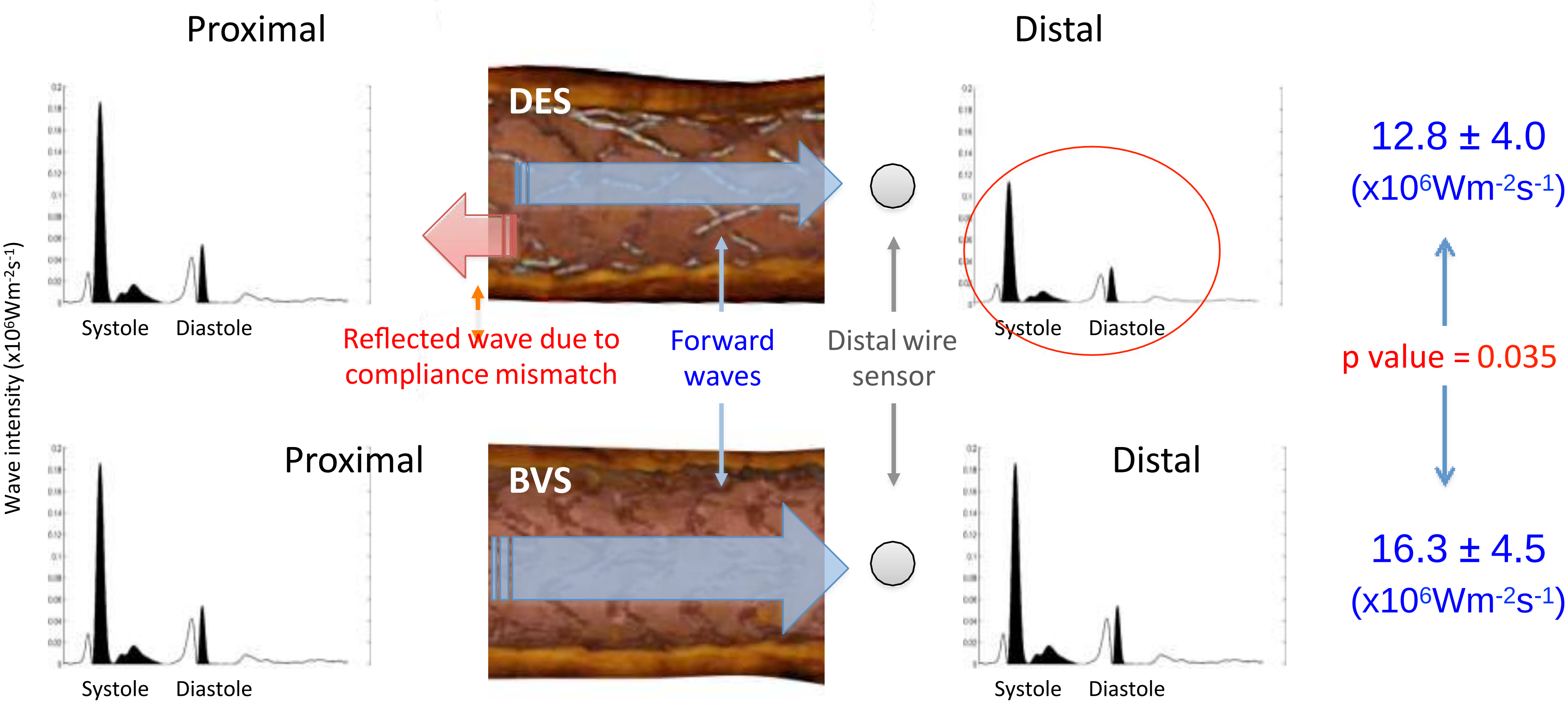
Indices derived from wave intensity analysis:

- Forward compressive waves
- Backward expansion wave



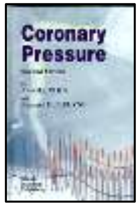
J. Davies Circulation 2012

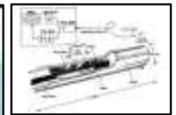
Schematic representation of forward wave transmission through coronary segments with and without a metallic cage

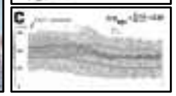


In coronary segments with a metallic DES the magnitude of travelling waves distal to the stent is decreased, as a result of energy loss in the generaNon of secondary reflected waves caused by compliance mismatch .

Part 1:
Future of physiology







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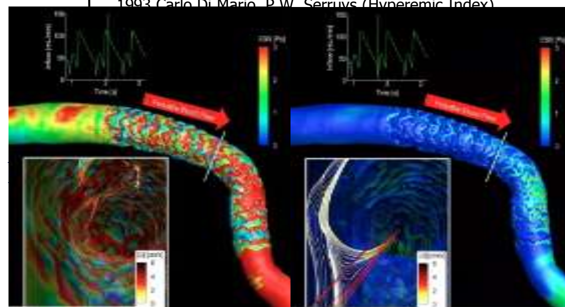


iFR®

ADVISE
ADVISE II
SYNTAX II

iFR®

DEFINE-FLAIR
SWEDEHEART

2001 **ANGUS**
Slager C, P.W. Serruys

Non-Newtonian Pulsatile
Shear-stress microenvironment (fusion OCT/IVUS and angiography).

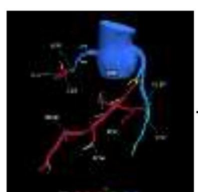
2002 **Shear stress**
Thury A, Wentzel J, P.W. Serruys

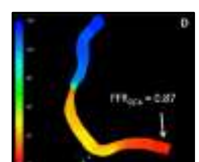
3D Angiography
+
"CFD"
+ Papafaklis, P.W. Serruys
TIMI Frame Count
Tu S

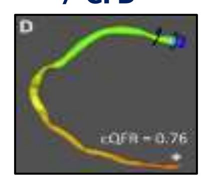
3D Angiography, or
2D Angiography
+
Lance Gould
"≠ CFD"

2010 **FFR$_{CT}$**

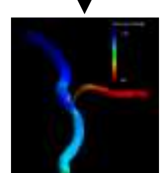
DISCOVER
FLOW
DE FACTO
NXT TRIAL
PLATFORM
SYNTAX III





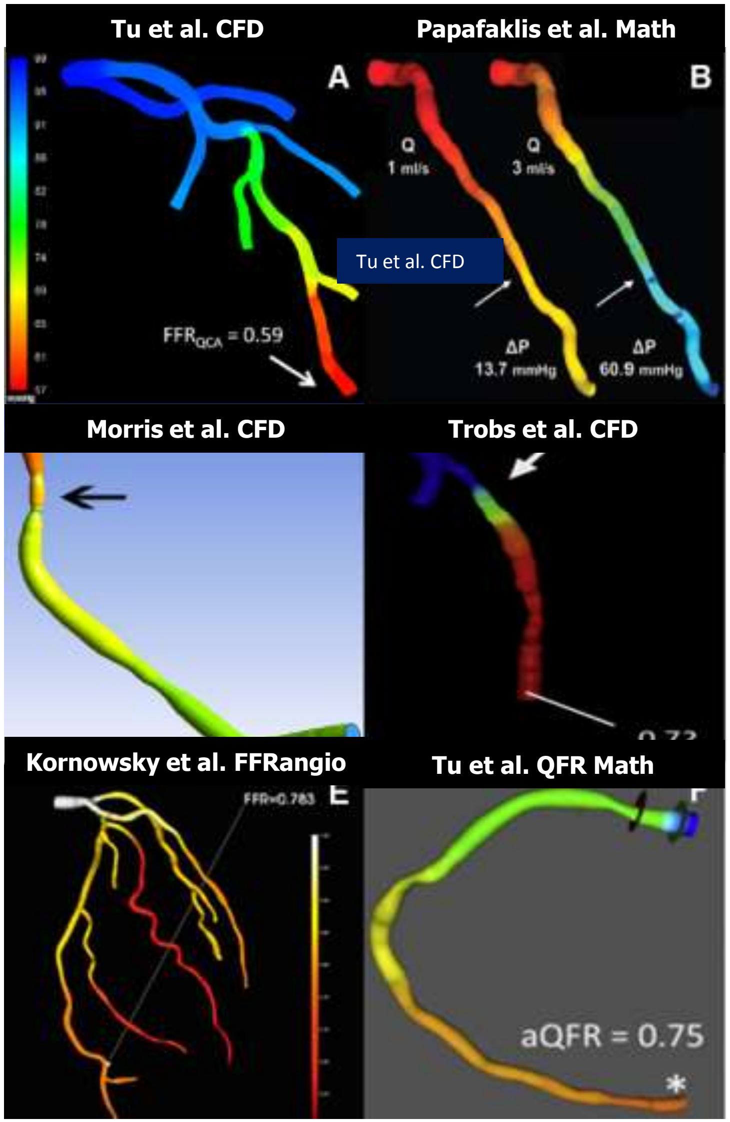


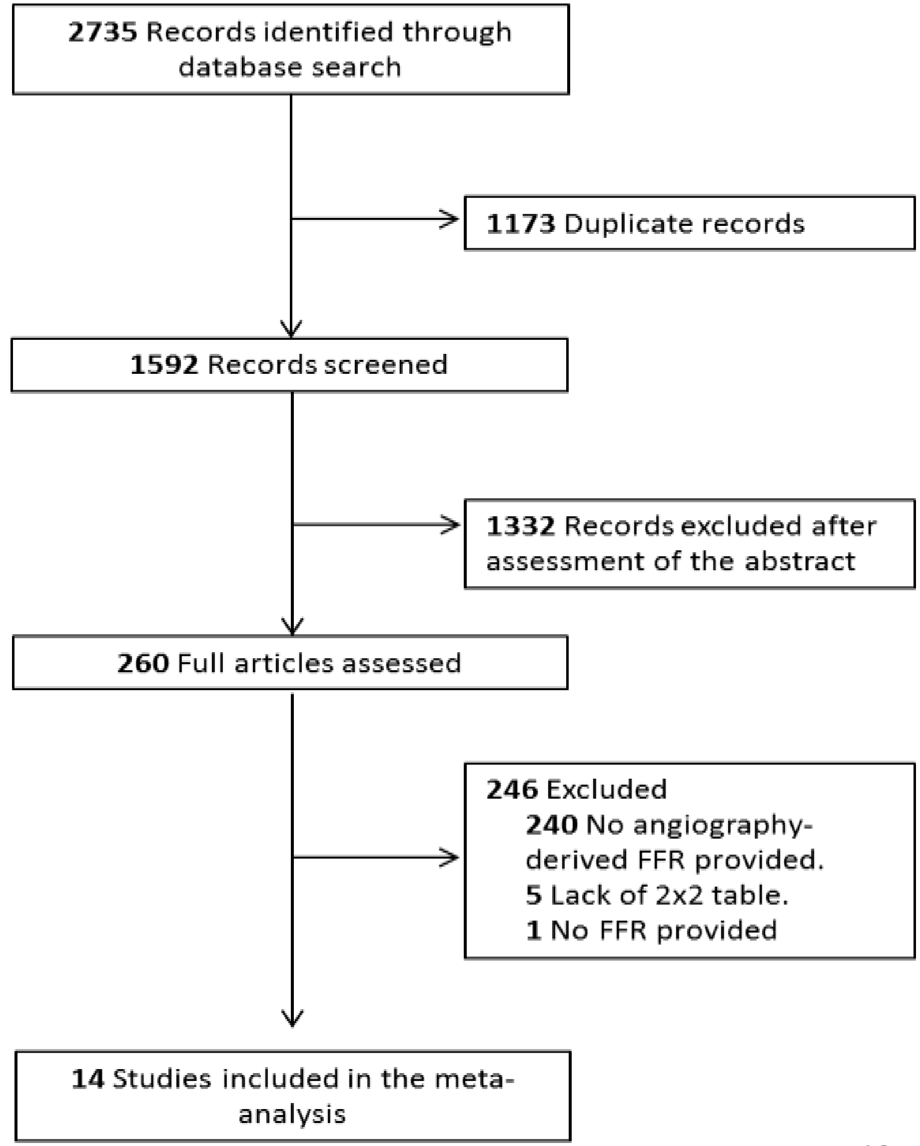
FFR$_{CT}$ PLANNER



3D Bifurcation QCA
CFD
Finite Elements
Navier-Stokes

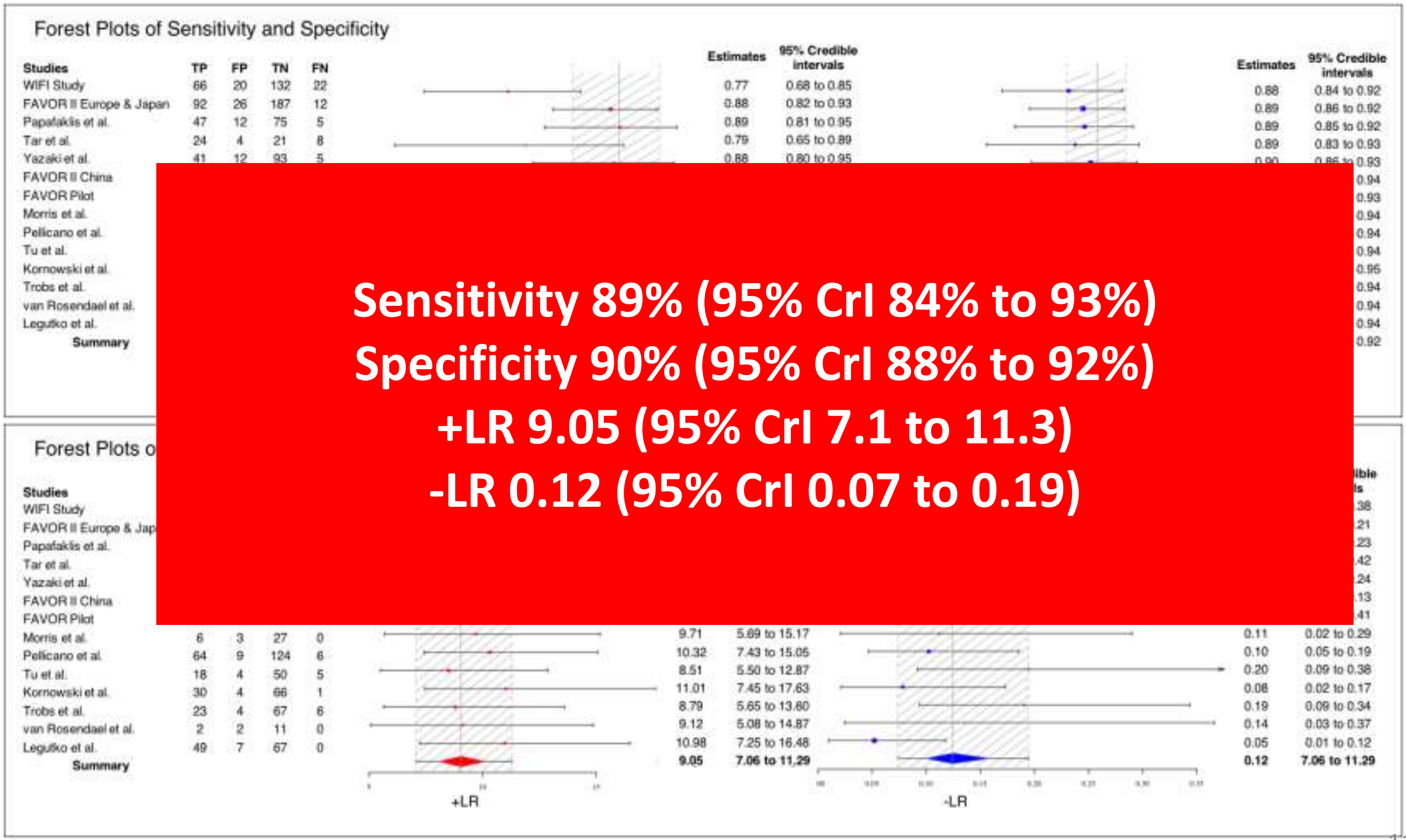
Angiography-derived FFR





Collet et al. under review

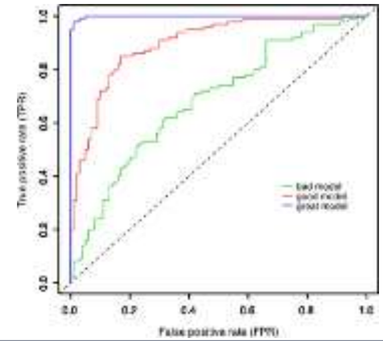
Angio-derived FFR Bayesian Meta-Analysis

