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FFR and outcome: The mechanistic link

Bernard De Bruyne
Cardiovascular Center Aalst
Belgium

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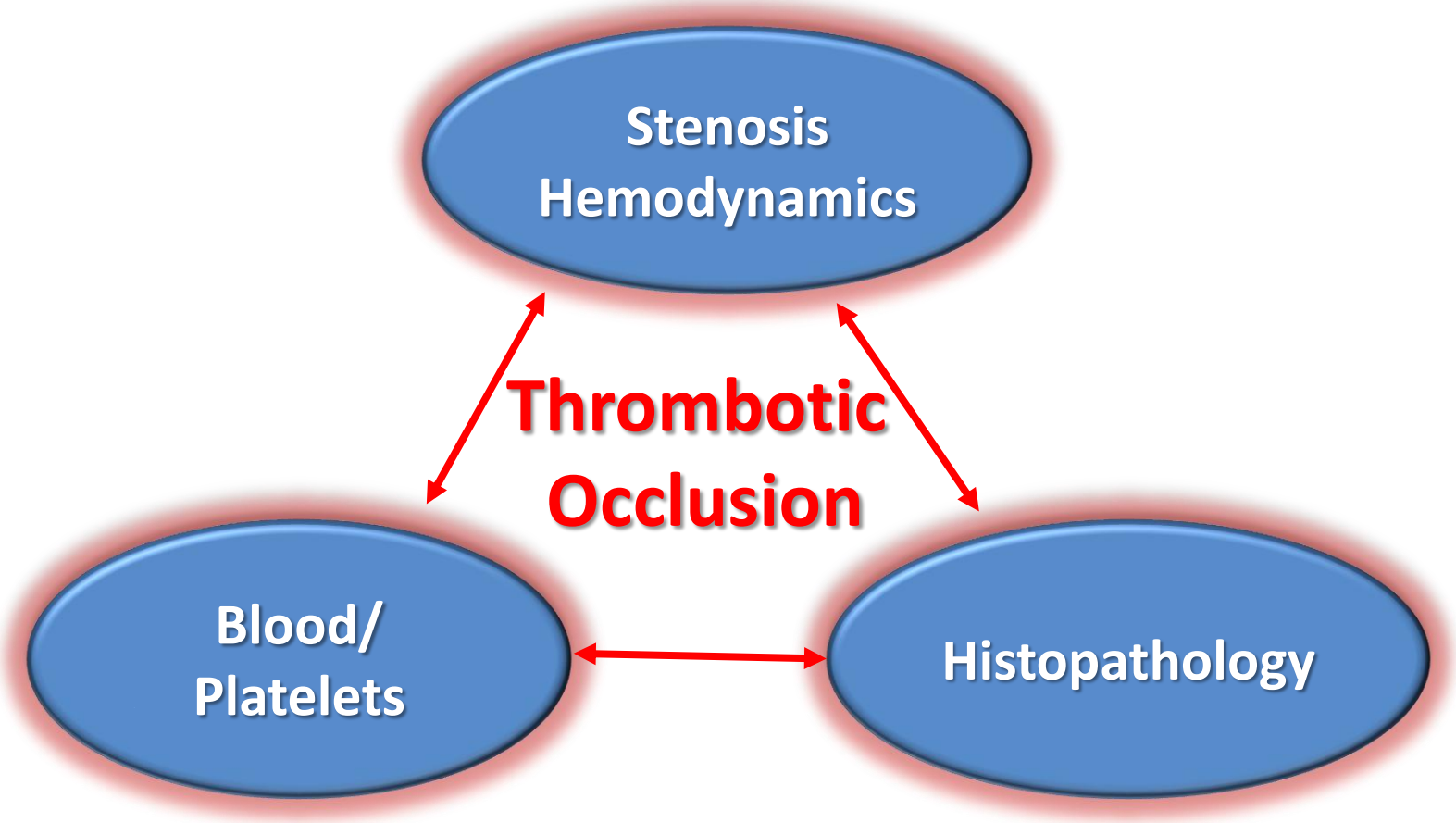
Mechanisms of Plaque Destabilization



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Factors that Contribute to Abrupt Coronary Occlusion

1. Blood/Platelets/… (Biochemistery/Cytology)

2. Histopathology of the wall (Histology)

3. Hemodynamic factors (Physics)

- *Plaque stress*
- *Venturi effect*
- *Vasa vasorum*
- *Shear stress*
- *Cholesterol crystal*
- *Exercise...*

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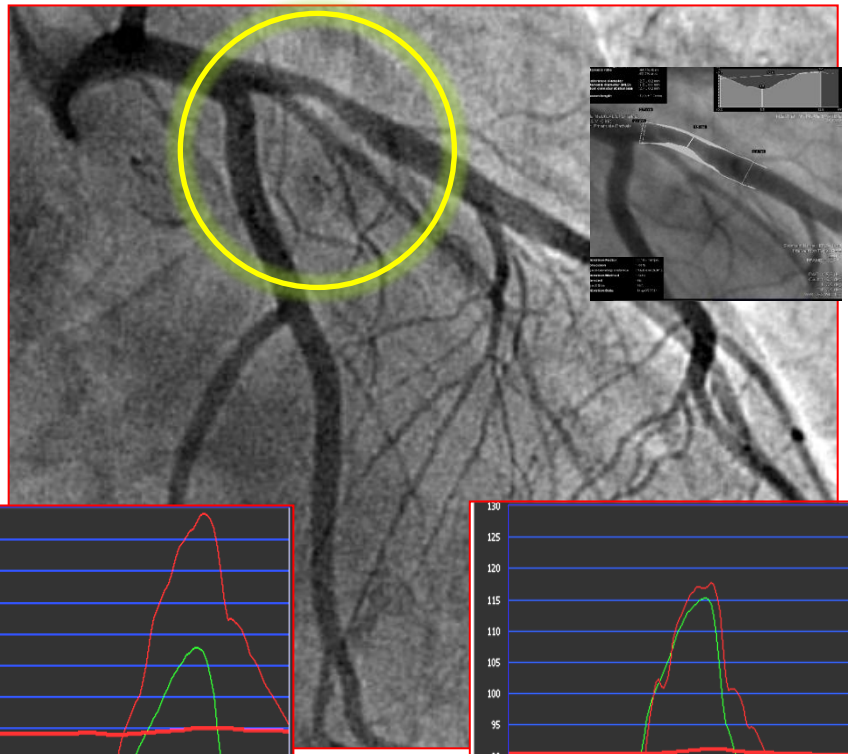
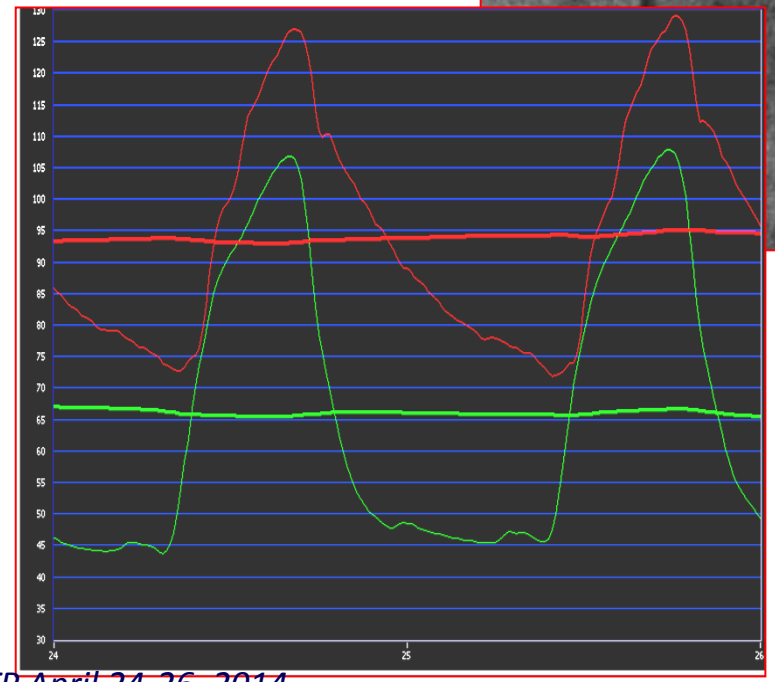
Mechanisms of Plaque Destabilization: Role of Physical Forces





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Mechanical constraints on coronary stenoses

