Mechanical, Chemical and Software Manipulation in the Prevention of De Novo Plaque Formation and post-PCI In-Stent Restenosis

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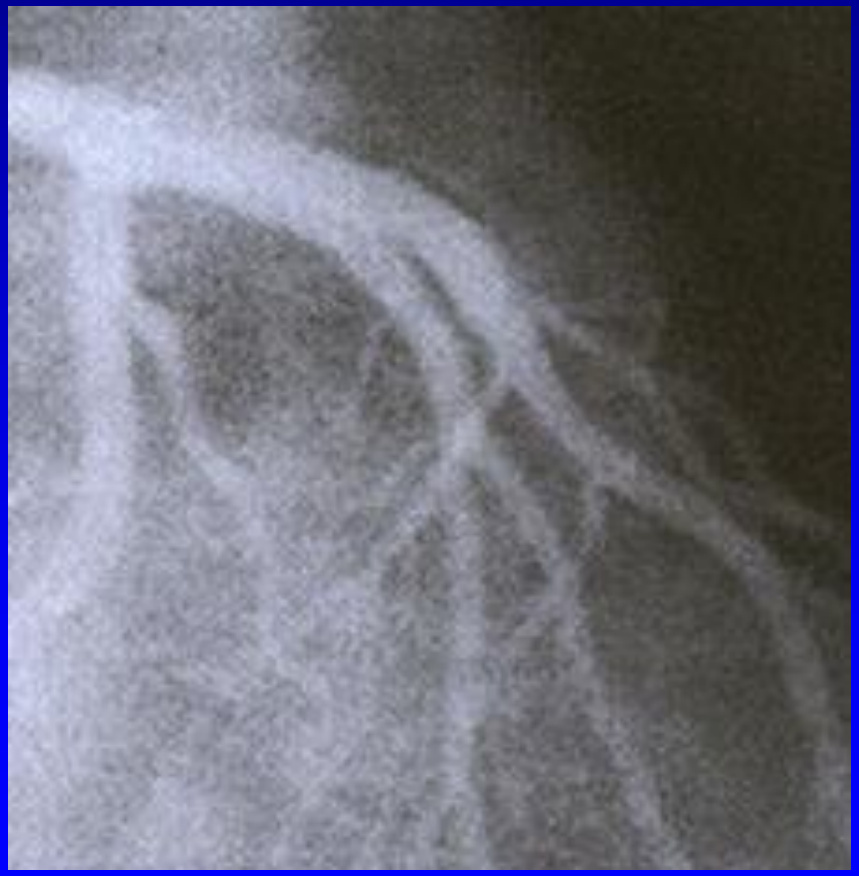
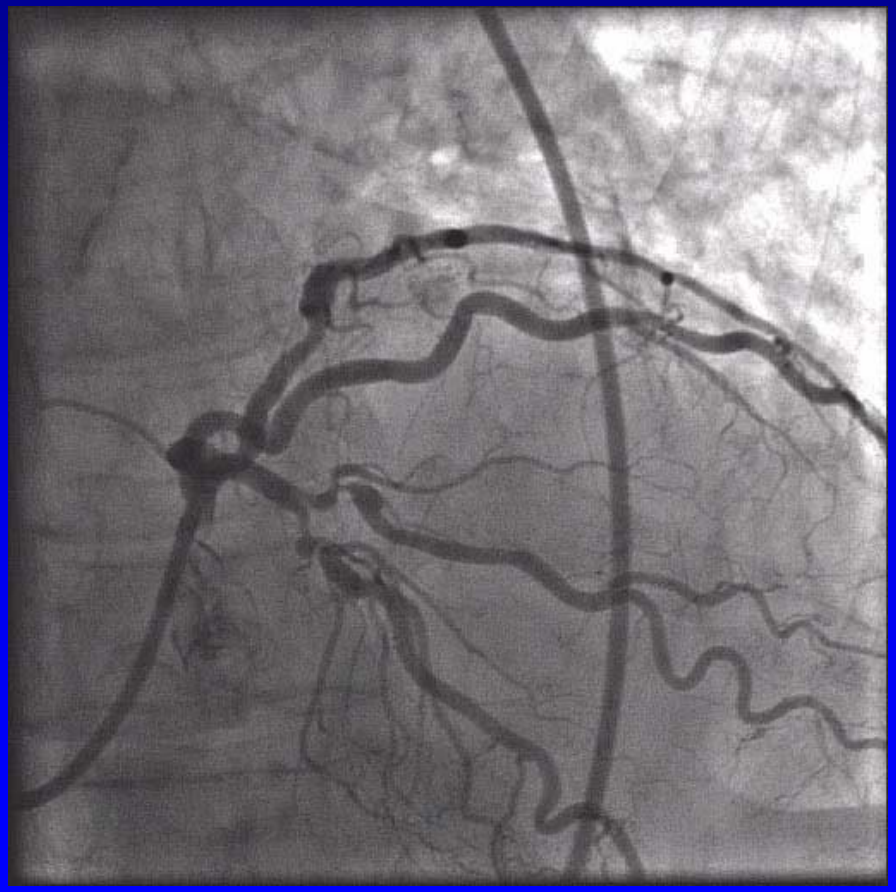
QUESTIONS

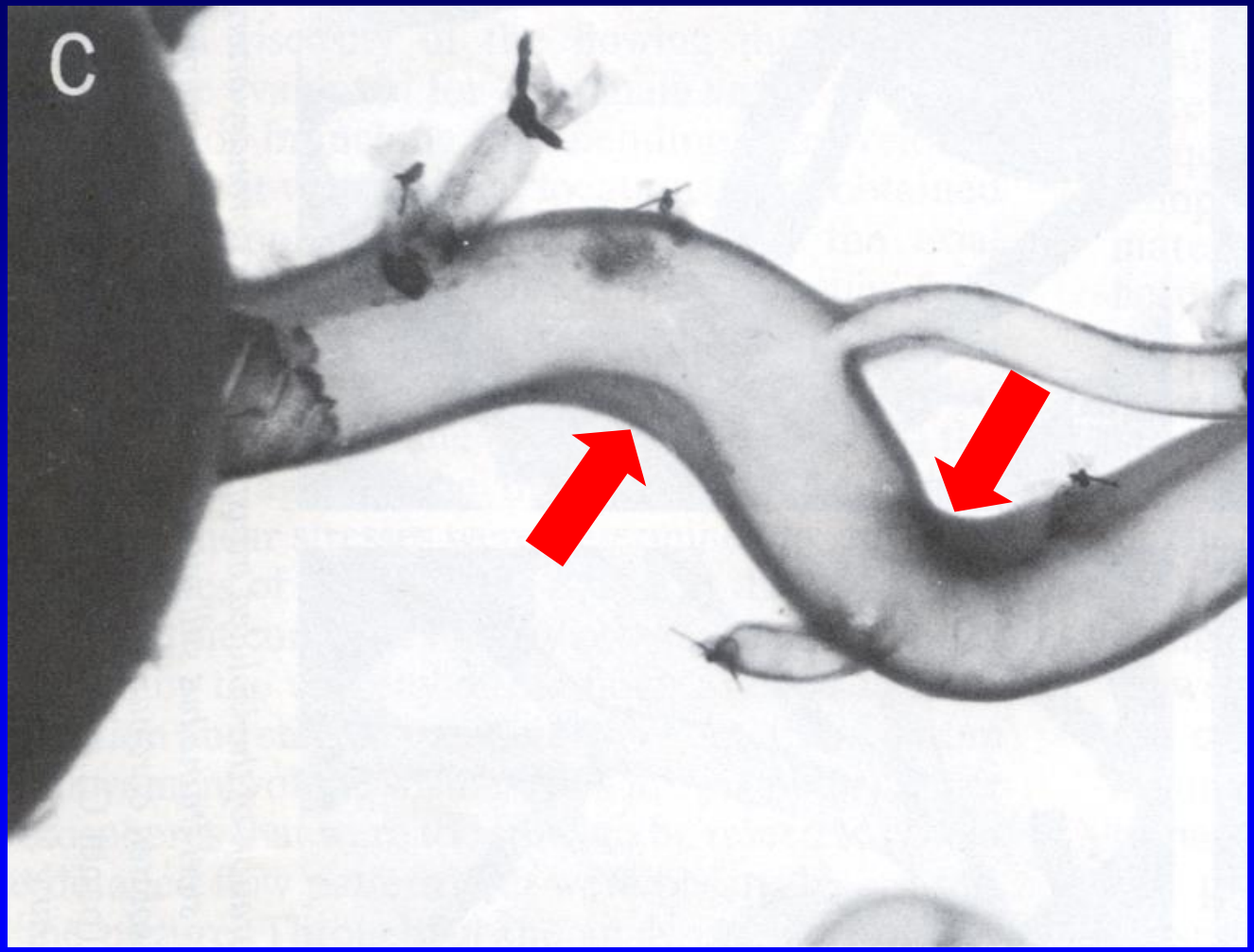
- 1. Why does atheroslerotic plaques form in the inner curve of the artery (de novo) ? Why they do not?
- 2. A patient coming with a lesion on the coronary, why we have to do PCI in this case and not continue to give medical treatment?
- 3. Why there are less in-stent restenosis after DES and not BMS?

