

**11th EBC, Athens, Greece
September 25 & 26, 2015**



Multicenter Clinical Trial on the Impact of Biomechanical Factors on Bifurcation Stent Restenosis and Thrombosis

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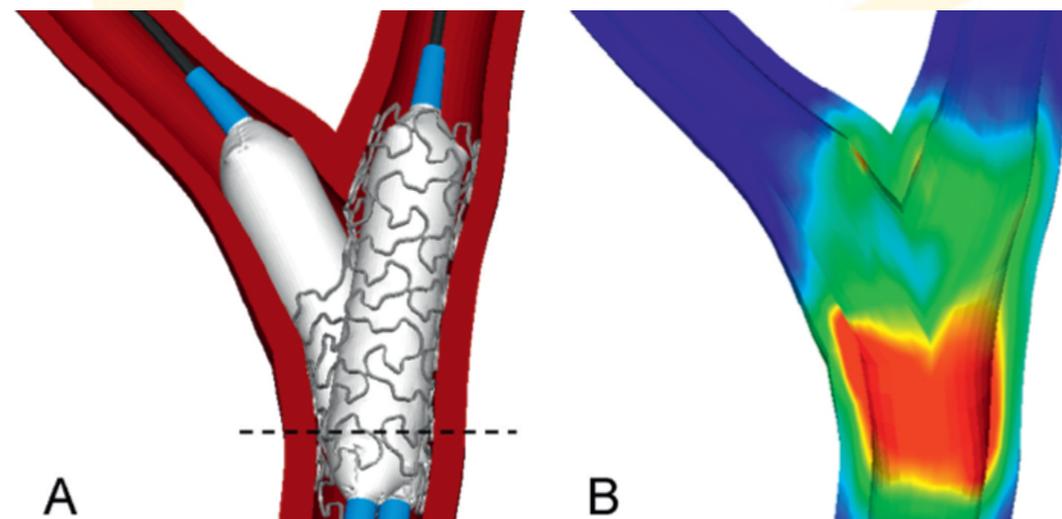
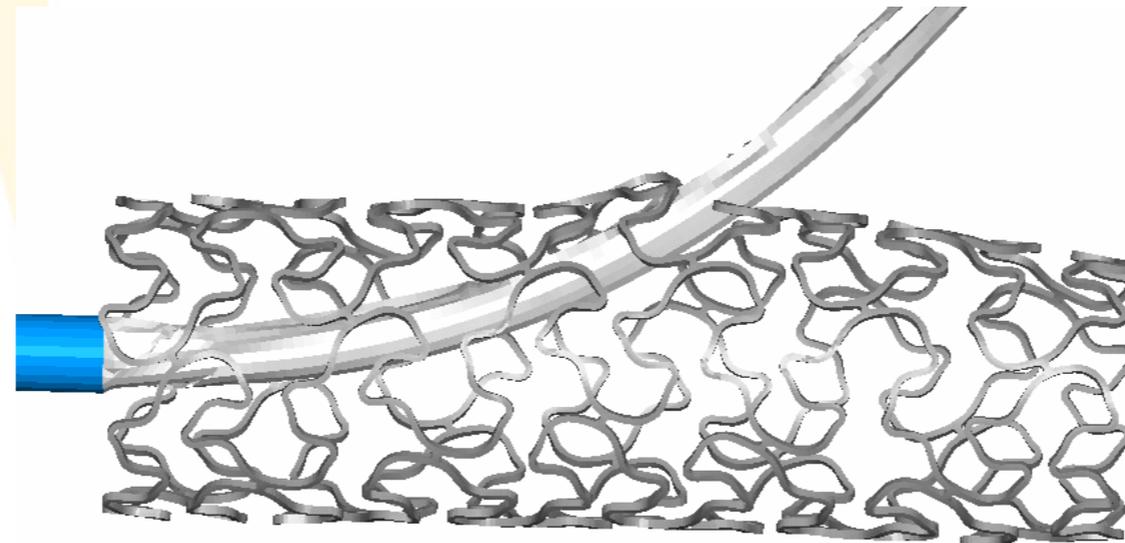
We have no conflicts of interest



My Last Slide...8th EBC, Barcelona 2012



From nice animations and colors to
clinically relevant simulations



Courtesy of Dr Mortier



FOCUS ISSUE ON BIFURCATION INTERVENTIONS

STATE-OF-THE-ART REVIEW

Biomechanical Modeling to Improve Coronary Artery Bifurcation Stenting

Expert Review Document on Techniques and Clinical Implementation

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Bifurcation Stenting



Bifurcations PCIs account for **one-fifth** of all coronary interventions Lassen JF, et al. Eurointervention 2014;10:545-60

Bifurcations PCIs exhibit **higher rates (10-20%)** of restenosis, thrombosis and recurrent adverse clinical events Abdel-Latif A, et al. JACC Intv 2015;8:561-3

Bifurcation PCI remains **challenging** and the ideal treatment strategy is still elusive



Role of ESS in Stent Restenosis and Thrombosis



Locally disturbed blood flow (i.e. low ESS) is a major determinant for the development and progression of atherosclerosis

Chatzizisis YS, et al. JACC 2007;49:2379-93

Experimental and **autopsy** evidence extend our current understanding of low ESS as a proatherogenic stimulus to a factor that also contributes to **stent restenosis and thrombosis**, clearly in conjunction with established risk factors

