공학적 이해와 임상적용을 위한
순환기질환 관련용어

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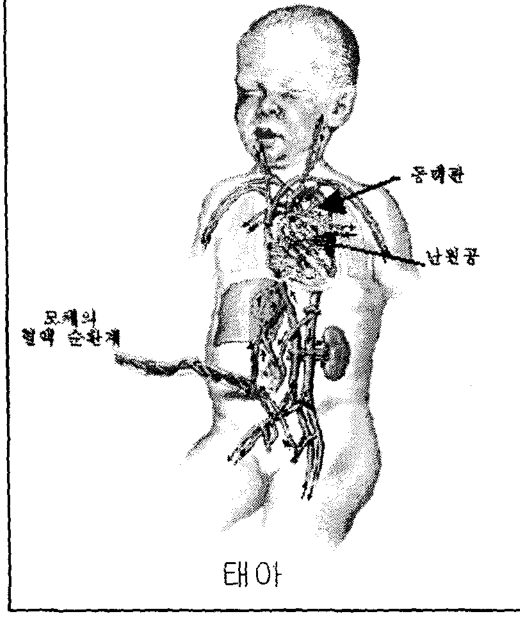
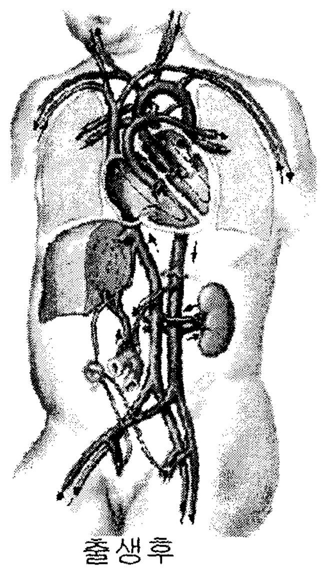
상계백병원 내과
이 병 권

출생전후의 순환계

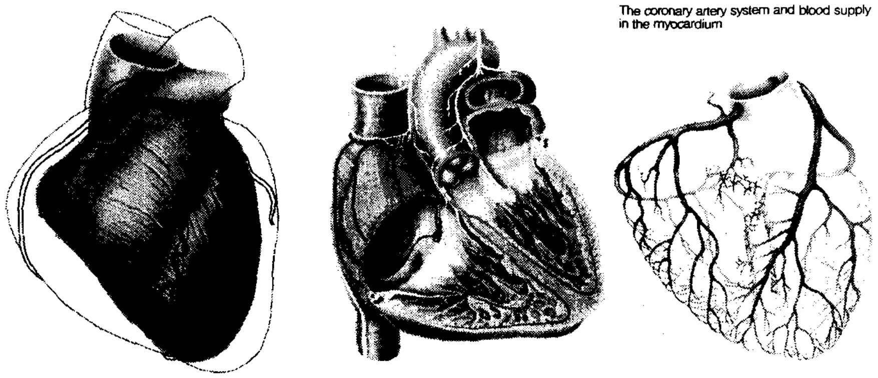


태아



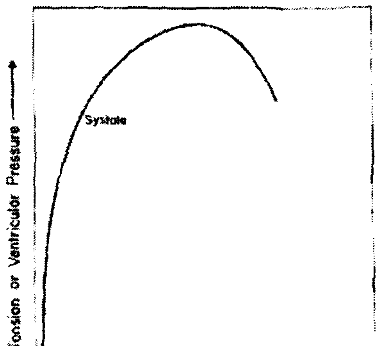
출생후

정상 심장의 해부학적 구조

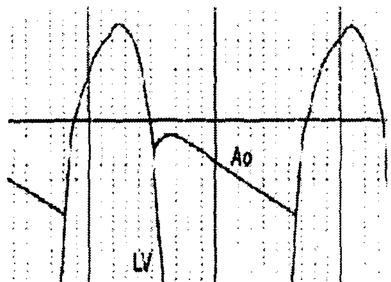


정상 순환계의 생리

심실의 압력-부피 곡선

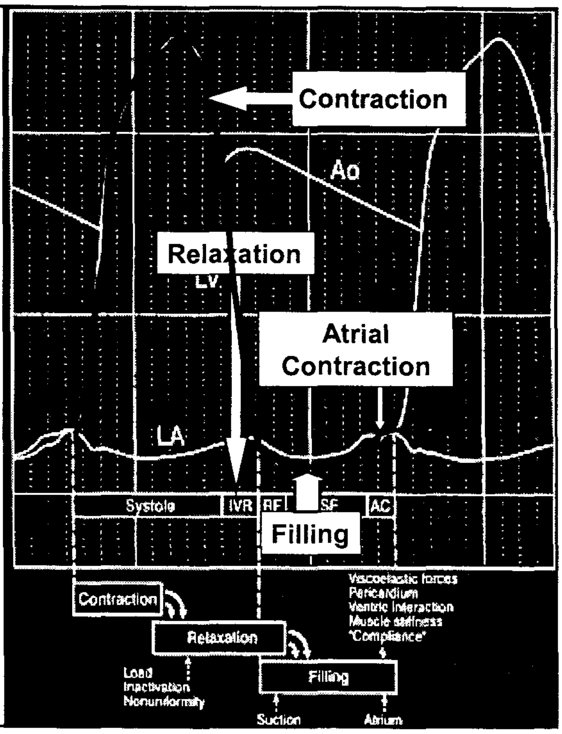


심실-심방-동맥의 압력 곡선



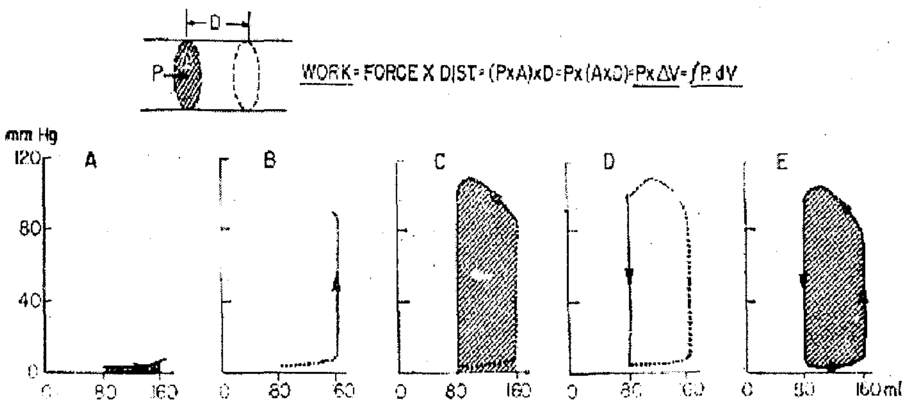
심장주기

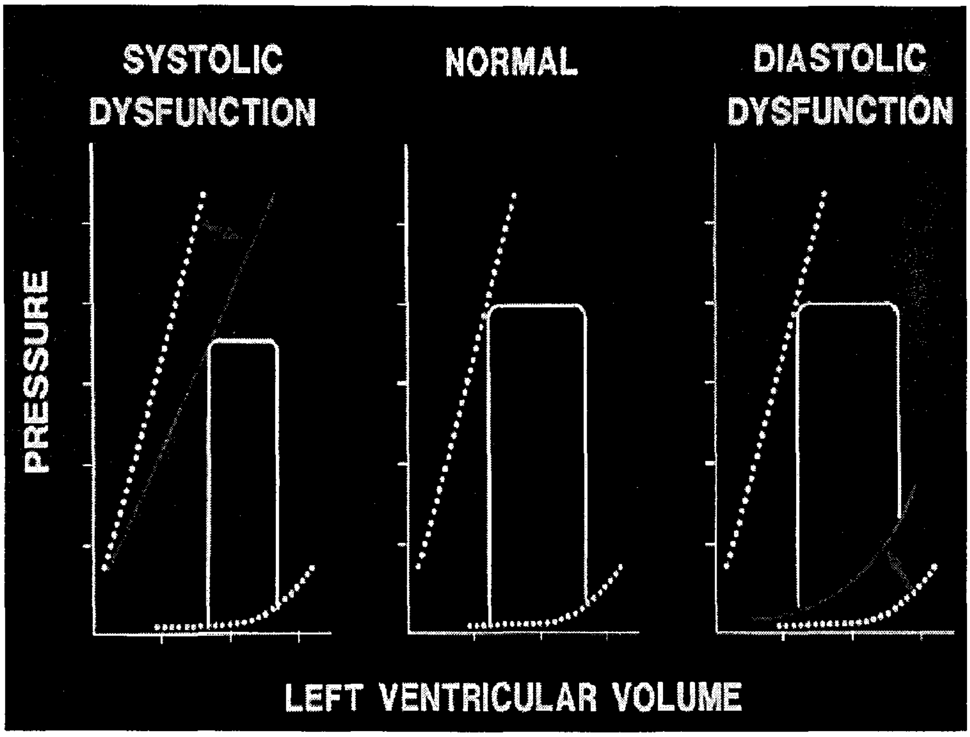
- **Contraction**
- **Relaxation**
- **Filling**
- **Atrial Contraction**



