Cardiovascular Center Aalst

Regulation of Coronary Blood Flow

… for the Interventionalists

Bernard De Bruyne
Cardiovascular Center Aalst
Belgium

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ETP April 24-26, 2014

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ABC of Coronary Physiology For the Interventionalist

1. **About Pressure, flow, mass, resistance, etc, ...**
2. **Epicardial vs microvascular compartments**
3. **Flow-function relationship**
4. **Coronary autoregulation**

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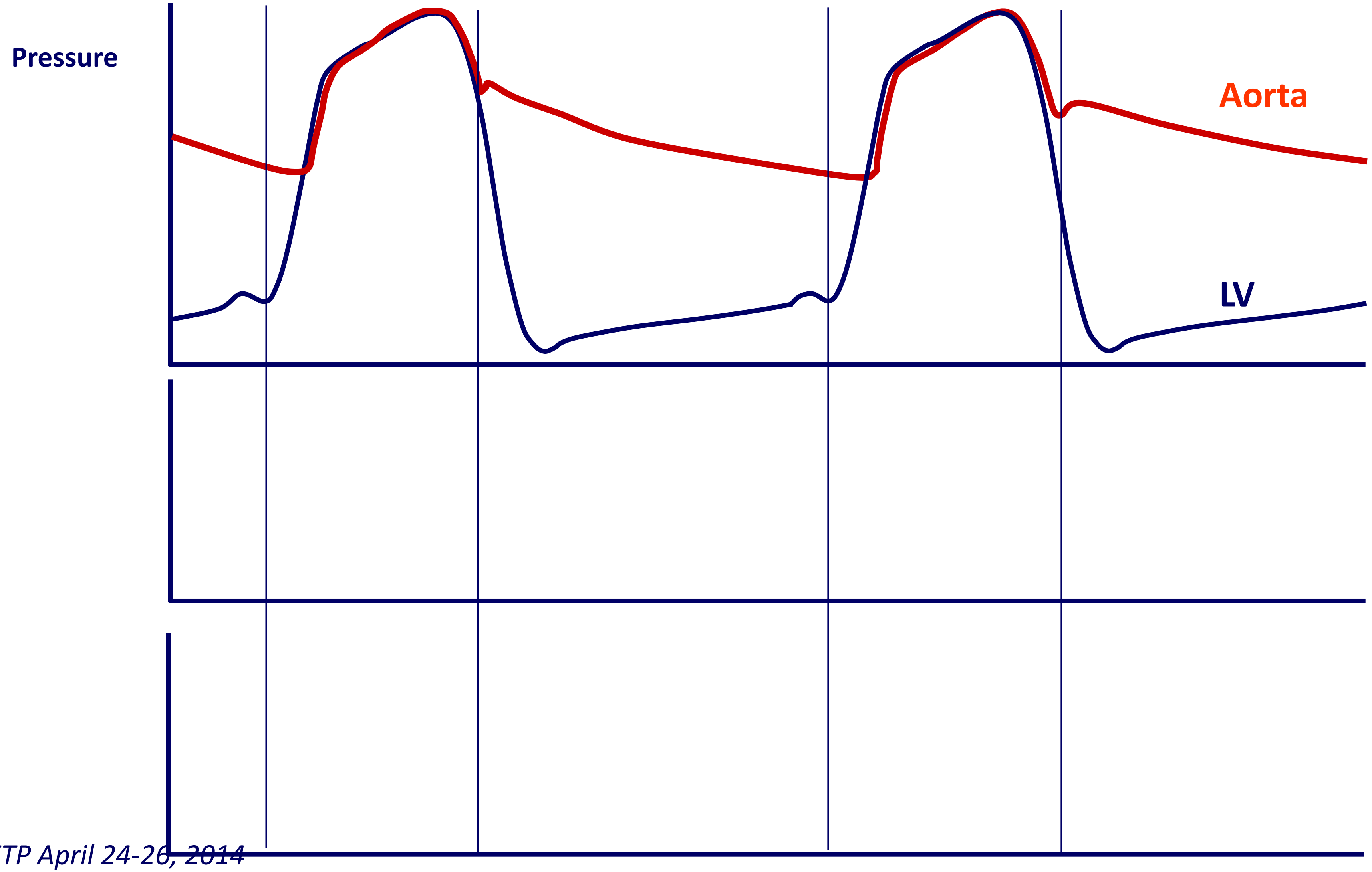
Extravascular Compressive Forces



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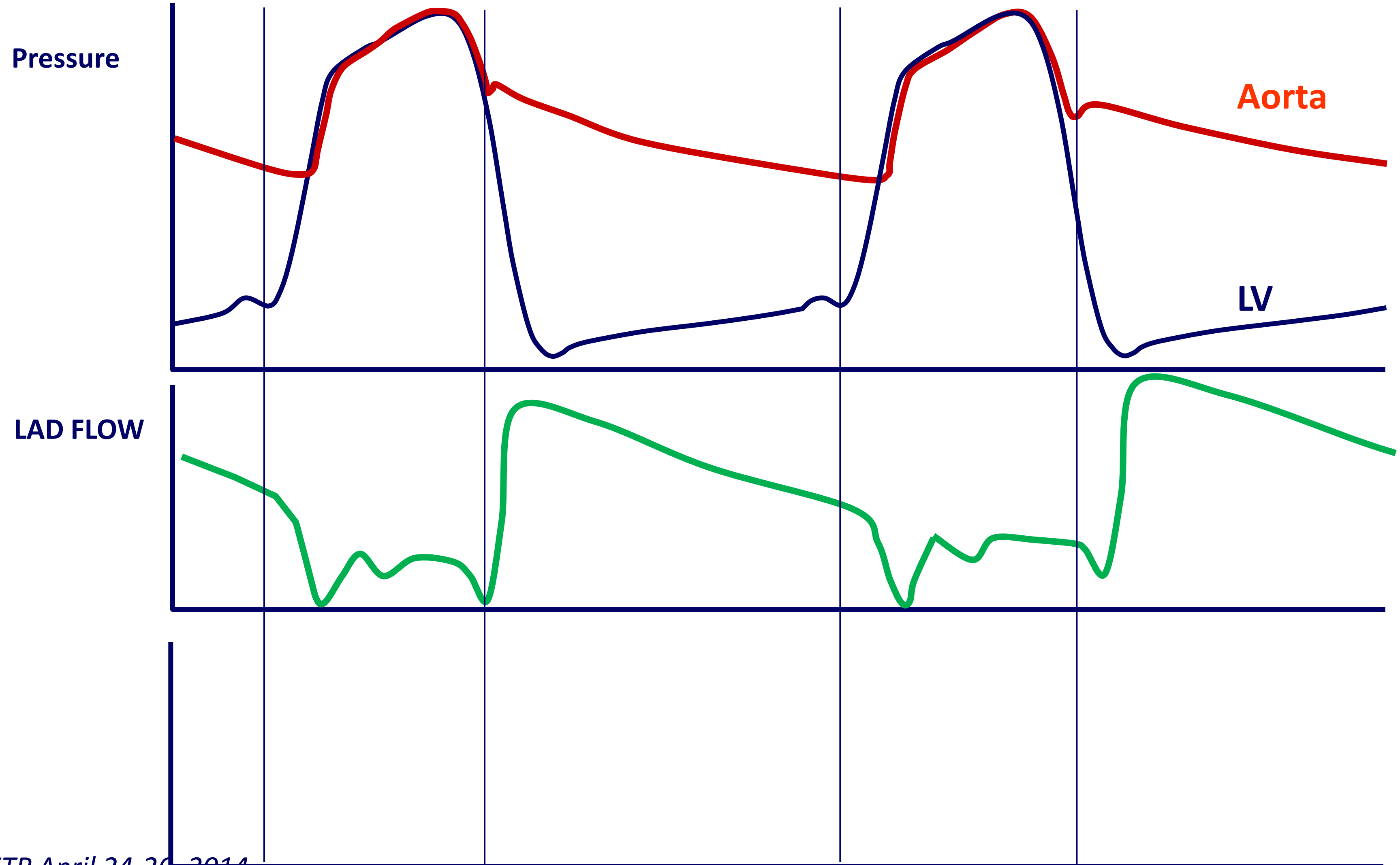

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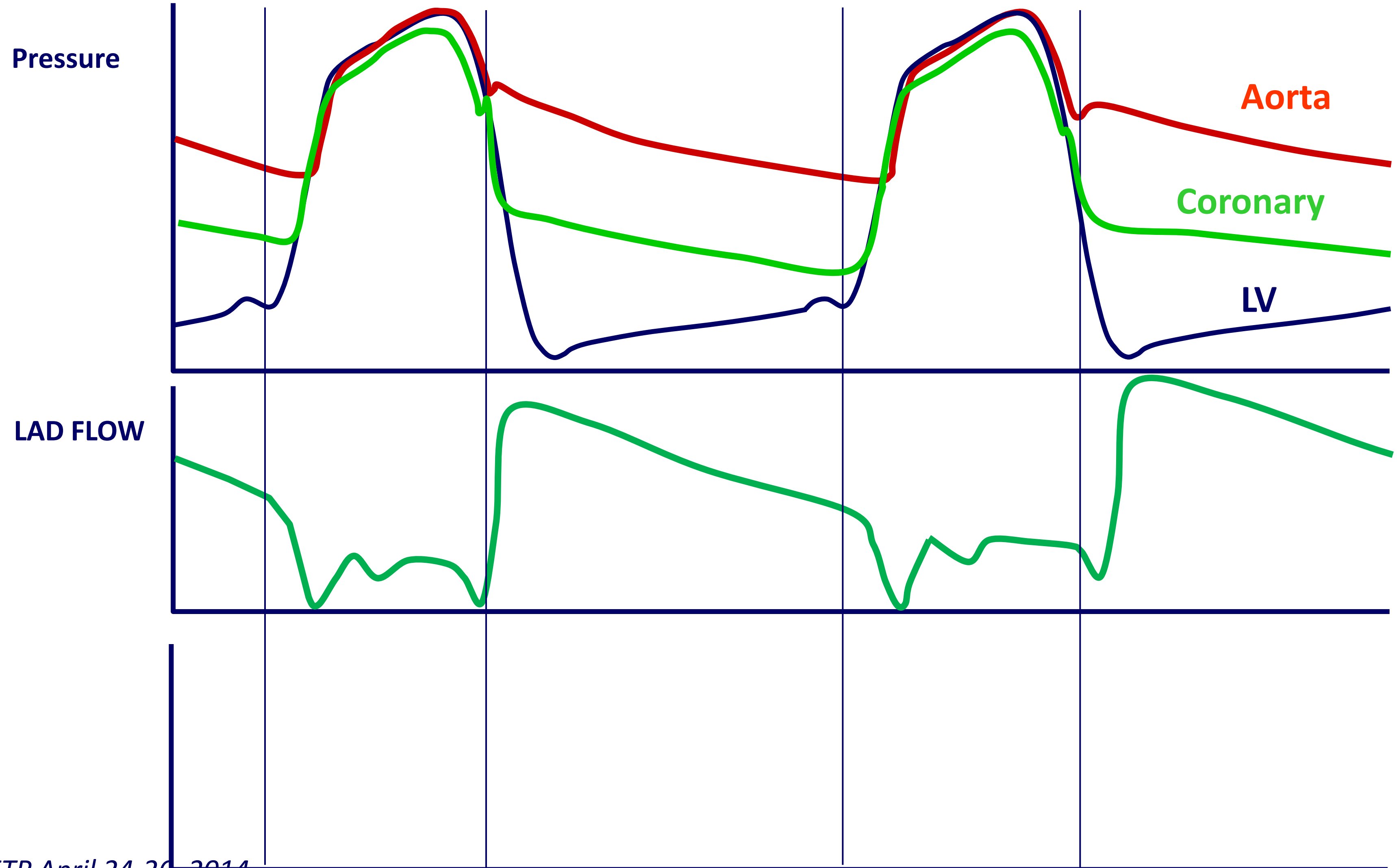

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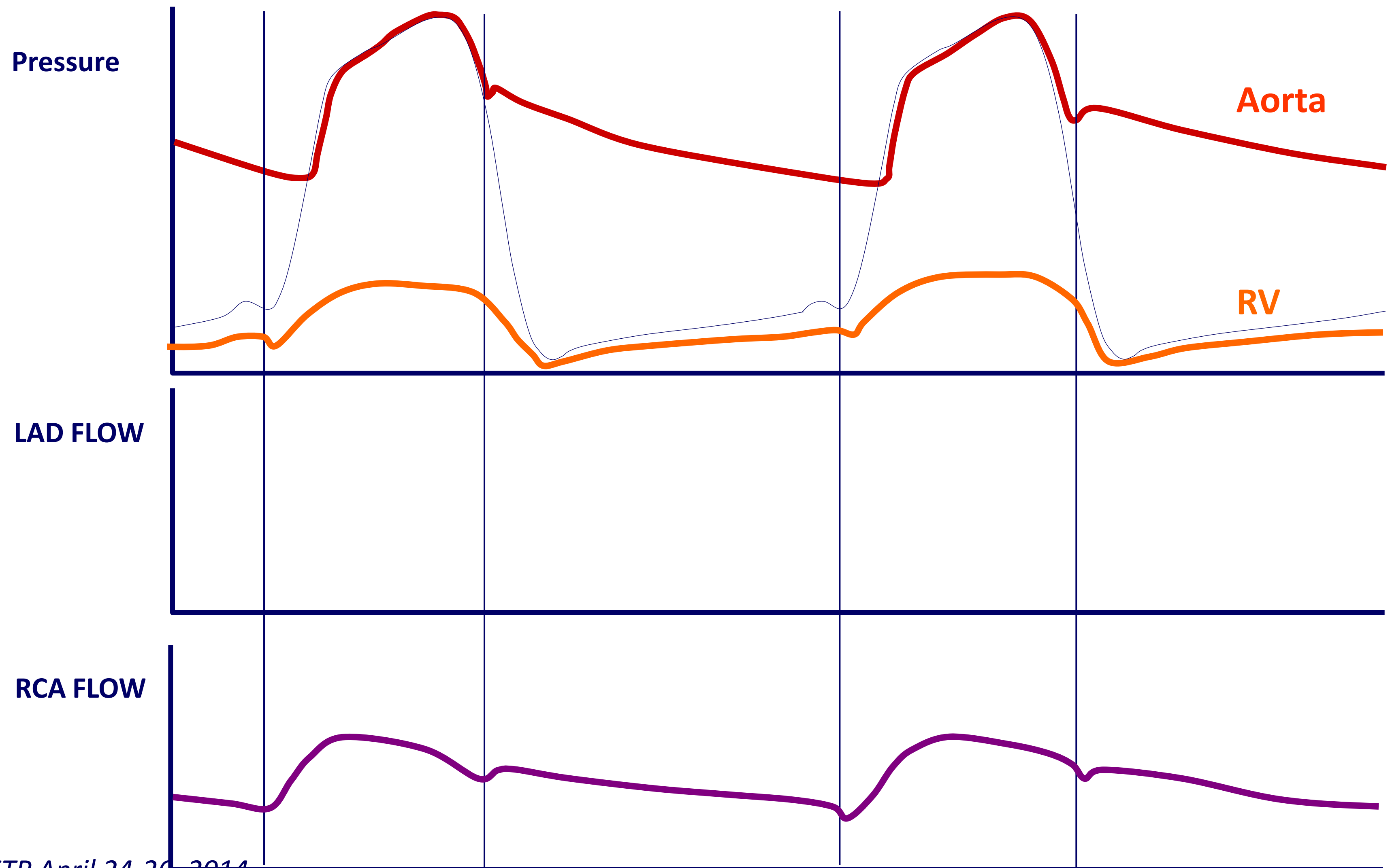

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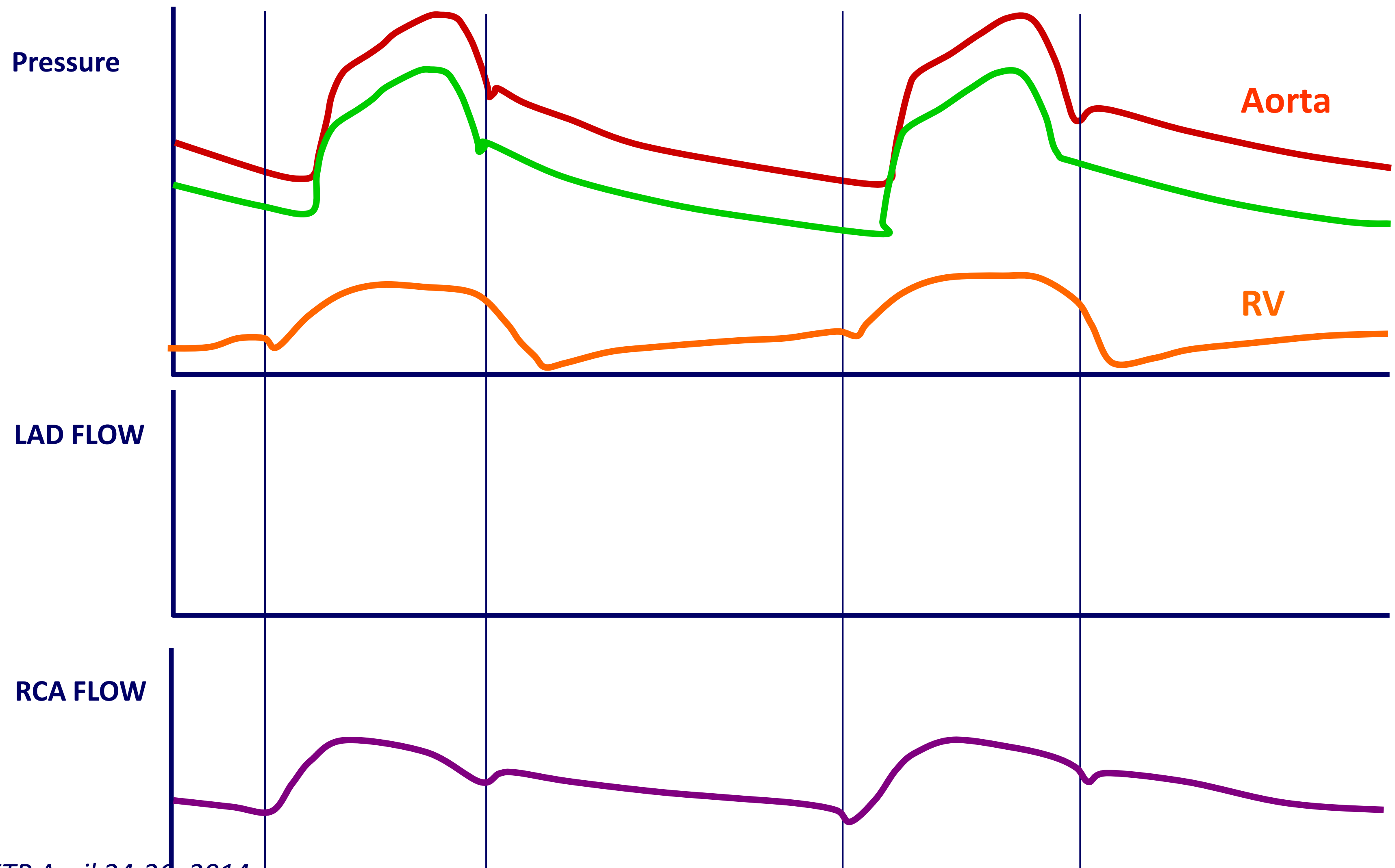

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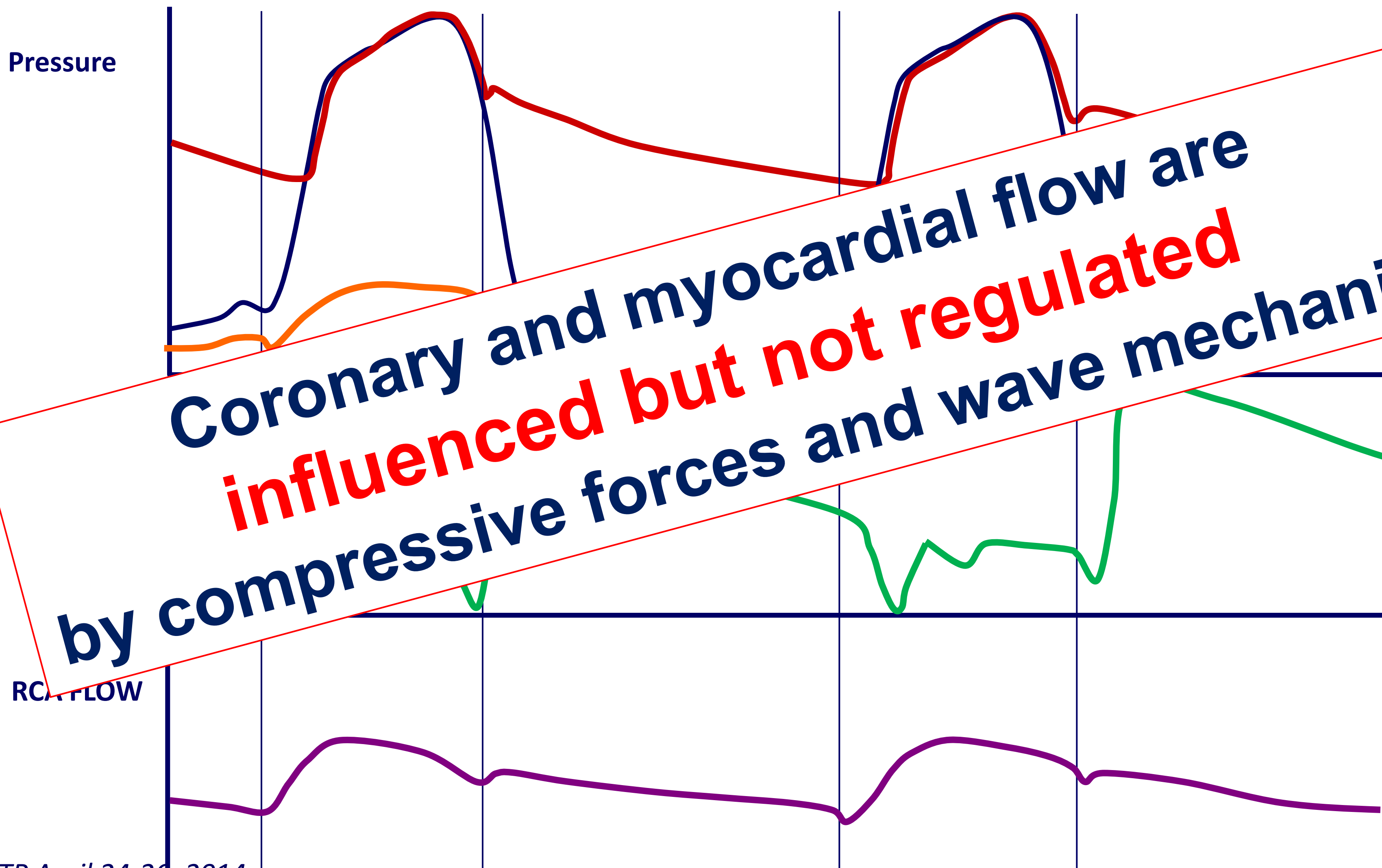
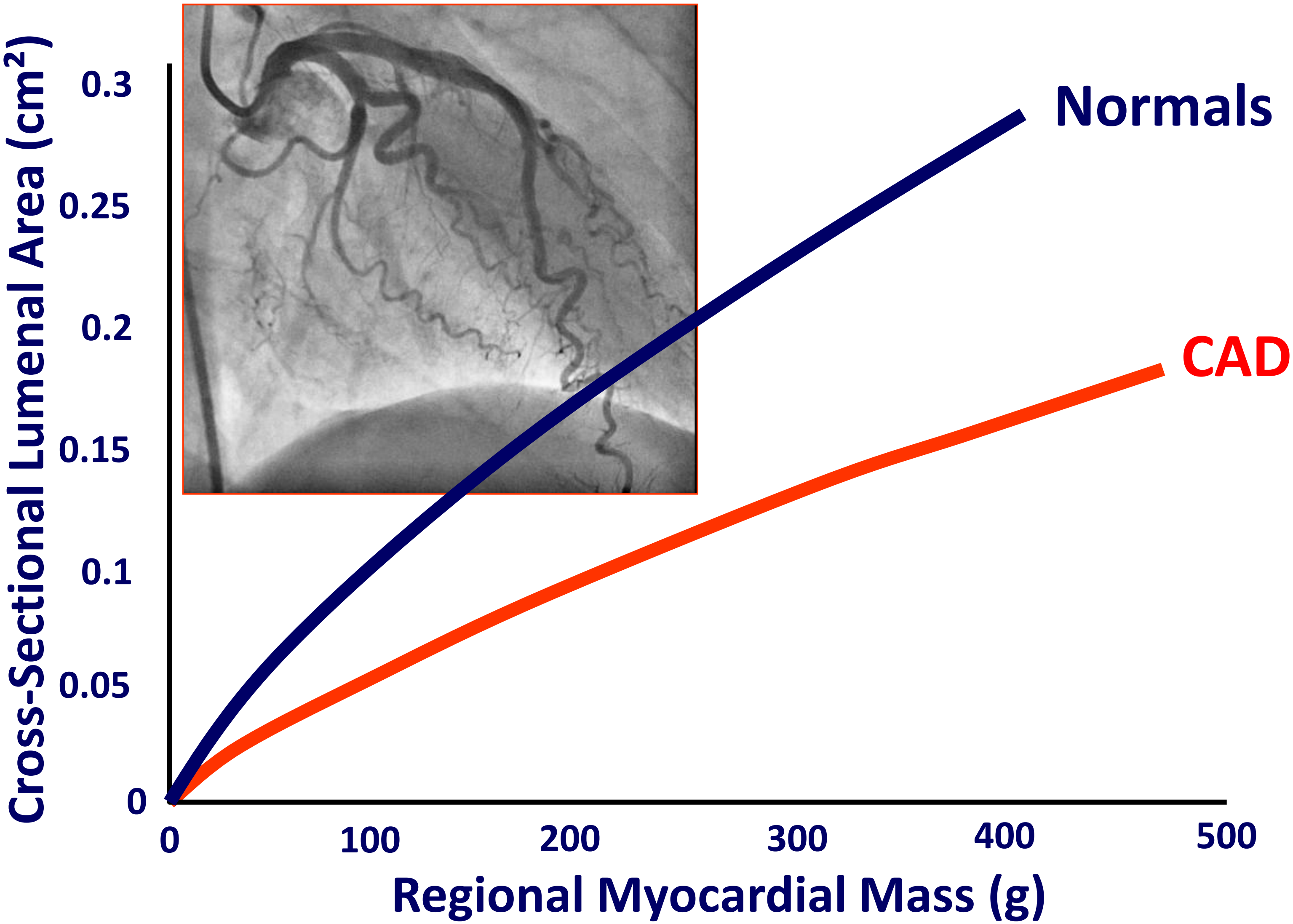
Extravascular Compressive Forces