Richter Y, et al. J Cin Invest 2004;113:1607-14

Nakazawa G, et al. JACC 2010;55:1679-87





Journal of the American College of Cardiology
© 2012 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 59, No. 15, 2012
ISSN 0735-1097/\$36.00
doi:10.1016/j.jacc.2011.10.903

FOCUS ISSUE: TRANSCATHETER CARDIOVASCULAR THERAPEUTICS

State-of-the-Art Paper

Role of Endothelial Shear Stress in Stent Restenosis and Thrombosis

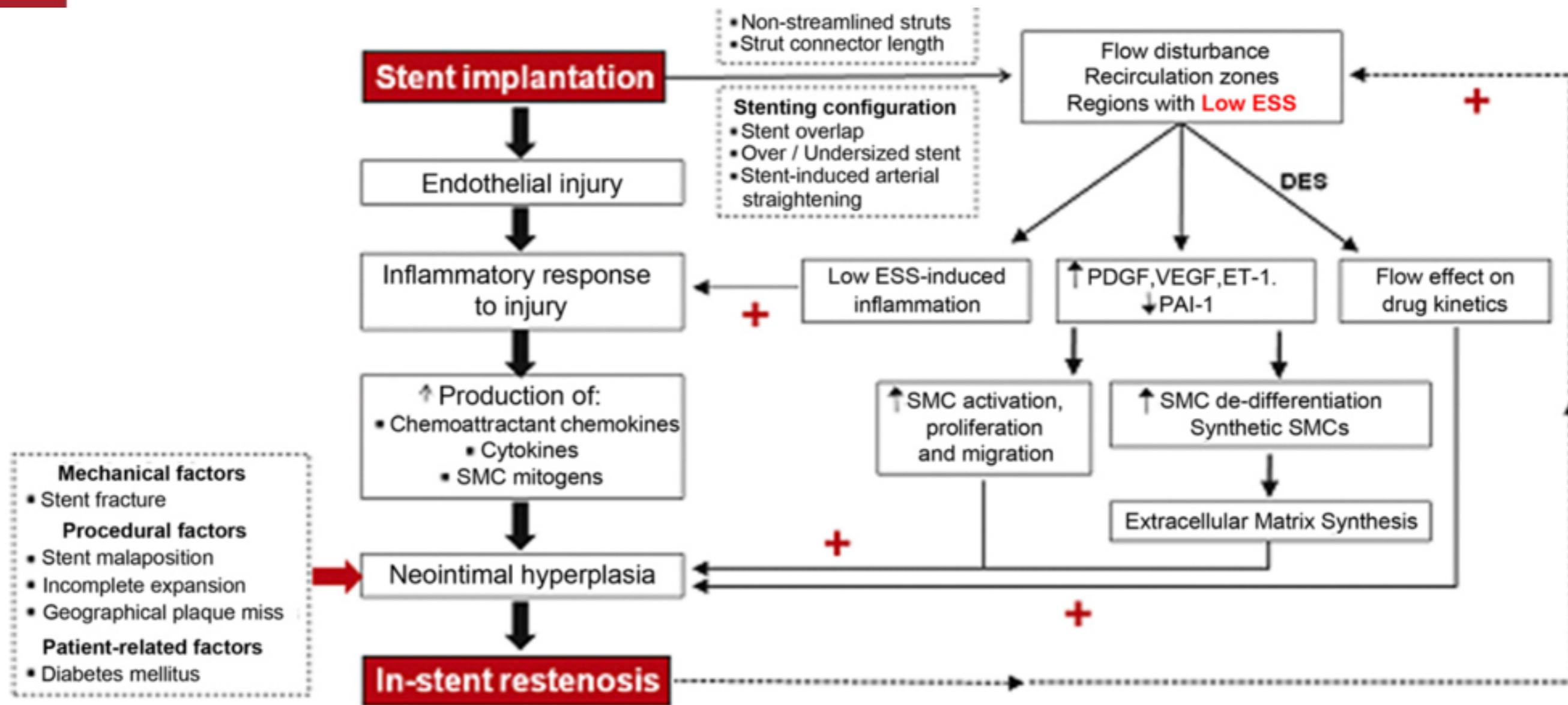
Pathophysiologic Mechanisms and Implications for Clinical Translation

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Pathobiologic Implication of Low ESS in ISR