- **Plaque stress**

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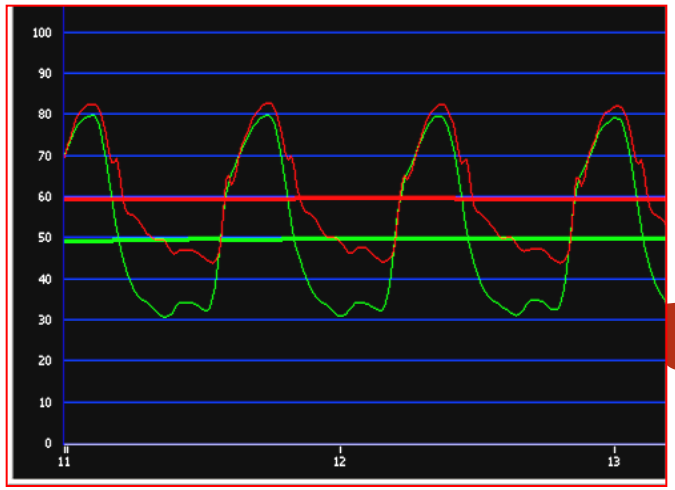
Mechanical constraints on coronary stenoses

40.000.000 / year



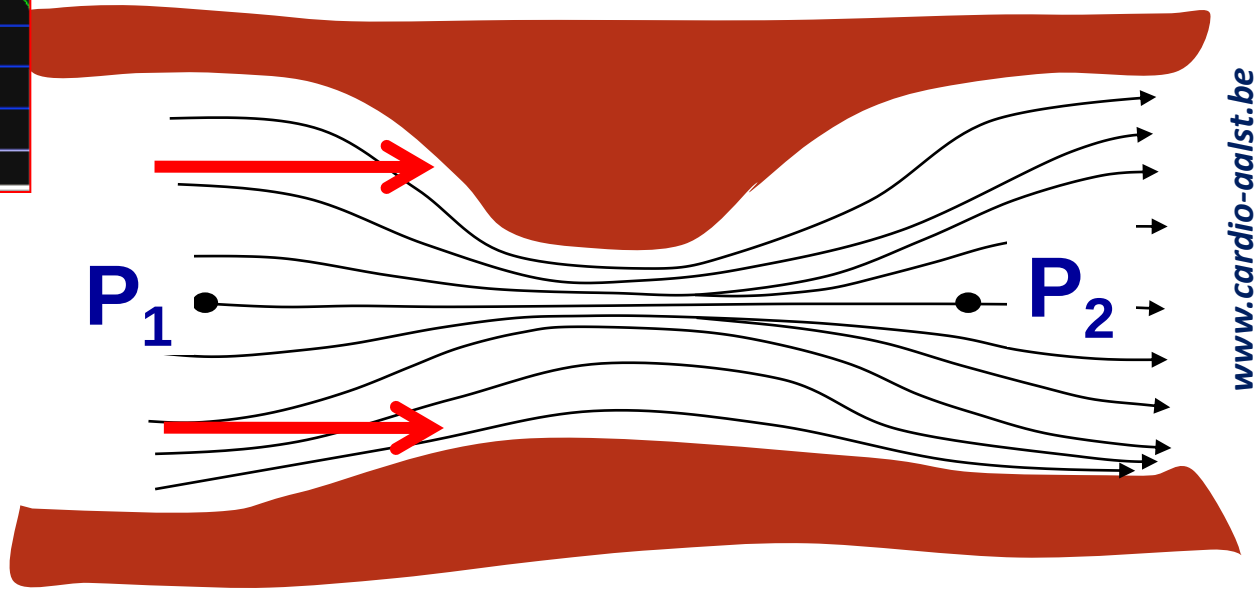
Pressure wave

↓

Slicing forces

↓

Plaque fatigue



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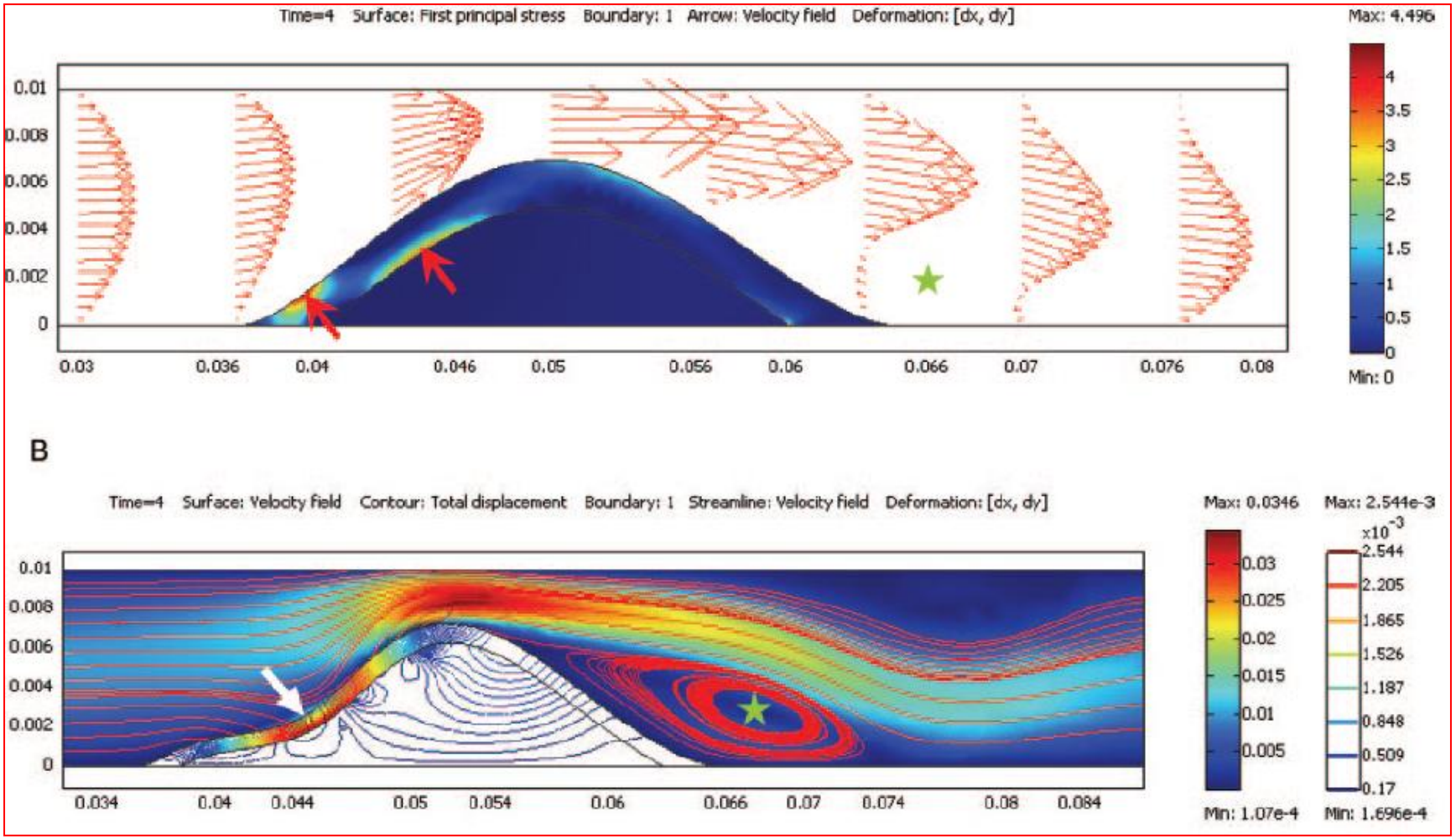
Computational Flow Dynamics
Plaque Stress and Strain Distribution



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Li Y.Z. et al Stroke 2006

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Mechanical constraints on coronary stenoses

