FFR vs. Acute Coronary Syndrome

Is there any link?

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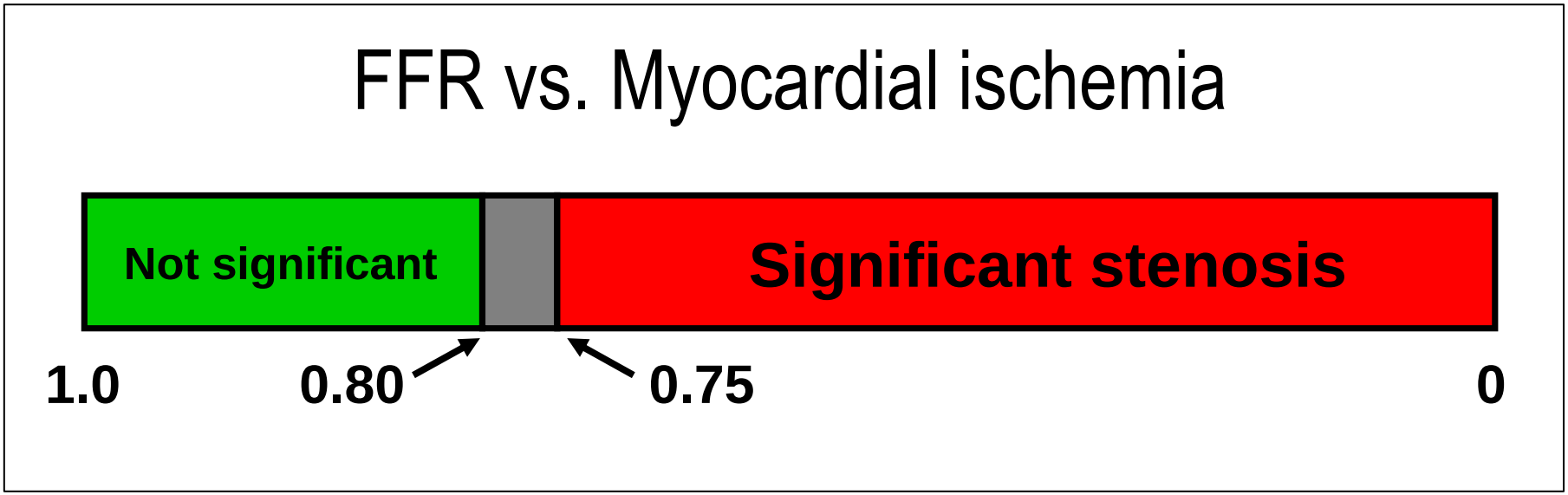
SNUH *Seoul National University Hospital*
Cardiovascular Center

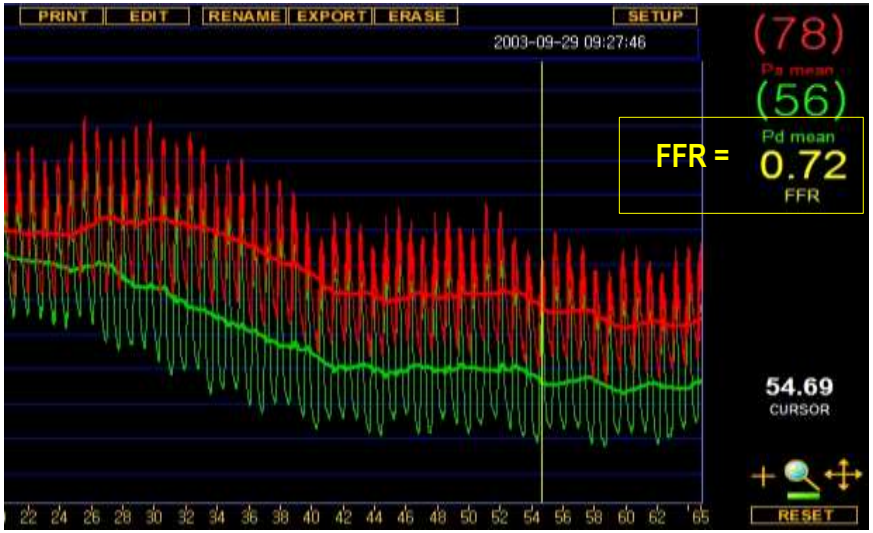
What we already know….

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

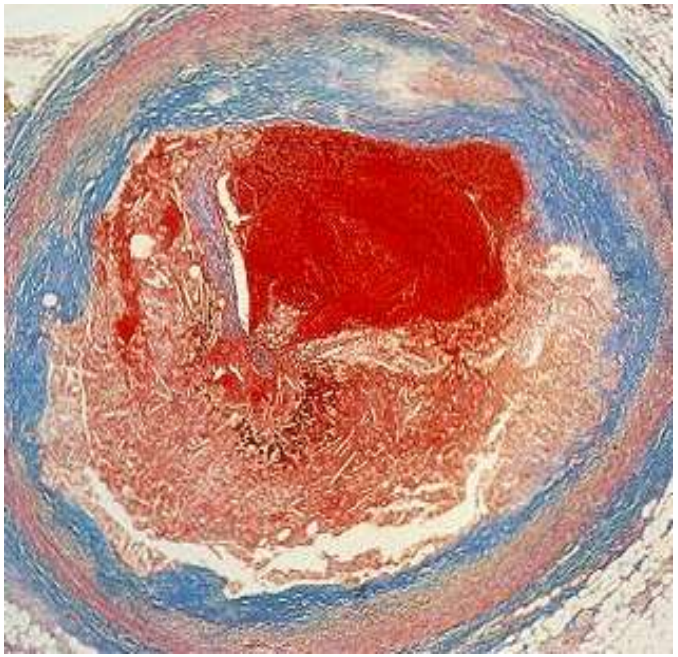


What we already know….

Both are bad, but ACS is worse!

