SUPPLEMENTAL MATERIAL

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Computational fluid dynamic measures of wall shear stress are related to coronary lesion characteristics

The List of Files

Supplemental Methods

Definition of Hemodynamic Metrics and Analysis Methods

Major components of stress in blood flow consist of local blood pressure and the deviatoric stress. The blood pressure and the normal component of the deviatoric stress act normal to the endothelial surface whereas the remaining components of the deviatoric stress act tangential to the endothelial surface. A mathematical definition of the stress vector ($\vec{\boldsymbol{t}}$), also referred to as the traction vector, which acts on the surface of the blood vessel is as follows:

$$\vec{\boldsymbol{t}} = \widetilde{\boldsymbol{T}}\vec{\boldsymbol{n}} = -p\vec{\boldsymbol{n}} + \mu((\nabla\vec{\boldsymbol{v}}) + (\nabla\vec{\boldsymbol{v}})^T)\vec{\boldsymbol{n}}, \tag{1}$$

where $\widetilde{\boldsymbol{T}}$ is the Cauchy stress tensor defined by $-p\boldsymbol{I} + \mu((\nabla\vec{\boldsymbol{v}}) + (\nabla\vec{\boldsymbol{v}})^T)$ for a Newtonian fluid, p is the blood pressure, $\boldsymbol{I}$ is the 3×3 identity matrix, μ is the dynamic viscosity of blood, $\vec{\boldsymbol{v}}$ is the velocity of blood, and $\vec{\boldsymbol{n}}$ is the normal vector on the luminal surface of the blood vessel.

If the amount of force per unit area acting at any location on the endothelial surface is the quantity of interest, the magnitude of the traction vector needs to be considered. However, since the primary interest in the present study is the net resultant force acting over a defined lesion, the vector sum of the traction was computed in the direction along the axis of the coronary vessel. Specifically, since the pressure drop predominantly occurs in the longitudinal direction of the coronary artery, the line integral of the traction vector along the centerline (defined as slicing force) was computed as follows:

$$\boldsymbol{F_s} = \int_{\boldsymbol{a}}^{\boldsymbol{b}} A \cdot \vec{\boldsymbol{t}} \cdot d\vec{\boldsymbol{s}}, \tag{2}$$

where $\vec{\boldsymbol{t}} \cdot d\vec{\boldsymbol{s}}$ is the dot product of the traction vector and the unit tangential vector of the centerline, [$\boldsymbol{a}, \boldsymbol{b}$] is the defined interval of the centerline encompassing the lesion, and A is the area of surface mesh associated with the traction vector (see Supplemental Figure 1).

Other hemodynamic metrics are described as follows.

First, the wall shear stress is the tangential stress resulting from the friction between the blood flow and the endothelial surface of the vessel wall. From the definition of the traction vector (1), the wall shear stress vector ($\overrightarrow{\boldsymbol{t}_s}$) is defined by

$$\vec{\boldsymbol{t}}_s = \vec{\boldsymbol{t}} - (\vec{\boldsymbol{t}} \cdot \vec{\boldsymbol{n}})\vec{\boldsymbol{n}}, \tag{3}$$

The magnitude of the wall shear stress vector is referred to herein by the acronym, WSS. In a simple form, applicable to an idealized circular vessel under assumptions of fully developed steady or pulsatile flow, WSS can be expressed as the product of the blood dynamic viscosity (μ) and the gradient of the axial velocity, v, at the vessel wall, i.e., $WSS = \mu \frac{\mathrm{dv}}{\mathrm{dy}}|_{y=0}$, (y is the distance from the wall) in units of force per unit area [Pascal (Pa) or dyne/cm^2] (Supplemental Figure 1).