- Plaque stress
- **Venturi Effect**

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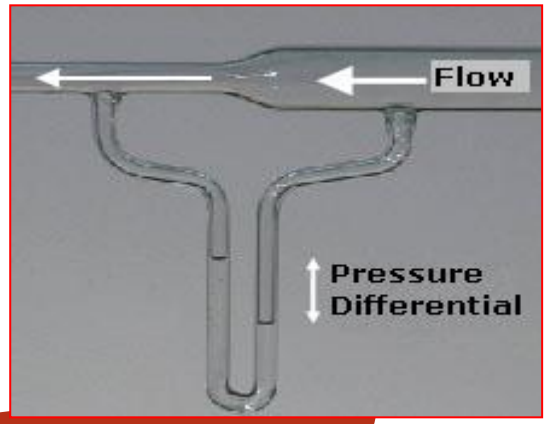
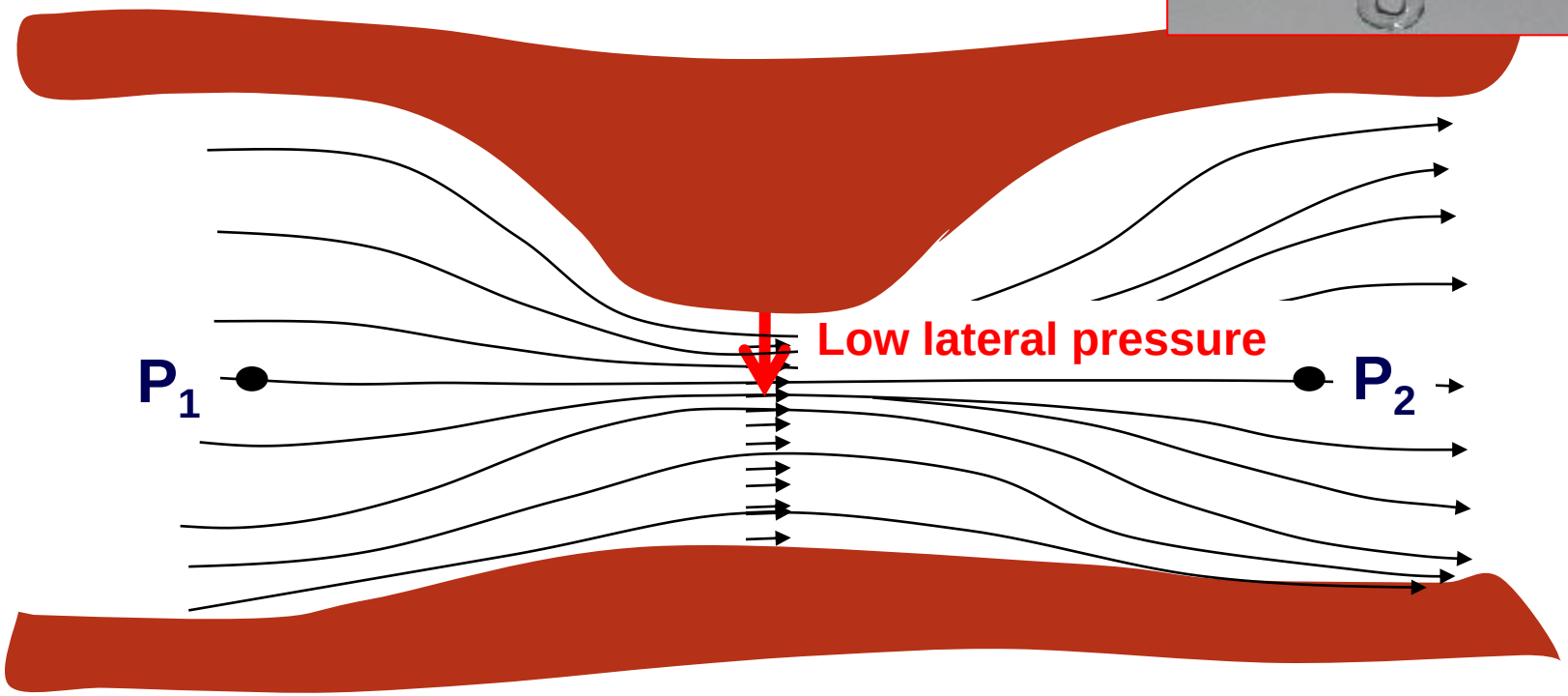
Mechanical constraints on coronary stenoses

Decreased lateral pressure (Venturi Effect)





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Mechanical constraints on coronary stenoses

- Plaque stress
- Venturi Effect
- **Vasa Vasorum**

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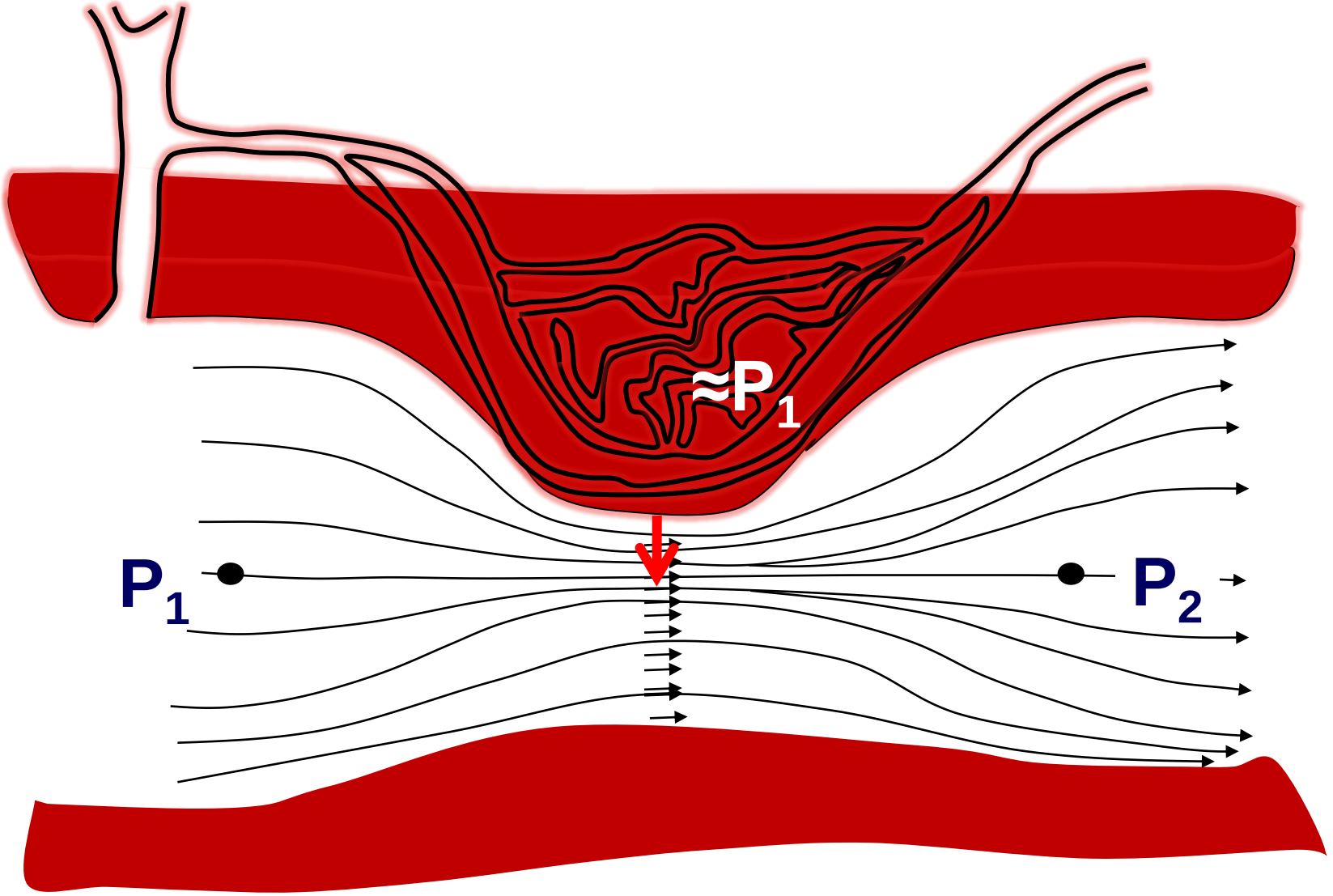
Importance of Vasa Vasorum And Vasa Plaquorum

Mechanical constraints on coronary stenoses



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Paterson JC , J Occupational Medicine 1961

