FFR_{CT}: Beyond FFR

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Patient-specific non-invasive coronary hemodynamic assessment

Non-invasive, Pt-specific

Hemodynamics
- Pressure
  - Pressure difference
  - Pressure gradient
  - Pressure recovery
  - FFR
- Flow velocity
- Flow rate
- Shear rate
- Shear stress – average, peak, gradient
- Traction
- Oscillatory shear index
- Particle residence time
- Turbulent kinetic energy
- ..................

- Static
- Pulsatile
- Resting
- Hyperemic
- Exercise – mild, moderate, peak
Non-invasive hemodynamic parameter measurement using computational fluid dynamics and cCTA

Hemodynamics
- Pressure
  - Pressure difference
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Image-based computerised modelling of coronary circulation: Potentials

- Static flow - hyperemic
- Pulsatile flow - rest
- Pulsatile flow - Hyperemia
- Pulsatile flow - Exercise

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Why Does the Plaque Rupture?

Mechanistic link between Hemodynamics and Acute Coronary Syndrome
We already know....

- Coronary plaque rupture is a critical event that triggers the initiation of acute coronary syndrome (ACS).
- Risk assessment for ACS
  - **Plaque Vulnerability**: cap thickness, lipid core, inflammation, neovascularization, posterior attenuation......
Why does the plaque rupture?
:Mechanism of material failure

Durability = Vulnerability

The broken cap was much thinner in the rest-onset group than in the exertion group (50 vs. 90 μm, P<0.01)

Information on external force in addition to vulnerability can lead to better discrimination of the risk of plaque rupture.
What kind of forces are acting on the plaque?

Wall shear stress (magnitude scaled by 10)

Axial plaque stress

Traction Pressure
Low wall shear stress

\(\rightarrow\) Proliferative, pro-inflammatory, pro-thrombotic stimulus
Very high WSS vs. Vulnerability

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 MENG¹,²,³,⁵

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

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: $52.3 \pm 12.4\%$

### WSS in stenotic segments - Resting

- WSS = 0 – 20: 26.4%
- WSS = 20 – 40: 34.1%
- WSS = 40 – 60: 15.6%
- WSS = 60 – 80: 8.0%
- WSS = 80 – 100: 4.6%
- WSS >100: 11.2%

### WSS in stenotic segments - Hyperemic

- WSS = 0 – 20: 0.2%
- WSS = 20 – 40: 2.2%
- WSS = 40 – 60: 4.8%
- WSS = 60 – 80: 7.5%
- WSS = 80 – 100: 7.5%
- WSS >100: 77.8%

Koo BK. International Symposium on Biomechanics 2014
Relationship between WSS and pressure gradient

Koo BK. International Symposium on Biomechanics 2014
### Relationship between WSS and lesion characteristics

<table>
<thead>
<tr>
<th>Determinants</th>
<th>( \beta )</th>
<th>95% CI</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressure Gradient</td>
<td>1.281</td>
<td>0.35 – 2.25</td>
<td>0.007</td>
</tr>
<tr>
<td>Blood flow</td>
<td>0.683</td>
<td>0.34 – 1.02</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Distance from LM ostium</td>
<td>-0.298</td>
<td>-0.56 – -0.04</td>
<td>0.024</td>
</tr>
<tr>
<td>Minimal lumen area</td>
<td>-1.676</td>
<td>-2.44 – -0.92</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lesion length</td>
<td>-1.157</td>
<td>-1.81 – -0.51</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Koo BK. International Symposium on Biomechanics 2014
Regional distribution of hemodynamic forces: Pressure gradient vs. WSS
FFR vs. ACS

Koo BK. International Symposium on Biomechanics 2014
Pressure, FFR and WSS are high at the upstream segment of a plaque. Therefore, these parameters cannot explain the occurrence of downstream rupture.

Location of rupture

WSS and pressure, then what else?

- Traction is the total force (stress) acting on vessel wall (plaque), and can be decomposed

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

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

Axial plaque stress ($\overrightarrow{APS}$)

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

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JACC imaging 2015, in press
Distribution of “Axial Plaque Stress”

Idealized stenosis models (n=264)

- Distal segment
  - N=264
  - Median: -7801.3 dyne/cm²
  - IQR: -11954.3, -4603.1

- Proximal segment
  - N=264
  - Median: 11629.4 dyne/cm²
  - IQR: 11954.3, 4603.2

Patients’ lesions (n=114)

- Distal segment
  - N=114
  - Median: -7912.4 dyne/cm²
  - IQR: -12366.7, -5632.7

- Proximal segment
  - N=114
  - Median: 7885.6 dyne/cm²
  - IQR: 6055.9, 12707.9

Distribution of axial plaque stress is similar between idealized models and patients lesions.

JACC imaging 2015, in press
Distribution of Axial Plaque Stress in patients

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Proximal segment
Distal segment

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Lesion geometry vs. Hemodynamic forces

- **Flow**
  - **Same morphology**
  - **Different severity**

- **Proximal segment**
- **Distal segment**

<table>
<thead>
<tr>
<th>WSS (dyne/cm$^2$)</th>
<th>Proximal segment</th>
<th>Distal segment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>500</td>
<td>1000</td>
</tr>
<tr>
<td>500</td>
<td>1500</td>
<td>3000</td>
</tr>
<tr>
<td>1000</td>
<td>2000</td>
<td>4000</td>
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<tr>
<td>1500</td>
<td>2500</td>
<td>5000</td>
</tr>
<tr>
<td>2000</td>
<td>3000</td>
<td>6000</td>
</tr>
</tbody>
</table>

| |APS| (dyne/cm$^2$) |
|-----------------|----------------|
| 0               | 500             |
| 500             | 1000            |
| 1000            | 1500            |
| 1500            | 2000            |
| 2000            | 2500            |

- **Upstream dominant lesion**
- **Downstream dominant lesion**

Same morphology
Different severity

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Influence of “Lesion Shape” on Hemodynamic Parameters (n=114)

% Diameter Stenosis  \[ \text{FFR}_{\text{CT}} \]  | Axial Plaque Stress | (dyne/cm²)

- Upstream-dominant lesion (n=56)
- Downstream-dominant lesion (n=58)

- Proximal segment
  - P<0.001
- Distal segment
  - P<0.001

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Future perspective

2011-04 CT, Asymptomatic

2012-06 Acute MI
Future perspective

2011-04 CT, Asymptomatic

2012-06 Acute MI

Upstream  9960 dyne/cm²
Downstream  1740 dyne/cm²

APS
Conclusion

• Hemodynamic forces acting on the plaque can be measured non-invasively using coronary CT angiography and computational fluid dynamics.

• Very high wall shear stress (WSS) promotes plaque vulnerability and is mainly determined by pressure gradient. Therefore, WSS and pressure gradient can be the link between FFR and the risk of ACS.

• Axial plaque stress uniquely characterizes the stenotic segment and can provide additional information on the risk of plaque rupture.

• Clinical application of these non-invasive hemodynamic parameters can be helpful to assess the future risk of plaque related clinical events.