Grundlagen der Biomechanik – 719.009
Sommersemester 2016, TU Graz

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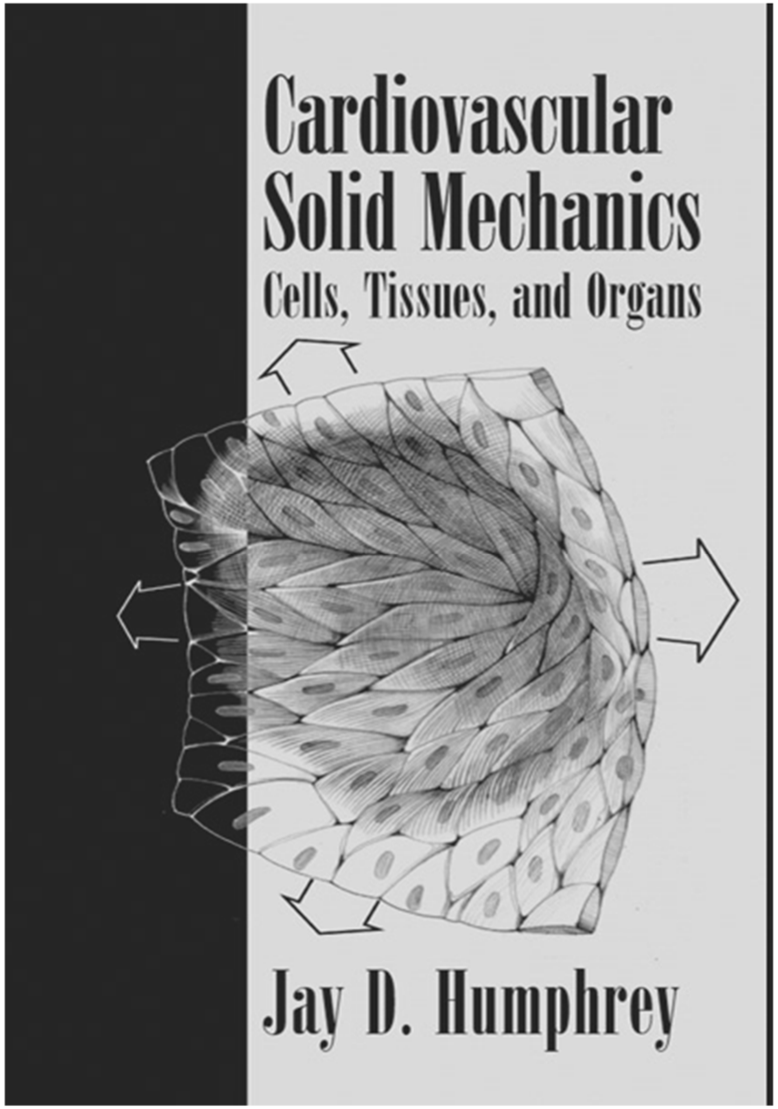
Vorlesung – 17 :

Arterial Wall Mechanics

- **Motivation**
- **Anatomy and Histology**
- **Components of the Vessel Wall**
- **Functions of Arterial Layers**
- **Aging and Pathology**

Literature



Humphrey (2002)

Motivation

Motivation

Purpose of arterial wall mechanics:

1. Better understanding of the arterial physiology

2. Better understanding of the arterial pathophysiology

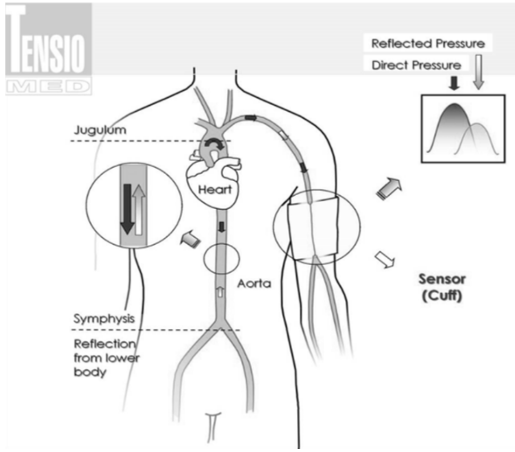
3. Better understanding of the (mechanical) treatment methods of arterial diseases

1. Better understanding of the arterial physiology

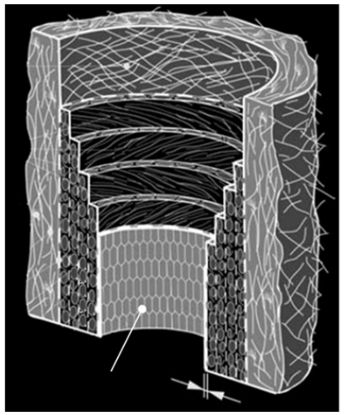
Korteweg-Moens Equation (1879):

$$c = \sqrt{\frac{Et}{\rho D}}$$

c...pulse-wave velocity; E...modulus of wall elasticity (Young's modulus); t...wall thickness; D...inner diameter of the vessel; ρ...density of the fluid (blood)



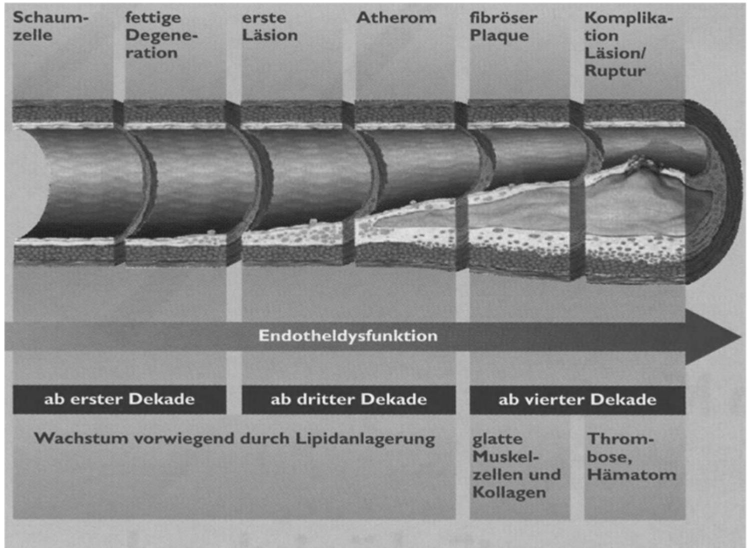
http://www.unimedic.co.uk/images/upload/Erek.jpg



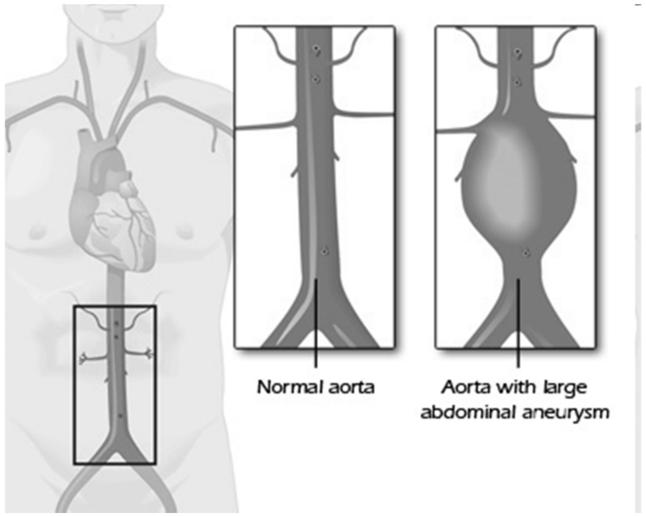
Histomechanics
→ multiscale modeling

Motivation

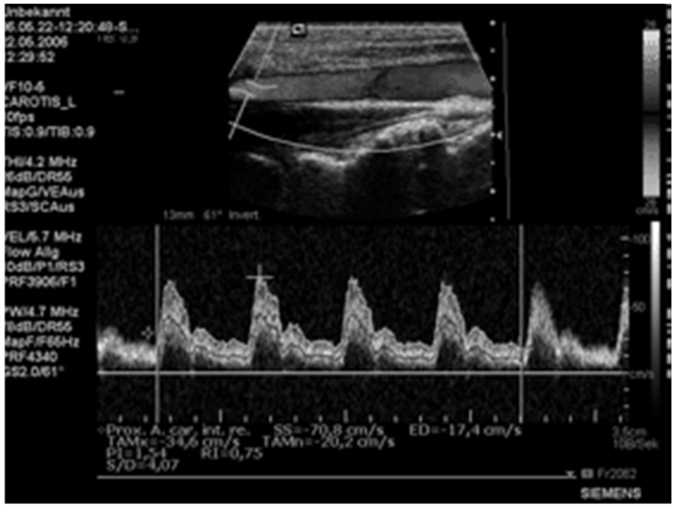
2. Better understanding of the arterial pathophysiology



Nach Stary HC et al. Circulation 1995; 92:1355-1374

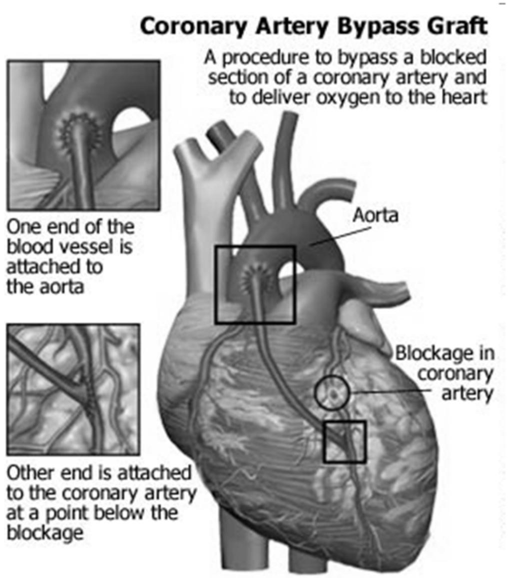


http://www.newmedical.co.uk/library/folder.2005-10-13.9893989721/aneurysm_diagram3.jpg