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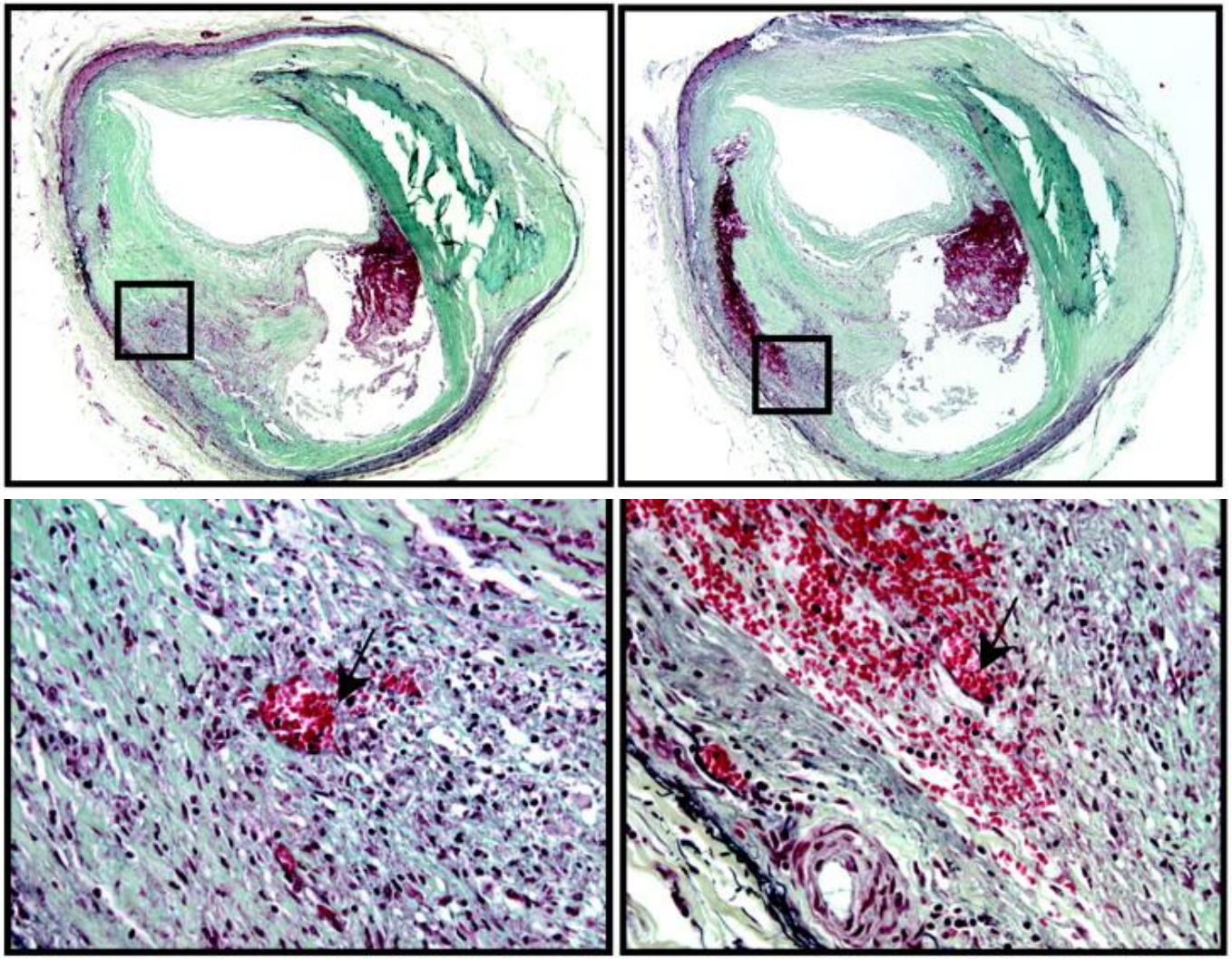
Recent intraplaque hemorrhage in a thin-cap fibroatheroma



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Virmani, R. et al. Arterioscler Thromb Vasc Biol 2005

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Mechanical constraints on coronary stenoses

- Plaque stress
- Venturi Effect
- Vasa Vasora
- **Shear stress**
  - ❖ **Wall (Endothelial) shear stress**
  - ❖ **Blood shear stress**

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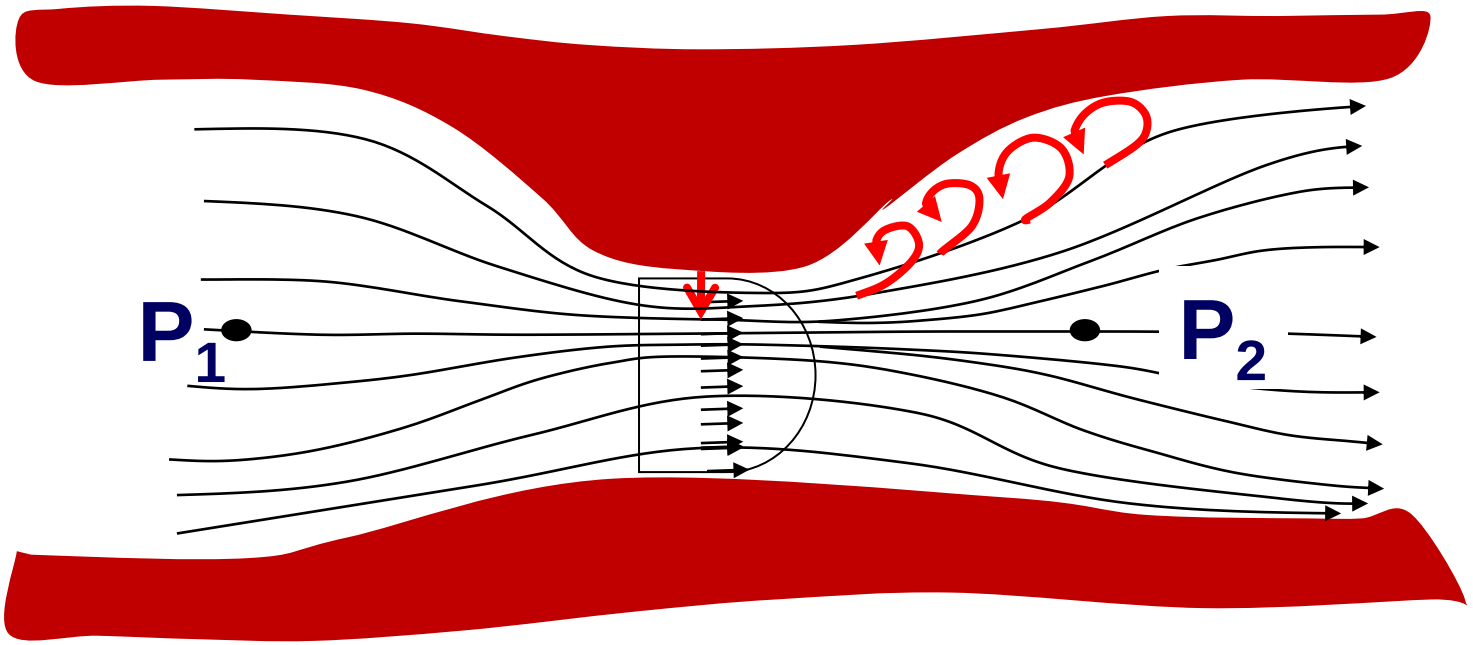
Mechanical constraints on coronary stenoses

Acceleration/deceleration/turbulences = unfavorable rheologic conditions



Low Wall Shear Stress ➔ Pro-atherogenic

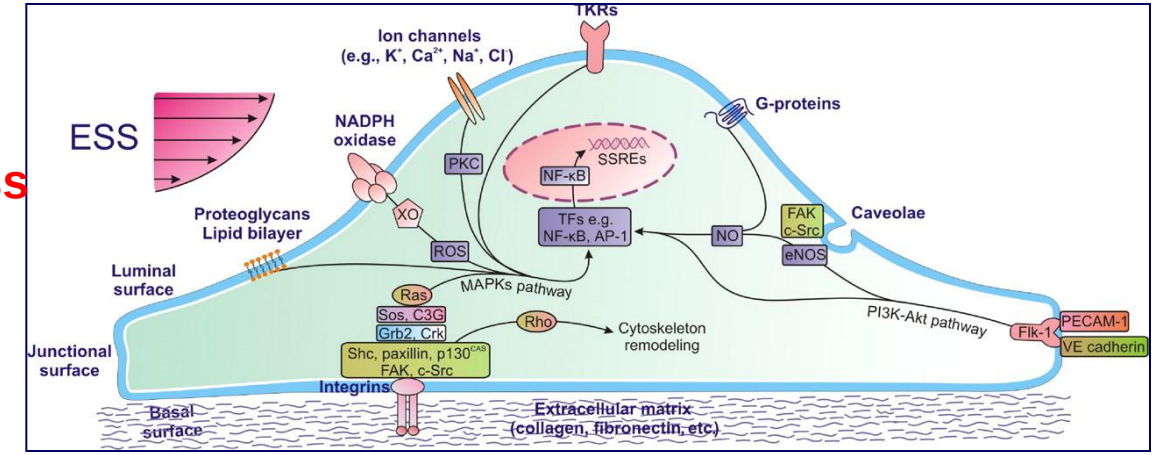
Cross-talks between rheology and biology