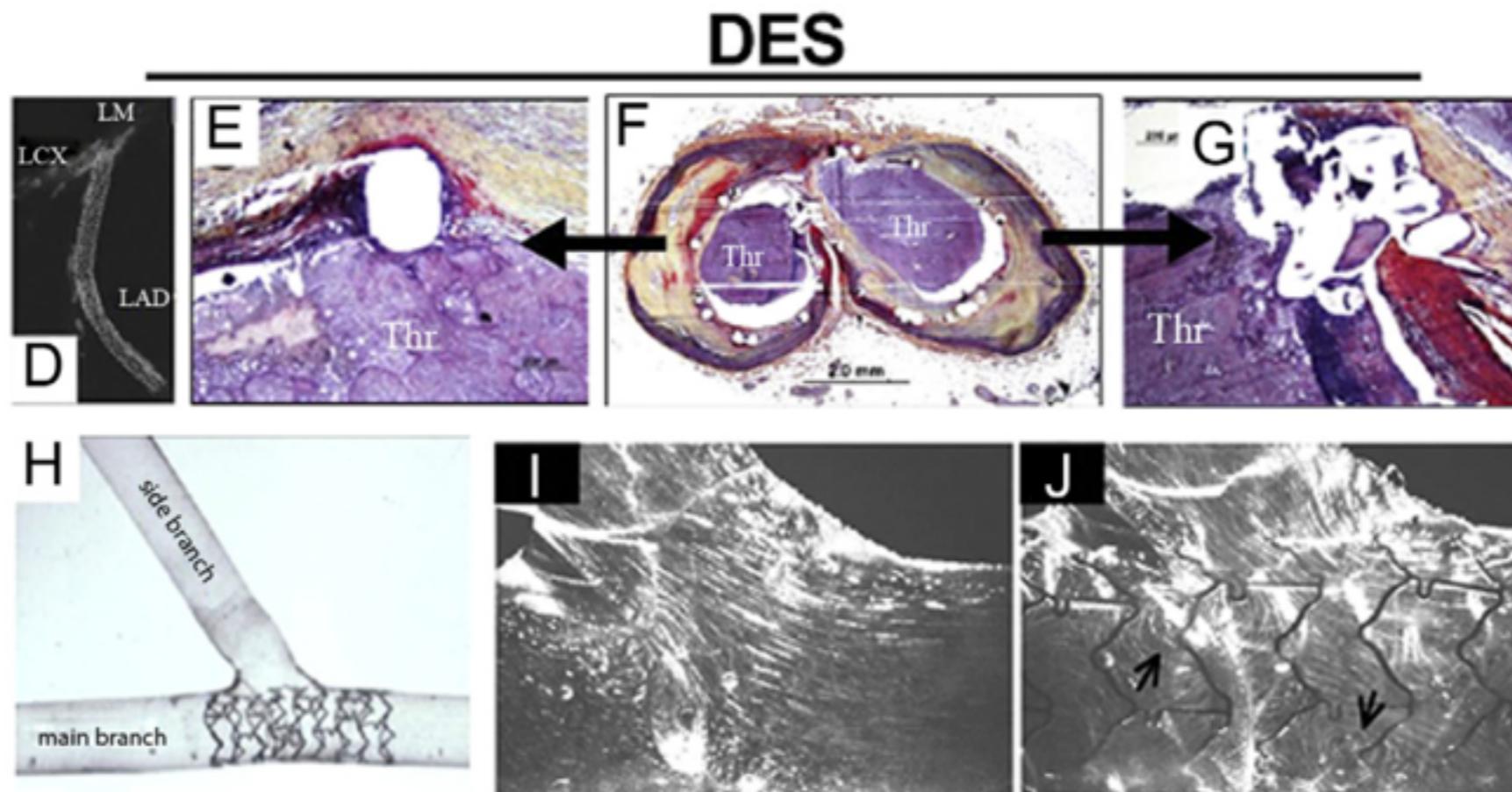
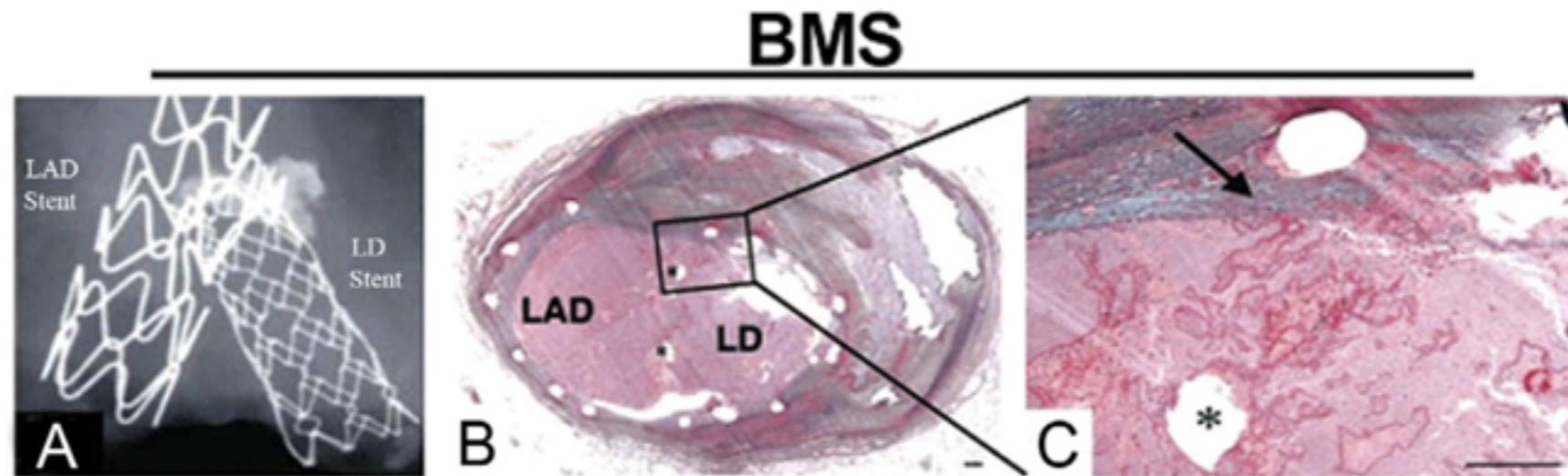
Determinants of ESS within Stents