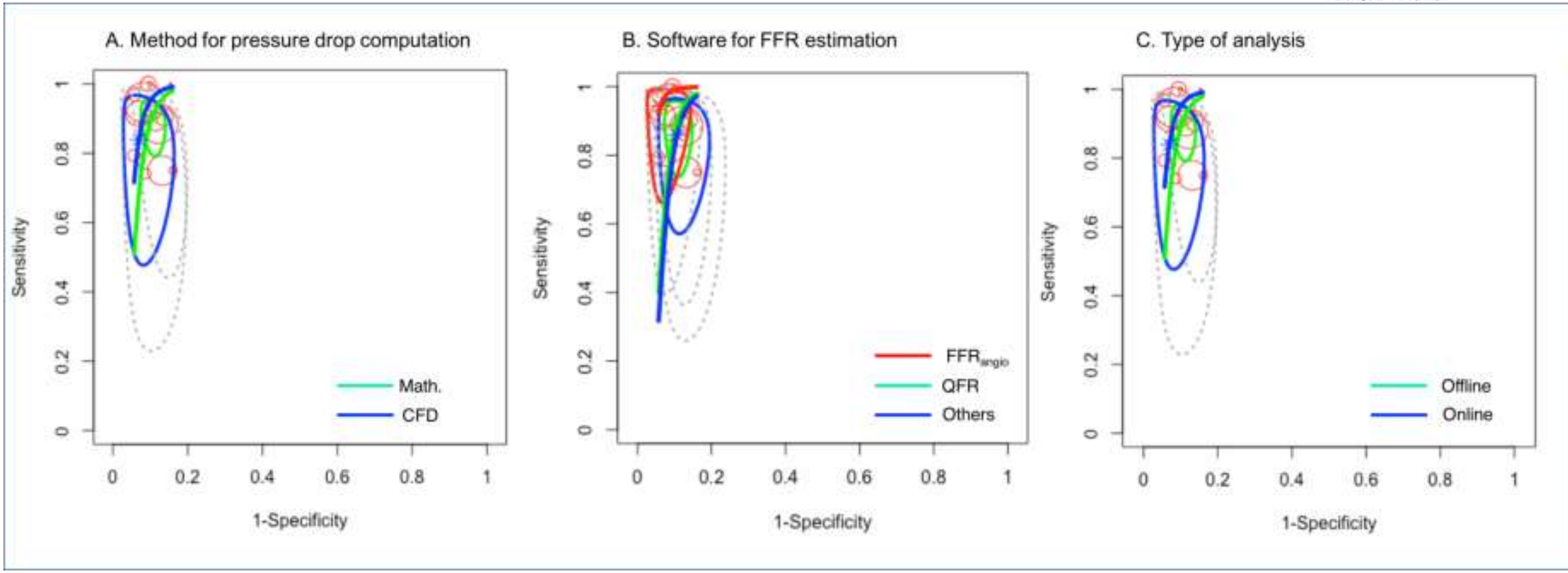


Sensitivity 89% (95% CrI 84% to 93%)
Specificity 90% (95% CrI 88% to 92%)
+LR 9.05 (95% CrI 7.1 to 11.3)
-LR 0.12 (95% CrI 0.07 to 0.19)

Collet et al. under review

Bayesian Meta-regression





No difference in Diagnostic Performance (AUC) between type of method for pressure drop computation, Software or online/offline analysis.

Collet et al. under review

Conclusion in coronary physiology

- Since more than a quarter of century (1993-2018), we have the technology (pressure/velocity wire) to analyze in great details the coronary physiology (epicardial conductance / micro vasculature resistance).

- However, we have no specific treatments for the microcirculation disease (e.g. L-arginine).

- The use of the current single pressure velocity wire is cumbersome, time consuming and costly - will probably remain a research tool.

- ”Color coded angiography” with QFR, virtual FFR and FFR_{angio} etc... will be embraced by busy operators who want to have at low cost and swiftly the “physiological justification” of their treatment of the epicardial vessels.

- When conventional fluoroscopic angiography will be replaced by CT angiography, FFRCT might become a surrogate of the angio and pressure derived FFR.

Part II

Taylor & Francis
Taylor & Francis Group

Expert Review of Medical Devices

ISSN: 1743-4440 (Print) 1745-2422 (Online) Journal homepage: http://www.tandfonline.com/loi/ierd20

What does the future hold for novel intravascular imaging devices: a focus on morphological and physiological assessment of plaque

Yuki Katagiri, Erhan Tenekecioglu, Patrick W. Serruys, Carlos Collet, Athanasios Katsikis, Taku Asano, Yosuke Miyazaki, Jan J Piek, Joanna J. Wykrzykowska, Christos Bourantas & Yoshinobu Onuma

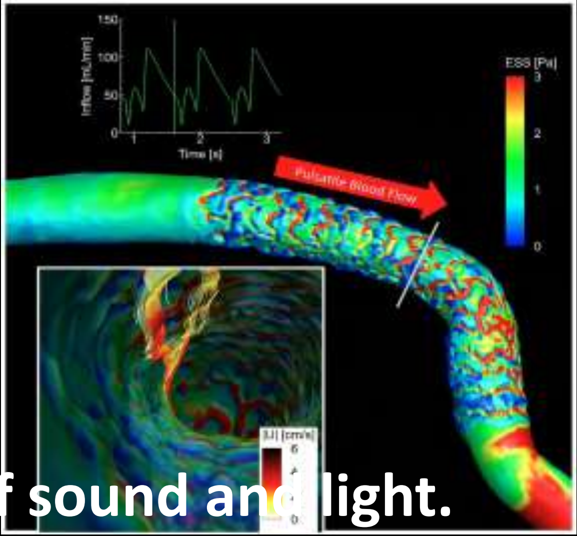
OVERVIEW

1) Fusion methodology of OCT, grayscale IVUS, VH and angiography

2) High definition IVUS

3) OCT

- Ultra high speed (UHS) OCT.
- Hybrid catheter (IVUS and OCT).
- Tissue characterization and 3D.
- Photoacoustic Imaging: The merging of sound and light.



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- Software for collagen detection.
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  Fluorescence lifetime imaging (Flim)

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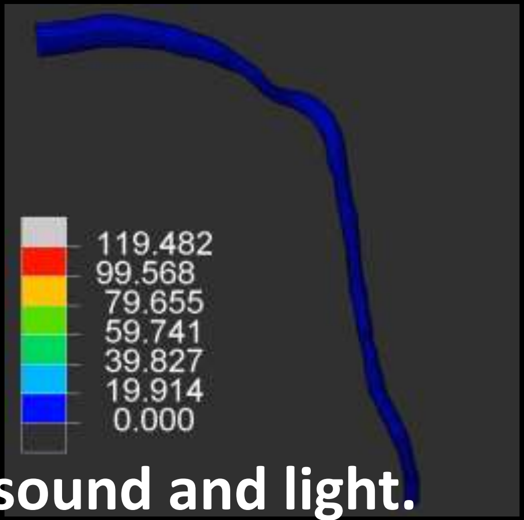

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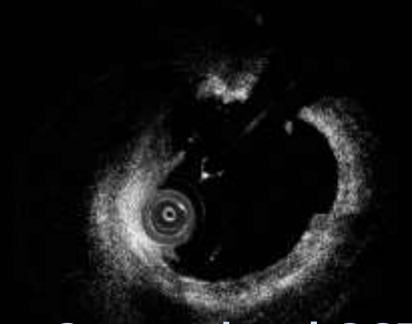

Conventional OCT
100rps

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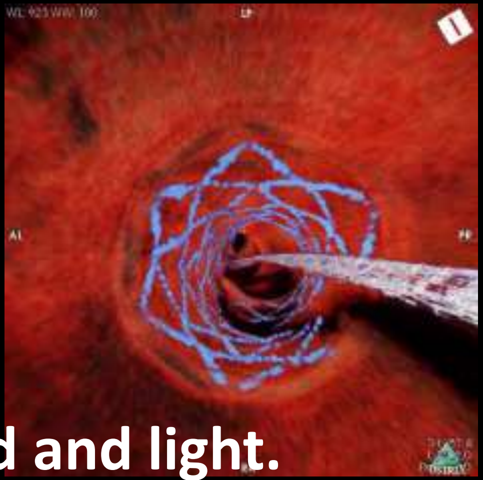

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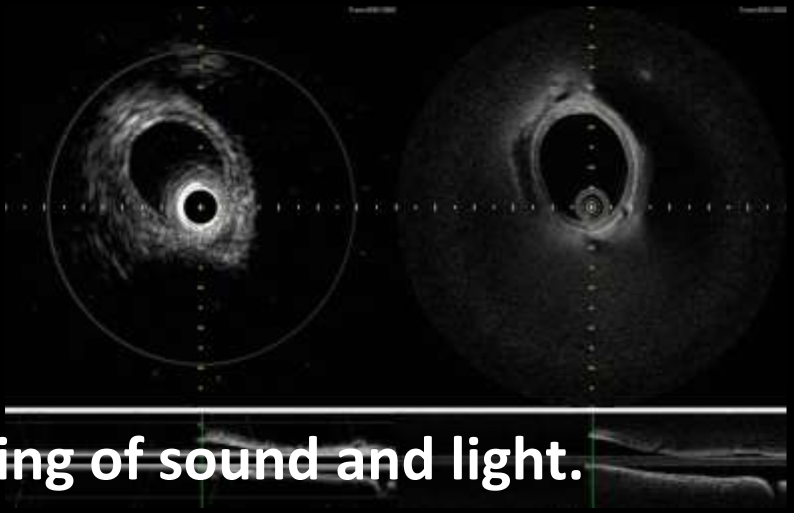

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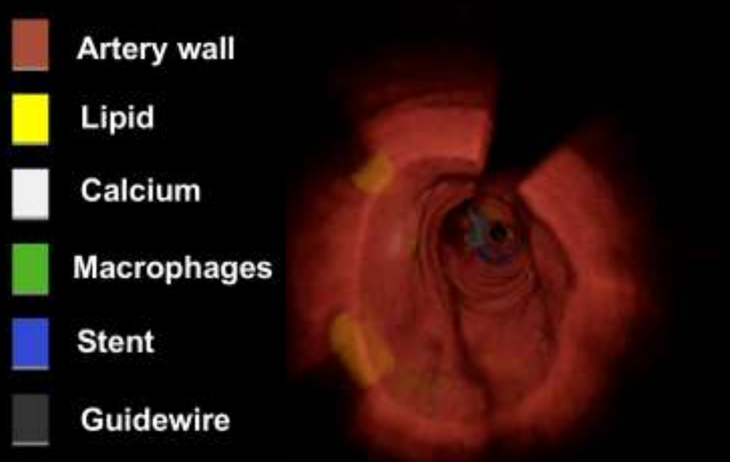

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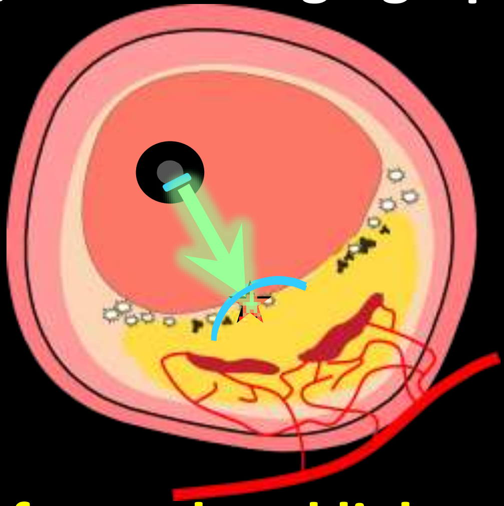

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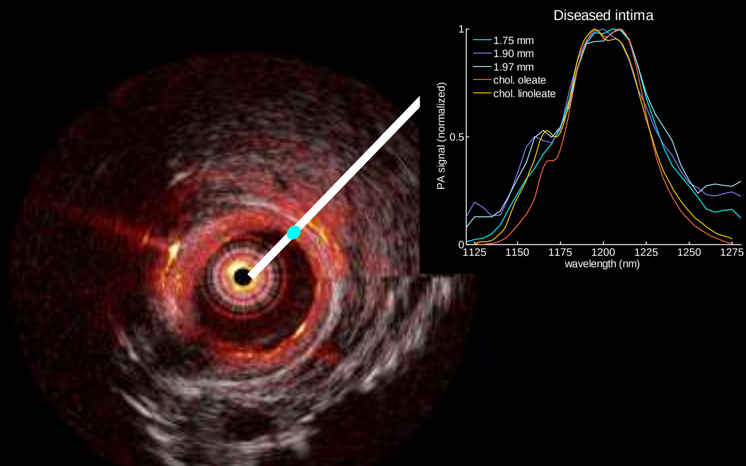

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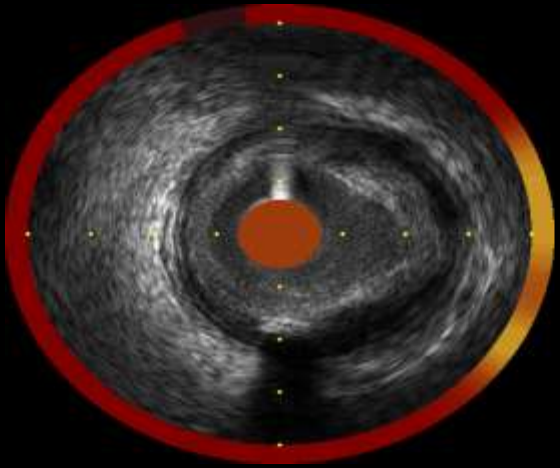

