Novel Non-invasive Indices to Define Hemodynamic Forces Acting on Coronary Plaque

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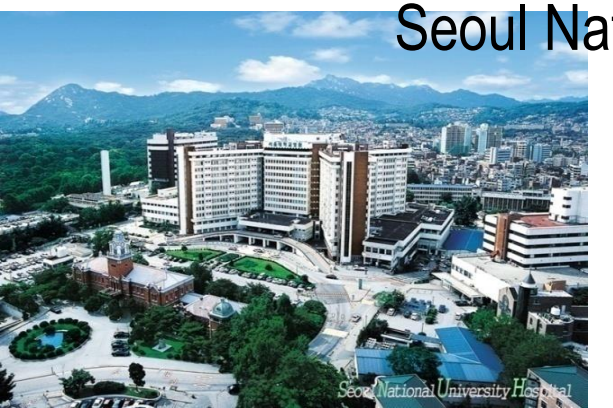
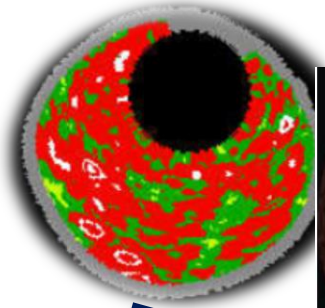
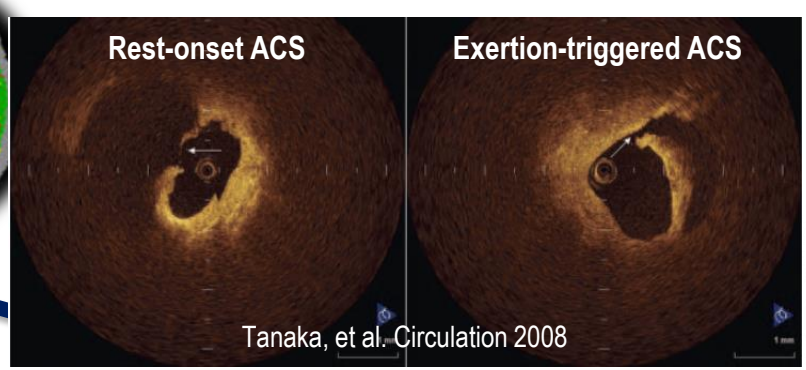


SNUH Seoul National University Hospital
Cardiovascular Center

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, $P<0.01$)

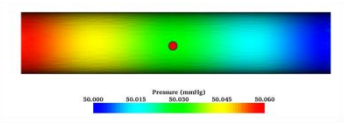
External force

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

How to calculate or measure forces acting on the plaque?

How can we obtain the traction $\bar{t}$ at a given point $\bar{x}$ of the domain?

Take for instance $\bar{x} = \begin{Bmatrix} x_r \\ x_\theta \\ x_z \end{Bmatrix} = \begin{Bmatrix} R \\ 0 \\ 0.5L \end{Bmatrix}$ (cylindrical coordinates)



We know that $\bar{t}_{\bar{n}} = \underset{\sim}{T}\bar{n}$ therefore, we need to define $\underset{\sim}{T}$ and $\bar{n}$

Velocity
Pressure

$\underset{\sim}{T}$ is therefore given as a function of the velocity and pressure fields:

$$\underset{\sim}{T} = -p\underset{\sim}{I} + \mu\left(\nabla\bar{v} + \nabla\bar{v}^T\right)$$

In cylindrical coordinates, $\nabla\bar{v} = \begin{bmatrix} \frac{\partial v_r}{\partial r} & \frac{1}{r}\left(\frac{\partial v_r}{\partial \theta} - v_\theta\right) & \frac{\partial v_r}{\partial z} \\ \frac{\partial v_\theta}{\partial r} & \frac{1}{r}\left(\frac{\partial v_\theta}{\partial \theta} + v_r\right) & \frac{\partial v_\theta}{\partial z} \\ \frac{\partial v_z}{\partial r} & \frac{1}{r}\frac{\partial v_z}{\partial \theta} & \frac{\partial v_z}{\partial z} \end{bmatrix}$

For this problem,

$$\bar{v} = \begin{Bmatrix} v_r \\ v_\theta \\ v_z \end{Bmatrix} = \begin{Bmatrix} 0 \\ 0 \\ -\frac{dp}{dz}\frac{1}{4\mu}\left(R^2 - r^2\right) \end{Bmatrix} \Rightarrow \nabla\bar{v} = \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ \frac{\partial v_z}{\partial r} & 0 & 0 \end{bmatrix} = \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ \frac{dp}{dz}\frac{r}{2\mu} & 0 & 0 \end{bmatrix}$$

Therefore,

$$\underset{\sim}{T}(x_r, x_\theta, x_z) = -p(z)\underset{\sim}{I} + \mu\begin{bmatrix} 0 & 0 & \frac{dp}{dz}\frac{r}{2\mu} \\ 0 & 0 & 0 \\ \frac{dp}{dz}\frac{r}{2\mu} & 0 & 0 \end{bmatrix} = \begin{bmatrix} -p(z) & 0 & \frac{dp}{dz}\frac{r}{2} \\ 0 & -p(z) & 0 \\ \frac{dp}{dz}\frac{r}{2} & 0 & -p(z) \end{bmatrix}$$

At our point of interest: $\bar{x} = \begin{Bmatrix} x_r \\ x_\theta \\ x_z \end{Bmatrix} = \begin{Bmatrix} R \\ 0 \\ 0.5L \end{Bmatrix}$

$$\underset{\sim}{T}(R, 0, 0.5L) = \begin{bmatrix} -\frac{(P_o + P_L)}{2} & 0 & \frac{dp}{dz}\frac{R}{2} \\ 0 & -\frac{(P_o + P_L)}{2} & 0 \\ \frac{dp}{dz}\frac{R}{2} & 0 & -\frac{(P_o + P_L)}{2} \end{bmatrix}$$

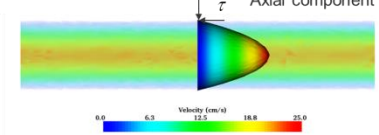
And finally:

$$\bar{t}_{\bar{n}} = \underset{\sim}{T}\bar{n} = \begin{bmatrix} -\frac{(P_o + P_L)}{2} & 0 & \frac{dp}{dz}\frac{R}{2} \\ 0 & -\frac{(P_o + P_L)}{2} & 0 \\ \frac{dp}{dz}\frac{R}{2} & 0 & -\frac{(P_o + P_L)}{2} \end{bmatrix} \begin{Bmatrix} 1 \\ 0 \\ 0 \end{Bmatrix} = \begin{Bmatrix} -\frac{(P_o + P_L)}{2} \\ 0 \\ \frac{dp}{dz}\frac{R}{2} \end{Bmatrix}$$

At that point, the fluid experiences a traction $\bar{t}_{\bar{n}} = \begin{Bmatrix} -\frac{(P_o + P_L)}{2} \\ 0 \\ \frac{dp}{dz}\frac{R}{2} \end{Bmatrix}$

Normal component (pressure) p

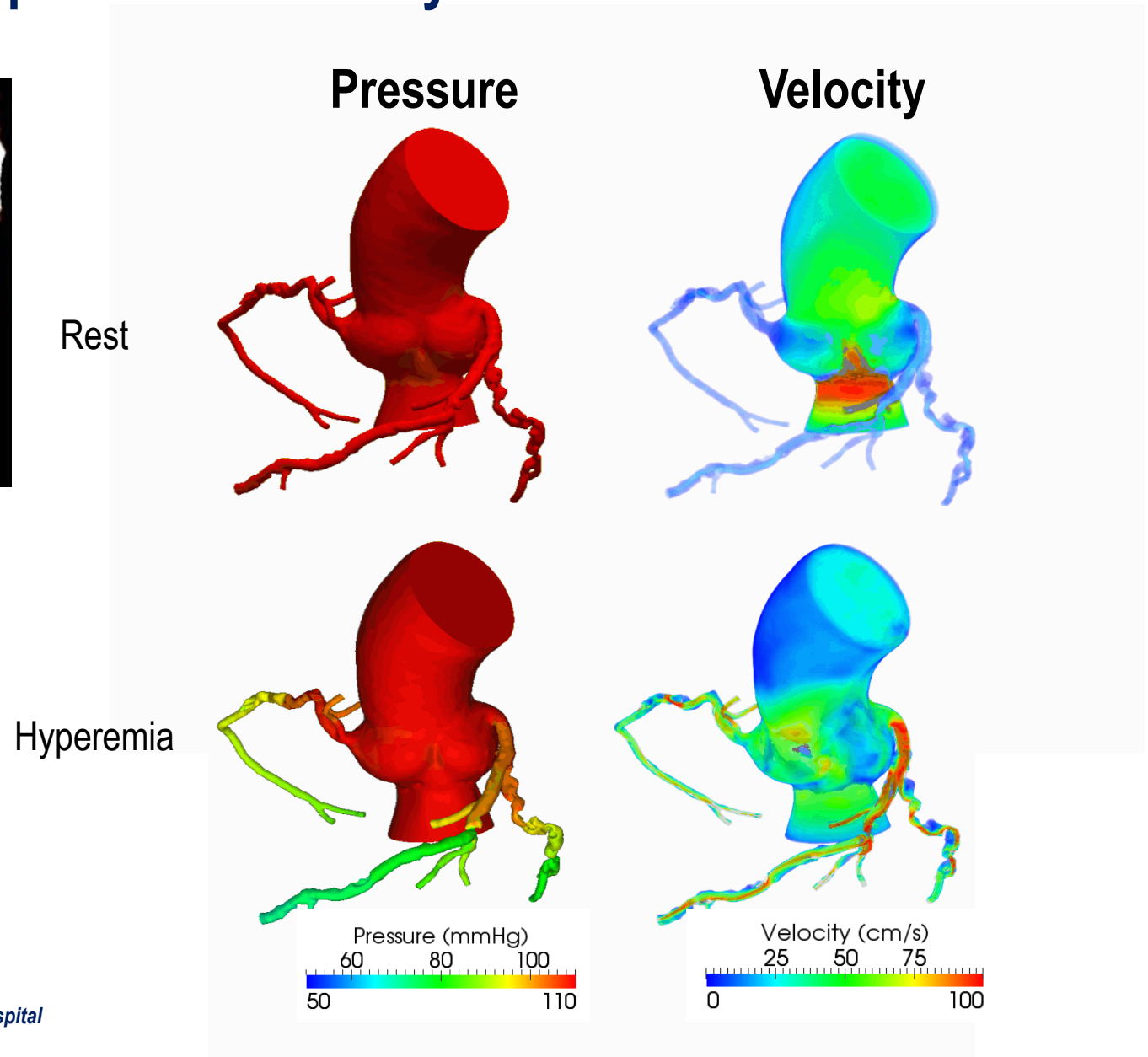
τ Axial component (shear), note that dp/dz is negative



