Mechanistic Link between Hemodynamics and Acute Coronary Syndrome

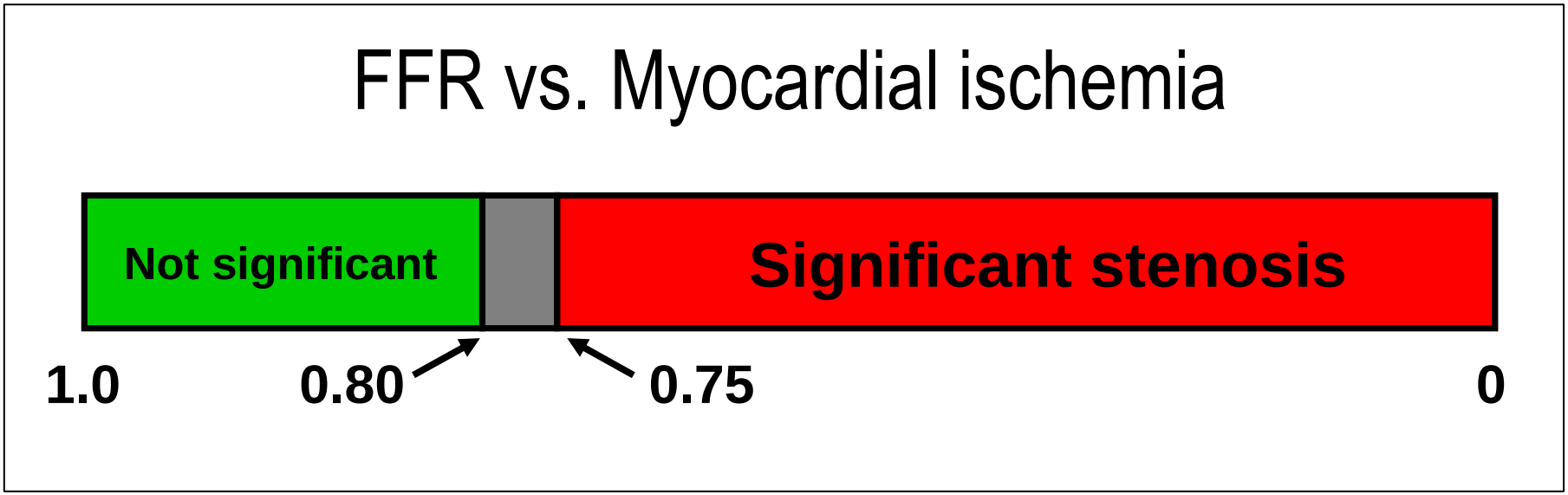
Bon-Kwon Koo, MD, PhD

Seoul National University Hospital, Seoul, Korea

SNUH *Seoul National University Hospital*
Cardiovascular Center

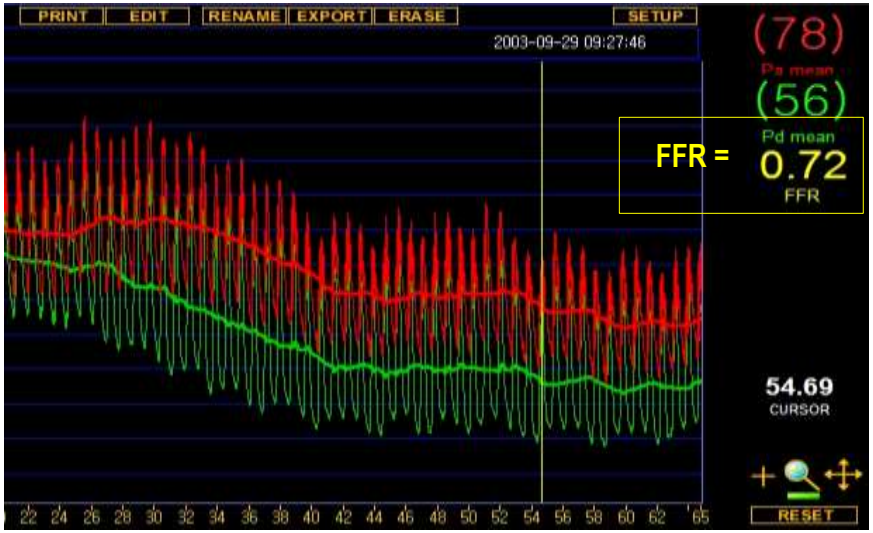
What we already know….

- **Fractional Flow Reserve (FFR)**
  - Invasive index to assess the hemodynamic influence of epicardial stenosis
  - Surrogate for “ischemia”

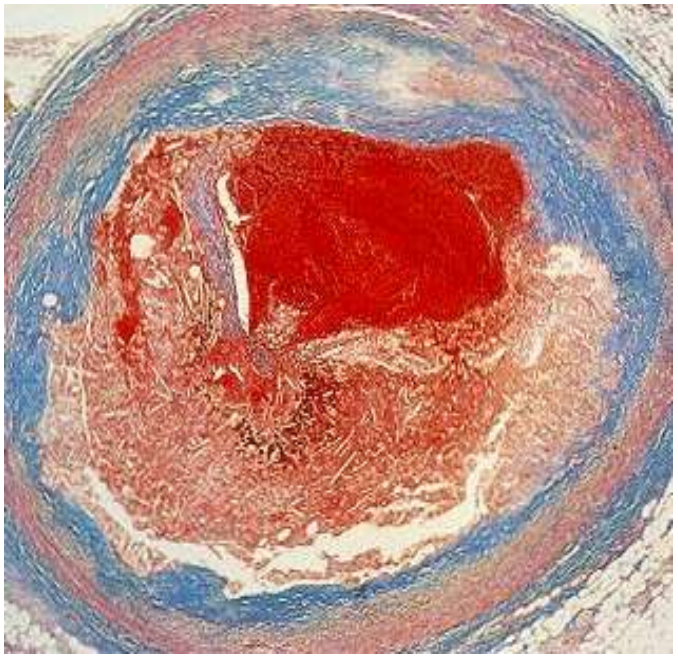


What we already know….

Both are bad, but ACS is worse!