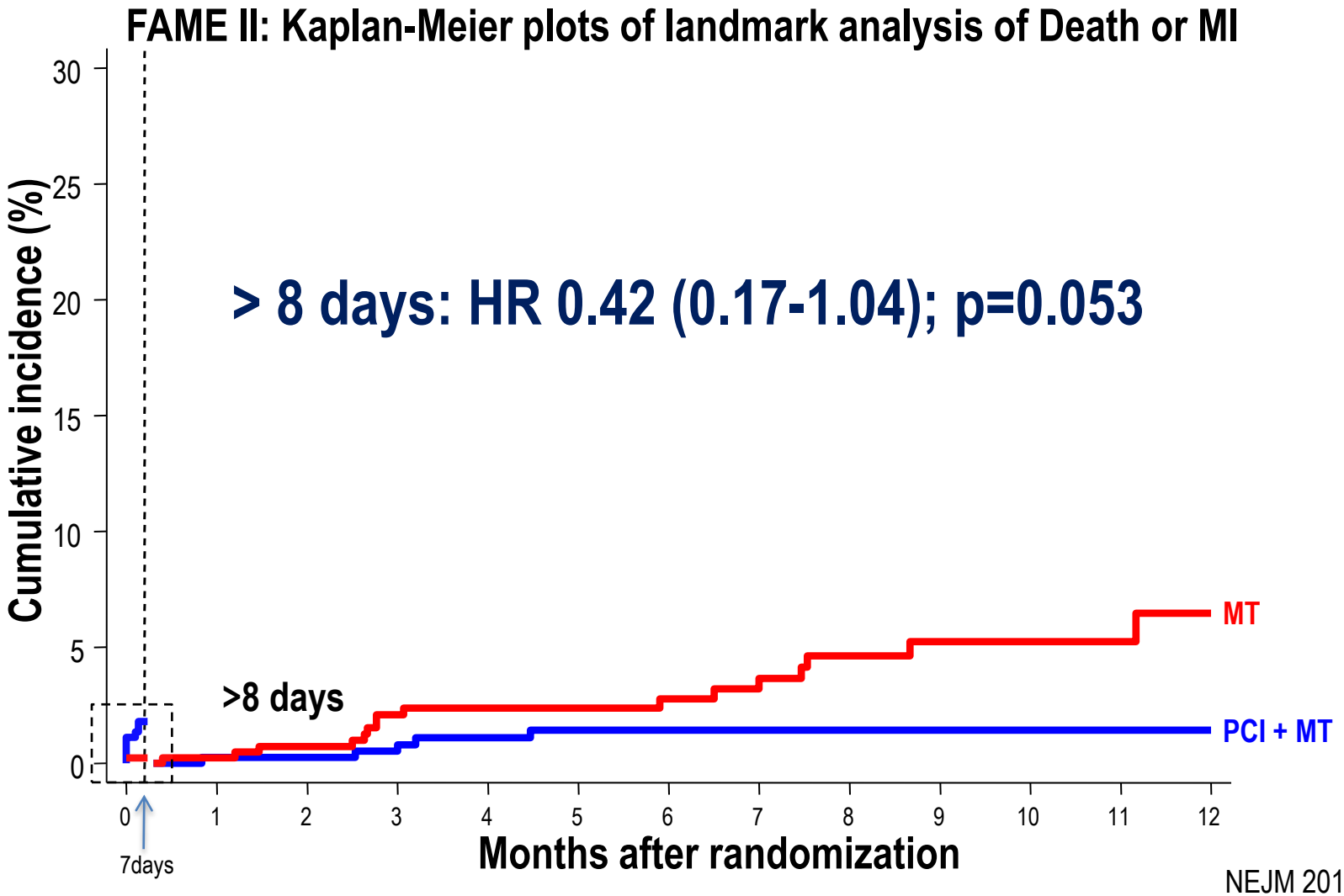


Angina or Ischemia



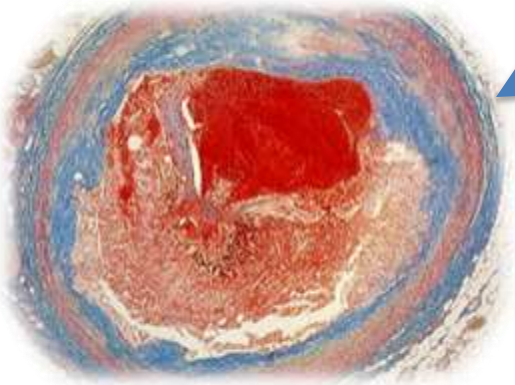
Acute coronary syndrome (ACS)

Link between FFR and ACS?



NEJM 2012

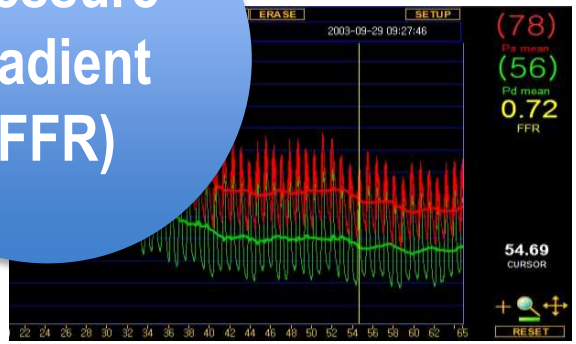
Looking for the links between FFR and ACS…



ACS

?

Pressure gradient (FFR)



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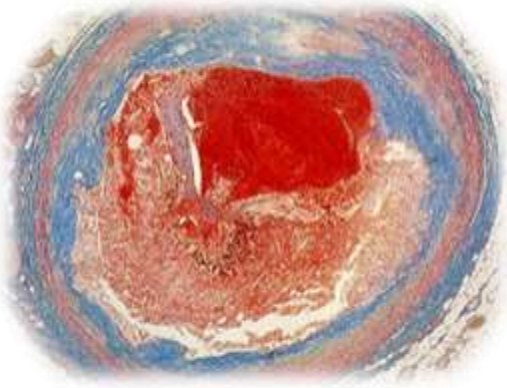


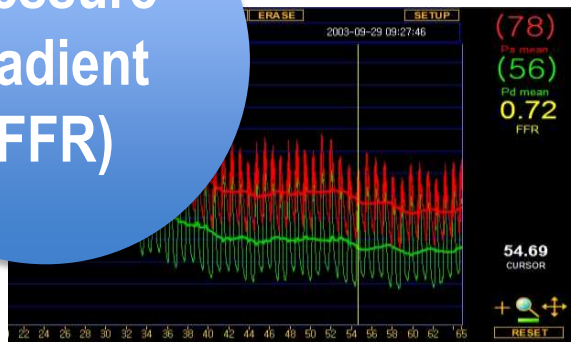
ACS

Thrombosis

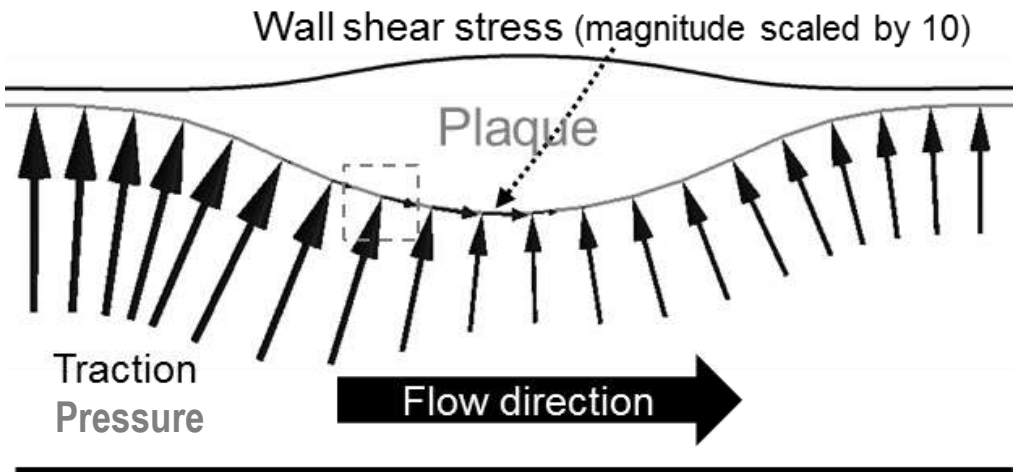
External Force

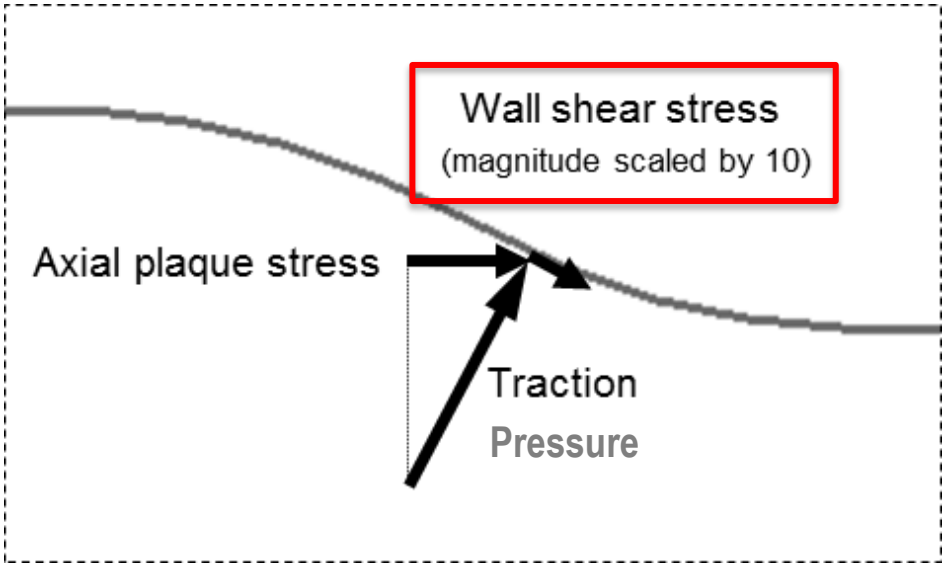
Plaque vulnerability

Pressure gradient (FFR)