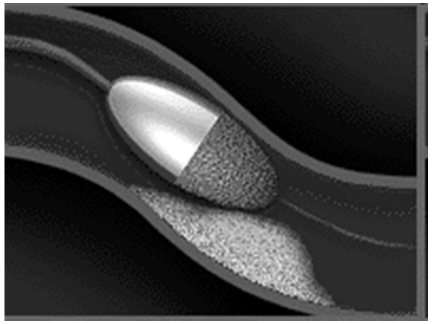
Motivation

3. Better understanding of the (mechanical) treatment methods of arterial diseases



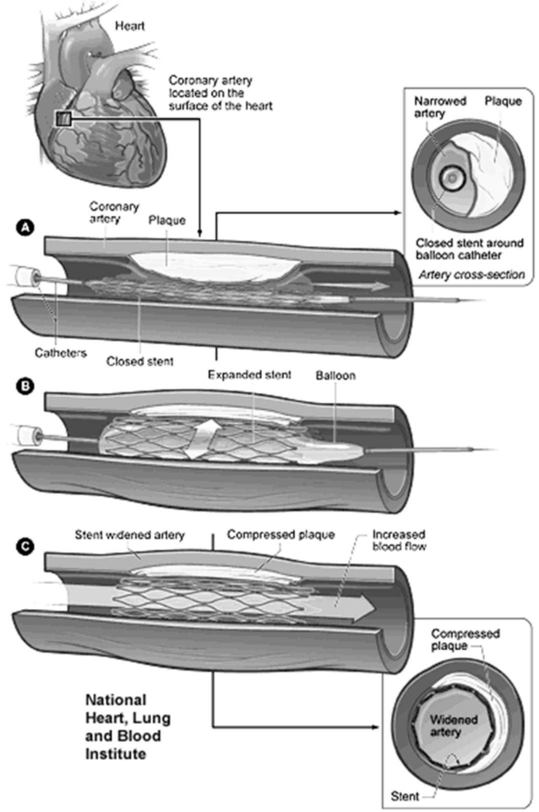
http://www.heartonline.org/images/BypassGraft.jpeg

Rotablator



http://www.vascular-intervention.de/images/rotablator2.gif

Balloon angioplasty with stenting



http://seniorjournal.com/images/Symbols/StentPlacement.gif

Artificial heart

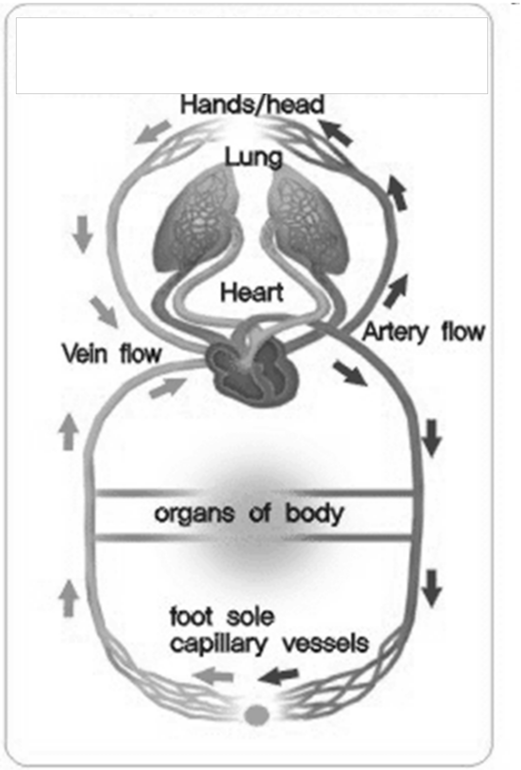
http://www.spiegel.de/img/0,1020,117002,00.jpg