A. First Observation: Same bifurcation angle, why ones develops lesion and ones does not? What makes the differences?





Common Locations of Atherosclerotic Plaques Caused by Disturbed Flow

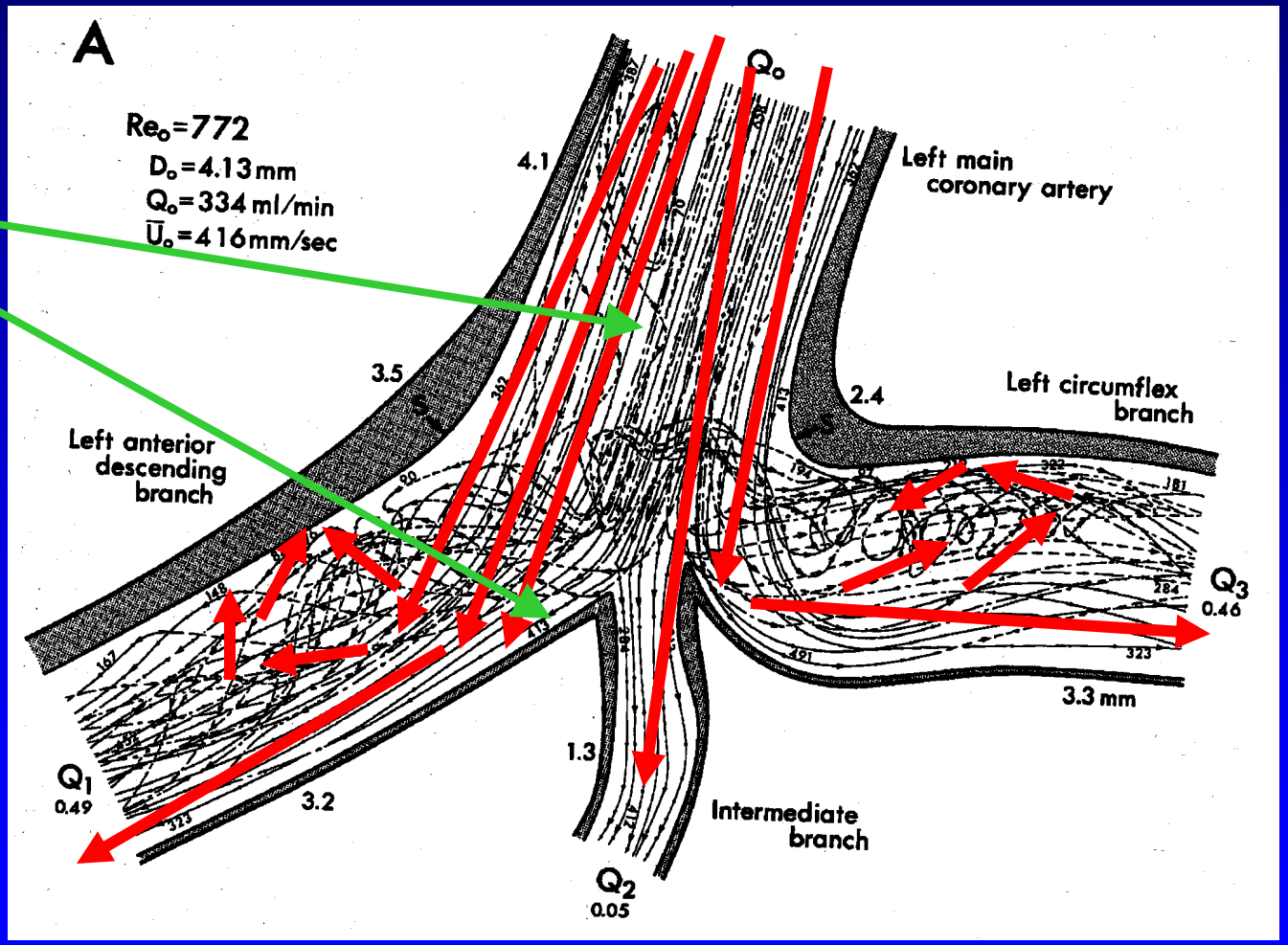


(Asakura and Karino. Circ Res 1990;66:1045)

Disturbed Flow in Inner Curvature at Bifurcation

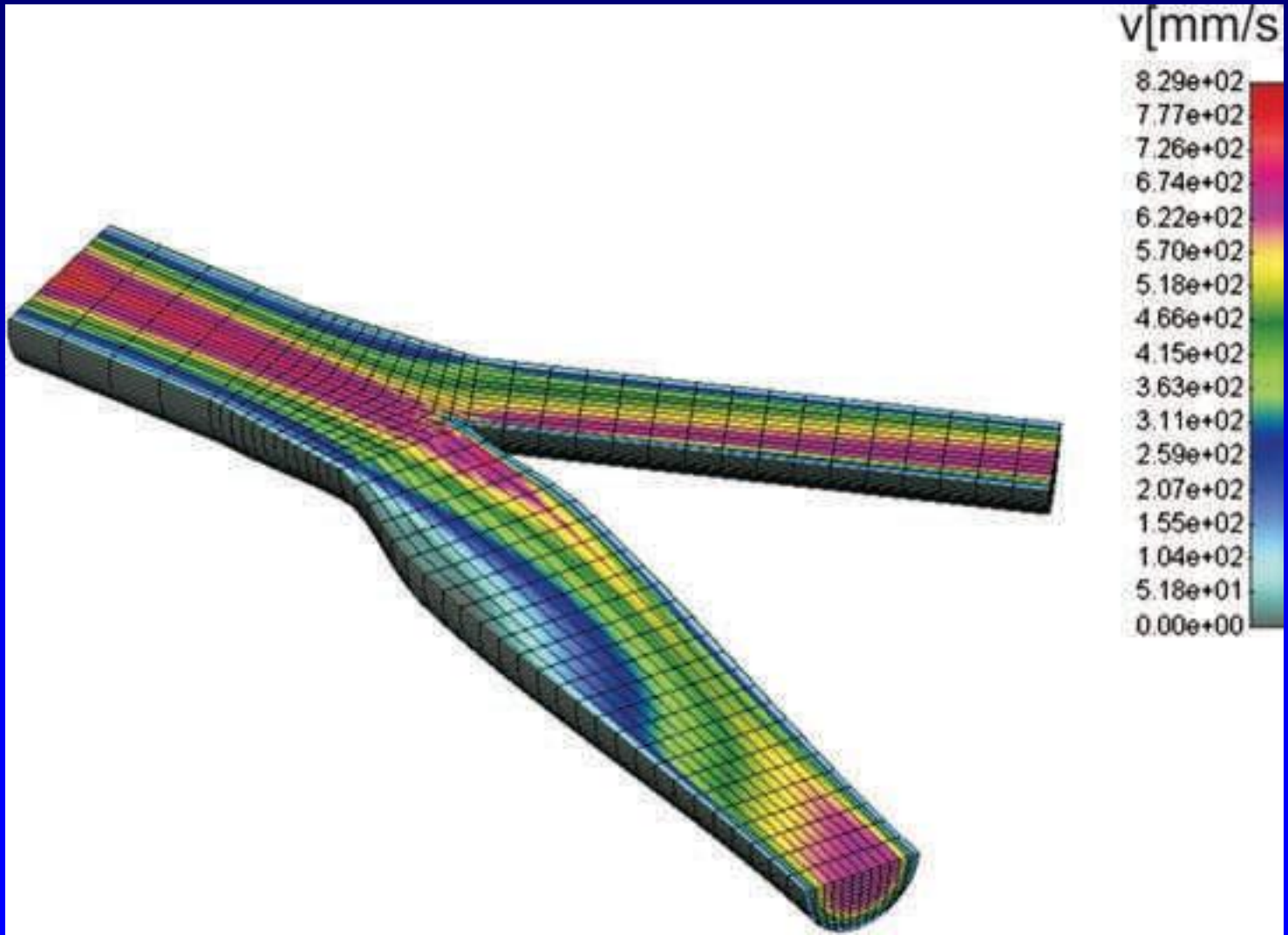
Undisturbed laminar flow

Low and oscillatory disturbed laminar flow



(Asakura and Karino. Circ Res 1990;66:1045)