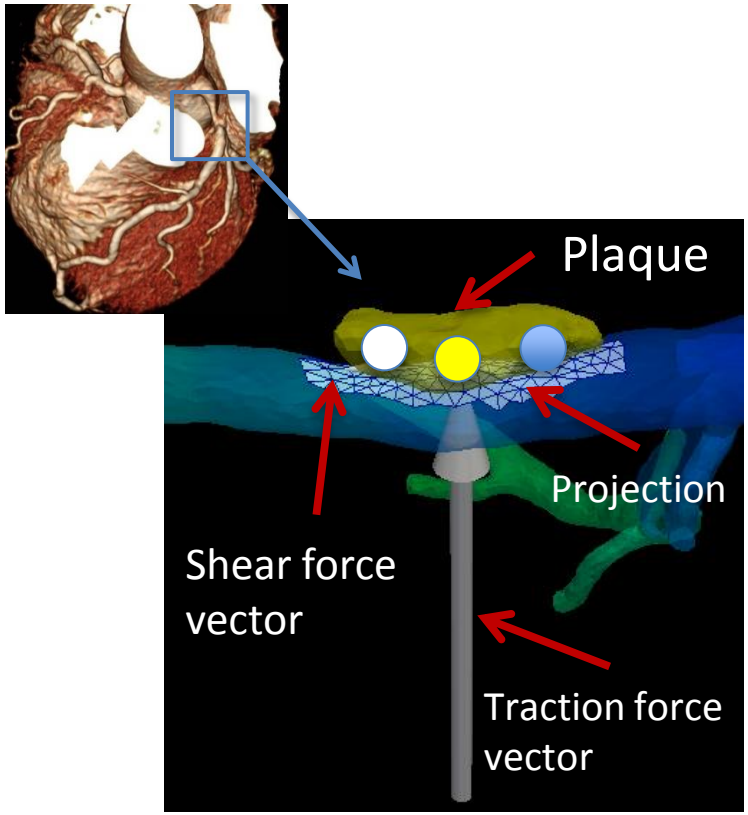
Same result as with formula:

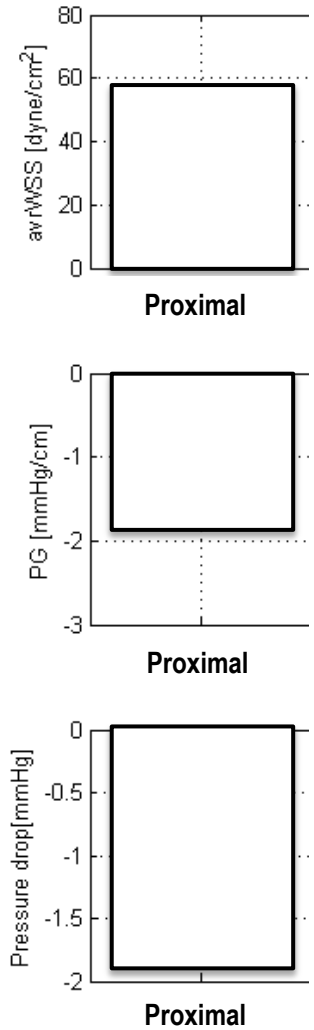
$$\tau = \mu\left.\frac{dv}{dr}\right|_{r=R} = \mu\frac{d}{dr}\left[-\frac{dp}{dz}\frac{1}{4\mu}\left(R^2 - r^2\right)\right] = \frac{dp}{dz}\frac{R}{2}$$

Non-invasive hemodynamic force measurement using computational fluid dynamics and cCTA

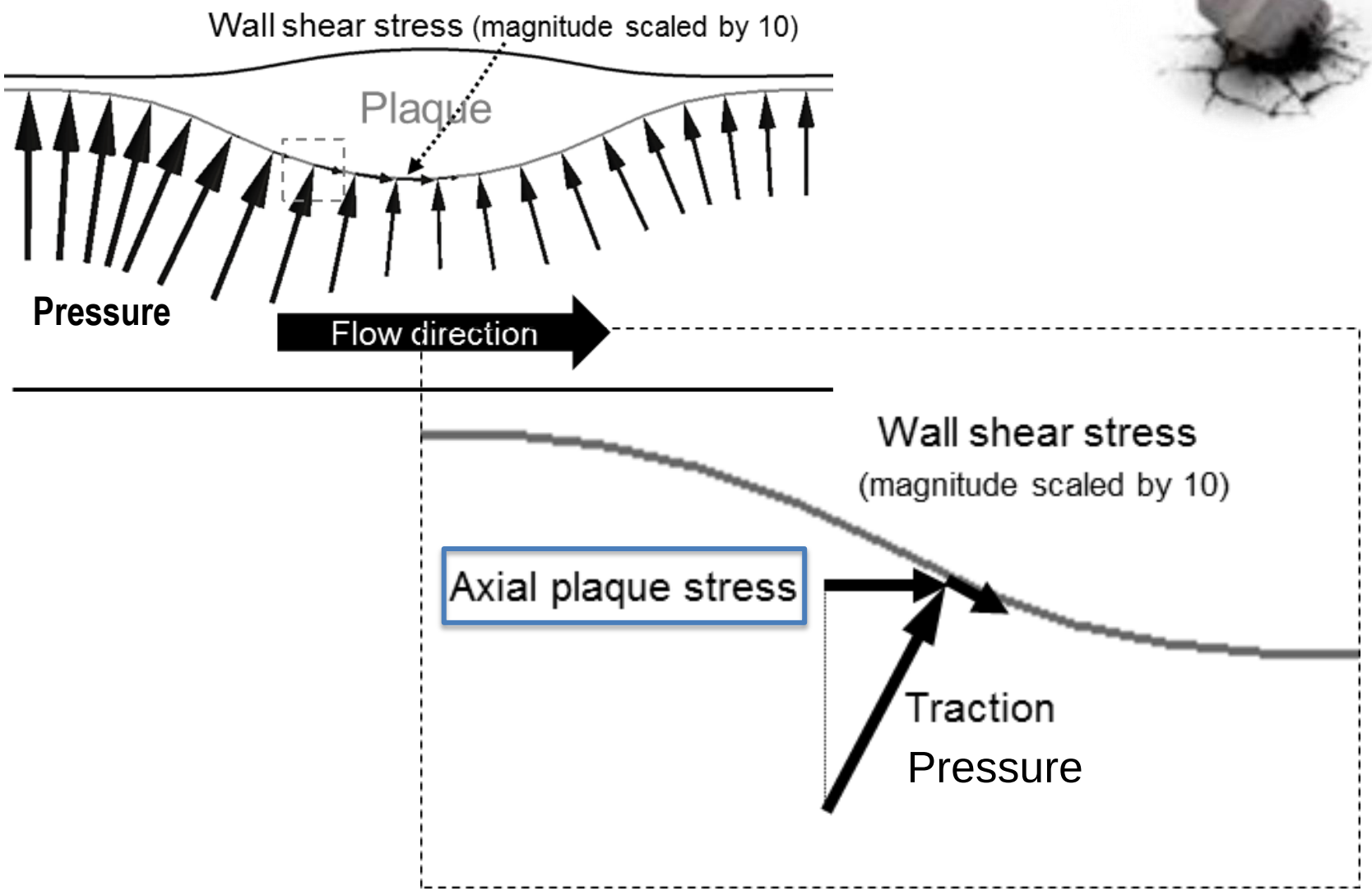


Non-invasive assessment for regional distribution of hemodynamic forces: WSS and Pressure