Second, the spatial derivative of pressure is a physical quantity that describes the direction and rate of change of pressure at a given location and is expressed in units of pressure per unit length (e.g., mmHg/cm). Although this metric is a vector quantity as represented by $(\frac{\partial \mathrm{P}}{\partial \mathrm{x}}, \frac{\partial \mathrm{P}}{\partial \mathrm{y}}, \frac{\partial \mathrm{P}}{\partial \mathrm{z}})$, it predominantly varies in a direction aligned with the vessel longitudinal axis since pressure drop mainly occurs along the direction of flow.

Third, fractional flow reserve from coronary computed tomography angiography data (FFR_{CT}) is defined by the ratio of mean downstream coronary pressure divided by the upstream pressure (i.e., aortic pressure) derived from the computational fluid dynamics (CFD) analysis under a simulated hyperemic condition. The FFR_{CT} traces provide information on the normalized pressure drop across lesions in the entire epicardial coronary arteries.

Lastly, flow in each coronary vessel is also derived from the CFD analysis by using the principle of mass conservation. Flow rate in each parent vessel is computed by summing all the flows in daughter vessels following the hierarchical structure of the coronary vascular trees.

For the statistical analysis over the given patient populations, the aforementioned hemodynamic quantities were evaluated along the coronary centerline for each patient. Specifically, a thin strip (2 mm in thickness) of the coronary model was sliced with 0.5 mm intervals along the coronary centerlines and the average values of FFR_{CT}, WSS, and pressure gradient (∇P) were computed over the strip as follows:

$$\mathbf{FFR_{CT}}(\boldsymbol{s}) = \frac{1}{A(s)}\int_{s-\Delta s/2}^{s+\Delta s/2} FFR_{CT}dA,$$

$$\mathbf{WSS}(\boldsymbol{s}) = \frac{1}{A(s)}\int_{s-\Delta s/2}^{s+\Delta s/2}\|\vec{\boldsymbol{t}}_{\boldsymbol{s}}\|dA, \text{ and}$$

$$\boldsymbol{\nabla}\mathbf{P}(\boldsymbol{s}) = \frac{1}{A(s)}\int_{s-\Delta s/2}^{s+\Delta s/2}\|\nabla P\|dA,$$

where $A(s)$ is the area of strip at s, and Δs is the slice thickness (2 mm).

To analyze the spatial variation of hemodynamic quantities in each lesion, average WSS ($\overline{\mathbf{WSS}}$) and pressure drop ($\Delta\mathbf{P}$) were evaluated over upstream, minimal lumen area (MLA), and downstream segments as follows.

$$\overline{\mathbf{WSS}} = \frac{1}{A(s)}\int_{a}^{b}\|\vec{\boldsymbol{t}}_{\boldsymbol{s}}\|dA$$

$$\Delta\mathbf{P} = \mathbf{P}(b) - \mathbf{P}(a)$$

where $[a, b]$ is the specified region of interest (e.g., total lesion, upstream, MLA, or downstream) and **P** is the computed coronary pressure.

Supplemental Tables

Supplemental Table 1. Influence of Lesion Location on Anatomic and Hemodynamic Parameters

Parameter	Left main	Proximal LAD	Mid LAD	*p* value
Anatomic variables				
Reference diameter, mm	3.5 ± 0.5	3.1 ± 0.5	2.6 ± 0.4	<0.001
% diameter stenosis	47.6 ± 8.5	53.2 ± 14.8	52.5 ± 15.2	0.618
MLA, mm^2	3.2 ± 1.0	2.2 ± 1.1	1.8 ± 0.7	<0.001
Lesion length, mm	13.5 ± 7.7	20.1 ± 9.0	21.4 ± 10.1	0.110
Hemodynamic variables				
Resting				
Δpressure, mmHg	2.6 ± 2.1	2.5 ± 2.4	1.8 ± 2.0	0.342
Average WSS, dyne/cm^2	87.6 ± 57.7	49.4 ± 25.7	37.5 ± 24.9	<0.001
Hyperemic				
ΔFFR_{CT}	0.16 ± 0.12	0.14 ± 0.09	0.10 ± 0.07	0.057
Δpressure, mmHg	14.8 ± 11.3	12.9 ± 8.8	9.5 ± 8.3	0.163

Average WSS, dyne/cm^2	388.6 ± 152.3	252.6 ± 89.7	184.4 ± 90.5	<0.001

Values given as mean ± standard deviation.