3D Bifurcation Model with Areas of ESS in Color



ESS= Gradient of Velocity at Wall x Viscosity

Shear Stress: Frictional force/unit area acting on endothelial cells from the flow of viscous blood

Low ESS and disturbed flow (< 6-12 dynes/cm^2)

- Intensely atherogenic

Normal ESS and laminar flow (12-20 dynes/cm^2)

- No plaque

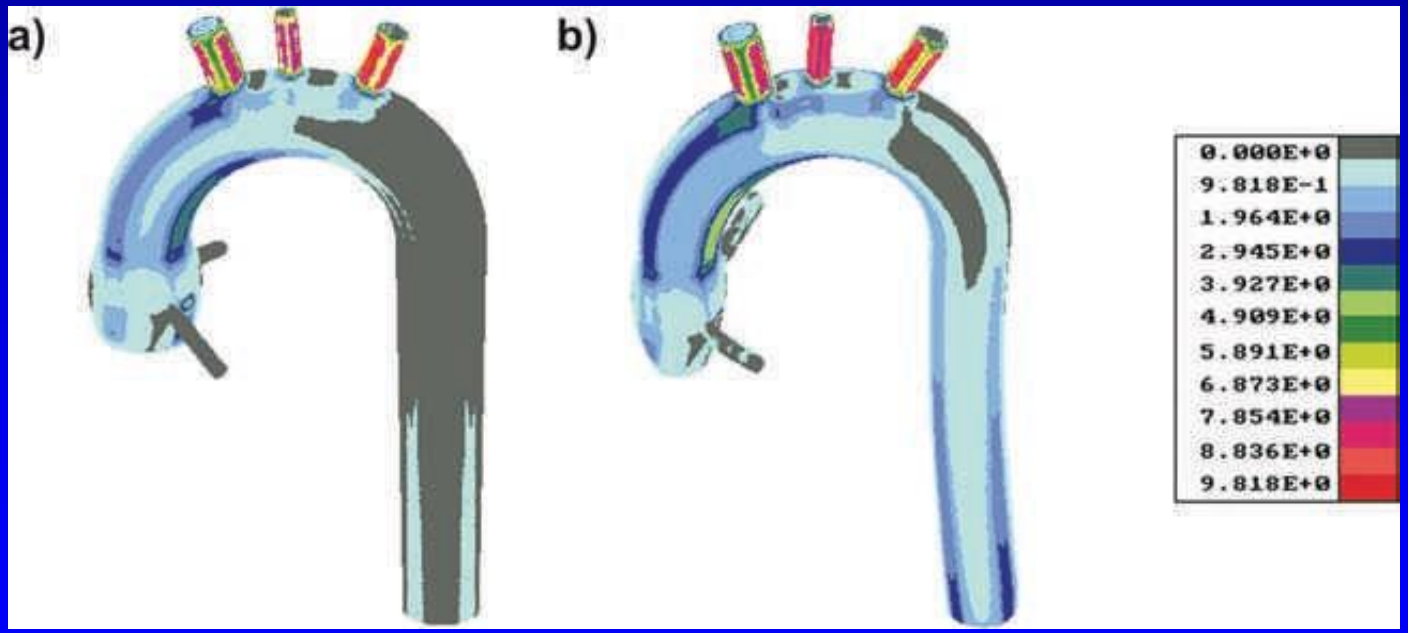
High ESS and turbulent flow (> 20 dynes/cm^2)

- Thrombus formation, and possibly plaque rupture

How do the Coronary Arteries Prevent from Having De Novo Plaque Formation?

1. A Young Aorta Avoids Low ESS in BIF by Vasoconstriction (Good vascular tone)

If the wall is flexible, not stiff from calcification, then the wall can constrict (smaller lumen, higher velocity so higher ESS)