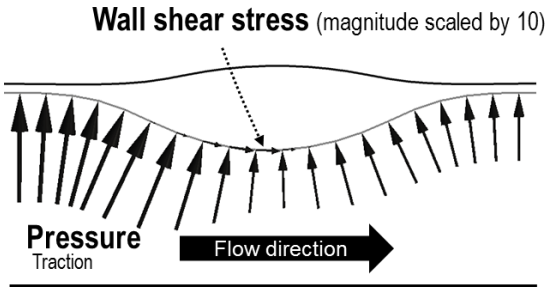




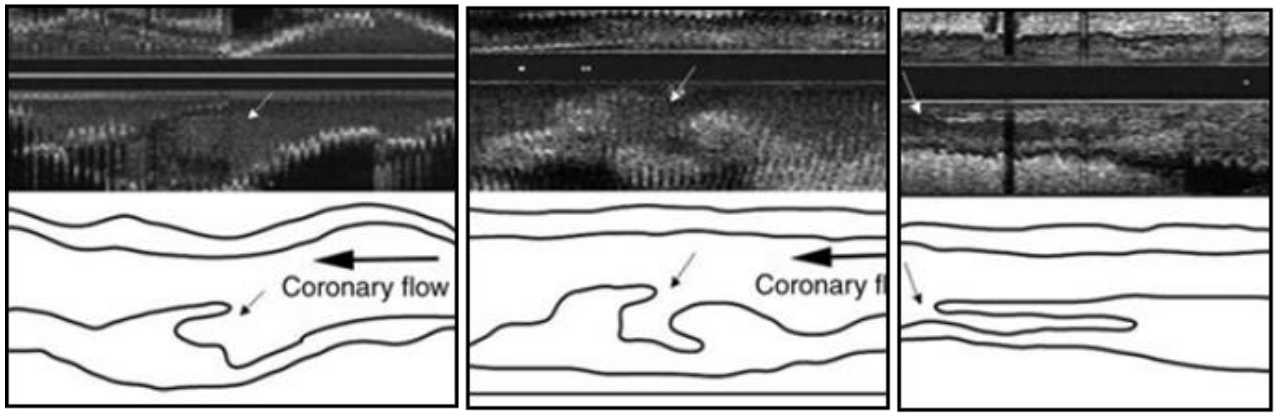
What kind of forces are acting on the plaque?



WSS and pressure, are they enough?



Location of rupture

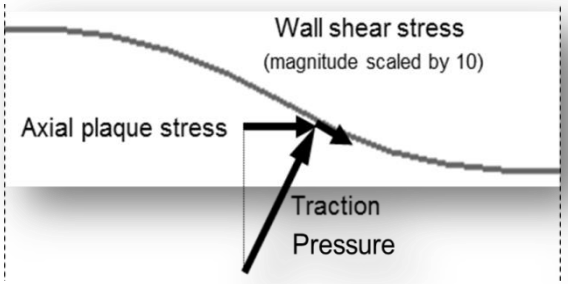


Upstream (39%) **Mid (25%)** **Downstream (36%)**

Tanaka, et al. Eur Heart J 2008;29:38-44

Pressure, FFR and WSS are high at the *upstream segment* of a plaque. Therefore, these parameters cannot explain the occurrence of *downstream rupture*.

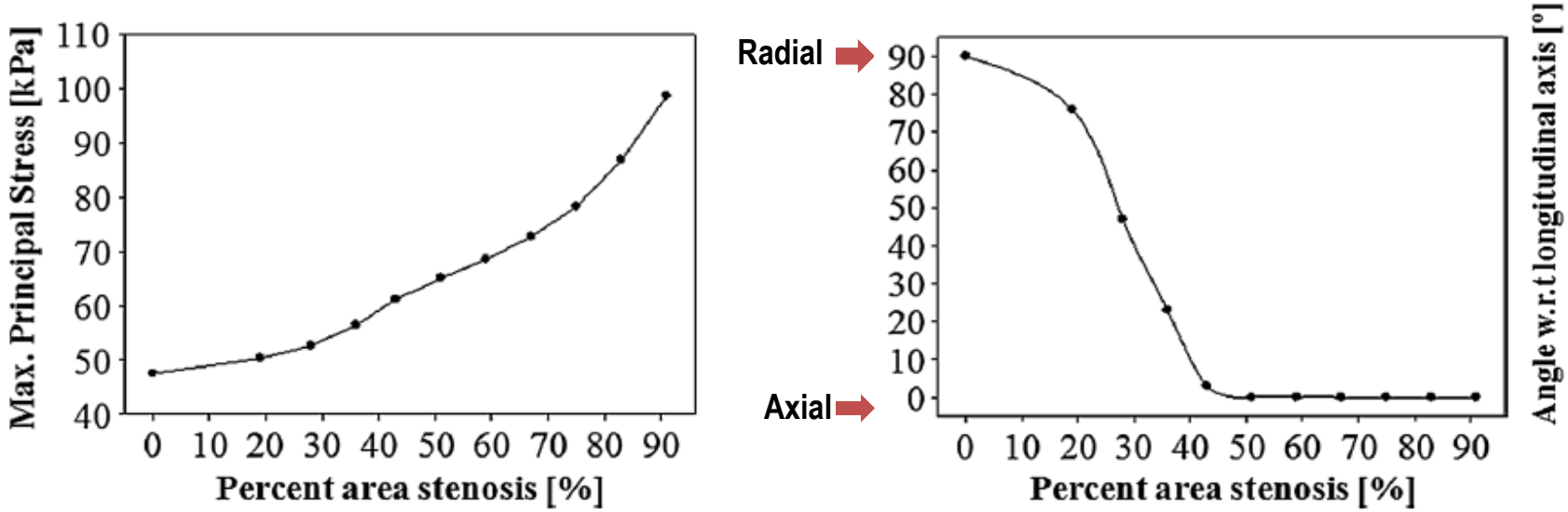
Pressure and WSS, then what else?



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

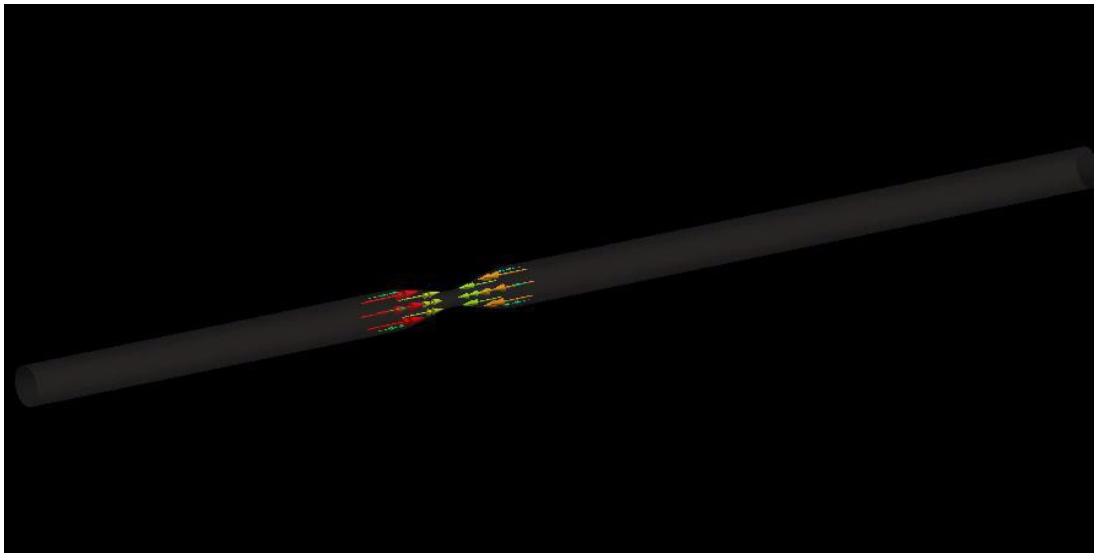
In relation to lumen surface: $\|\mathbf{Traction}\|^2 = \|\mathbf{WSS}\|^2 + \|\mathbf{Pressure}\|^2$

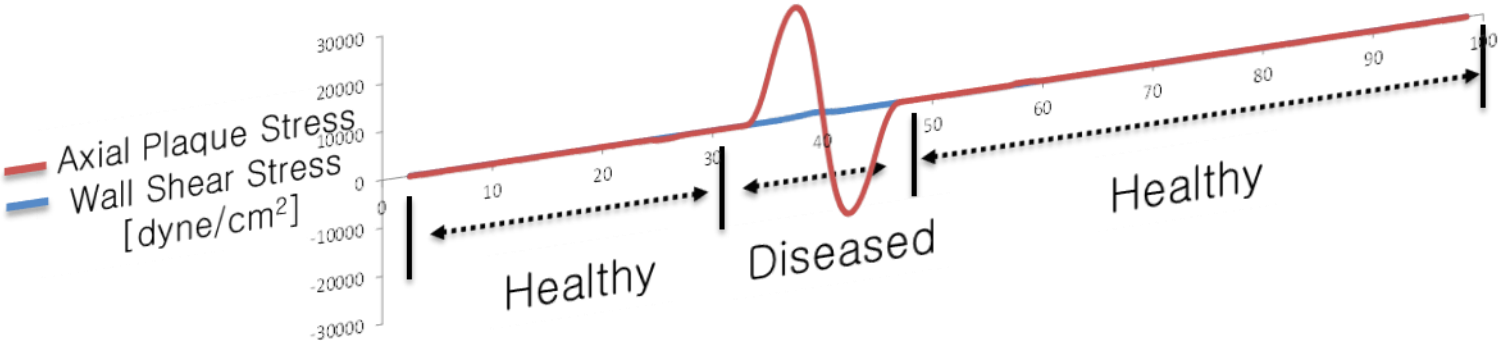
In relation to centerline: $\|\mathbf{Traction}\|^2 = \|\mathbf{Axial\ Stress}\|^2 + \|\mathbf{Radial\ Stress}\|^2$



Pagiatakis C, et al. Med Biol Eng Comput 2015

Novel hemodynamic index: Axial Plaque Stress





- **Axial plaque stress** uniquely characterizes the diseased segment of both upstream and downstream.
- **Axial plaque stress** is much higher than wall shear stress.