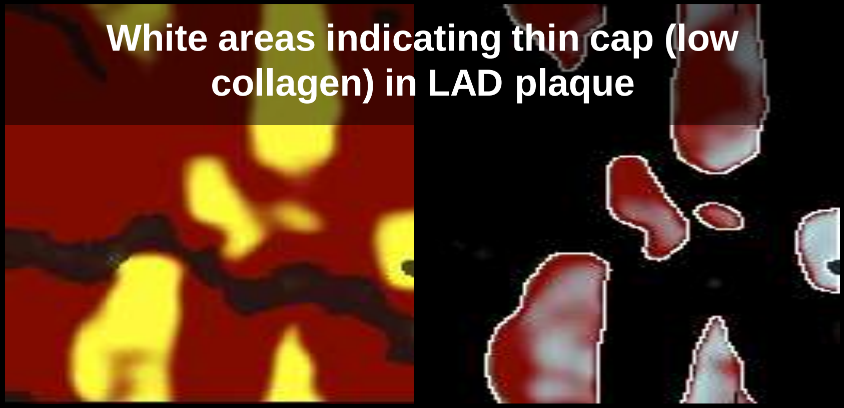

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OVERVIEW

- NIRF imaging agents – Translatable
  - ProSense VM110: All refs above; *EHJ CV imaging* 2016 (Calfon)
  - Indocyanine Green: *Sci Transl Medicine* 2011 (Vinegoni, Botnaru);
    - *JACC CV Imaging* 2016 (Verjans, Osborn)
  - Fibrin (FTP11): *JACC CV Imaging* 2012; *European HJ 2015* (Hara)
  - Oxidized LDL (LO1): *Scientific Reports* 2016 (Khamis, Haskard)
  - Macrophages (CLIO-CyAm7) *Circulation CV Imaging* 2017 (Stein-Merlob)

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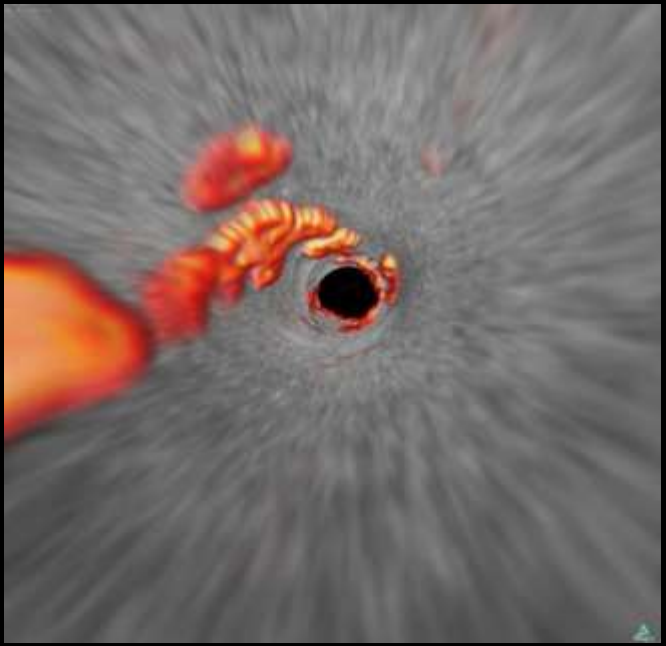

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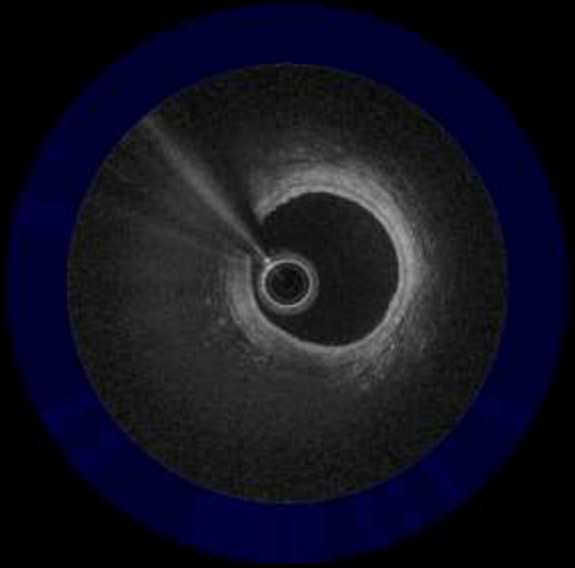

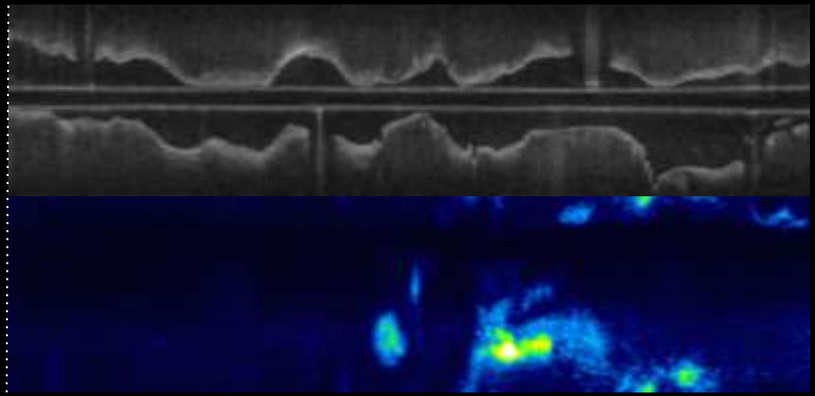

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OVERVIEW

TRFS relies on the assessment of the fluorescence emission **decay time (nsec)** of molecules being excited with pulsed light

- ✓ Elastin: ~4.5 ns
- ✓ Collagen (type I): ~ 6 ns
- ✓ Lipids: ~2 ns* up to ~13 ns^{+}

*: LDL $^{+}$: Cholesteryl linoleate

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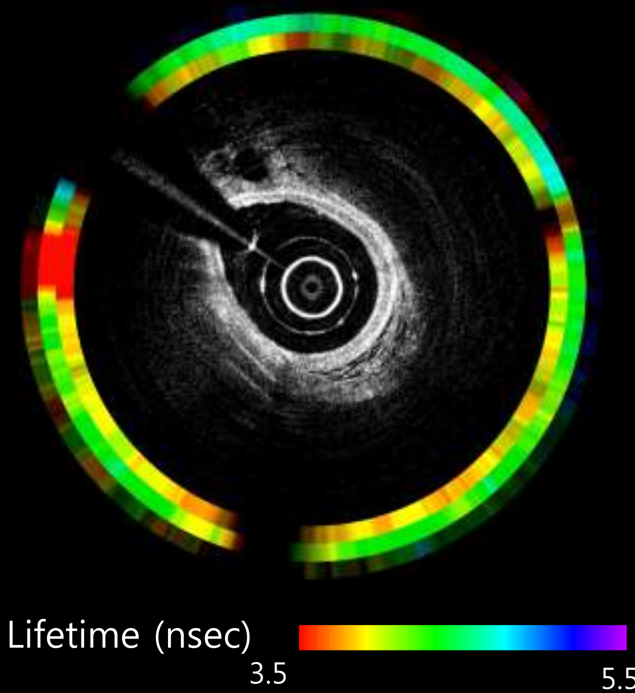
Fluorescence lifetime imaging (Flim)

OVERVIEW

TRFS relies on the assessment of the fluorescence emission decay time (nsec) of molecules being excited with pulsed light



4) Near infrared spectroscopy

- **Software for collagen detection.**
- **Intravascular molecular imaging of plaque biology**
- **Near infrared auto fluorescence spectroscopy.**
- **Time resolved fluorescence spectroscopy.**

  Fluorescence lifetime imaging (Flim)

Conclusion-1

- Hybrid dual-probe catheters allow

1) Evaluation of the plaque micro-features such as:

    cholesterol crystals detected by OCT, inflammation (provided by NIRF), macrophages, and neovessels by IVPA), that were unseen by stand-alone IVUS

2) established markers of plaque vulnerability such as plaque burden and lipid component at the same time.

- Vulnerable plaque detection by new hybrid imaging modalities may have an impact on decision-making in terms of treatment indication and procedural optimization.

Conclusion-2

- Within 5 years, most of the hybrid imaging techniques now in preclinical phase will be utilized in the clinical arena.

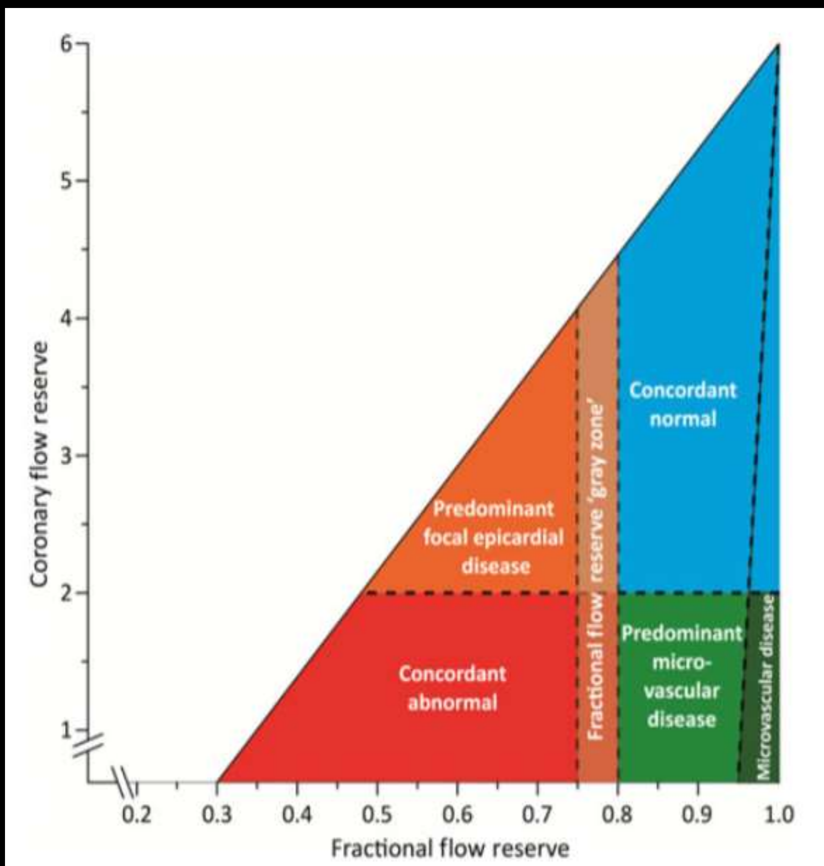
- Software for online blood simulation is likely to be developed that will enable ESS and wall stress calculation.

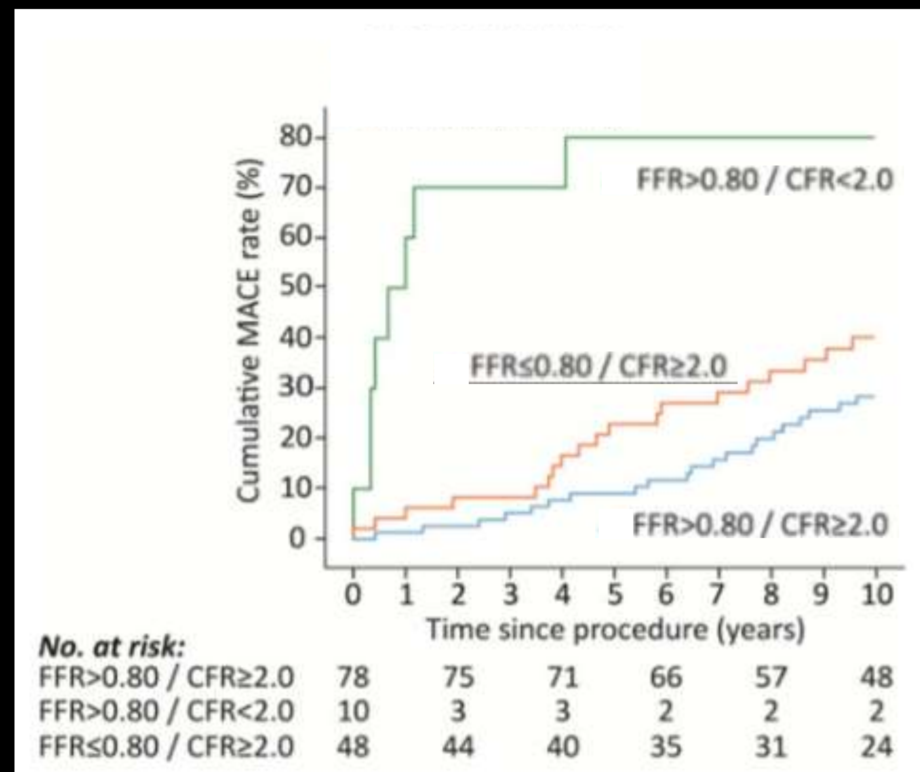
- Future studies of intravascular imaging devices are expected to shed light into the mechanisms of atherosclerotic evolution and precise risk stratification of vulnerable plaque.