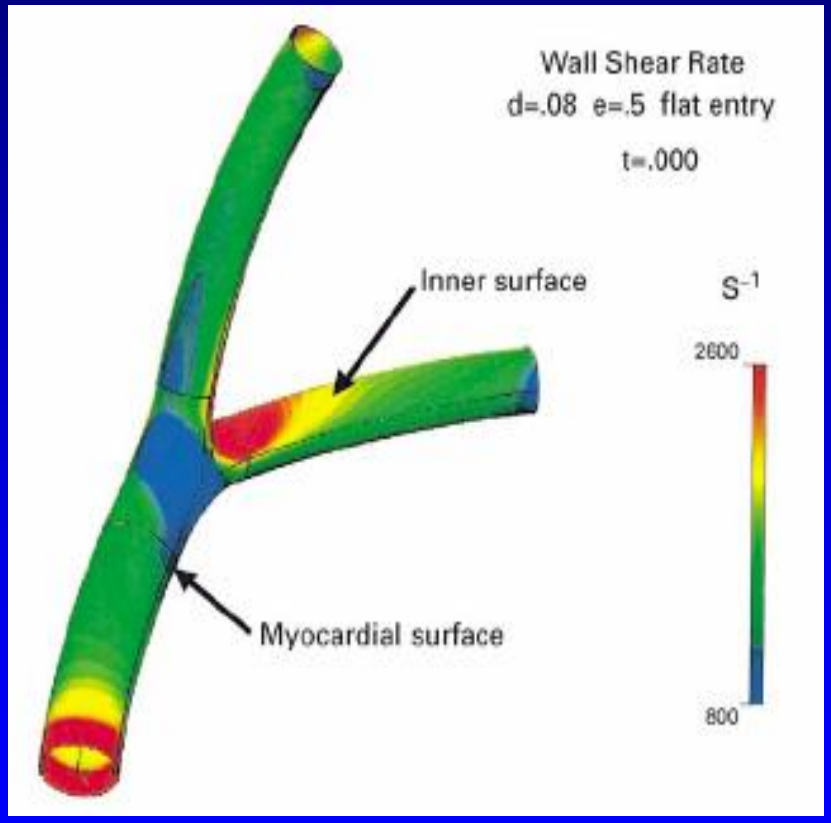


Diastole Systole

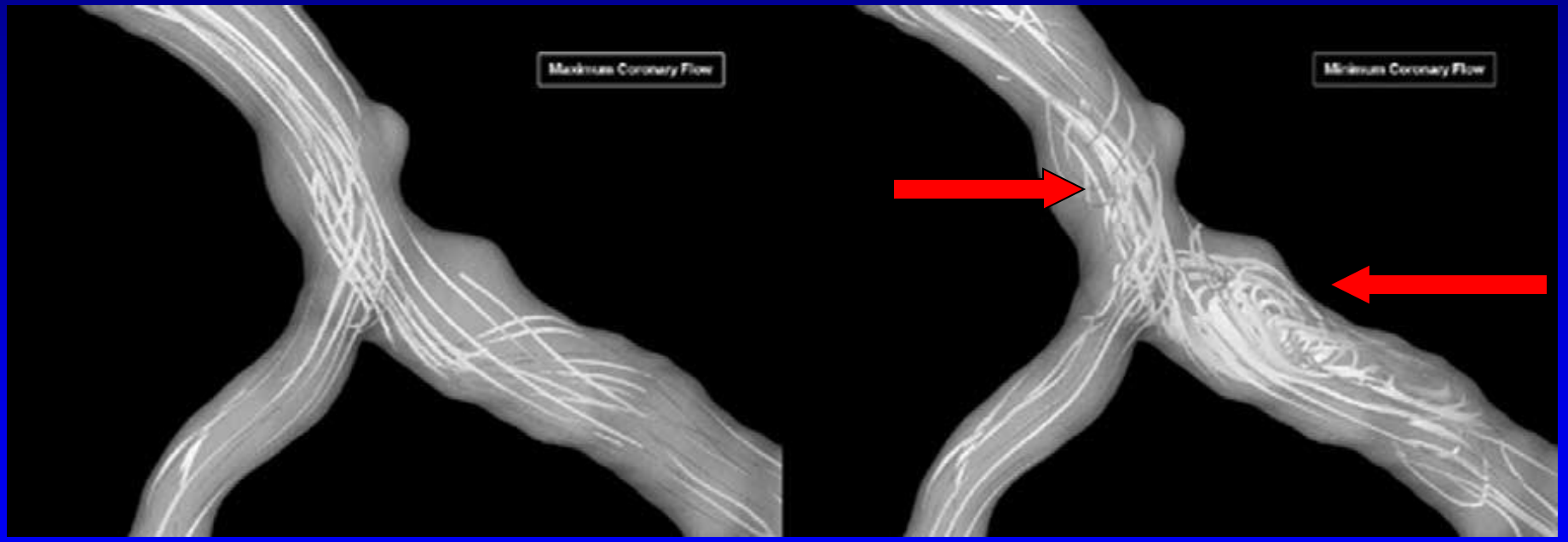
2. How the Young People Avoid Causing Low WSS in Bifurcation? By Vasoconstriction

If the wall is flexible, not stiff from calcification, then the wall can constrict (smaller lumen, higher velocity so higher WSS)

This is also the mechanism of negative remodeling. With a smaller lumen, the flow is higher and so the WSS



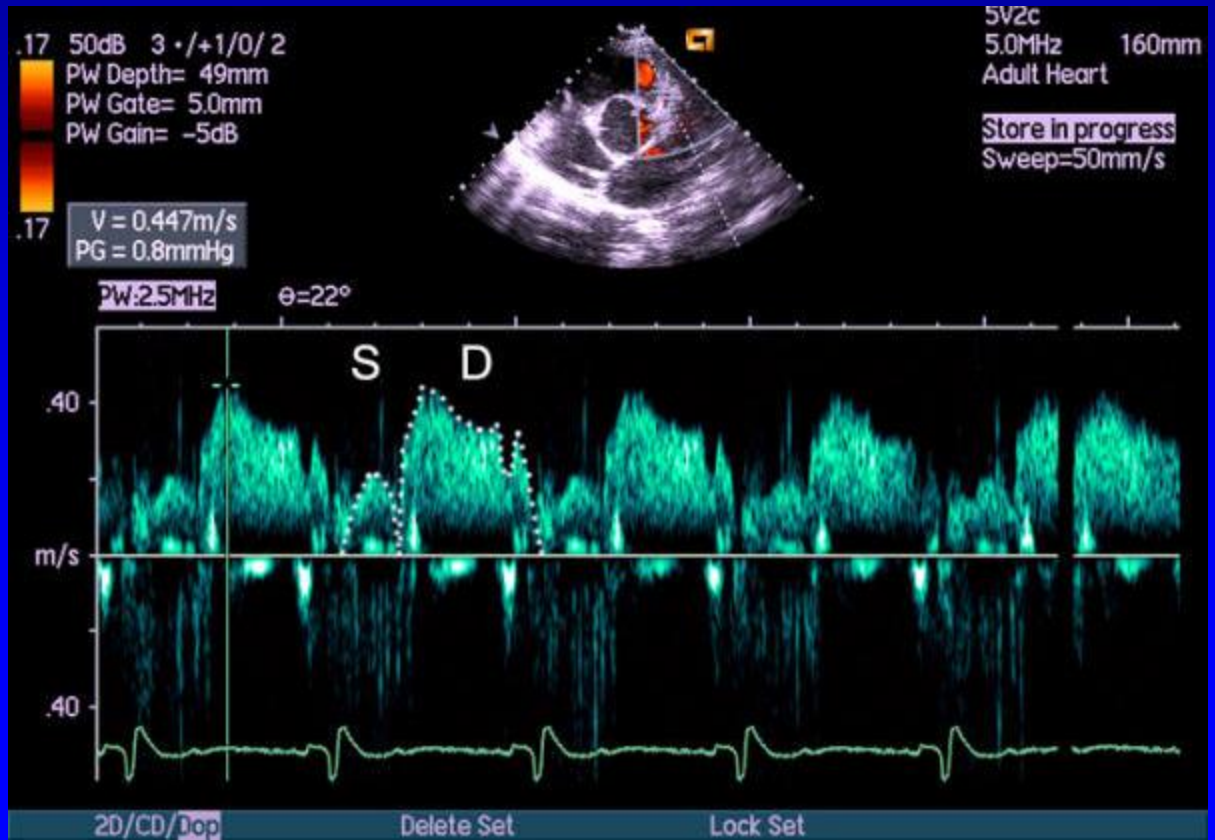
3.High Flow Causes Less Low ESS (while awake and when exercise)



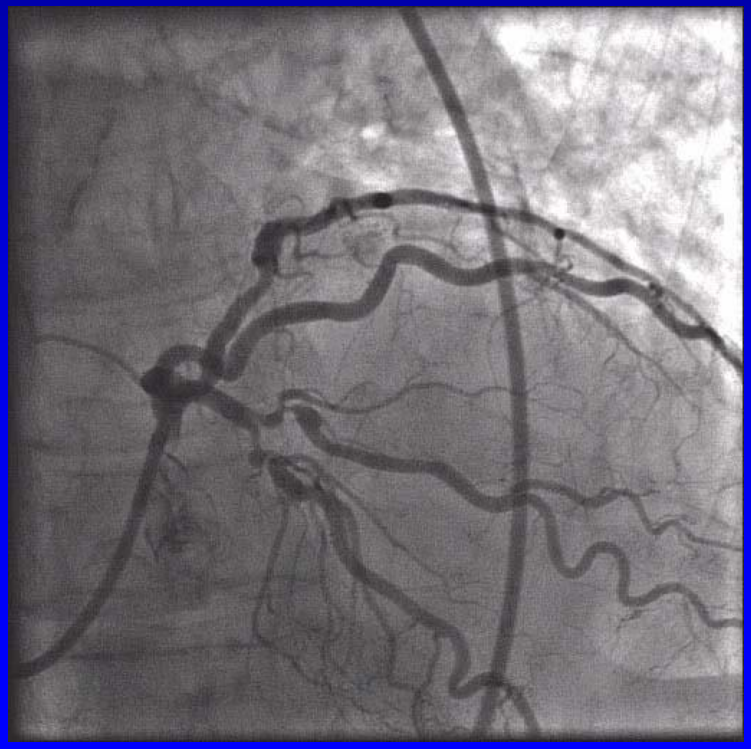
- Exercise with higher speed
- Resting with lower speed

4. ESS= Role of BetaBlockers

Betablocker slows the heart rate, prolong diastole, provide a higher flow in the coronary arteries



B. Second Observation: Why We have to Intervene at this Junction ? (Why we have to do PCI now?) Why we should not continue medical therary?



What are the Differences Between Medicine of the 20th Century and of the 21st Century?