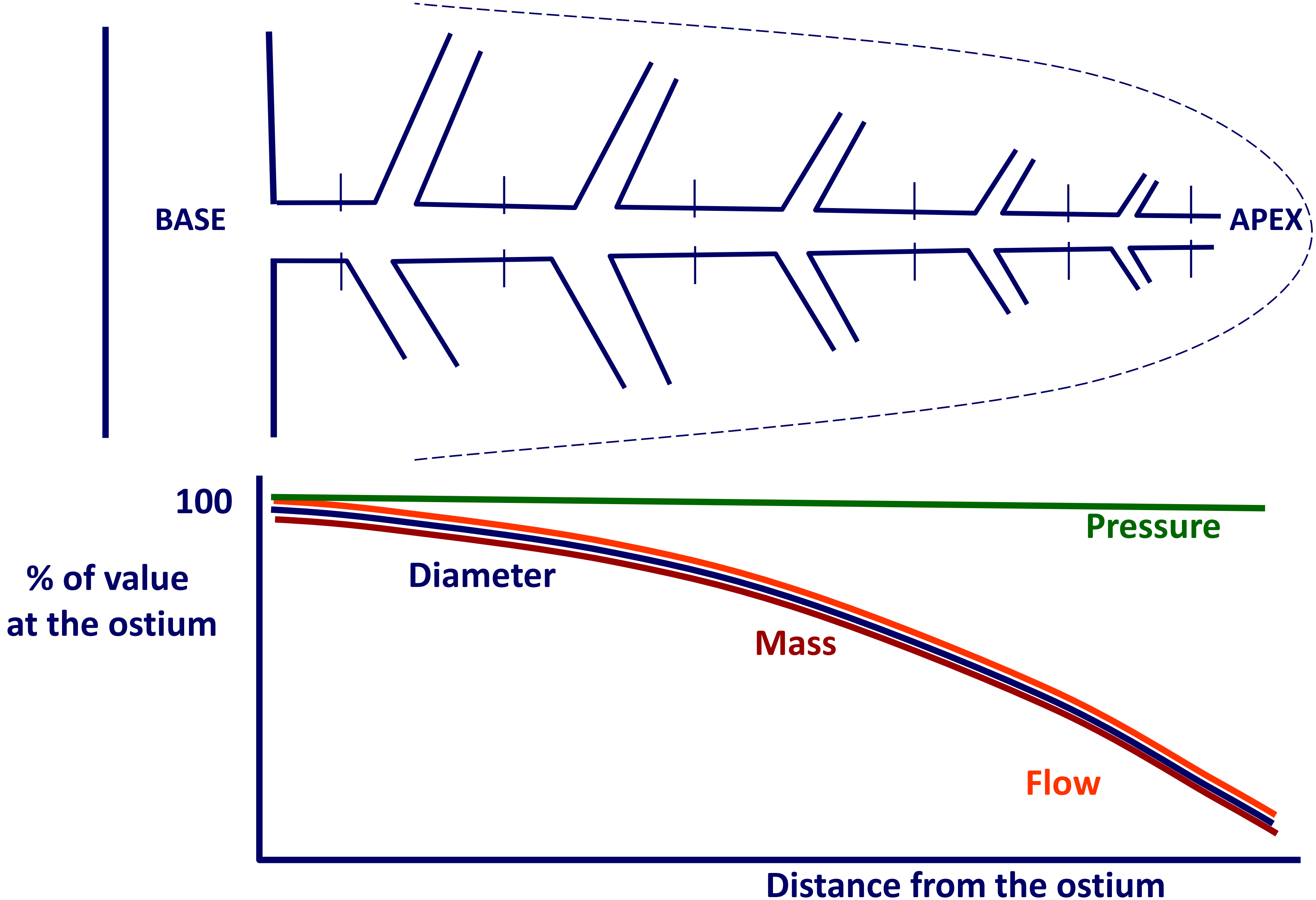
Coronary and myocardial flow are influenced but not regulated by compressive forces and wave mechanics

Relation between Vessel Size and Myocardial Mass



C. Seiler et al Circulation 1992

About Pressure, Flow, Resistance, and Vessel Size

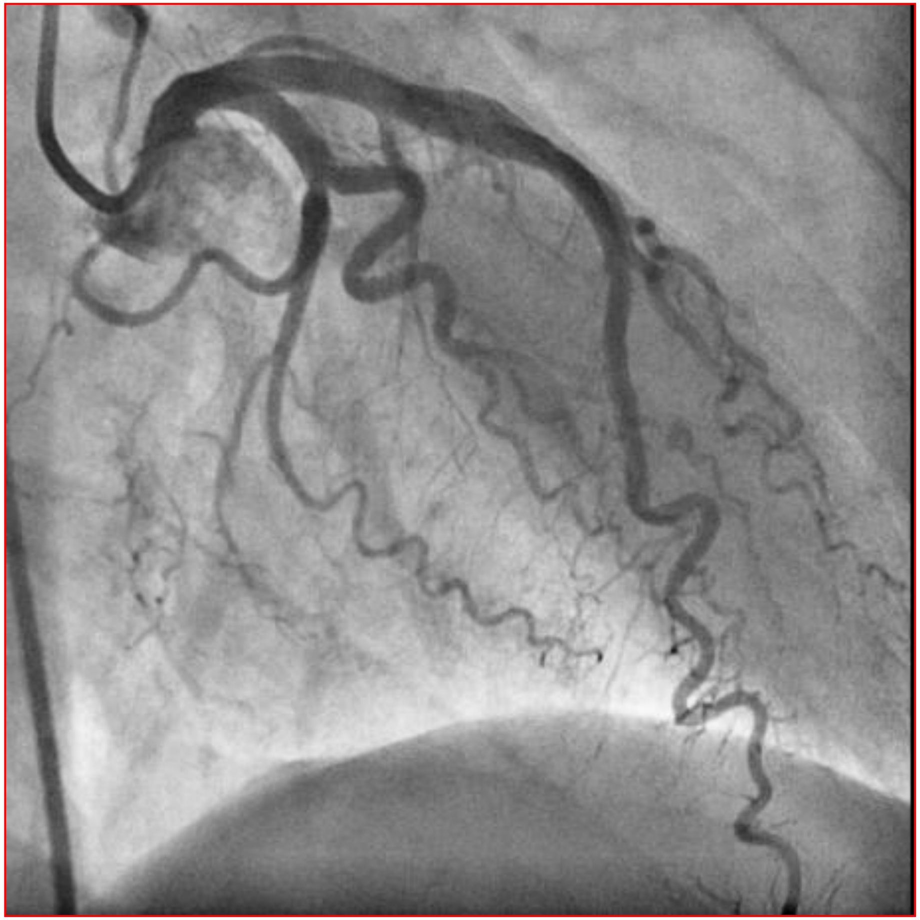


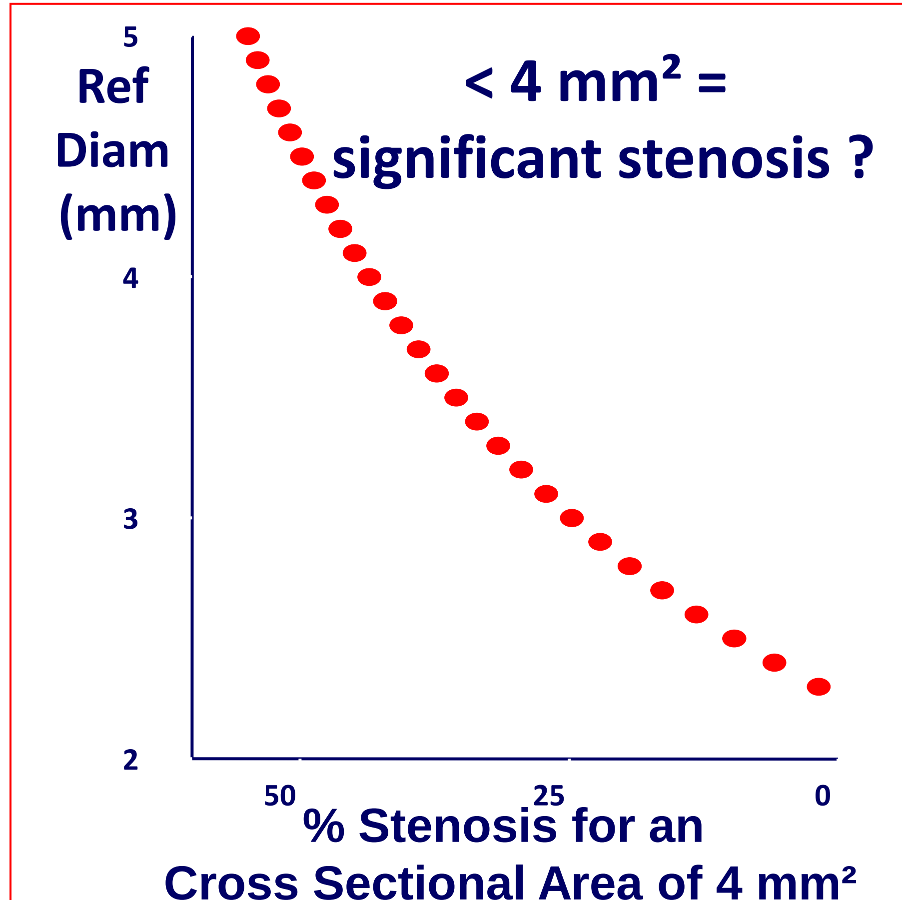
About Pressure, Flow, Resistance, and Vessel Size



	Tree Shrew	Human	Blue Whale
Body Mass [kg]	0.005	70	100,000
Heart Weight [kg] (~M^1)	$3.3x10^{-5}$	0.46	660
Stroke Volume [ml] (~M^1)	0.0033	46	66,000
Heart Rate[s^{-1}] (~$M^{-1/4}$)	11 (>600 bpm)	1	0.16 (<10 bpm)
Cardiac Output [L/min] (~$M^{3/4}$)	0.003	5	1000
Radius of Aorta [cm] (~$M^{3/8}$)	0.02	1	15
Mean Aortic Velocity [cm/sec] (~M^0)	10	10	10
Mean Aortic Pressure [mmHg] (~M^0)	100	100	100
Mean Aortic Reynold's No. (~$M^{3/8}$)	15	530	8080 (turbulent!)
Mean Aortic Shear Stress [dynes/cm^2] (~$M^{-3/8}$)	180	5	0.3

About Pressure, Flow, Resistance, and Vessel Size





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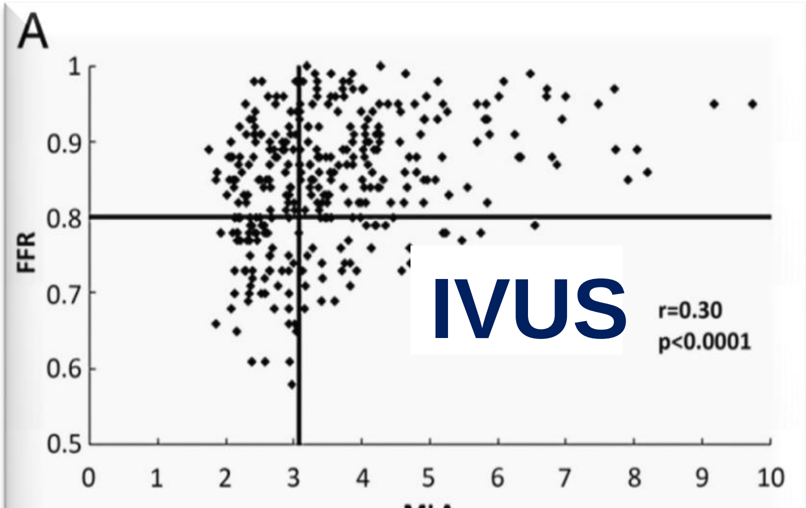
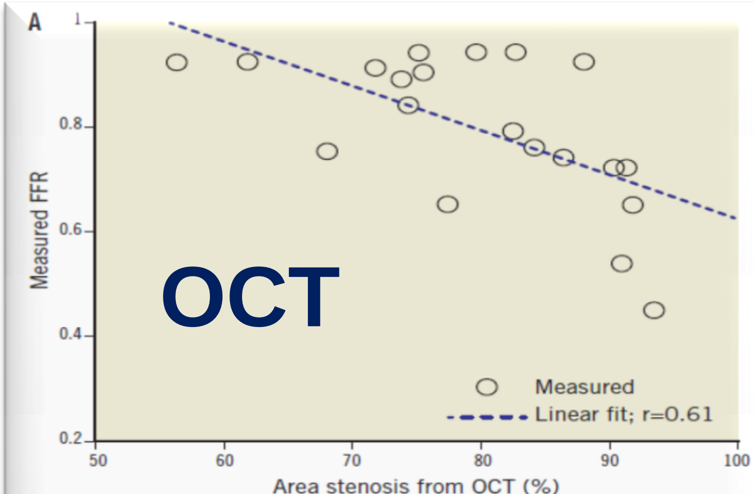
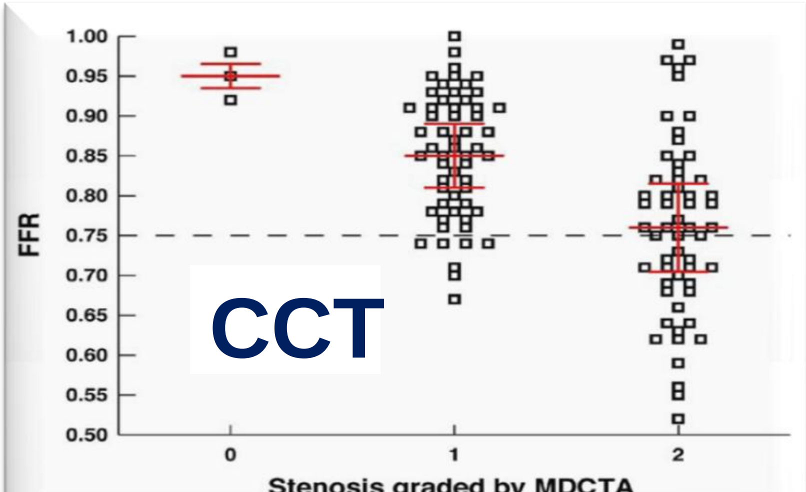
Anatomy vs Physiology: the Chimeric Link



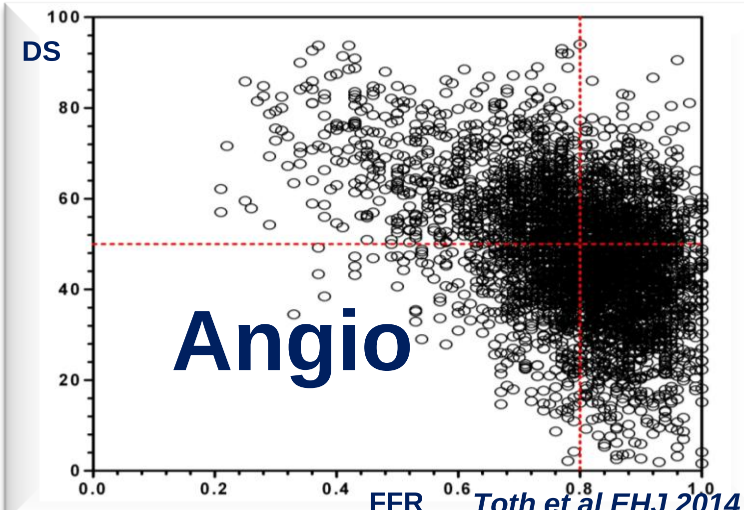
Waksman et al. JACC 2013



Guagliumi et al EuroInterv 2013



Sarno et al JACC 2009



Toth et al EHJ 2014

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Statistical (mechanistic) relation but little clinical relation

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ABC of Coronary Physiology For the Interventionalist

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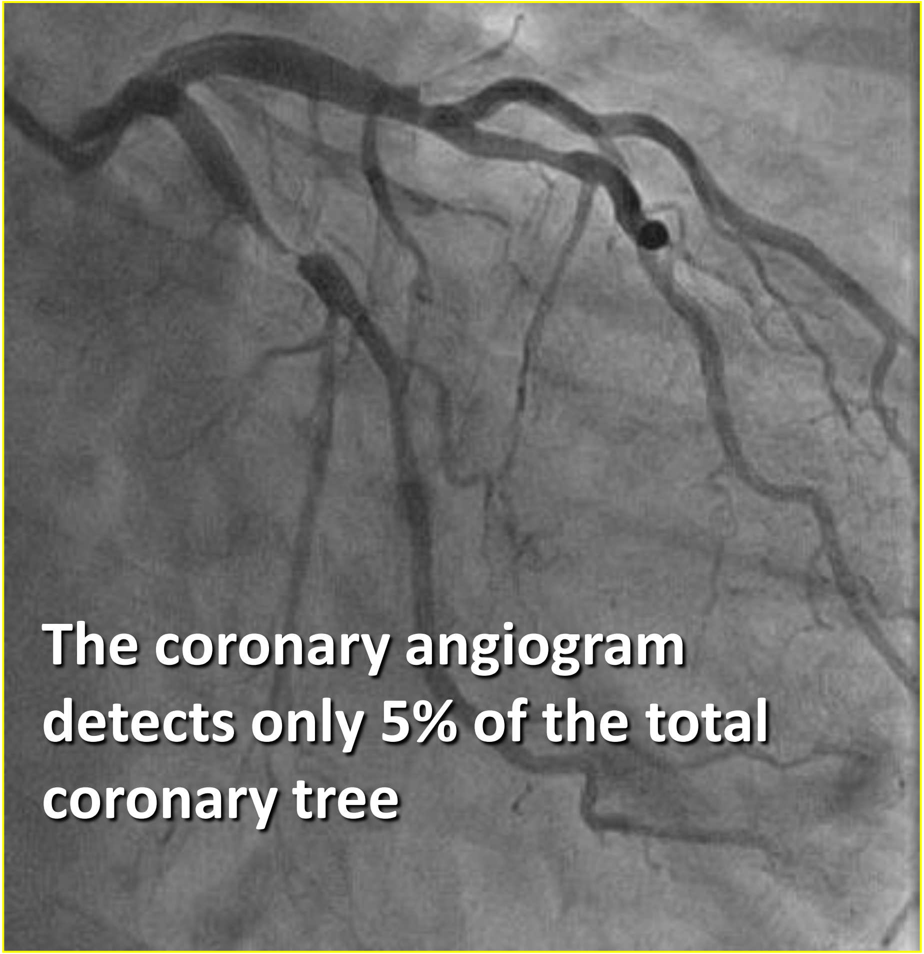
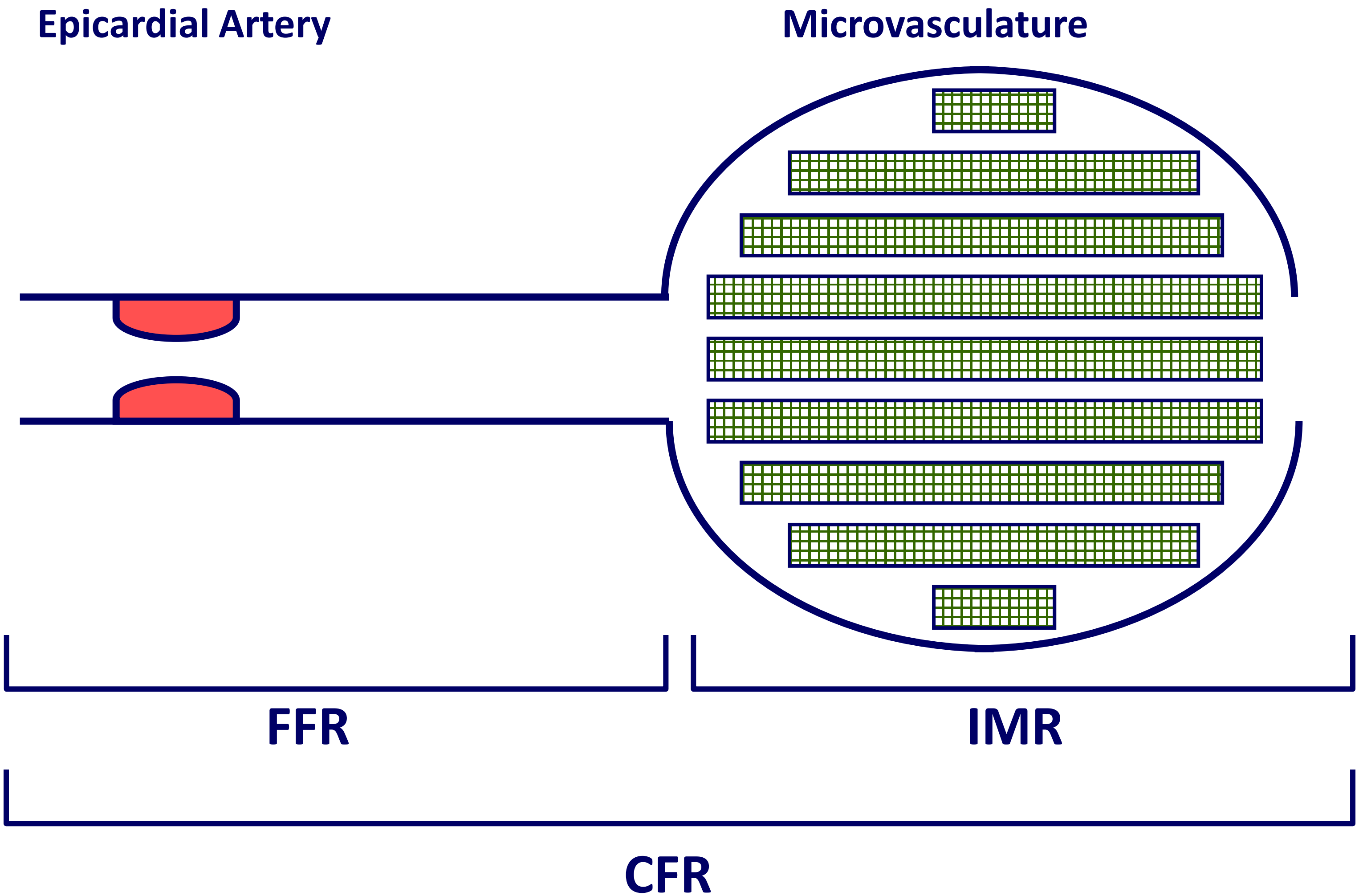
Two-Compartment Model of the Coronary Circulation