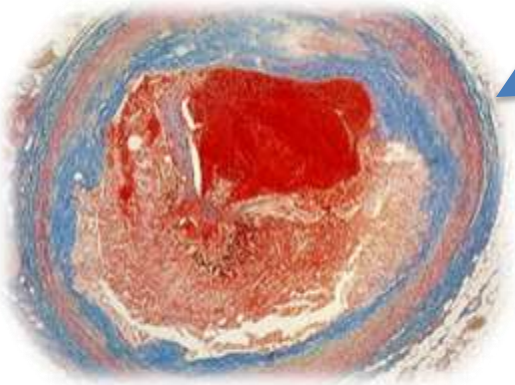


Angina or Ischemia



Acute coronary syndrome (ACS)

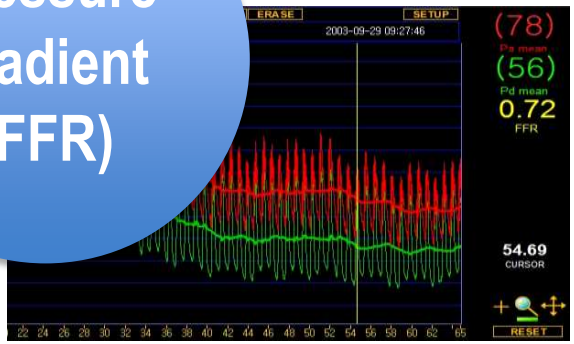
Looking for the links between FFR and ACS…



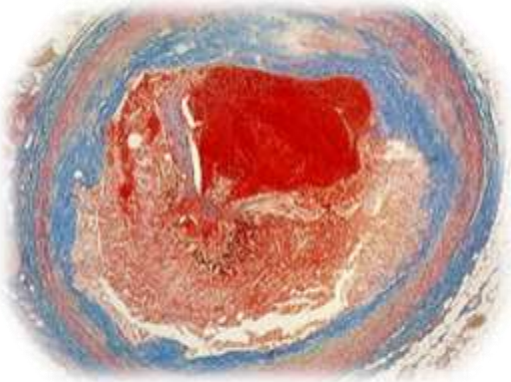
ACS

?

Pressure gradient (FFR)



Looking for the links between FFR and ACS…



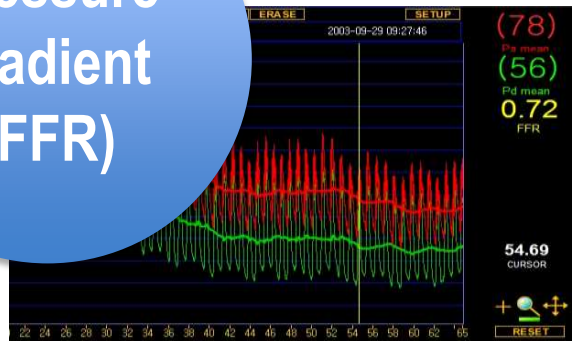
ACS

Thrombosis

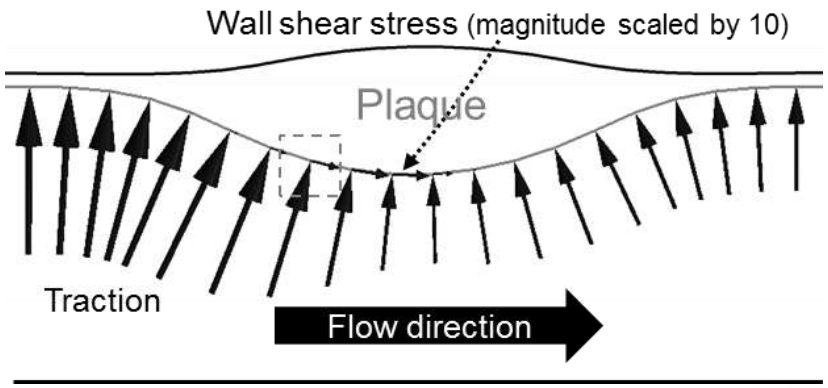
External Force

Plaque vulnerability

Pressure gradient (FFR)



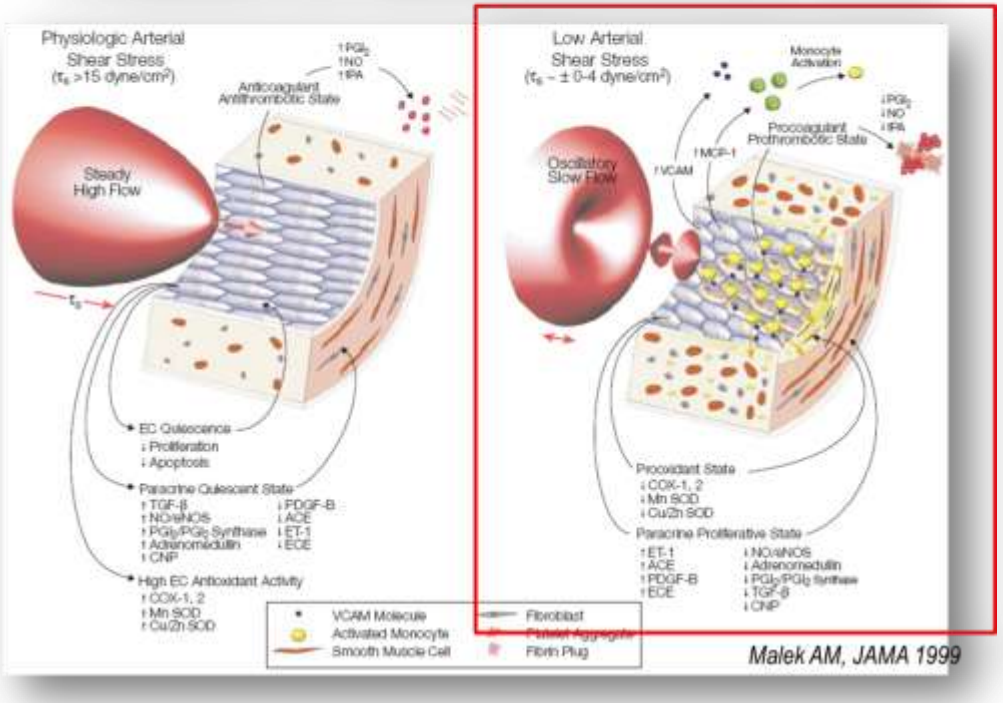
Wall shear stress: Small, but important



Wall shear stress
: Tiny tangential force of flowing blood on endothelial surface

Low wall shear stress

→ ***Proliferative, pro-inflammatory, pro-thrombotic stimulus***



Malek AM, JAMA 1999

Very high WSS vs. Vulnerability

Annals of Biomedical Engineering, Vol. 41, No. 7, July 2013 (© 2012) pp. 1411–1427
DOI: 10.1007/s10439-012-0695-0