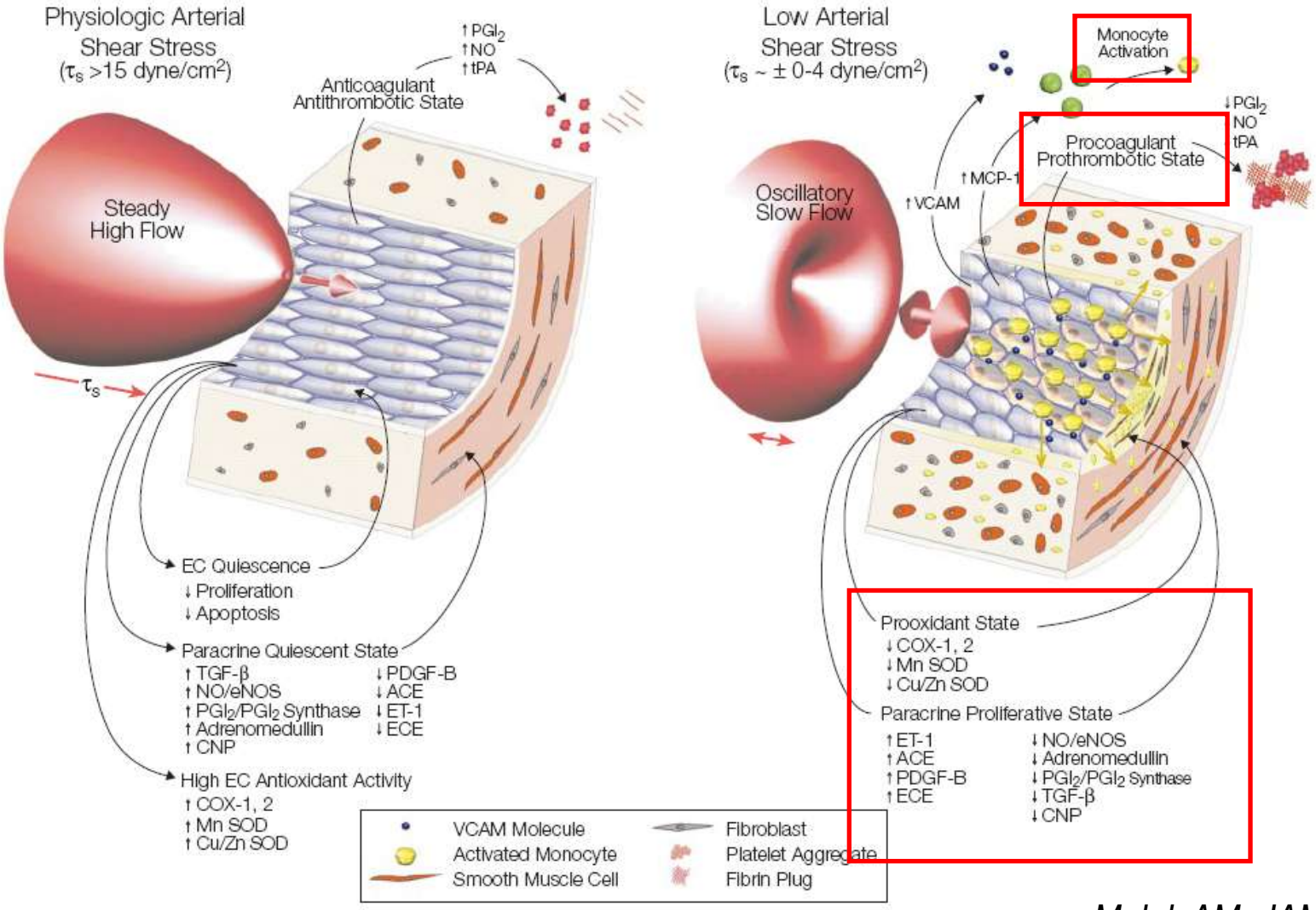
Hemodynamic forces…..





Initiation of plaque: Low wall shear stress

→ Proliferative, pro-inflammatory, pro-thrombotic stimulus



Malek AM, JAMA 1999

High wall shear stress, always good?

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

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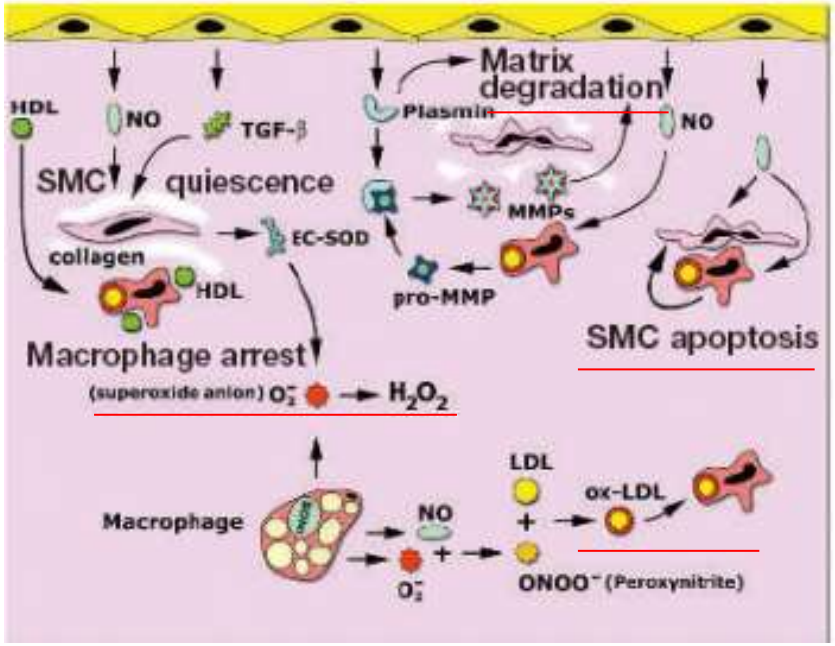
High Wall Shear Stress and Spatial Gradients in Vascular Pathology: A Review