Two-Compartment Model of the Coronary Circulation



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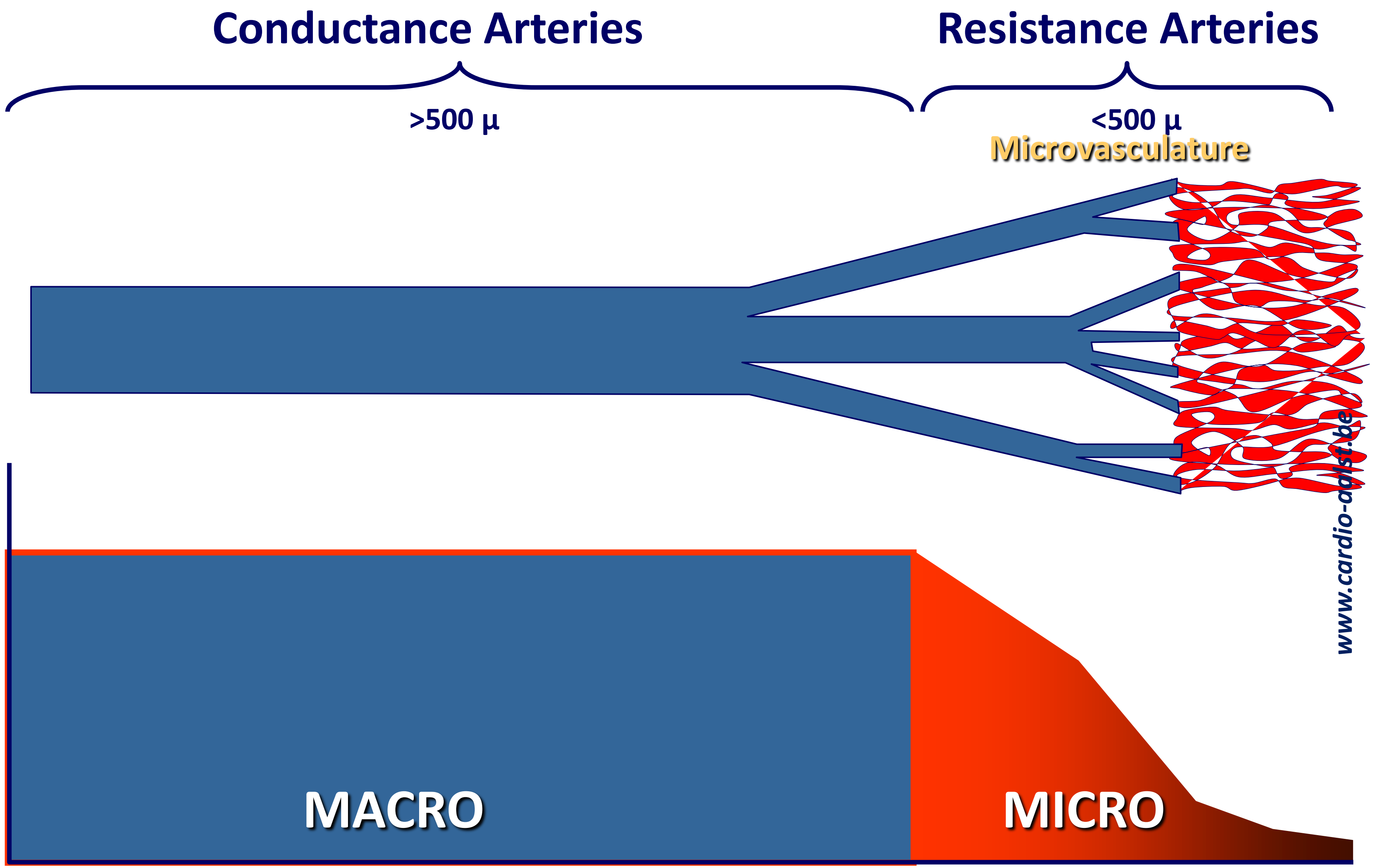
Two-Compartment Model of the Coronary Circulation



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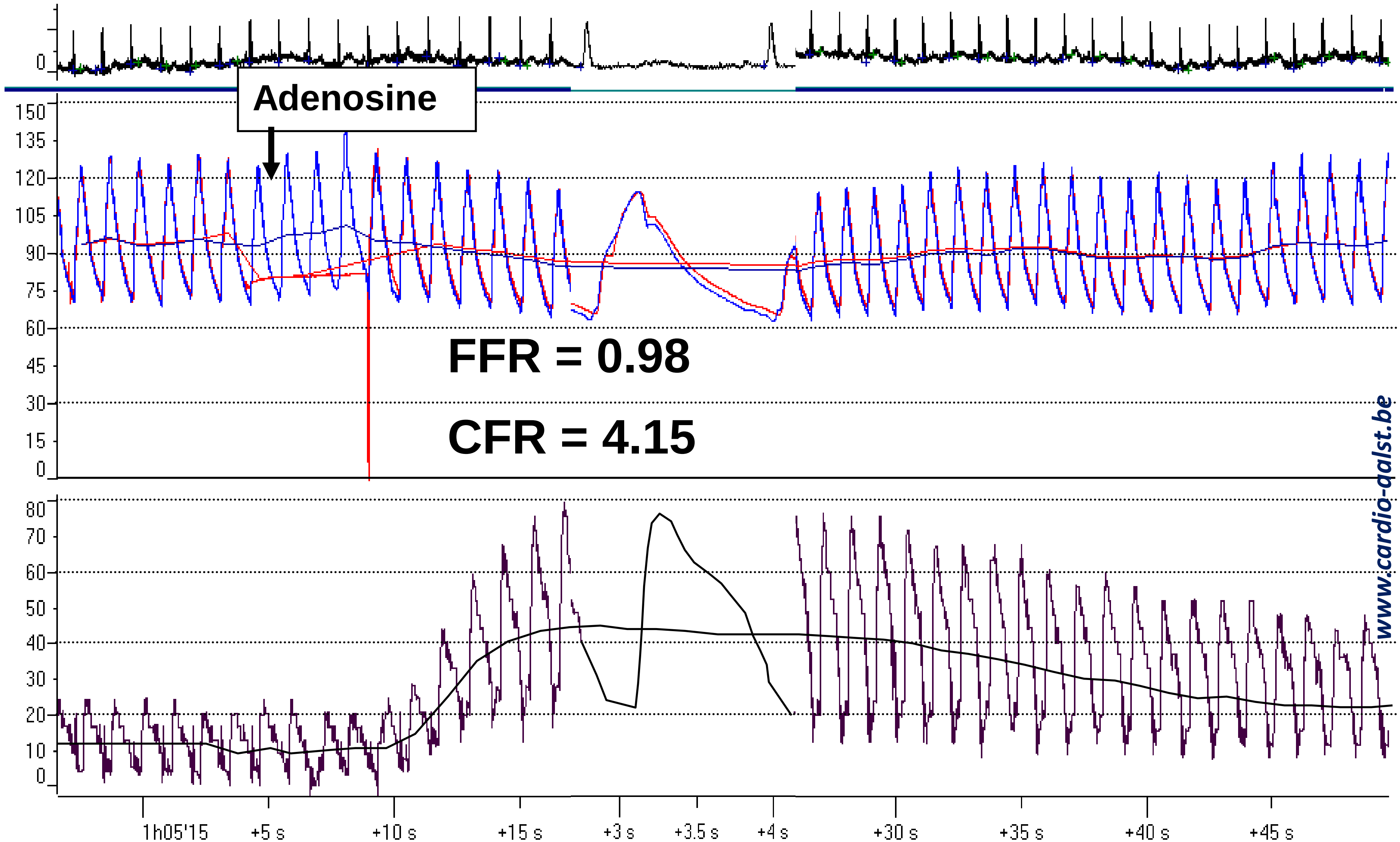
Pressure and Flow Velocity in Normal Coronary Arteries



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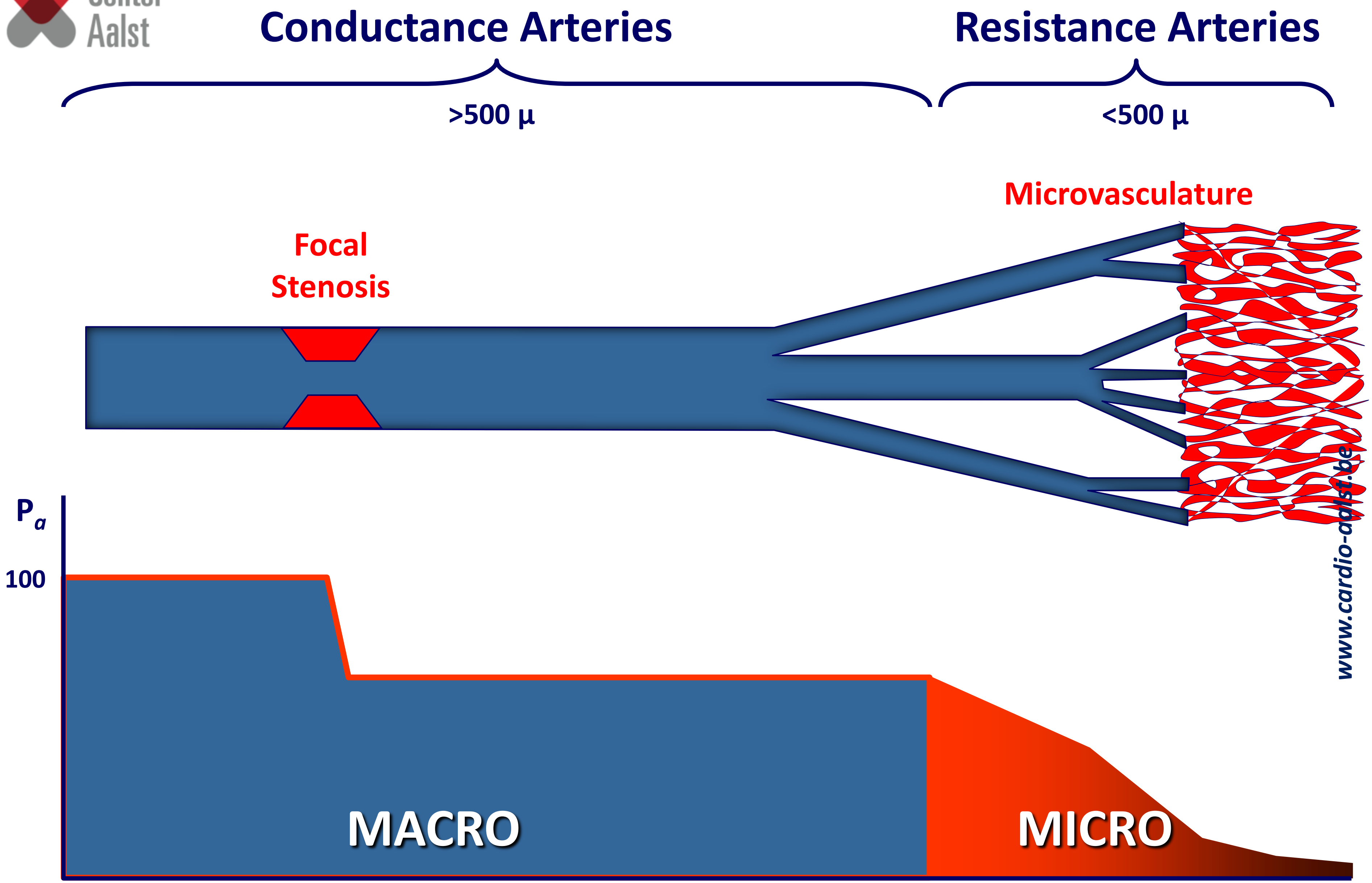
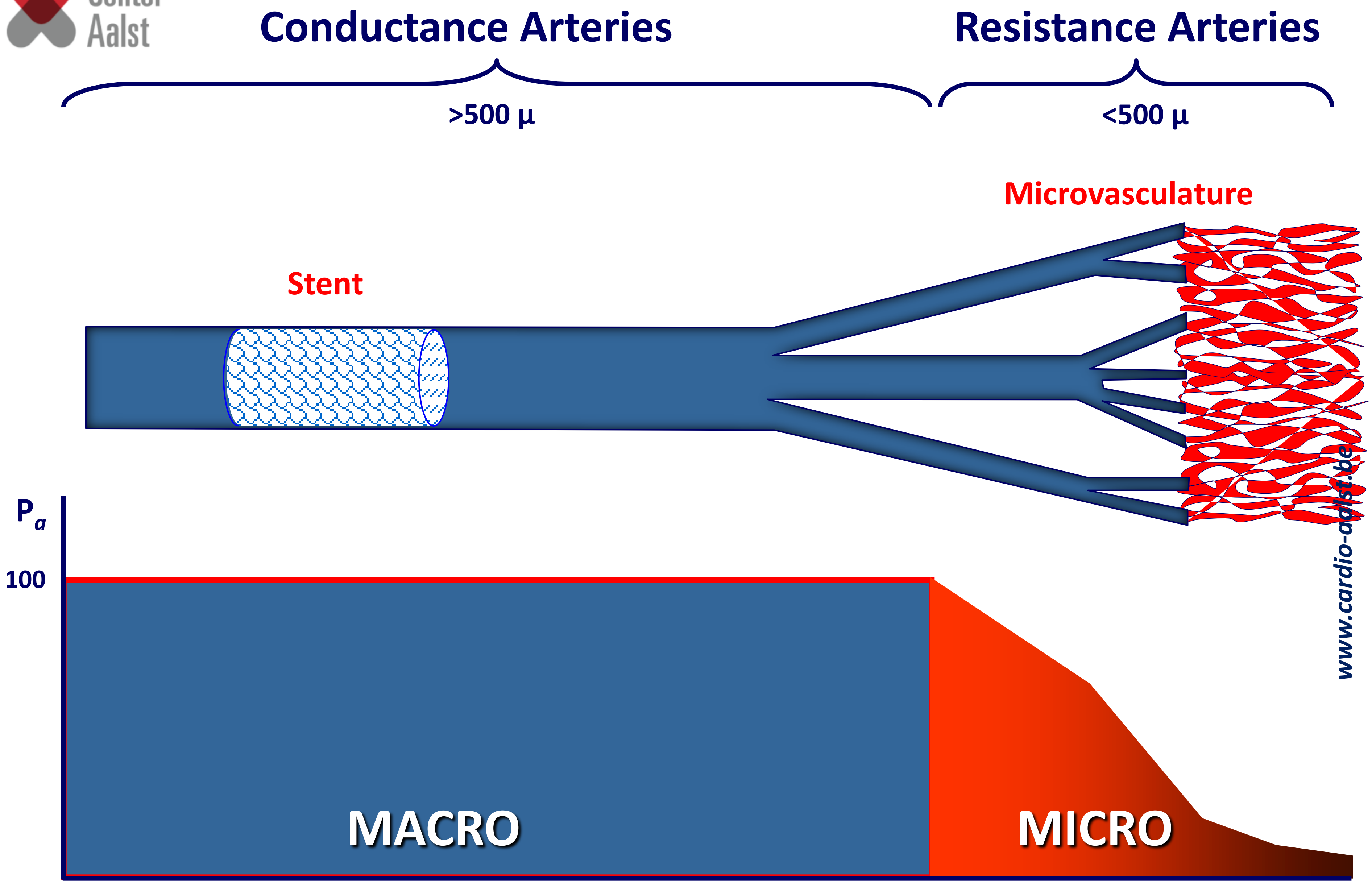
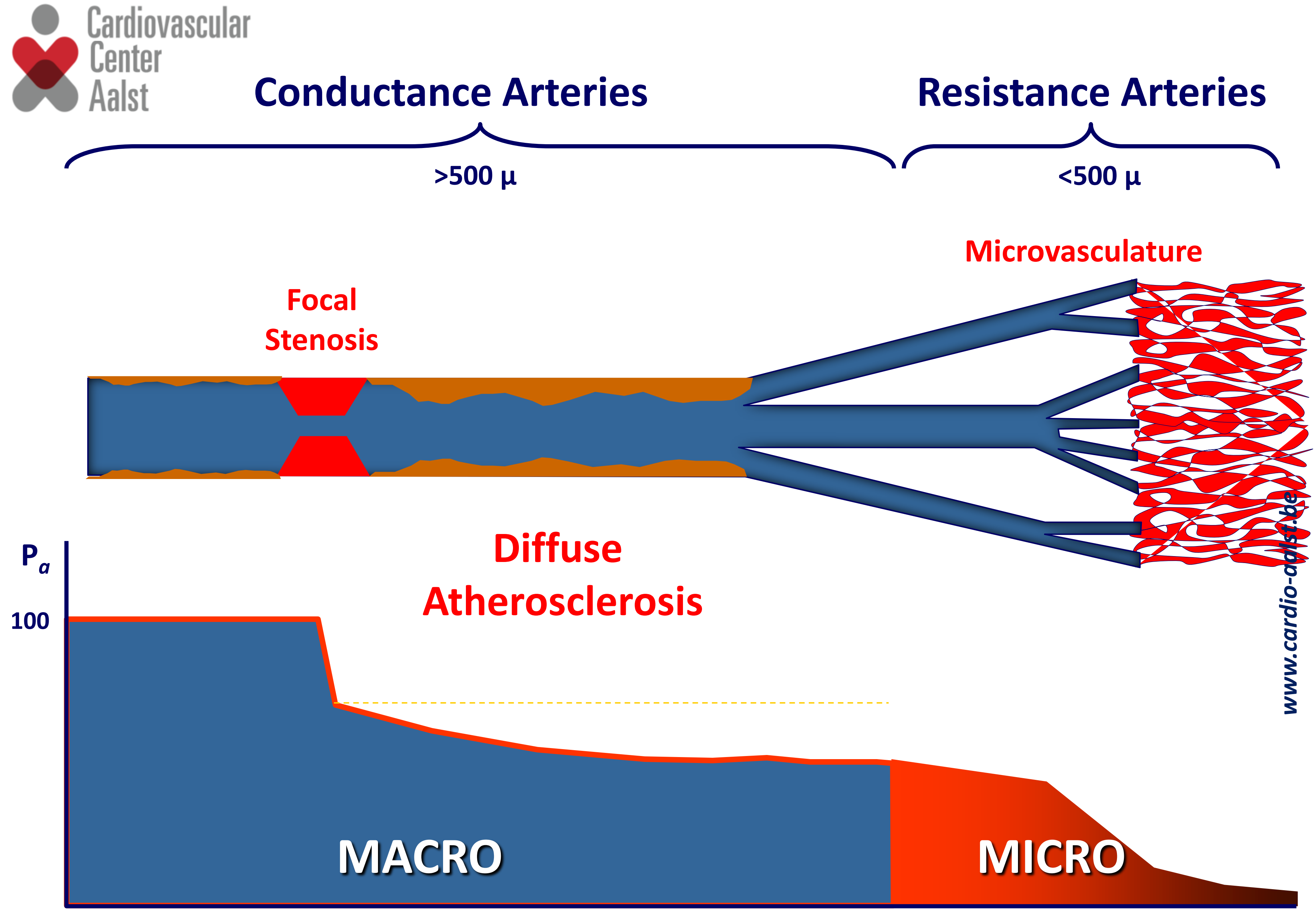



Conductance Arteries
Resistance Arteries
>500 µ
<500 µ
Microvasculature
Stent
P_a
100
MACRO
MICRO
www.cardio-aalst.be


Cardiovascular Center Aalst
Conductance Arteries
Resistance Arteries
>500 µ
<500 µ
Microvasculature
Focal Stenosis
Diffuse Atherosclerosis
P_a
100
MACRO
MICRO
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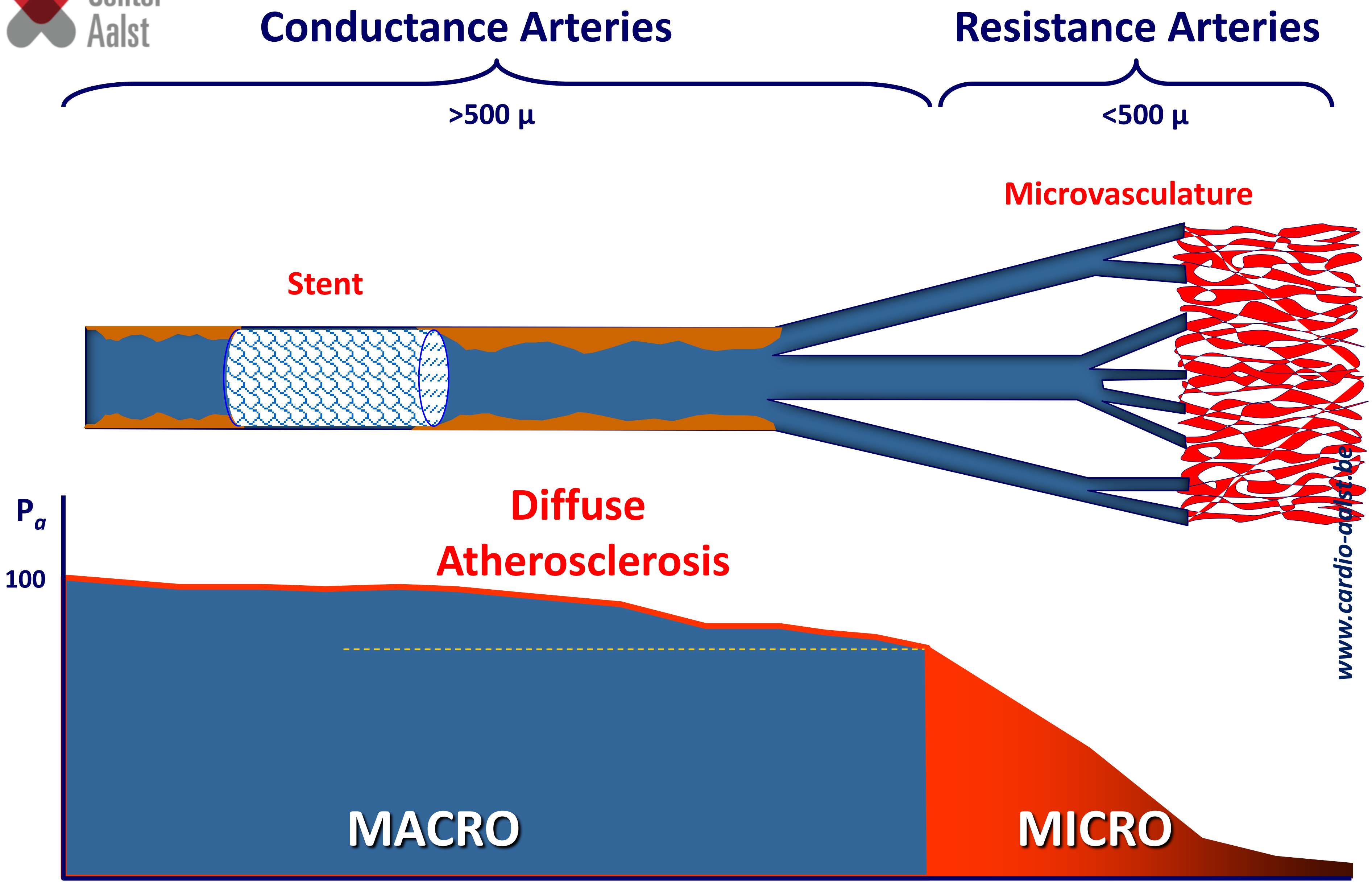