심장의 작업량

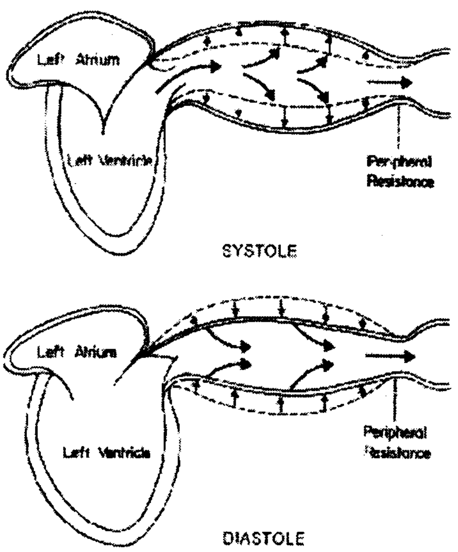
심장이 한 주기 동안 좌심실에서 일어난 압력과 용적의 변화

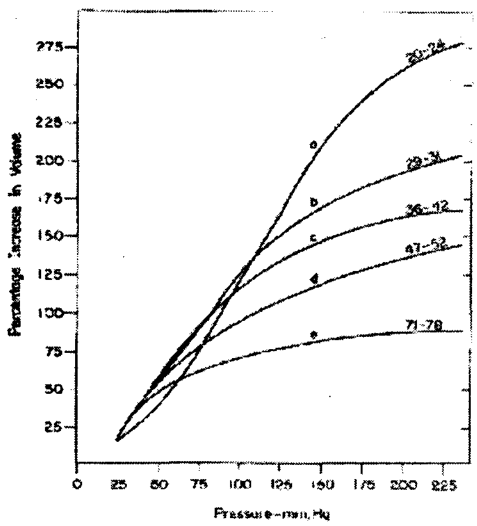




동맥

수압필터(hydraulic filter)로서의역할 ; compression chamber, pressure tank

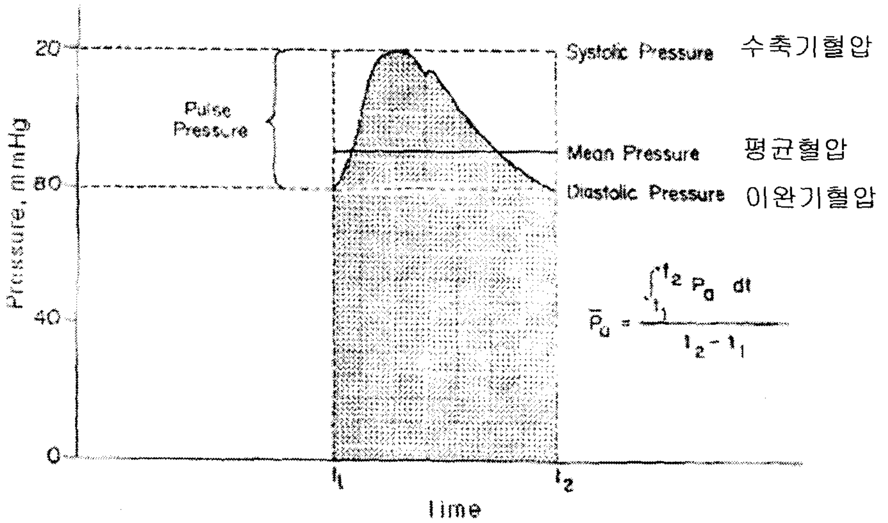




나이에 따라 compliance감소

혈압

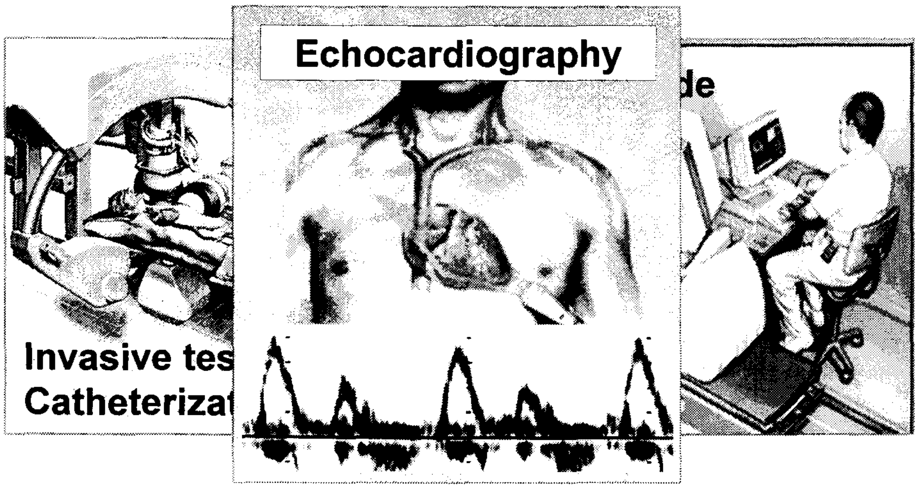
심근의 수축력, 동맥의 저항



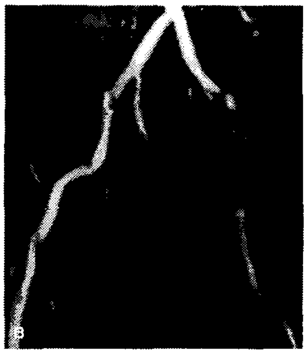
정상 순환계의 혈역학 수치

***Pressures* (mmHg)**	
Systemic arterial	
Peak systolic/end-diastolic	100-140/60-90
Mean	70-105
Left ventricle	
Peak systolic/end-diastolic	100-140/3-12
Left atrium (or pulmonary capillary wedge)	
Mean	2-10
a wave	3-15
v wave	3-15
Pulmonary artery	
Peak systolic/end-diastolic	15-30/4-12
Mean	9-18
Right ventricle	
Peak systolic/end-diastolic	15-30/2-8
Right atrium	
Mean	2-8
a wave	2-10
v wave	2-10
***Resistances* [(dyn×s)/cm5]**	
Systemic vascular resistance	700-1600
Pulmonary vascular resistance	20-130
Cardiac index [(L/min)/m2]	2.6-4.2
Oxygen consumption index [(L/min)/m2]	110-150
Arteriovenous oxygen difference (mL/L)	30-50

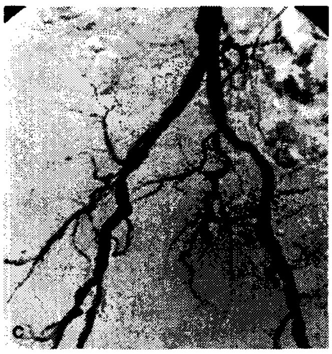
순환계 구조 및 기능의 평가



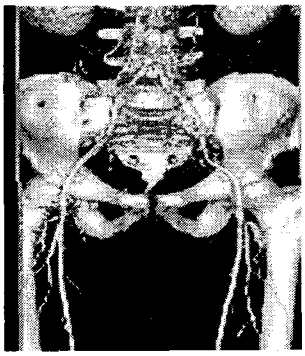
순환계 구조 및 기능의 평가



MRA



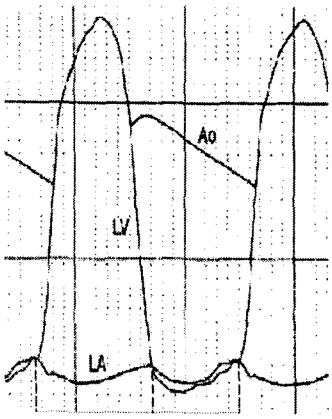
Angio

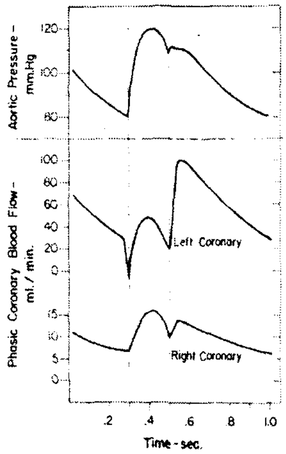


CTA

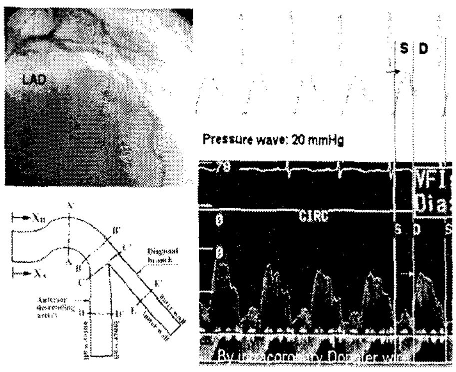
서로 다른 형태의 압력파형

- **Aorta**
- **Coronary**
- **Left ventricle**

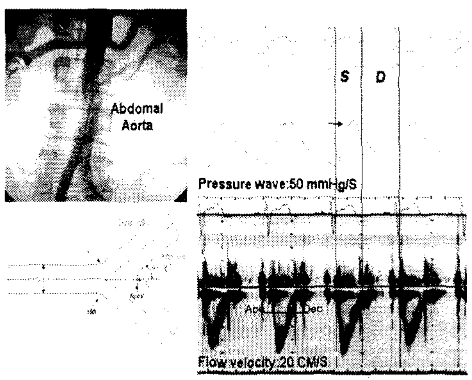




서로 다른 형태의 압력-혈류 파형



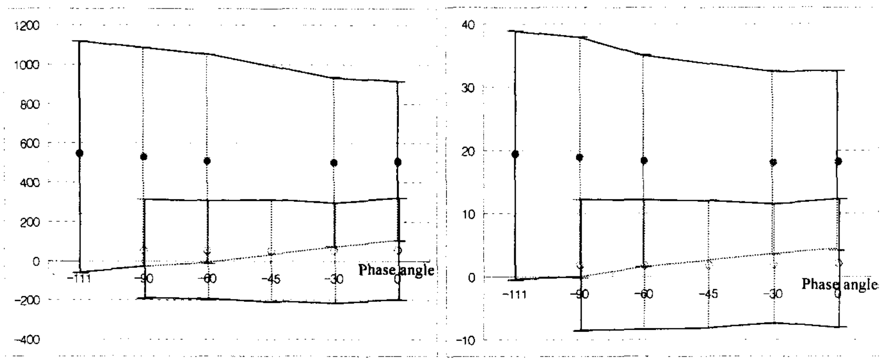
(a) Left coronary artery



(b) Abdominal aorta

서로 다른 형태의 전단응력 분포

○□ Coronary artery ○□ Abdominal Aorta



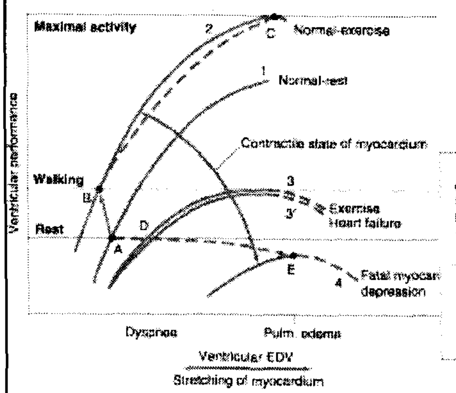
(a) Wall shear rate(1/sec) (b) Wall shear stress($dyne/cm^2$)

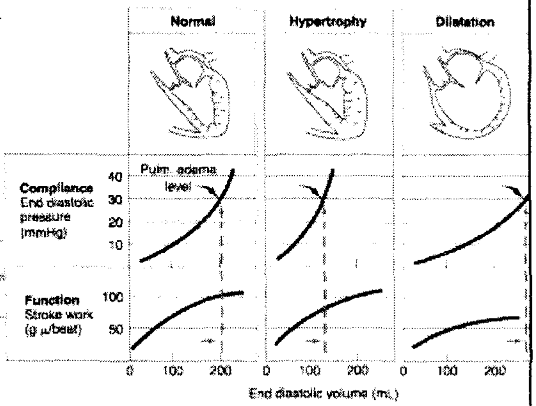
Influence of phase angle on the wall shear stresses for the coronary artery and abdominal aorta. The mean wall shear rate(WSR) and wall shear stress(WSS) of the coronary artery was more than 10 times higher than that of the abdominal aorta while the amplitude of WSR and WSS was double of the abdominal aorta.