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

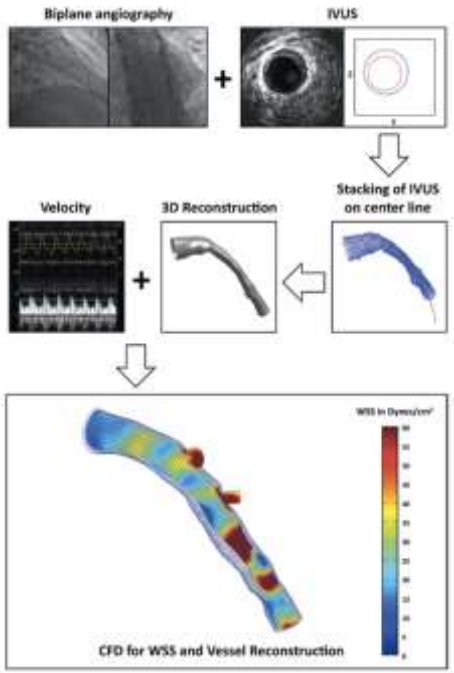
Very High SS

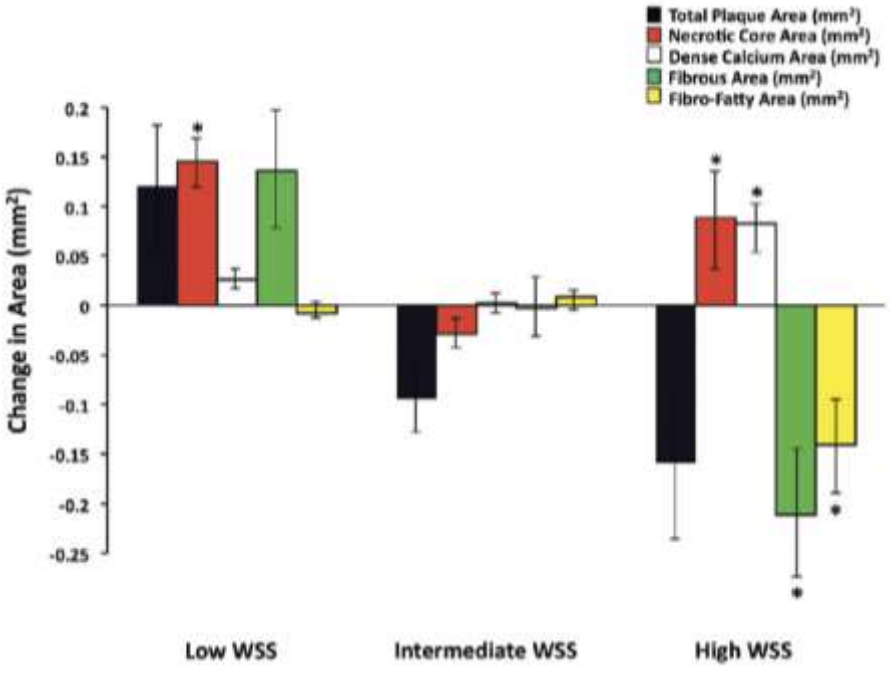


Slager, et al. Nature Clin Pract 2005

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

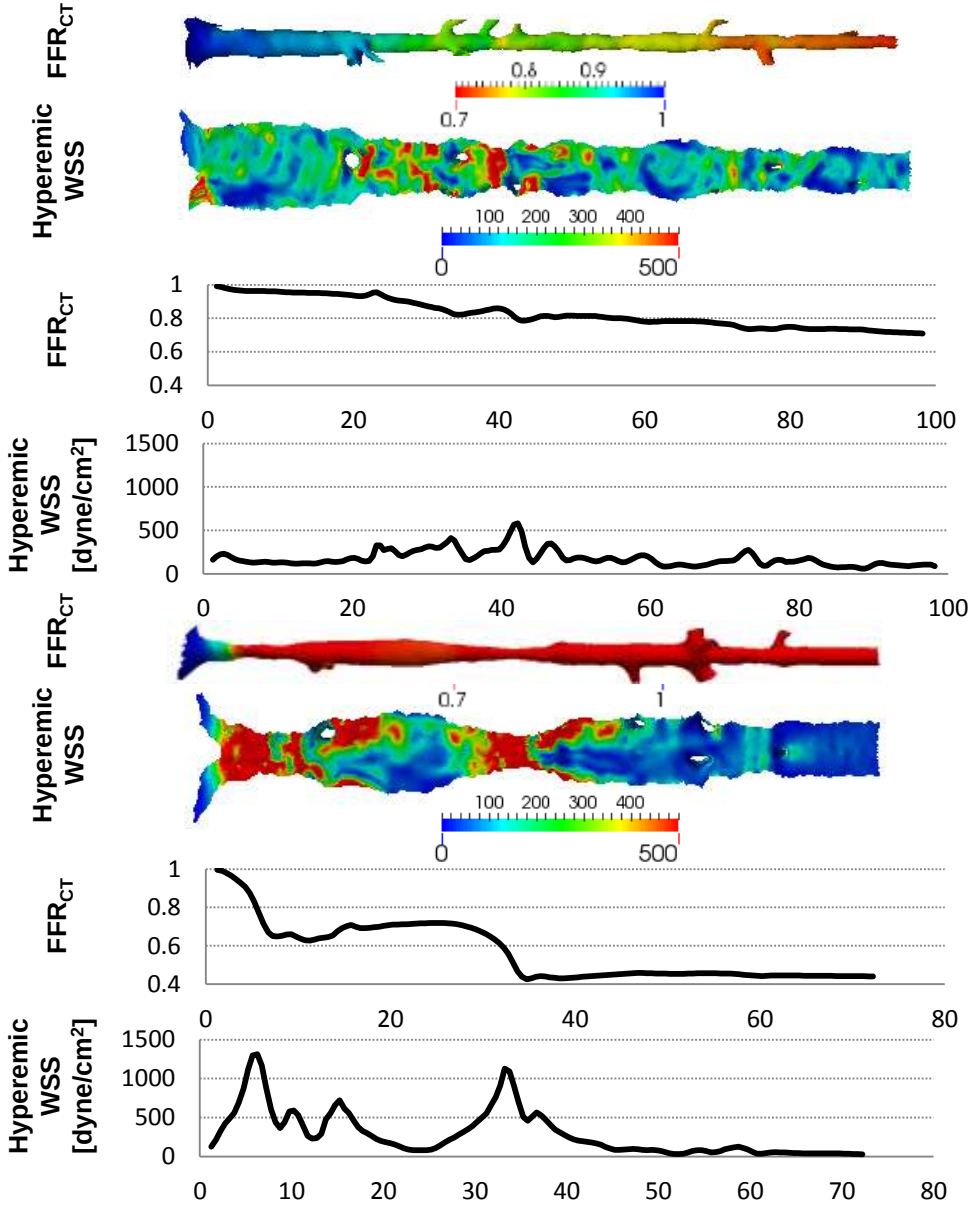
Habib Samady, MD; Parham Eshtehardi, MD; Michael C. McDaniel, MD; Jin Suo, PhD; Saurabh S. Dhawan, MD; Charles Maynard, PhD; Lucas H. Timmins, PhD; Arshed A. Quyyumi, MD; Don P. Giddens, PhD





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.

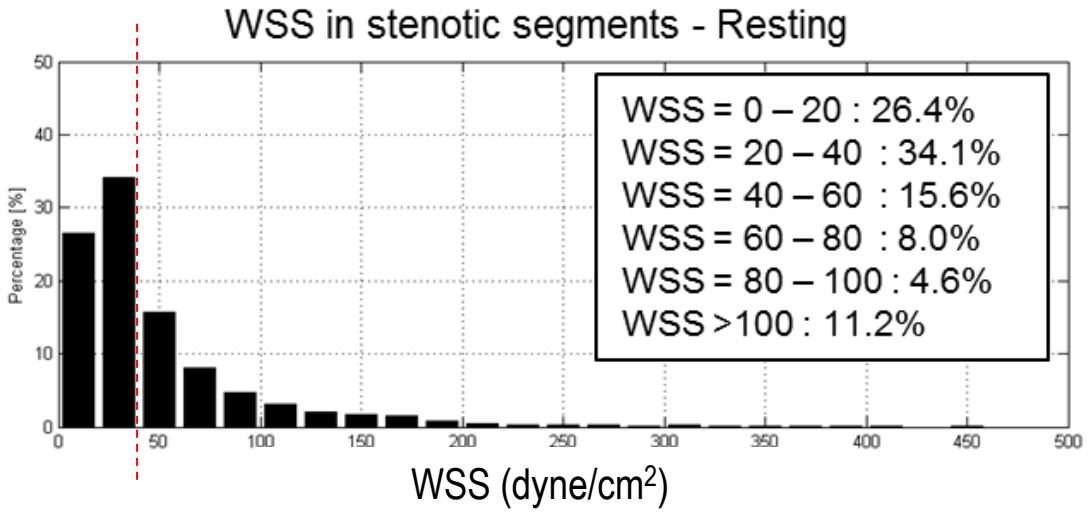
Measurement of hemodynamic parameters in a patient using cCTA and computational fluid dynamics

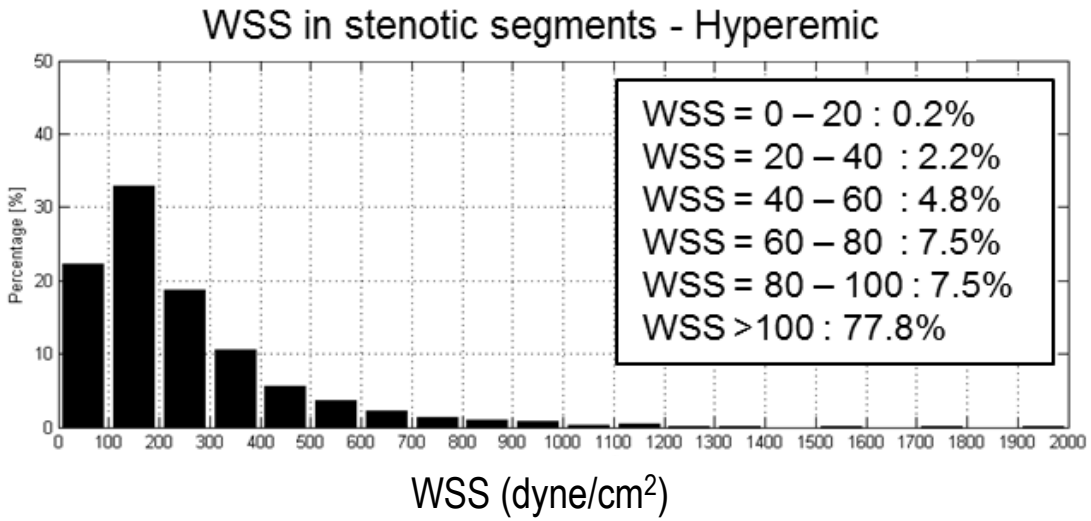


Koo BK. International Symposium on Biomechanics 2014

WSS in clinically relevant lesions

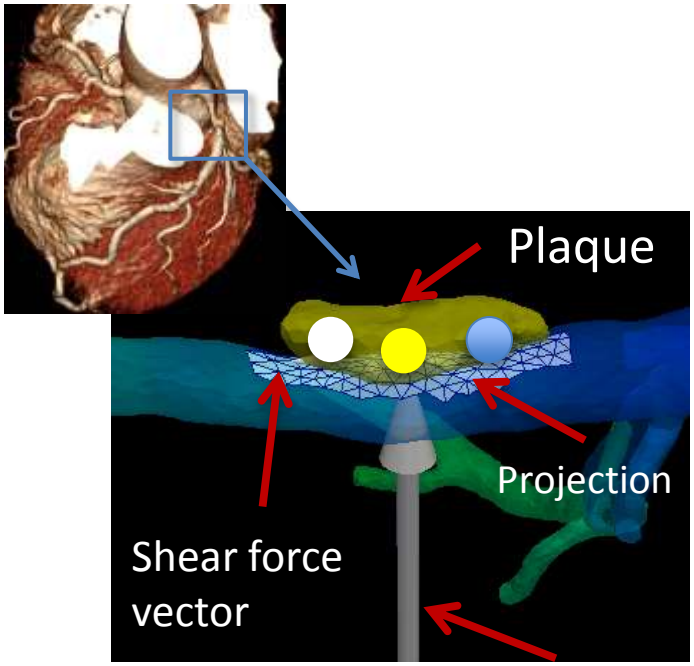
- 80 patients
- Clinically driven invasive coronary angiography and CT angiography
- Average % diameter stenosis: 52.3±12.4%