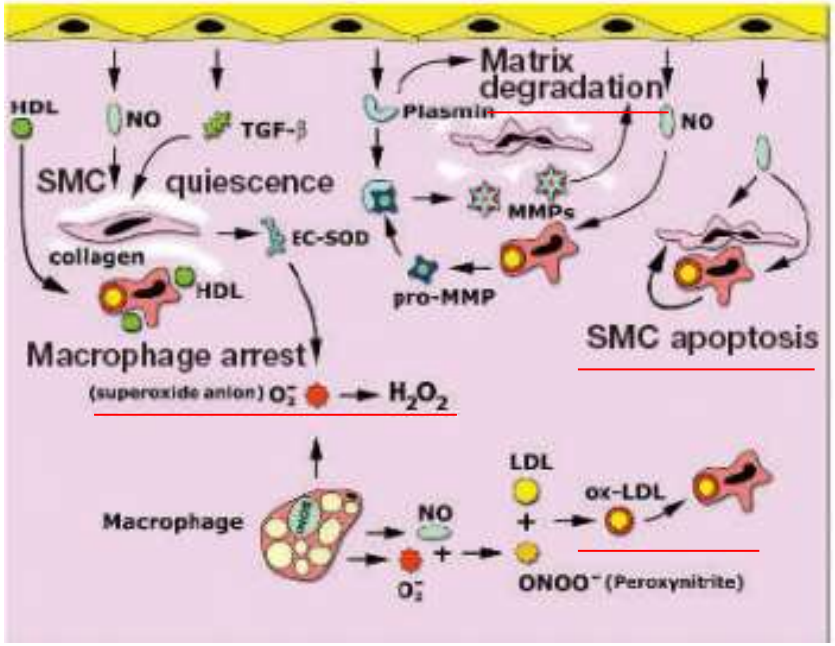
BMES BIOMEDICAL ENGINEERING SOCIETY™ www.bmes.org

High Wall Shear Stress and Spatial Gradients in Vascular Pathology: A Review

JENNIFER M. DOLAN,[1,3,4] JOHN KOLEGA,[1,3,4] and HUI MENG[1,2,3,5]

Abstract—Cardiovascular pathologies such as intracranial aneurysms (IAs) and atherosclerosis preferentially localize to bifurcations and curvatures where hemodynamics are complex. While extensive knowledge about low wall shear stress (WSS) has been generated in the past, due to its strong relevance to atherogenesis, high WSS (typically >3 Pa) has emerged as a key regulator of vascular biology and pathology as well, receiving renewed interests. As reviewed here, chronic high WSS not only stimulates adaptive outward remodeling, but also contributes to saccular IA formation (at bifurcation apices or outer curves) and atherosclerotic plaque destabilization (in stenosed vessels). Recent advances in understanding IA pathogenesis have shed new light on the

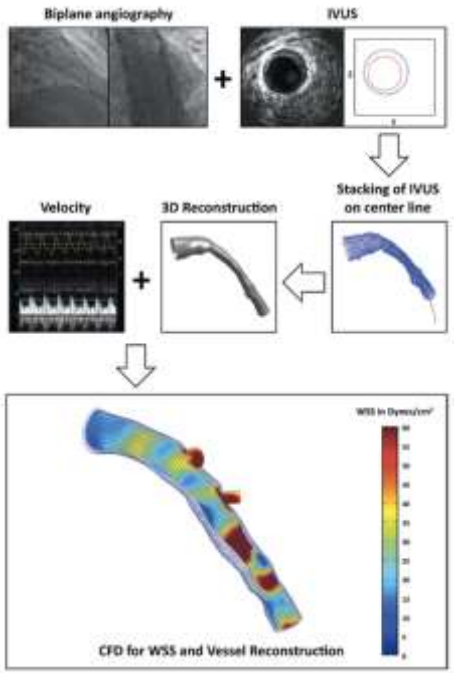
Very High SS

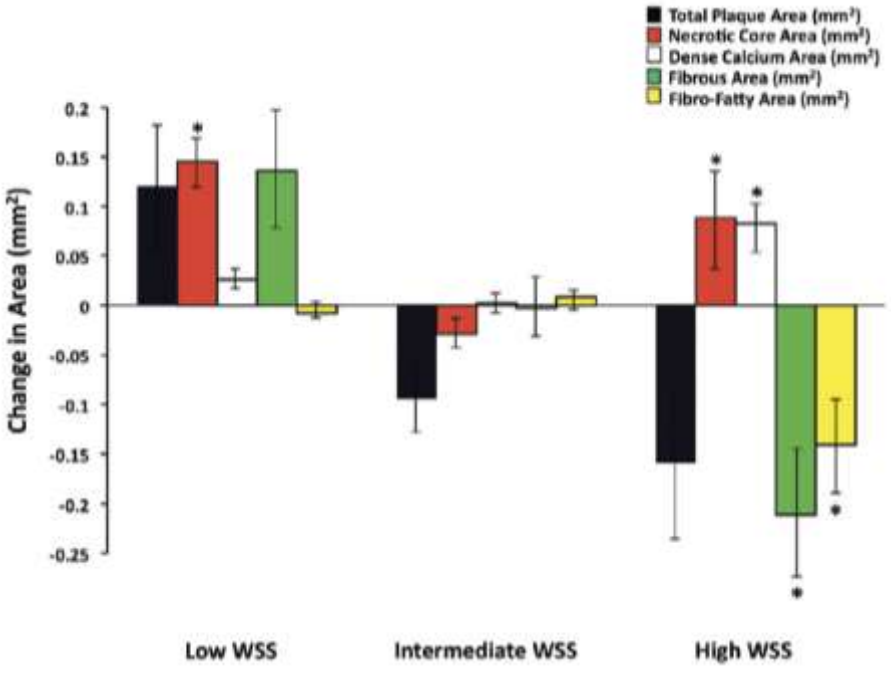


Slager, et al. Nature Clin Pract 2005

Coronary Artery Wall Shear Stress Is Associated With Progression and Transformation of Atherosclerotic Plaque and Arterial Remodeling in Patients With Coronary Artery Disease

Habib Samady, MD; Parham Eshtehardi, MD; Michael C. McDaniel, MD; Jin Suo, PhD; Saurabh S. Dhawan, MD; Charles Maynard, PhD; Lucas H. Timmins, PhD; Arshed A. Quyyumi, MD; Don P. Giddens, PhD





Conclusions—Compared with intermediate-WSS coronary segments, low-WSS segments develop greater plaque and necrotic core progression and constrictive remodeling, and high-WSS segments develop greater necrotic core and calcium progression, regression of fibrous and fibrofatty tissue, and excessive expansive remodeling, suggestive of transformation to a more vulnerable phenotype.