순환기질환; 심장 및 혈관의 질환

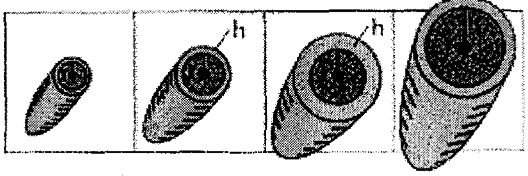
- 혈관질환
  관동맥질환
  말초혈관질환; 대동맥, 경동맥, 상하지 동맥, 내장 동맥
- 심장근육질환
  비후성, 확장성, 제한성
- 심장판막질환
  승모판, 대동맥판, 삼첨판, 폐동맥판
- 선천성 심장질환
- 부정맥
- 고혈압
- 심부전

심부전의 생리



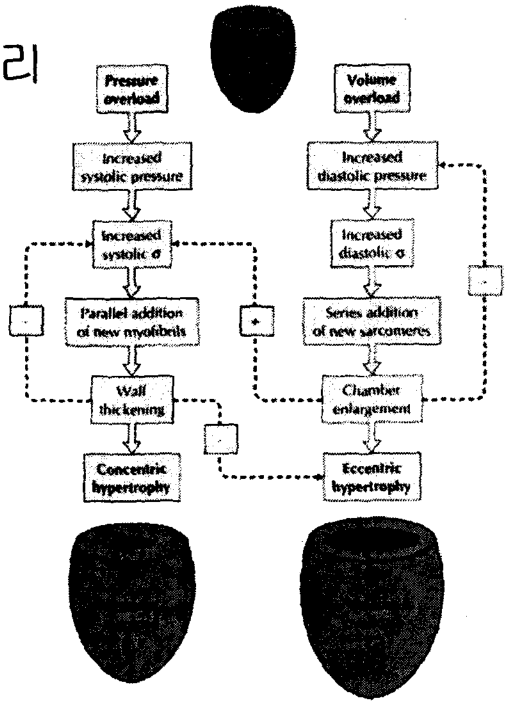


심부전의 생리

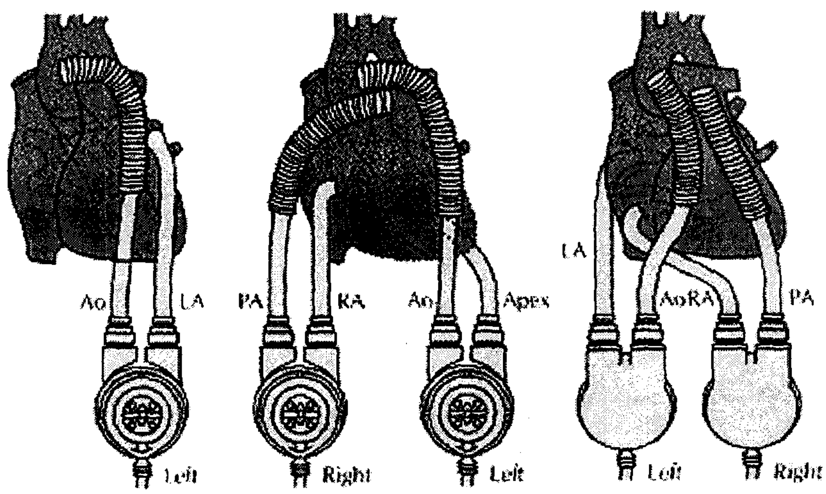


	Normal	Acute load	Compensatory hypertrophy	Cardiac failure
LV systolic pressure	N	+	+	+
LV radius	N	+	+	+
LV wall thickness	N	N	+	+
LV diastolic volume	N	+	+	++
Systolic wall stress	N	+	N	+
Diastolic wall stress	N	+	N	+

심부전의 생리

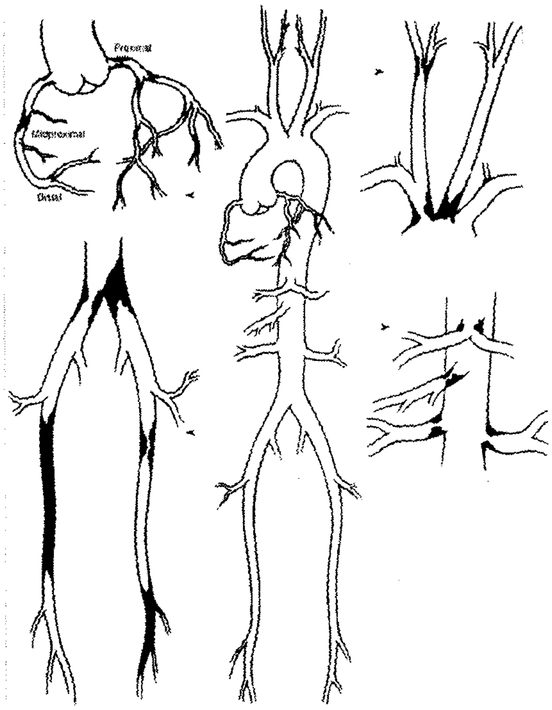


심부전의 보조 장치; **VAD**

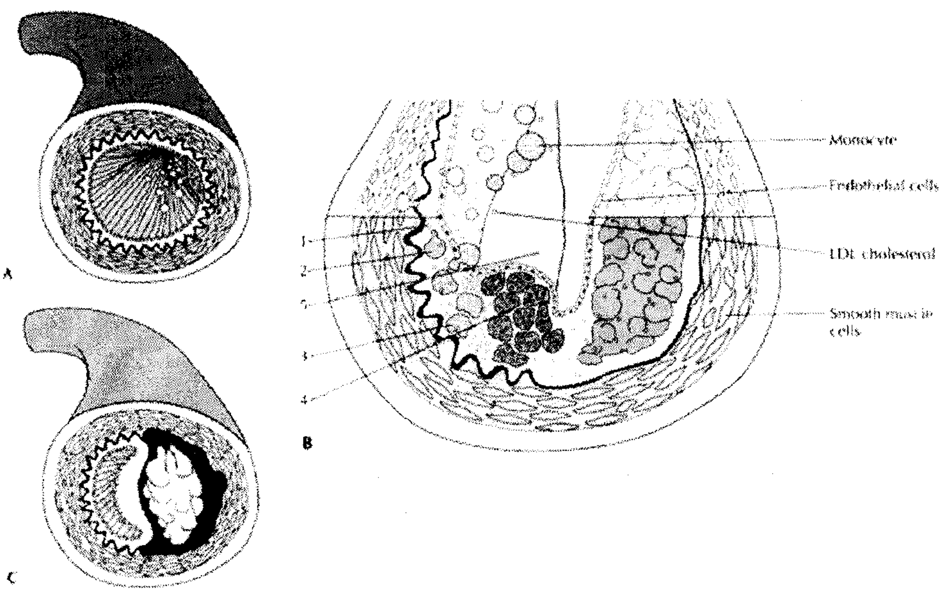


동맥경화의 호발부위

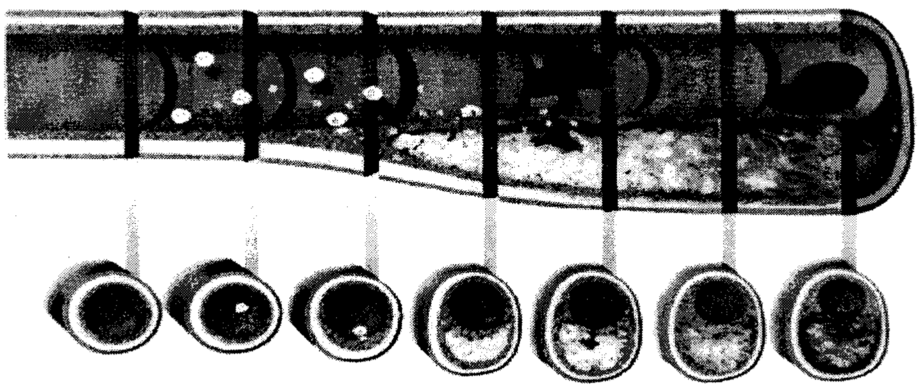
분지부, 만곡부



동맥경화의 발생기전



동맥경화의 발생기전



Circulation.2001;104:365-372. Libby P, et.al.