Back up files

Physiological Basis and Long-Term Clinical Outcome of Discordance Between Fractional Flow Reserve and Coronary Flow Velocity Reserve in Coronary Stenoses of Intermediate Severity

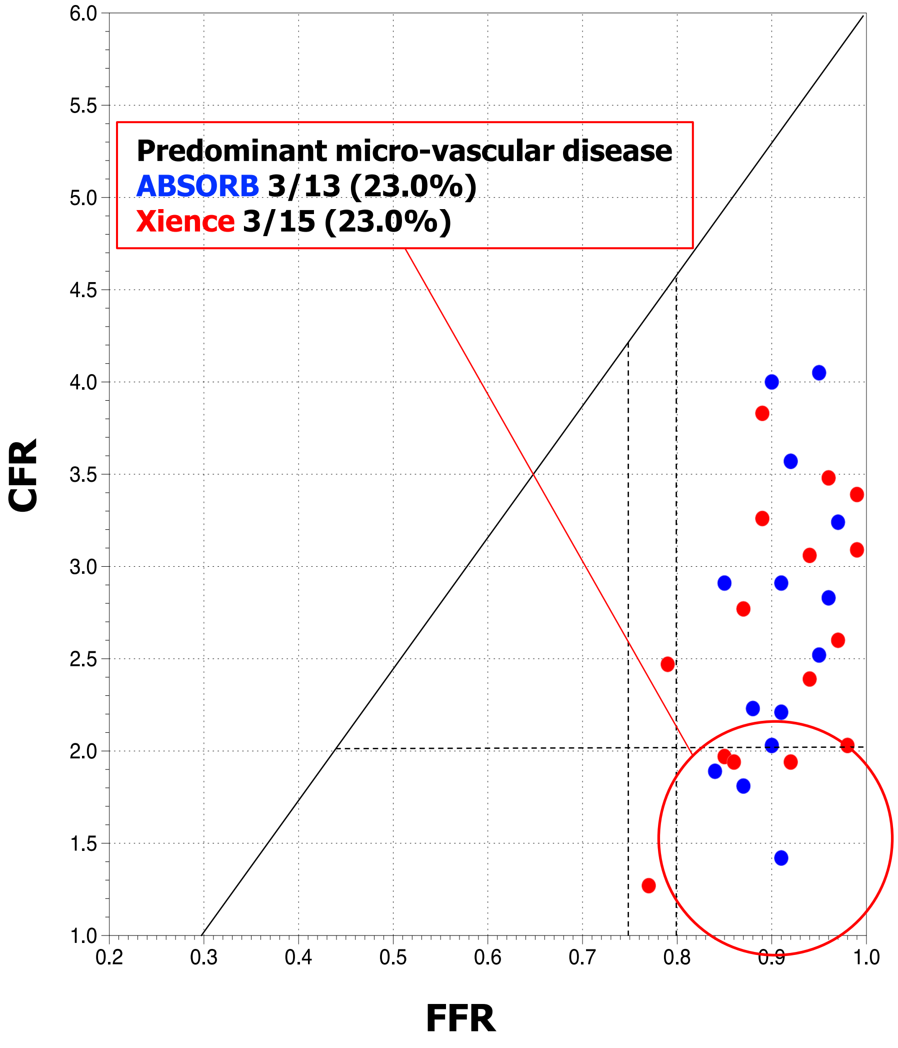
Tim P. van de Hoef, MD; Martijn A. van Lavieren, MSc; Peter Damman, MD, PhD; Ronak Delewi, MD; Martijn A. Piek; Steven A.J. Chamuleau, MD, PhD; Michiel Voskuil, MD, PhD; José P.S. Henriques, MD, PhD; Karel T. Koch, MD, PhD; Robbert J. de Winter, MD, PhD; Jos A.E. Spaan, PhD; Maria Siebes, PhD; Jan G.P. Tijssen, PhD; Martijn Meuwissen, MD, PhD; Jan J. Piek, MD, PhD

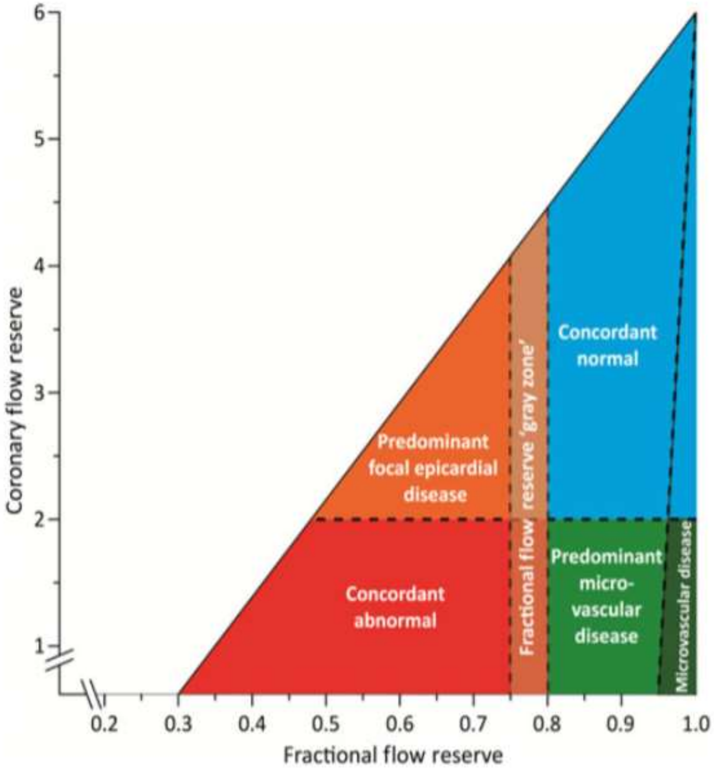




Van de Hoef et al. Circ Cardiovasc Interv 2014

Today we are still using these parameters to compare at 3 years Xience and Absorb in an attempt to understand their different impact on physiology





Circ Cardiovasc Interv 2014;7:301–311

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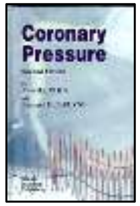
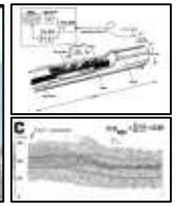
Part 1:
Future of physiology





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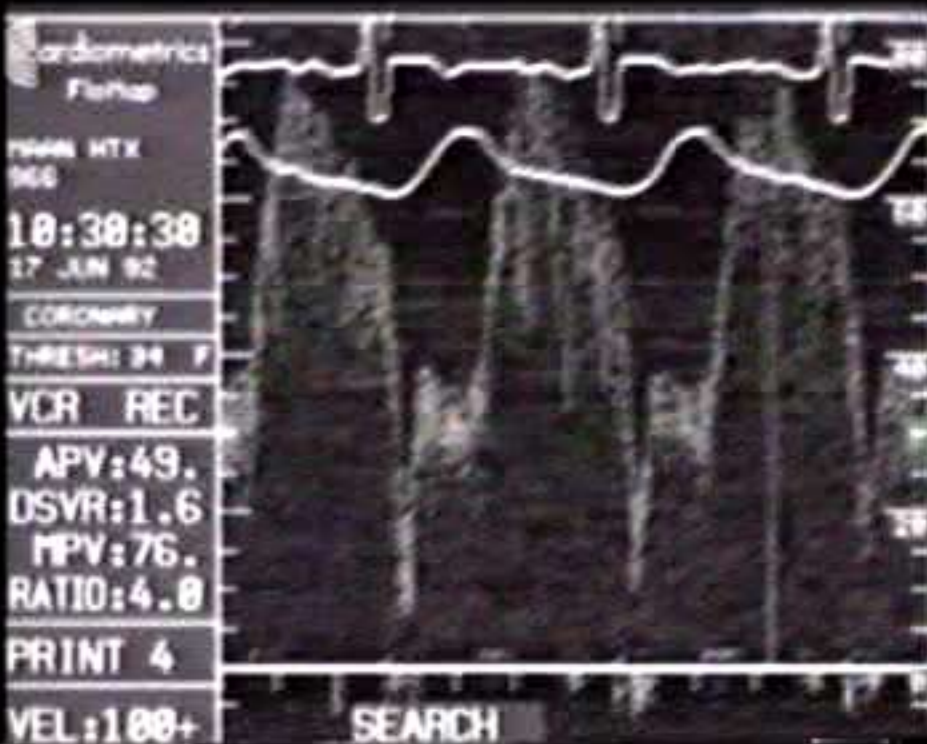
- 1993 Carlo Di Mario, P.W. Serruys (Hyperemic Index)
- 2004 M. Siebes, J.J Piek (Single wire Pressure-velocity)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DSVR:1.6
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PRINT 4
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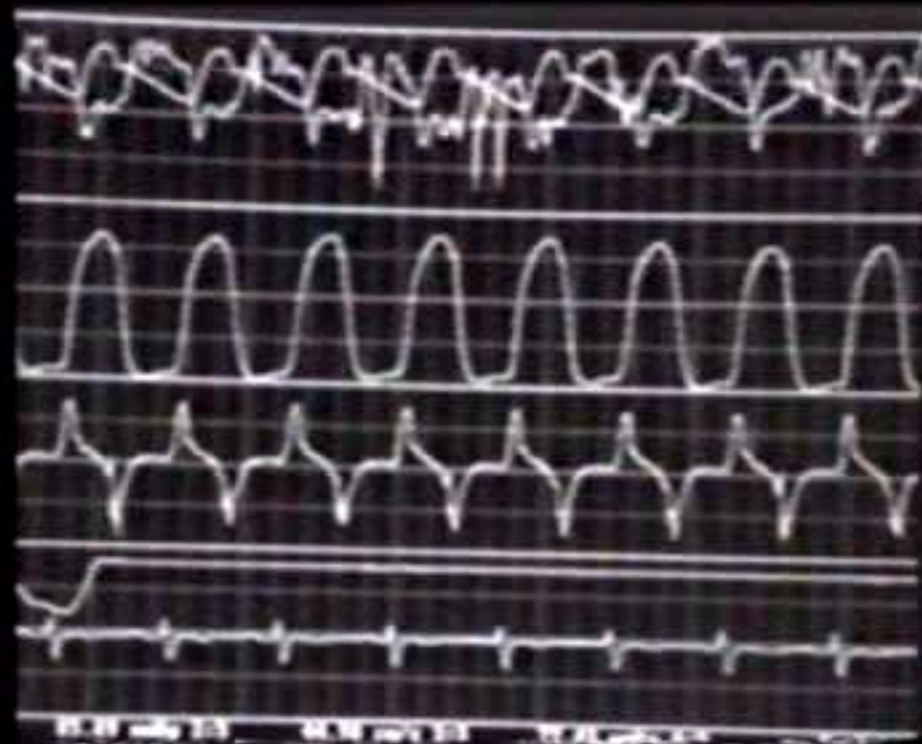
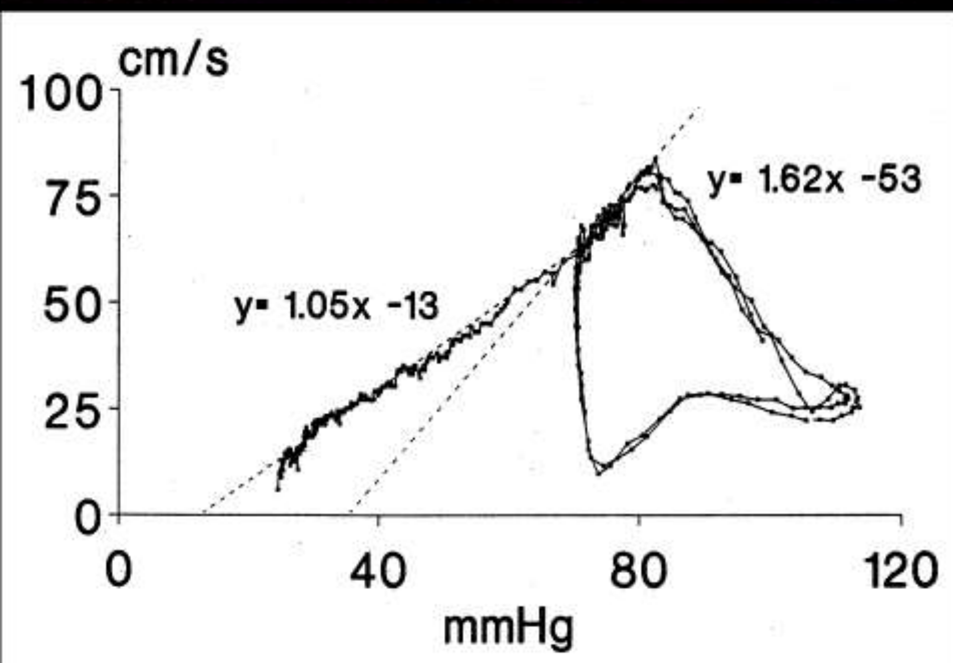
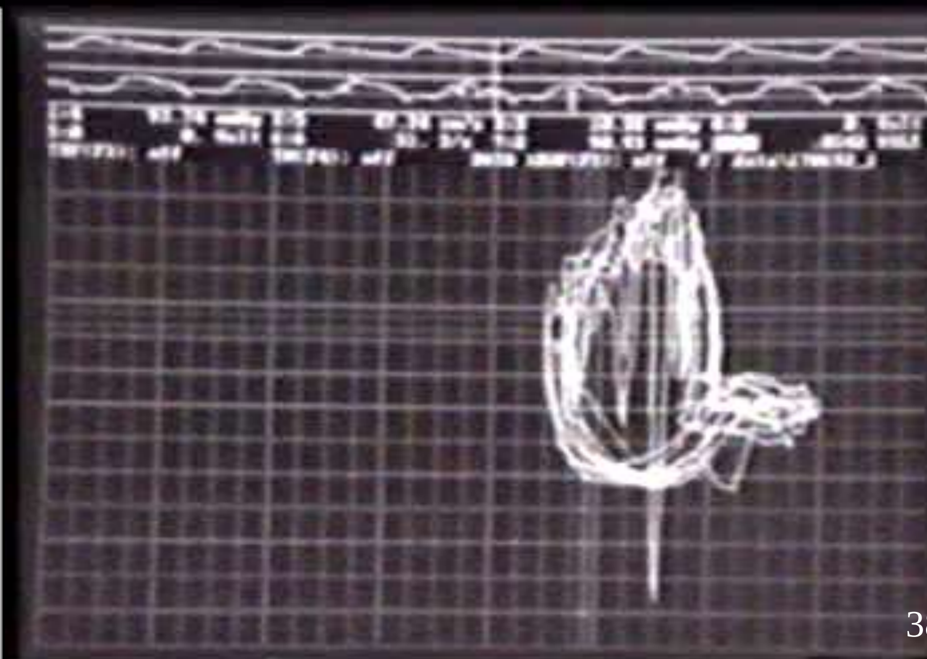
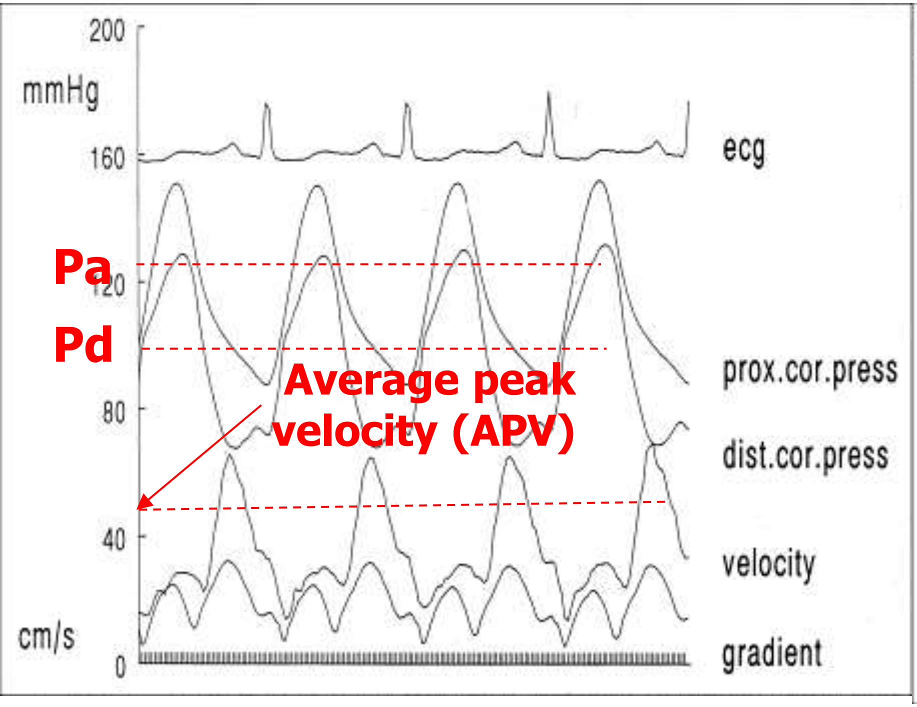
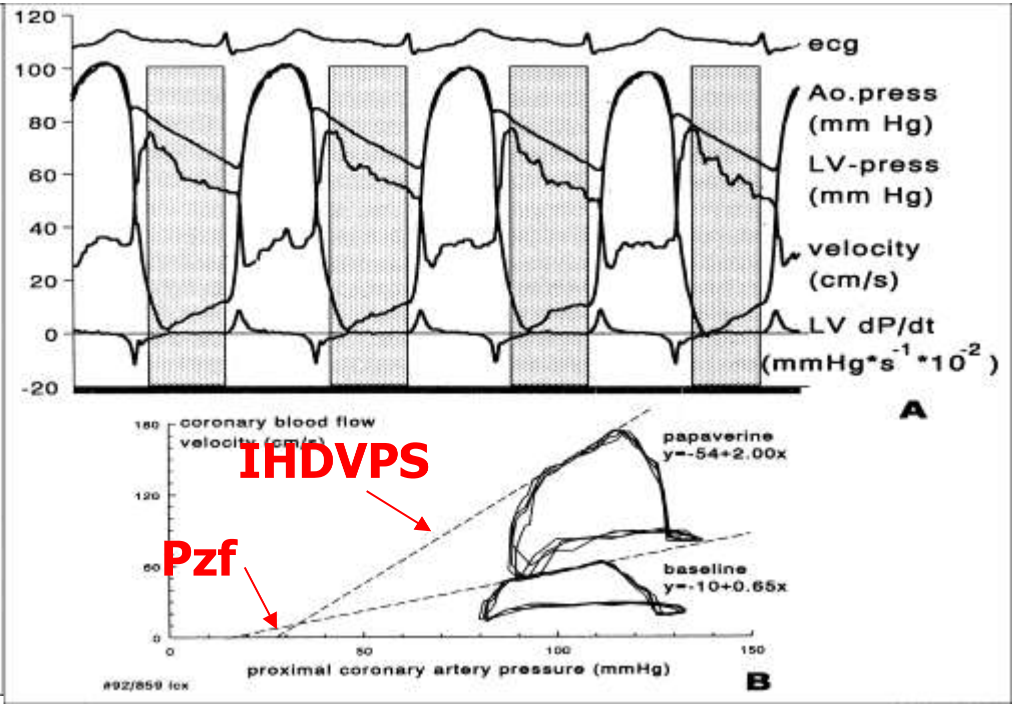