LAD denotes left anterior descending coronary artery; MLA, minimal lumen area; WSS, wall shear stress; and FFR_{CT}, coronary computed tomography angiography-derived fractional flow reserve.

Supplemental Table 2. Discriminating Ability of Wall Shear Stress and % Diameter Stenosis for Adverse Plaque Characteristics

	AUC (95% CI)	*p* value	Cutoff value	Sensitivity (%)	Specificity (%)
WSS					
Any of high-risk features	0.673 (0.559 – 0.775)	0.005	72.5	68	71
Low density plaque	0.682 (0.568 – 0.783)	0.011	104.0	61	75
Positive remodeling	0.654 (0.538 – 0.757)	0.019	72.5	70	69
Napkin ring sing	0.817 (0.714 – 0.895)	<0.001	104.0	75	78
Spotty calcification	0.677 (0.562 – 0.778)	0.072	81.6	80	59
% diameter stenosis					
Any of high-risk features	0.540 (0.424 – 0.653)	0.539	40	34	89
Low density plaque	0.558 (0.442 – 0.670)	0.418	53	57	63
Positive remodeling	0.576 (0.460 – 0.686)	0.245	40	35	87
Napkin ring sing	0.639 (0.524 – 0.744)	0.064	53	65	64
Spotty calcification	0.633 (0.517 – 0.739)	0.175	42	90	45

AUC denotes the area under the curves; CI, confidential interval; and other abbreviations are as in Supplemental Table 1.

Supplemental Figure Legends

Supplemental Figure 1. Visualization of Computational Fluid Dynamics Results in Straightened and Unfolded Configuration

The initial cut-plane direction at LAD bifurcation ($\vec{v}_{cut}$) was determined by cross-product of LAD ($\vec{v}_{LAD}$) and LCX ($\vec{v}_{LCX}$) directions. Then the 3D curvilinear cut-plane was defined by transforming the initial direction parallel to the vessel centerline.

LAD denotes left anterior descending coronary artery; LCX, left circumflex coronary artery; 3D, three dimension; and FFR_{CT}, coronary CT angiography-derived fractional flow reserve.

Supplemental Figure 2. Definition of Hemodynamic Parameters

(A) A schematic demonstration showing the definition of WSS, traction, and slicing stress in an idealized stenosis model (diameter: 3.5 mm, % diameter stenosis: 60%, flow: 3.5 cc/second).

(B) The distribution and change of FFR_{CT}, WSS, pressure, and pressure gradient across a stenotic segment.

FFR_{CT} denotes cCTA-derived fractional flow reserve.

Supplemental Figure 3. A representative example of the napkin-ring sign

(Left panel) Straightened multiplanar reconstruction and cross-sectional images of coronary CT angiography show the plaque with a napkin-ring sign (upper red box) in the left main coronary artery (upper red box). The napkin-ring sign is a qualitative plaque characteristic demonstrating a ring-like peripheral high attenuation tissue (blue dashed line) surrounding a central lower attenuation portion of the plaque (asterisk). There is another plaque in the mid left anterior descending coronary artery without a napkin ring sign (lower blue box).

(Right panel) Wall shear stress derived from coronary CT angiography was the highest in the segment with a napkin ring sign.