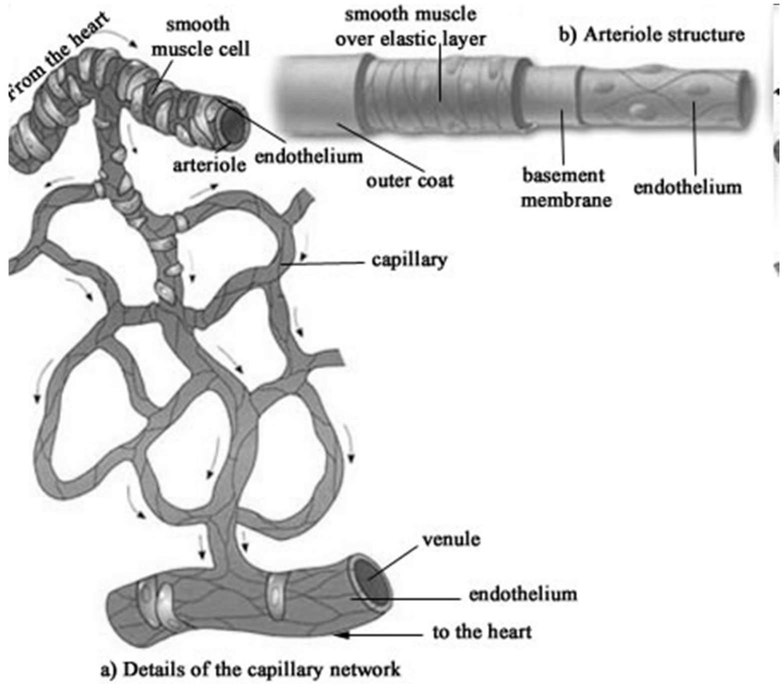
Pharmacotherapy

http://www.berlin.de/special/umwelt/medikamente/

Anatomy and Histology

Anatomy and Histology

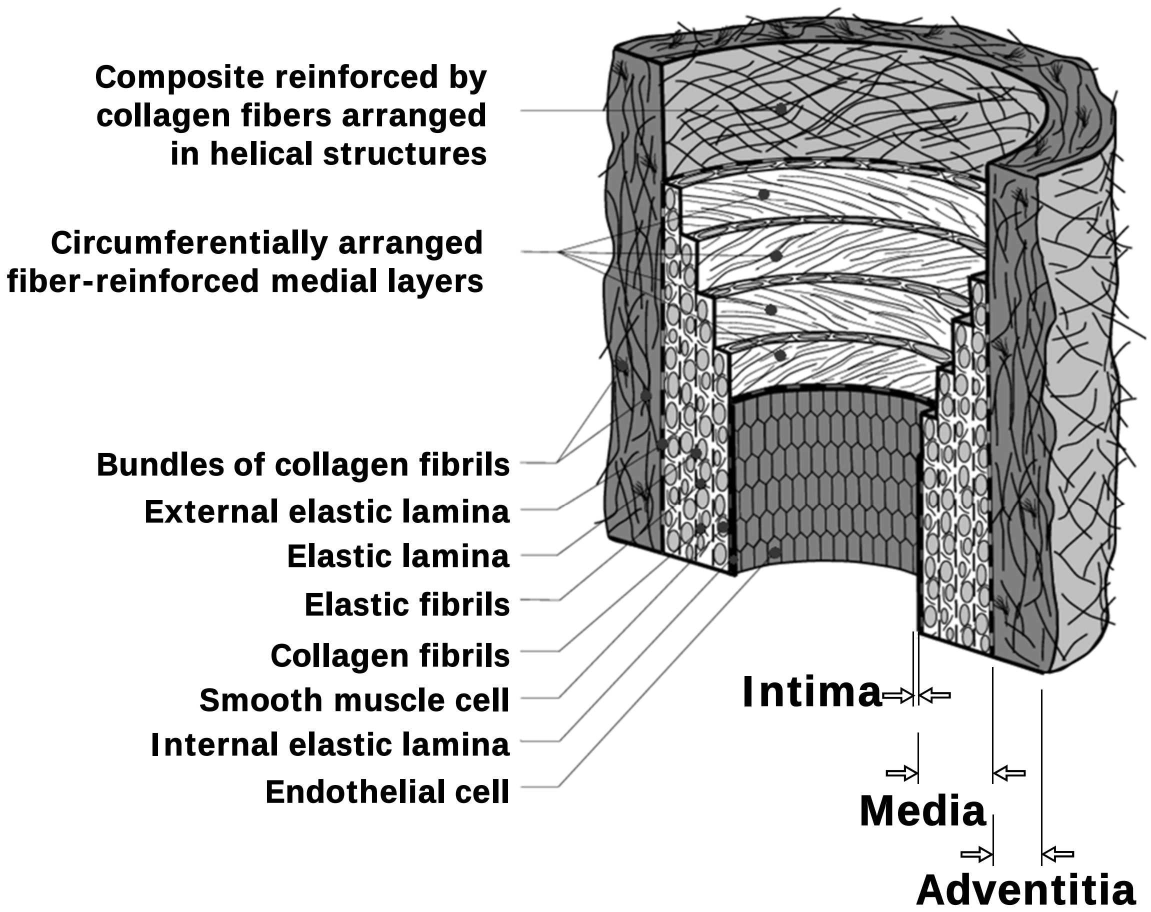


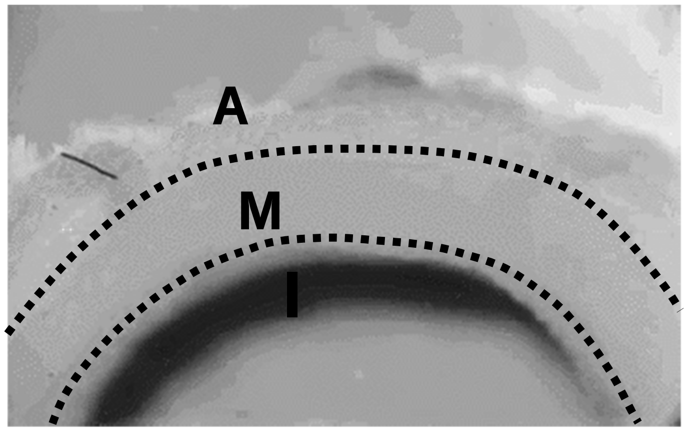


http://www.harunyahya.de/bucher/wissenschaft/blut_herz/images/arteriole_2.jpg

http://www.anyhaus.com/mdk/jjeng_img/sub/sub72_03.gif

Anatomy and Histology

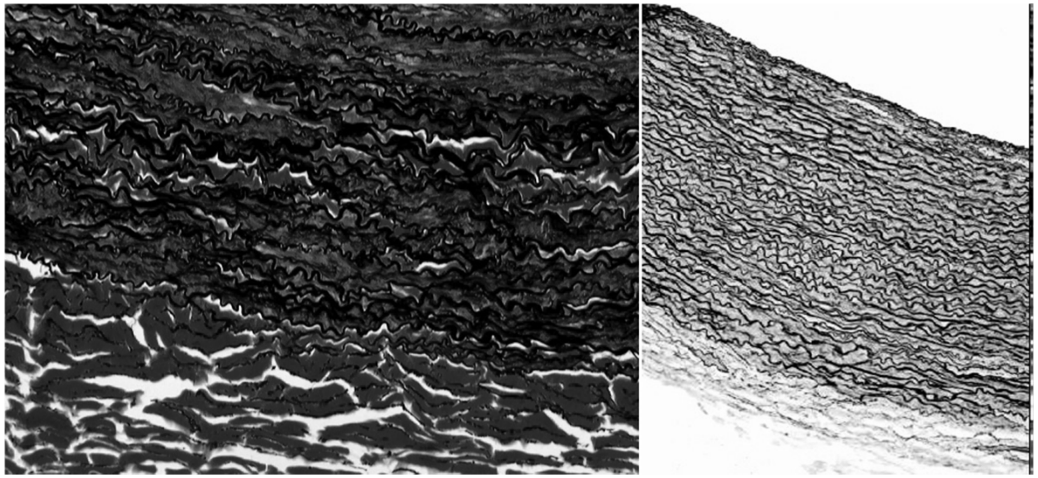


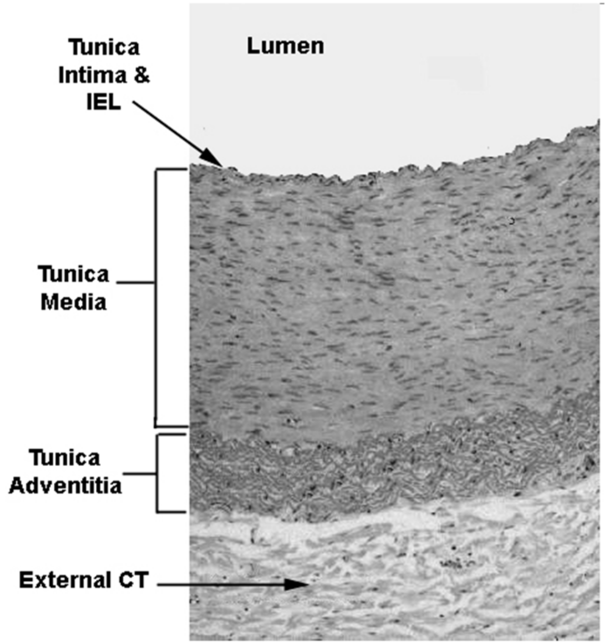


Macroscopic view of
an arterial ring

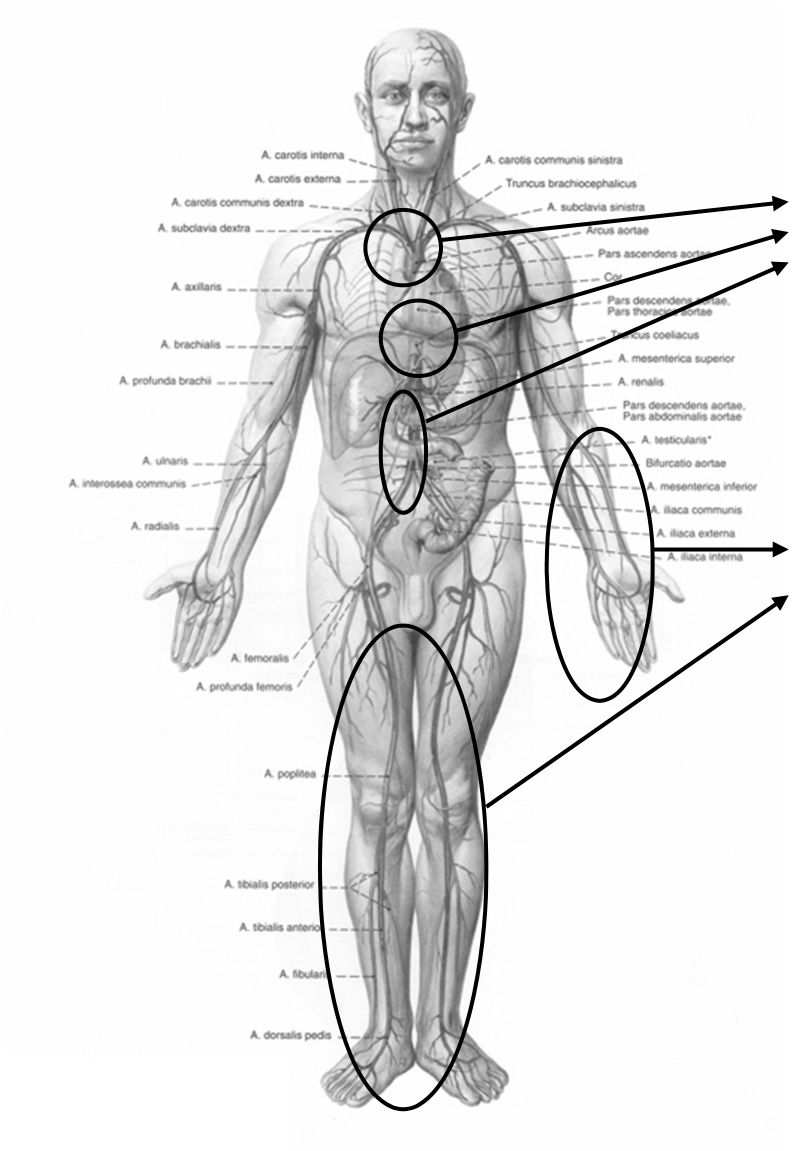
Anatomy and Histology

- Two sub-groups of arteries:
  - elastic arteries: larger diameter and closer to the heart (e.g. aorta)
  - muscular arteries: smaller vessels, more peripherally (e.g. coronaries, femorals and renals)





Anatomy and Histology



Types of Arteries

***Elastic* arteries**

***Muscular* arteries**

Components of the Arterial Wall

Components of the Vessel Wall

• The vessel wall consists of cellular and non-cellular components.

Mechanically important are:

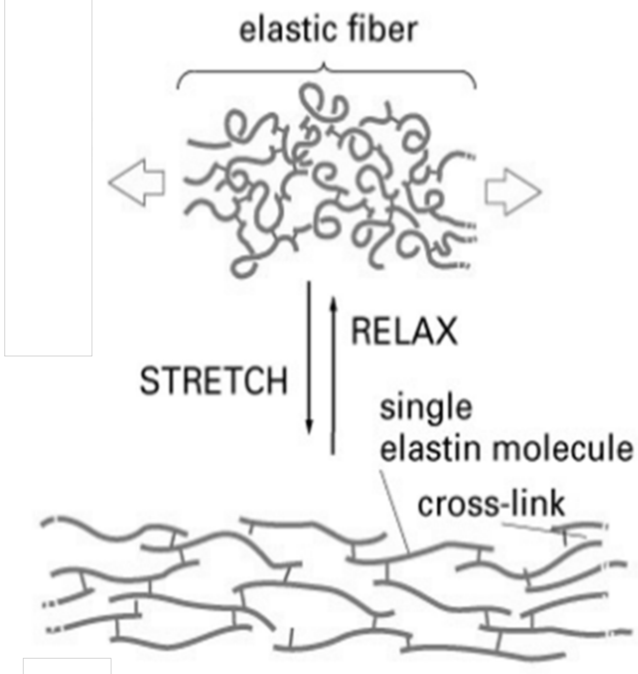
- Scleroproteins: collagen and elastin
- Smooth muscle cells
- Ground substance

Elastin

- Clew shaped (knäuelförmige) amino acid chains are three-dimensional cross-linked with desmosine bridges

- Macroscopically, these structures appear yellowish → see also Tunica media

- In contrast to collagen, elastin has no ordered macromolecular structures → basis for the mechanically isotropic behavior of elastin structures



http://www.accessexcellence.org/RC/VL/GG/ecb/collagen_elastin.php

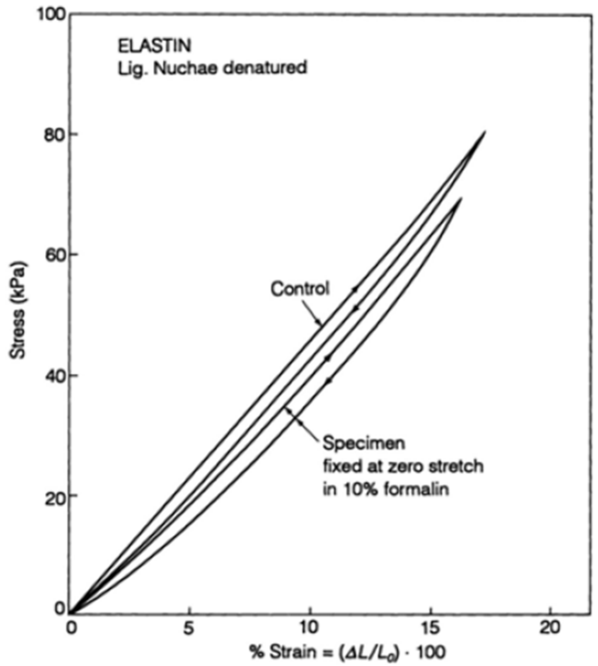
Elastin

• Elastin is the most linear and softest elastic biomaterial, with E =0.6 MPa

• During cyclic stress-stretch tests, elastin shows very small hysteresis until a stretch of 1.6 (Fung, 1993) → Elastin is predisposed as a component for elastic arteries (e.g. elastin content in an human thoracic aorta: 30g/100g dry weight)

• An further interesting property is the thermal stability of elastin: the mechanical behavior remains unchanged after exposition in boiling water for 1 hour (Fung, 1993)