Circulation 2011

High WSS vs. Platelet activity

High-Shear Stress Sensitizes Platelets to Subsequent Low-Shear Conditions

JAWAAD SHERIFF,[1] DANNY BLUESTEIN,[1] GAURAV GIRDHAR,[1] and JOLYON JESTY[2]

[1]Department of Biomedical Engineering, T18-030 Health Sciences Center, Stony Brook University, Stony Brook, NY 11794-8181, USA; and [2]Division of Hematology/Oncology, T15-040 Health Sciences Center, School of Medicine, Stony Brook University, Stony Brook, NY 11794-8151, USA

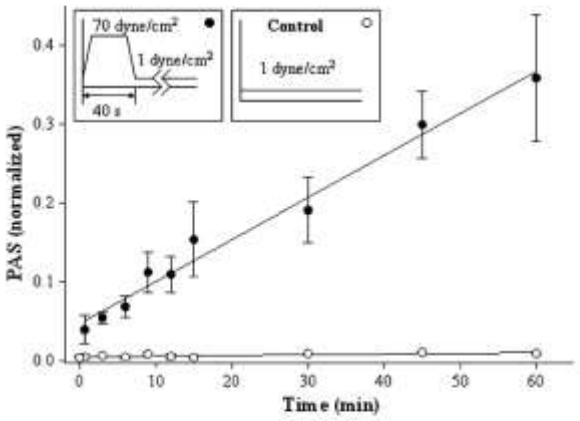


FIGURE 1. Pre-exposure to high-shear stress, 40 s duration. Platelets were pre-exposed to shear stresses of 1 (control), and 70 dyne/cm^2, as shown in the top bar, followed by exposure to 1 dyne/cm^2 for 59 min. The means of four experiments are shown ±SEM.

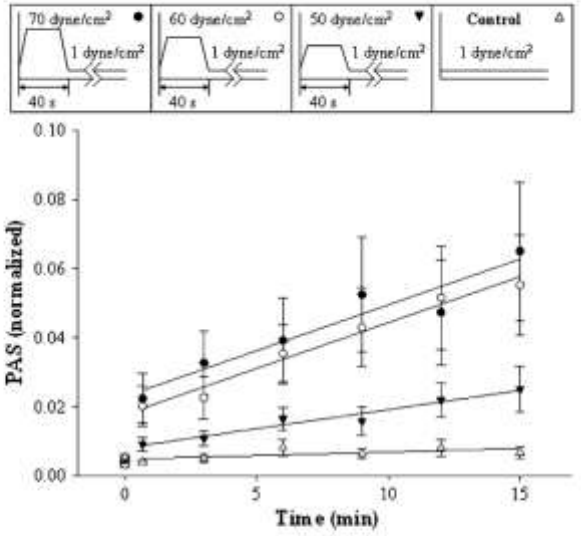
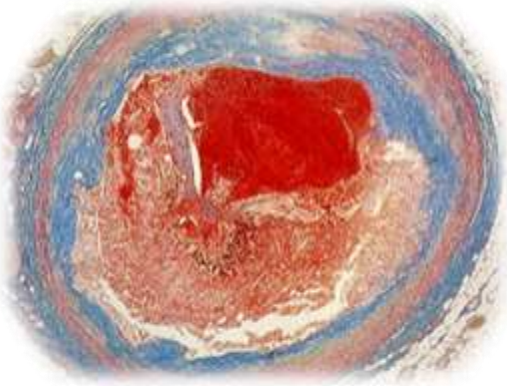


FIGURE 2. Pre-exposure to varying shear stress, 40 s duration. Platelets were pre-exposed to shear stresses of 1 (control), 50, 60, and 70 dyne/cm^2, as shown in the top bar, followed by exposure to 1 dyne/cm^2 for 14 min. The means of nine experiments are shown ±SEM.