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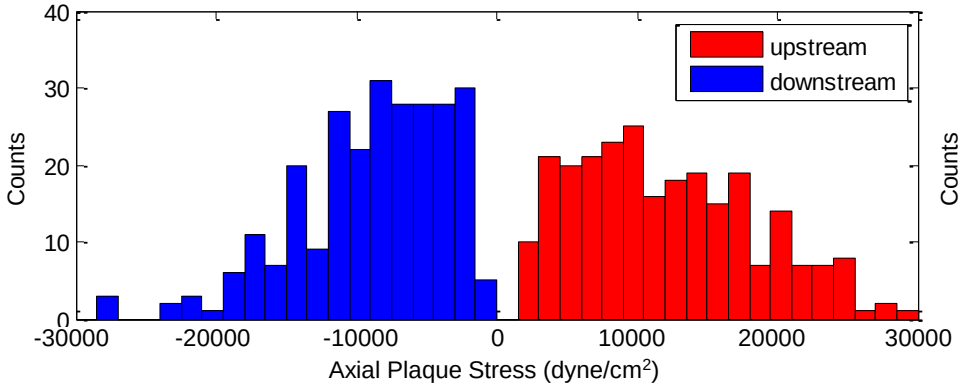
Distribution of Axial plaque stress

Idealized stenosis models (n=264)



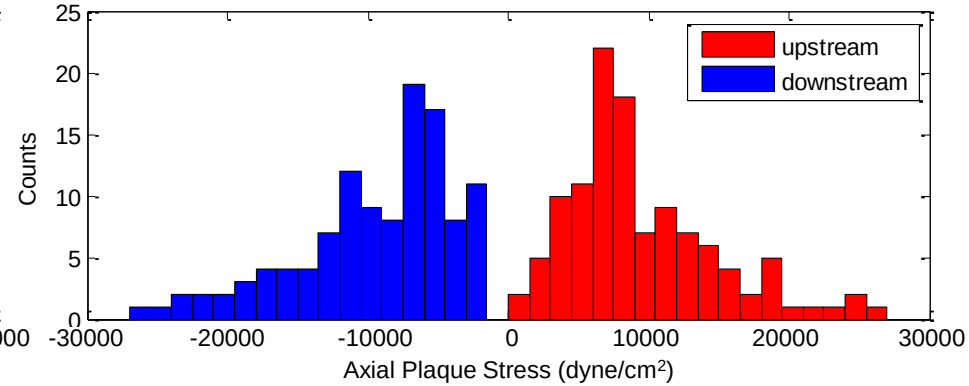
Downstream segment

- N=264
- **Median: -7801 dyne/cm²**
- IQR: -11954, - 4603

Upstream segment

- N=264
- **Median: 11629 dyne/cm²**
- IQR: 11954, 4603

Patients' lesions (n=114)



Downstream segment

- N=114
- **Median: -7912 dyne/cm²**
- IQR: -12366, - 5632

Upstream segment

- N=114
- **Median: 7886 dyne/cm²**
- IQR: 6055, 12707

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

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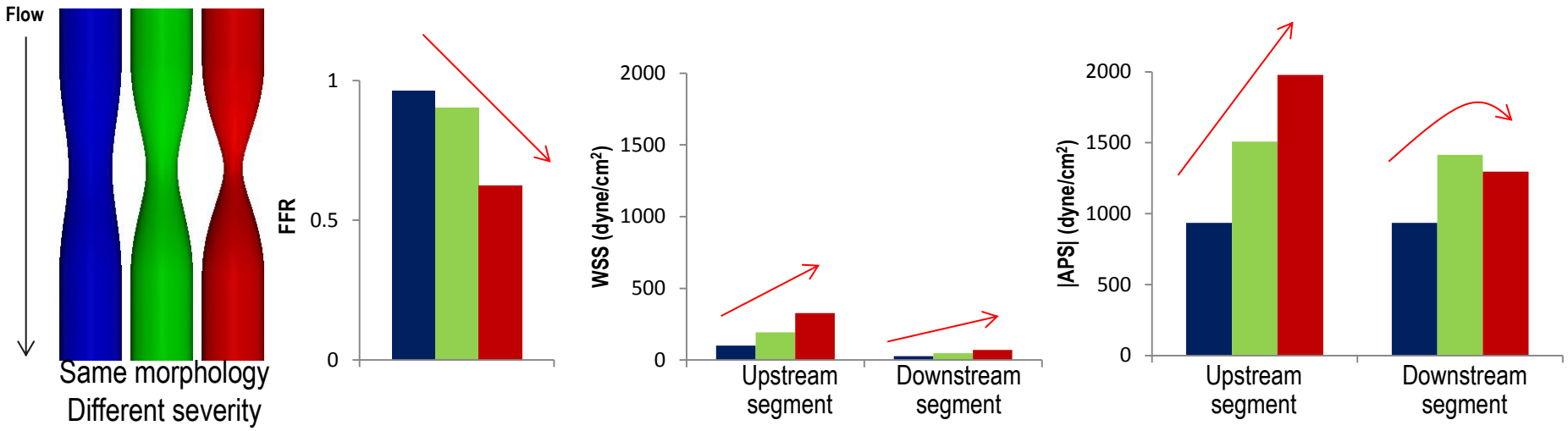
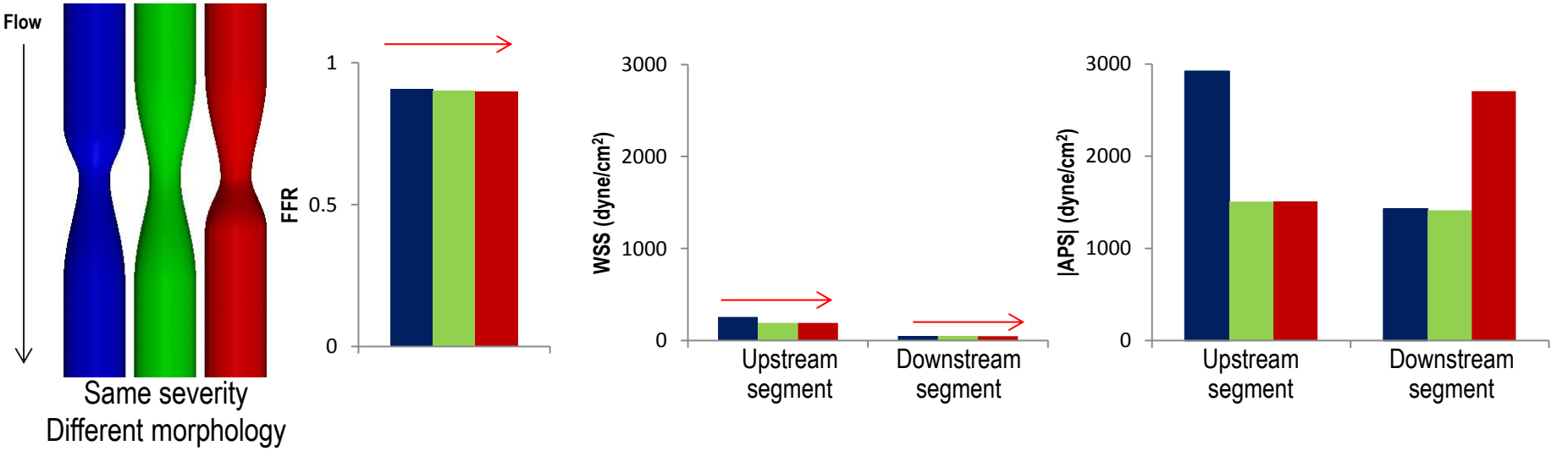
Lesion geometry vs. Hemodynamic forces