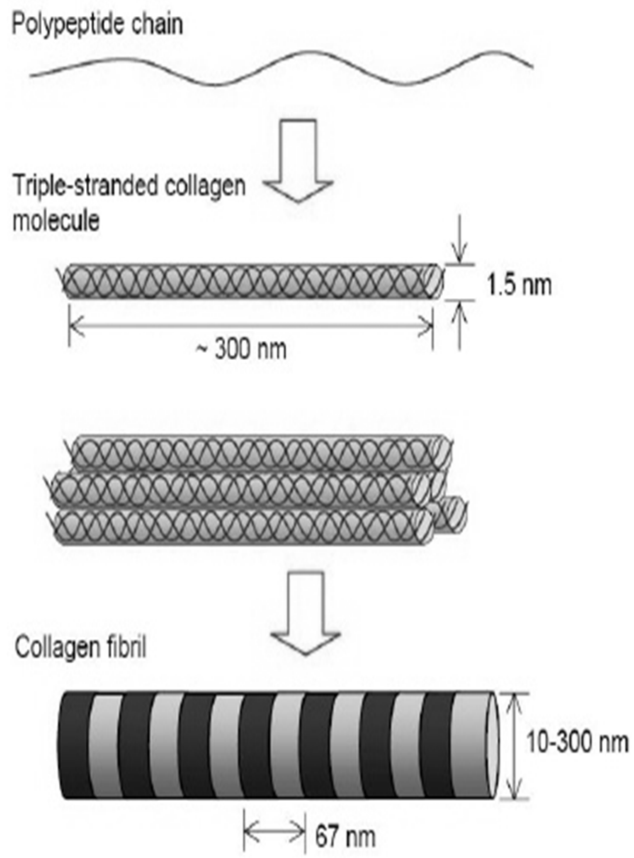
• Elastin is generated during development and degrades during aging → arteries become stiffer



Collagen

• Collagen consists of counterclockwise helical amino acid chains, the so-called α-chains. Three counterclockwise helices, α-chains, are twisted together into a clockwise coiled coil, a triple helix or "super helix" , the so-called procollagen (length 280 nm, diameter 1.5 nm, molecular weight 300000). These rod-shaped procollagen molecules are parallel assembled, with a shift of approx. ¼ of the molecule length (67 nm), to form collagen fibrils (diameter 20 – 40 nm).

• Macroscopically, collagen appears white → compare to tunica adventitia.



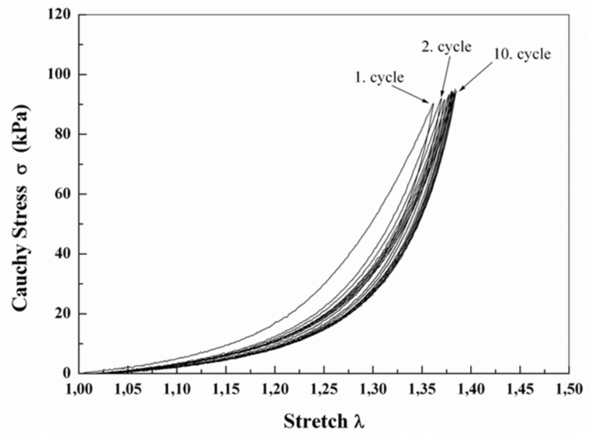
http://www.azonano.com/images/Article_Images/ImageForArticle_2267(2).jpg

Collagen

- In stress-strain tests of tissues (consisting almost only of collagen fibers (e.g. ligaments)), the Young's modulus was determined to be 1000 MPa (Fung, 1993), where a strong non-linear stress-strain relationship was observed.

- This nonlinear behavior is not only the consequence of the wavy form of the collagen fibers in the unloaded state (Rhodin, 1962). Under increasing loading, the number of load-bearing collagen fibers increase (recruiting), so that the tissue stiffens.

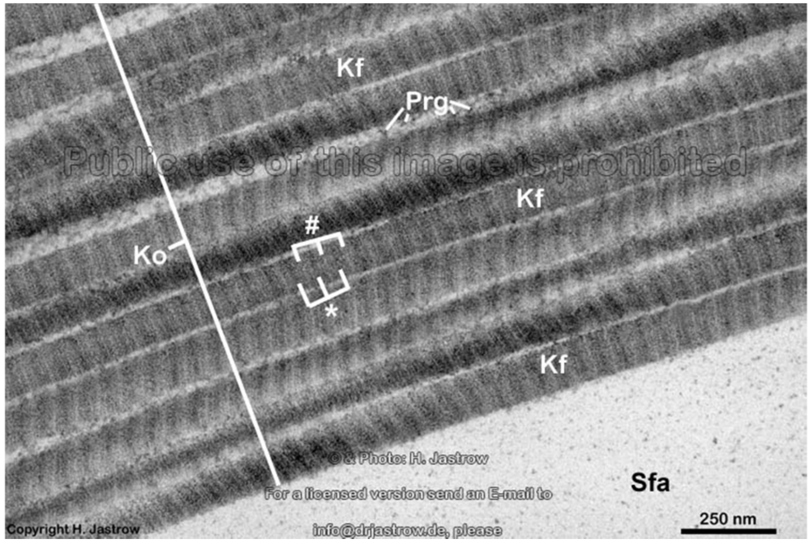
  - The hysteresis is bigger than for elastin. Furthermore, relaxation phenomenon under constant stretch, and preconditioning under cyclic loadings occur.



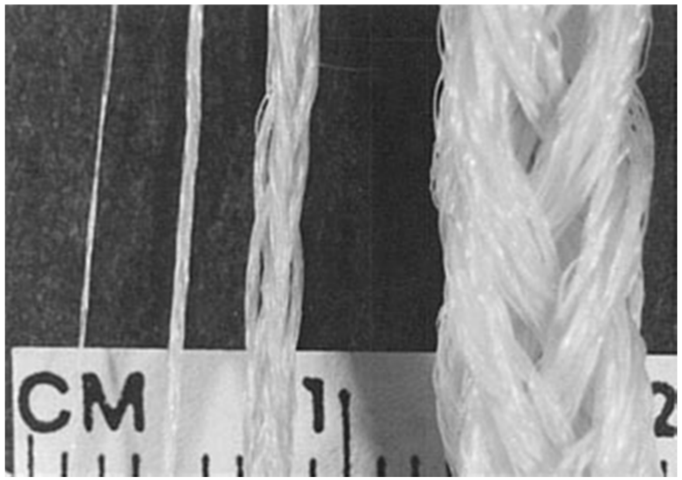
Collagen

• Collagen act as main load-bearing structures in all soft tissues

• Collagen shows a small thermal stability in contrast to elastin, e.g. at 65°C collagen shrinks about 1/3 of its original length, loses its fibrillar structure, becomes rubber-like, and shows a Young's modulus of only 1 MPa (shrunken head).



http://www.uni-mainz.de/FB/Medizin/Anatomie/workshop/EM/eigeneEM/BG/HomoBG7okb.jpg

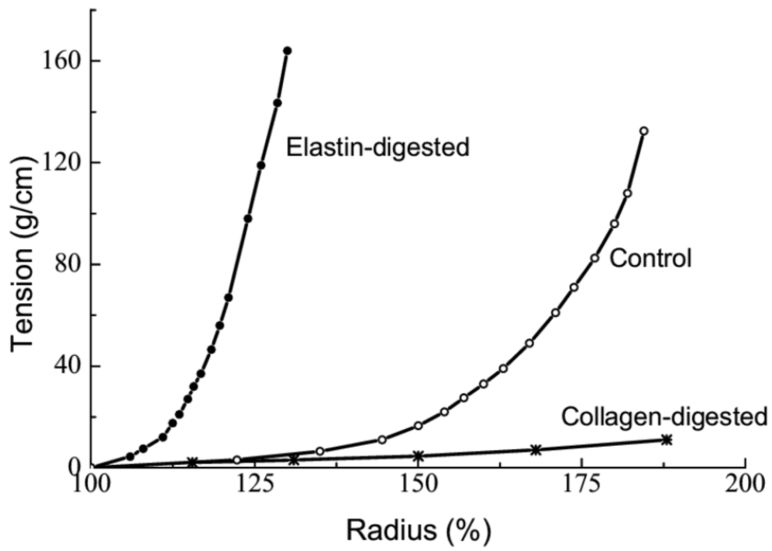


http://www.atp.nist.gov/eao/sp950-2/tissue_1lo.jpg

Collagen and Elastin

• The collagen-elastin ratio in arteries depends on the anatomical localization and from the age (higher collagen content at higher age (Cox, 1977)).

• Elastin acts in the low pressure domain, elastin and collagen in the middle (physiological) pressure domain, and just collagen in the high pressure domain (Roach and Burton, 1957).

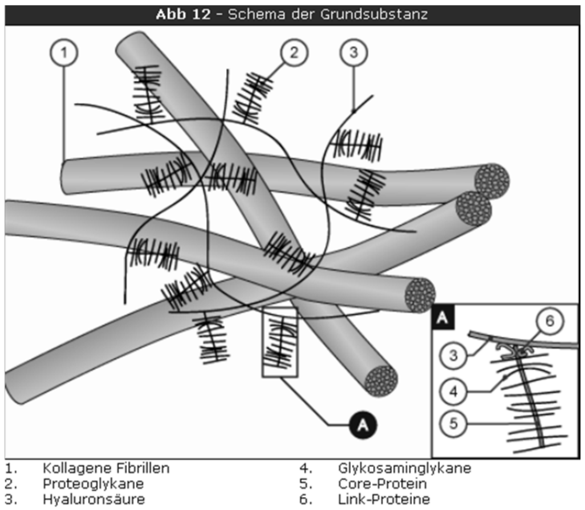


Ground substance

• The ground substance is gel-like and consists of proteoglycans.

• The mechanical behavior of basic substance have minor contribution to the mechanical behavior of blood vessels.

• Biomechanically meaningful is the property of the ground substance as a molecular filter. Therefore, it acts like the governing structure for fluid flows within the tissue.



http://www.unifr.ch/anatomy/elearningfree/allemand/bindegewebe/sfa/grundsubstanz/d-grundsubstanz.php

Smooth muscle cells

• Vessel muscle cells are 30 - 60 μm long with a diameter ranging from 1 to 5 μm.