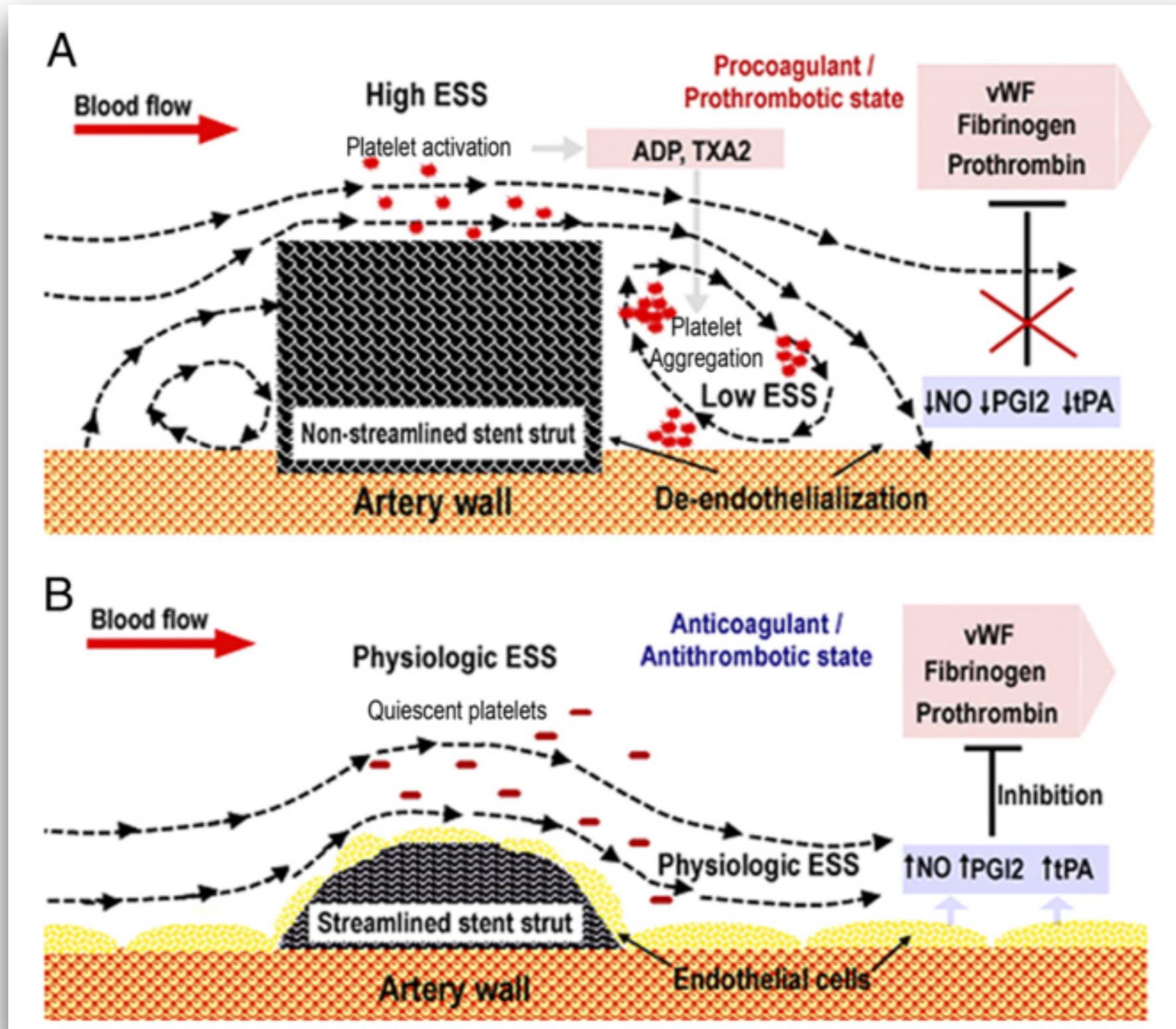
- Stent type: BMS vs. DES
- Stent design: Strut thickness and shape
- Stent diameter: Under- and over-expansion
- Stenting technique: Single long stent vs. two overlapping stents
- **Bifurcation stenting**