Looking for the links between FFR and ACS…



ACS

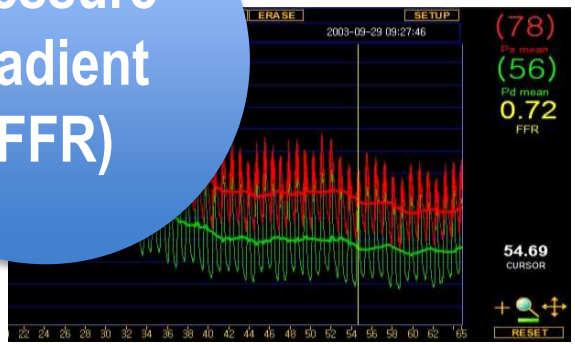
External Force

Thrombosis

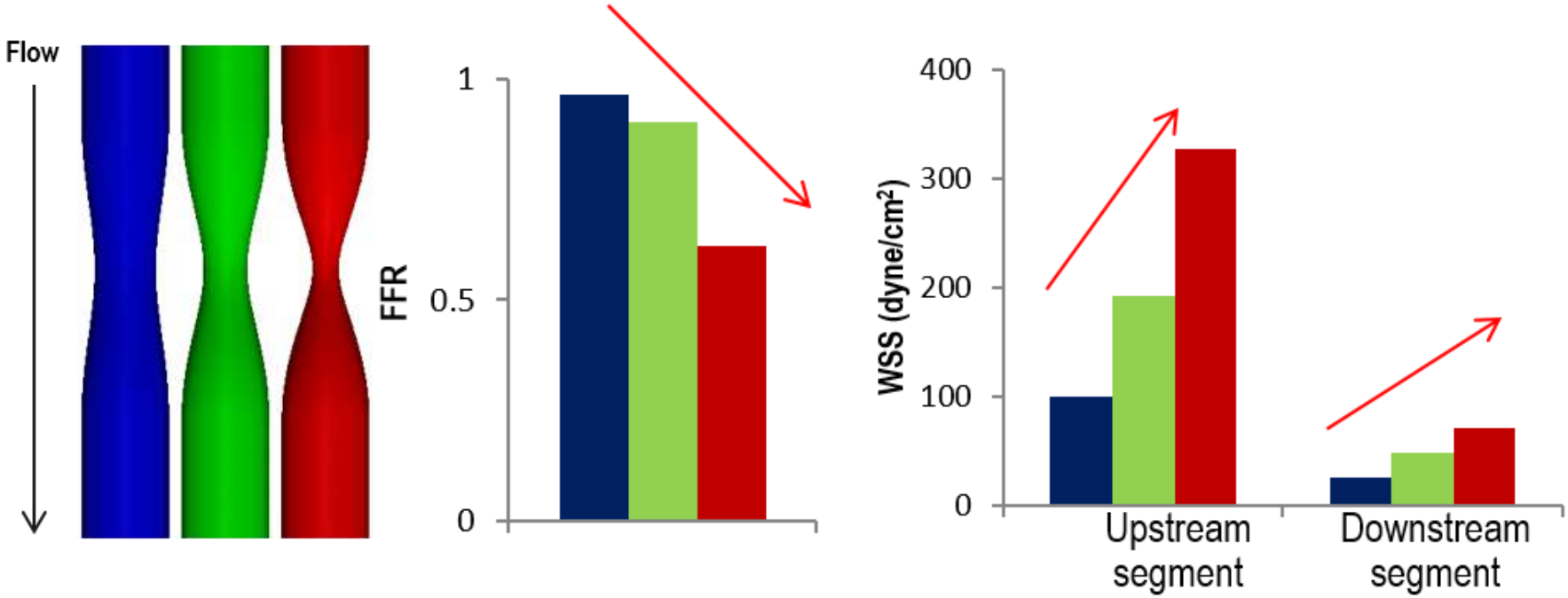
High WSS
High WSS gradient

Plaque vulnerability

Pressure gradient (FFR)