Thinking and Expressing with the Language and Tools of the 21st Century

The Heart Functions like a Computer

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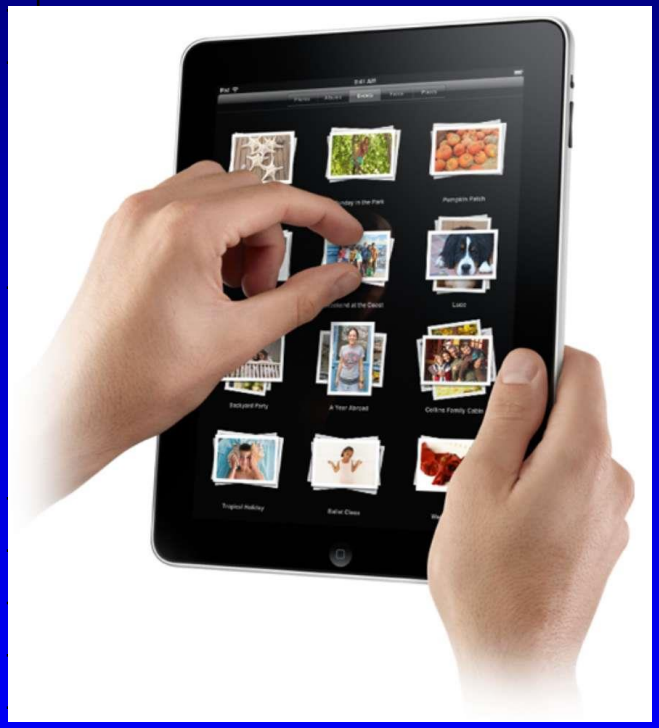
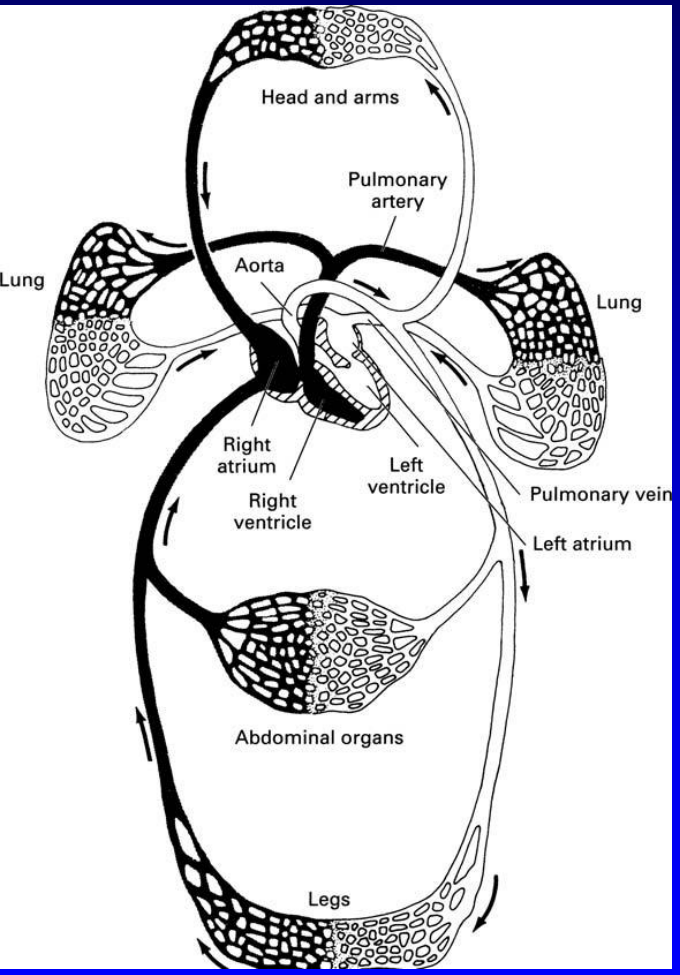


The HARDWARE 1

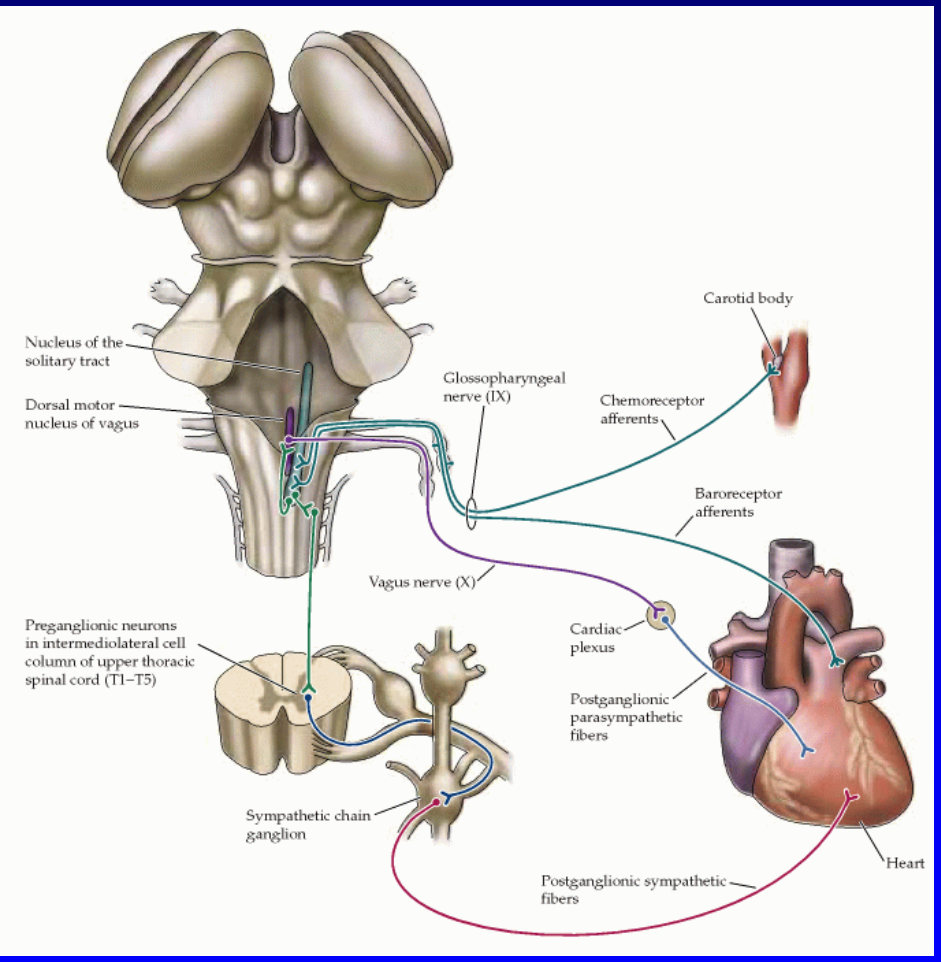


The pump = the heart

The irrigation network = the arterial and venous system

The carrier of data = the column of blood

The HARDWARE 3



The electrical system = The sympathetic and parasympathetic nervous system

The SOFTWARE

1. Programs to contract and relax the atria and ventricles

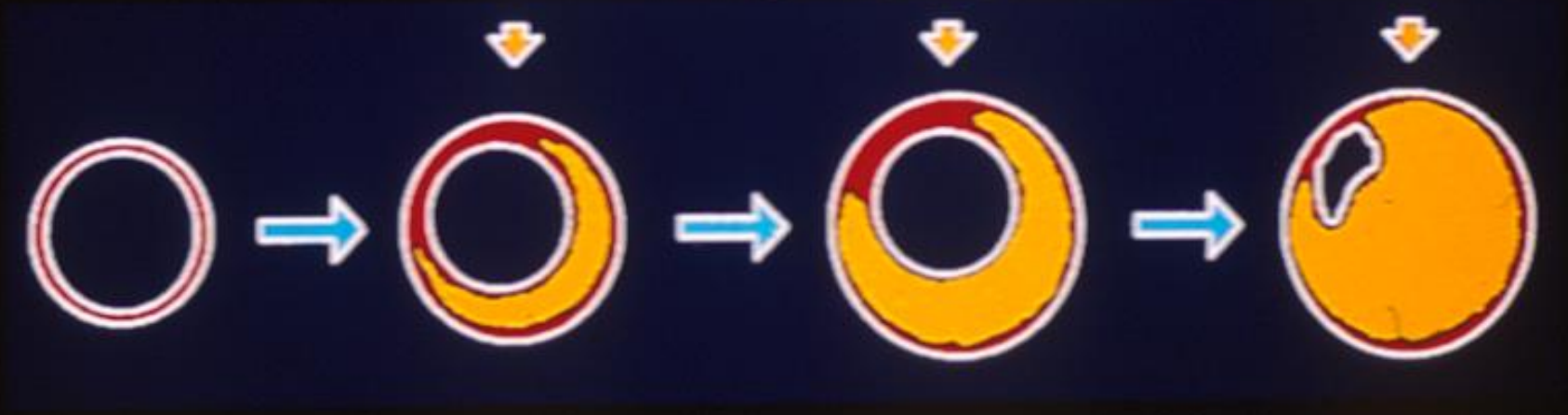
2. Programs to increase or decrease the heart rate