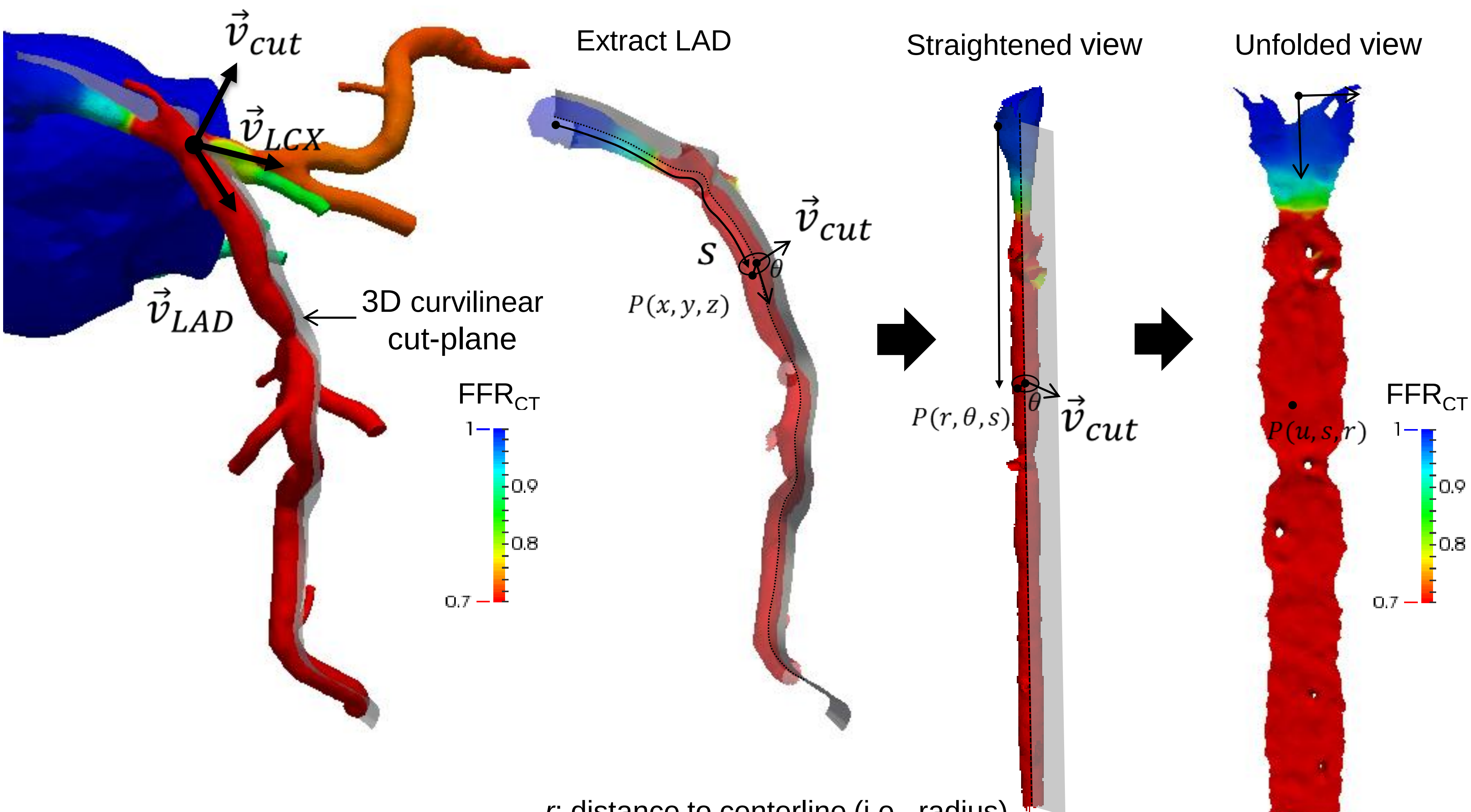
L denotes coronary lumen; NRS, napkin-ring sign; and WSS, wall shear stress.

Supplemental Figure 4. Association between Wall Shear Stress and Pressure Gradient across the Lesion

The magnitude of WSS was highly correlated with that of pressure gradient at both resting (A) and hyperemic (B) conditions.