Influence of Endothelial Shear Stress on Plaque Progression

Normal

High Endothelial Shear Stress

- Vasodilation
- ↓ platelet aggregation



Chatzizisis et al JACC 2007;49:2379

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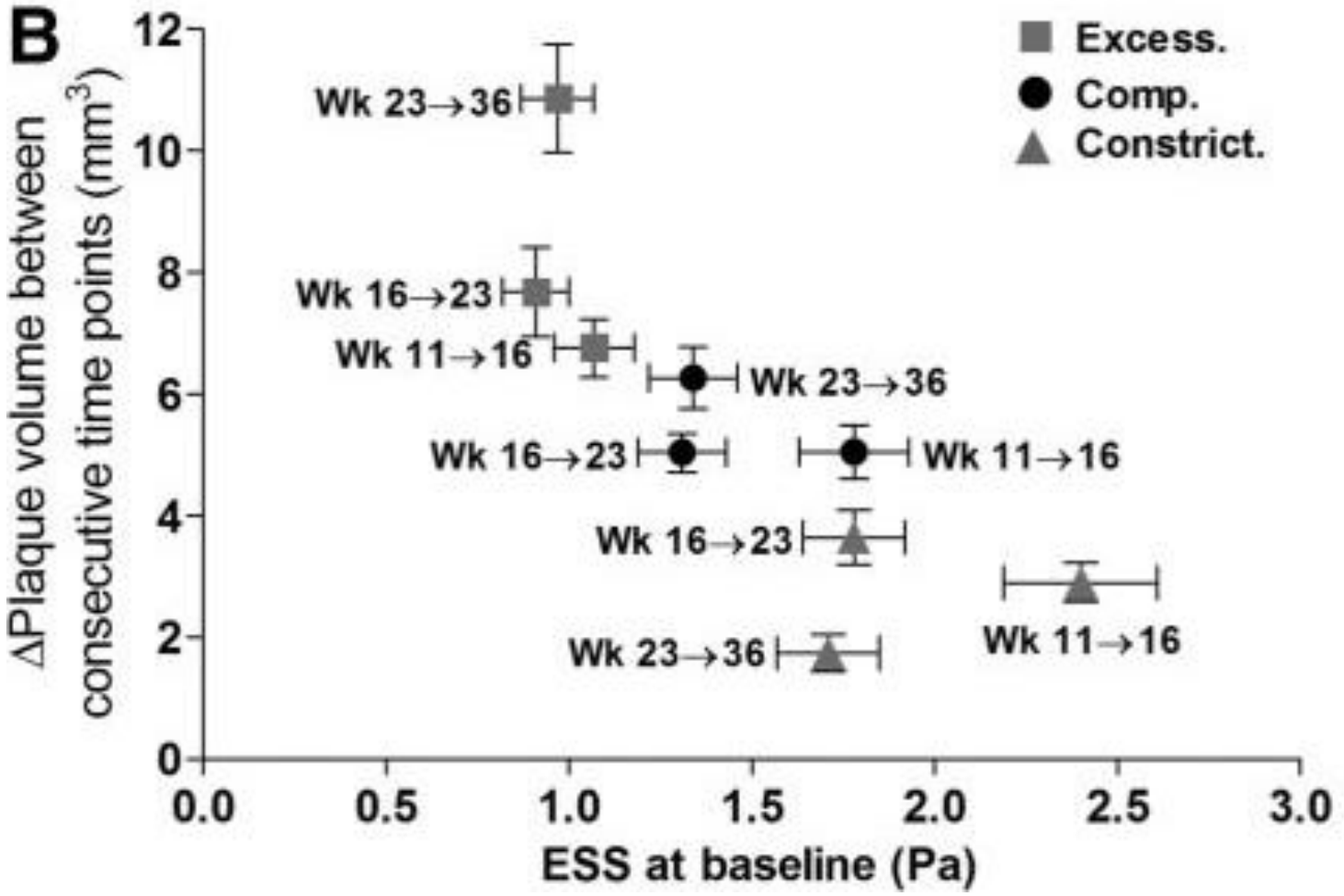
Cross-talks between rheology and biology



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Koskinas KC et al Circulation May 2010

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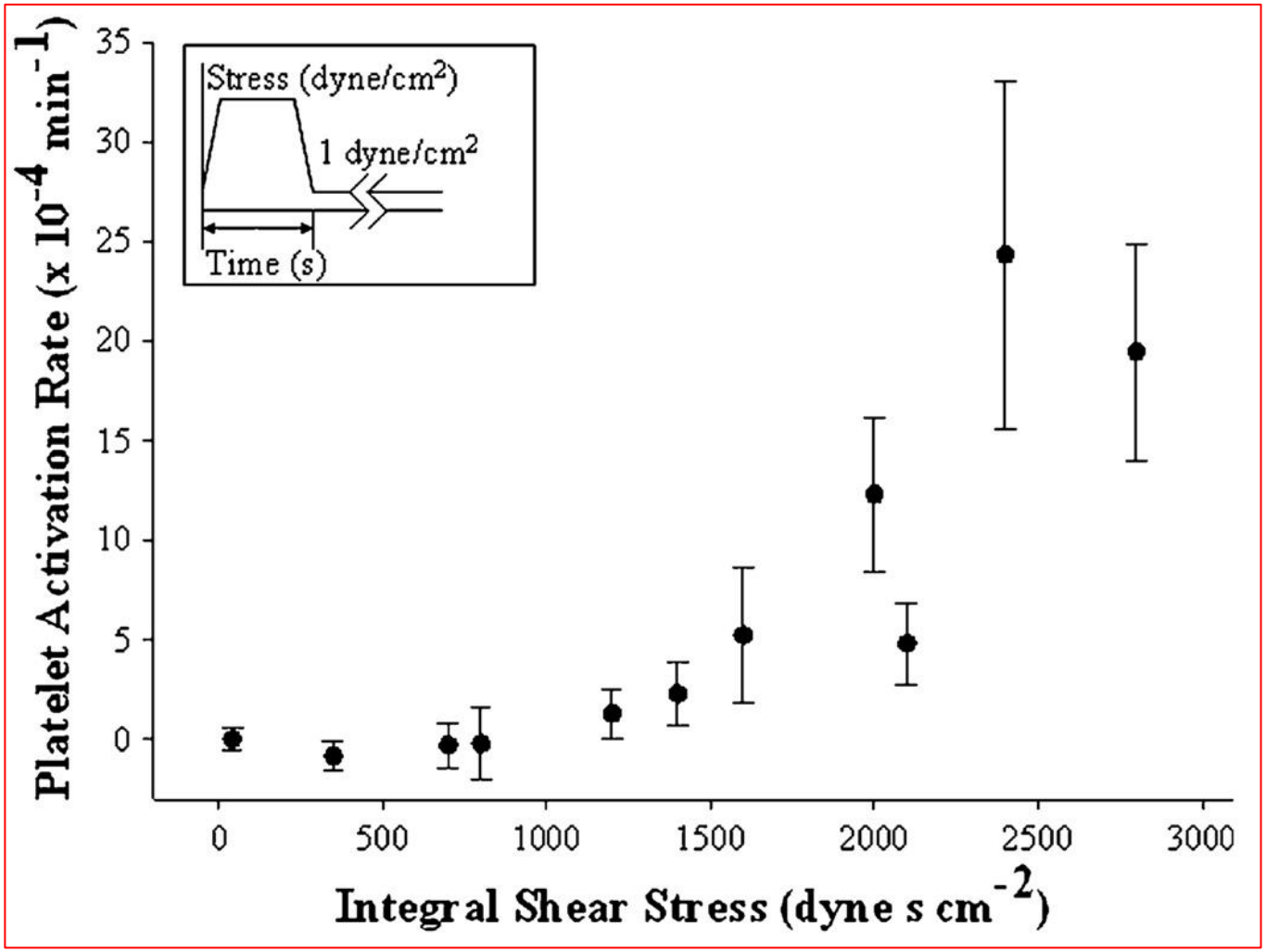
Cross-talks between rheology and biology