cm/s
100
75
50
25
0
0
40
80
120
mmHg
y= 1.62x -53
y= 1.05x -13



Hemodynamic parameters of PV analysis

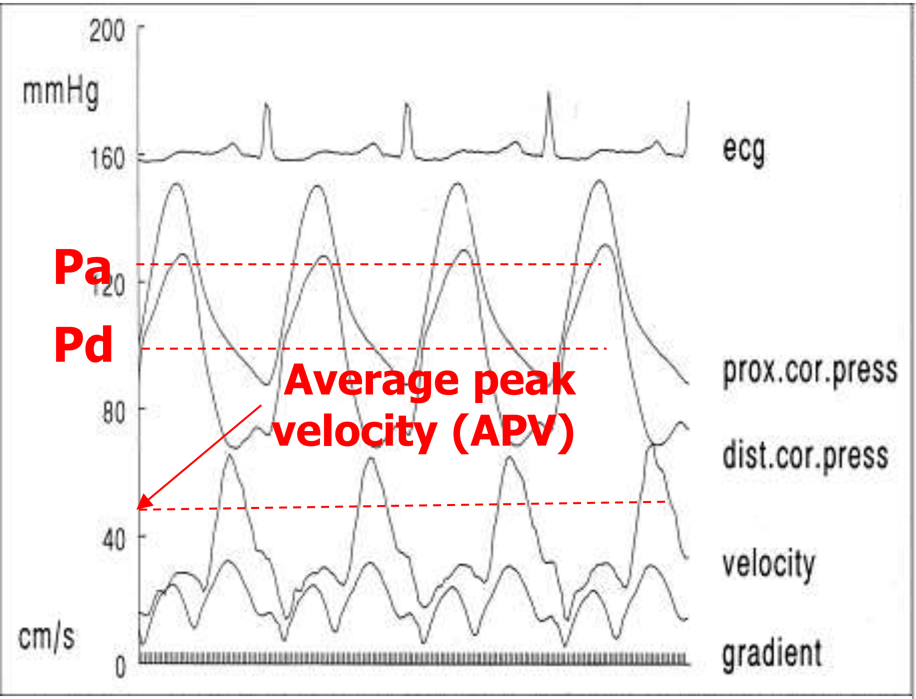


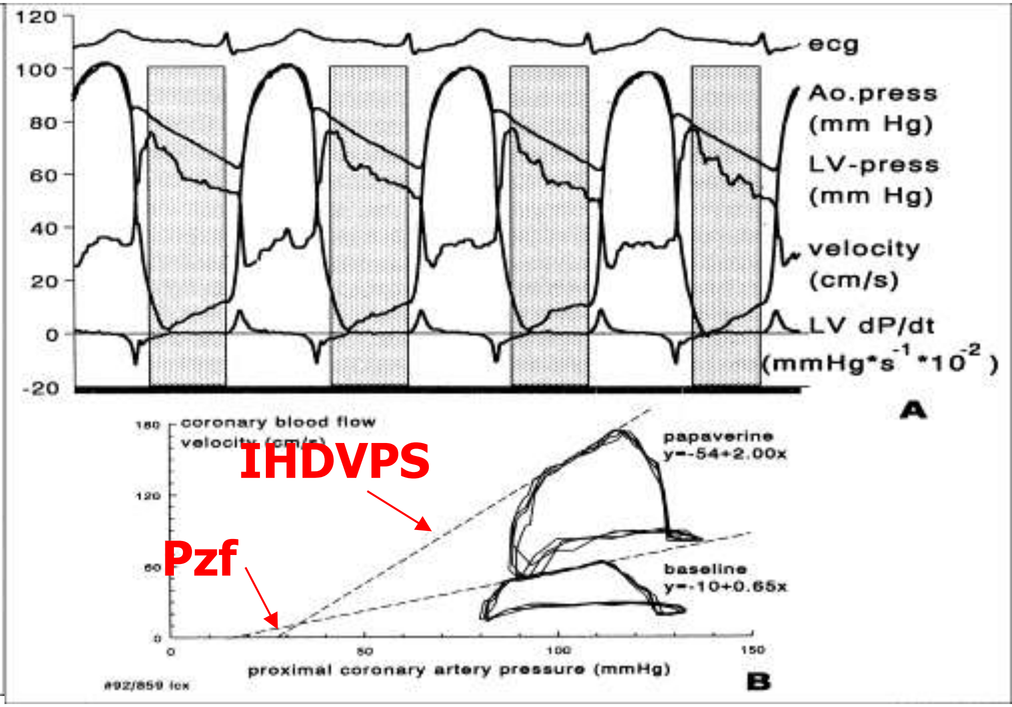


Intracoronary Pressure and Flow Velocity with Sensor-Tip Guidewires: A New Methodologic Approach for Assessment of Coronary Hemodynamics Before and After Coronary Interventions

P.W. Serruys et al., Am J Cardiol 1993;71:41-53

Hemodynamic parameters of PV analysis





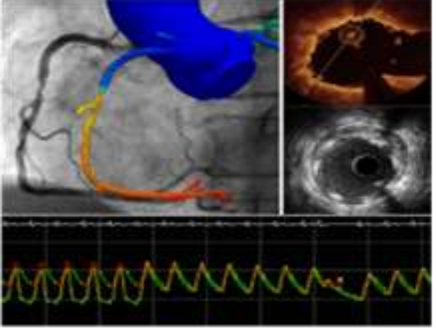
FFR =

Stenotic resistance (SR) =

CFR =

(CFVR)

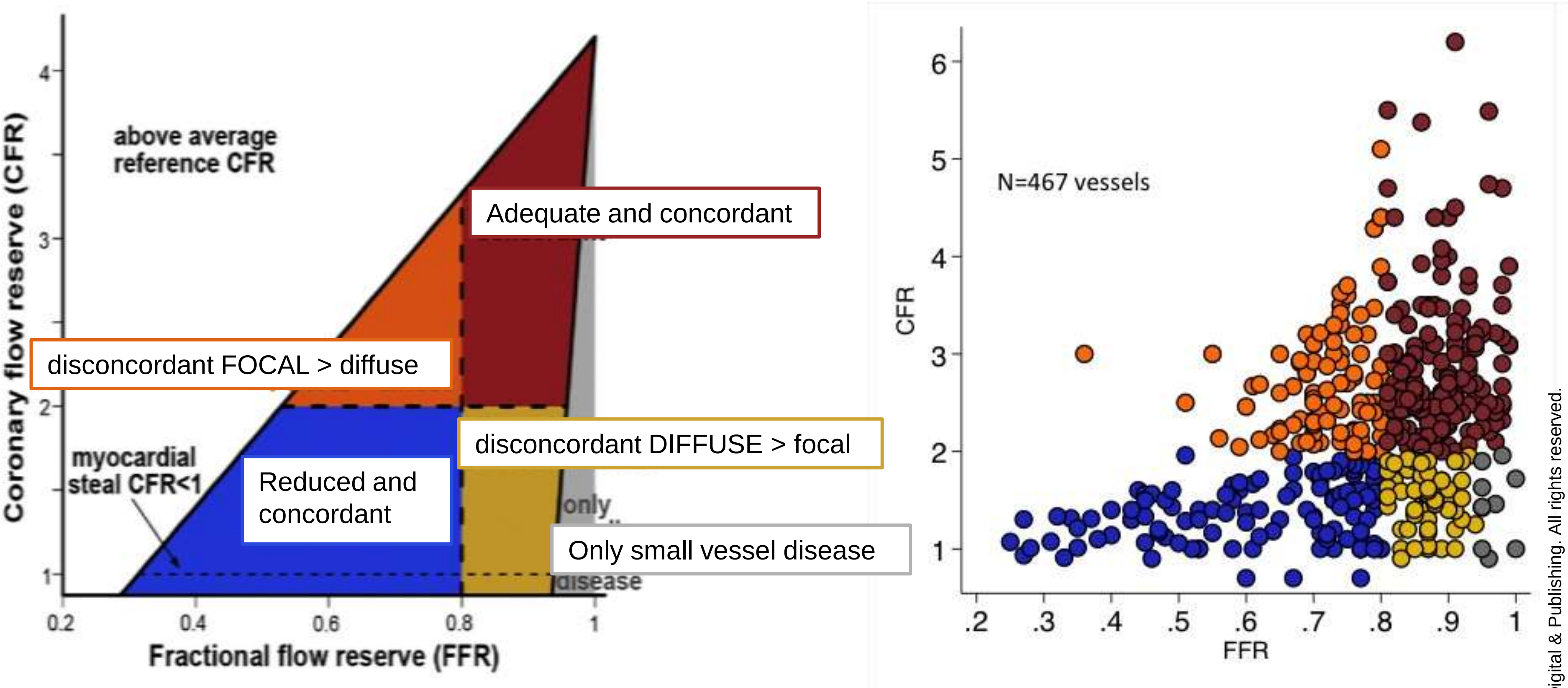
Microvascular resistance (MR) =



- SECOND EDITION -

CORONARY STENOSIS IMAGING, STRUCTURE AND PHYSIOLOGY

Edited by Javier Escaned and Patrick W. Serruys



Combined use of intracoronary pressure and flow to assess ischemic heart disease

Mauro Echavarría-Pinto, Tim P. van de Hoef, Hector M. Garcia-Garcia, Enrico Cerrato, Chris Broyd, Patrick W. Serruys, Jan J. Piek, Javier Escaned

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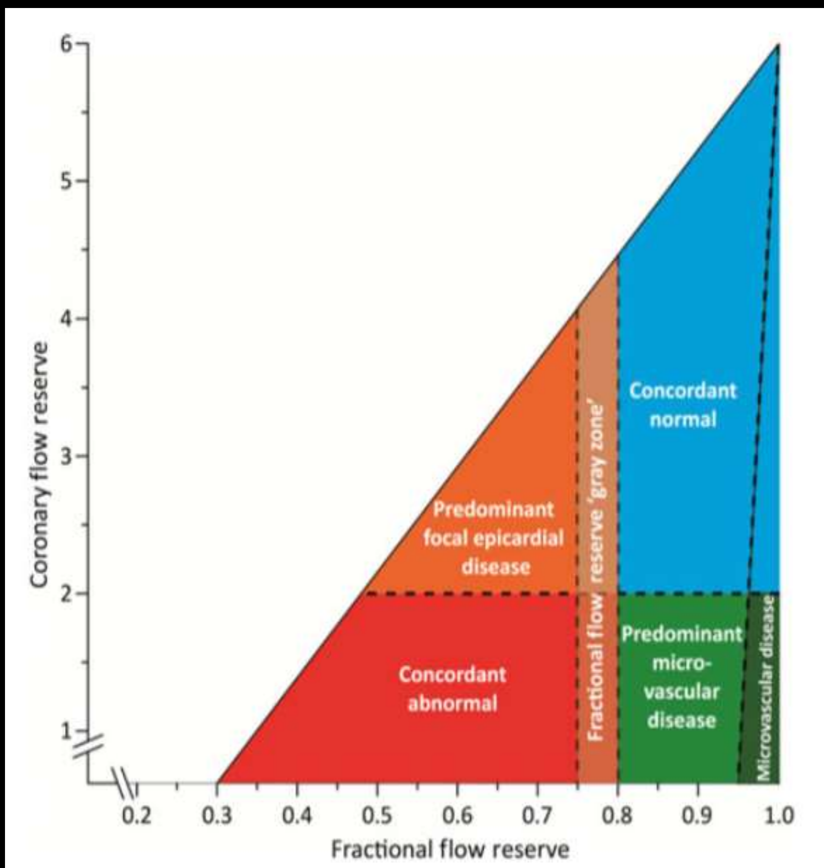