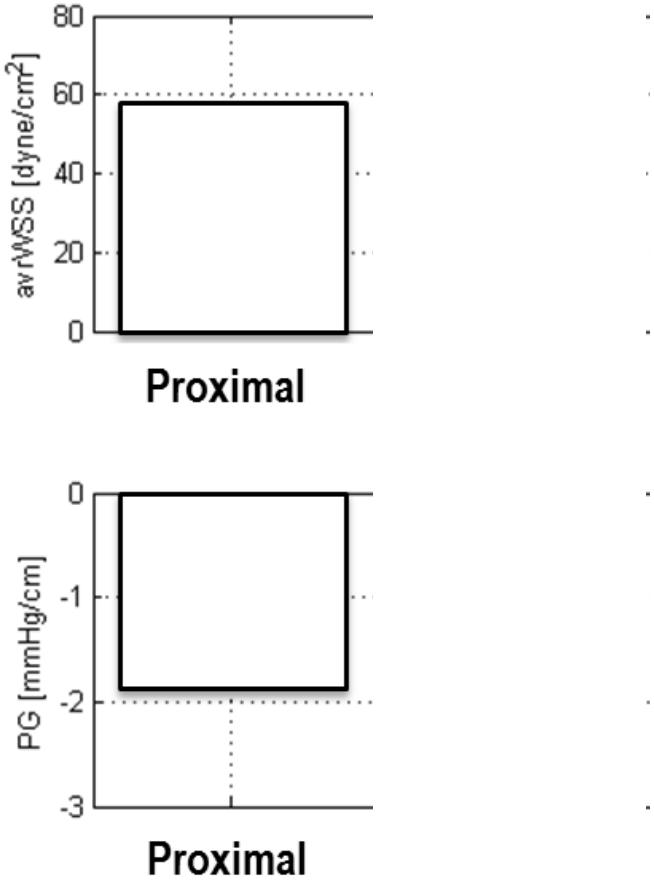




Koo BK. International Symposium on Biomechanics 2014

Regional distribution of hemodynamic forces
: WSS vs. Pressure gradient





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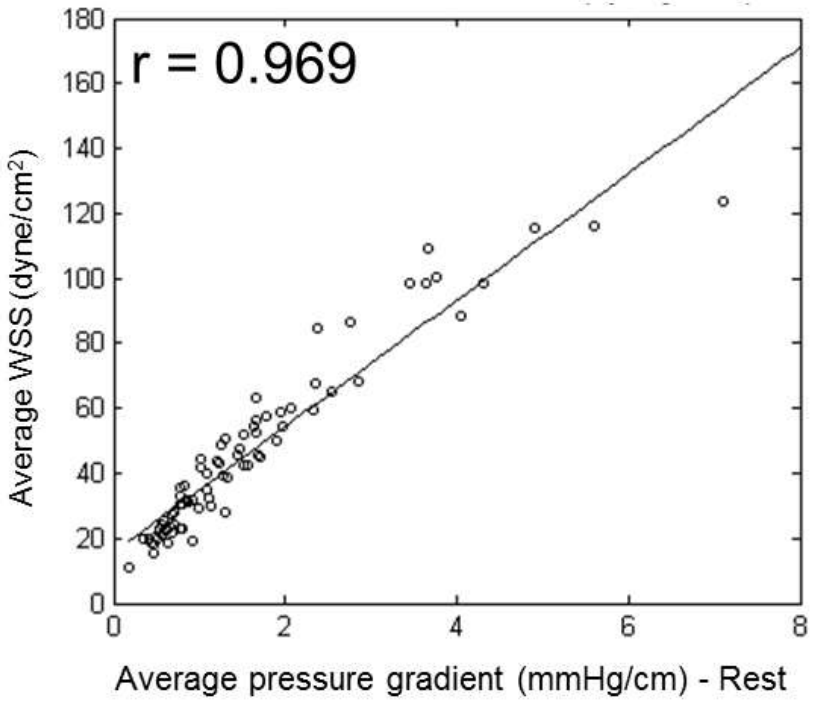
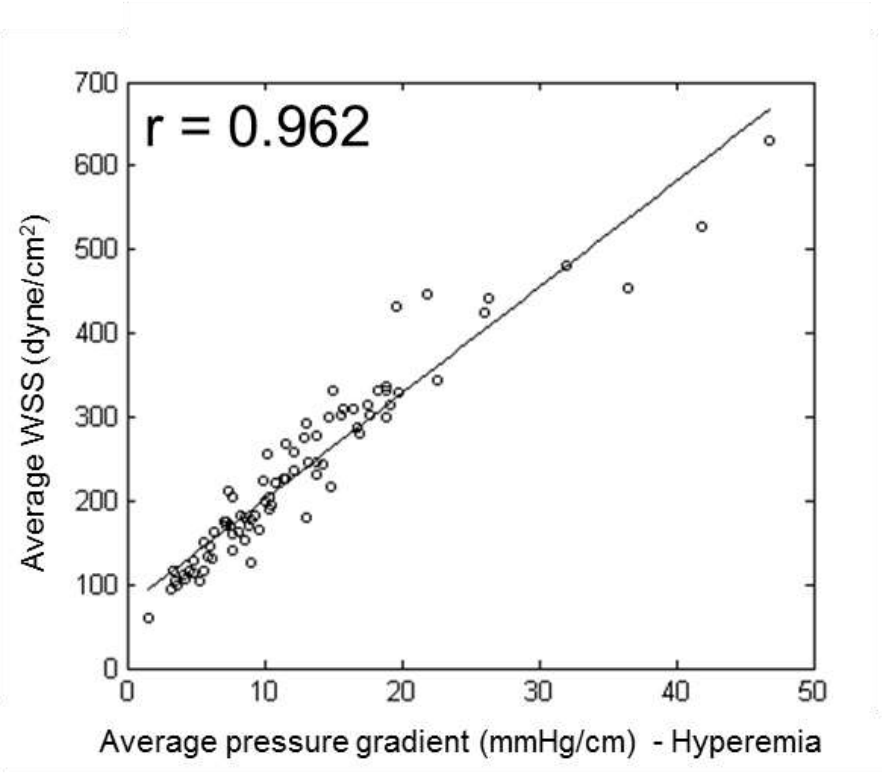
Relationship between WSS and pressure gradient





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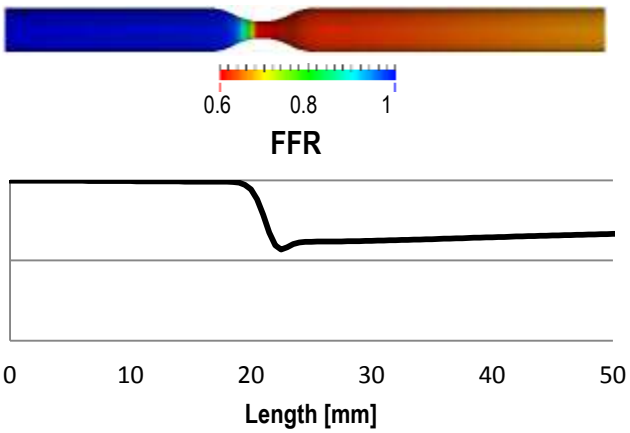
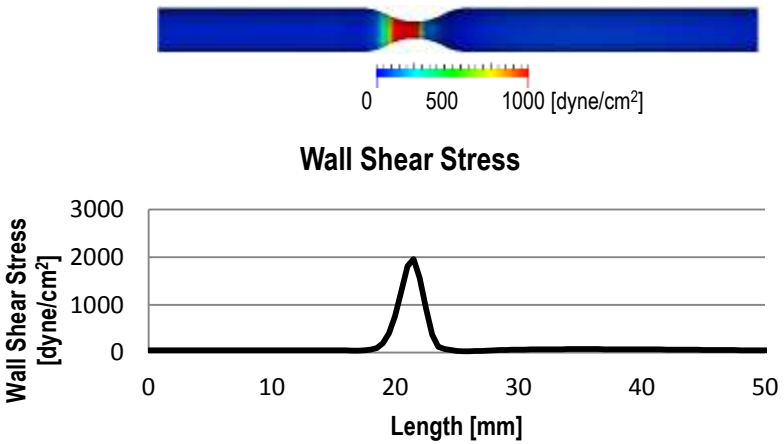
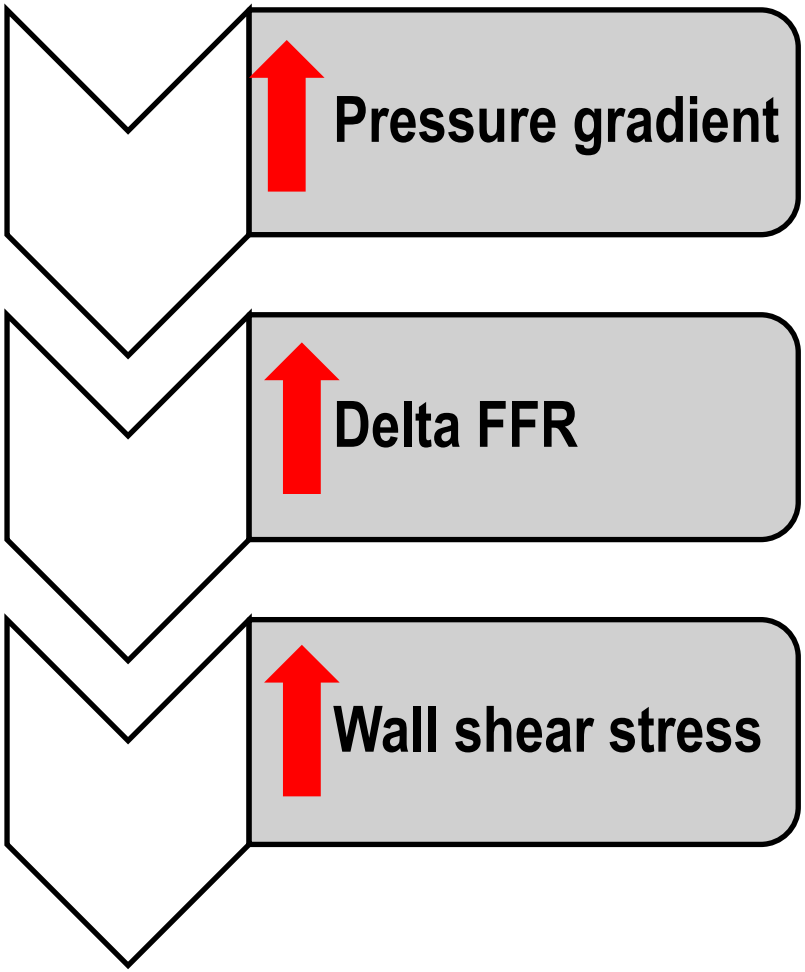
Relationship between FFR (pressure gradient) and WSS