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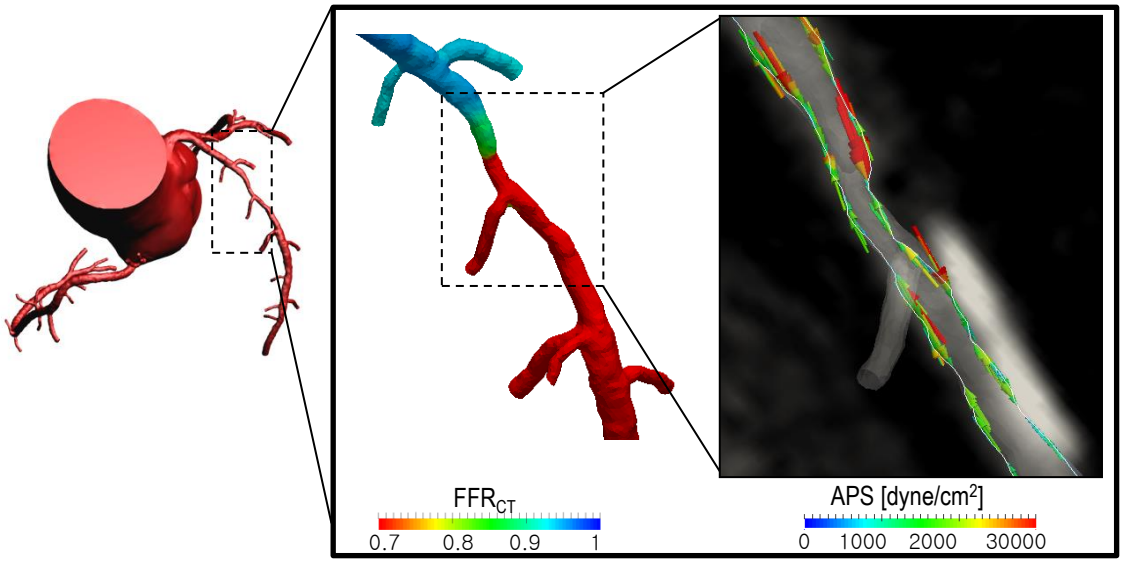
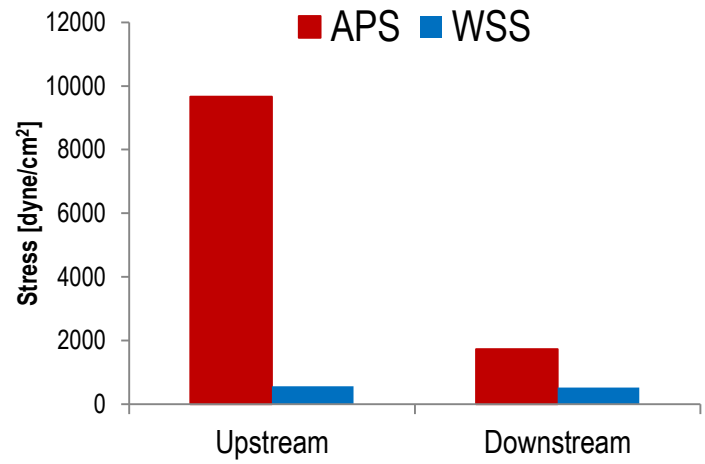
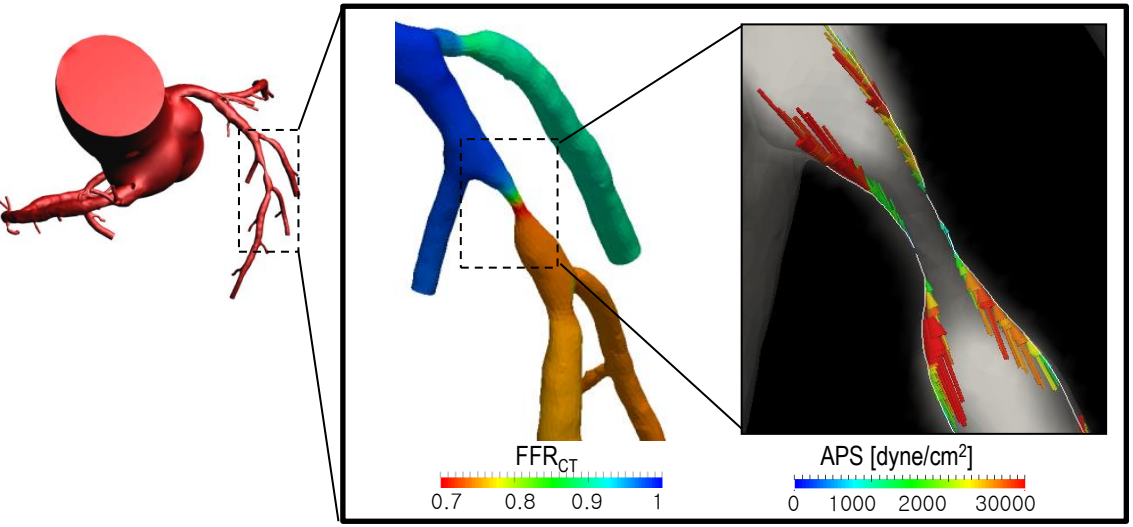
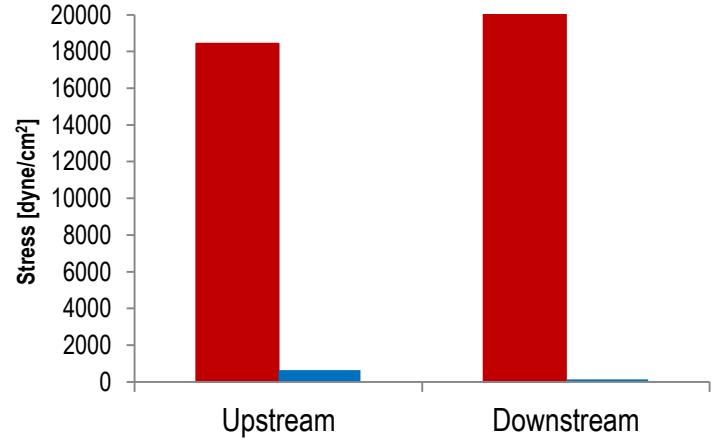
Distribution of Axial Plaque Stress in patients









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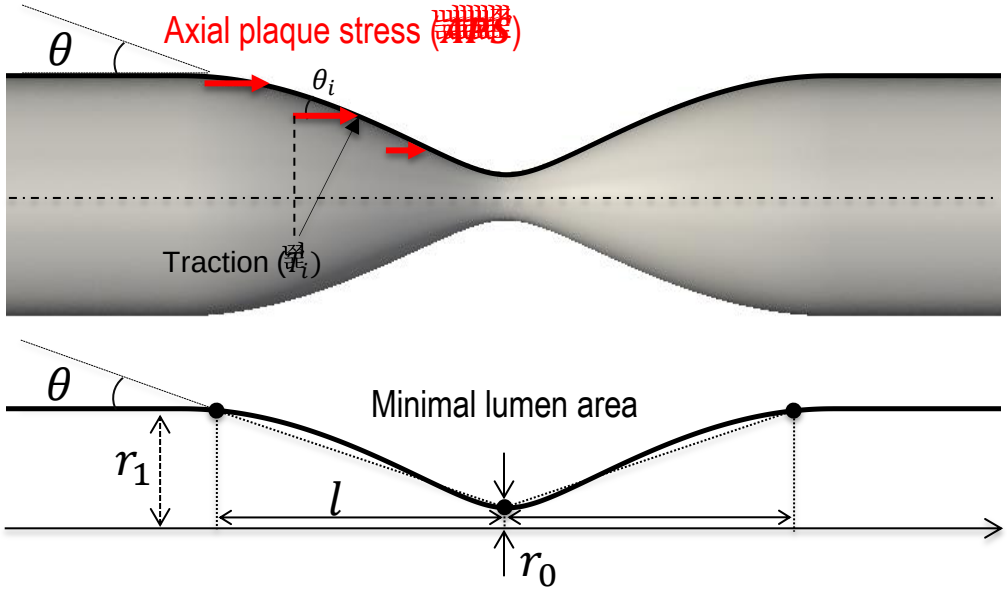
Novel geometric index: **Radius Gradient**



$$\mathbf{APS_{upstream}} = \text{깹}\,\text{뫋}_i sin\theta_i \approx Pressure\frac{r_1 - r_0}{\text{깎}\,l^2 + (r_1 - r_0)^2}$$

$$= Pressure\frac{\frac{r_1 - r_0}{l}}{\text{깐}\,1 + (\frac{r_1 - r_0}{l})^2} \approx Pressure\frac{r_1 - r_0}{l}$$