3. Programs to contract or to dilate the arteries

CORONARY REMODELING

Expansion Overcome: Lumen Narrows

Compensatory Expansion
- outluminal plaque growth



Normal Vessel

Minimal CAD

Moderate CAD

Severe CAD

Glagov S et al. *NEJM* 1987;316:1371-1375

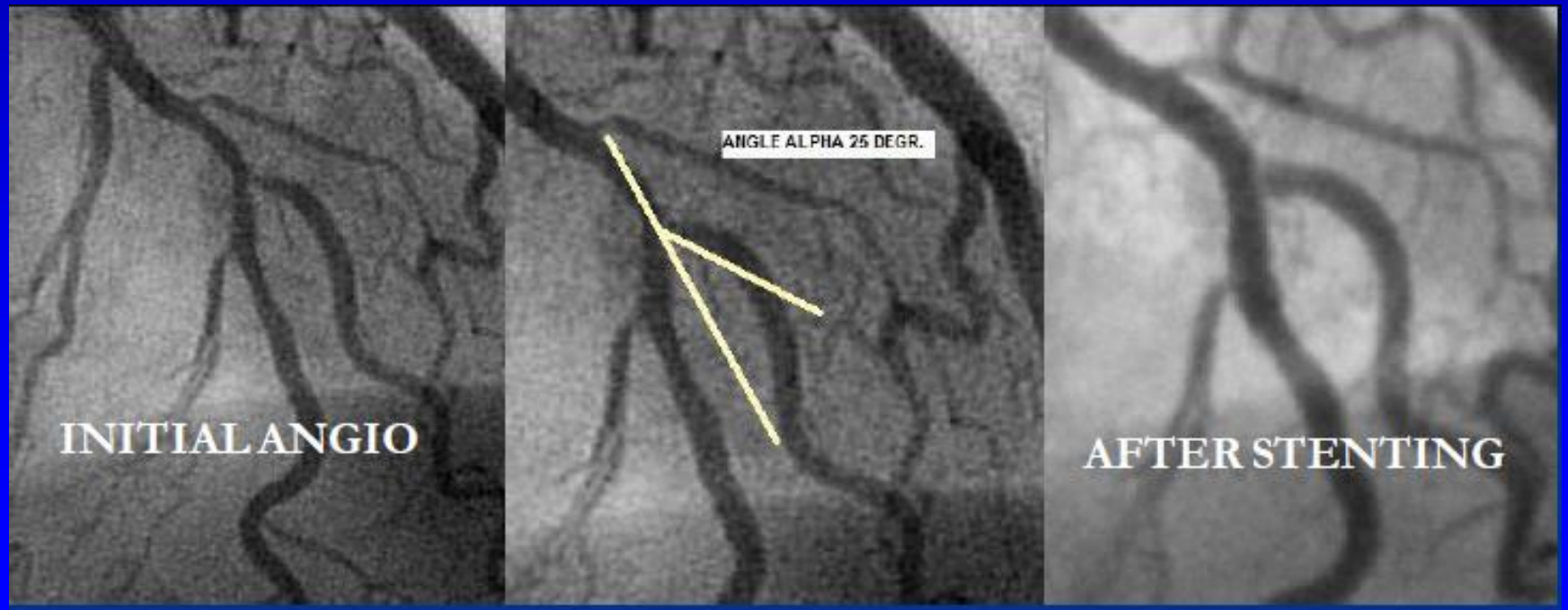
We have to Intervene at this Junction because the Software of the heart fails to keep the patient asymptomatic

C. Third Observation

Manipulation of Hardware, Software and Programming in PCI

1. Which are the Criteria for a Acute Perfect Hardware Correction in PCI of BIF Lesion?

Wide open SB and TIMI 3 flow in MB



2. Which are the Criteria for a Perfect Software Control after PCI?

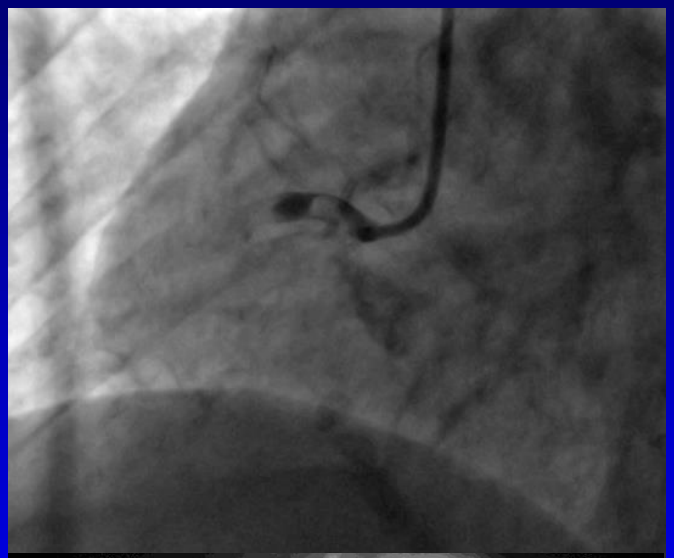
In the acute phase, the main goal is to avoid

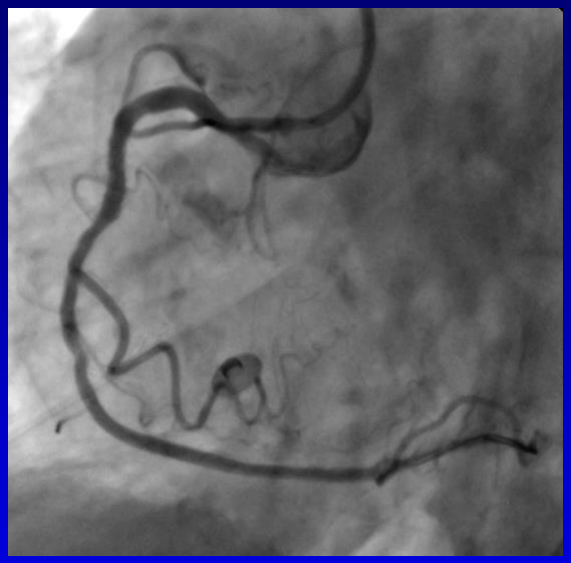
1. **Acute thrombotic formation** in the intrinsic and extrinsic pathway
2. **Platelet activation**

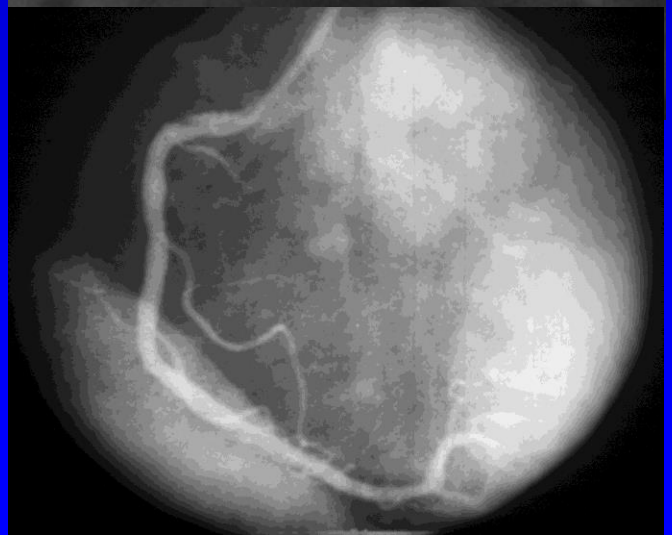
It is done by reprogramming the function of the coagulation cascade and of the platelets