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

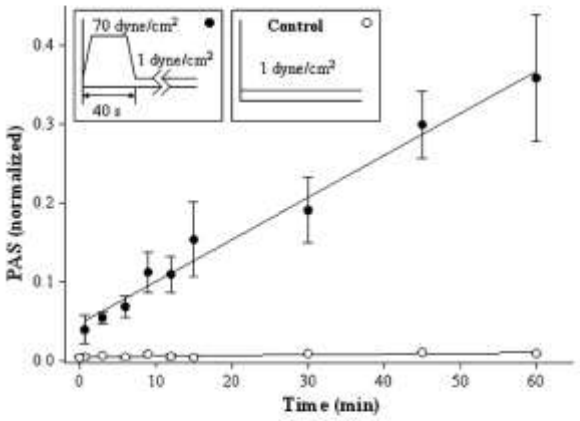


FIGURE 1. Pre-exposure to high-shear stress, 40 s duration. Platelets were pre-exposed to shear stresses of 1 (control), and 70 dyne/cm^2, as shown in the top bar, followed by exposure to 1 dyne/cm^2 for 59 min. The means of four experiments are shown ±SEM.

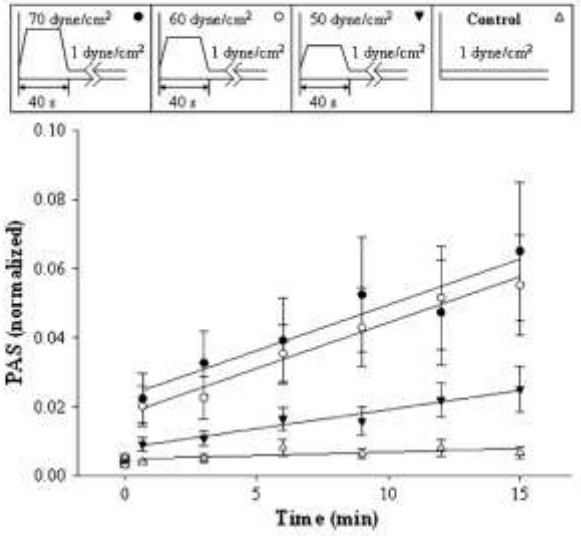
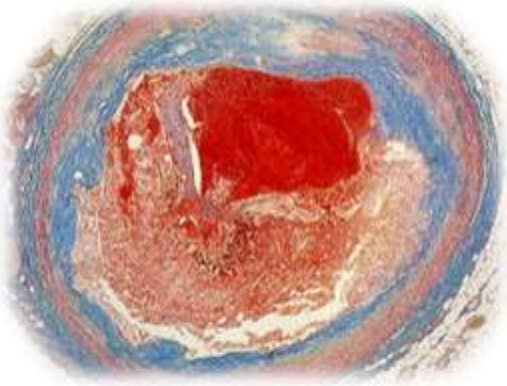


FIGURE 2. Pre-exposure to varying shear stress, 40 s duration. Platelets were pre-exposed to shear stresses of 1 (control), 50, 60, and 70 dyne/cm^2, as shown in the top bar, followed by exposure to 1 dyne/cm^2 for 14 min. The means of nine experiments are shown ±SEM.

Looking for the links between FFR and ACS…



ACS

External Force

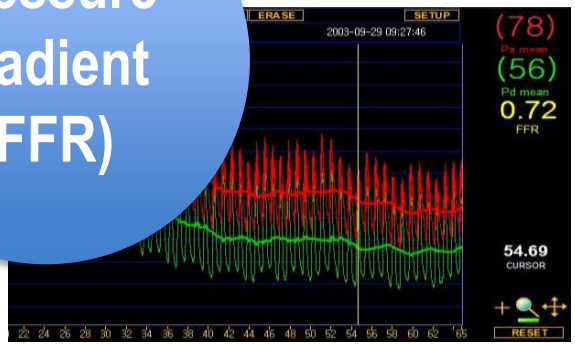
Thrombosis

High WSS
High WSS gradient

Plaque vulnerability

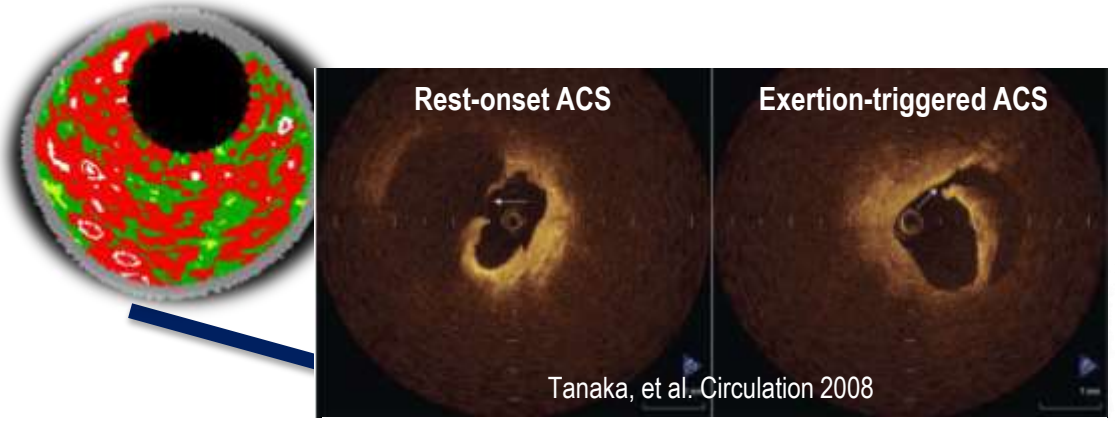
High WSS
High WSS gradient

Pressure gradient (FFR)



Why does the plaque rupture?
:Mechanism of material failure

Vulnerability = Durability



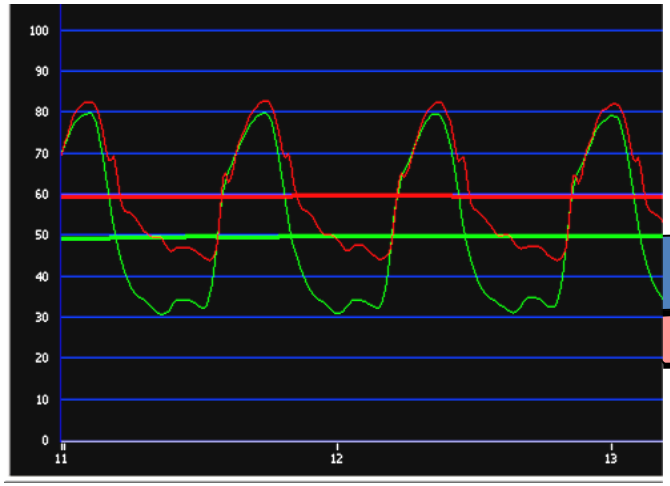
The thickness of the broken fibrous cap in the exertion group was significantly higher than in the rest-onset group (50 vs. 90 μm, *P*<0.01)

External force

Information on external force in addition to vulnerability can lead us to better discriminate the risk of plaque rupture.