Caro CG, et al, 1969, Nature

Low shear area near bifurcation et al

↓

Prolong resident time for lipid, blood vessel cells (pleatlets, mononuclear cells)

↓

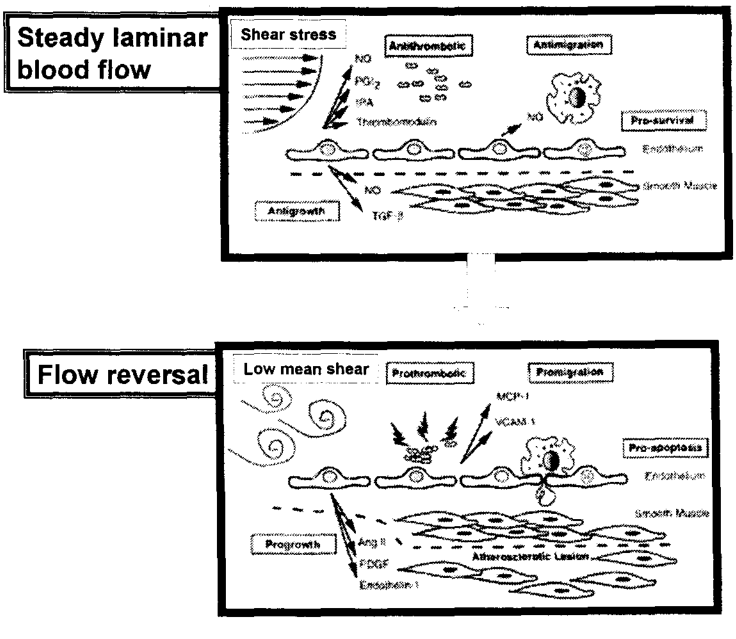
Favoring localized attachment, infiltration into arterial wall

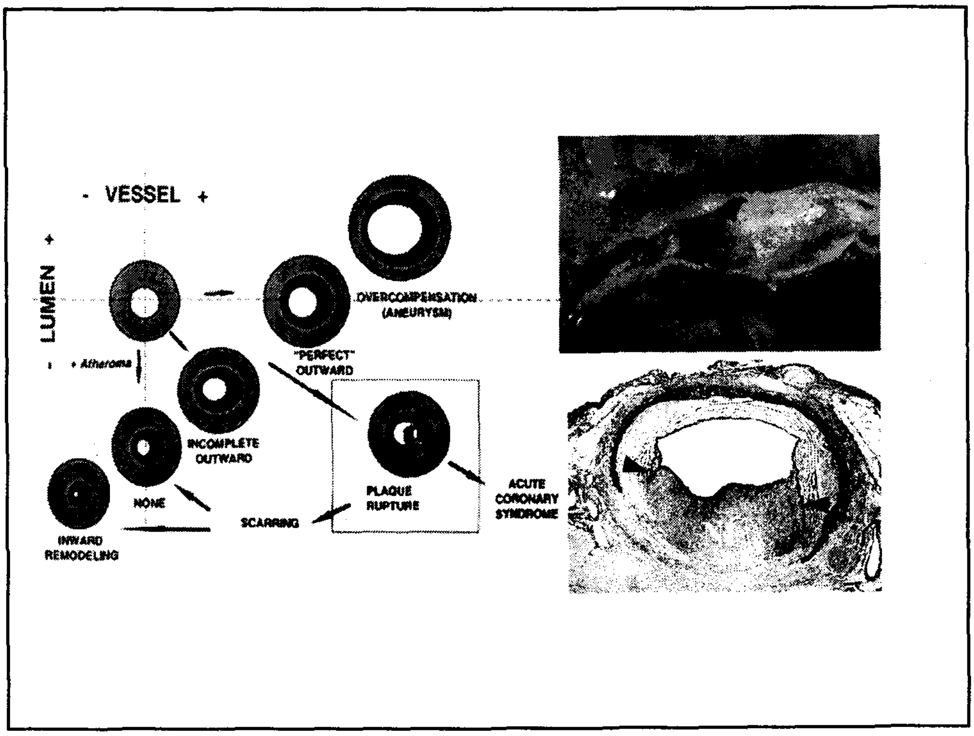
↓

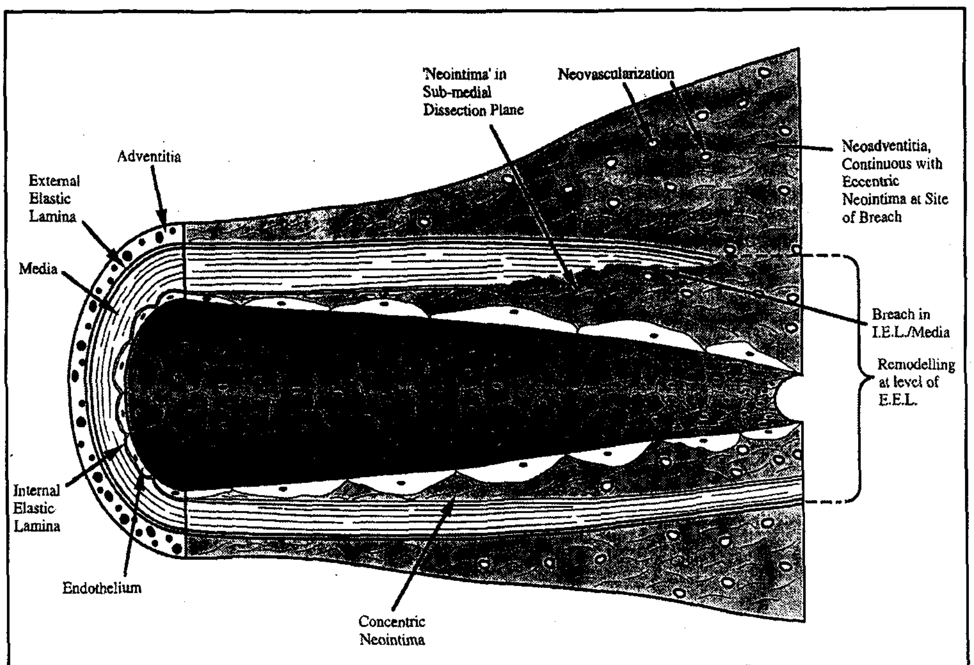
Localized accumulation of cytokines, growth factors, reactive oxygen species

$$\tau = \mu \frac{\delta U_T}{\delta n}$$

Shear stress(전단 응력) : The tractive or tangential forces generated at a surface by the flow of a viscous fluid
(unit of force per area = dyn/cm^2)




- VESSEL +
+ LUMEN -
+ Atheroma
OVERCOMPENSATION (ANEURYSM)
"PERFECT" OUTWARD
INCOMPLETE OUTWARD
NONE
INWARD REMODELING
PLAQUE RUPTURE
SCARRING
ACUTE CORONARY SYNDROME


'Neointima' in Sub-medial Dissection Plane
Neovascularization
Adventitia
External Elastic Lamina
Media
Internal Elastic Lamina
Endothelium
Concentric Neointima
Neoadventitia, Continuous with Eccentric Neointima at Site of Breach
Breach in I.E.L./Media
Remodelling at level of E.E.L.
NO TRAUMA
INCREASING TRAUMA

Temporal Gradients in Shear, but Not Spatial Gradients, Stimulate Endothelial Cell Proliferation

Charles R. White,* PhD; Mark Haidekker,* PhD; Xuping Bao, MD; John A. Frangos, PhD

Background—The effect of temporal and spatial gradients in shear on primary human endothelial cell (HUVEC) proliferation was investigated. The sudden-expansion flow chamber (SEFC) model was used to differentiate the effect of temporal gradients in shear from that of spatial gradients. With a sudden onset of flow, cells are exposed to both temporal and spatial gradients of shear. The temporal gradients can be eliminated by slowly ramping up the flow.

Methods and Results—HUVEC proliferation in the SEFC remained unstimulated when the onset of flow was slowly ramped. Sudden onset of flow stimulated a 109% increase of HUVEC proliferation relative to ramped onsets within the region of flow reattachment. To further separate temporal and spatial gradients, a conventional parallel-plate flow chamber was used. A single 0.5-second impulse of 10 dyne/cm² increased HUVEC proliferation 54±3% relative to control. When flow was slowly ramped over 30 seconds, HUVEC proliferation was not significantly different from controls. Steady laminar shear over 20 minutes inhibited HUVEC proliferation relative to controls regardless of step (36±8%) or ramp (21±5%) onsets of flow.

Conclusions—The results indicate that temporal gradients in shear stress stimulate endothelial cell proliferation, whereas spatial gradients affect endothelial proliferation no differently than steady uniform shear stress. (*Circulation*. 2001;103:2508-2513.)

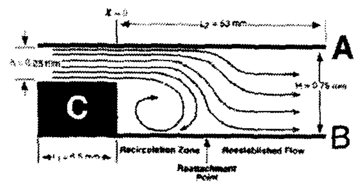


Figure 1. Cross section of SEFC. Flow channel (21 mm wide) is formed between polycarbonate body (A) and glass slide (B), where cell monolayer is grown. Two silicone gaskets with different-size openings provide inflow channel and sudden-expansion step (C). Inflow channel is sufficiently long (6.5 mm) to ensure parabolic velocity profile before expansion point, and after ~15 mm, flow assumed parabolic profile that can be observed in equivalent PPFC. All locations are given relative to sudden-expansion point (x=0). Fluid flows from left to right in direction of arrows.

Hemodynamic forces have long been implicated in the initiation and localization of atherosclerosis. Given the focal nature of plaque formation within regions of arterial curvatures, branches, and bifurcations, it has been suggested that certain characteristics of fluid shear stress unique to these regions may potentiate atherogenesis.[1] Detailed analyses of *fluid mechanics in atherosclerosis-susceptible regions of the* vasculature have identified unique patterns of disturbed flow characterized by regions of flow separation, recirculation, reattachment, and perhaps most importantly, significant temporal and spatial gradients of shear stress.[1,2] Temporal shear stress gradients are defined as the increase or decrease of shear stress over a small period of time at the same location, whereas spatial shear stress gradients are defined as the difference of shear stress between 2 close points of a cell at the same point in time. To date, the role of temporal and spatial gradients of shear stress in the pathogenesis of atherosclerosis remains unclear. Some studies link atherogenesis to the large temporal gradients in shear due to the change of shear direction,[2,3] whereas others relate this to different spatial distributions of mean wall shear stress.[4]

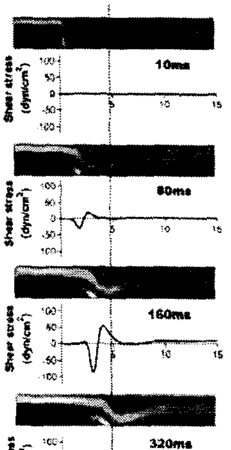


Figure 2. Development of recirculation eddy during onset phase of flow. Top frame shows flow in channel after 10 ms, where small eddy has already developed. *Blue colors indicate forward* flow, whereas red tint represents flow to left (backward). White bars indicate approximate direction of flow. Graphs show corresponding wall shear stress. Frames that follow show developing primary eddy after 80 and 160 ms. Secondary eddy at top becomes visible. Bottom frame shows fully established steady flow after 320 ms. Final steady-state reattachment point is indicated by dotted line.