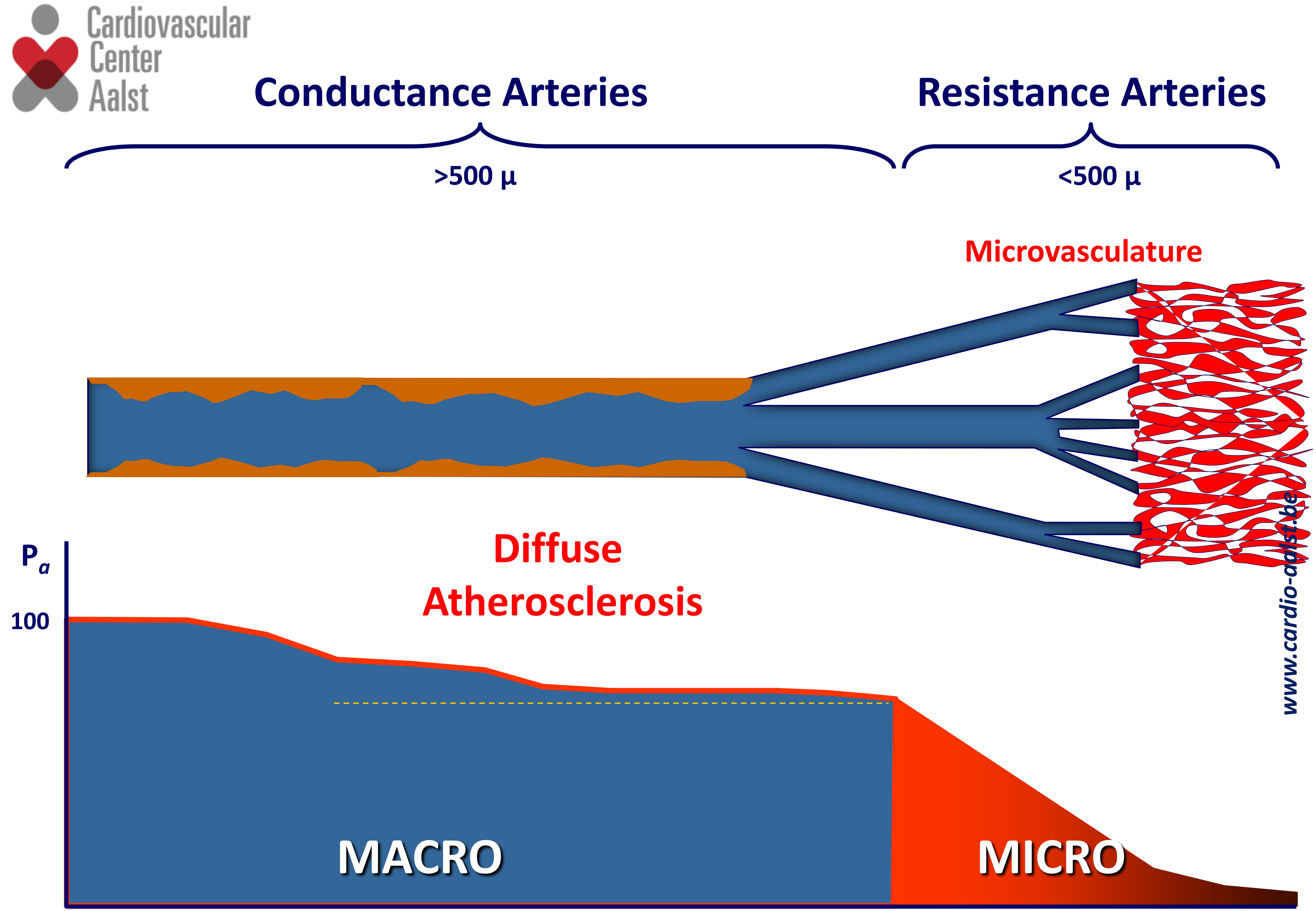

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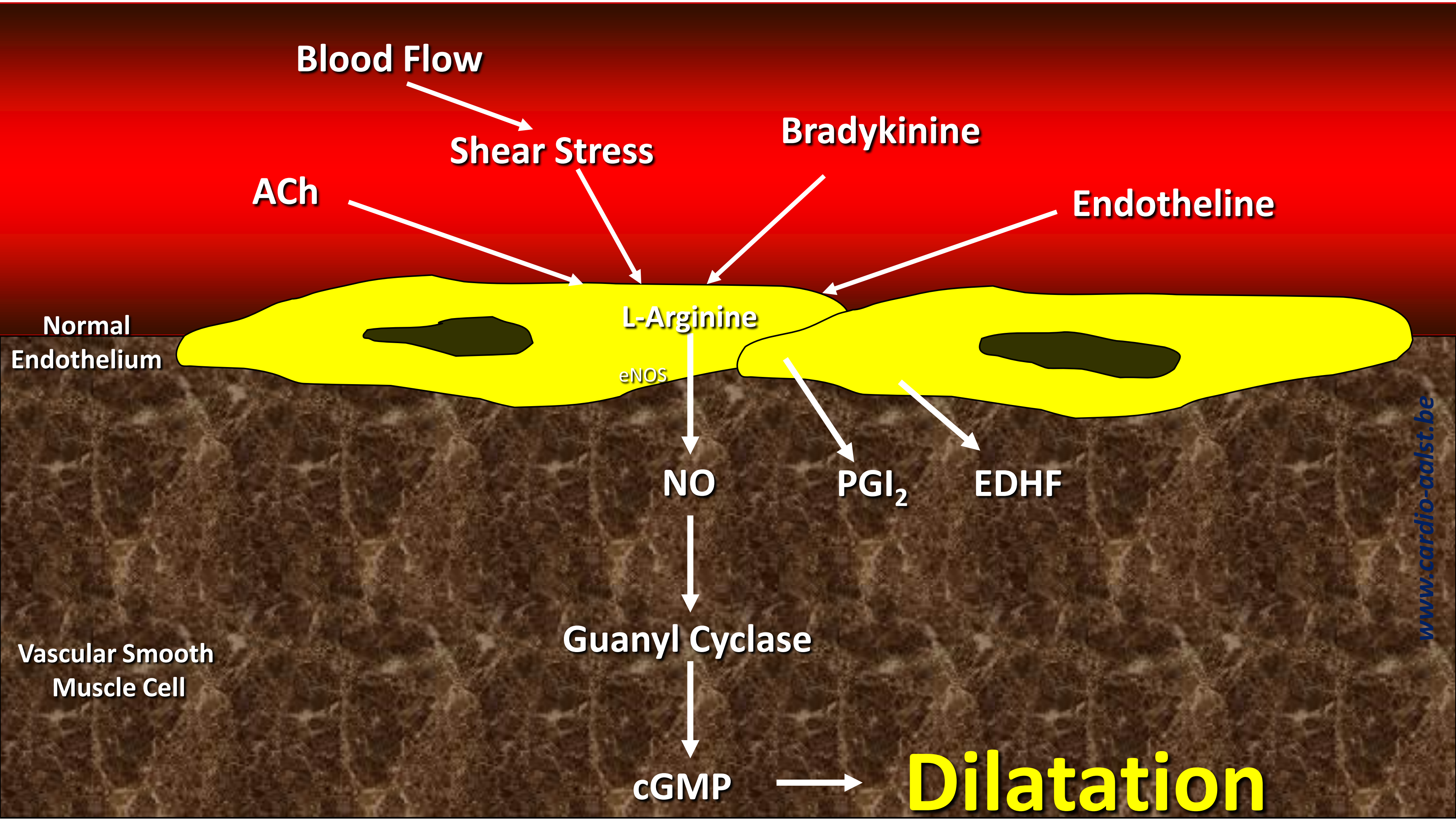
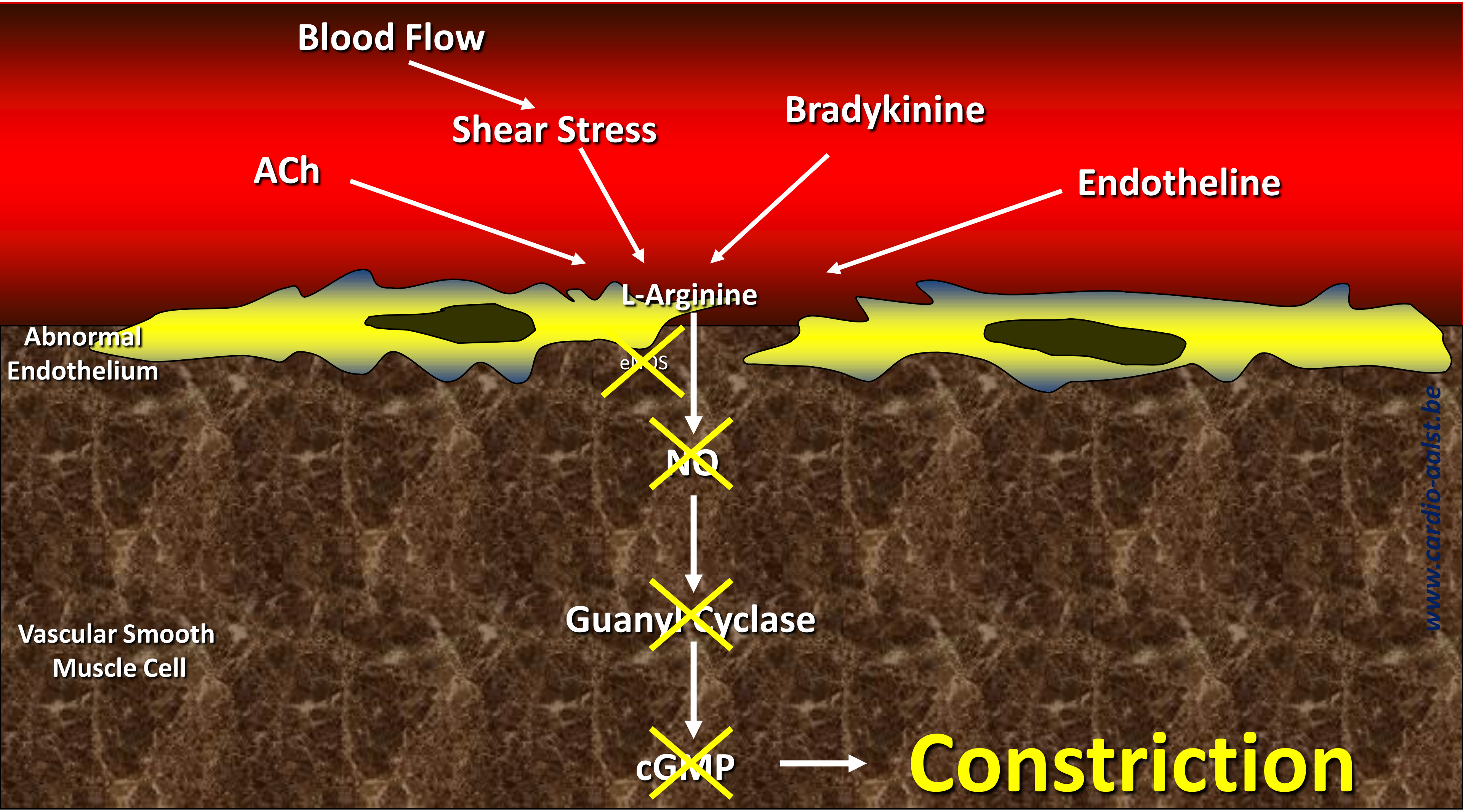
Endothelial Control of Coronary Blood Flow



Endothelial Control of Coronary Blood Flow



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Importance of Maximal Vasodilation

Epicardial

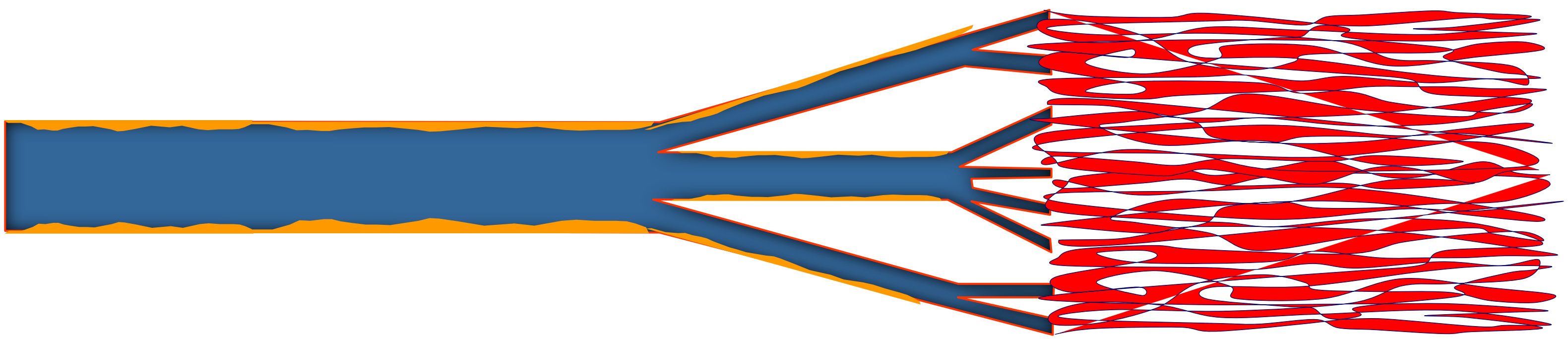
= Conductance

Arteries > 550 µ

Microvasculature

= Resistance

Arteries < 550 µ



Nitrates

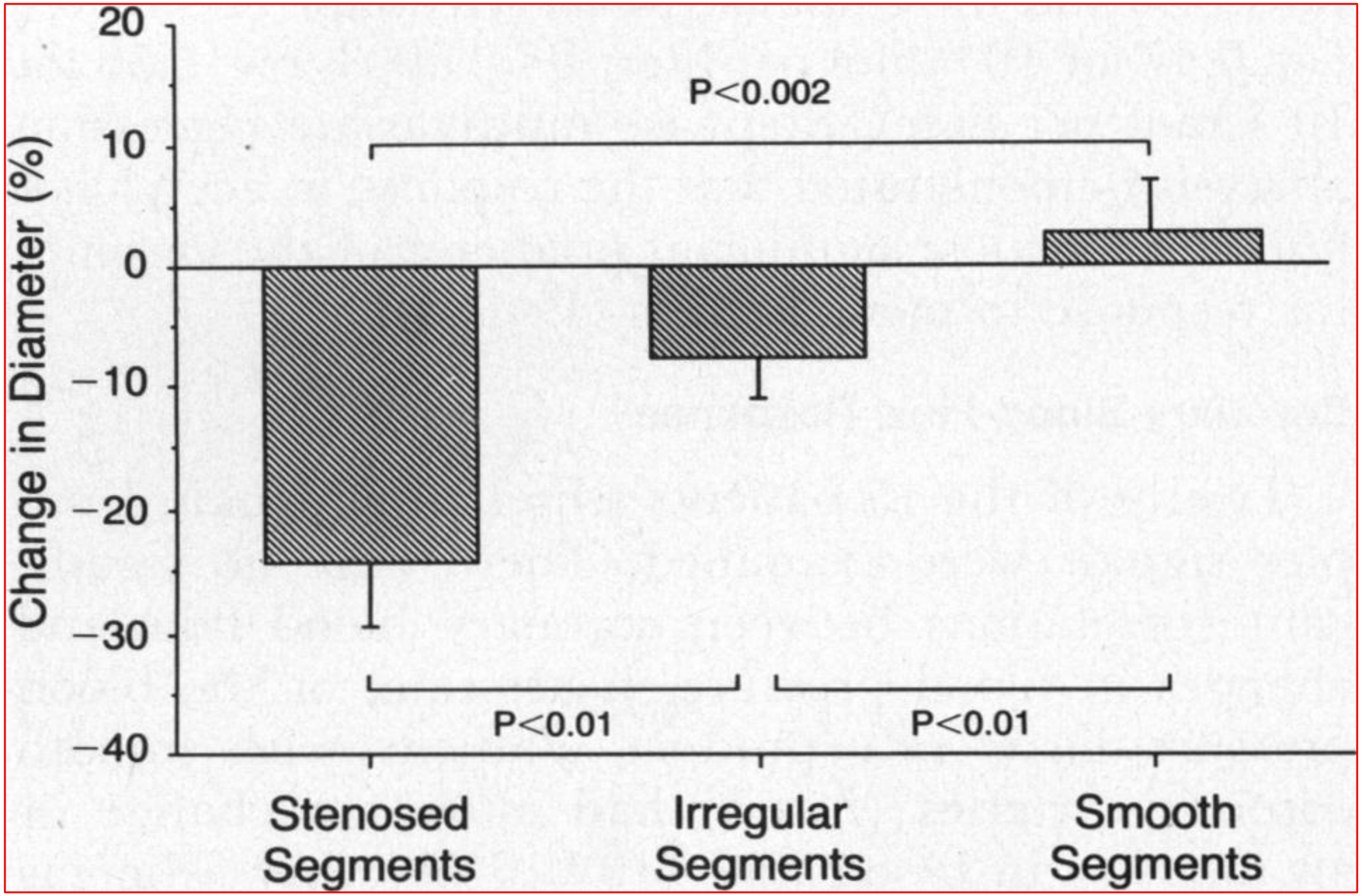
~~Vasospasm~~

Adenosine

~~Autoregulation~~

Endothelial Control of Coronary Blood Flow

Effect of Mental Stress on the Diameter of Coronary Arteries



Yeung AC et al. N Engl J Med 1991;325:1551-1556.

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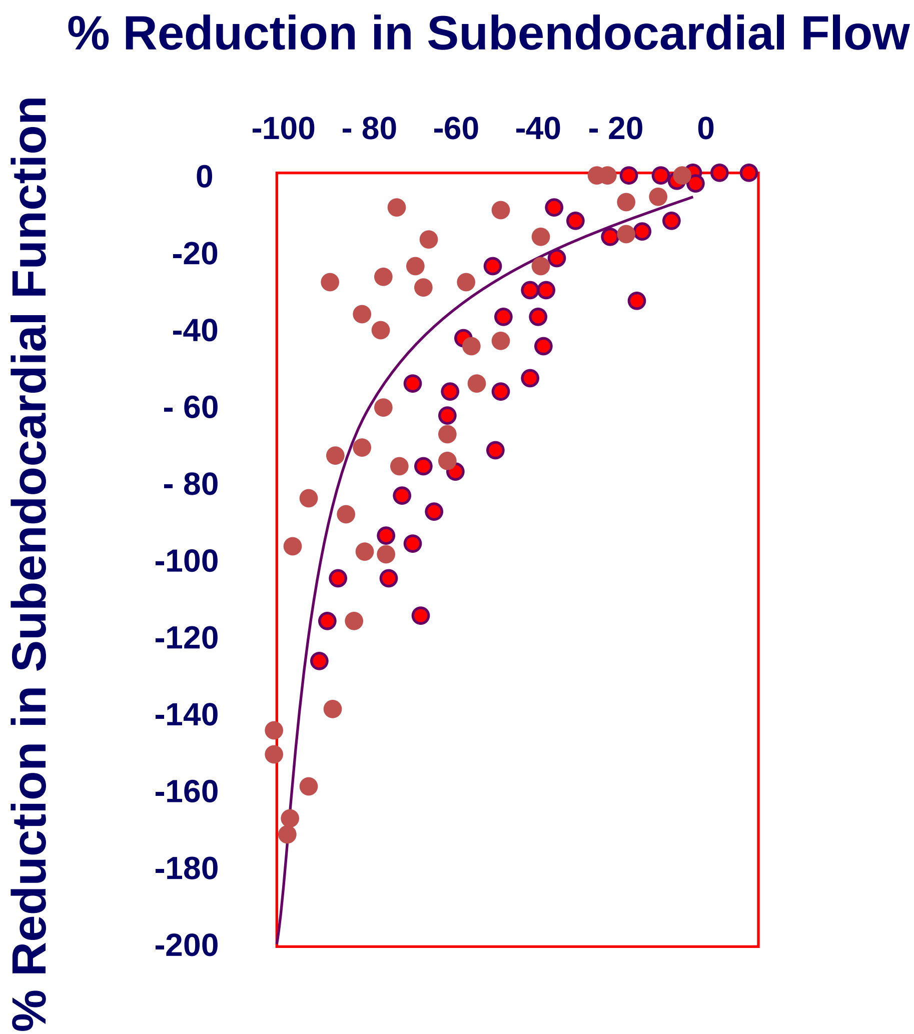
Flow-Function Relationship