ESS and Stent Thrombosis



Pathobiologic Implication of Low ESS in Stent Thrombosis

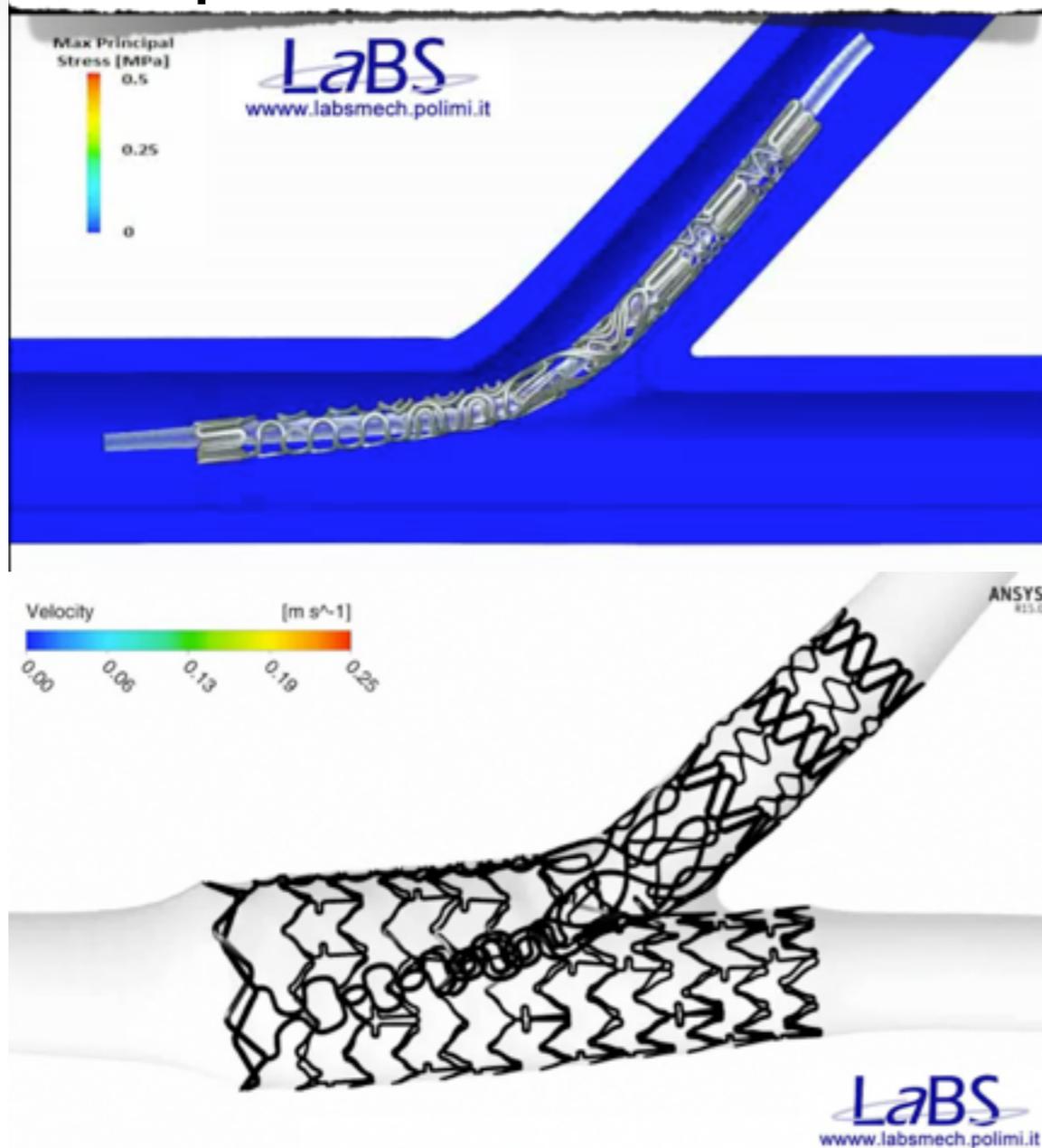


Consideration of **local biomechanical factors**, as well as **anatomic parameters**, in bifurcation lesions might optimize the post-stenting ESS distribution and in-stent drug kinetics in this challenging lesion subset