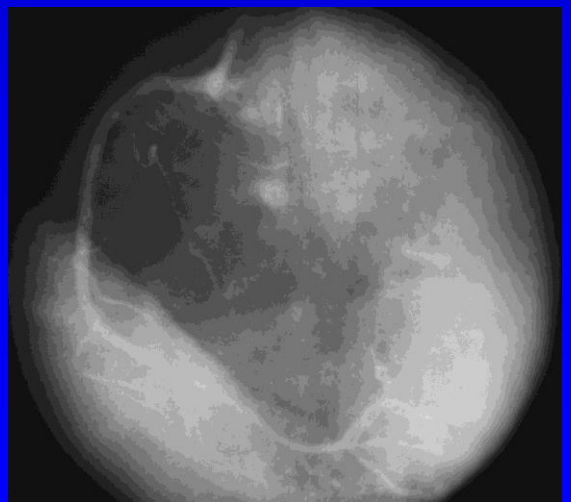
Observation 3.1a

Patient A had PTCA, Patient B had PCI with BMS and Patient C had DES. All had TIMI 3 Flow

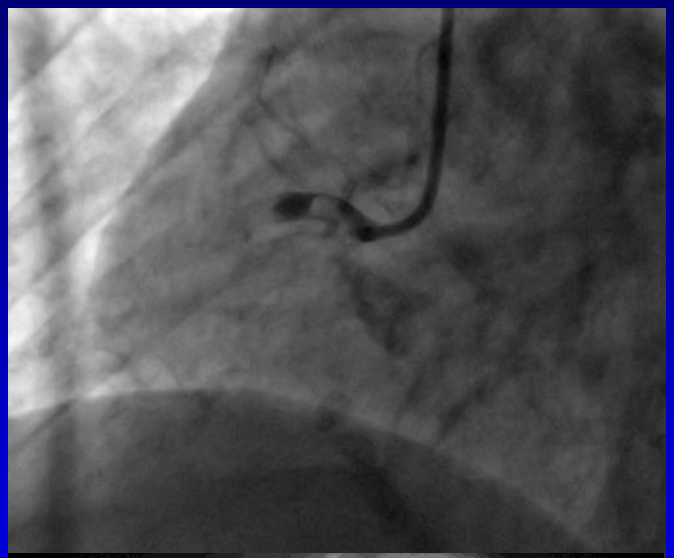


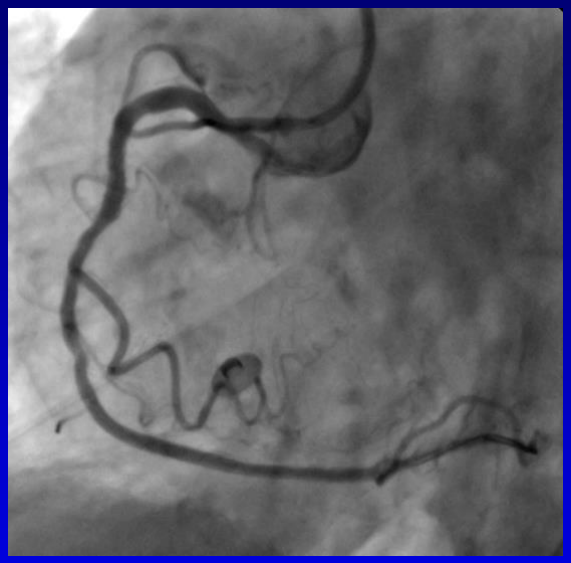


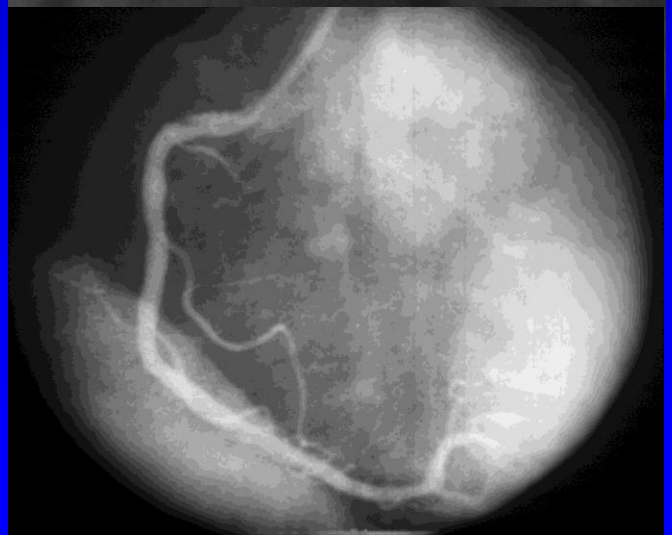


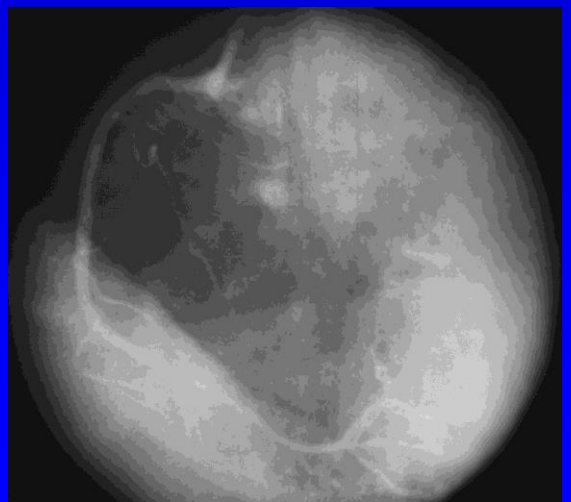


Observation 3.1b In 6 months what is the restenosis rate? and ejection fraction?

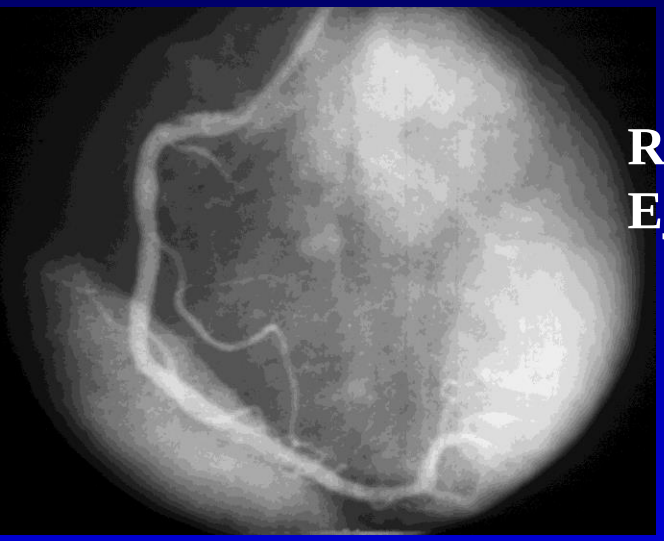




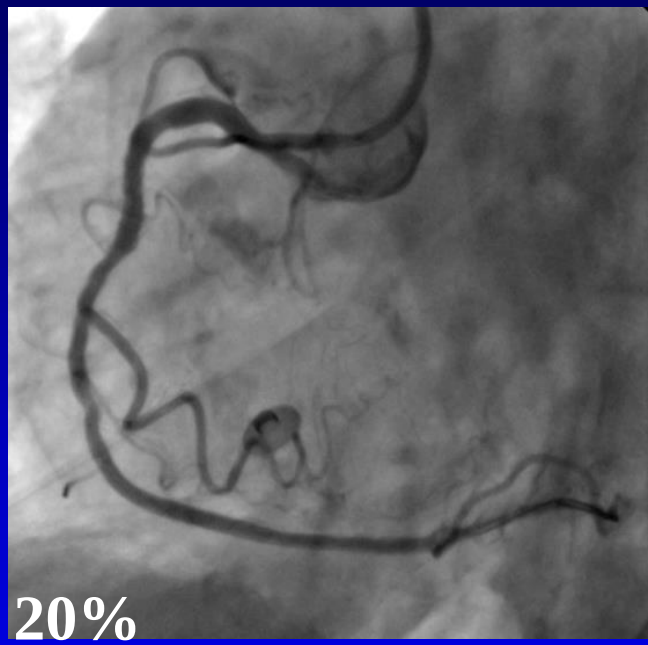




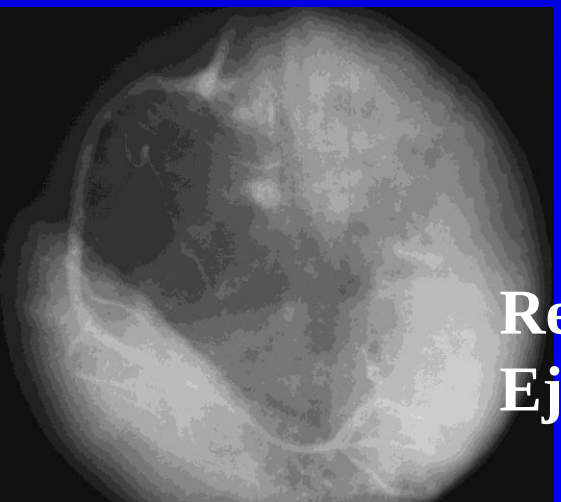
Observation 31.c In 6 months the restenosis rate and ejection fraction are:



Restenosis: 33%
Ejection fraction = 45%

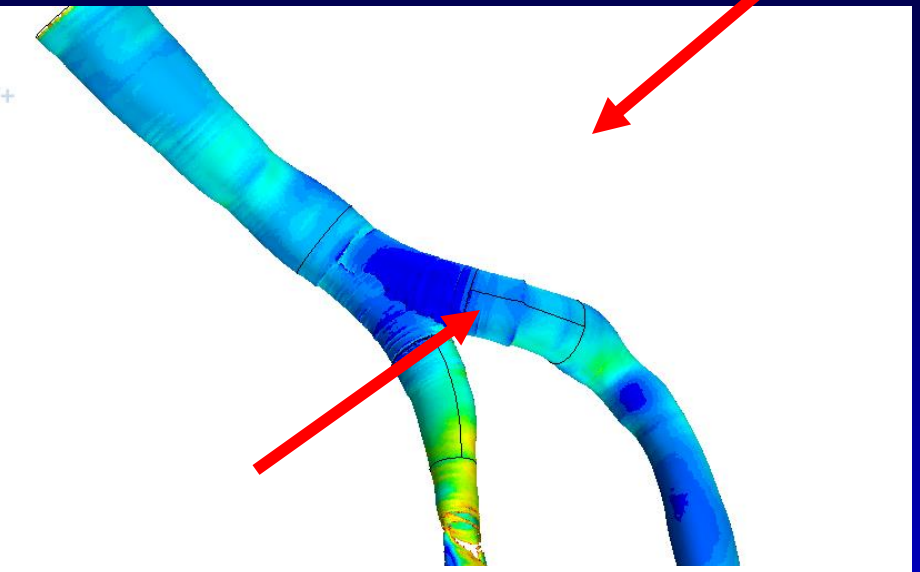


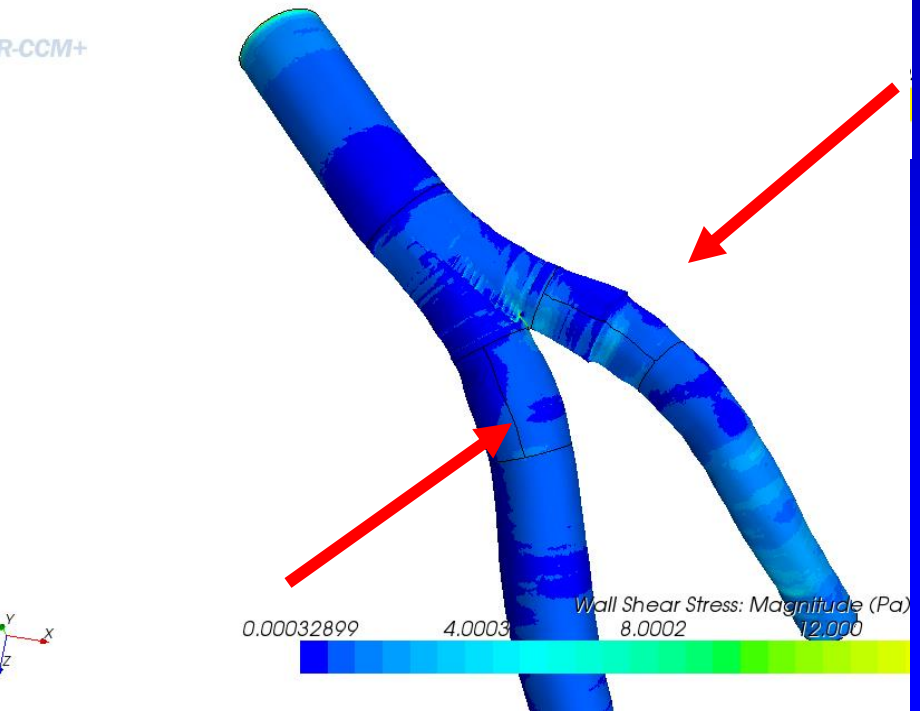
Restenosis: 20%
Ejection fraction = 45%

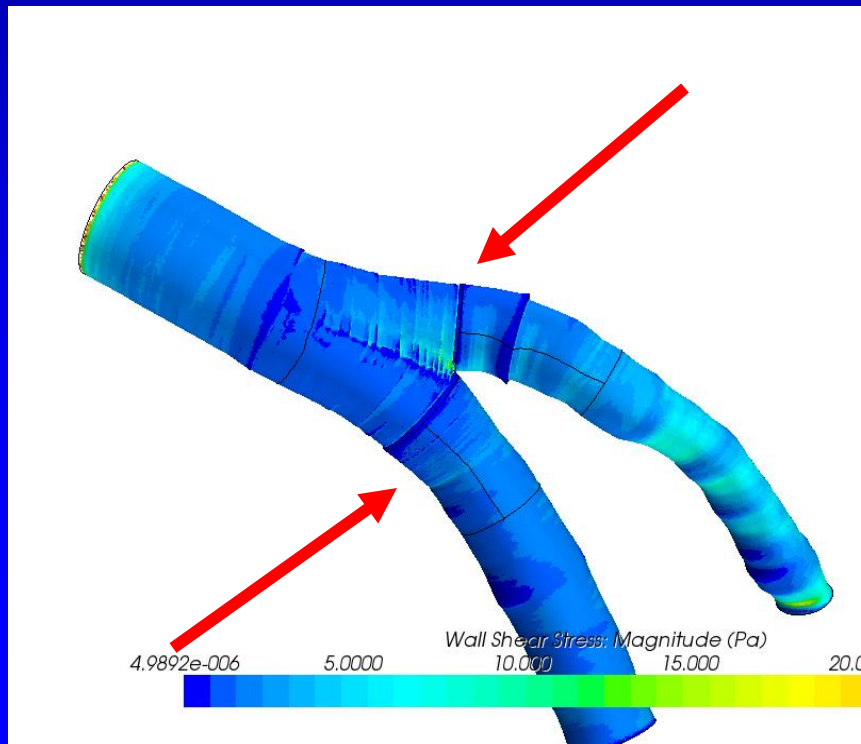


Restenosis: 10%
Ejection fraction = 55%

3. Why Low Shear Stress after DES does not cause Restenosis?







SOFTWARE overcomes the Detrimental EFFECT of HARDWARE

In patient receiving DES, effective programming of the drug (e.g. sirolimus) on the stent overcomes the detrimental mechanical effect of shear stress and prohibits the formation of scar tissue inside the stent and so prevents in-stent-restenosis

Conclusion 1: Priority Rank of Risk Factors Reduction for Primary Prevention (Prevention of Forming De Novo Lesion) SOFTWARE MANIPULATION

- 1. Prevent low shear stress (with normal vasoreactivity of the arterial wall)
- 2. Control high cholesterol level
- 3. No smoking
- 4. Control hypertension

Conclusion 2: Priority Rank of Goals for Prevention of Acute Occlusion Within 30 Days after Percutaneous Coronary Intervention (Hardware and Software Manipulation)

- 1. Excellent TIMI 3 flow
- 2. Low shear stress because the arterial wall is well covered by the metal struts
- 3. Wide open ostium of the sidebranch

Conclusion 3: Priority Rank of Goals for Long term Prevention of In-Stent Restenosis after PCI (Software Manipulation)

- 1. Endothelium well covered by drug
- 2. Persistent low shear stress
- 3. Low cholesterol level
- 4. Controlled blood pressure
- 5. No smoking

Thank You