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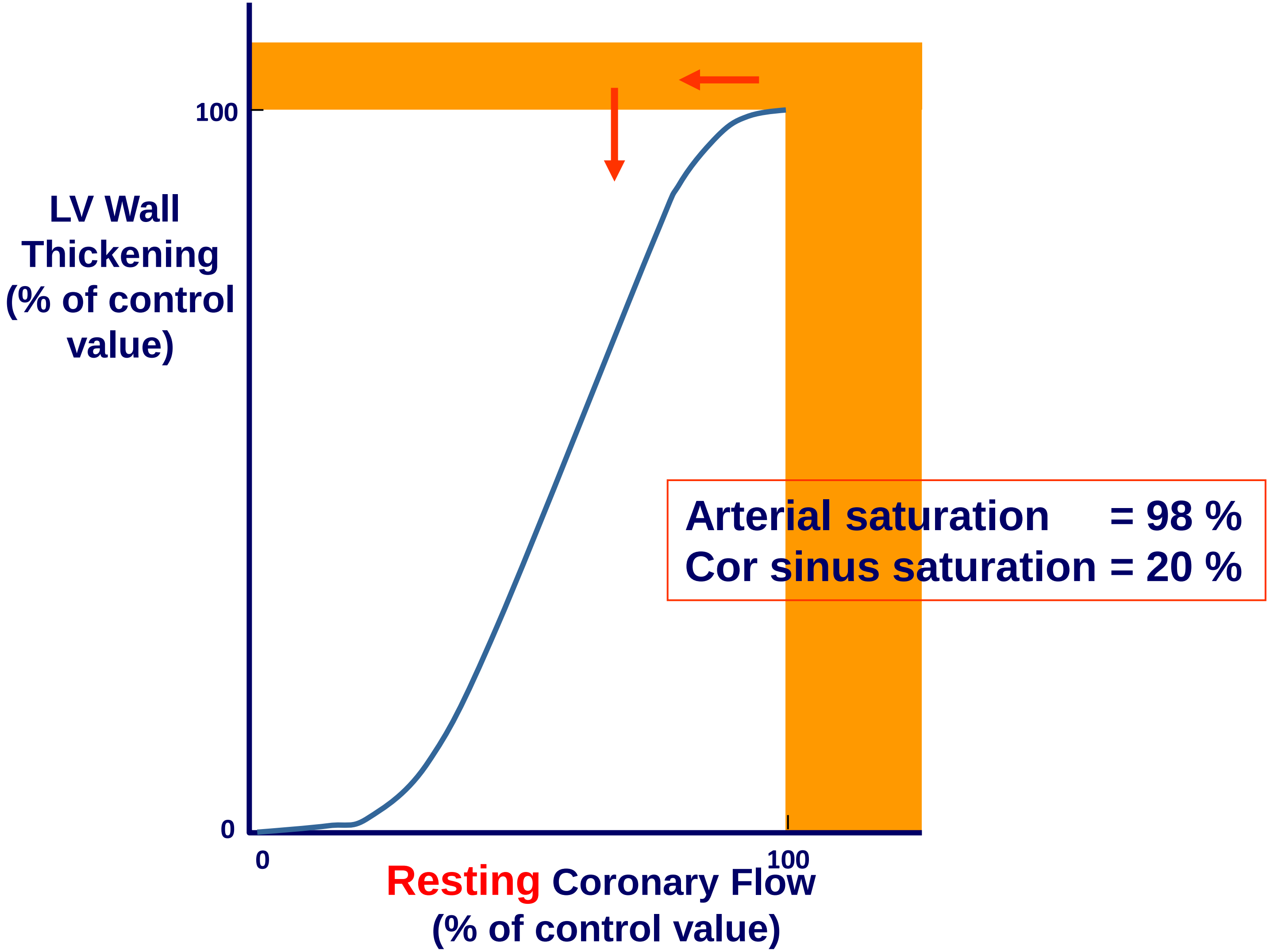
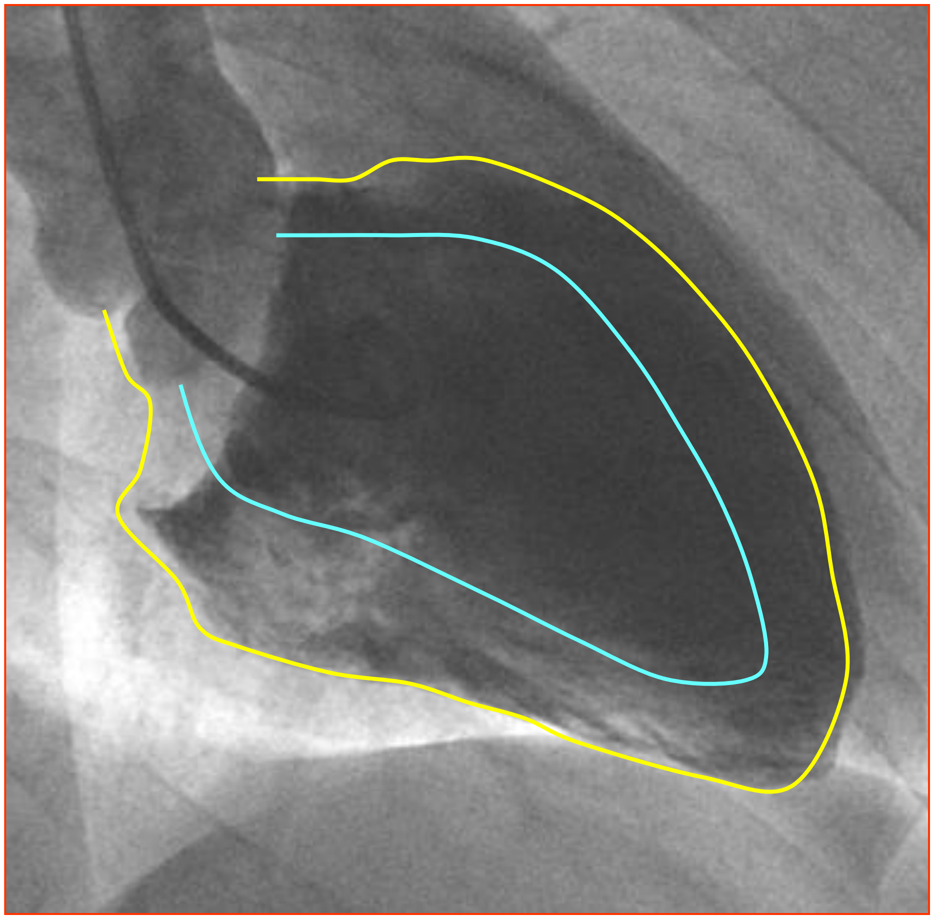
S. Vatner Circ Res 1980;47:201

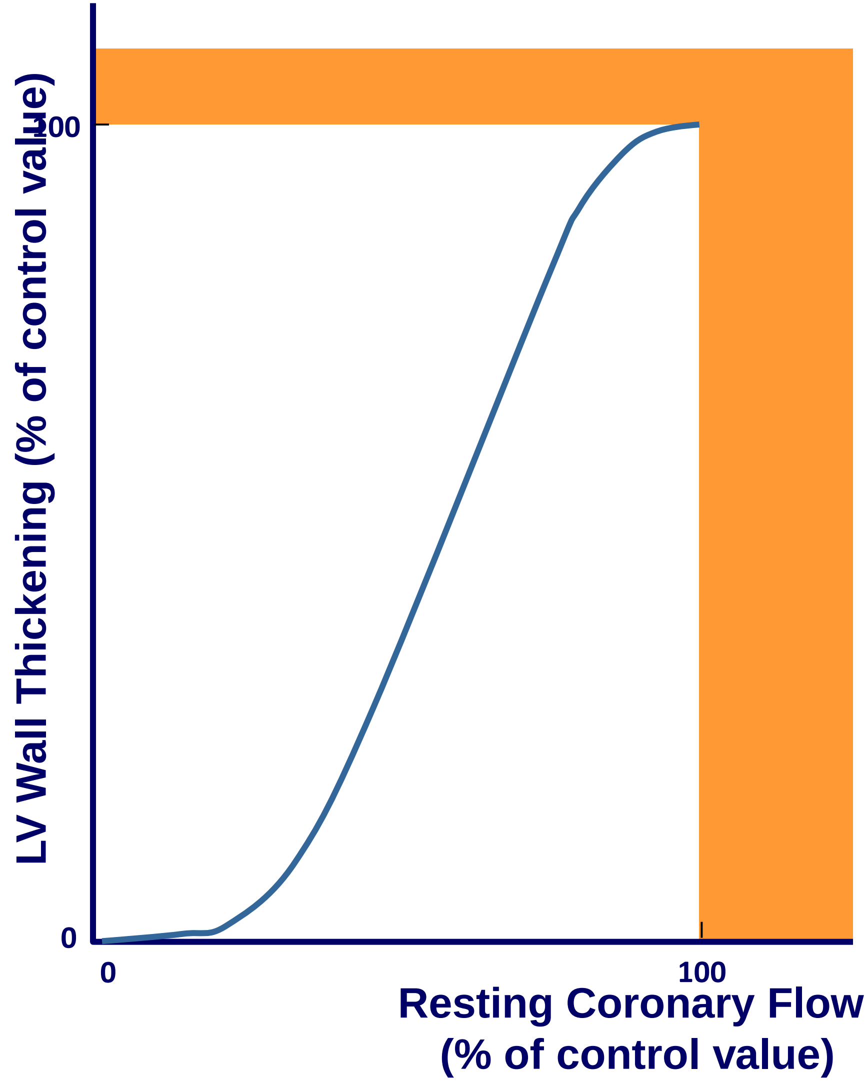
Flow-Function Relationship



J. Canty Circ Research 1988;63:821-836

Flow-Function Relationship





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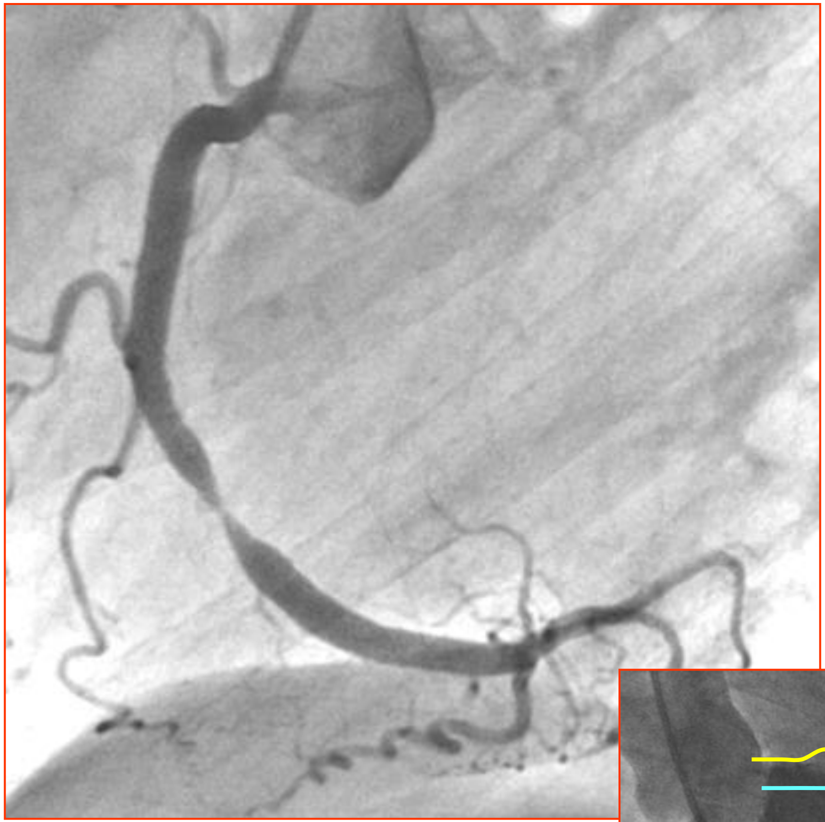
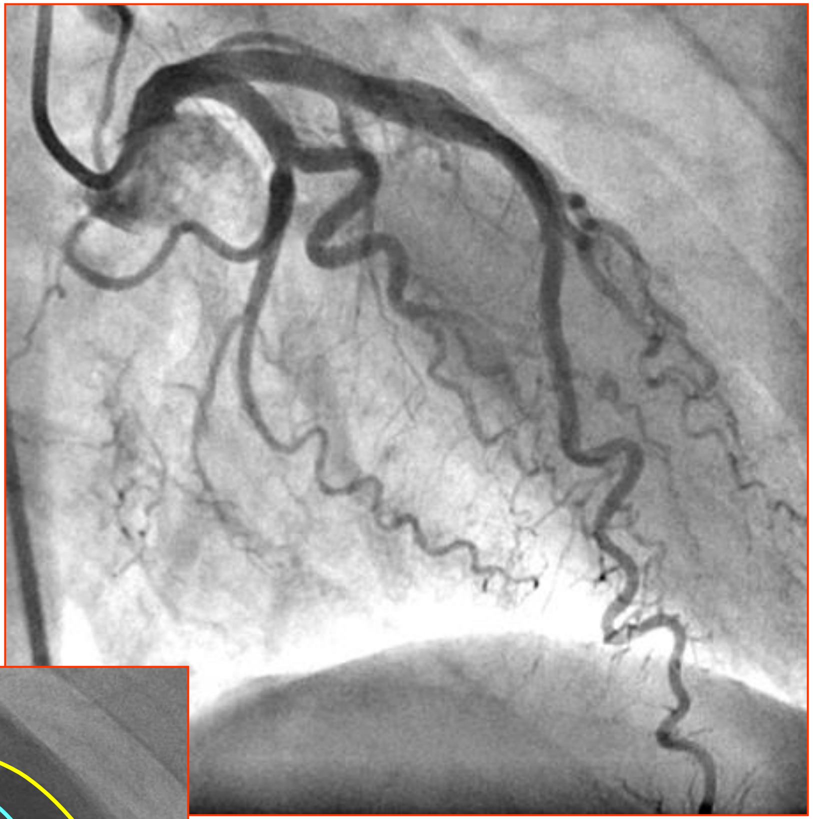
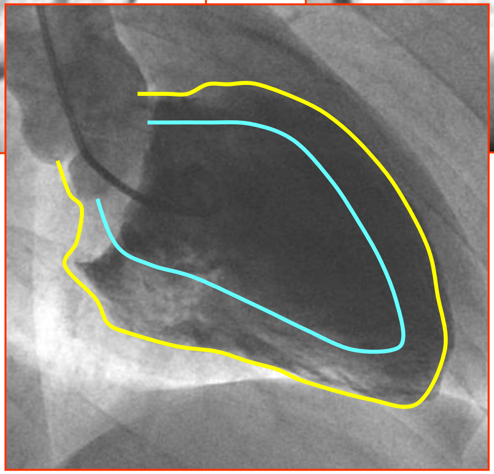
Flow-Function Relationship







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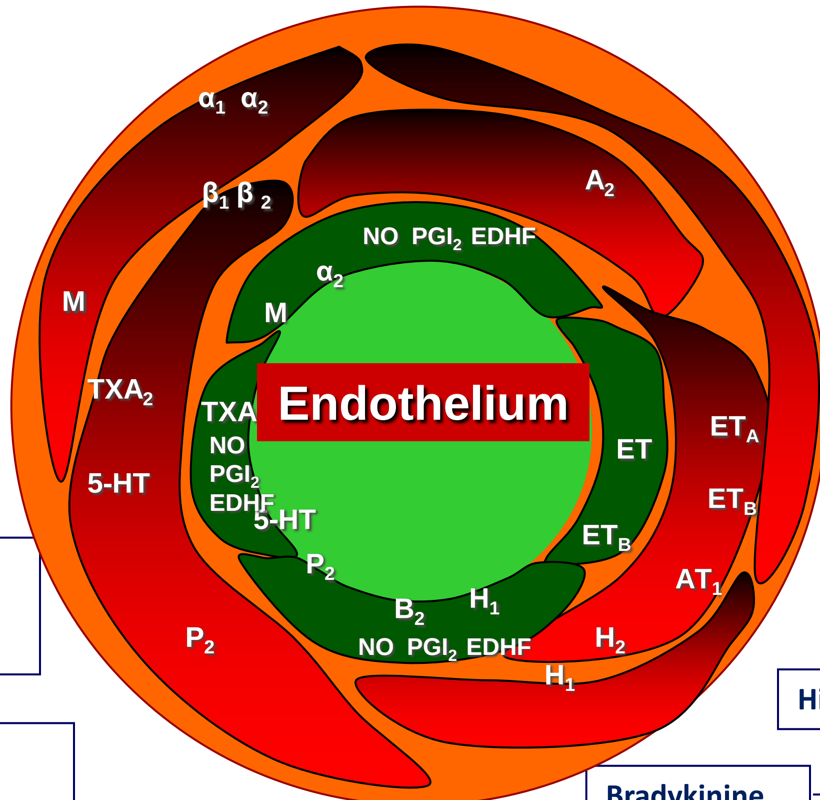
The Control of Myocardial Blood Flow

Neuro-humoral factors

- Noradrenaline
  Adrenaline
- Acethylcholine

Metabolic factors

- adenosine
- PO_2
- PCO_2, H^+, K^+



Physical factors

- Arterial Pressure
  Coronary pressure
  RAP, LVDP and $P_{f=0}$
- Systolic compression
  Diastolic compression

Endo- and paracrine factors

- Angiotensine II
- Histamine
- Bradykinine

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Adapted from D.J.G.M. Duncker

The Control of Myocardial Blood Flow

Endothelium

Metabolic factors

Physical factors

Neuro-humoral factors

Endo- and paracrine factors

Multiple, interacting, cumulative, nonlinear mechanisms

Coronary Autoregulation

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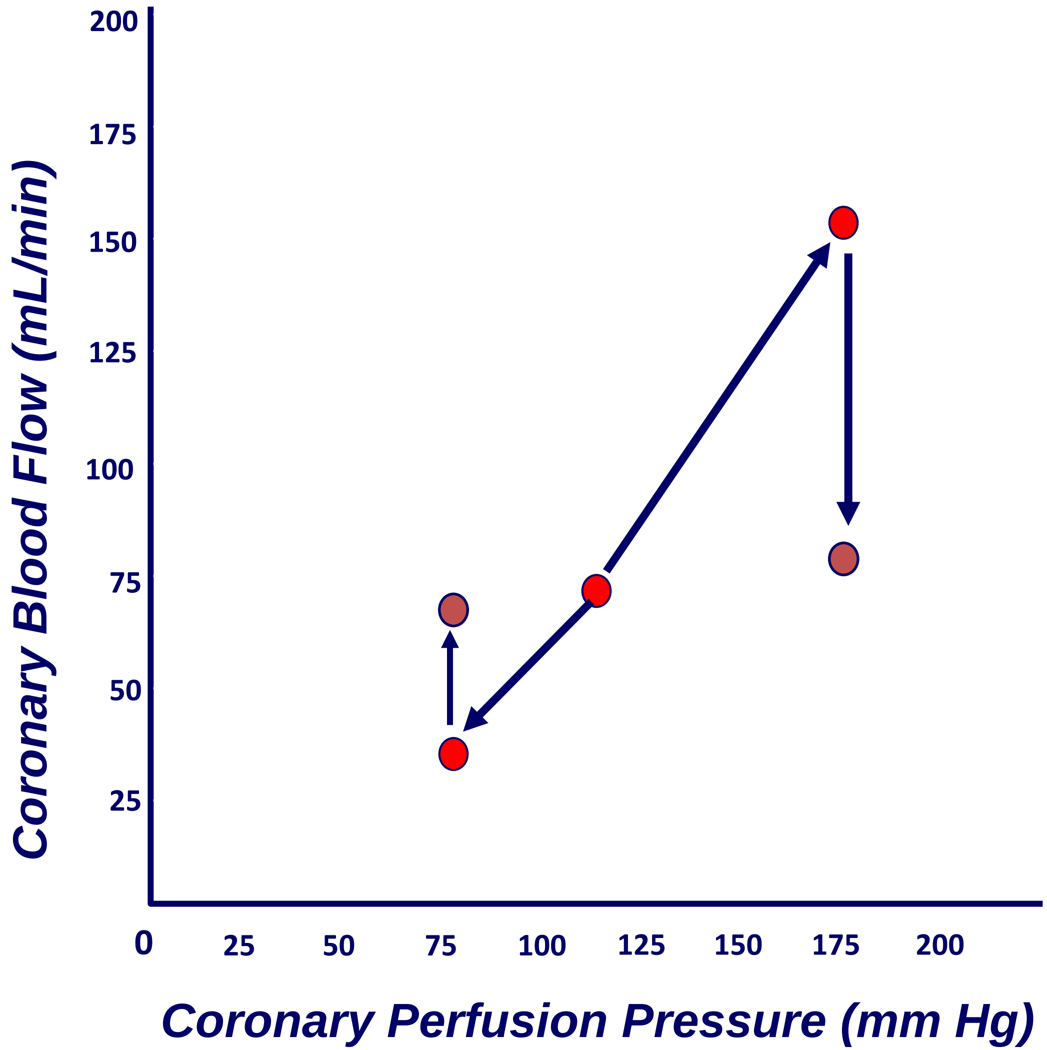
Adapted from D.J.G.M. Duncker

Autoregulation

The ability of the heart of maintaining flow constant in case of change of perfusion pressure without the intervention of any other external mechanism

Coronary Autoregulation



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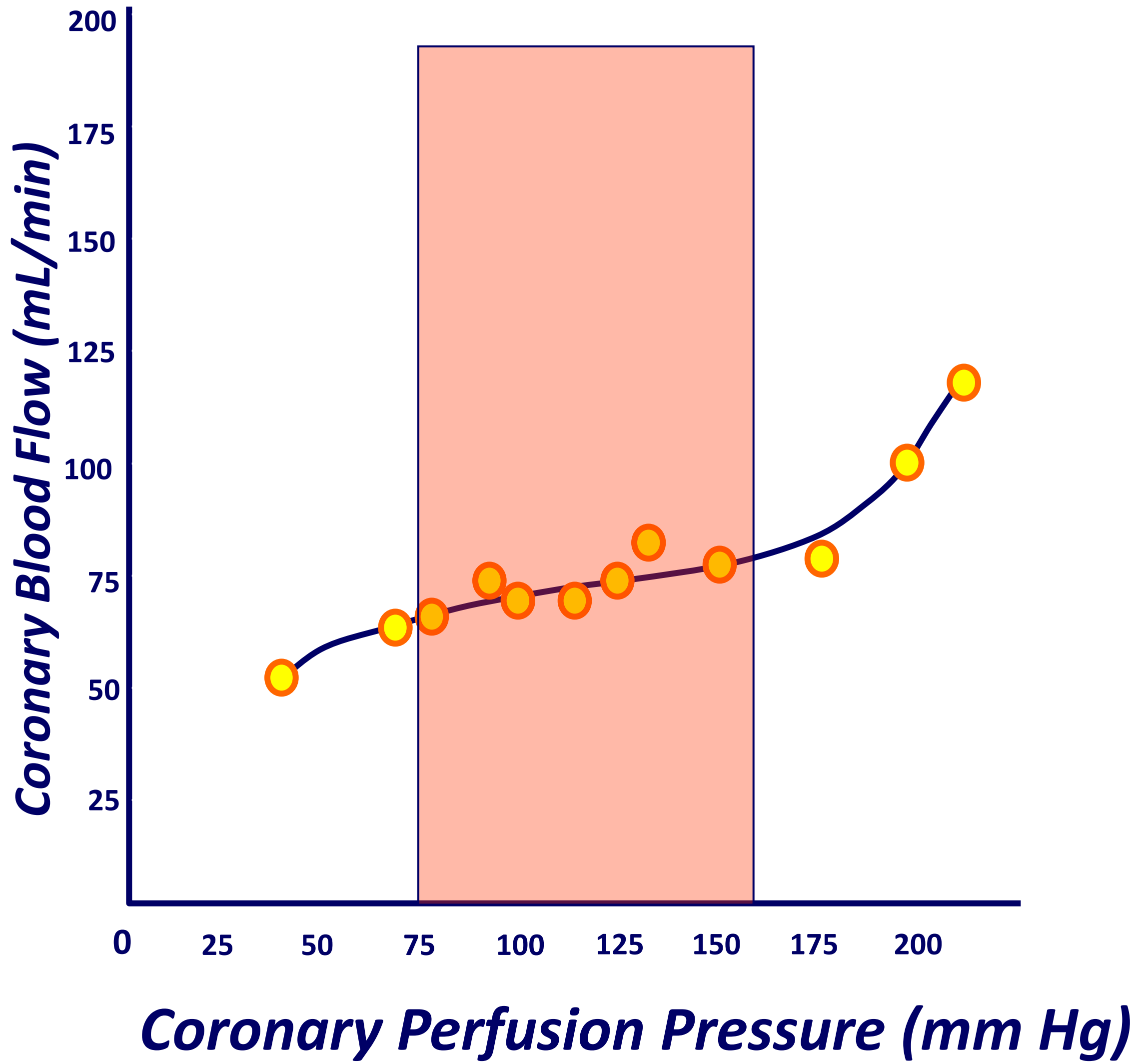
Rubio and Berne, Prog CV Disease 1975

Autoregulatory Range



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Rubio and Berne, Prog CV Disease 1975