Influence of BLOOD Shear Stress on Platelets



Sheriff J et al Ann Biomed Eng. 2010;38(4):1442-50

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Mechanical constraints on coronary stenoses

- Plaque stress
- Venturi Effect
- Vasa Vasora
- Shear stress
- **Cholesterol Crystals**

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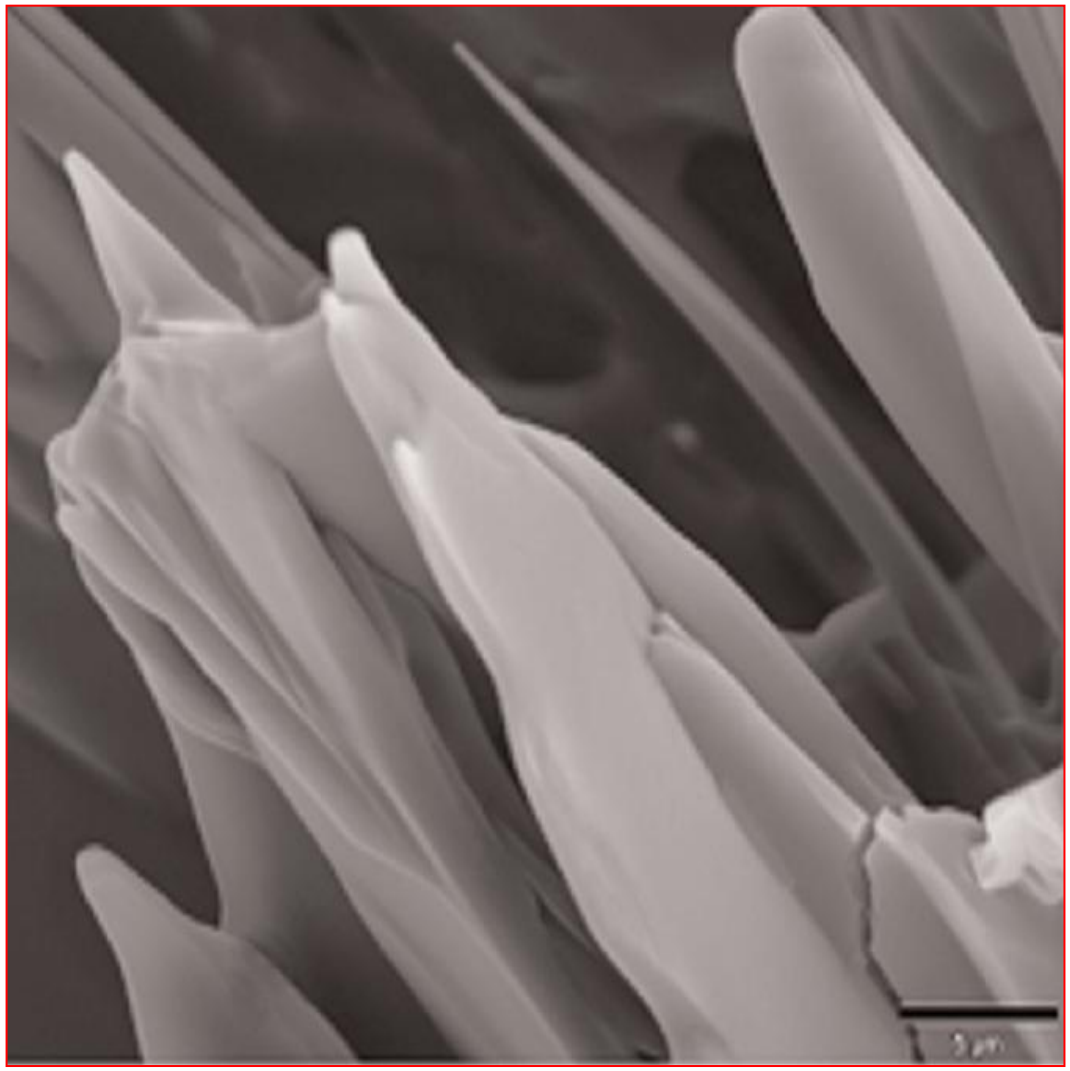
Physical Factors Trigger Crystallization and Volume Expansion of Intraplaque Cholesterol



Crystallization and Volume increase with

- ↓ Temperature
- ↑ pH
- ↑ Hydration
- ↑ Pressure ("very likely")

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Abela GS et al Am J Cardiol 2011;107:1710

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Mechanical constraints on coronary stenoses

- Plaque stress
- Venturi Effect
- Vasa Vasora
- Shear stress
- Cholesterol Crystals
- **Physical exercise**

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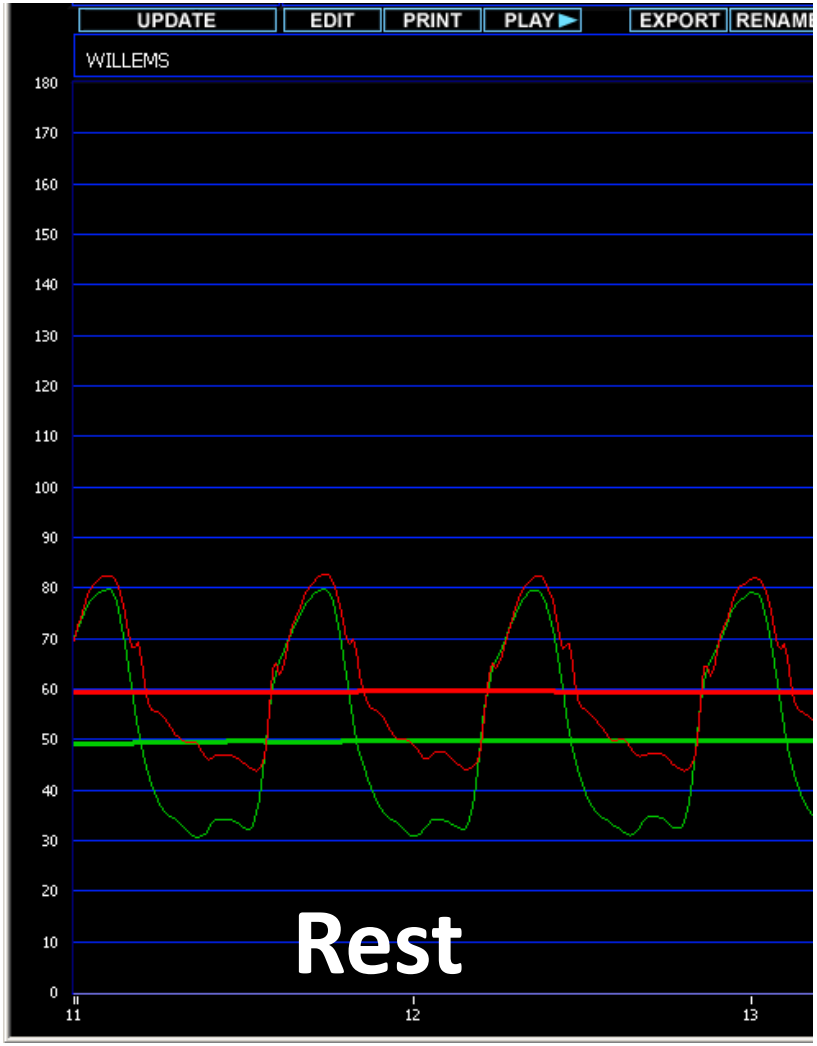
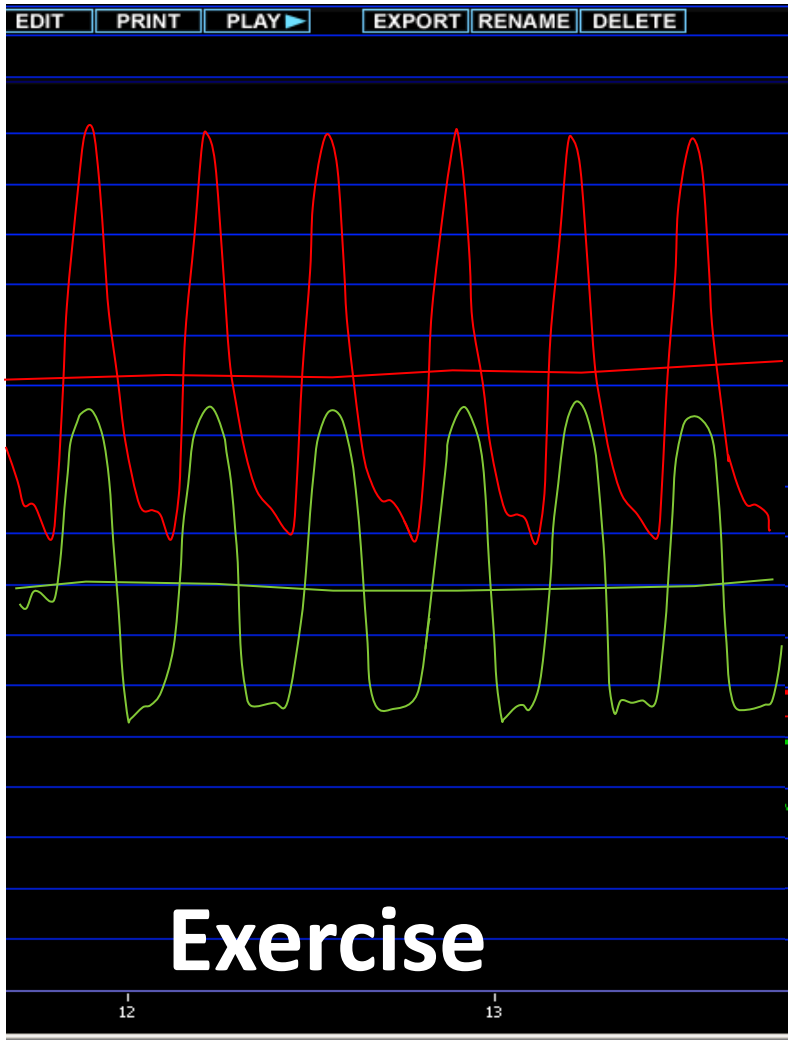
Mechanical constraints on coronary stenoses
Effect of Physical Exercise