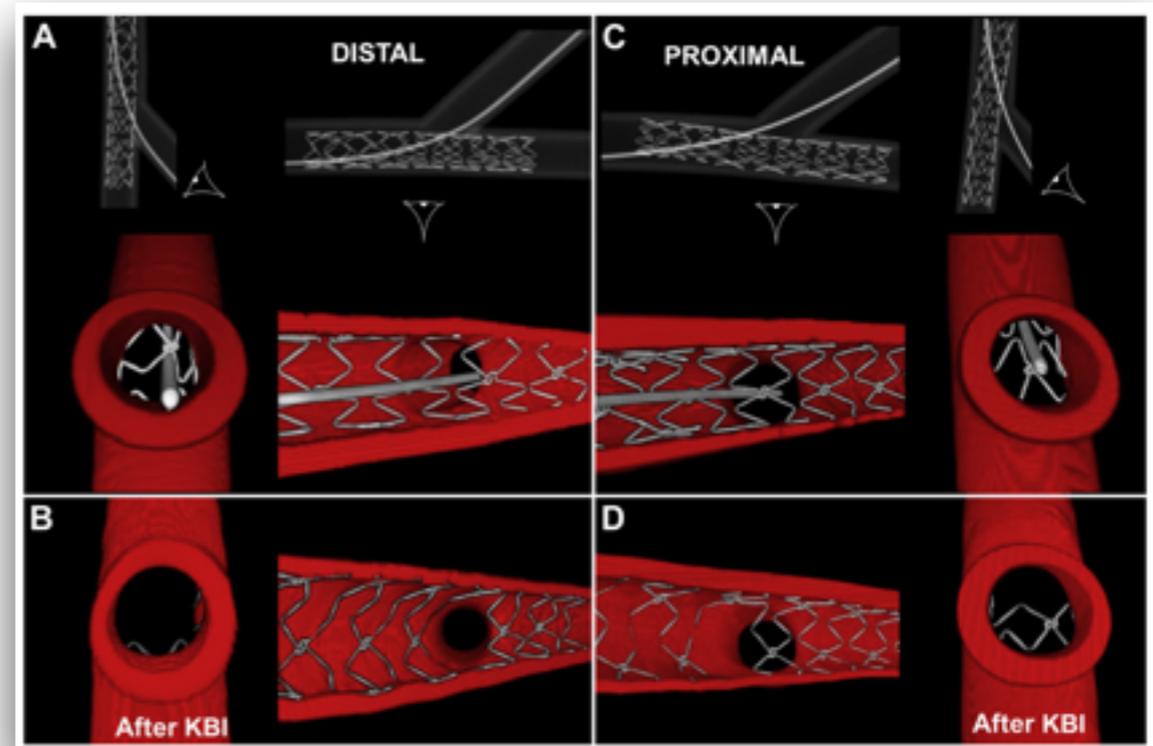
Biomechanical Modeling



Computational Simulations



In-vitro Bench Testing



Foin N, et al. Int J Cardiol 2013;168:3623-8

Migliavacca F, et al. Eurointervention 2015;Suppl V:V31-4



Modern Tools for Effective Biomechanical Modeling of Stenting



- High-resolution invasive (OCT) and non-invasive (CCTA) imaging of pre- and post-stenting
- Improved 3D reconstruction techniques (including stent struts)
- 3D printing methods
- Improved materials for in-vitro bench testing
- Fast and refined flow and mechanical computer simulations





Clinical Trial

EBC-driven, Prospective, Multicenter, Randomized, Single-blind, Controlled Clinical Trial



Objectives



- 1. Local biomechanical factors (i.e. low ESS, high wall stress) are implicated in bifurcation stent restenosis and thrombosis**
- 2. Biomechanical modeling can improve coronary bifurcation stenting and clinical outcomes**