Mechanical constraints on coronary stenoses

40.000.000 / year



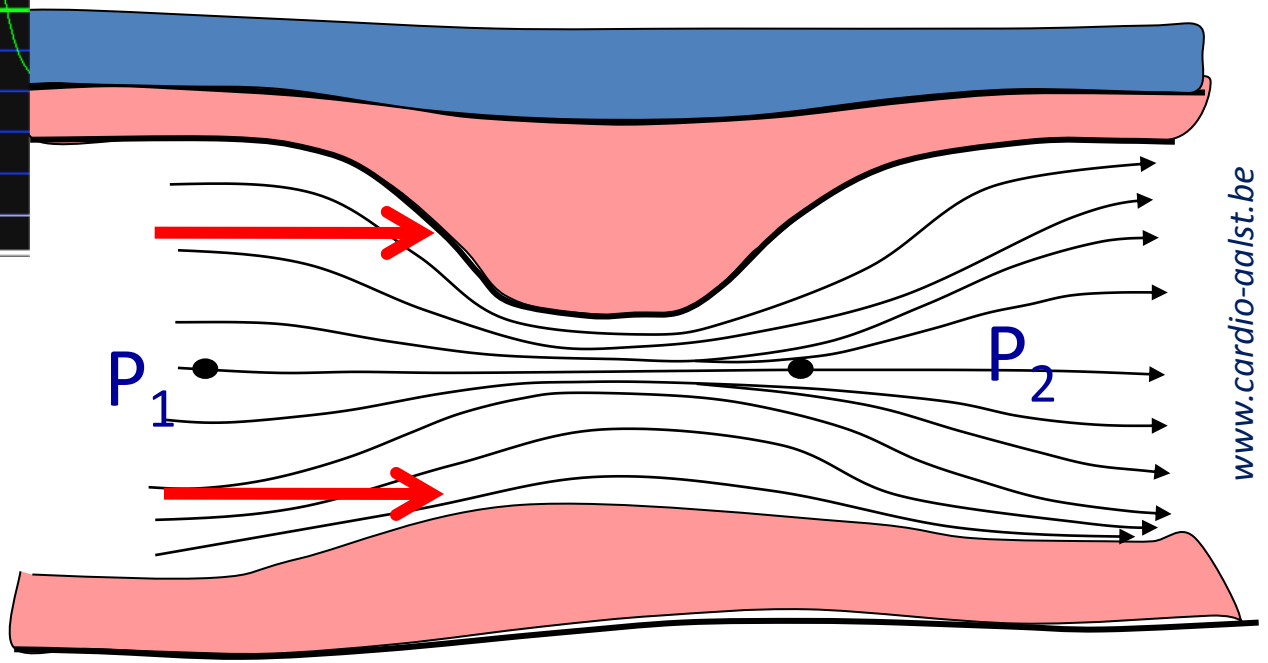
Pressure wave

↓

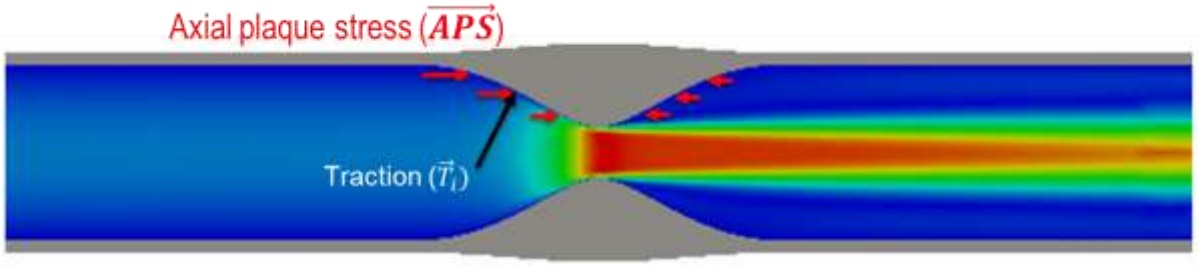
Slicing forces

↓

Plaque fatigue



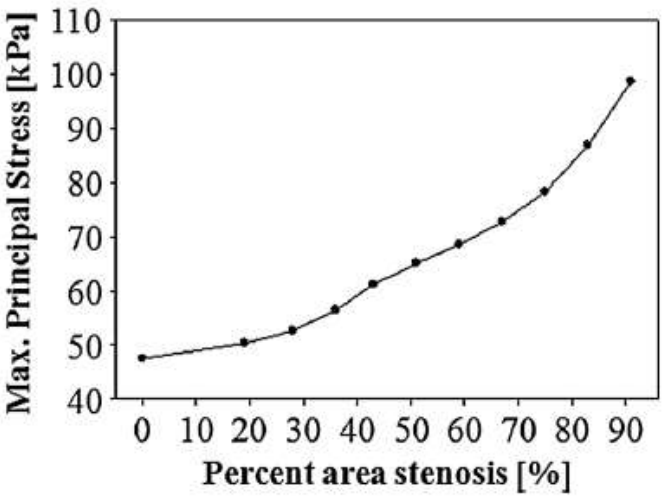
WSS and pressure, then what else?

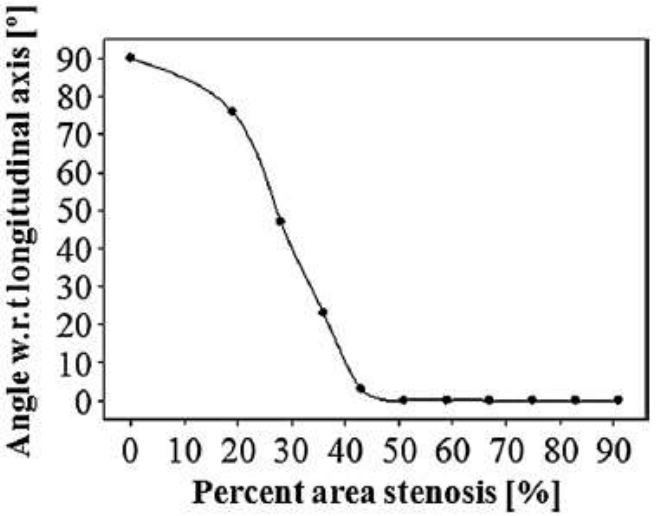


- Traction is the total force acting on vessel wall , and can be decomposed

In relation to lumen surface: $\|\mathbf{Traction}\|^2 = \|\mathbf{WSS}\|^2 + \|\mathbf{Pressure}\|^2$

In relation to centerline: $\|\mathbf{Traction}\|^2 = \|\mathbf{Axial\ Stress}\|^2 + \|\mathbf{Radial\ Stress}\|^2$





Pagiatakis C, et al. Med Biol Eng Comput 2015

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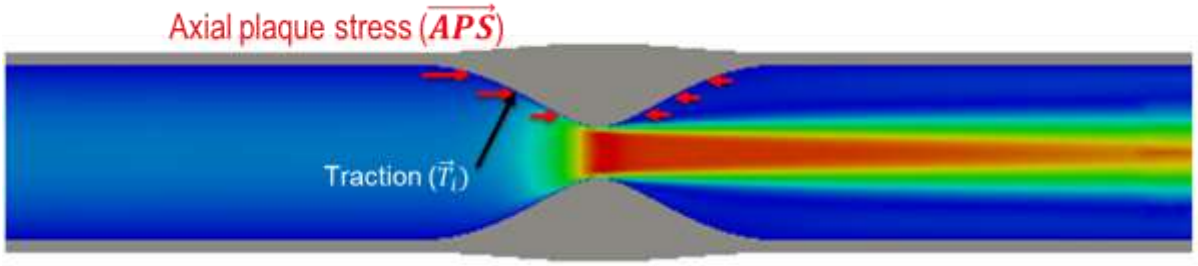