• There are presumably biological differences between the extracellular components discussed above and the smooth muscle cell:

- the muscle cell can divide and multiply
- as a myofibroblast (fiber-building cell) the cell is able to produce extracellular substance
- the cell can actively produce connections with its environment or rebuild them (i.e., the cell is able to alter the mechanical behavior of the tissue)
- contract actively (therefore, the cell is able to change its mechanical behavior and also its geometrical configuration)

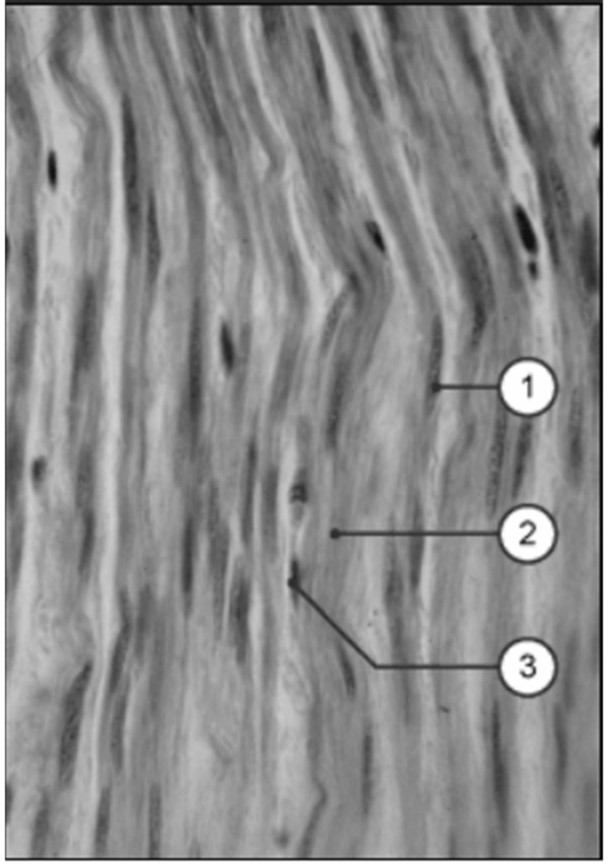
Smooth muscle cells

• These activities are controlled by nerval, hormonal (chemical messengers), and local factors

• Mechanically, smooth muscle cells reveal a strong viscoelastic (creep, relaxation) and nonlinear behavior (higher stiffness at higher loads), with large hysteresis at cyclic loading

• This behavior is strongly influenced from the contraction condition of the cell

Abb. 9 - Glatte Muskulatur



1. Zellkern einer glatten Muskelzelle
2. Actin-Myosin-Bündel
3. Zellkern eines Fibroblasten

http://www.unifr.ch/anatomy/elearningfree/allemand/biochemie/allg/muskel/d-muskel.php

In situ Tensile Testing of Human Aortas by Time-resolved Small-Angle-X-ray Scattering

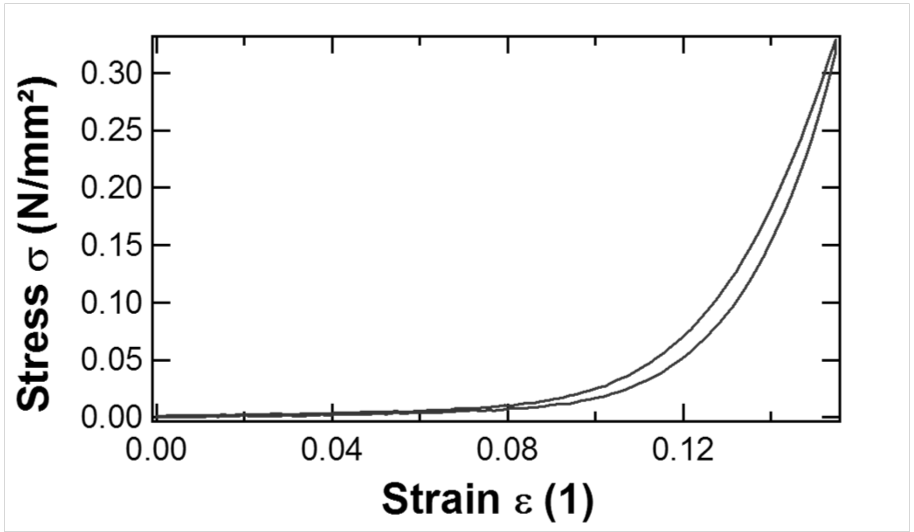
Mechanical Parameters

Macroscopic

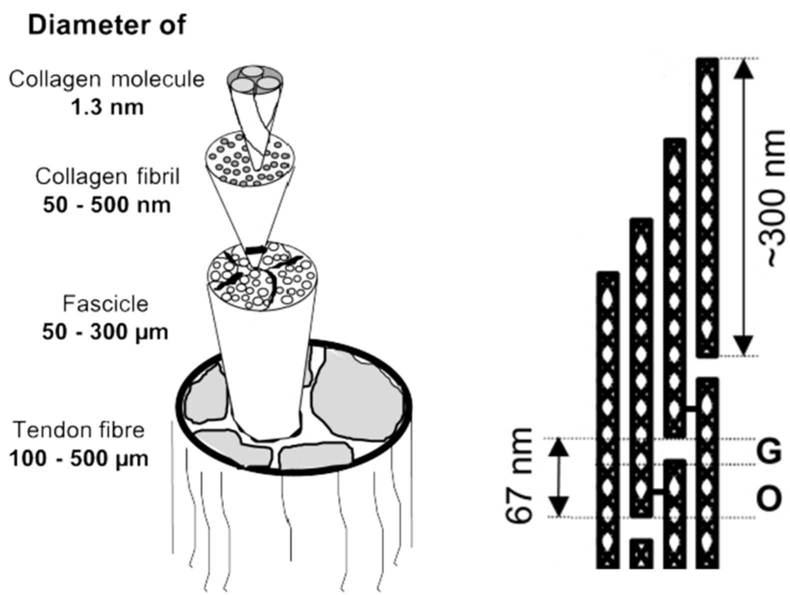
- geometric deformation
- stress
- strain