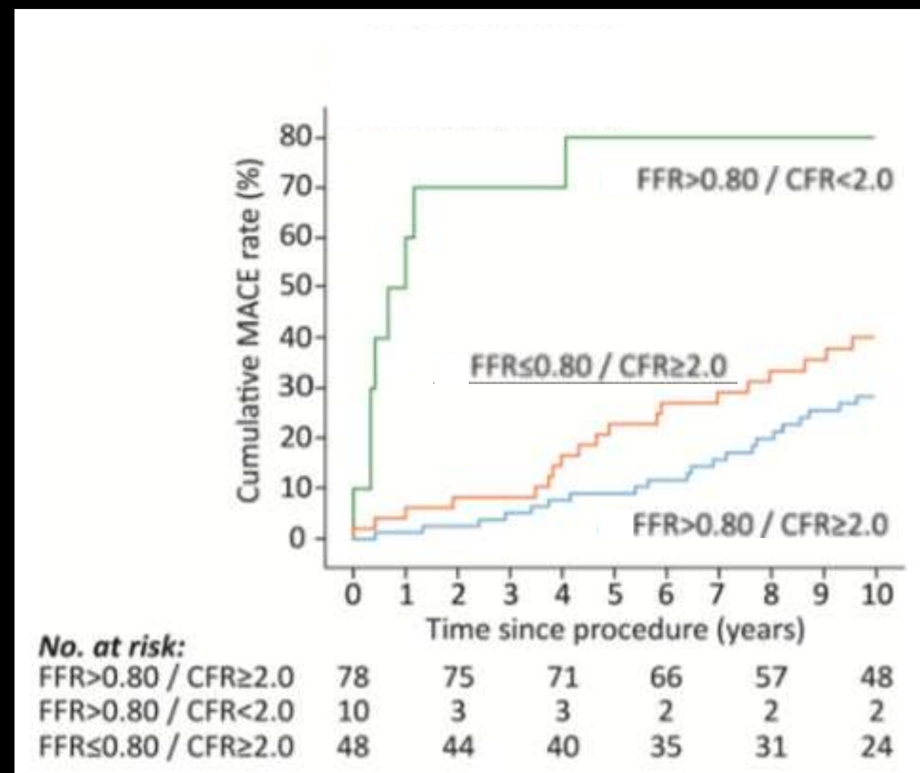

Van de Hoef et al. Circ Cardiovasc Interv 2014

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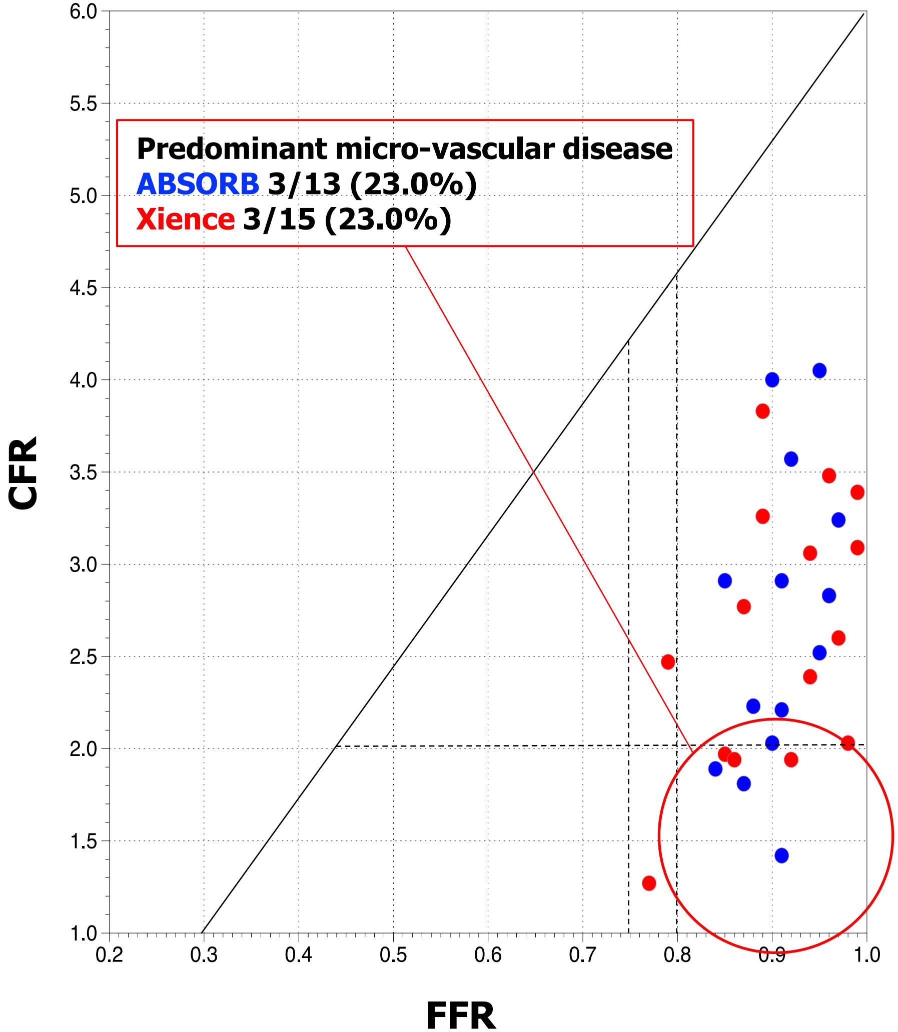

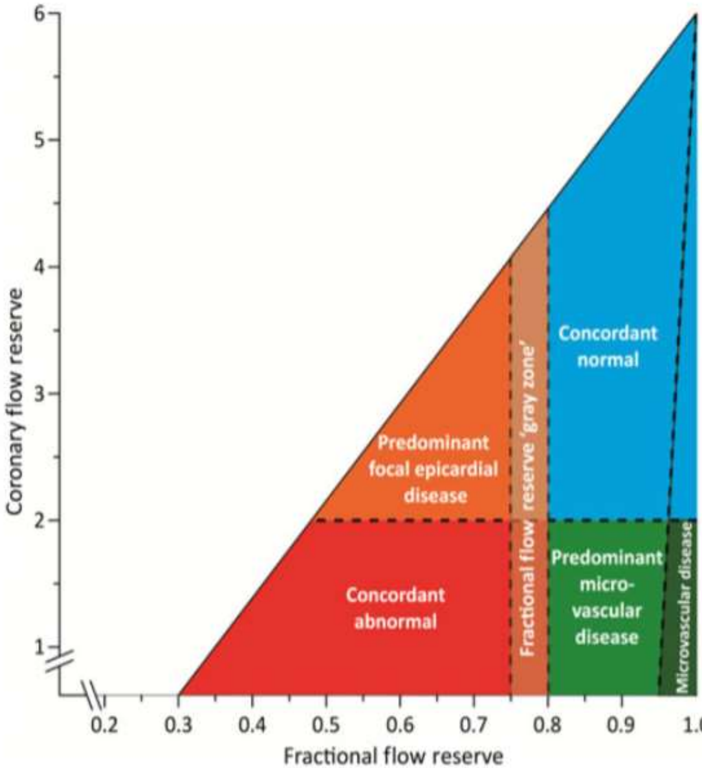

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Conventional indices:

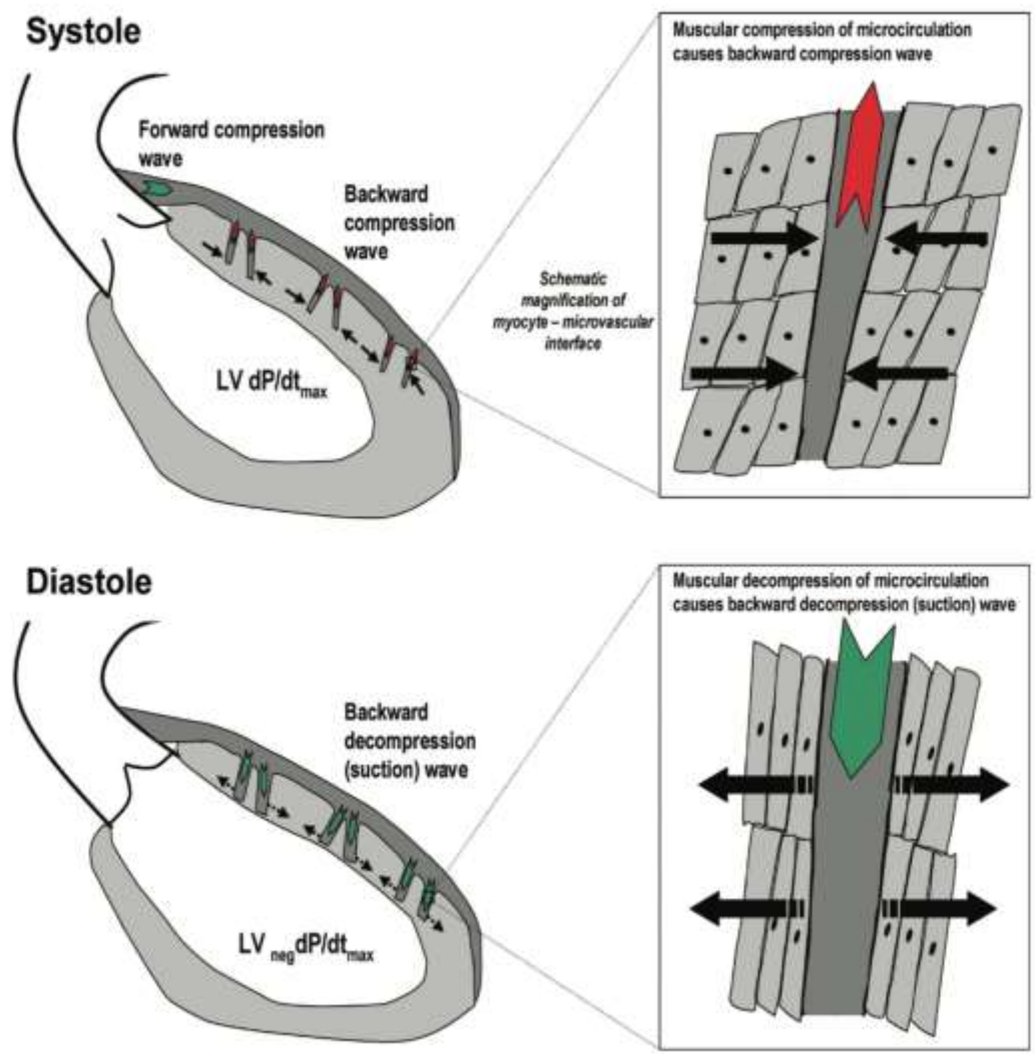
- FFR
- Coronary flow reserve (CFR)
- Hypereamic stenosis resistance (HSR)
- Hyperaemic microvascular resistance (HMR)

Indices derived from pressure-velocity loop analysis:

- Epicardial conductance (C_{epi})
- Microcirculatory conductance (C_{micro})

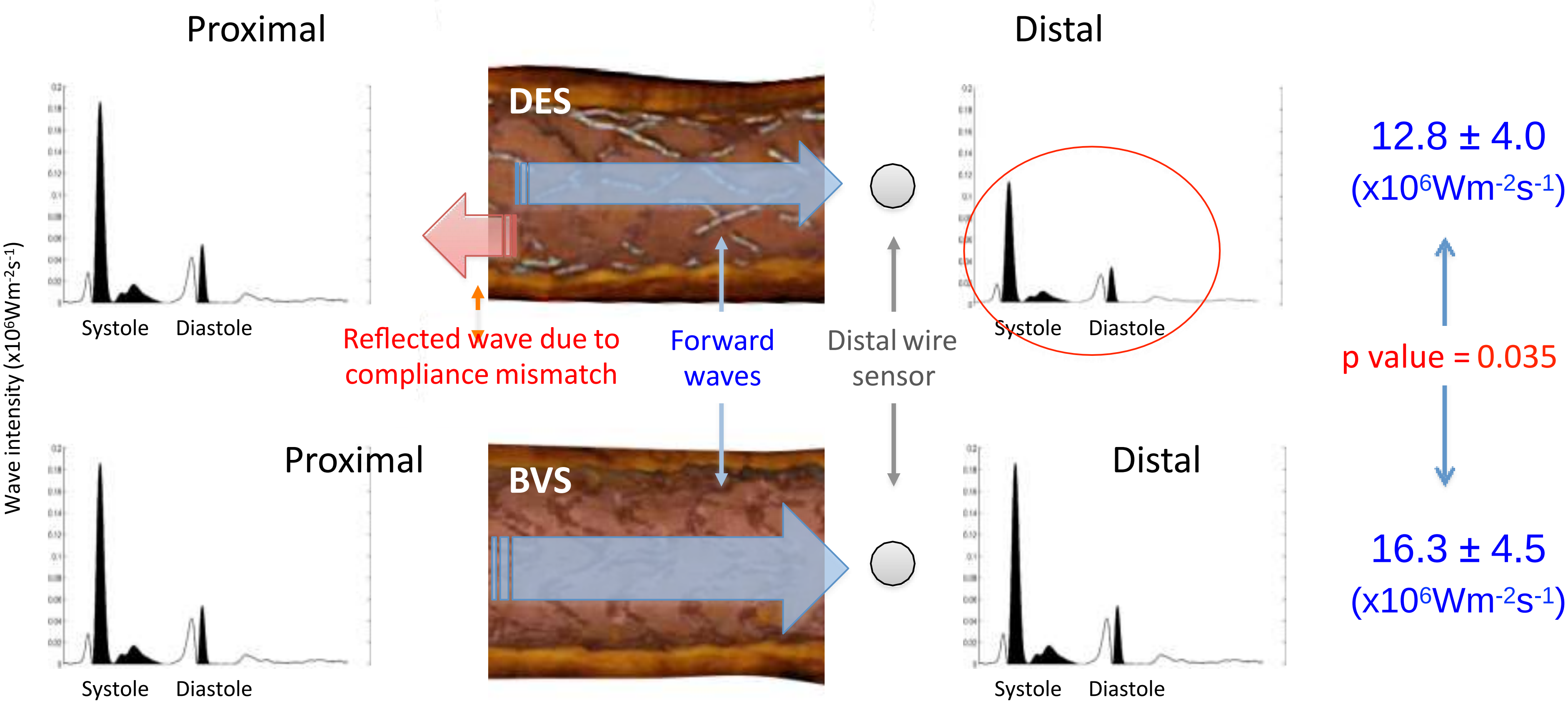
Indices derived from wave intensity analysis:

- Forward compressive waves
- Backward expansion wave



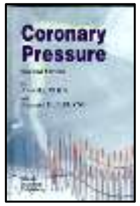
J. Davies Circulation 2012

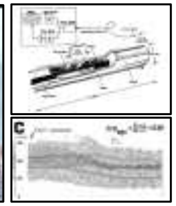
Schematic representation of forward wave transmission through coronary segments with and without a metallic cage



In coronary segments with a metallic DES the magnitude of travelling waves distal to the stent is decreased, as a result of energy loss in the generaNon of secondary reflected waves caused by compliance mismatch .

Part 1:
Future of physiology





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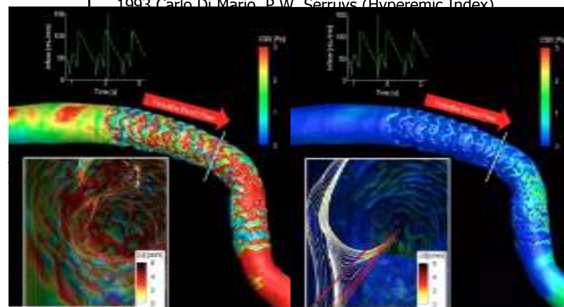


iFR®

ADVISE
ADVISE II
SYNTAX II

iFR®

DEFINE-FLAIR
SWEDEHEART

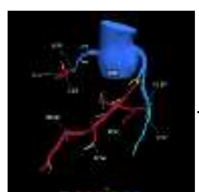
2001 ANGUS
Slager C, P.W. Serruys

Non-Newtonian Pulsatile
Shear-stress microenvironment (fusion OCT/IVUS and angiography).