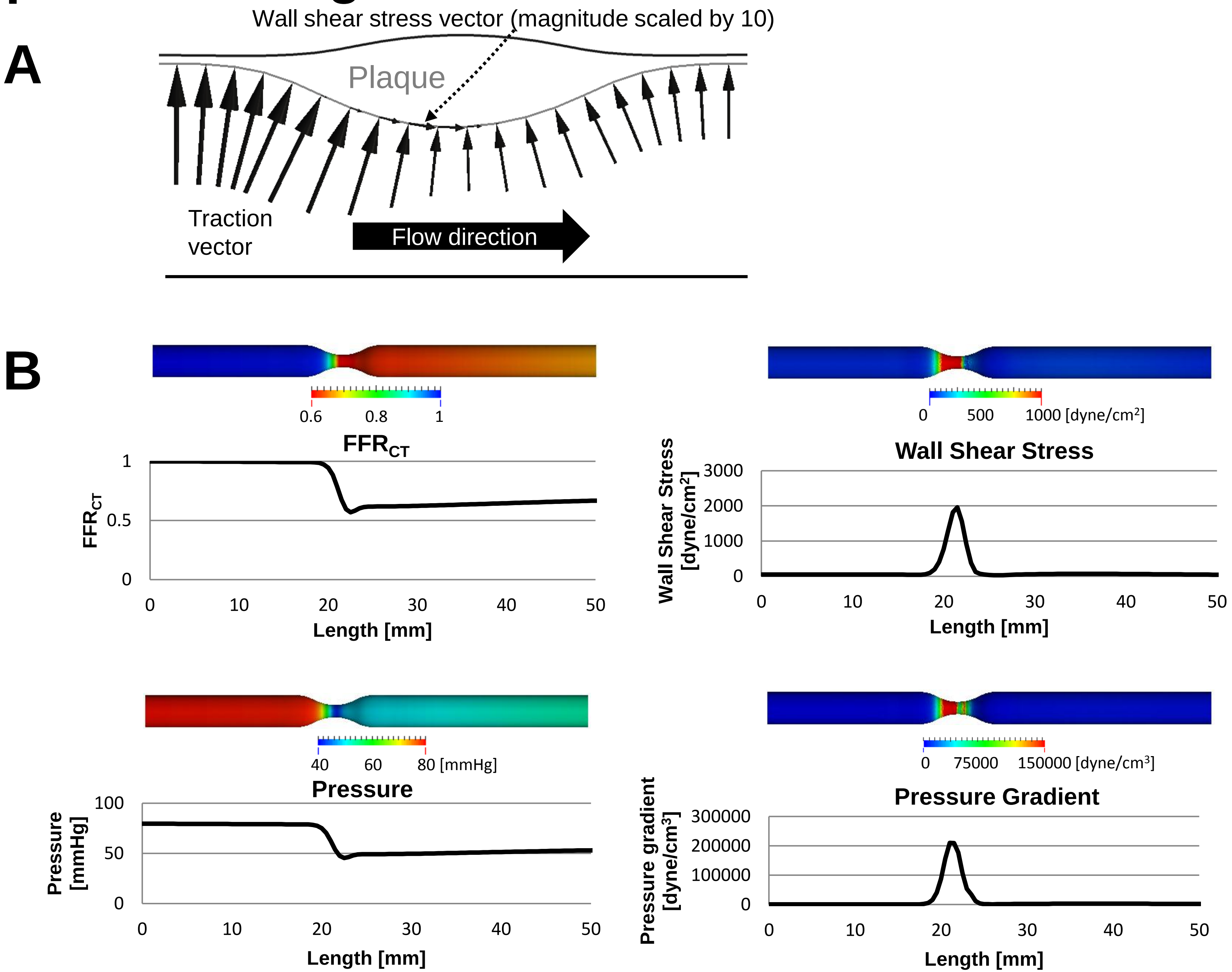
WSS denotes wall shear stress.