Nanoscopic

- fiber – matrix composite
- fiber alignment
- fiber strain

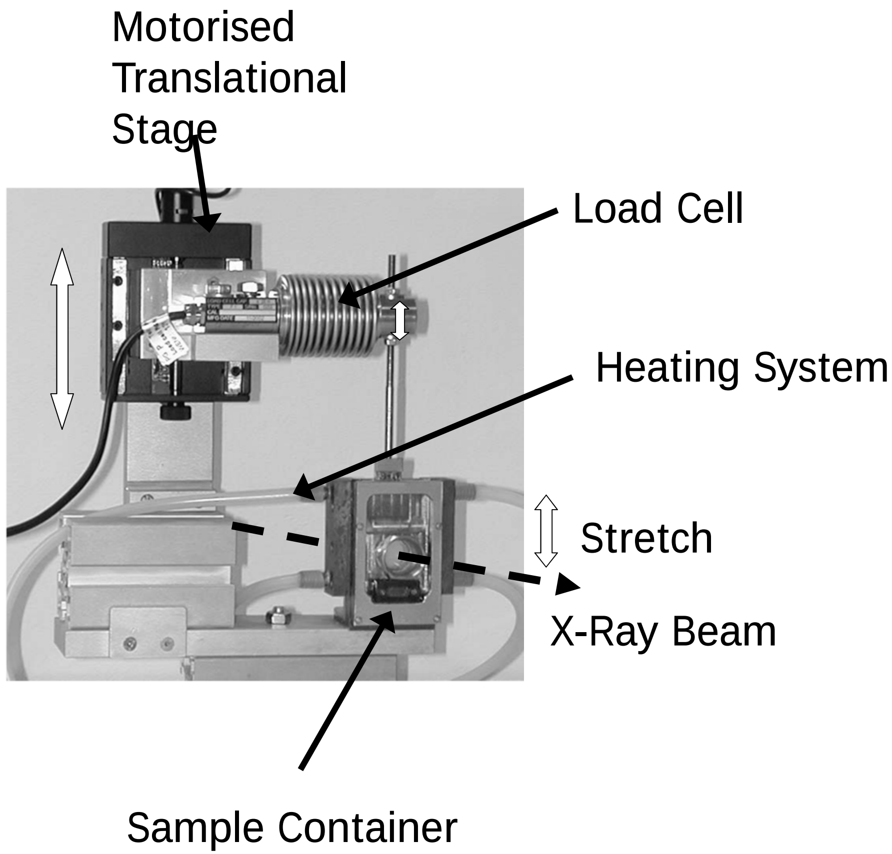


Collagen - The most abundant protein

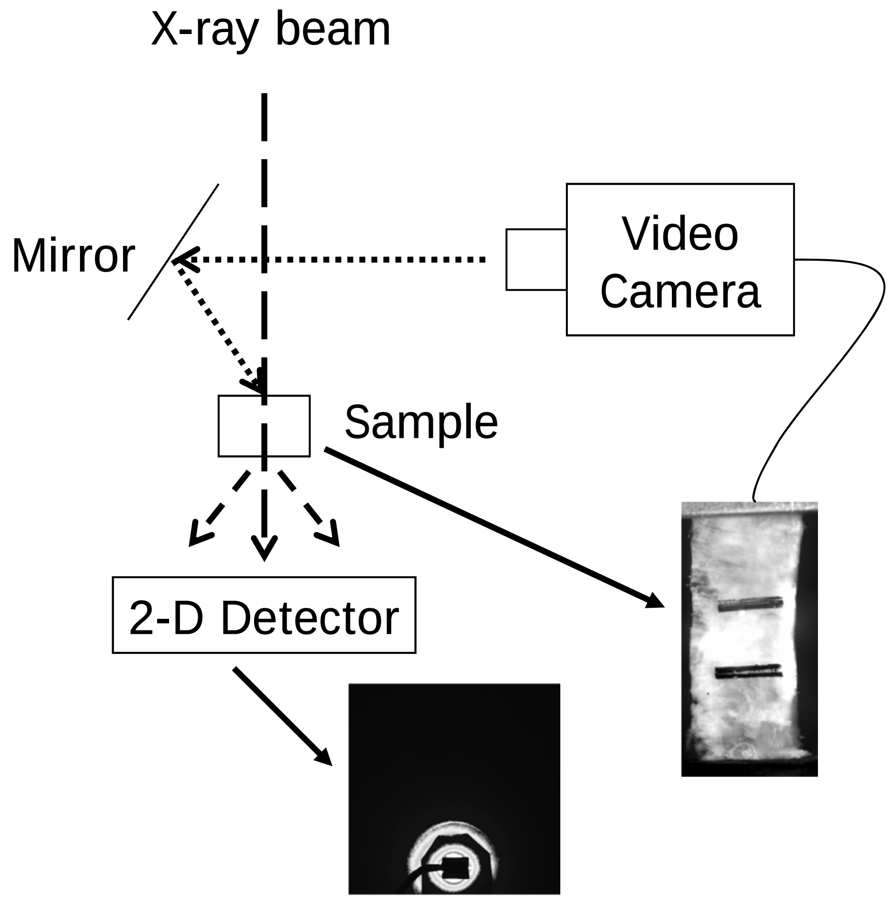


Methods: The Sample Stage

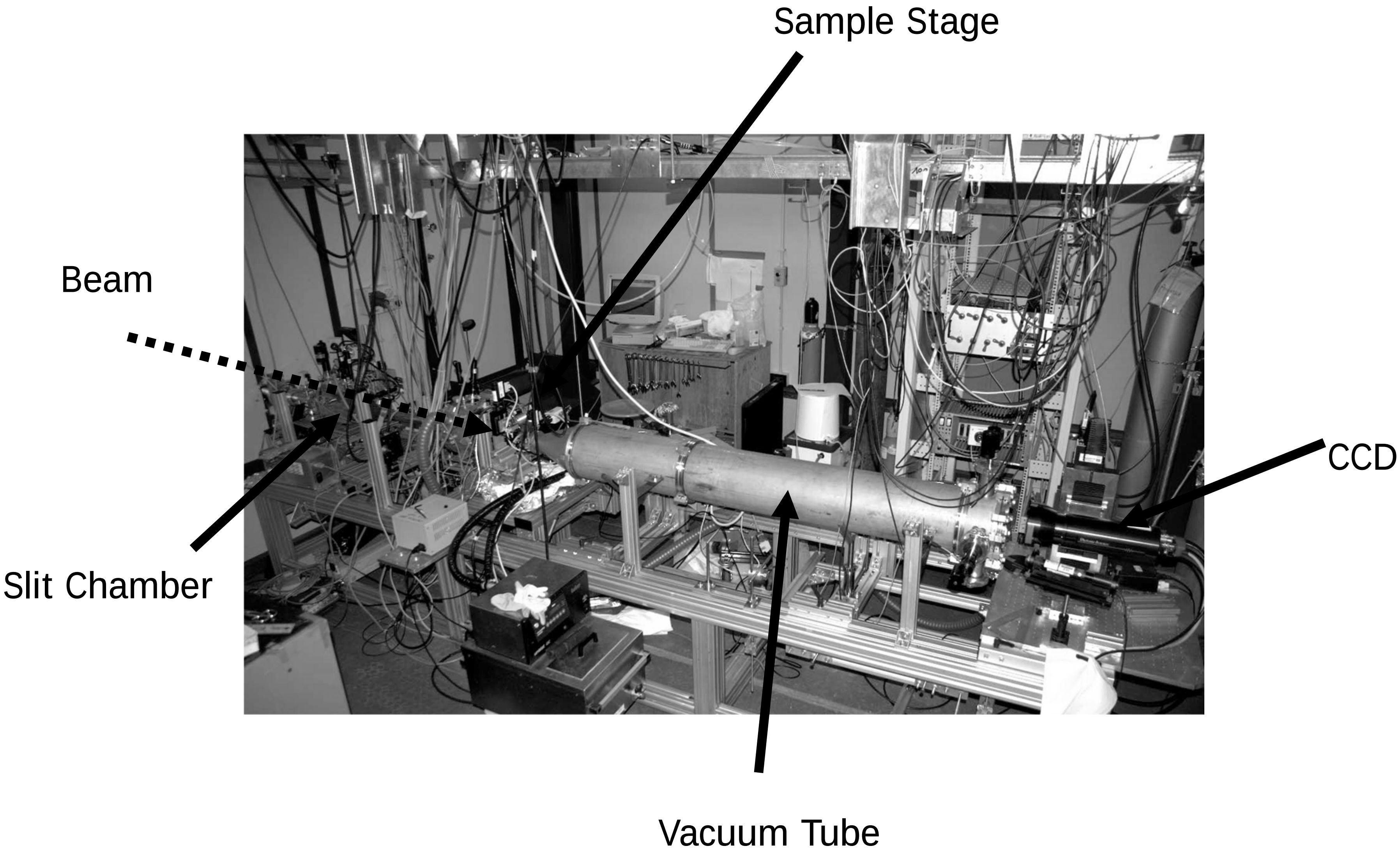
Stretching and mechanical data acquisition



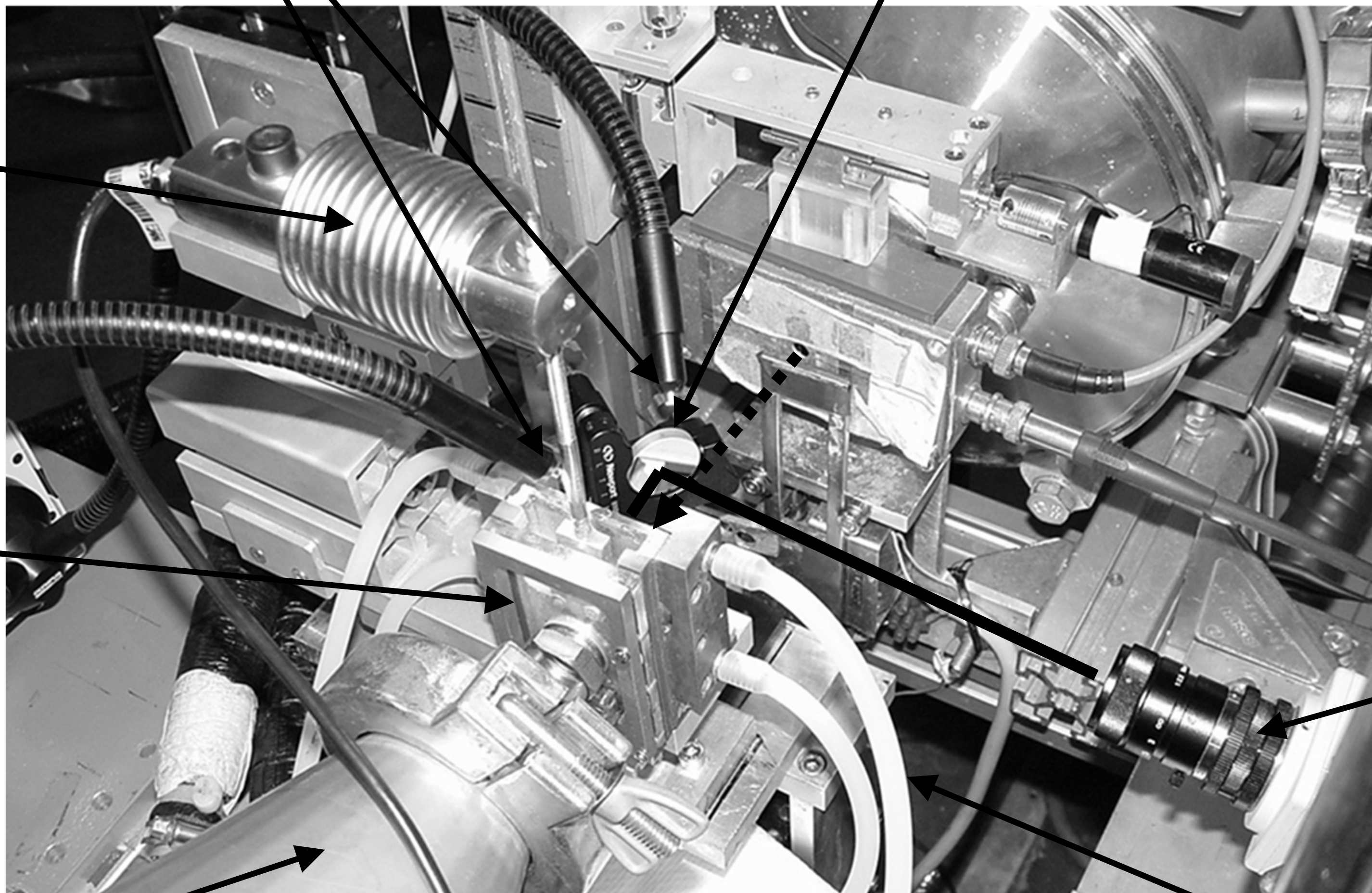
Recording geometrical changes during stretch; Top view