$$= \boldsymbol{Pressure \cdot Radius\ Gradient}$$

Radius Gradient: radius change over segmental lesion length

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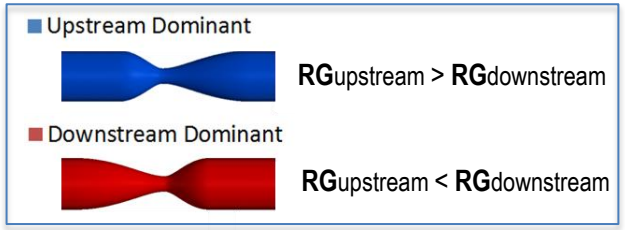
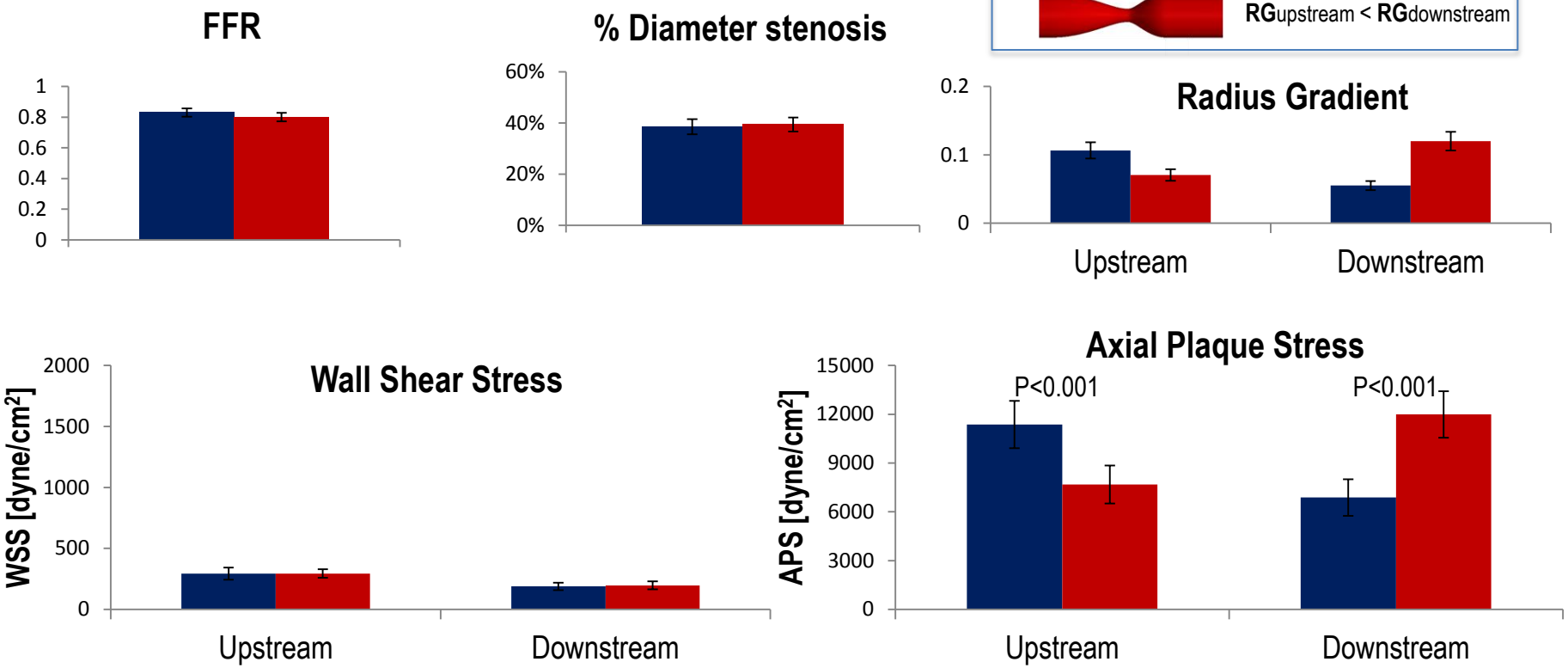
RG-derived lesion definition
Upstream-dominant vs. Downstream-dominant lesions

(n=114)





RG-derived lesion definition can provide additional information which conventional lesion definitions cannot provide.

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Influence of RG on hemodynamic parameters

: Segmental comparison in patients' lesions (n=114)

	Upstream-dominant stenosis (N=56)			Downstream-dominant stenosis (N=58)		
	Upstream	**Downstream**	p value	**Upstream**	**Downstream**	p value
Radius gradient	**0.11 ± 0.05**	0.06 ± 0.03	<0.001	0.07 ± 0.03	**0.12 ± 0.05**	<0.001
ΔPressure, mmHg	**9.8 ± 8.8**	0.2 ± 2.3	<0.001	11.5 ± 8.6	0.7 ± 1.2	<0.001
ΔFFR_{CT}	**0.10 ± 0.09**	0.002 ± 0.02	<0.001	0.12 ± 0.09	0.01 ± 0.01	<0.001
WSS, dyne/cm^2	**273 ± 181**	147 ± 92	<0.001	271 ± 124	154 ± 105	<0.001
APS, dyne/cm^2	**11372 ± 5575**	6878 ± 4320	<0.001	7681 ± 4557	**11991 ± 5557**	<0.001

FFR_{CT}, coronary CT angiography-derived FFR; WSS, wall shear stress, APS, axial plaque stress .

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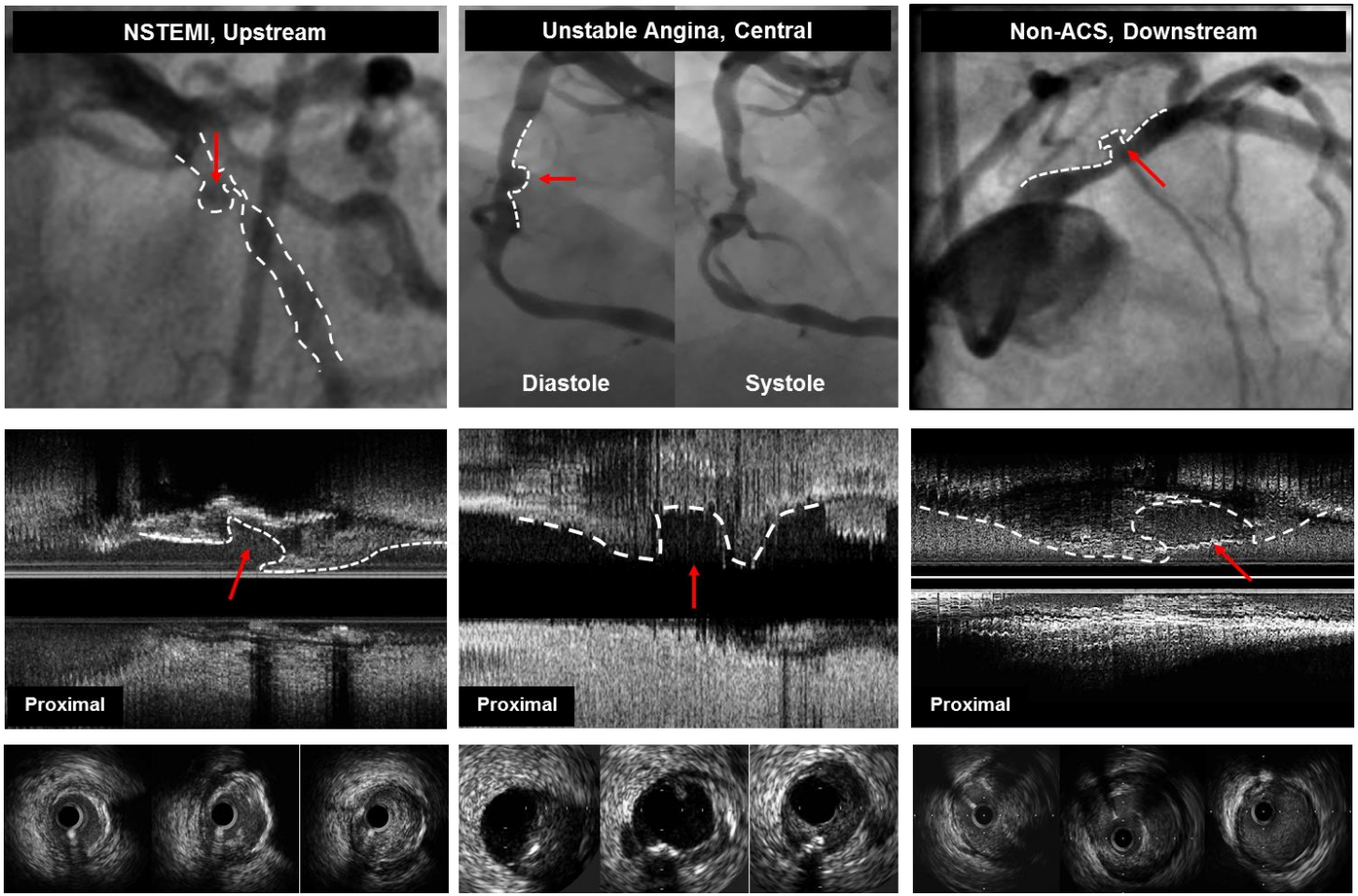
Lesion geometry vs. Rupture location: IVUS study