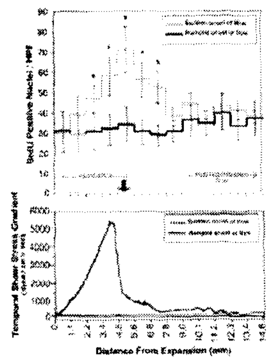
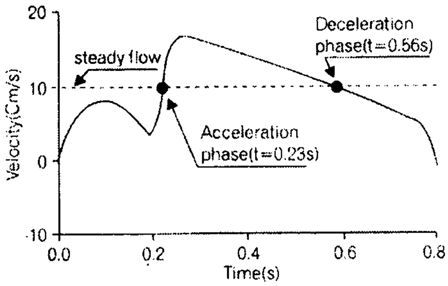
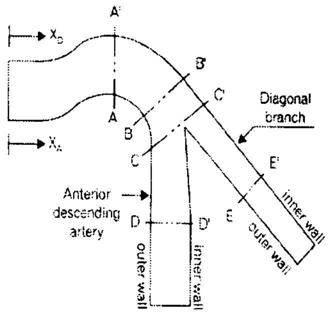


Figure 3. Effect of ramped and sudden onset of flow in SEFC on HUVEC proliferation. Top, Proliferation rate of HUVECs exposed to 4 hours of recirculating flow. Initial onset of flow was either 15-second ramped onset (n=5) or sudden onset (n=7). Arrow indicates calculated point of flow reattachment. Asterisks indicate significant difference between corresponding regions of ramped onset and sudden onset (P<0.05). Bottom, Profile of maximum temporal shear stress gradient downstream from expansion point for sudden onset of flow (maximum gradient 5200 dyne · cm^{-2} · s^{-1}) and for slowly ramped flow (maximum gradient 10 dyne · cm^{-2} · s^{-1}). Note that cells were subjected to range of temporal and spatial gradients. Significant stimulation of proliferation occurred in regions (segment 6.7 to 7.8 mm) corresponding to temporal gradients (955 dyne · cm^{-2} · s^{-1}) observed in vivo.[2] In contrast, a large range of spatial gradients (0 to 4000 dyne/cm³, calculation not shown), which include physiologically relevant gradients,[21] were unable to stimulate proliferation in absence of temporal gradients in ramp flow.

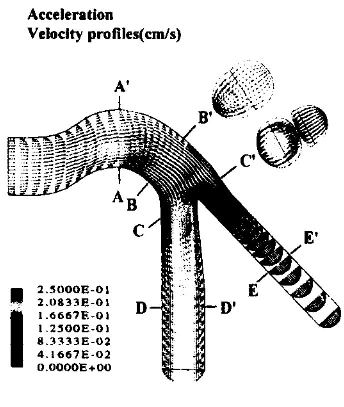
Coronary model

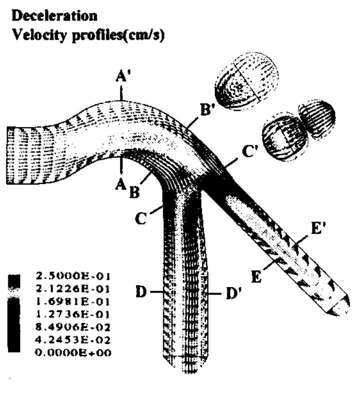


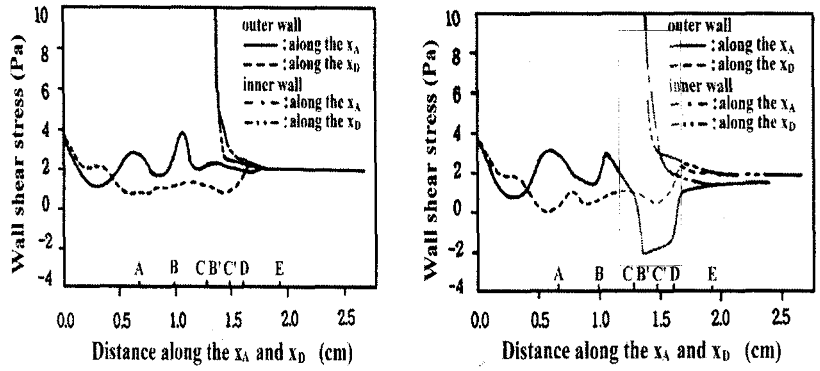


(a) Left coronary artery model

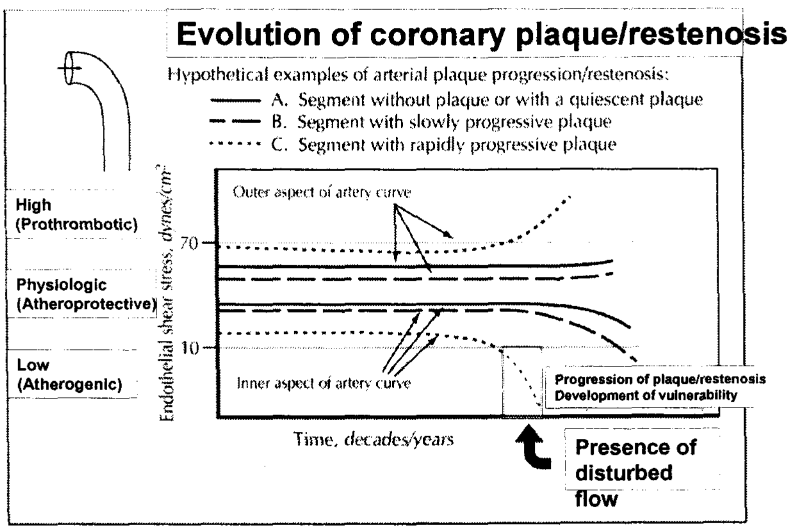
(b) Left coronary angiogram(LAO view)







(a) acceleration phase (b) deceleration phase



Feldman, et al, Curr Opin Caridiol, 15:430, 2000

Atherogenic arterial geometry

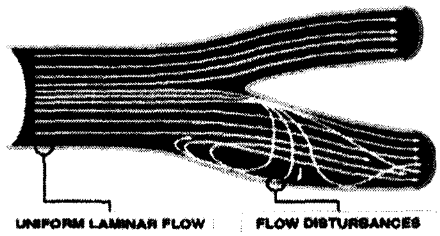
: Branch points, Bifurcations, Curves

Texon et al, Arch Intern Med, 99:418, 1957

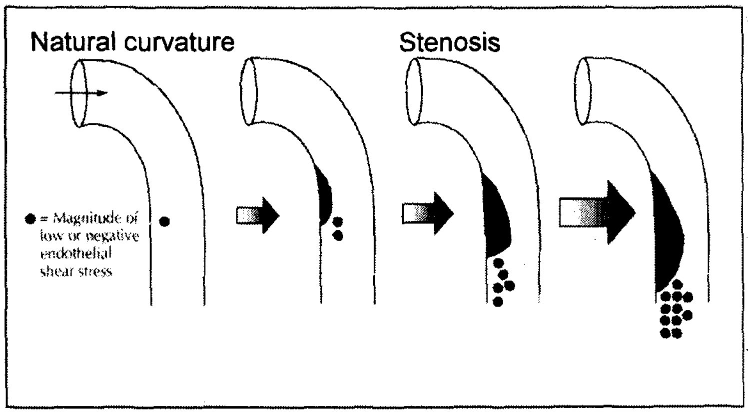
Disturbed laminar shear stress

- Flow seperation
- Recirculation
- Reattachment
- Temporal and spatial gradient of shear stress

El-Masry OA, et al, Circ Res, 43:608, 1978
Gidden DP, et al, J Biomech Eng, 115:588, 1993



Evolution of atherosclerotic plaque



Self-amplifying manner

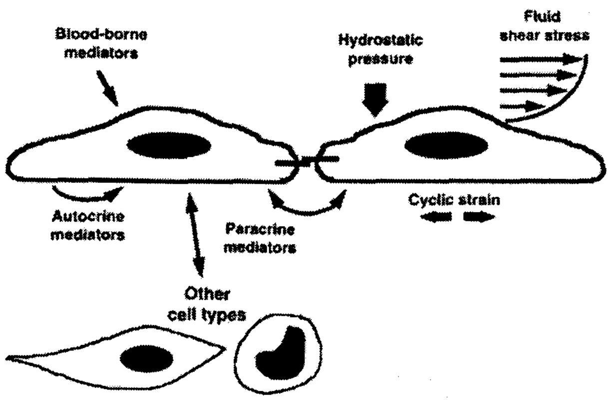
Nosovitsky VA et al. Computer and Biomed Res 1997, 9:575–580

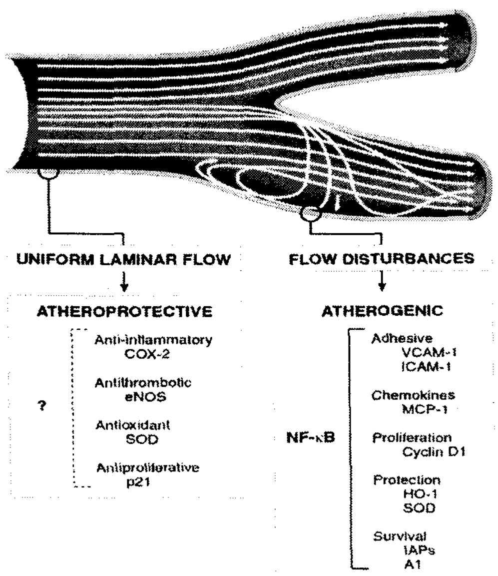
Shear stress

Cyclic strains(stretch)