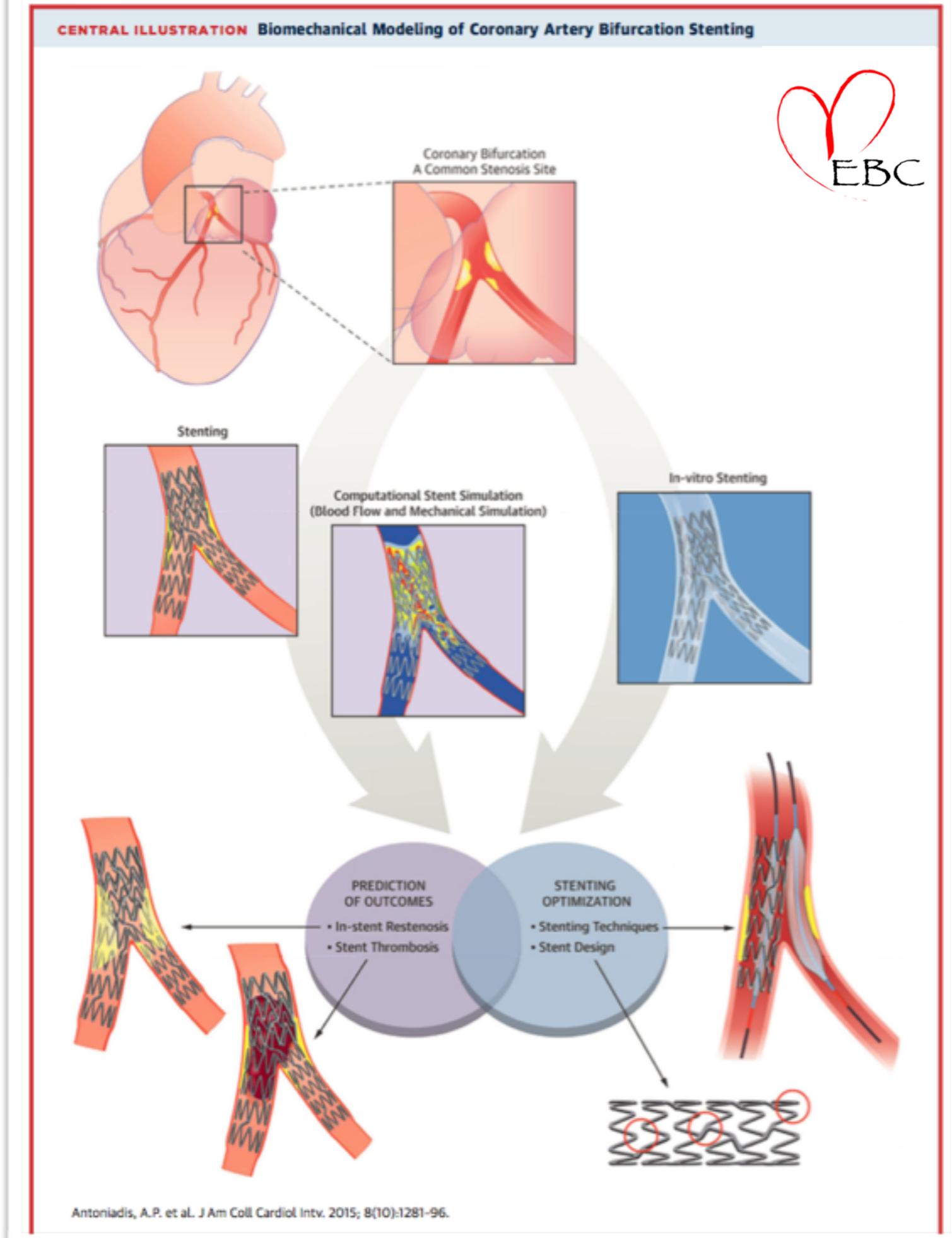
Clinical Significance



- Stenting simulation may provide an opportunity to translate biomechanical engineering breakthroughs into **quantifiable and patient-oriented clinical benefits**
- Stenting simulation can help in the **optimization of stenting techniques** and **development of new generation stents**, ultimately improving clinical outcomes
- Stenting simulation can be used in **real time** to guide young interventionalists (auto-pilot PCI)
- Also, excellent **educational** and **training** tool
- Such modeling techniques can be applied to **other vascular beds** (i.e. carotid artery bifurcation or aortic bifurcation) and to **structural interventions** (TAVR)