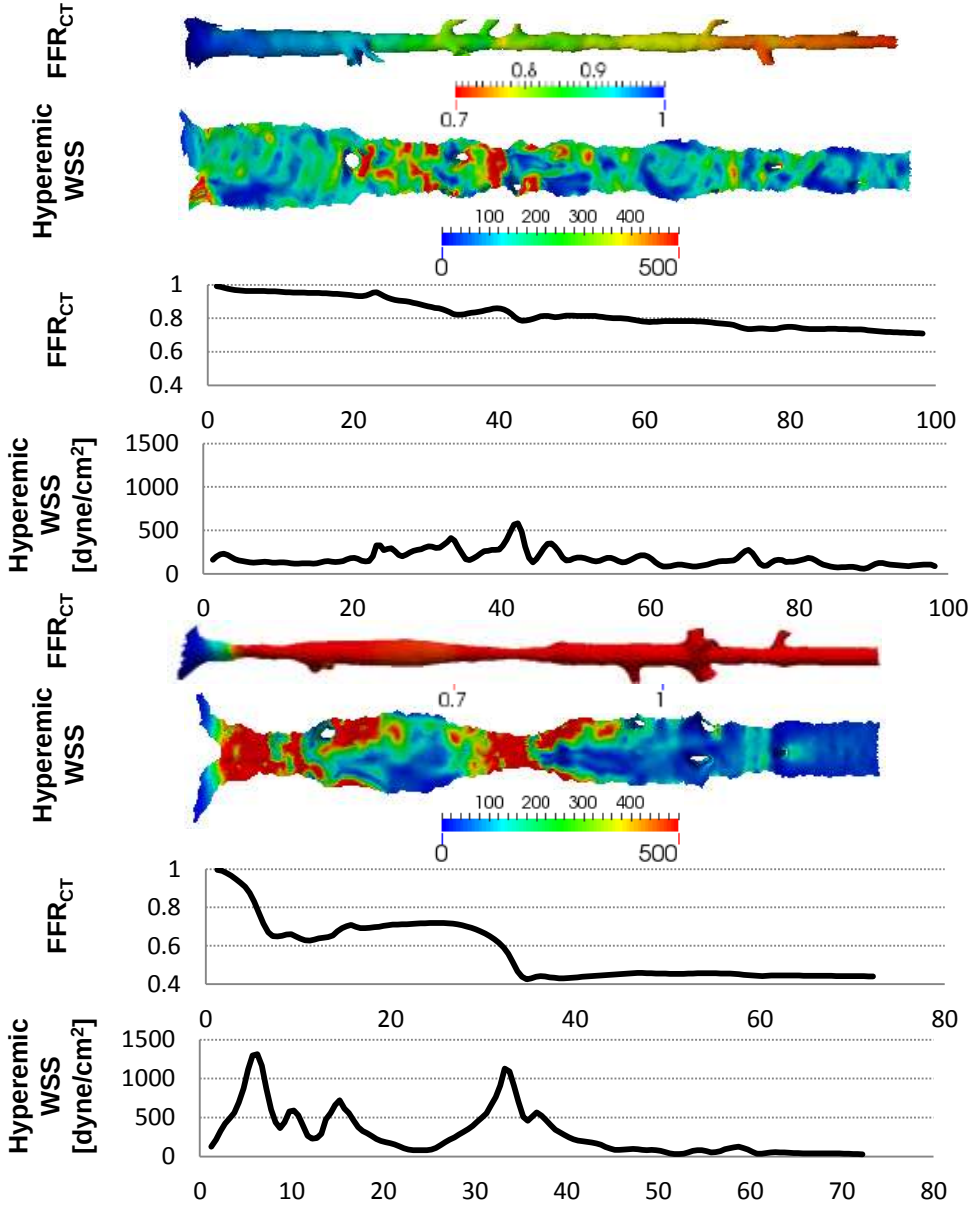


FFR vs. WSS



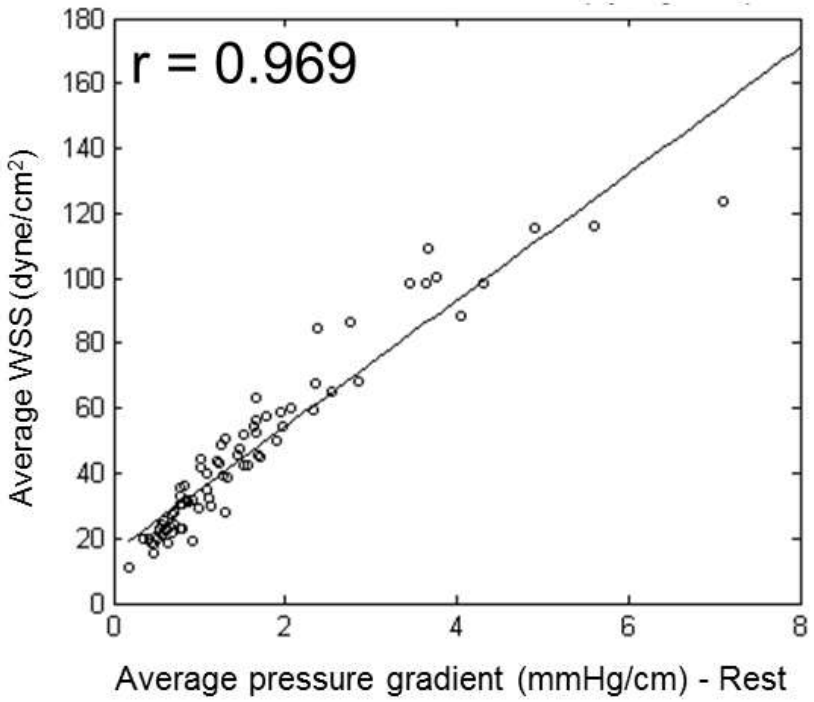
Lee JM…Koo BK. JACC imaging 2015

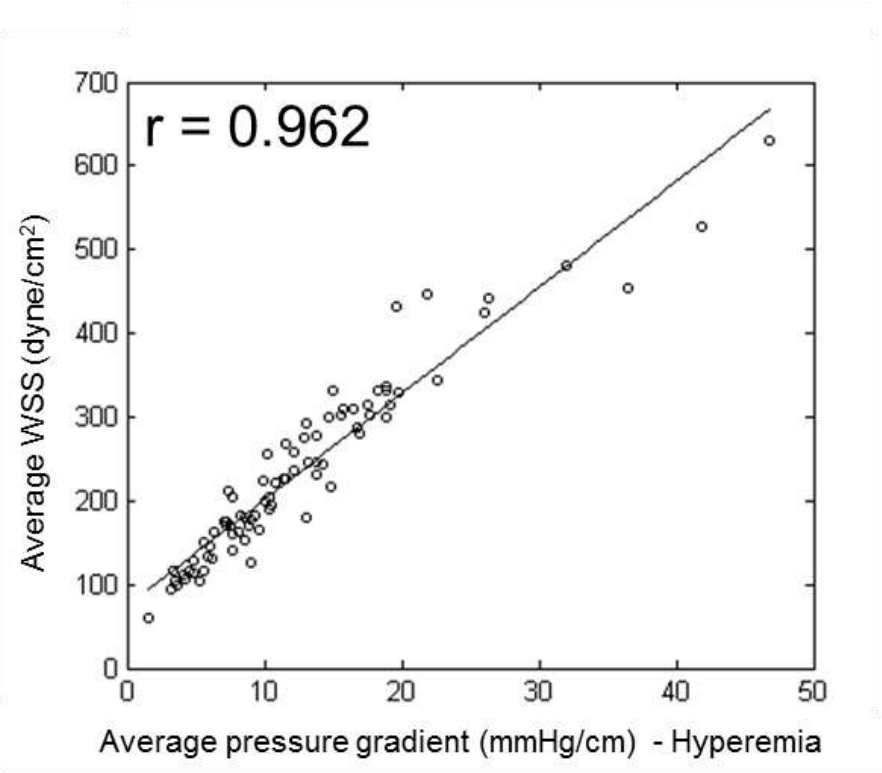
Non-invasive FFR and WSS assessment using cCTA and computational fluid dynamics



Koo BK. International Symposium on Biomechanics 2014

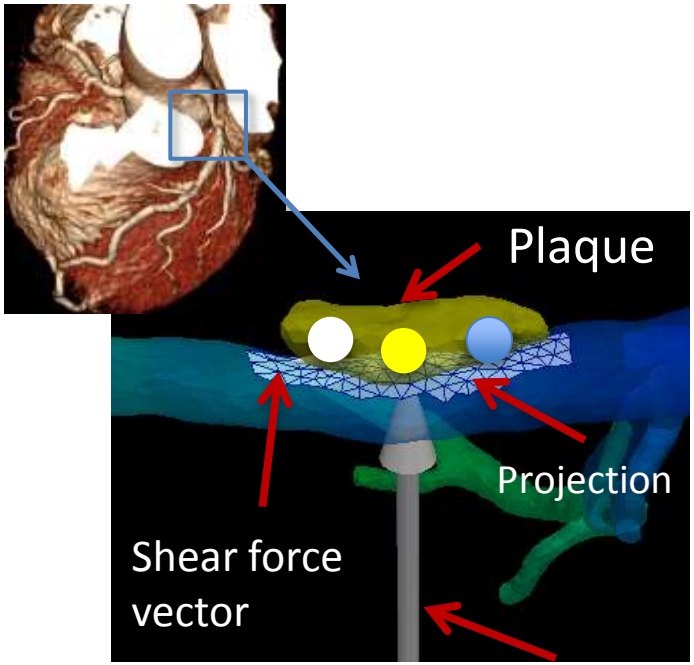
Relationship between WSS and pressure gradient