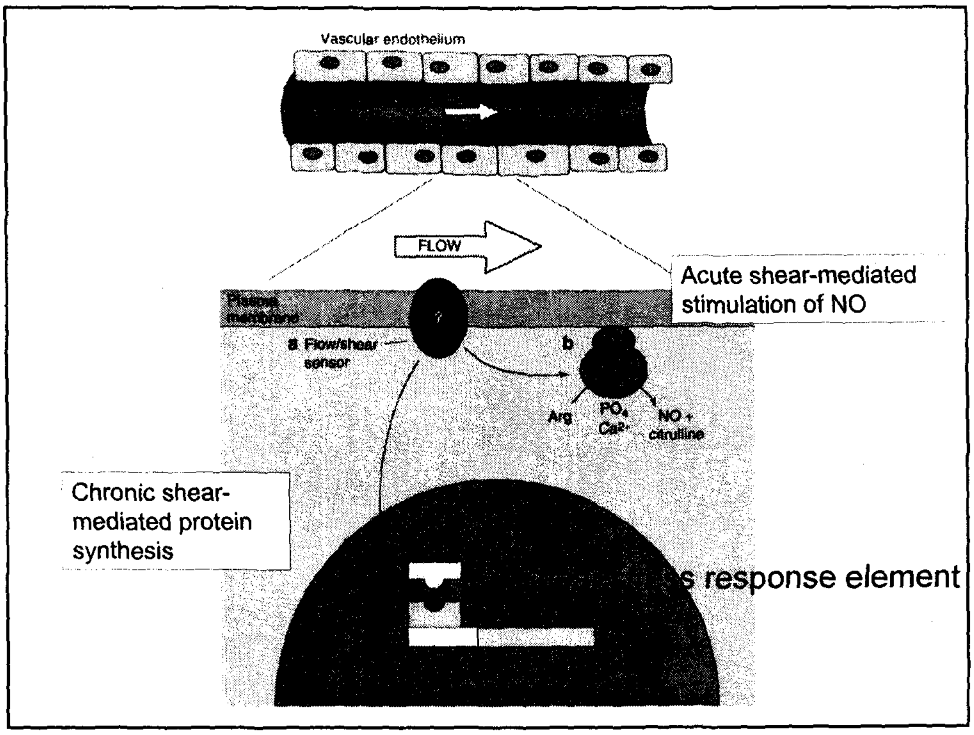
Hydrostatic pressure

Biochemical | **Biomechanical**

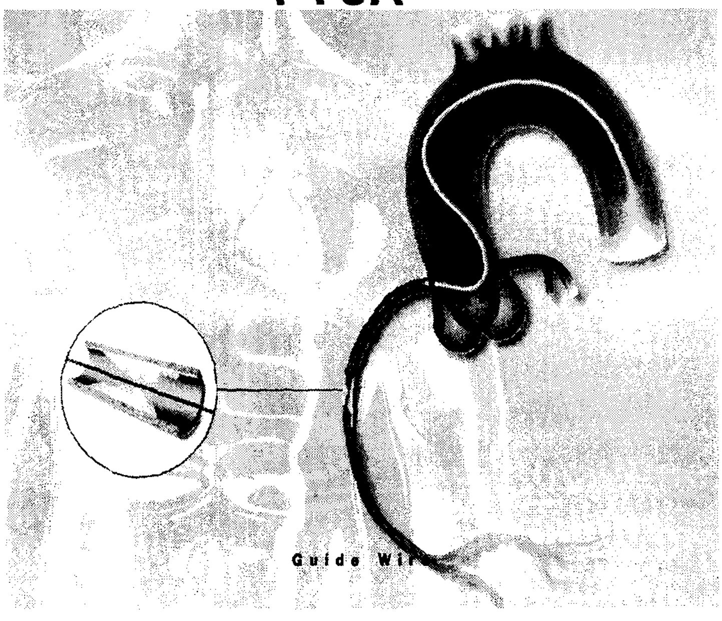




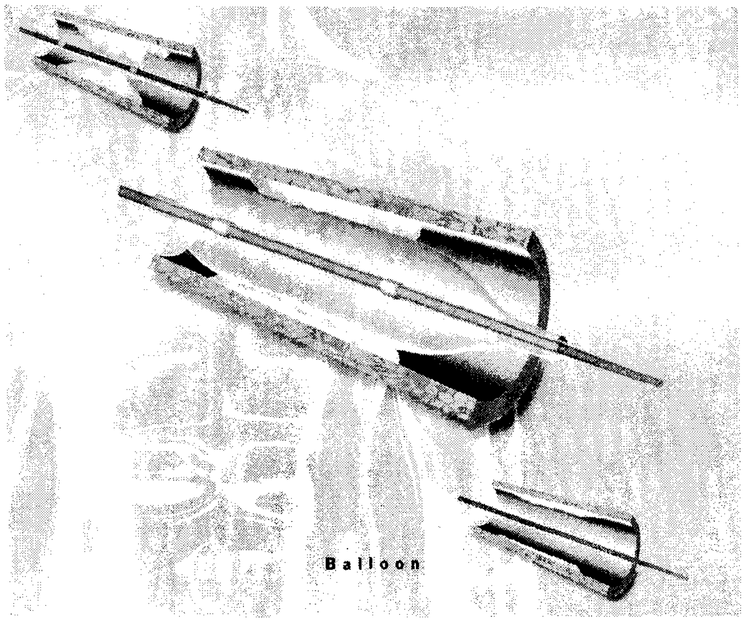
Tucker C et al, JCI. 2001;107:255


Vascular endothelium
FLOW
Acute shear-mediated stimulation of NO
Plasma membrane
a Flow/shear sensor
b
Arg
PO_4
Ca^{2+}
NO + citrulline
Chronic shear-mediated protein synthesis