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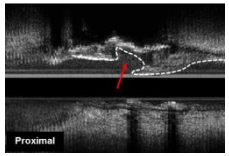
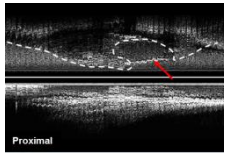
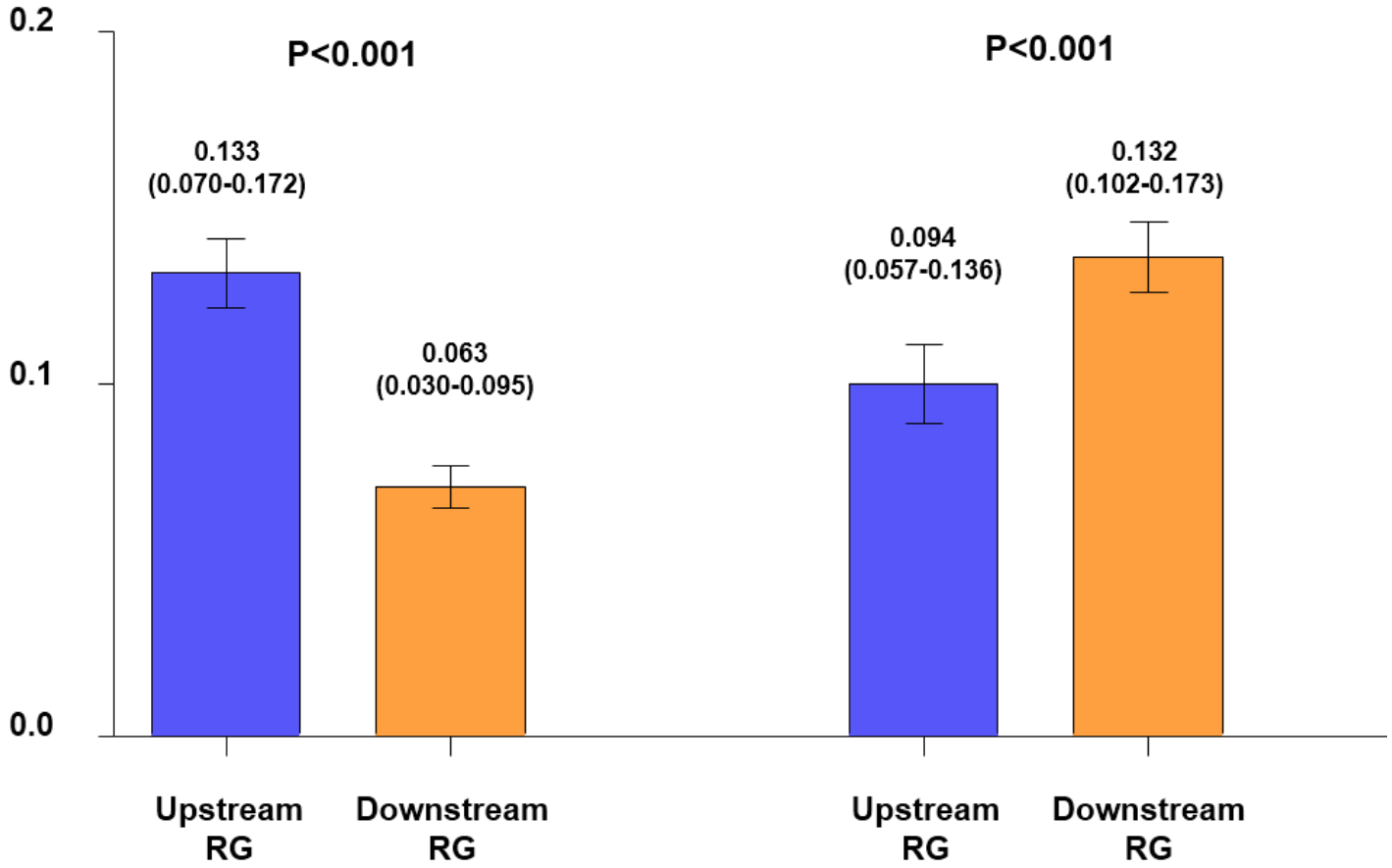
Comparison of Radius Gradient and Rupture Locations



Upstream Rupture

Downstream Rupture





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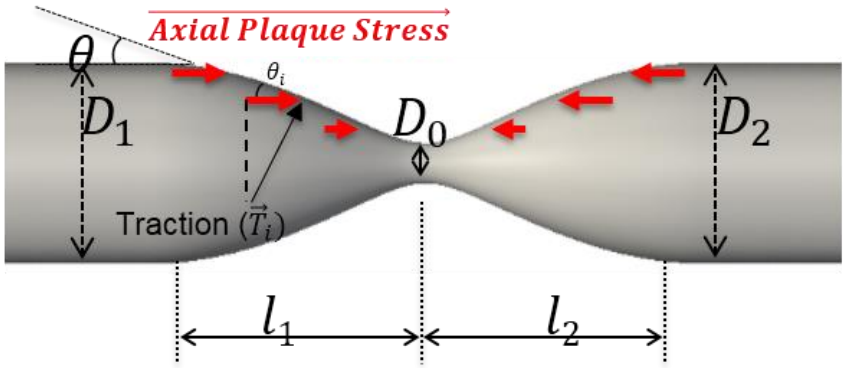
Influence of lesion severity on APS



$$\overrightarrow{\mathbf{APS}}_{\mathbf{upstream}} = \sum \vec{T}_i \sin\theta_i \approx \text{Pressure}\frac{\frac{D_1}{2} - \frac{D_0}{2}}{\sqrt{{l_1}^2 + (\frac{D_1}{2} - \frac{D_0}{2})^2}}$$

$$\approx \text{Pressure}\frac{\frac{D_1}{2} - \frac{D_0}{2}}{l_1} = \text{Pressure}\frac{\sqrt{\frac{A_1}{\pi}} - \sqrt{\frac{A_0}{\pi}}}{l_1}$$

$$= \underline{\mathbf{Pressure \cdot Radius\ Gradient}}$$

Severe stenosis

↓

Low distal pressure

↓

Low downstream APS

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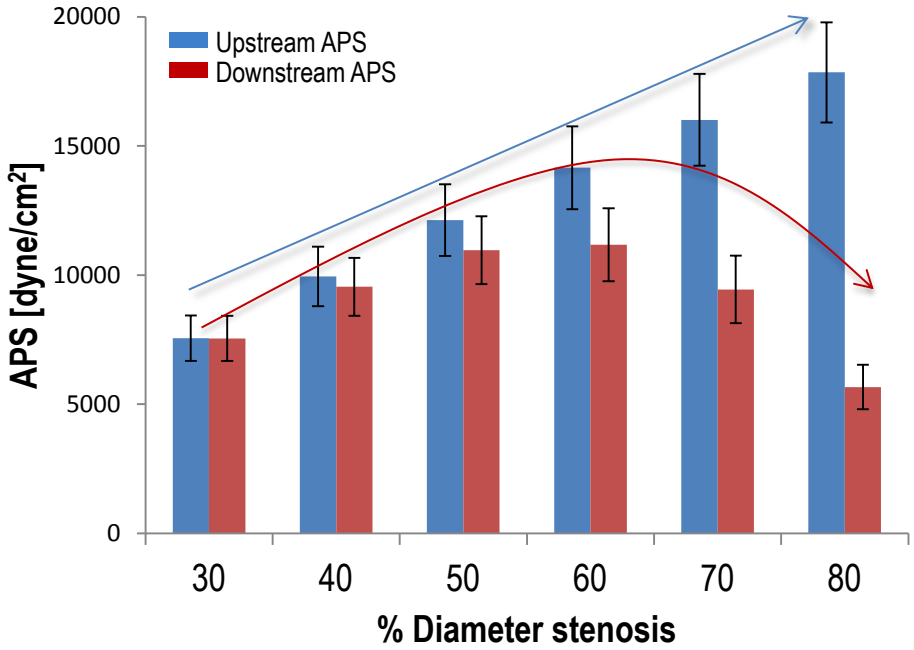
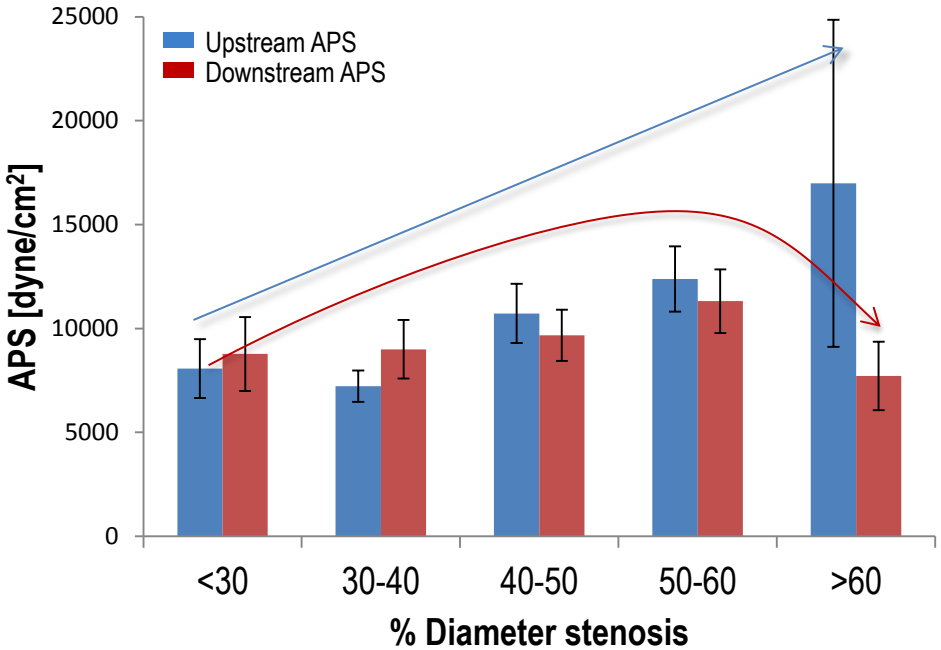
Influence of lesion severity on APS

Idealized Stenosis Models



Patient Lesions



- Upstream APS has linear relationship with stenosis severity.
- Downstream APS has a dual response to lesion severity.
- Downstream rupture may occur in less severe stenosis and its clinical consequence can be less severe than upstream rupture.