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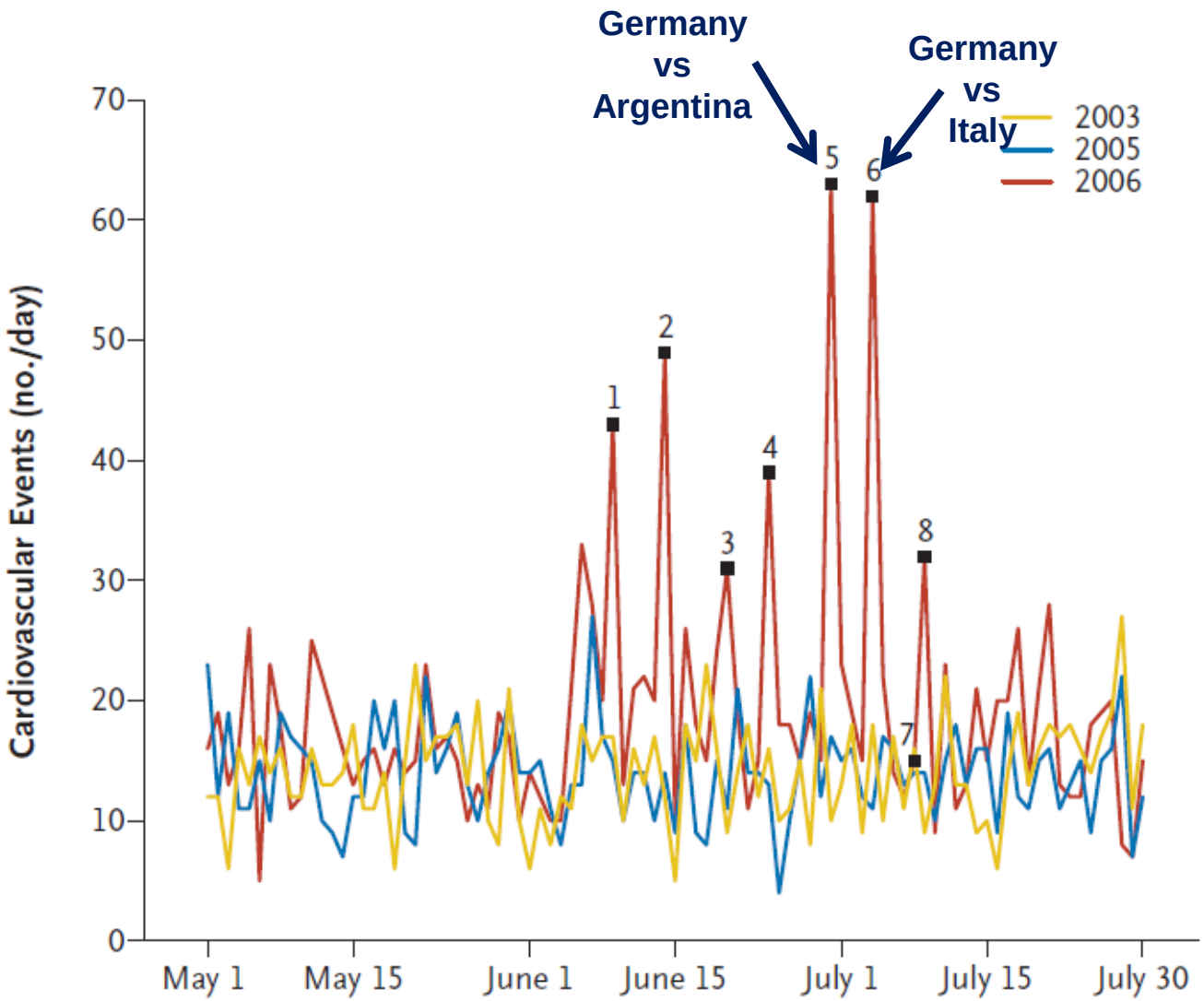
Mechanical constraints on coronary stenoses
Effect of WATCHING Football Matches



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Wilbert-Lampen U, N Engl J Med 2008

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Mechanical constraints on coronary stenoses

~~Pressure gradient~~

↓

- ~~Slicing forces → plaque fatigue~~
- ~~High flow velocities → Venturi Effect~~
- ~~Turbulences → low shear stress~~
- ~~Vasa Vasorum → gradient in/out~~