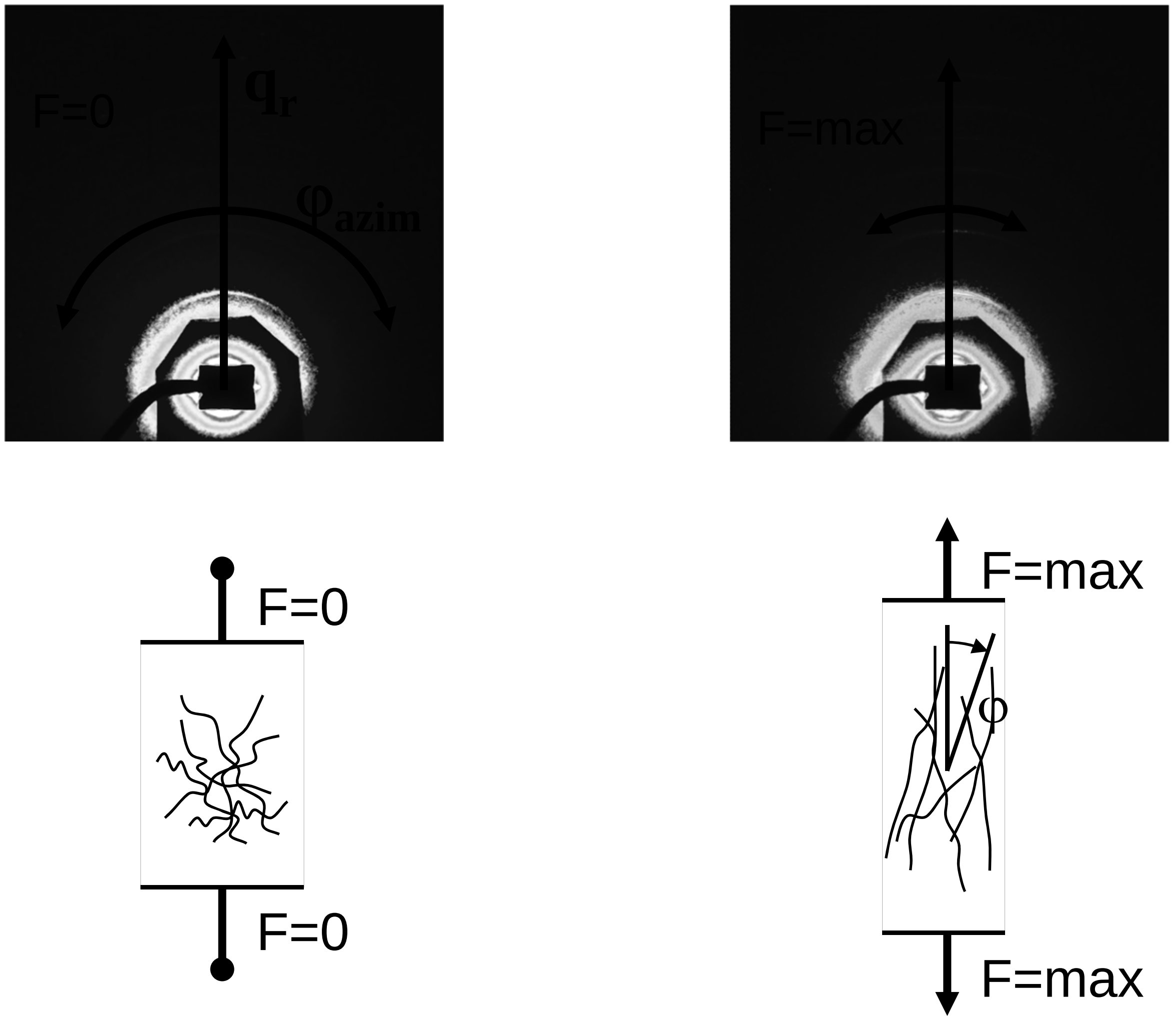
Experimental Hutch



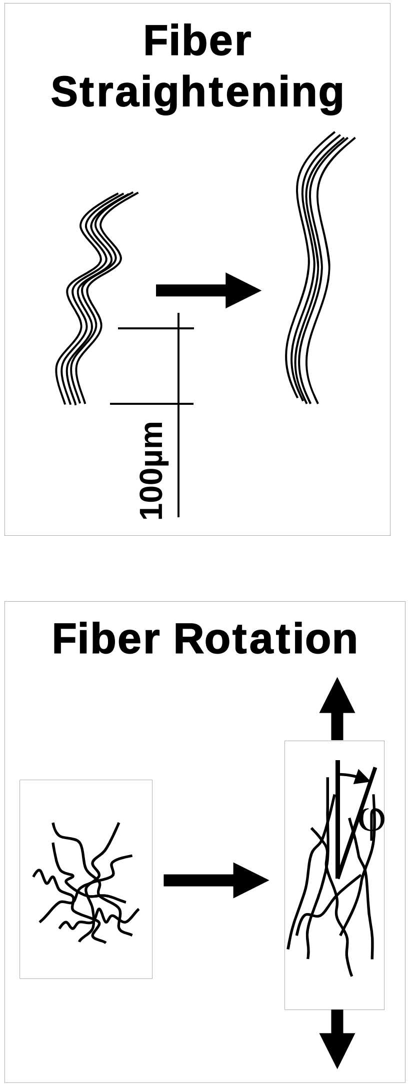
The Complete Setup

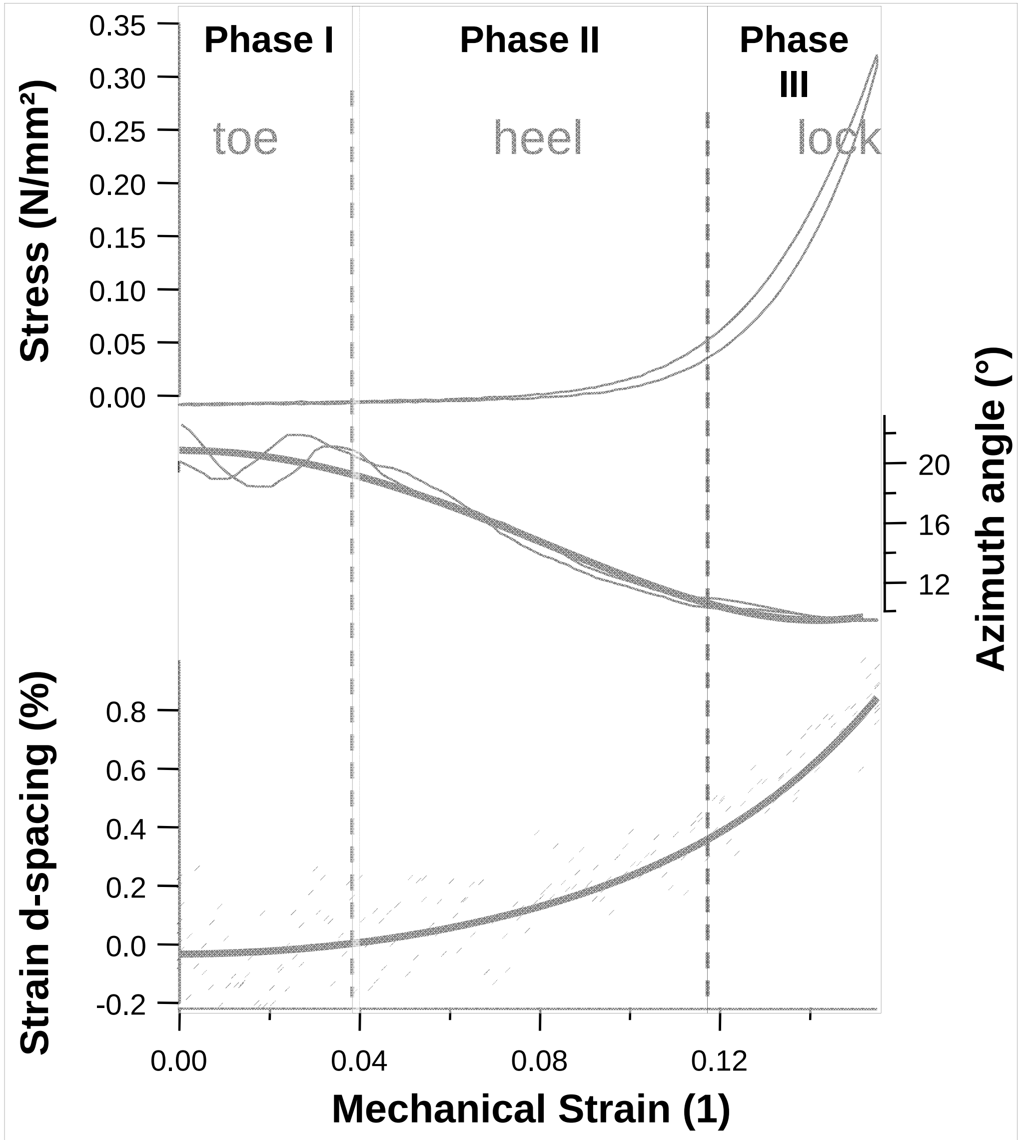


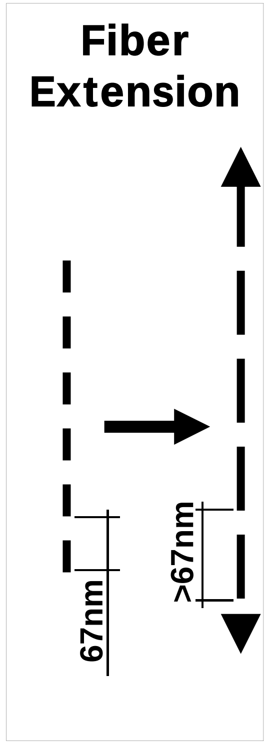
Results: Collagen Fiber Orientation



Results: Nano-Macro Coupling







Summary

Layer specific SAXS investigation of collagen network kinematics is feasible

Macroscopic response can be explained by nanoscopic structure

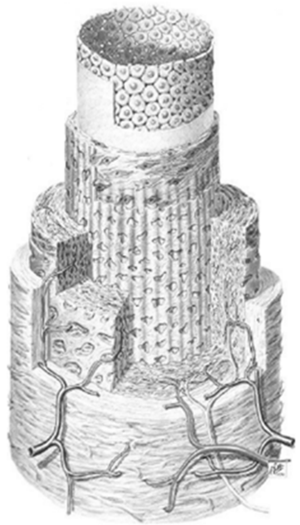
Functions of Arterial Layers

Intima

• The intima functions as a solid-fluid interface (the vessel lumen is coated with endothelial cells, where the blood coagulation is inactive)

• The healthy intima structure is mechanically negligible (Burton, 1954)

• However, the intima can strongly affect the vessel mechanics, since she is acting as a shear sensor. Dependent on the occurring shear forces from the flowing blood, the endothelial cells release messengers (e.g., ERDF – endothelium derived relaxing factor), which can locally modify the contraction condition or the growth behavior of the media muscle cells



Media

• The media consists of the complex three-dimensional network of elastin structures, collagen fibers and intermediary smooth muscle cells.