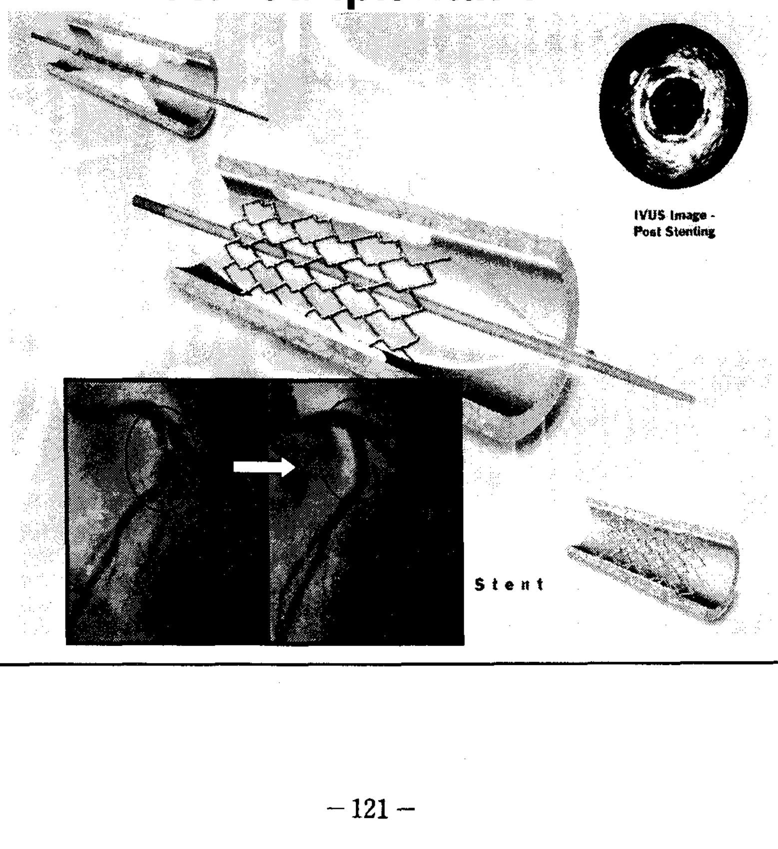
PTCA



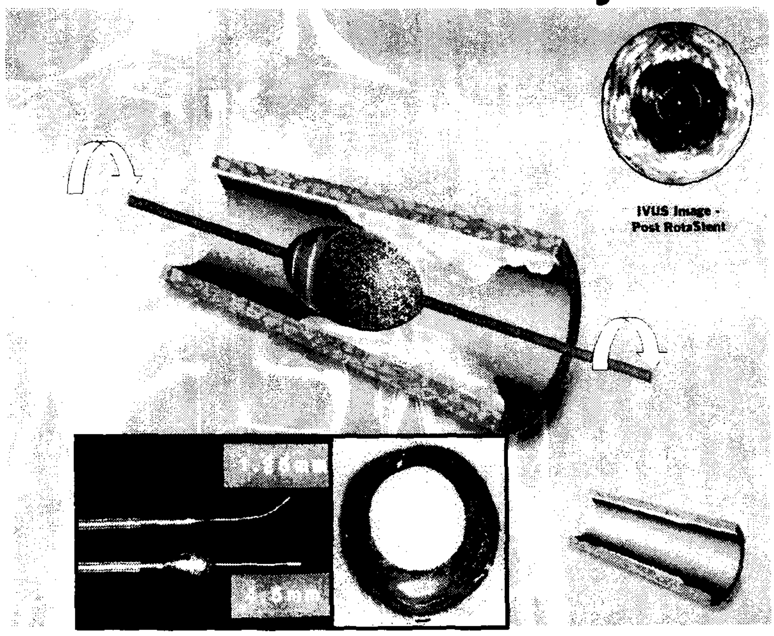
PTCA

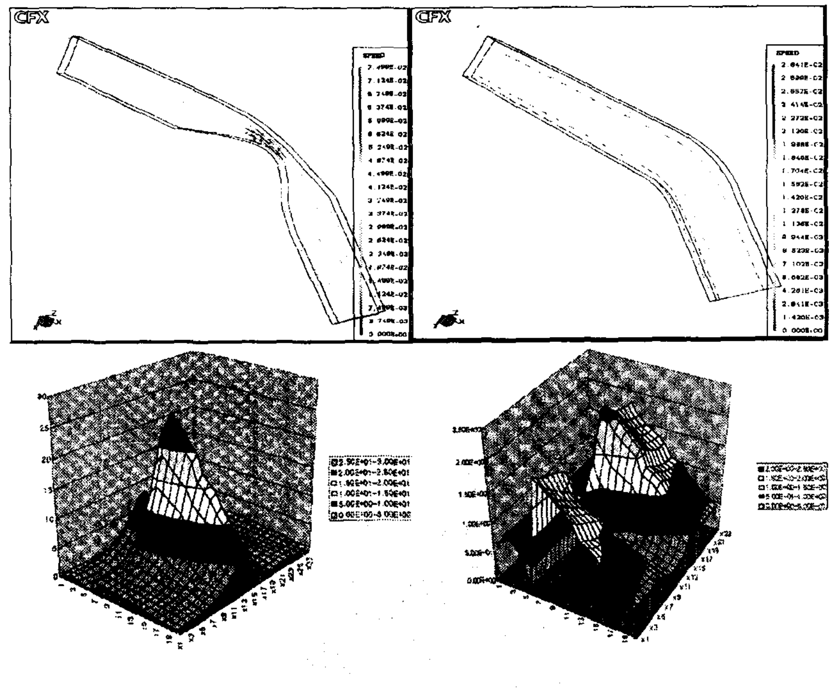


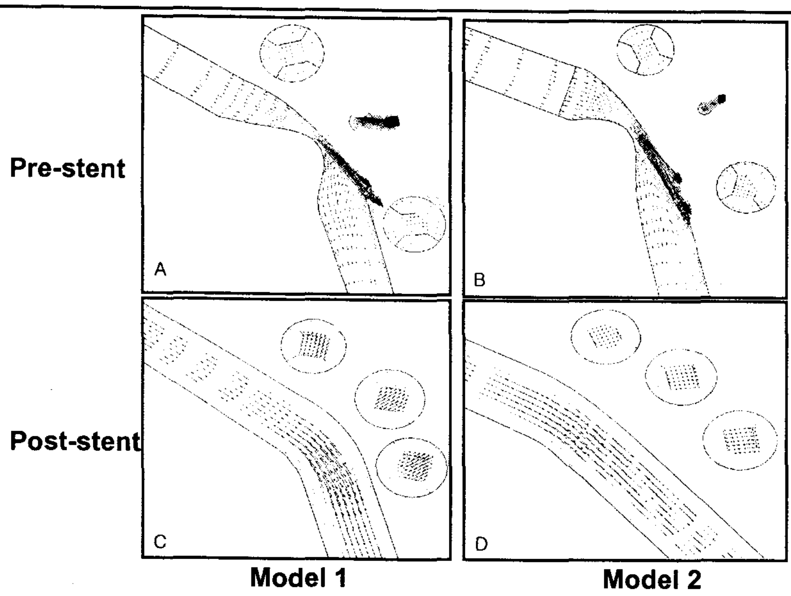
Stent Implantation



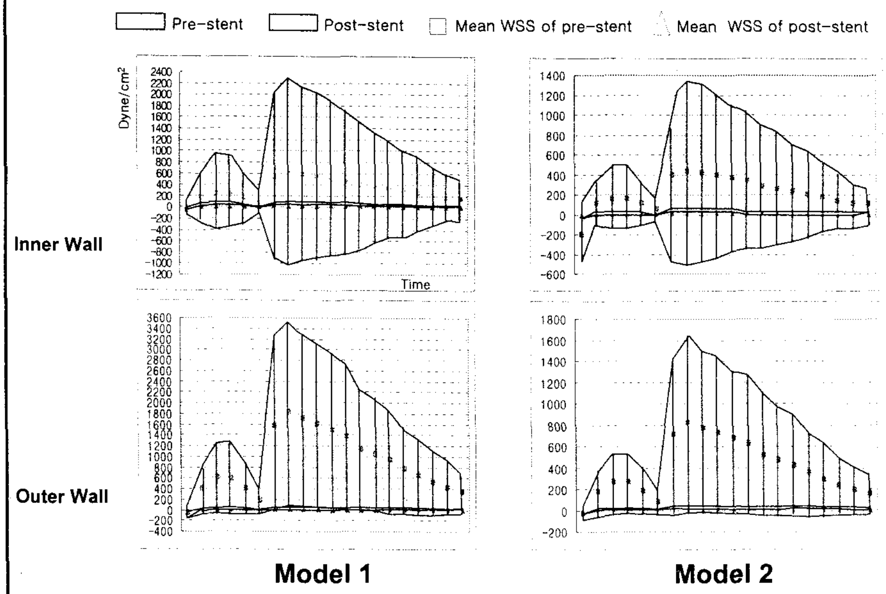
Rotational athrectomy





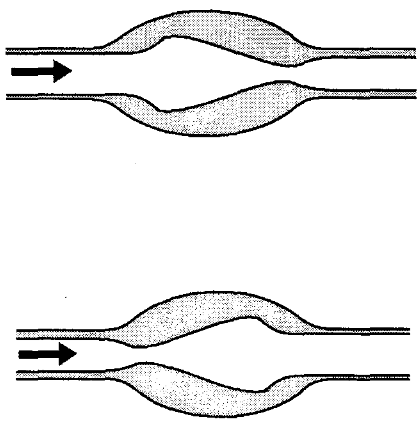


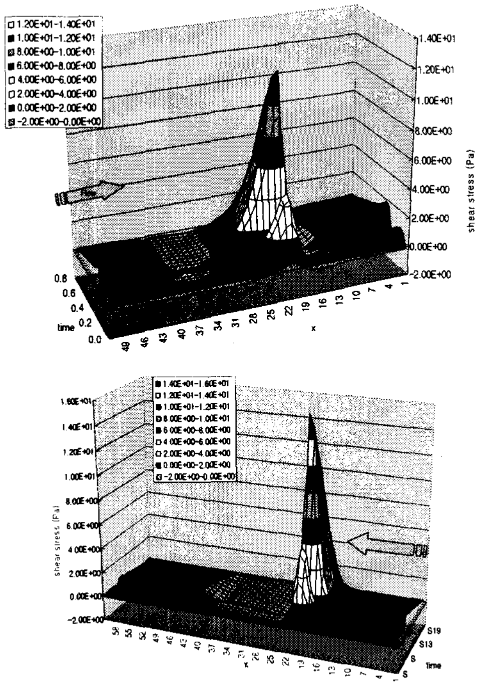
The flow-velocity vector of pre & post -stenting

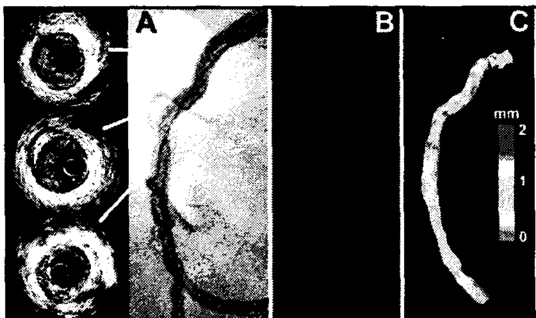


WSS according to pulsatile coronary circulation

Hemodynamics with Compensatory remodeling in pre/post stenotic segments

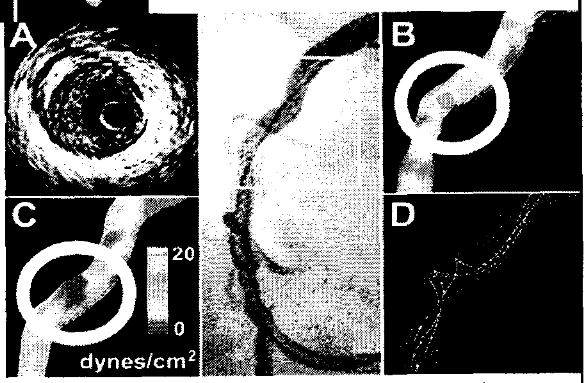






Left anterior oblique view of a stented right coronary artery (A) with IVUS images showing (from top to bottom) reference segment with slight intimal hyperplasia, focal fibrocalcific plaque, and stented segment (with only discrete neointimal formation). B, Flow paths of hypothetical red blood cells inside 3D reconstructed vessel. C, Local wall thickness, with color code ranging from 0 mm (blue) up to 2 mm (purple-red).

Detailed view of proximal part of RCA (white box) with IVUS image of a fibrocalcific plaque in a nontreated region (A), local wall thickness clearly demonstrating a "hot" (red) spot with increased thickness (B), computed local WSS with color code ranging from 0 to 20 dyne/cm² showing lower WSS values at site of interest (C), and helical flow patterns derived from computational fluid dynamics at site of increased vessel wall thickness (D).



Helical Velocity Patterns in a Human Coronary Artery : A Three-Dimensional Computational Fluid Dynamic Reconstruction Showingthe Relation With Local Wall Thickness G. Van Langenhove, Circulation 2000 102: e22 - e24.

Disturbed, low, and oscillatory shear stress condition (< 10 dynes/cm2)

- Atherogenic (accumulation of lipids , stimulate expression of leukocyte adhesion molecules, chemotactic factors, growth factors
- Proliferation, transmigration of monocytes/macrophage, SMC
- Prothrombotic, pro-inflammatory , pro-oxidant state

Malek AM, et al, JAMA, 282:2035, 1999

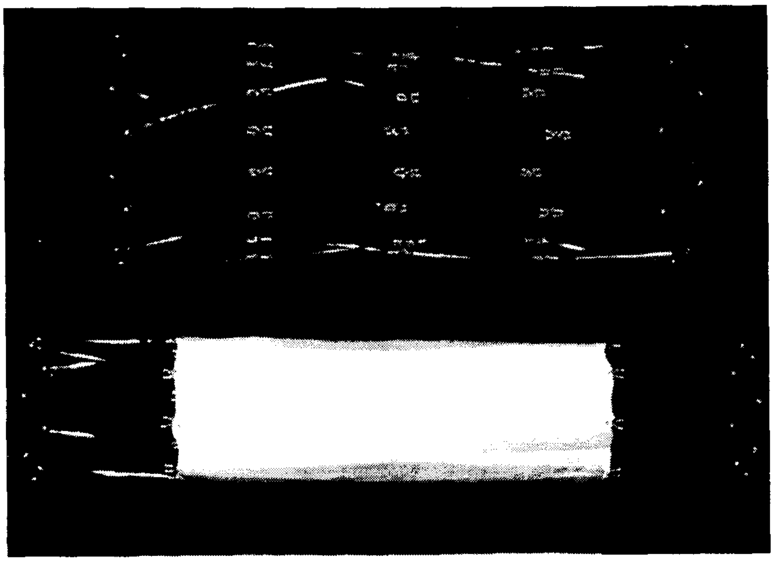
High Shear Stress (>70 dynes/cm2)