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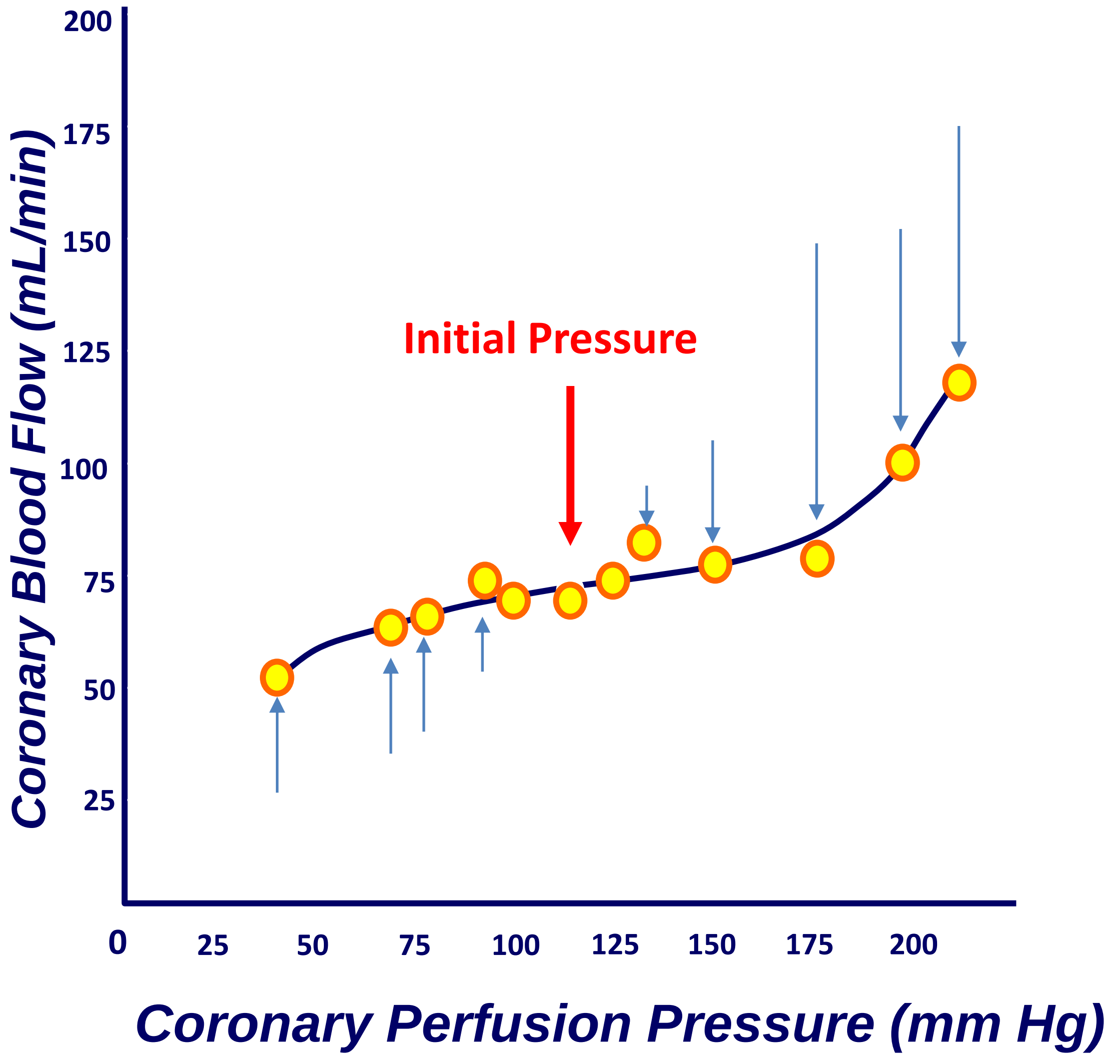
Autoregulatory Range



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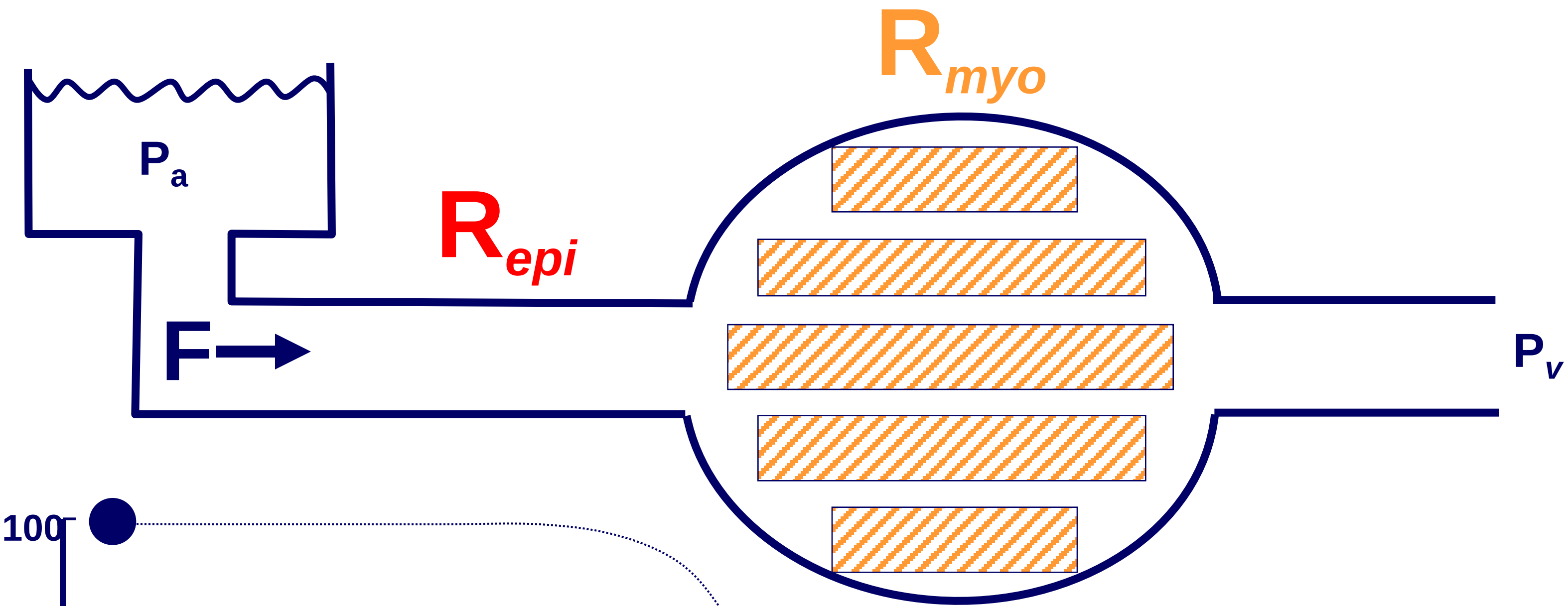
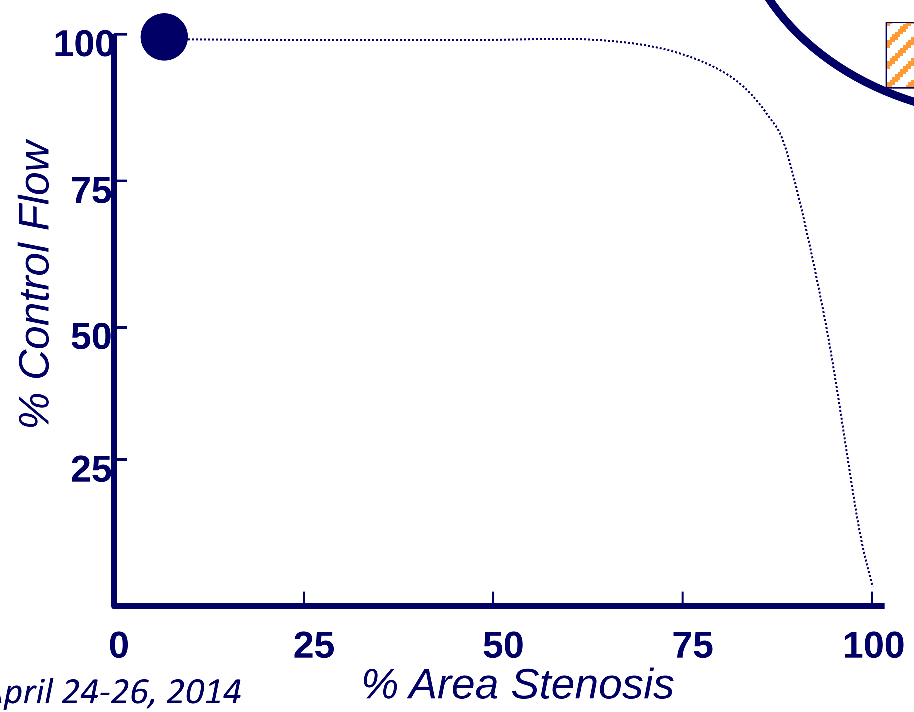
Rubio and Berne, Prog CV Disease 1975

Flow, Pressure, and Resistance

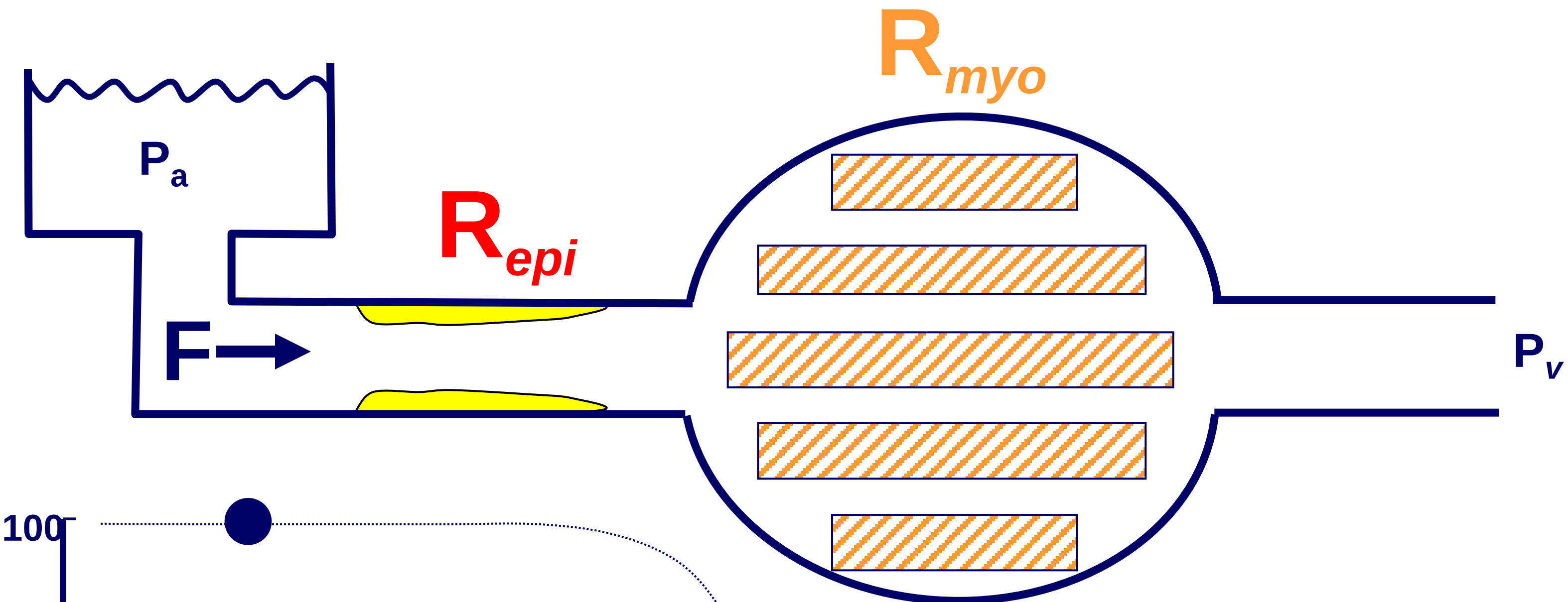


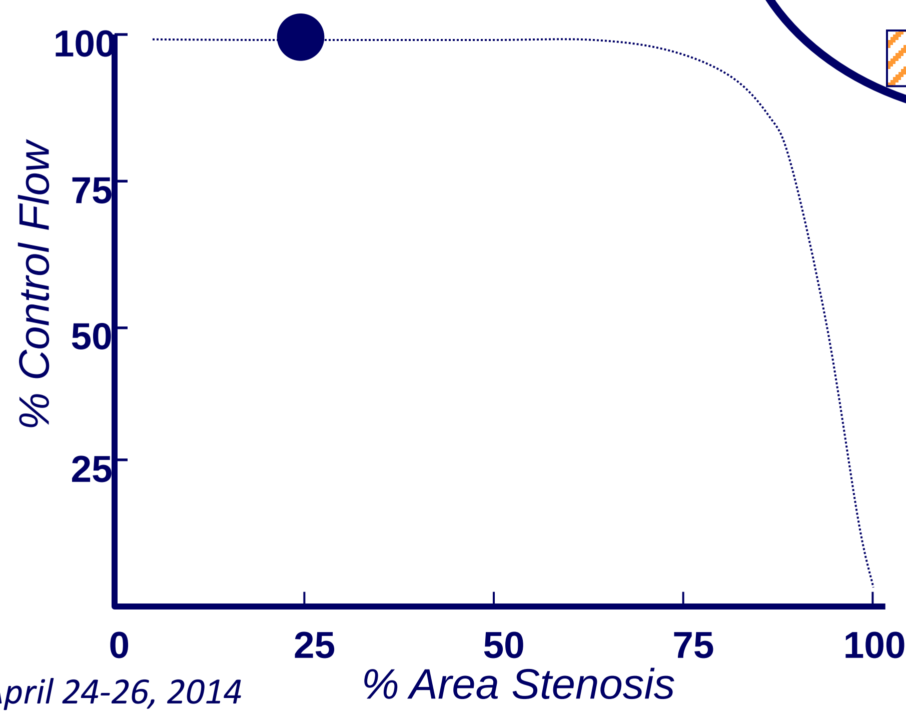


$$F = \frac{\Delta P}{R_{epi} + R_{myo}}$$

K. Lance Gould, 1974

Flow, Pressure, and Resistance

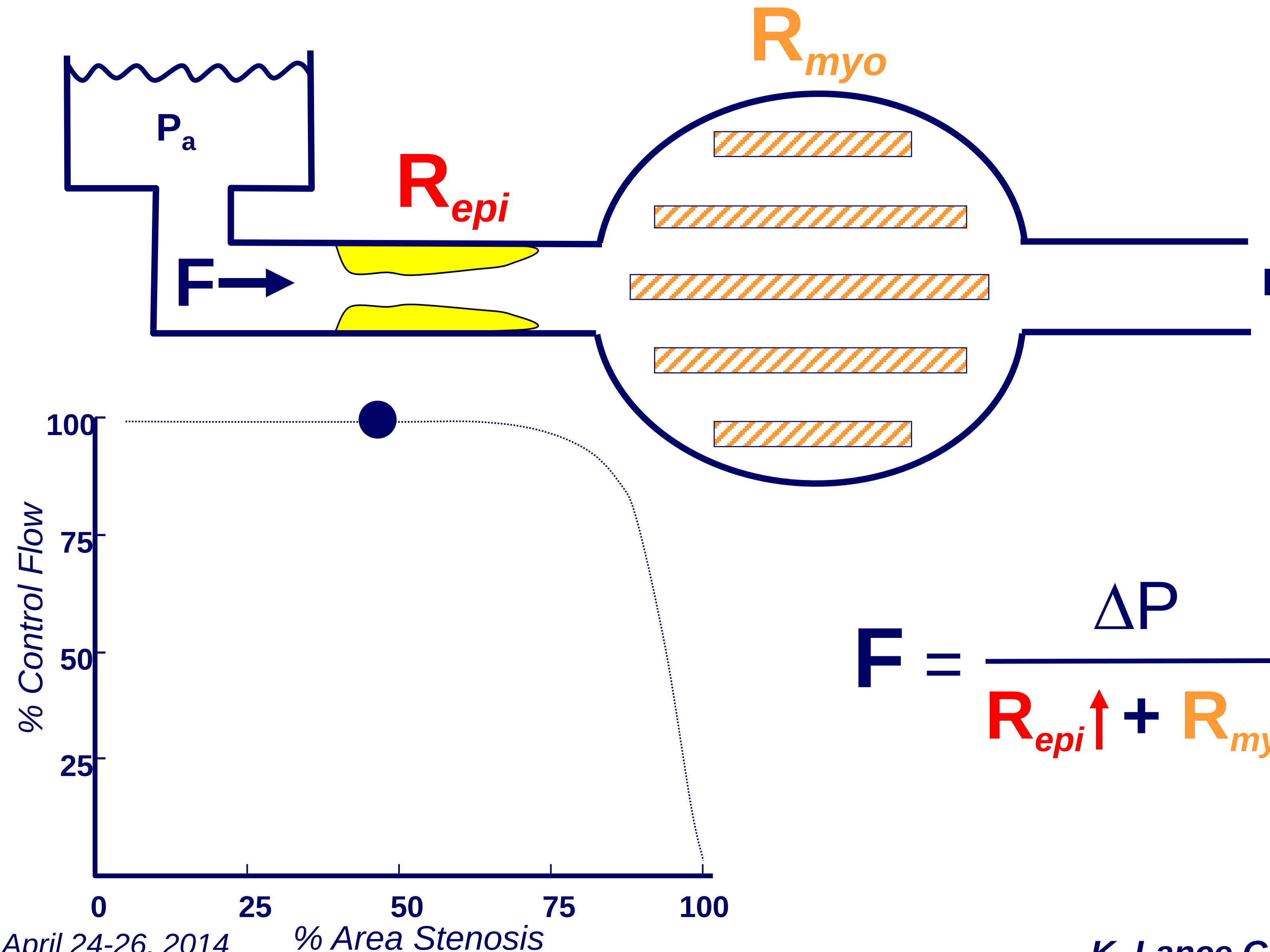




$$F = \frac{\Delta P}{R_{epi}\uparrow + R_{myo}\downarrow}$$

K. Lance Gould, 1974

Flow, Pressure, and Resistance



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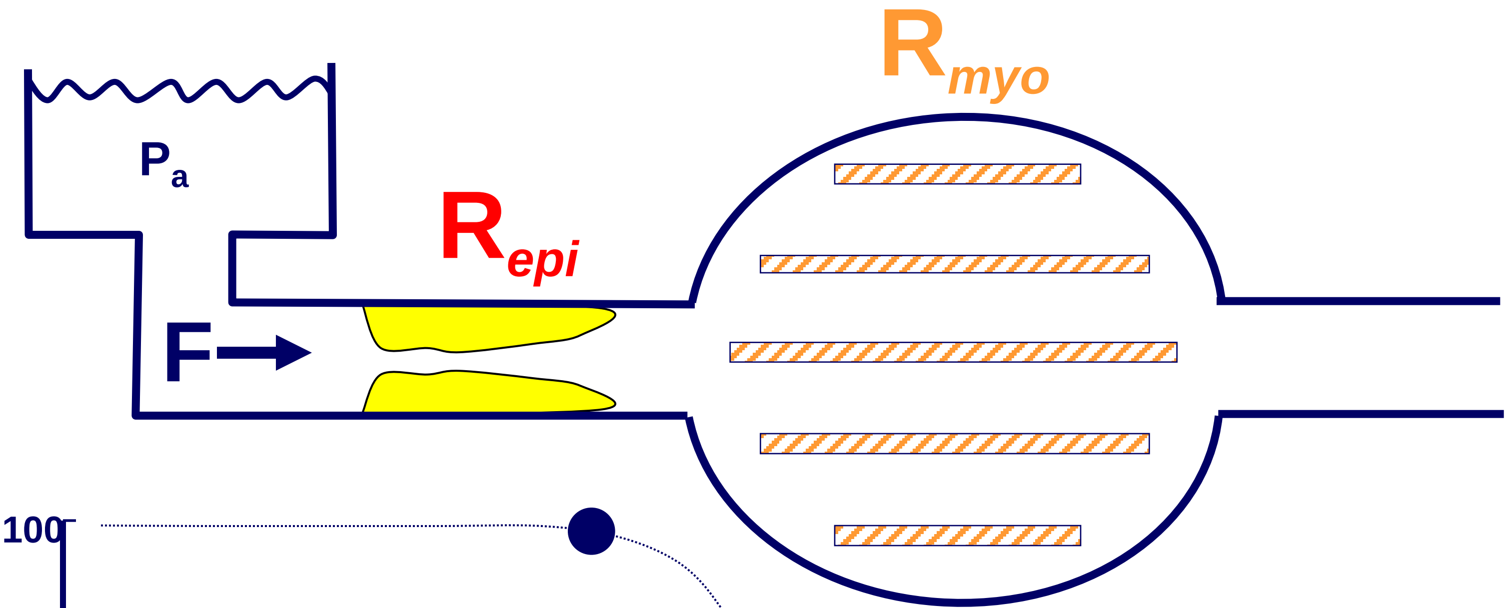