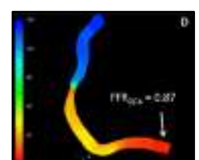
2002 Shear stress
Thury A, Wentzel J, P.W. Serruys

2010 FFR_{CT}

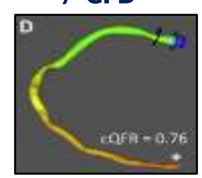
DISCOVER
FLOW
DE FACTO
NXT TRIAL
PLATFORM
SYNTAX III



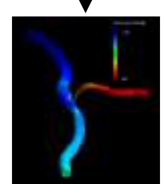
3D Angiography
+
"CFD"
+ Papafaklis, P.W. Serruys
TIMI Frame Count
Tu S



3D Angiography, or
2D Angiography
+
Lance Gould
"≠ CFD"

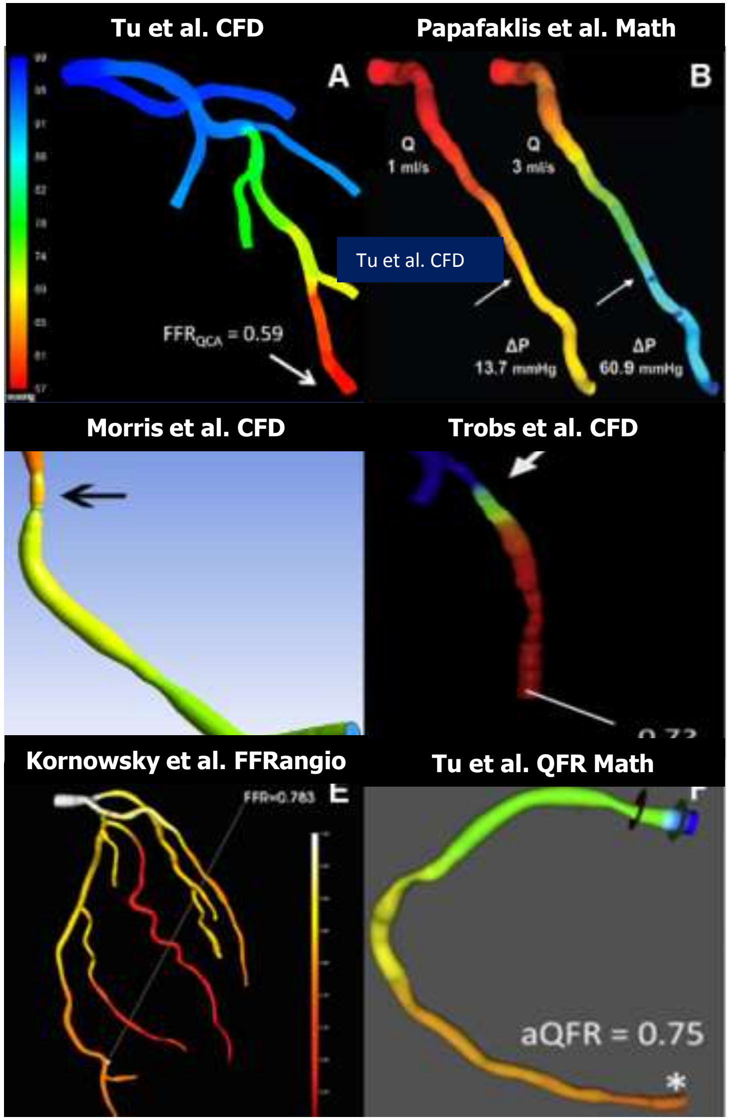


FFR_{CT} PLANNER



3D Bifurcation QCA
CFD
Finite Elements
Navier-Stokes

Angiography-derived FFR



2735 Records identified through database search

→ **1173** Duplicate records

1592 Records screened

→ **1332** Records excluded after assessment of the abstract

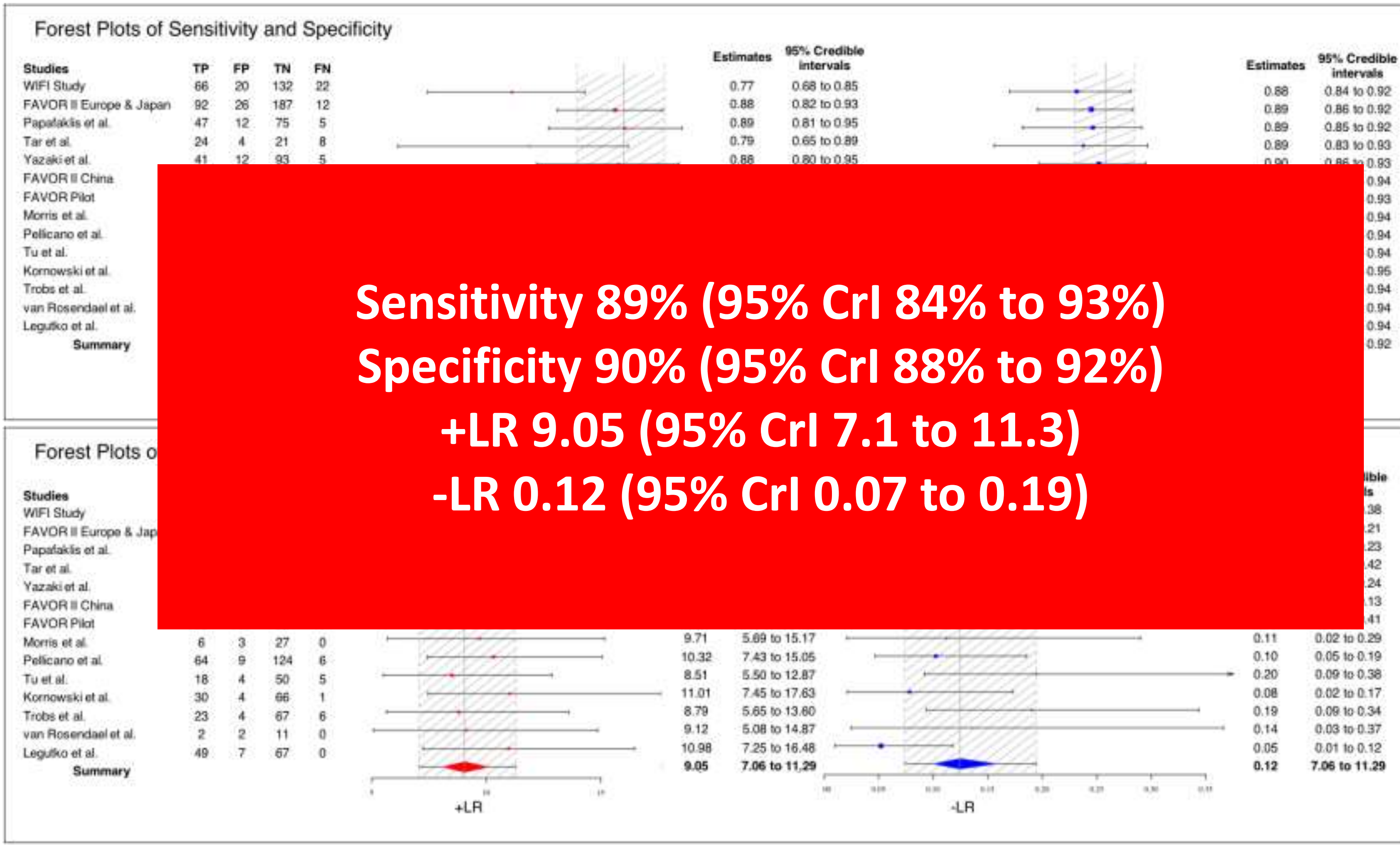
260 Full articles assessed

→ **246** Excluded
- **240** No angiography-derived FFR provided.
- **5** Lack of 2x2 table.
- **1** No FFR provided

14 Studies included in the meta-analysis

Collet et al. under review

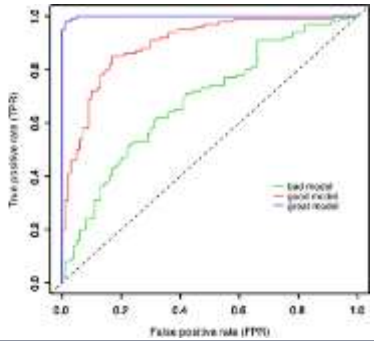
Angio-derived FFR Bayesian Meta-Analysis

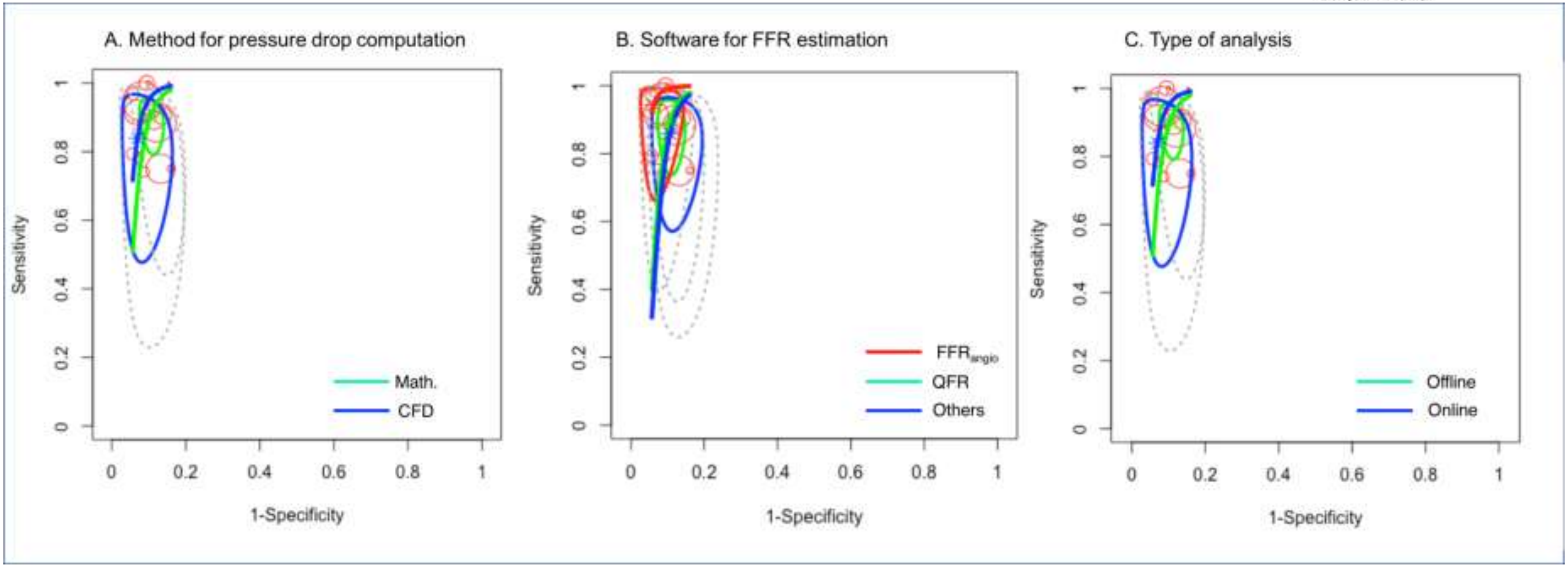


Sensitivity 89% (95% CrI 84% to 93%)
Specificity 90% (95% CrI 88% to 92%)
+LR 9.05 (95% CrI 7.1 to 11.3)
-LR 0.12 (95% CrI 0.07 to 0.19)

Collet et al. under review

Bayesian Meta-regression





No difference in Diagnostic Performance (AUC) between type of method for pressure drop computation, Software or online/offline analysis.

Collet et al. under review

Conclusion in coronary physiology

- Since more than a quarter of century (1993-2018), we have the technology (pressure/velocity wire) to analyze in great details the coronary physiology (epicardial conductance / micro vasculature resistance).

- However, we have no specific treatments for the microcirculation disease (e.g. L-arginine).

- The use of the current single pressure velocity wire is cumbersome, time consuming and costly - will probably remain a research tool.

- ”Color coded angiography” with QFR, virtual FFR and FFR_{angio} etc... will be embraced by busy operators who want to have at low cost and swiftly the “physiological justification” of their treatment of the epicardial vessels.

- When conventional fluoroscopic angiography will be replaced by CT angiography, FFRCT might become a surrogate of the angio and pressure derived FFR.

Part II

Taylor & Francis
Taylor & Francis Group

Expert Review of Medical Devices

ISSN: 1743-4440 (Print) 1745-2422 (Online) Journal homepage: http://www.tandfonline.com/loi/ierd20

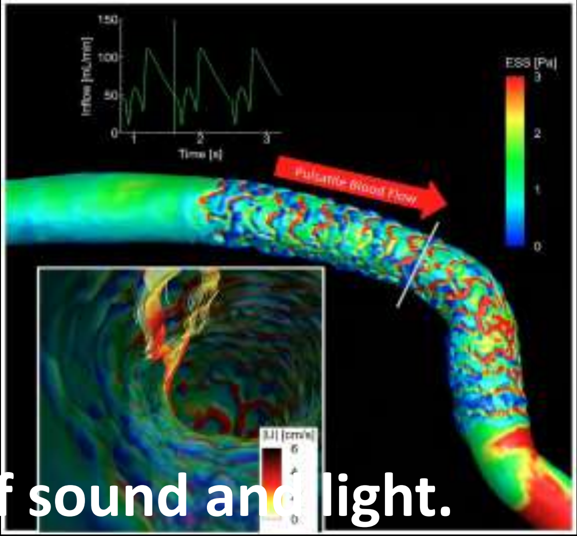
What does the future hold for novel intravascular imaging devices: a focus on morphological and physiological assessment of plaque

Yuki Katagiri, Erhan Tenekecioglu, Patrick W. Serruys, Carlos Collet, Athanasios Katsikis, Taku Asano, Yosuke Miyazaki, Jan J Piek, Joanna J. Wykrzykowska, Christos Bourantas & Yoshinobu Onuma

OVERVIEW

1) **Fusion methodology of OCT, grayscale IVUS, VH and angiography**

2) **High definition IVUS**



3) **OCT**

- **Ultra high speed (UHS) OCT.**
- **Hybrid catheter (IVUS and OCT).**
- **Tissue characterization and 3D.**
- **Photoacoustic Imaging: The merging of sound and light.**

4) **Near infrared spectroscopy**

- **Software for collagen detection.**
- **Intravascular molecular imaging of plaque biology**
- **Near infrared auto fluorescence spectroscopy.**
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  Fluorescence lifetime imaging (Flim)

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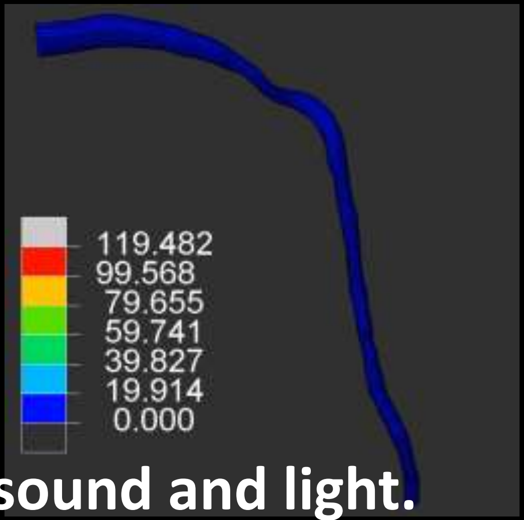