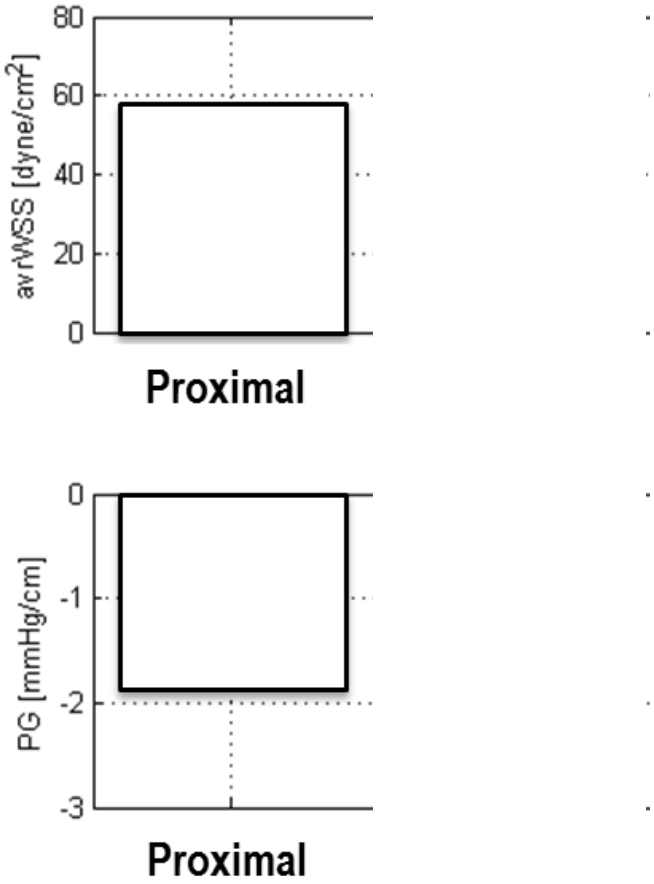




Koo BK. International Symposium on Biomechanics 2014

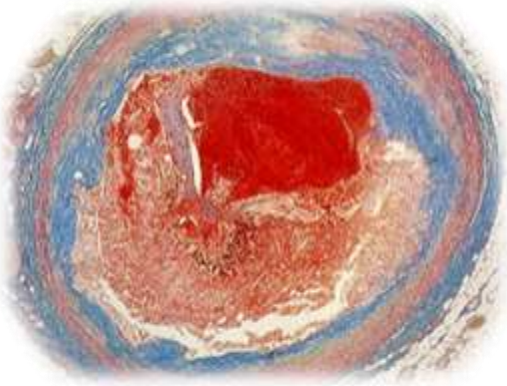
Regional distribution of hemodynamic forces
: WSS vs. Pressure gradient





Koo BK. International Symposium on Biomechanics 2014

Looking for the links between FFR and ACS…



ACS

External Force

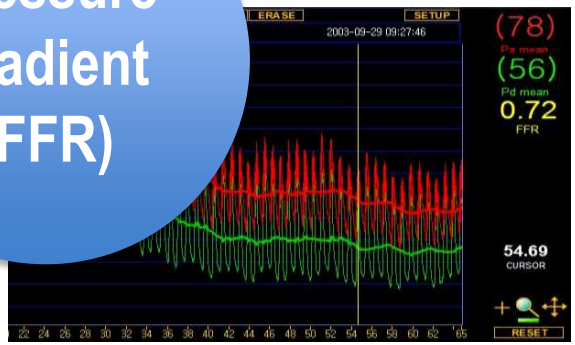
Thrombosis

High WSS
High WSS gradient

Plaque vulnerability

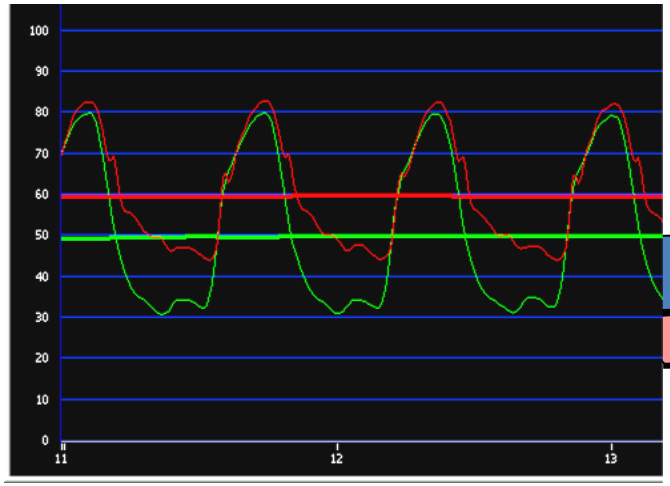
High WSS
High WSS gradient

Pressure gradient (FFR)