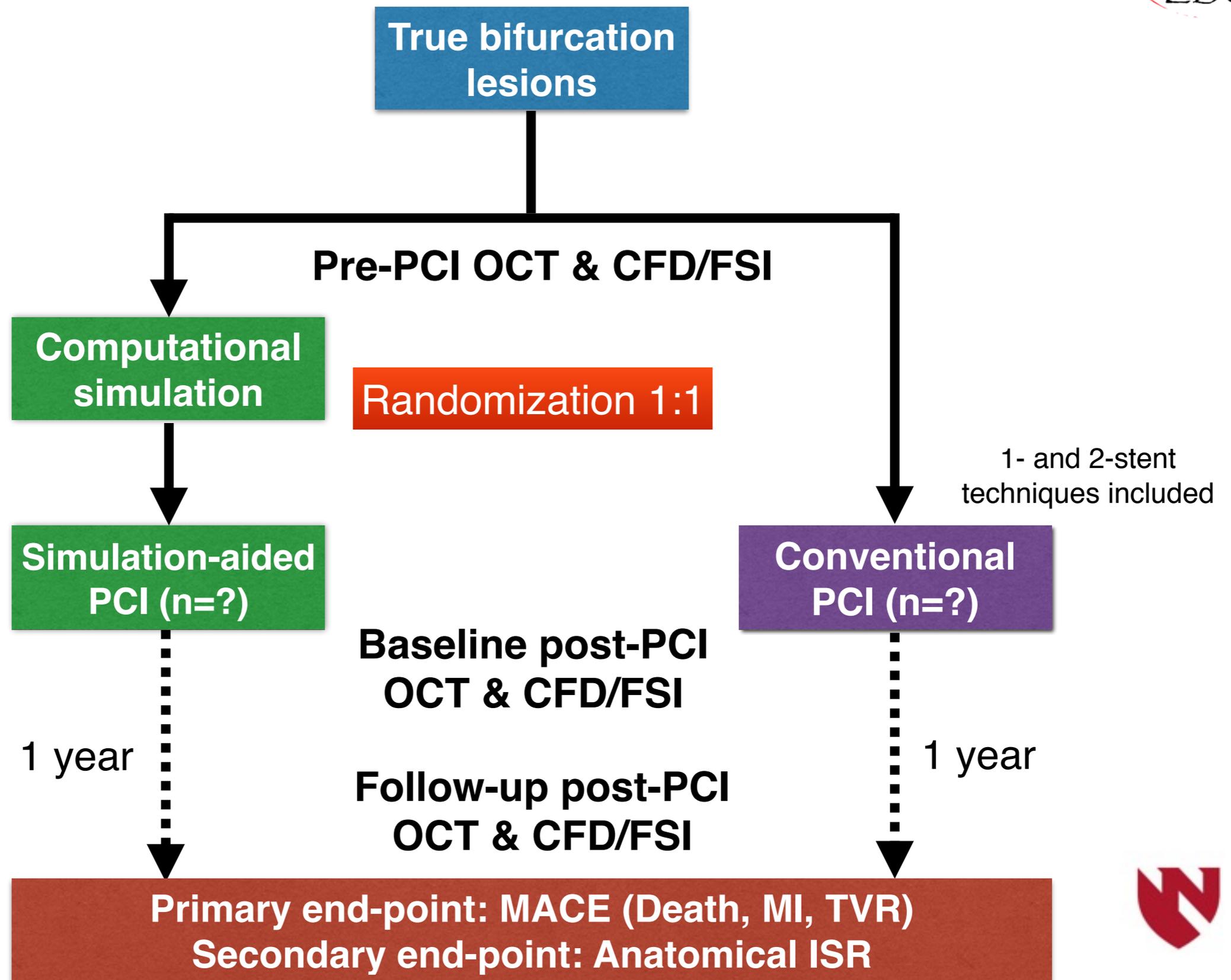


Study Concept



Antoniadis A, et al.
JACC Intv 2015;8:1281-96

Clinical Trial: Design



Adjusted Groups



Table 1 Risk Factors of Late Stent Thrombosis and Potential Role of ESS	
Risk Factor	Effect on In-Stent ESS/ Endothelial Response to ESS
Patient factors	
Diabetes	
Renal failure	
Acute coronary syndrome	
Stent factors	
Incomplete endothelialization	→ Attenuation of physiologic ESS-induced endothelial production of PGI ₂ , tPA, eNOS (2)
Hypersensitivity to the drug or polymer	
Procedural factors	
Bifurcation stenting	→ Adverse hemodynamic impact on the inherently complex ESS environment (68-70)
Lesion complexity	
Multivessel disease	
Excessive stent length	
Stent undersizing	→ Gaps between stent struts and arterial wall → increased flow resistance → low ESS (12)
Incomplete stent expansion (underexpansion)	
Overlapping stents	
Expansive vascular remodeling	→ Reduced flow rate → low ESS (2,4)
Antiplatelet therapy	
Premature discontinuation	
Clopidogrel resistance	

Koskinas KC, Chatzizisis YS, et al. JACC 2012;59:1337-49



Core Labs

- **Core Lab #1:**
 - Imaging data collection
 - 3D reconstruction
 - CFD and mechanical simulations (FSI)
- **Core Lab #2:** Computational simulations of bifurcation stenting

Independent Third-Party Contract Research Organization



- Clinical data collection and monitoring
- Statistical analysis



Potential Funding Sources



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- **Innovation**
- **Patient care**



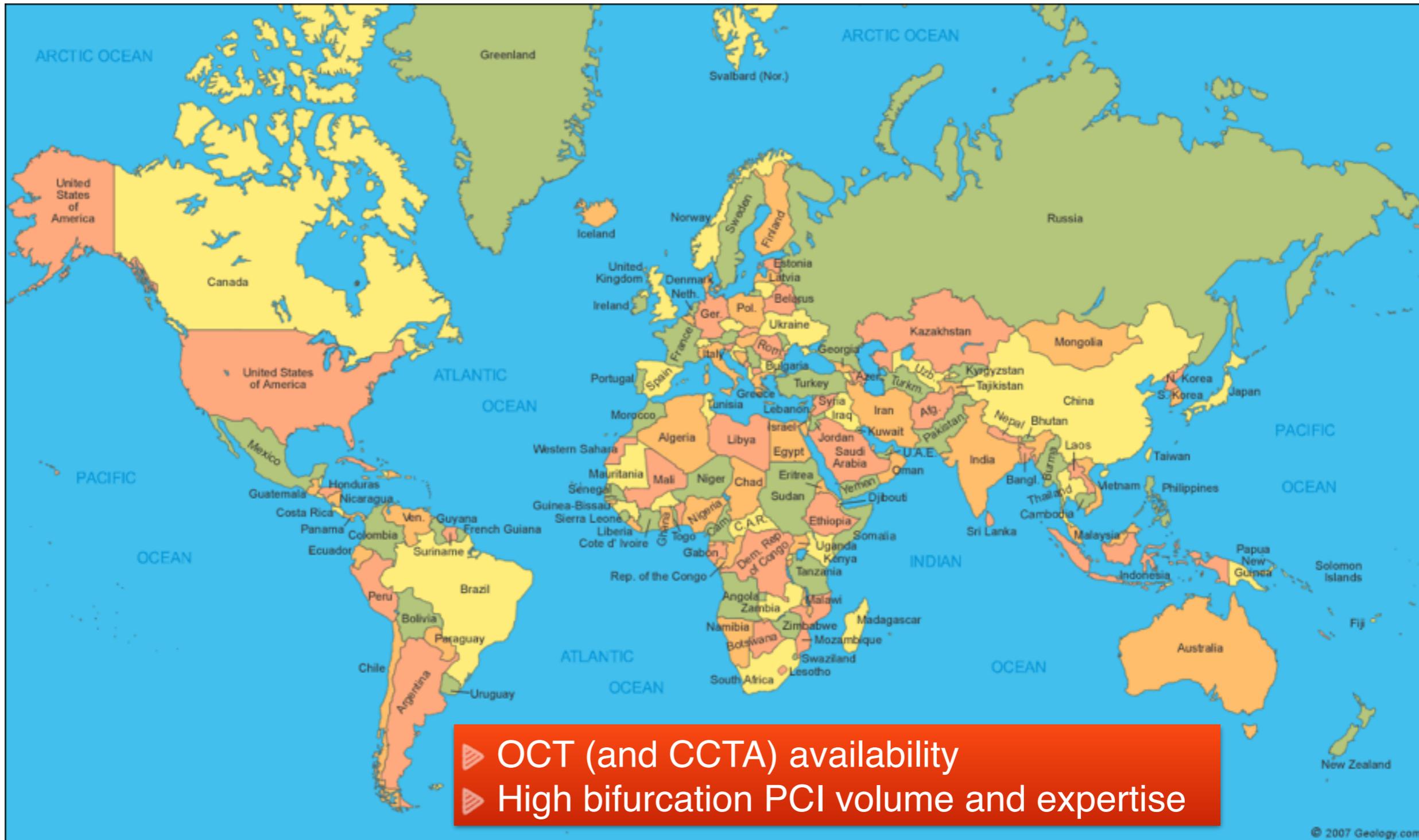
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Co-PIs



Yiannis Chatzizisis and Yves Louvard