Supplemental Figure 1

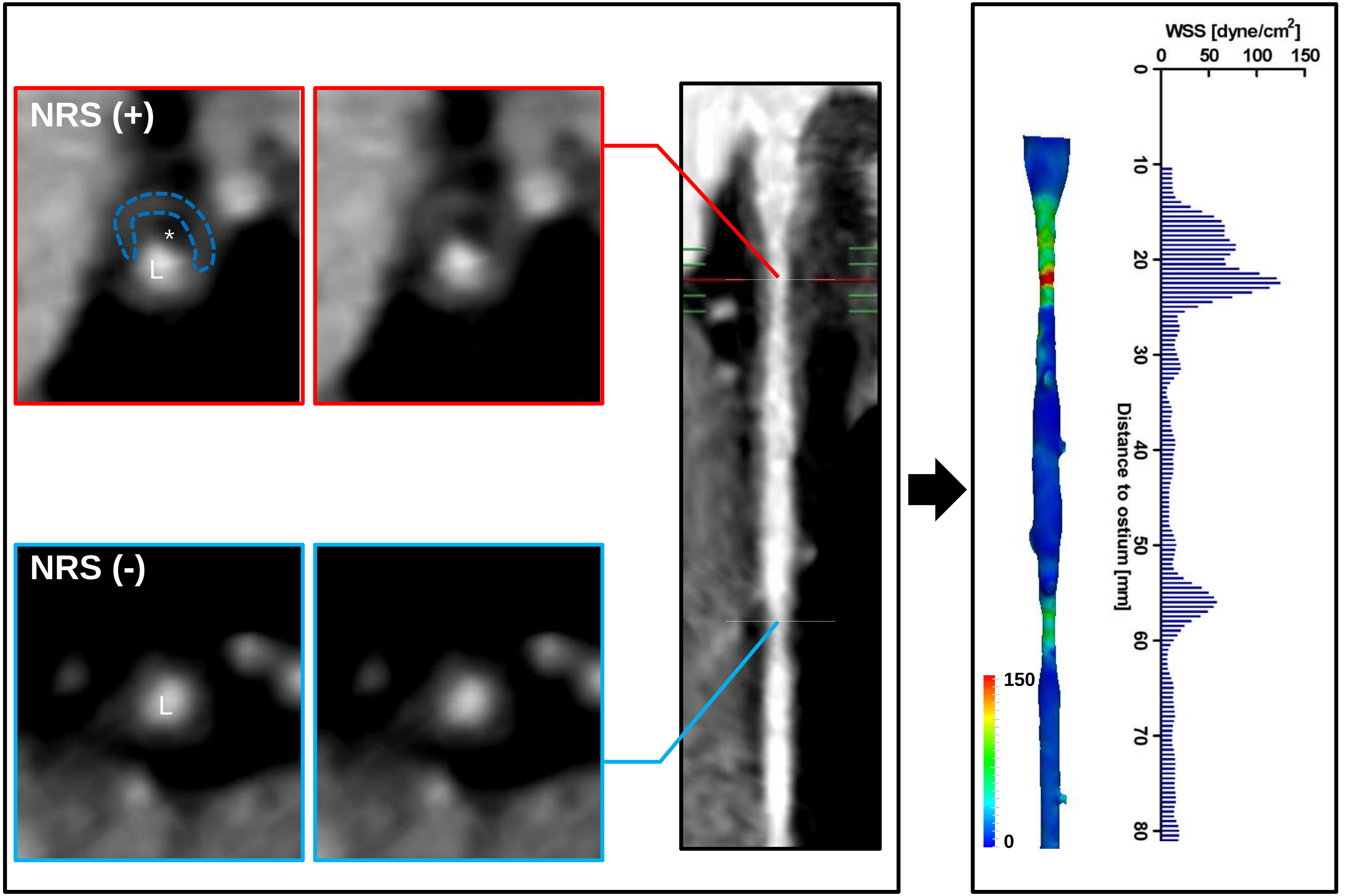


r: distance to centerline (i.e., radius)
θ: angle between radial and reference cut vectors
s: distance to ostium
u: circumferential distance regarding cut vector

Supplemental Figure 2



Supplemental Figure 3



Supplemental Figure 4