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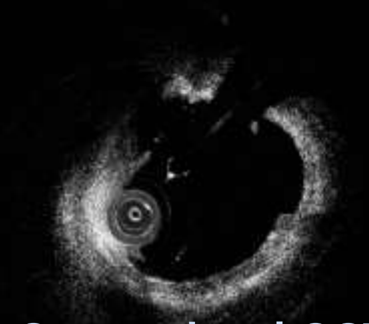

Conventional OCT
100rps

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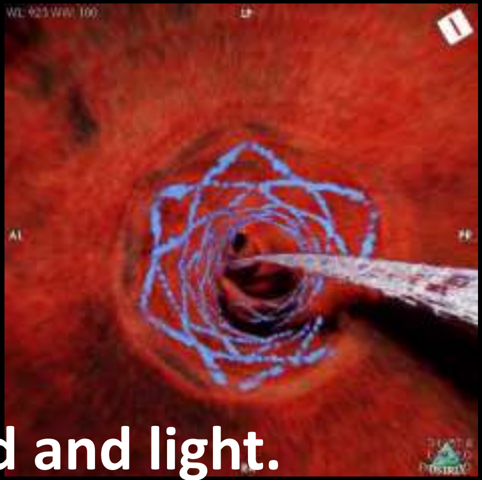

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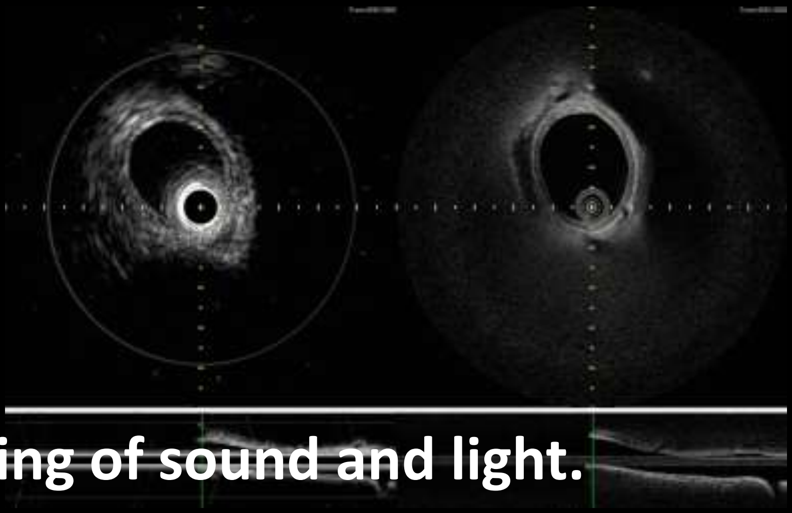
1) Fusion methodology of OCT, grayscale IVUS, VH and angiography

2) High definition IVUS

3) OCT

- Ultra high speed (UHS) OCT.
- Hybrid catheter (IVUS and OCT).
- Tissue characterization and 3D.
- Photoacoustic Imaging: The merging of sound and light.



4) Near infrared spectroscopy

- Software for collagen detection.
- Intravascular molecular imaging of plaque biology
- Near infrared auto fluorescence spectroscopy.
- Time resolved fluorescence spectroscopy.

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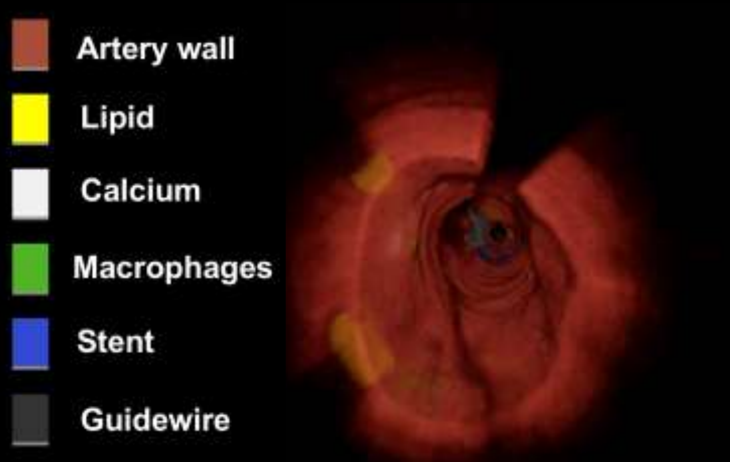

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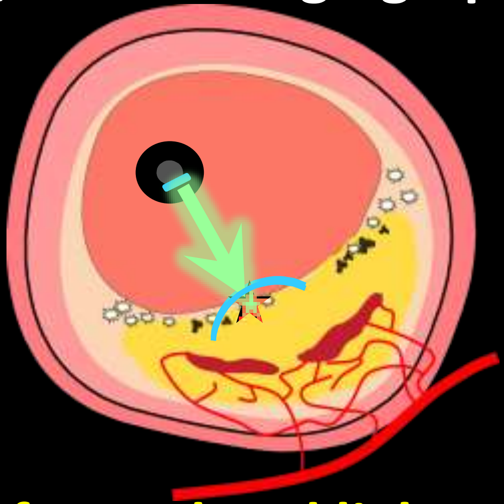

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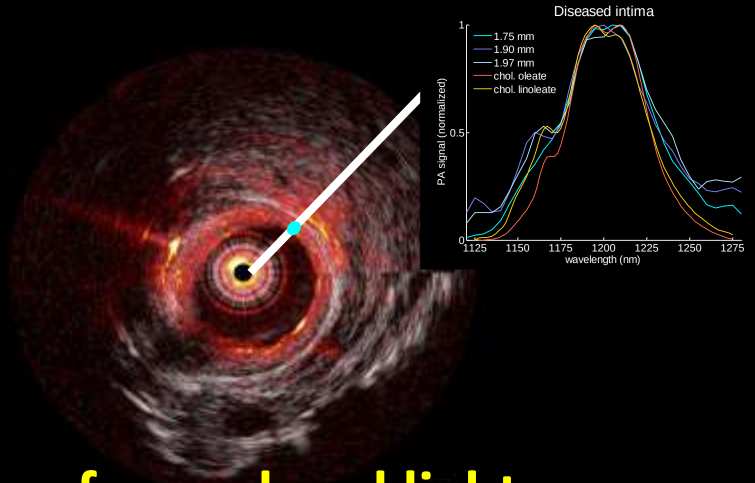

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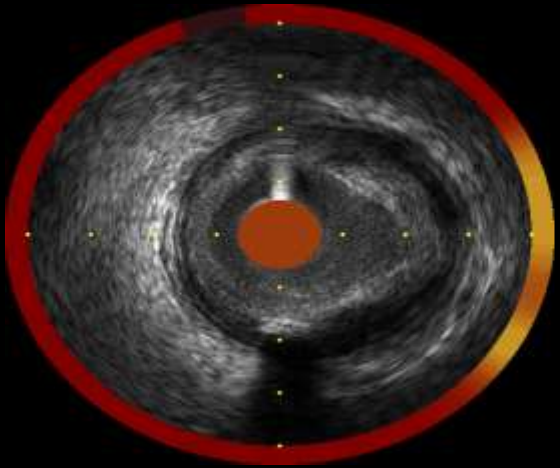

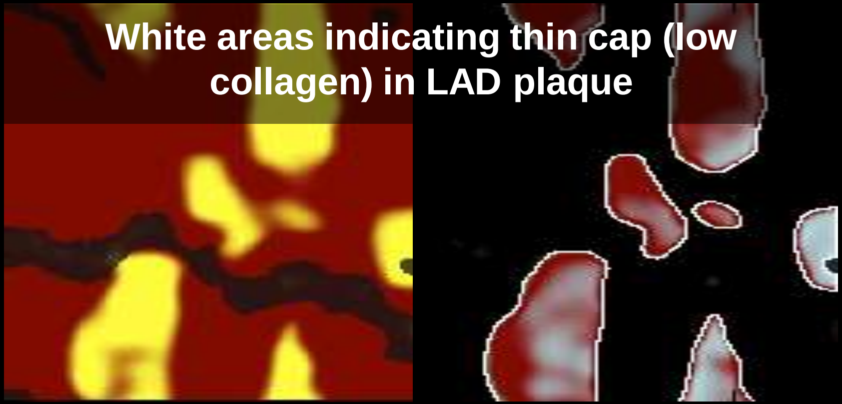

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OVERVIEW

- NIRF imaging agents – Translatable
  - ProSense VM110: All refs above; *EHJ CV imaging* 2016 (Calfon)
  - Indocyanine Green: *Sci Transl Medicine* 2011 (Vinegoni, Botnaru);
    - *JACC CV Imaging* 2016 (Verjans, Osborn)
  - Fibrin (FTP11): *JACC CV Imaging* 2012; *European HJ 2015* (Hara)
  - Oxidized LDL (LO1): *Scientific Reports* 2016 (Khamis, Haskard)
  - Macrophages (CLIO-CyAm7) *Circulation CV Imaging* 2017 (Stein-Merlob)

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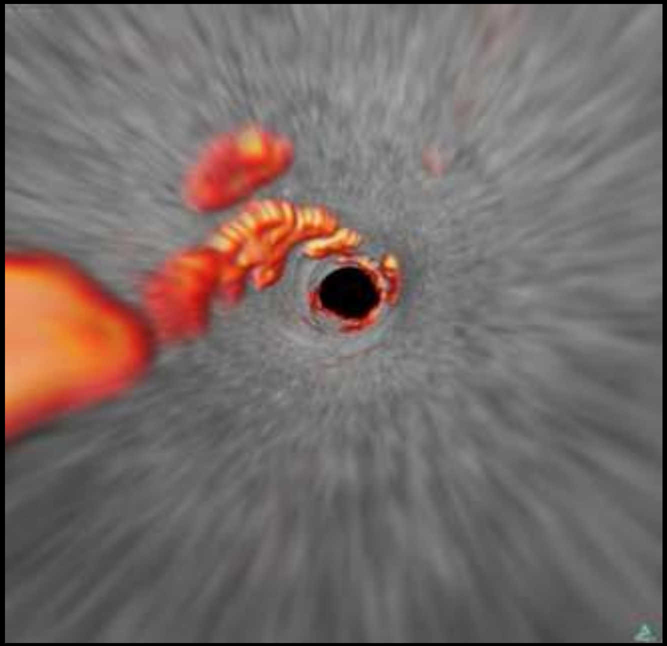

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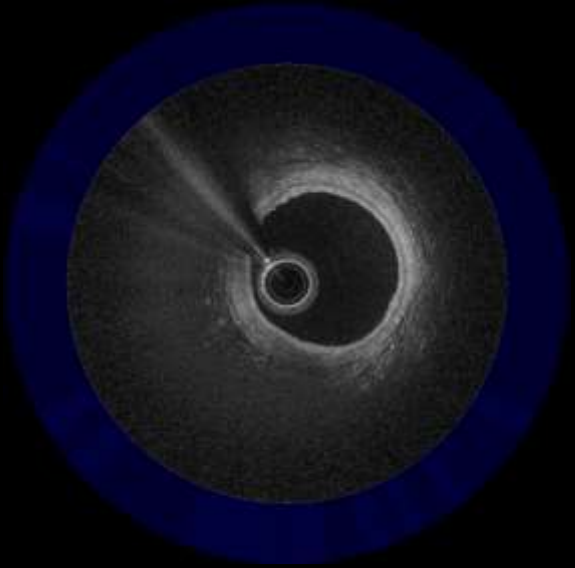

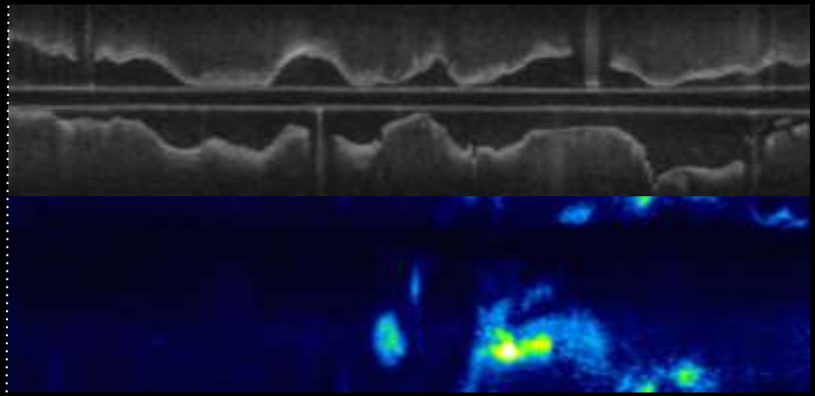

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OVERVIEW

TRFS relies on the assessment of the fluorescence emission decay time (nsec) of molecules being excited with pulsed light

- ✓ Elastin: ~4.5 ns
- ✓ Collagen (type I): ~ 6 ns
- ✓ Lipids: ~2 ns* up to ~13 ns⁺

*: LDL ⁺: Cholesteryl linoleate

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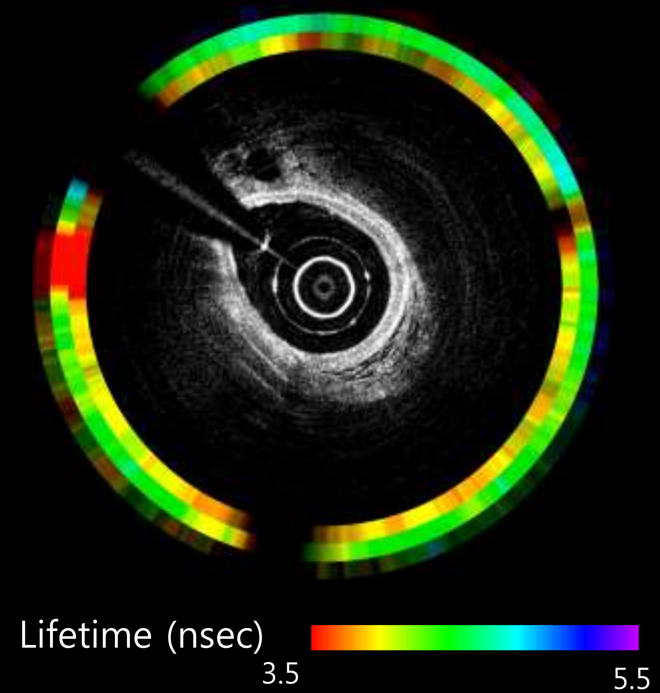

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Conclusion-1

- Hybrid dual-probe catheters allow

1) Evaluation of the plaque micro-features such as:

   cholesterol crystals detected by OCT, inflammation (provided by NIRF), macrophages, and neovessels by IVPA), that were unseen by stand-alone IVUS

2) established markers of plaque vulnerability such as plaque burden and lipid component at the same time.

- Vulnerable plaque detection by new hybrid imaging modalities may have an impact on decision-making in terms of treatment indication and procedural optimization.

Conclusion-2

- Within 5 years, most of the hybrid imaging techniques now in preclinical phase will be utilized in the clinical arena.
- Software for online blood simulation is likely to be developed that will enable ESS and wall stress calculation.
- Future studies of intravascular imaging devices are expected to shed light into the mechanisms of atherosclerotic evolution and precise risk stratification of vulnerable plaque.