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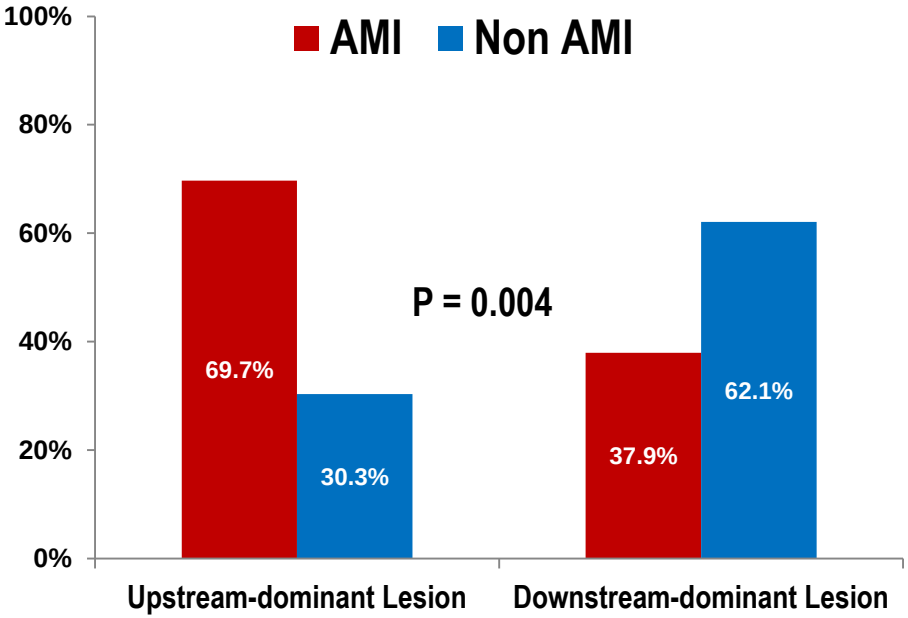
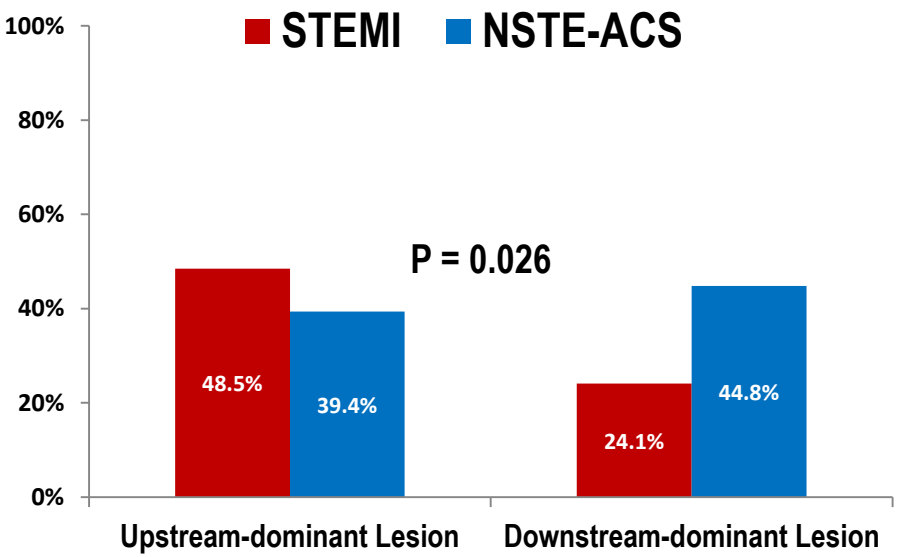
Clinical Presentations According to Longitudinal Lesion Geometry





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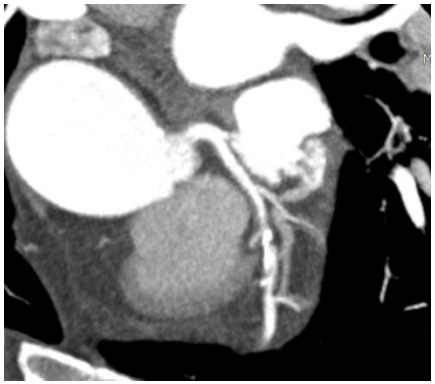
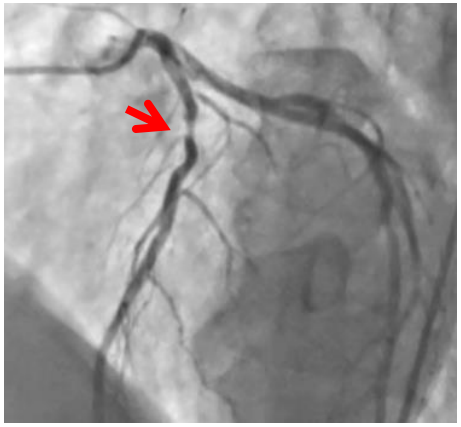
APS, RG and Future Event

2011-04 CT, Asymptomatic



2012-06 Acute MI



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APS, RG and Future Event

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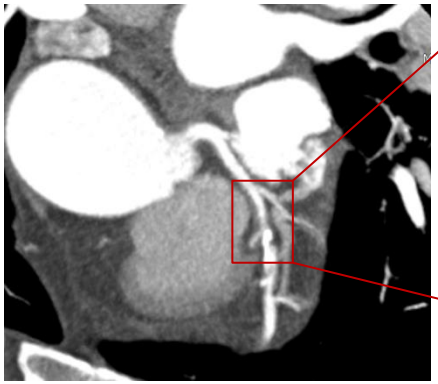
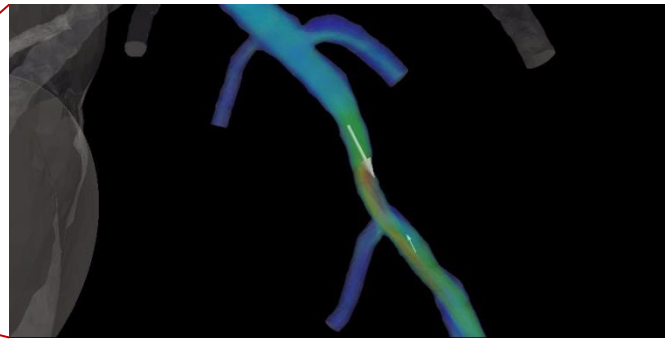
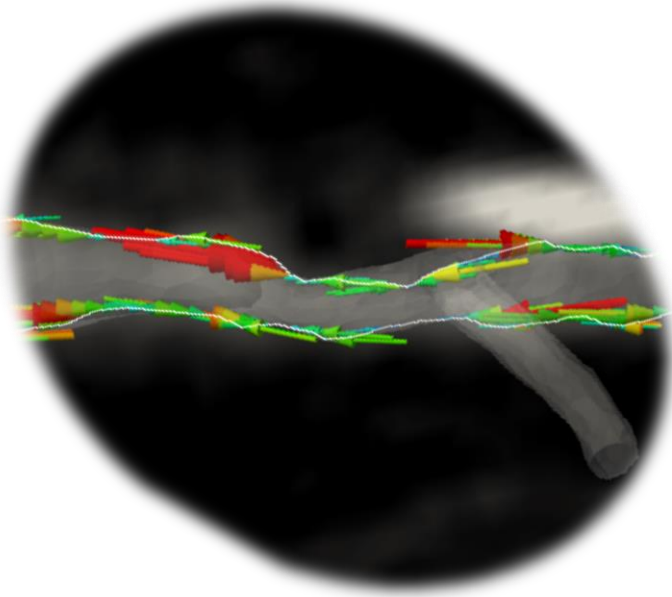
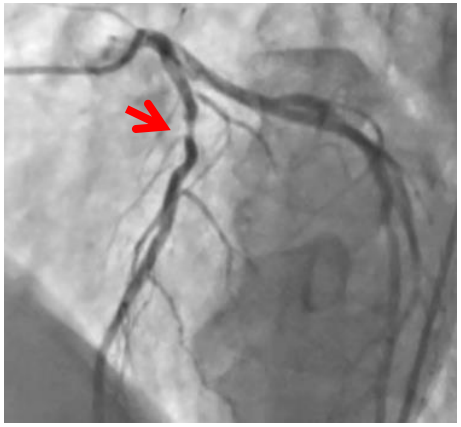


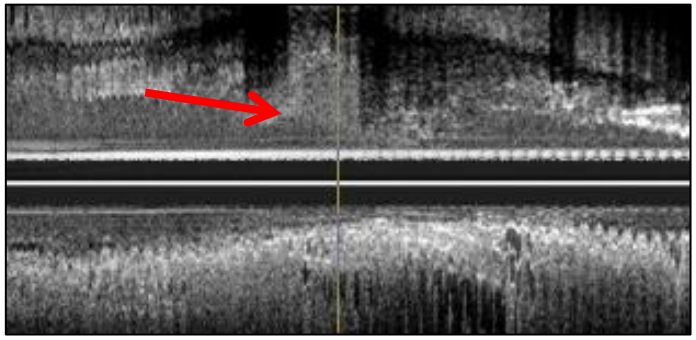


	RG	APS
Upstream	**0.14**	**9960 dyne/cm^2**
Downstream	0.05	1740 dyne/cm^2



2012-06 Acute MI





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Conclusion

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

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

- Clinical application of these novel indices can be helpful to better assess the future risk and to determine the treatment strategy for patients with coronary artery disease.