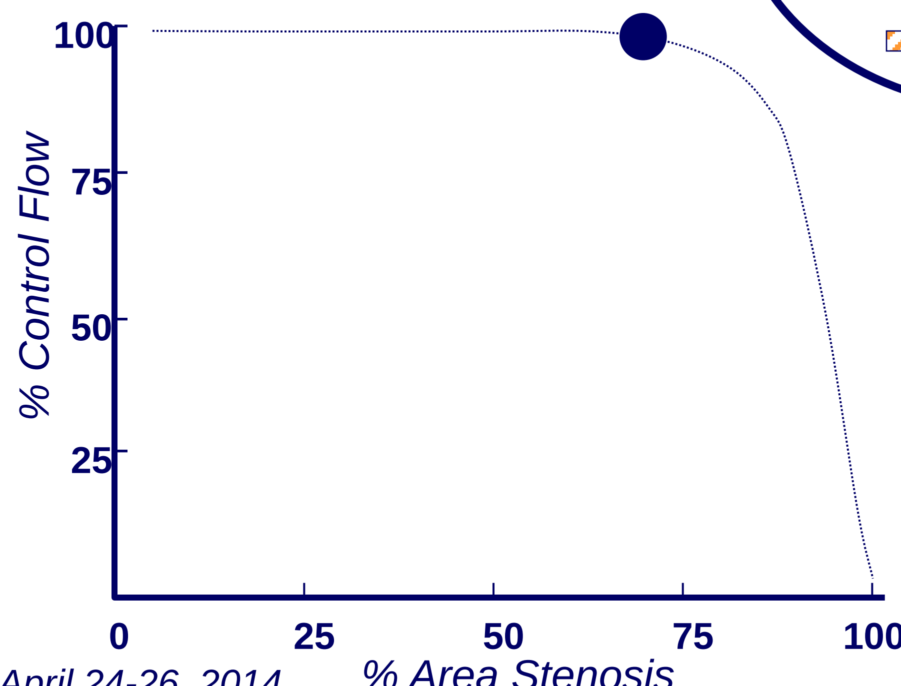

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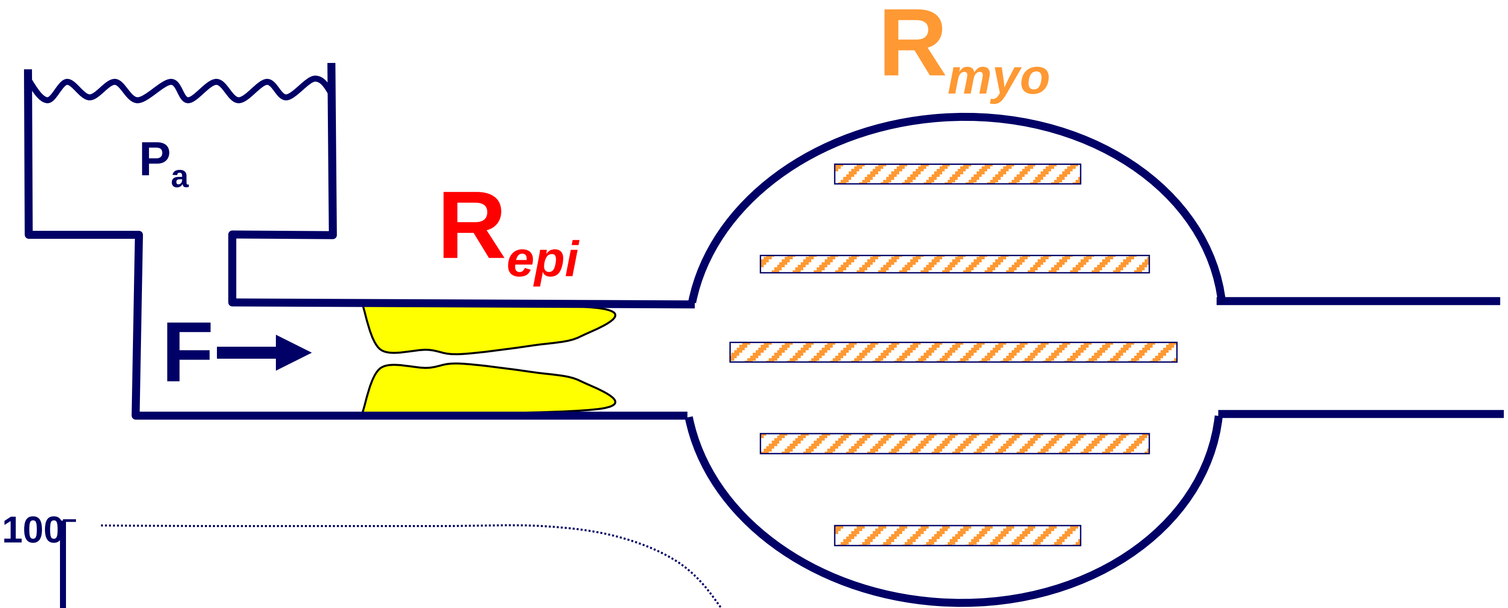
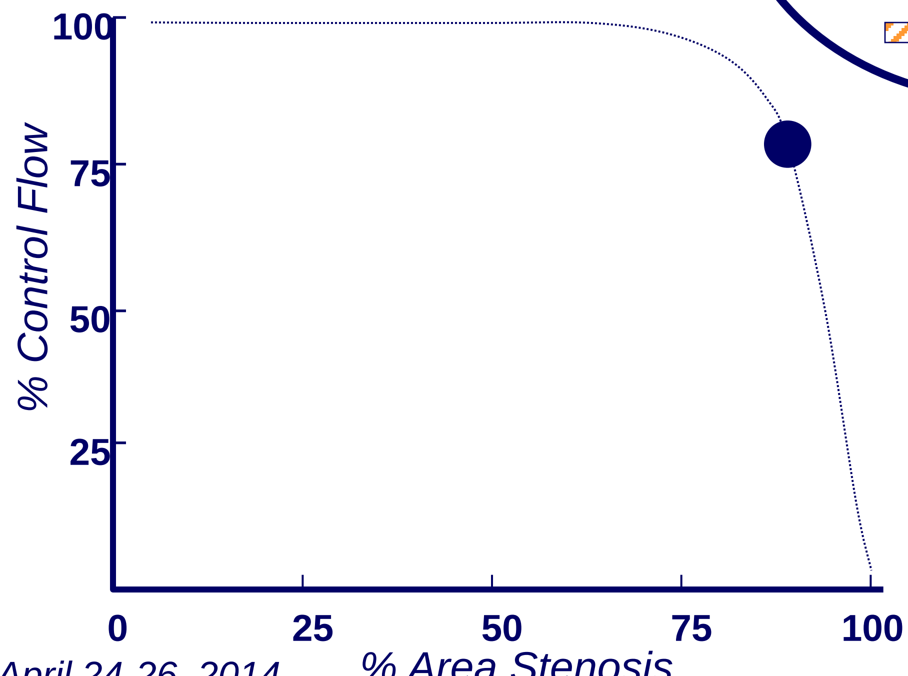
Flow, Pressure, and Resistance





$$F = \frac{\Delta P}{R_{epi}\uparrow + R_{myo}\downarrow}$$

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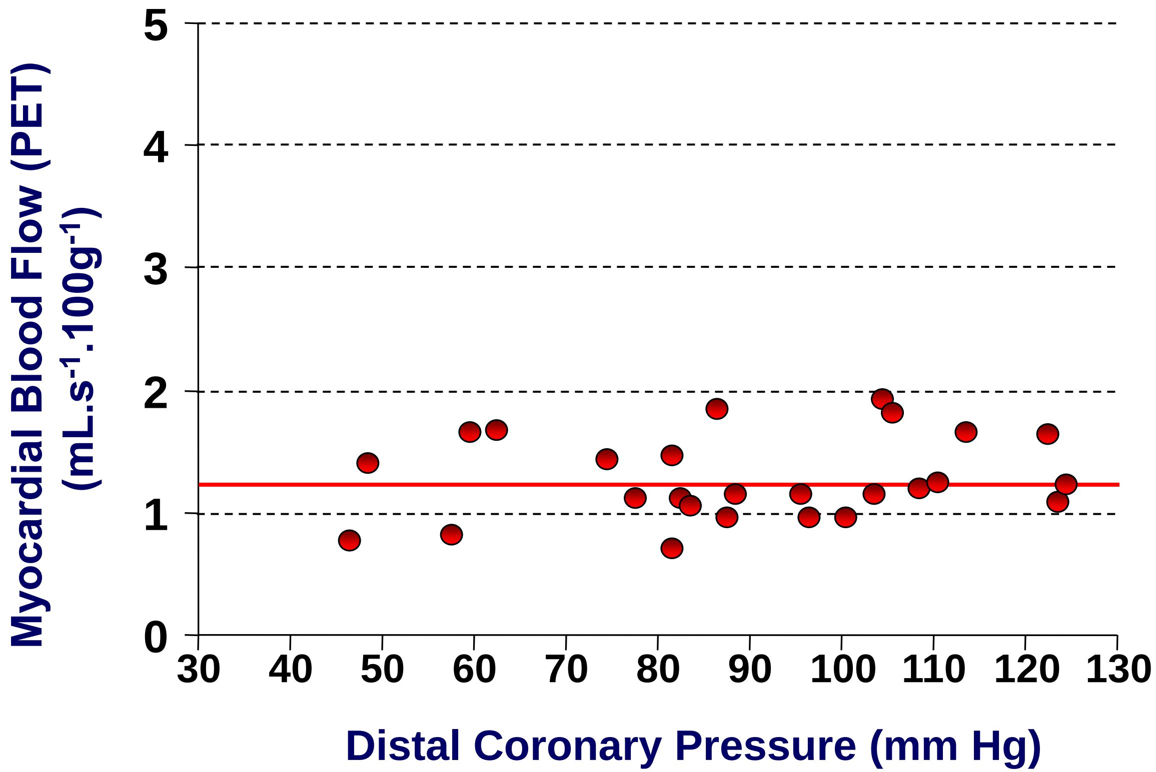
K. Lance Gould, 1974

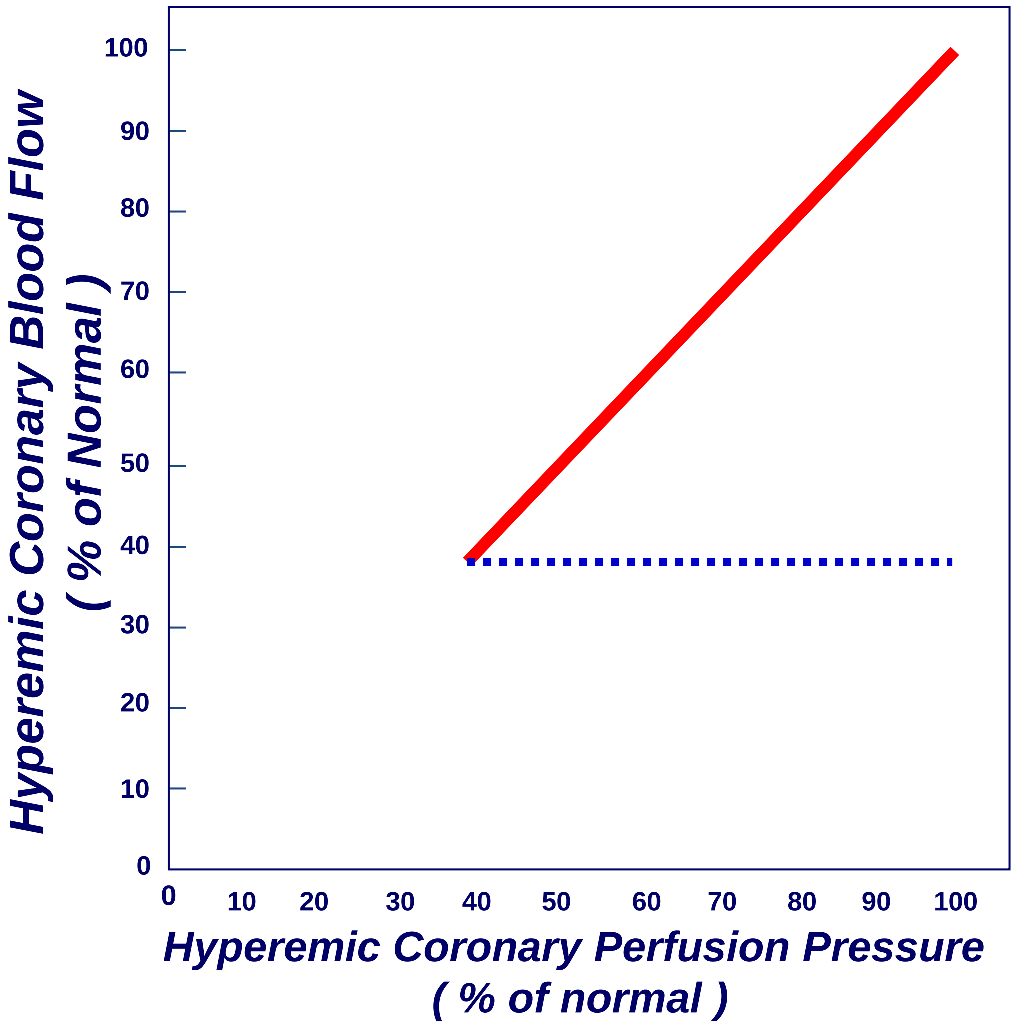
Autoregulation

- Proximal LAD stenosis (n = 26)
- Normal LV systolic function
- PET fow measurements (^{15}O-labeled water) at rest



De Bruyne et al, 1996

Pressure-Flow Relationship During Maximal Vasodilation



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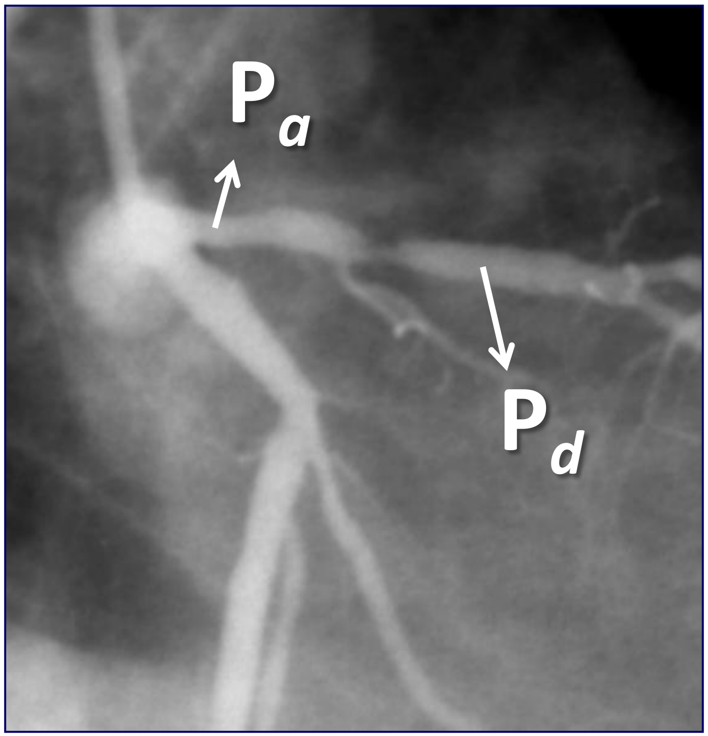
People who wish to treat patients with CAD without coronary physiology must settle for a suboptimal treatment

Fractional Flow Reserve

FFR = ratio of hypermic flow in the stenotic vessel to hyperemic flow in the same vessel but in the absence of the stenosis

FFR = extent to which (%) maximal myocardial flow is limited by the epicardial stenosis



$$FFR = \frac{Q^S_{max}}{Q^N_{max}} = \frac{P_d}{P_a}$$

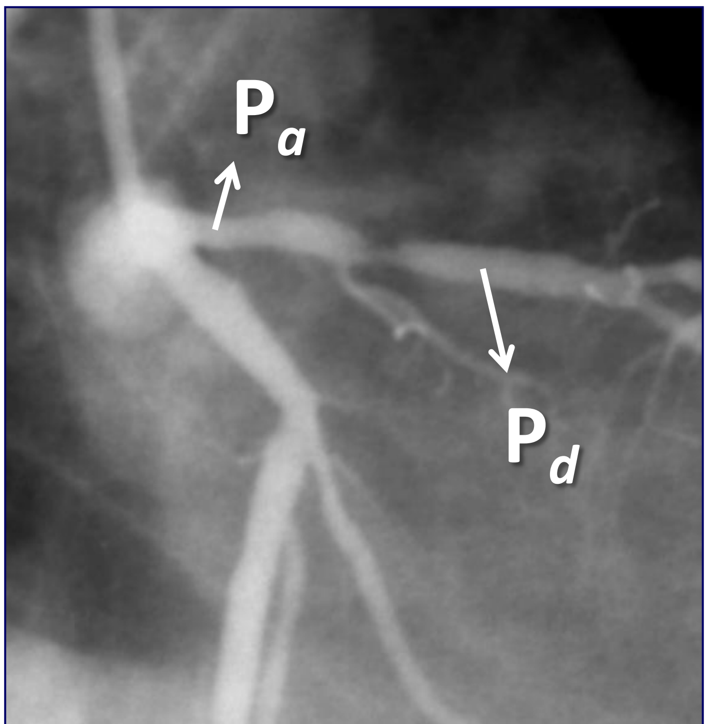
During maximal hyperemia

(i.e. during maximal transstenotic flow)

Fractional Flow Reserve

FFR = ratio of hypermic flow in the stenotic vessel to hyperemic flow in the same vessel but in the absence of the stenosis

FFR = extent to which (%) maximal myocardial flow is limited by the epicardial stenosis



$$FFR = \frac{Q_S^{max}}{Q_N^{max}}$$

?

$$FFR = \frac{P_d}{P_a}$$ (at hyperemia)

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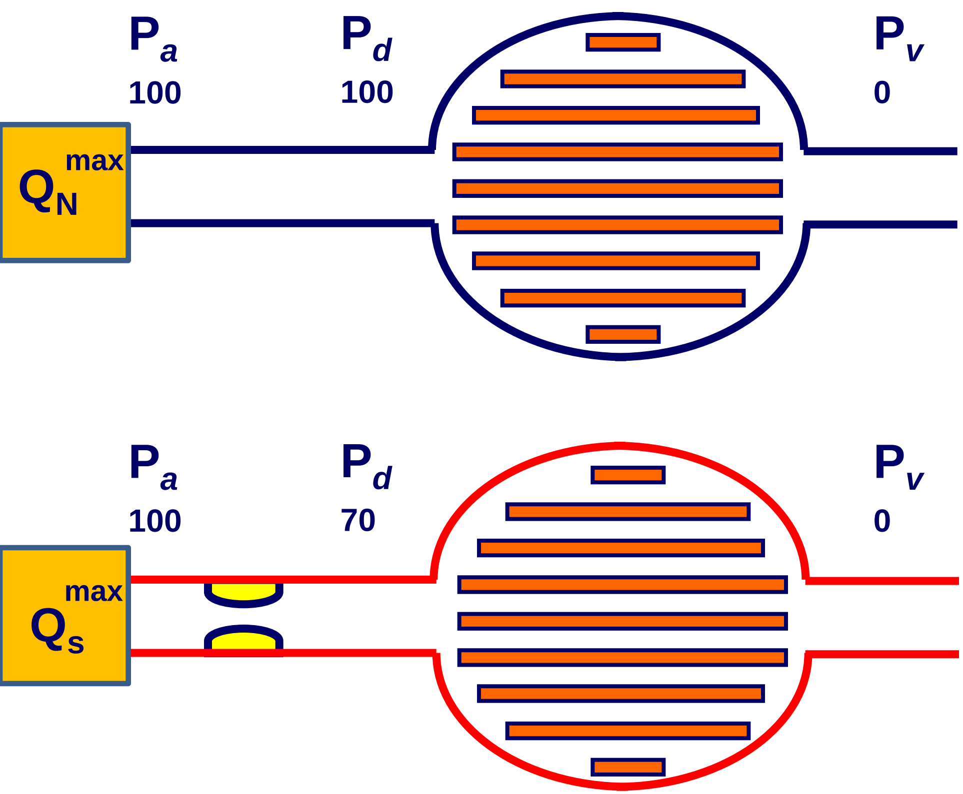
Definition

Fractional Flow Reserve is the ratio of maximal myocardial flow In the stenotic territory to normal maximal myocardial flow



$$FFR = \frac{Q_s^{max}}{Q_N^{max}}$$

$$FFR = \frac{(P_d - \cancel{P_v}) \;/\; \cancel{R_s^{max}}}{(P_a - \cancel{P_v}) \;/\; \cancel{R_N^{max}}}$$

- Hyperemia → $R_s = R_N$
- P_v <<< P_a and P_d

$$FFR = \frac{P_d}{P_a}$$

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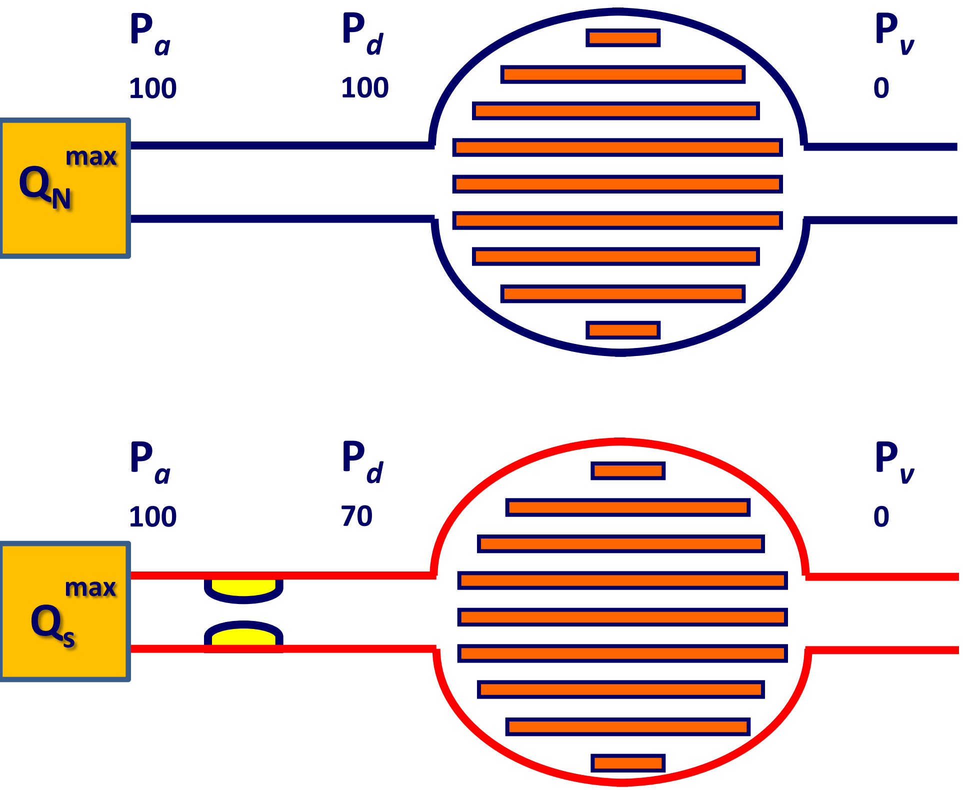
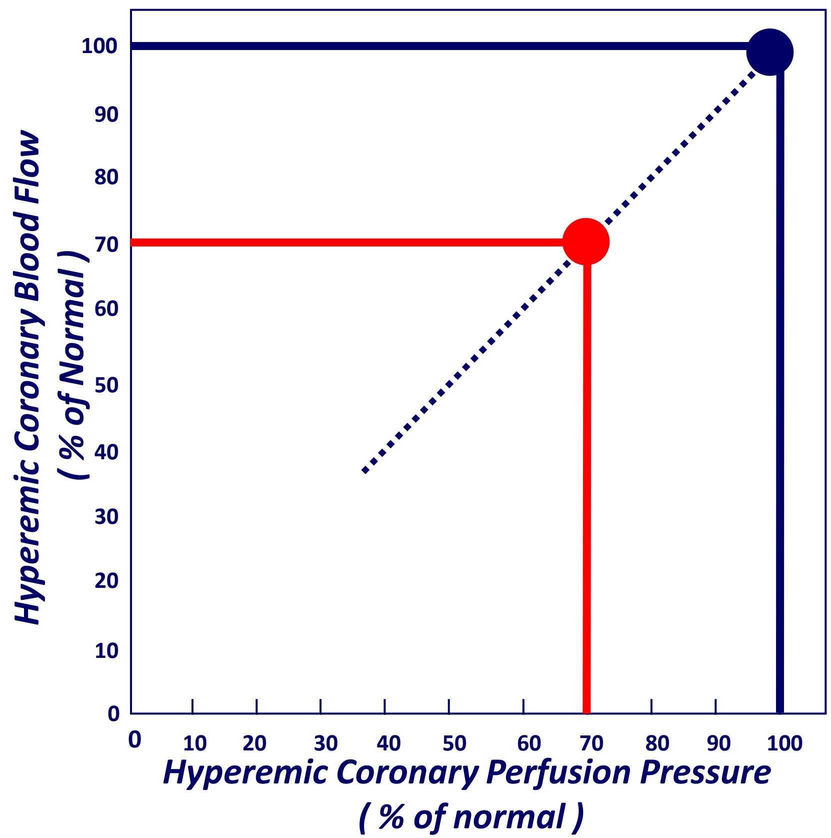
Pressure-Flow Relationship During Maximal Vasodilation





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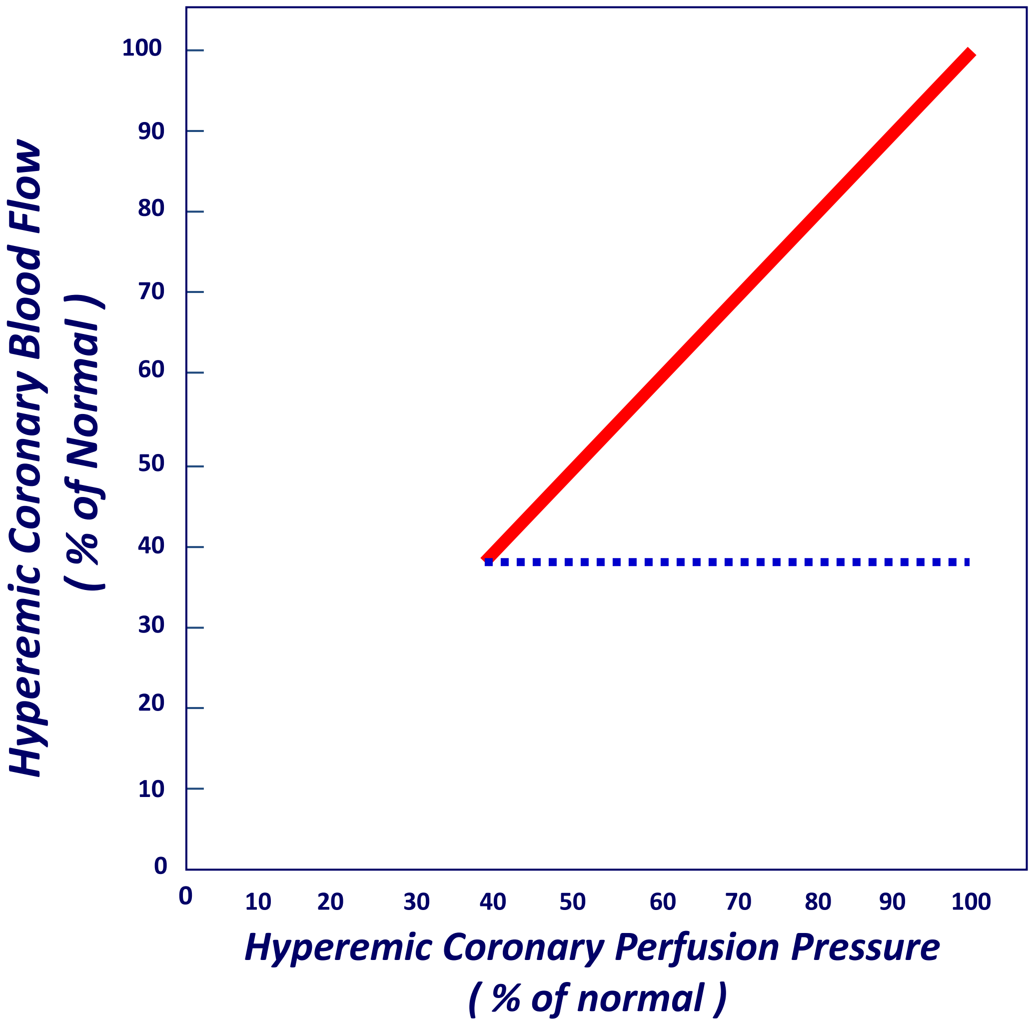