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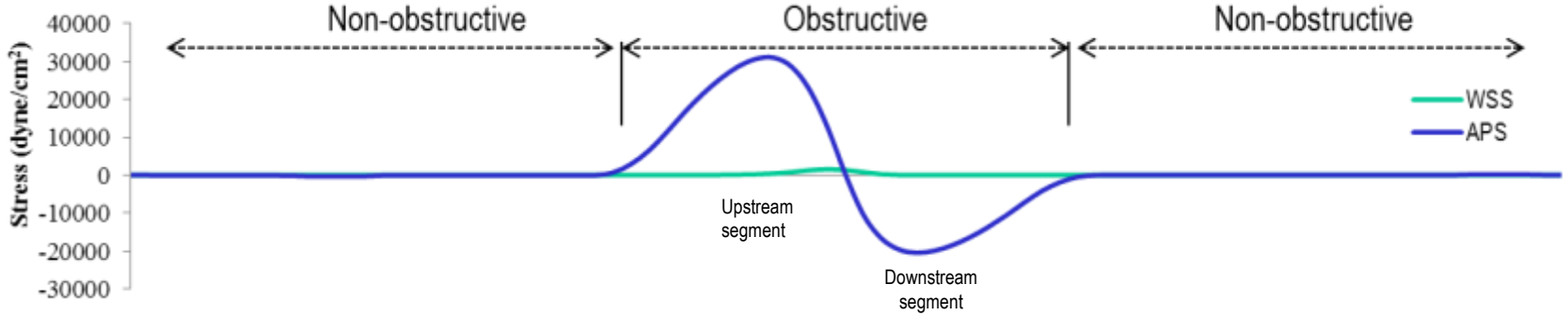
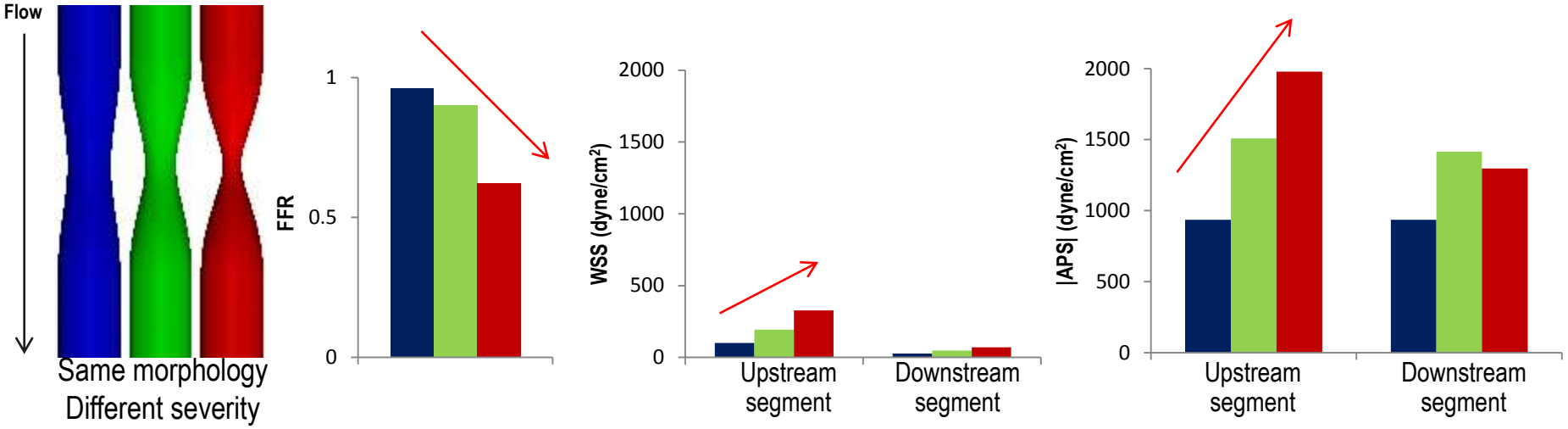


Axial plaque stress is much larger than WSS and uniquely characterizes the upstream and downstream segments of coronary stenosis.

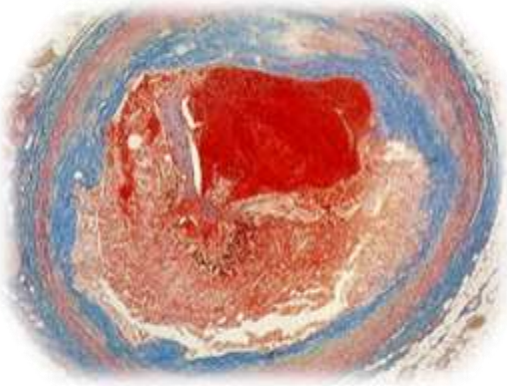
Lee JM…Koo BK. JACC imaging 2015 in press

Lesion severity vs. FFR vs. Axial plaque stress



Lee JM…Koo BK. JACC imaging 2015 in press

Looking for the links between FFR and ACS…



ACS

External Force

Thrombosis

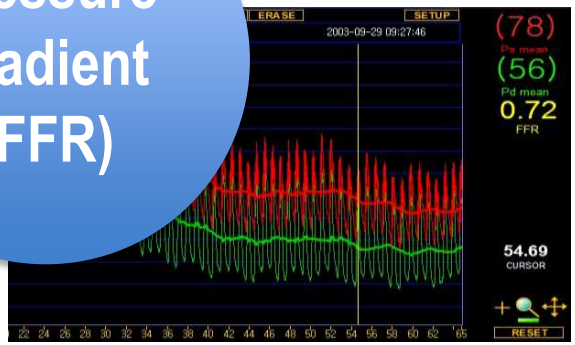
High plaque stress

High WSS
High WSS gradient

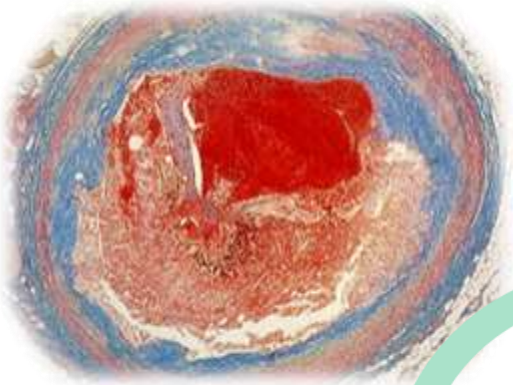
Plaque vulnerability

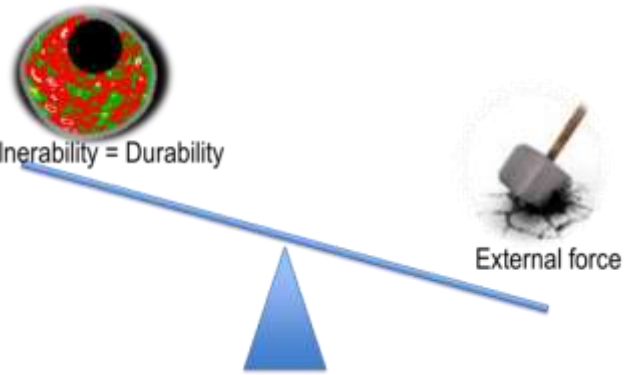
Pressure gradient (FFR)

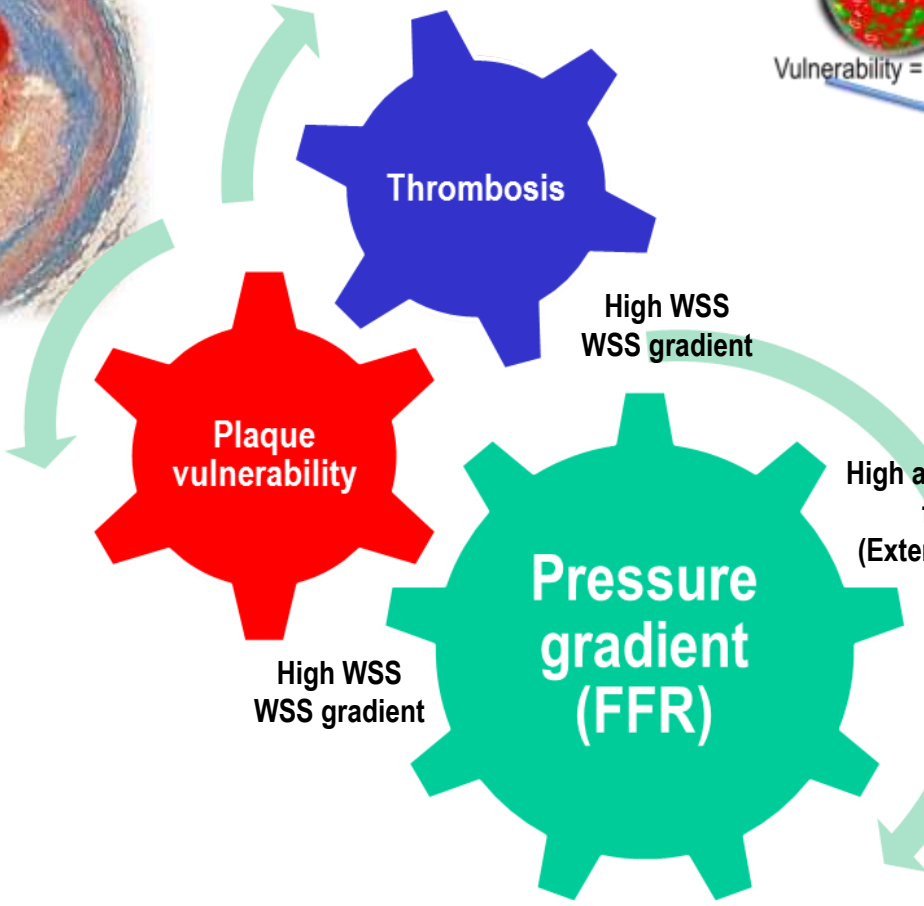
High WSS
High WSS gradient

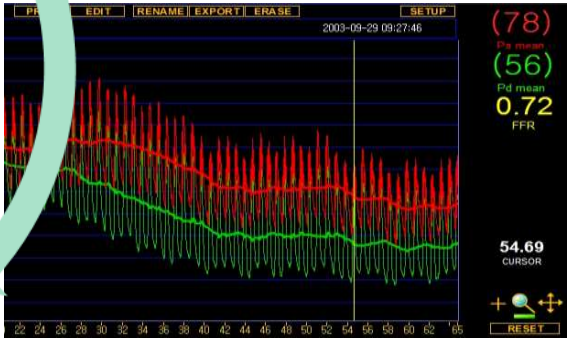


Links between FFR and ACS……









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