- Endothelial damage
- Promote platelet deposition
- Plaque rupture

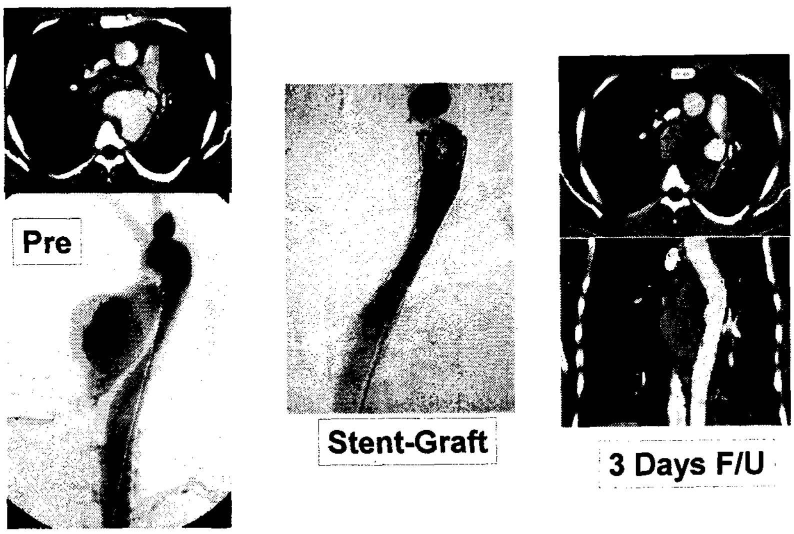
Physiological Shear Stress (10-70dynes/cm2)

- Atheroprotective
- Decrease expression of vasoconstrictors, paracrine growth factors, inflammatory mediators, adhesion molecules, oxidants
- Increase production of vasodilators, growth inhibitors, fibrinolytics, antiplatelet factors, antioxidants

Stent-Graft



대동맥 박리증



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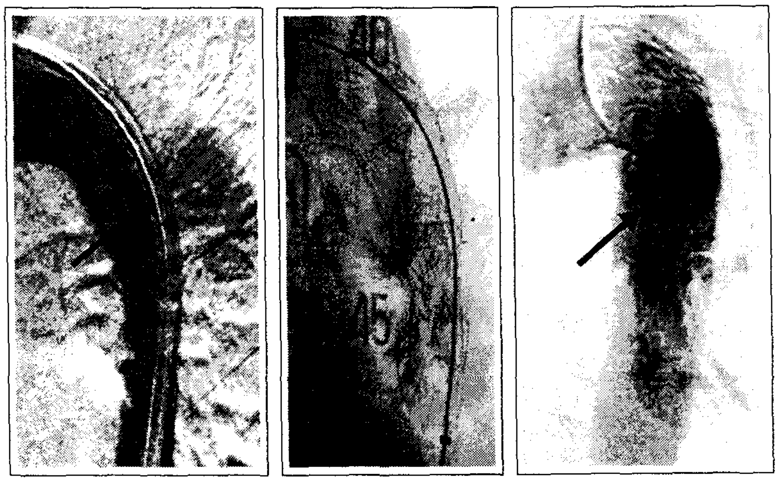

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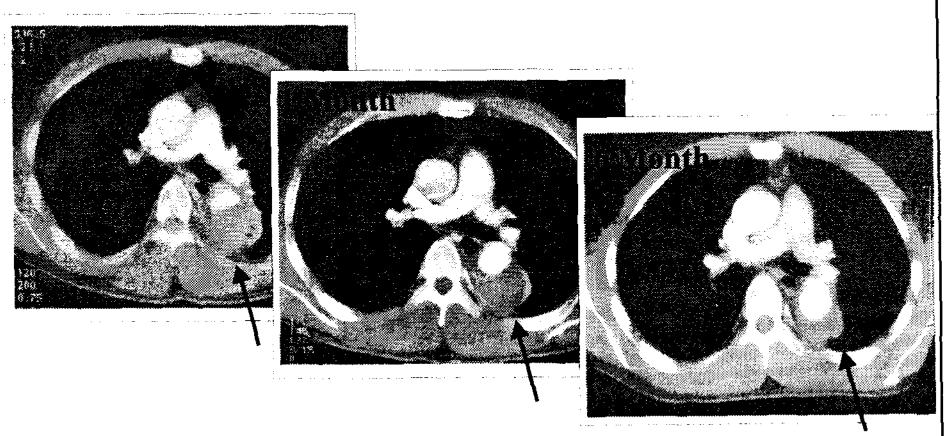

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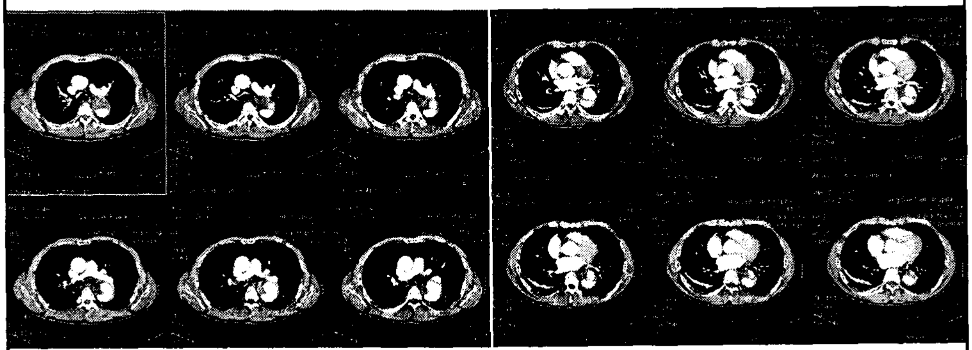
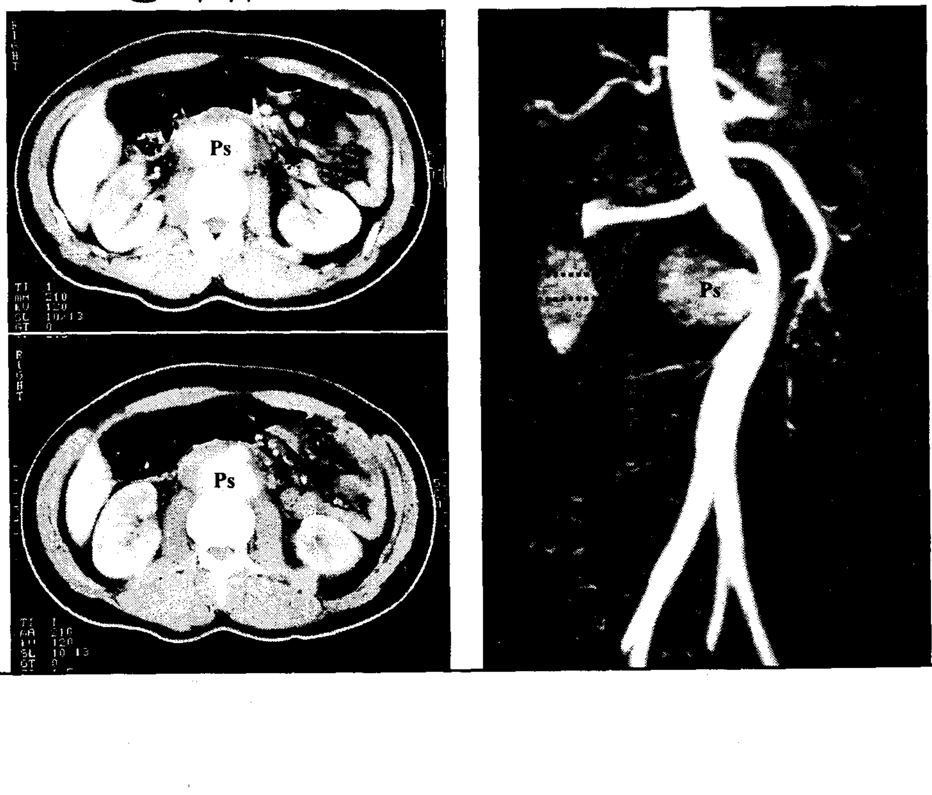
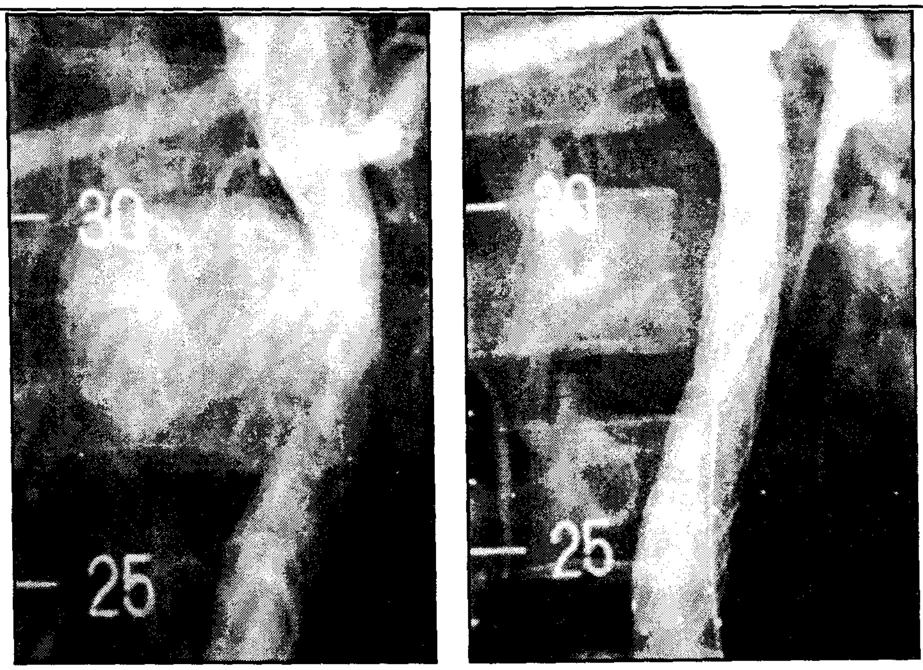


동맥 류





Graft-stent로 치료한 대동맥류