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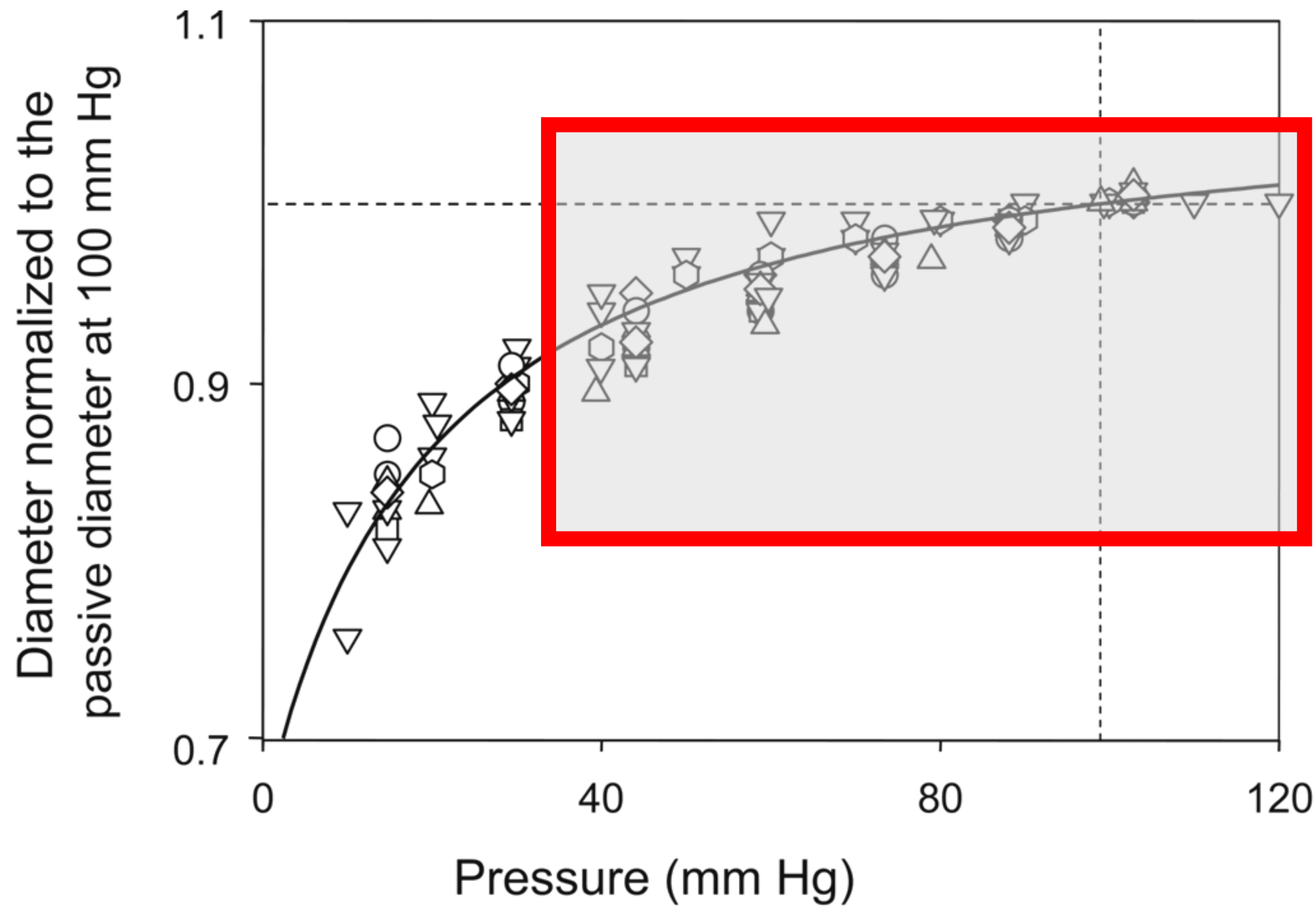
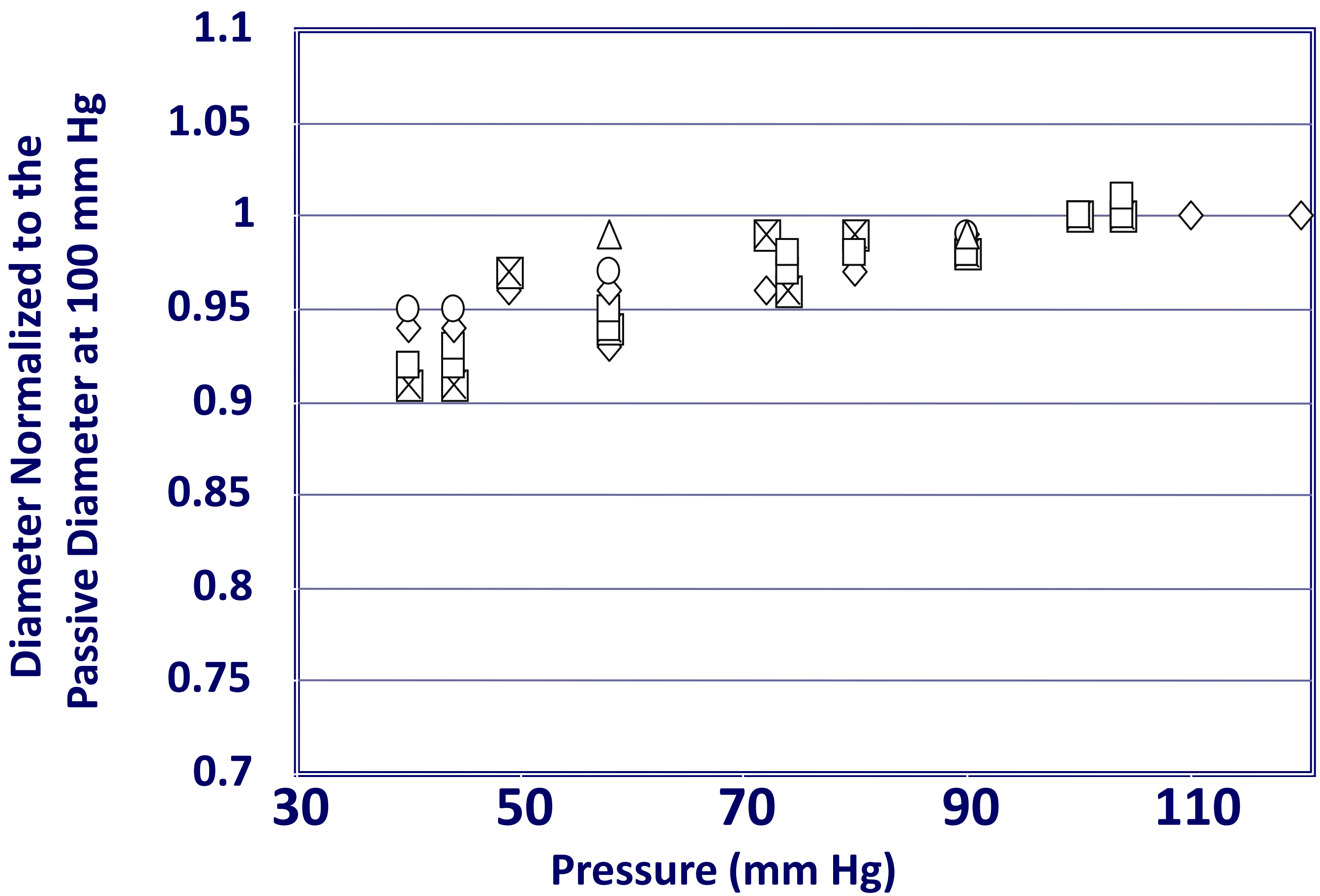
Non-Linearity of the Pressure-Resistance Relationship ?



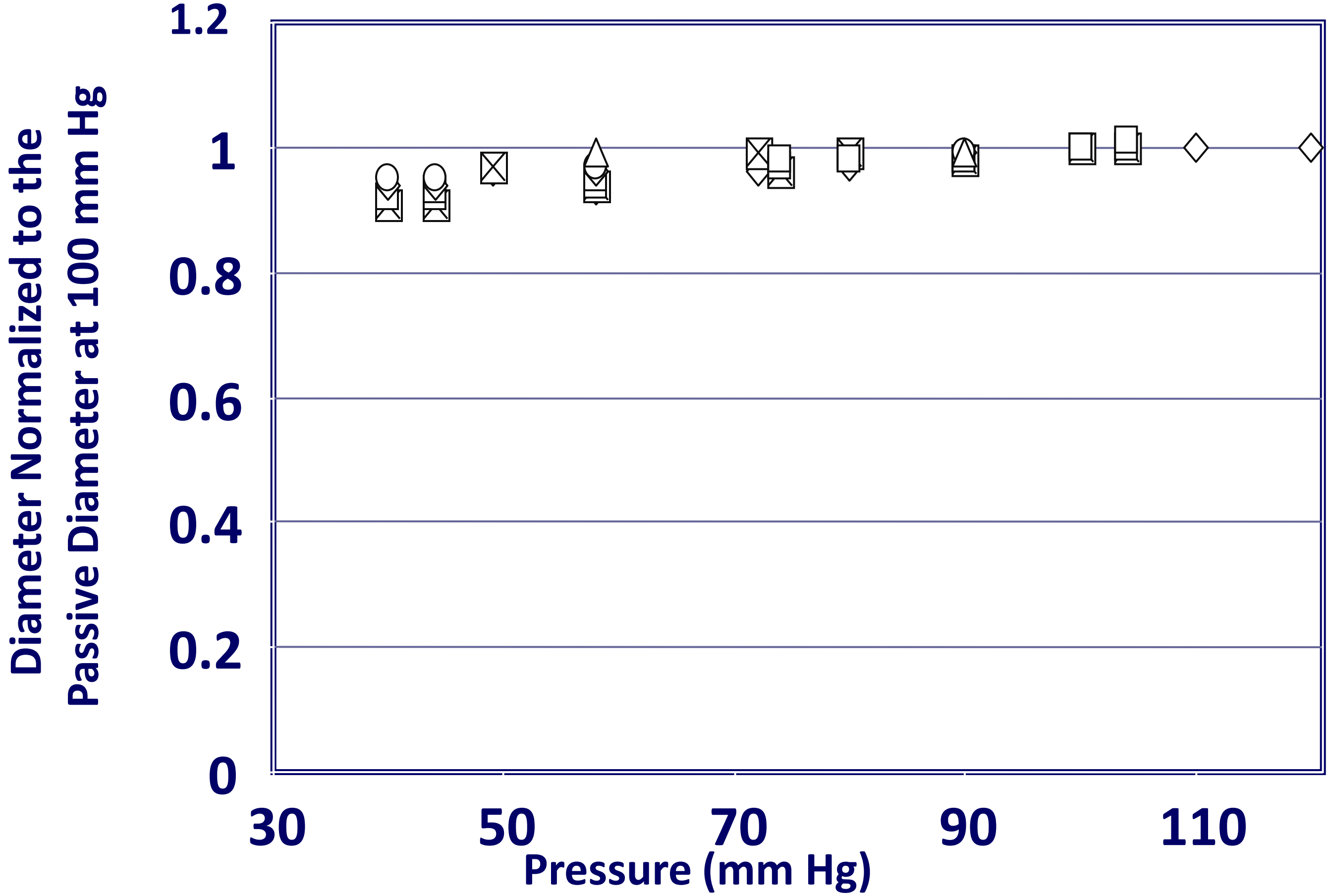
Spaan, J. A.E. et al. Circulation 2006

Non-Linearity of the Pressure-Resistance Relationship ?



Adapted from Spaan, J. A.E. et al. Circulation 2006

Non-Linearity of the Pressure-Resistance Relationship ?



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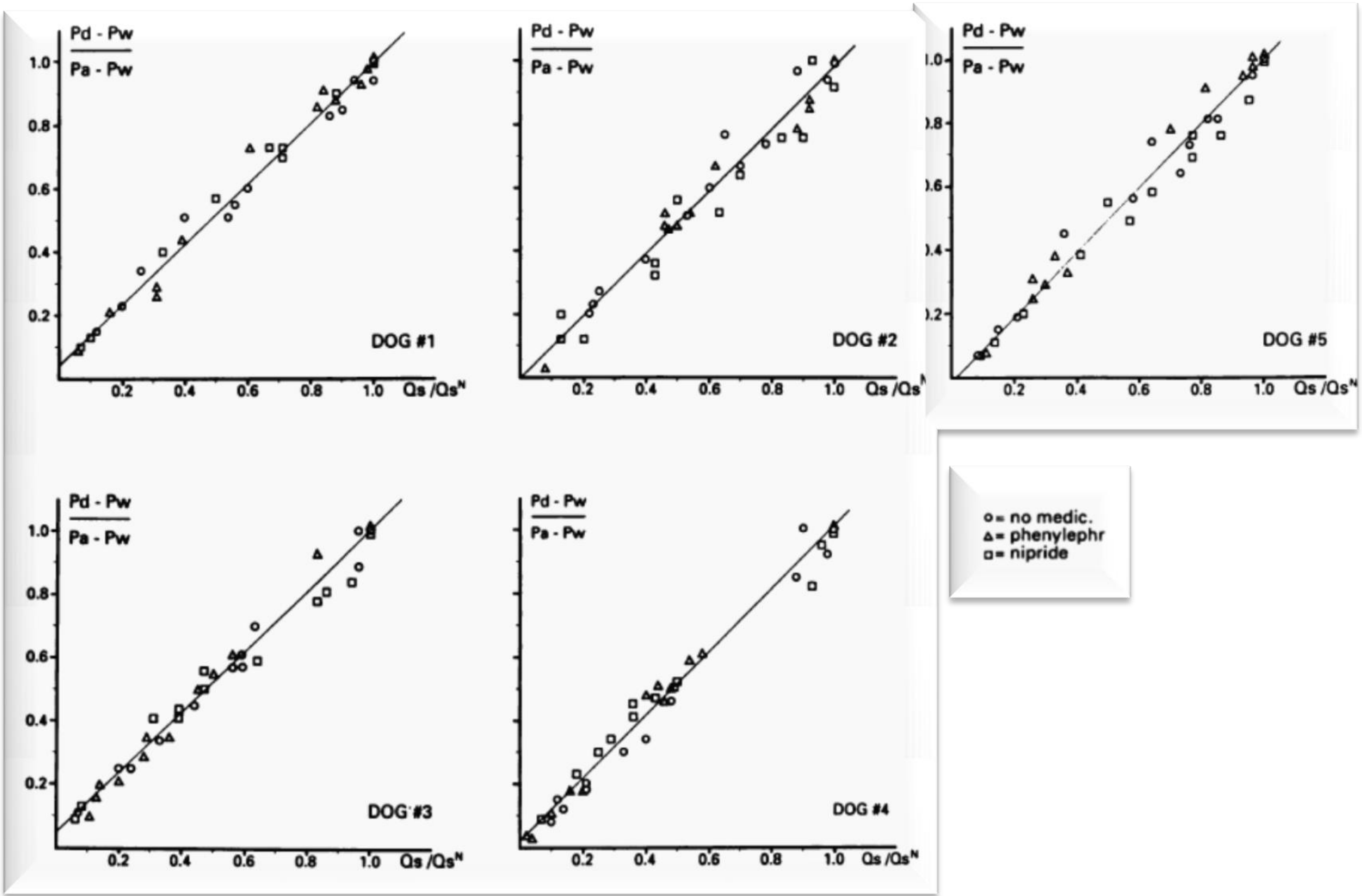
The relation between P_d/P_a and Q_S/Q_N *is LINEAR during HYPEREMIA*



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Pijls NHJ et al, Circulation,1993;86:1354

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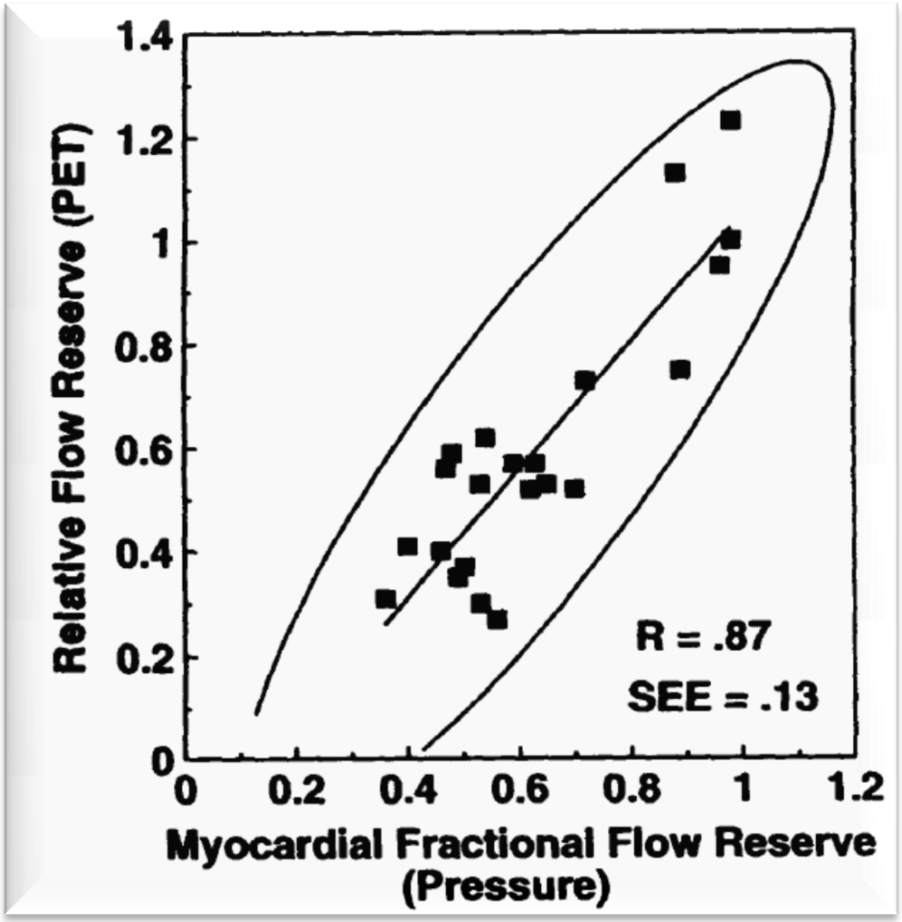
The relation between P_d/P_a and Q_S/Q_N *is LINEAR during HYPEREMIA*

- 22 Patients with an isolated proximal LAD stenosis
- $H_2^{15}O$ PET maximal flow in LAD vs normal territories
- FFR within 24 hours



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De Bruyne B et al, Circulation,1994;89:1013

FFR: Physiologic Meaning

$$FFR = \frac{Q^{S}_{max}}{Q^{N}_{max}} = \frac{P_d}{P_a}$$

During maximal hyperemia
(i.e. during maximal transstenotic flow)

FFR has a well defined physiologic meaning
(in sharp contrast to other indices like the ΔP, resting P_d/P_a, iFR, FFR_{diast})

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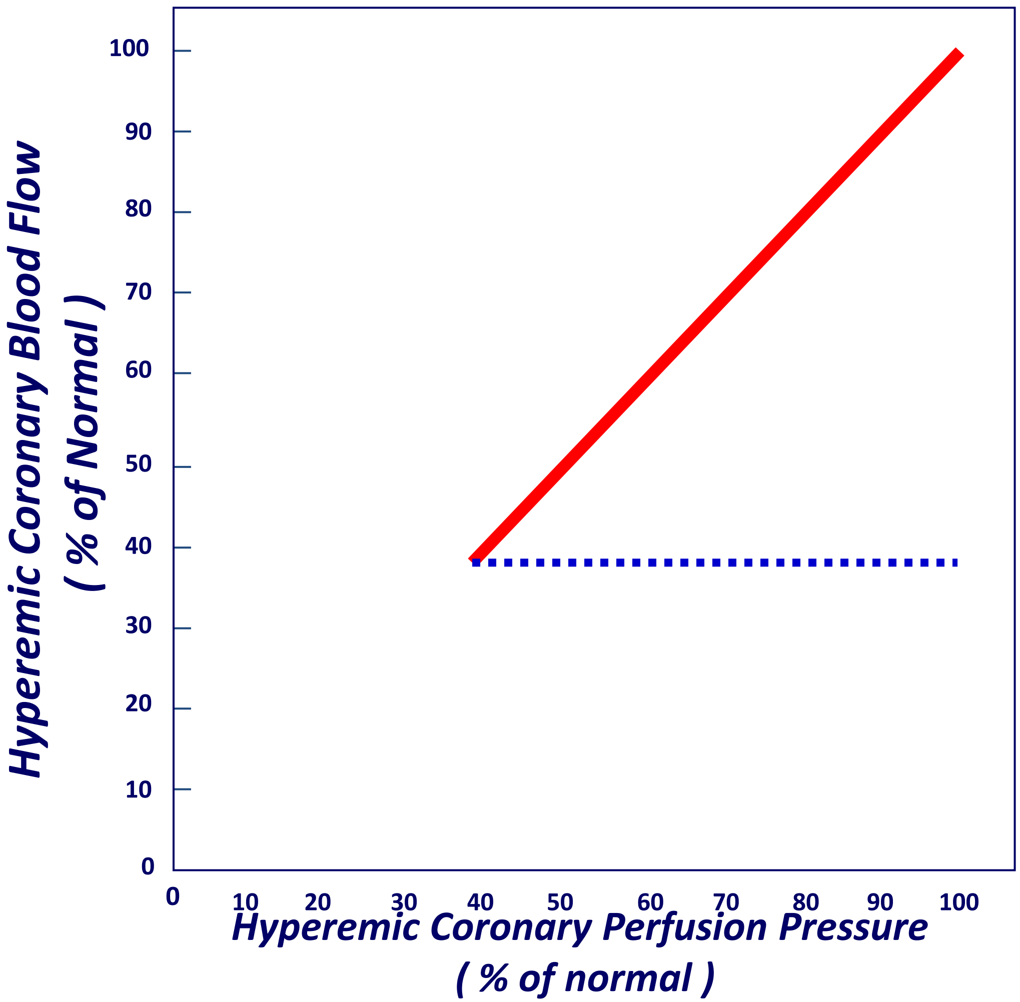

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People who wish to treat patients with CAD without coronary physiology must settle for a suboptimal treatment