↓

~~Plaque Rupture~~

~~(Especially when Thin Cap Fibro Atheroma)~~

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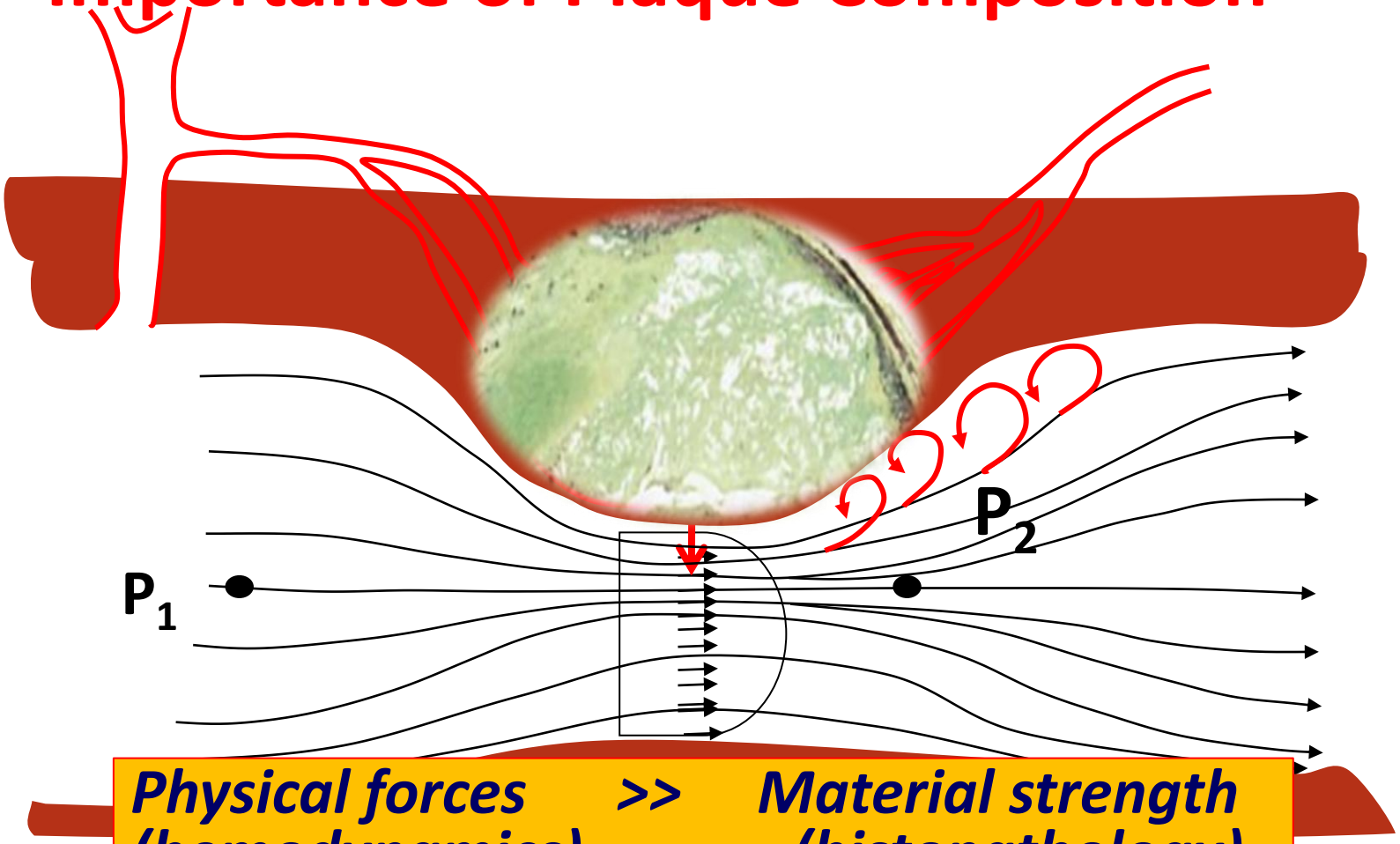
Mechanical constraints on coronary stenoses

Plaque Rupture

Importance of Plaque Composition



Physical forces (hemodynamics) >> Material strength (histopathology)

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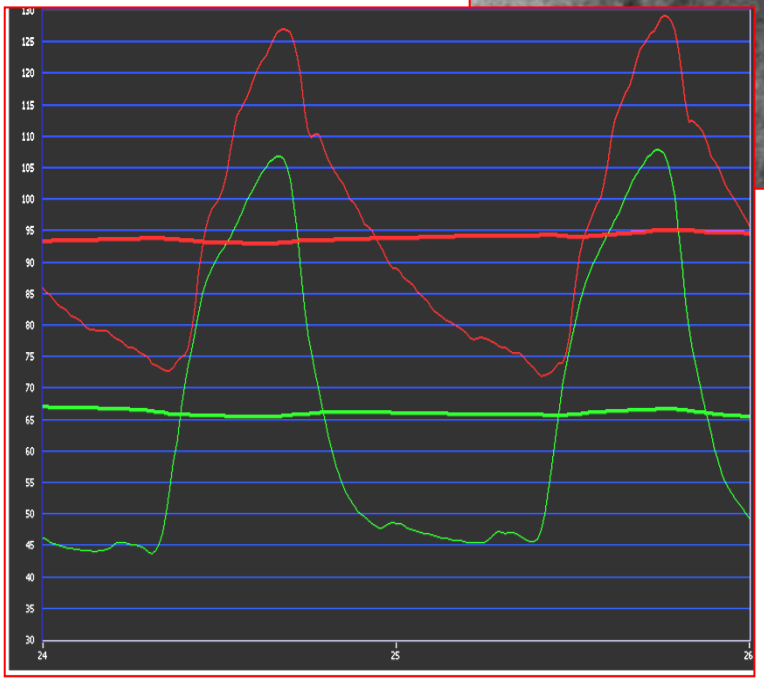

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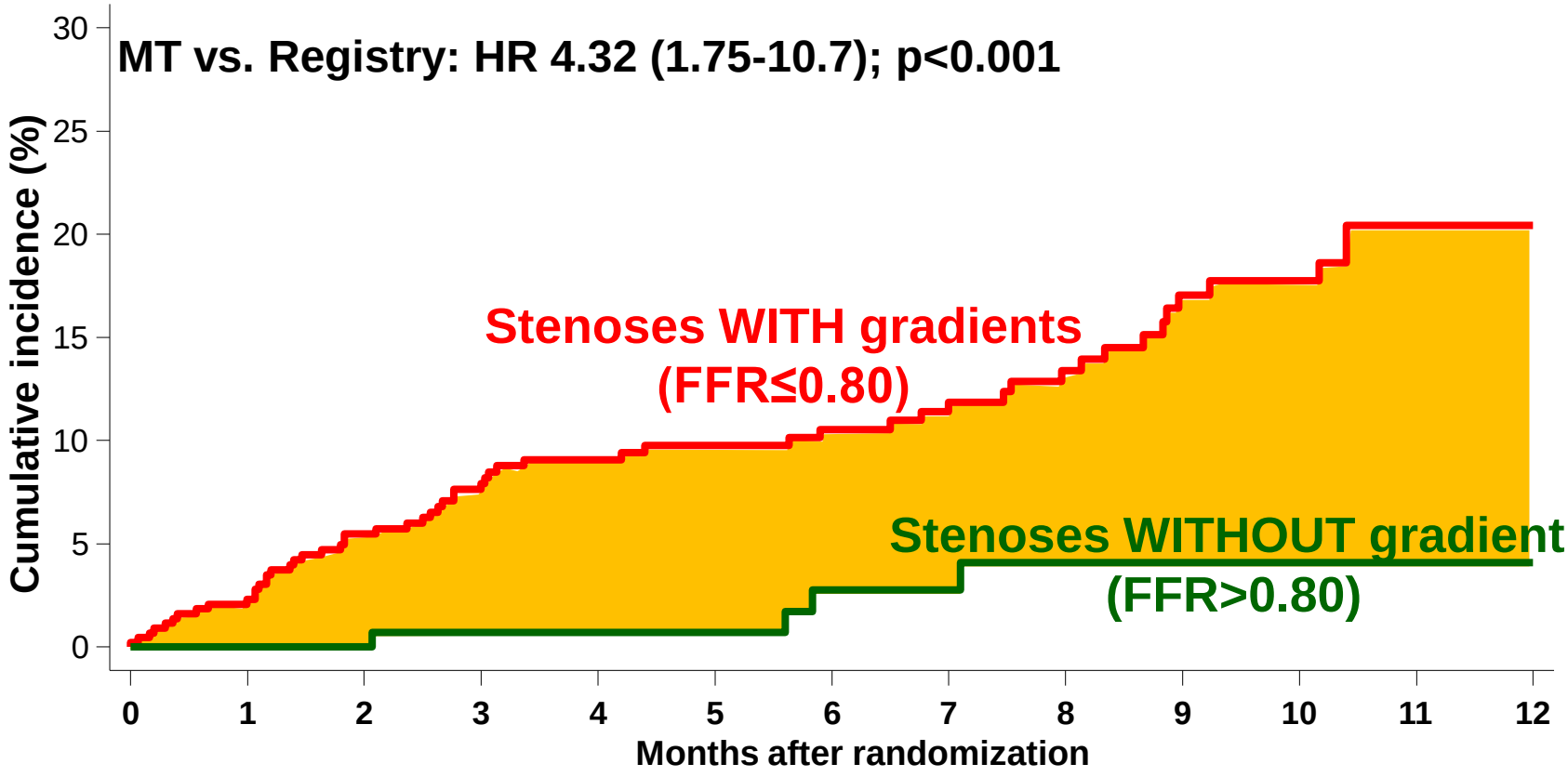
FAME 2 Trial
Primary Outcomes



No. at risk

MT	441	414	370	322	283	253	220	192	162	127	100	70	37
PCI+MT	447	414	388	351	308	277	243	212	175	155	117	92	53
Registry	166	156	145	133	117	106	93	74	64	52	41	25	13

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Conclusive Remarks

Ischemia is a marker of the abnormal physical forces that take place at the level of the epicardial vessels