Mechanical constraints on coronary stenoses

40.000.000 / year



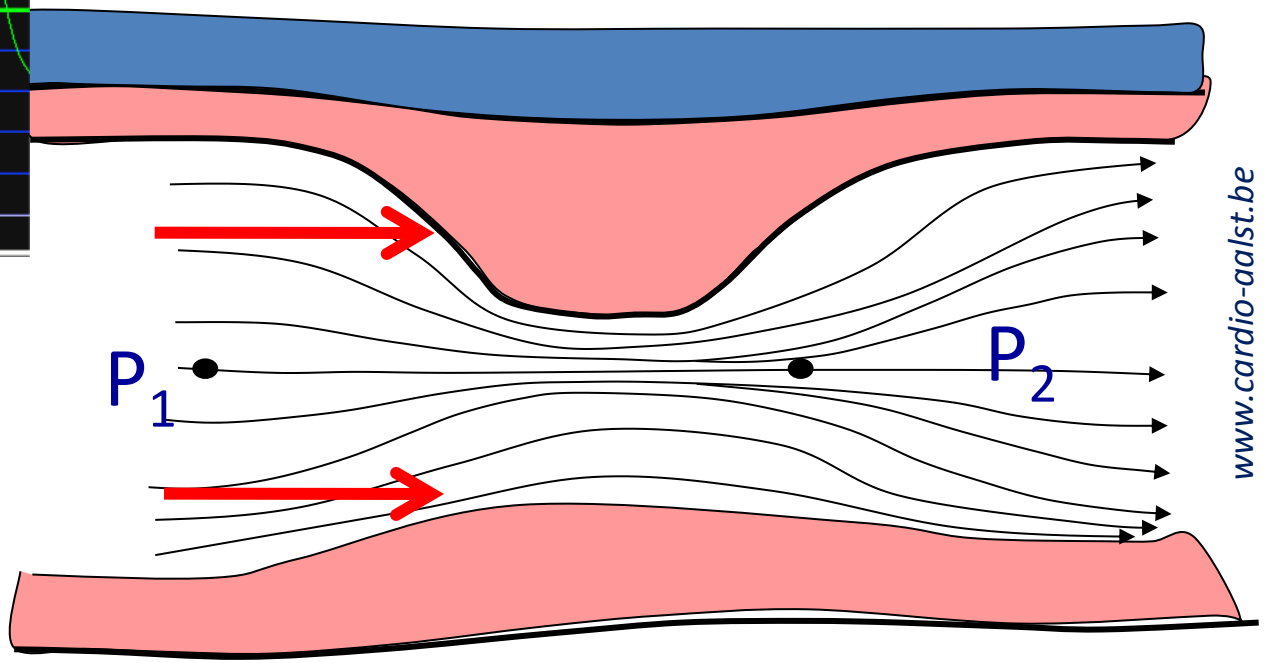
Pressure wave

↓

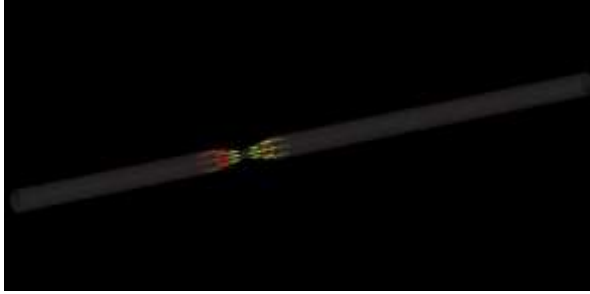
Slicing forces

↓

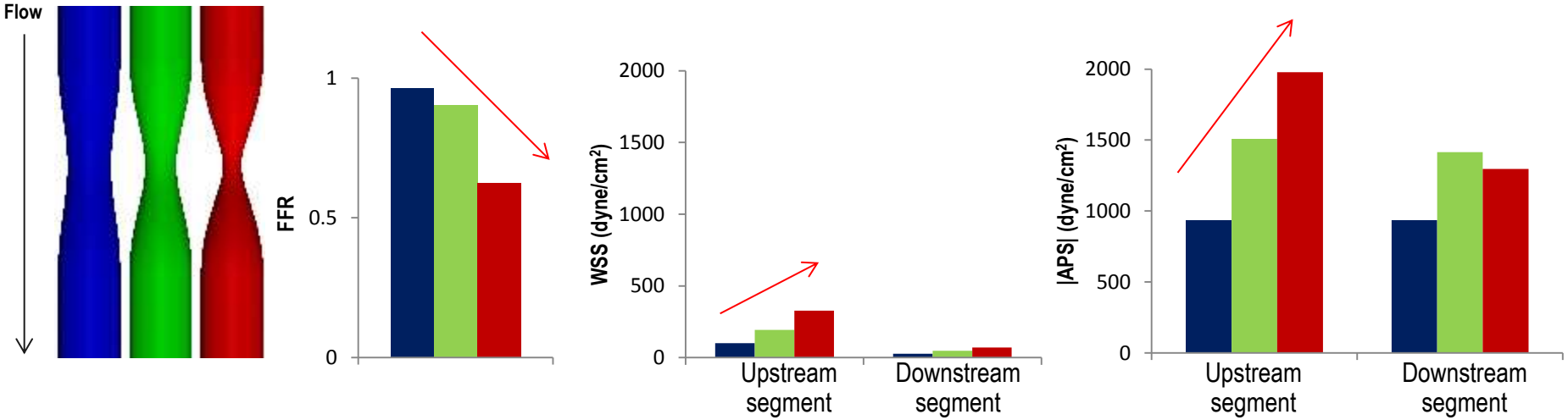
Plaque fatigue



www.cardio-aalst.be

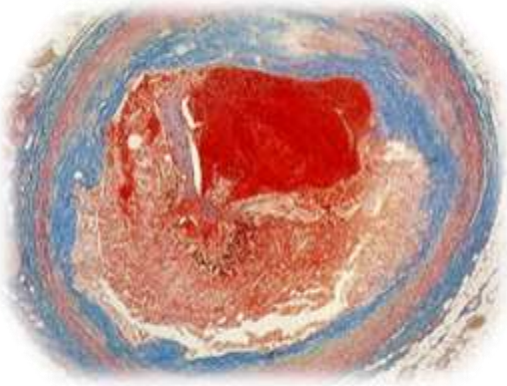


FFR vs. Axial plaque stress



Lee JM…Koo BK. JACC imaging 2015

Looking for the links between FFR and ACS…



ACS

External Force

High plaque stress
Stress imbalance

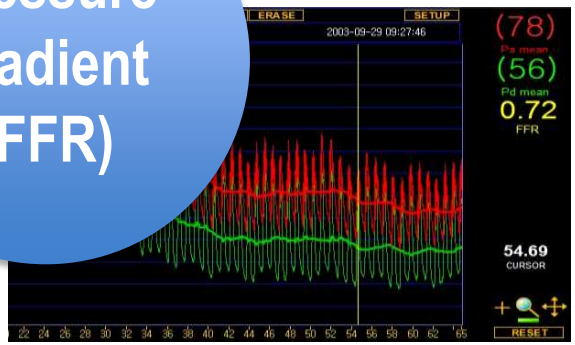
Thrombosis

High WSS
High WSS gradient

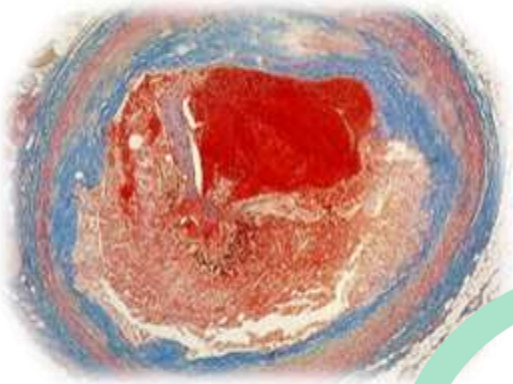
Plaque vulnerability

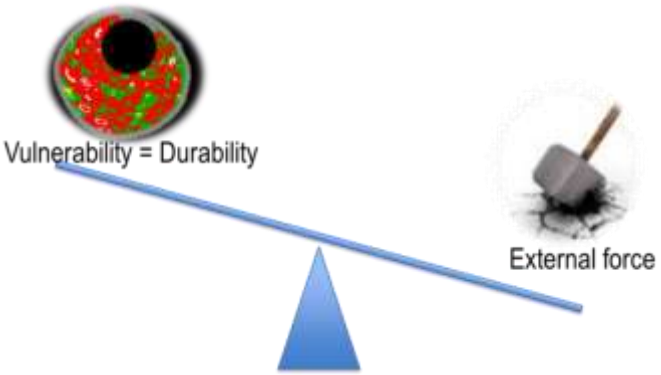
High WSS
High WSS gradient

Pressure gradient (FFR)



Links between FFR and ACS……





Thrombosis

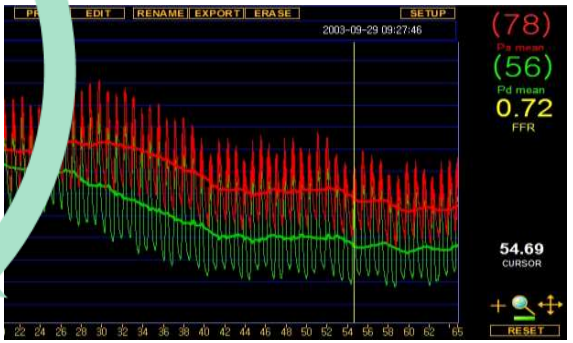
High WSS
High WSS gradient

Plaque vulnerability

Pressure gradient (FFR)

High axial plaque force
Stress imbalance

High WSS
High WSS gradient



In addition to define ischemia, FFR can tell the risk of ACS through the interaction with other hemodynamic parameters.