• Distribution, orientation, and connection of these elements and the contraction condition of the smooth muscle cells determine the mechanical behavior of the muscle-elastic system of the media.

• Muscle cells and collagen fibers form flat helical spirals, which are primarily oriented circumferentially (Rhodin, 1980).

Functions of Arterial Layers

Media

• The media defines mainly the mechanical behavior of the entire vessel, especially in the physiological loading domain.

• Contraction capability influences its mechanical characteristics

• Active tissue remodelling due to the capabilities of reproduction and synthesis (→ e.g. permanent high blood pressure → structural modifications → alterations of the vessel geometry and mechanical behavior)

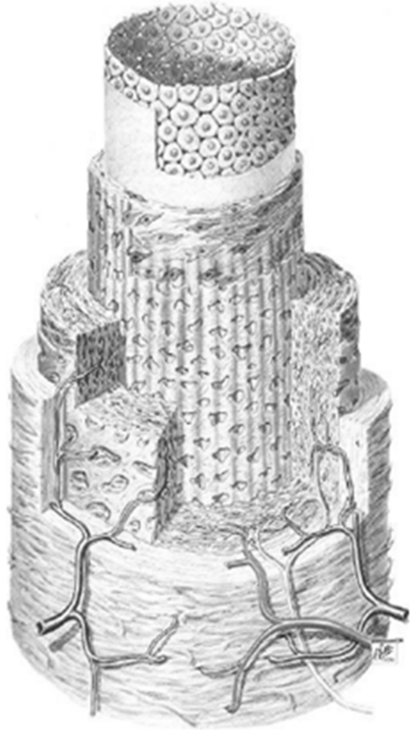
• The mechanical laws (which underlie the remodeling processes) are subject of current biomechanical research.

Adventitia

• The adventitia consists mainly of collagen fibers and only few elastin fibers, which form a complex three-dimensional network with predominant axial oriented fibers.

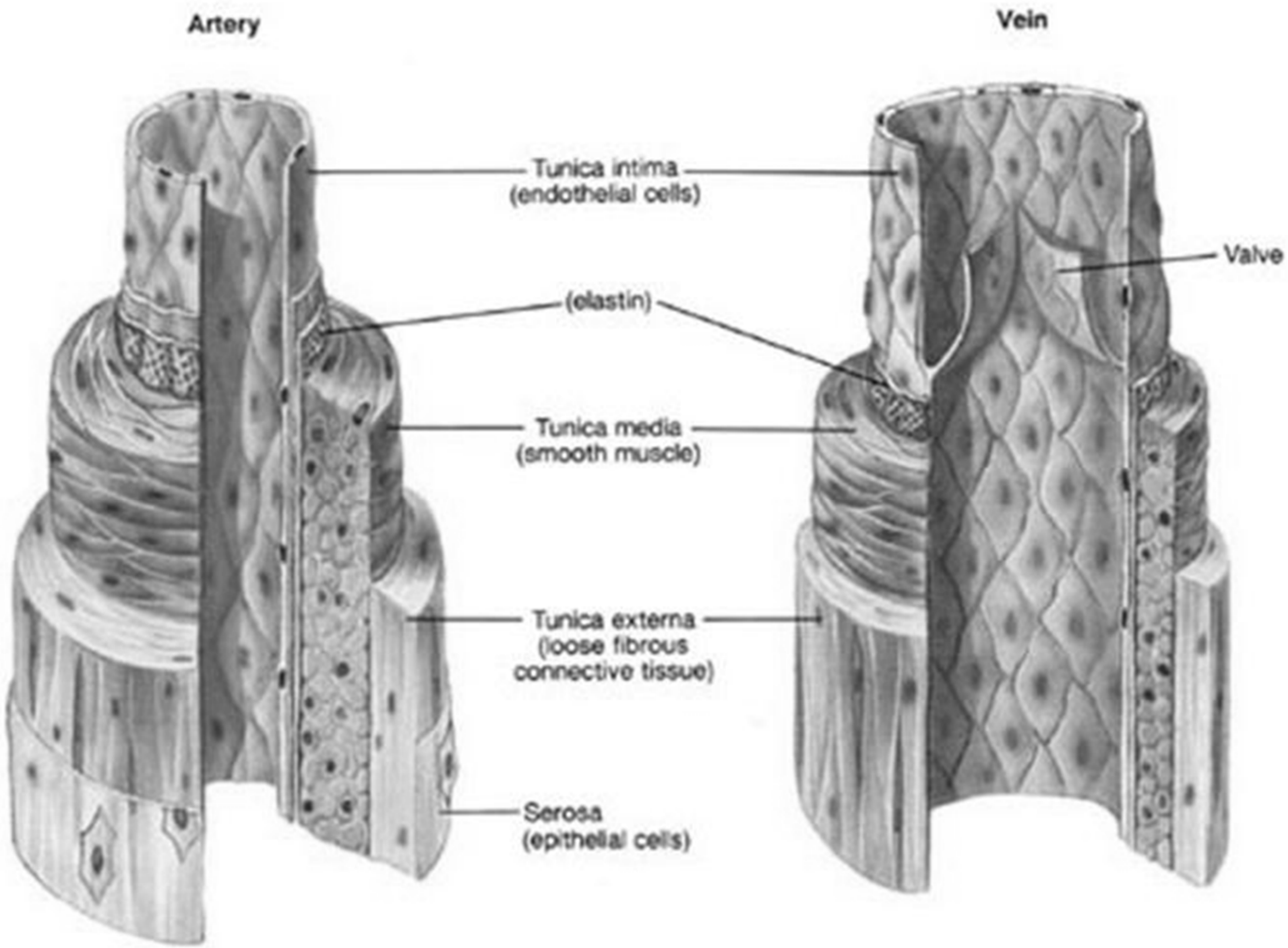
• The adventitia has a high deformable structure with different shape and orientation of its components at different loads.

• At non-physiological high pressure or axial tension (e.g. due to injuries), the collagen net stiffens and acts as a overstretch protection of the intima and media, where the latter has a small ultimate strength in the axial direction.



Functions of Arterial Layers

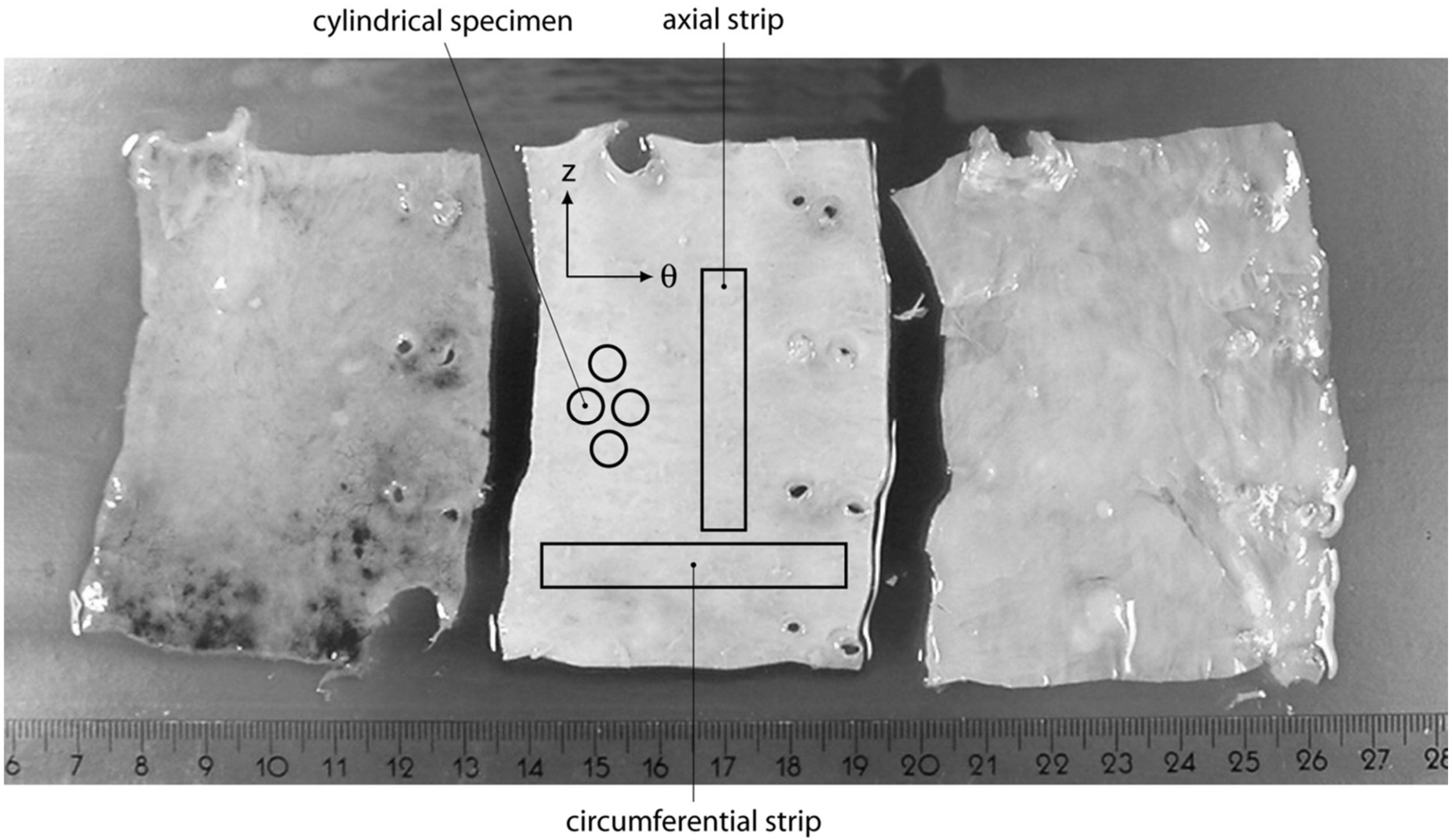
Artery vs. vein



Source: Fox, Stuart I. Human physiology 4th edition, Brown Publishers

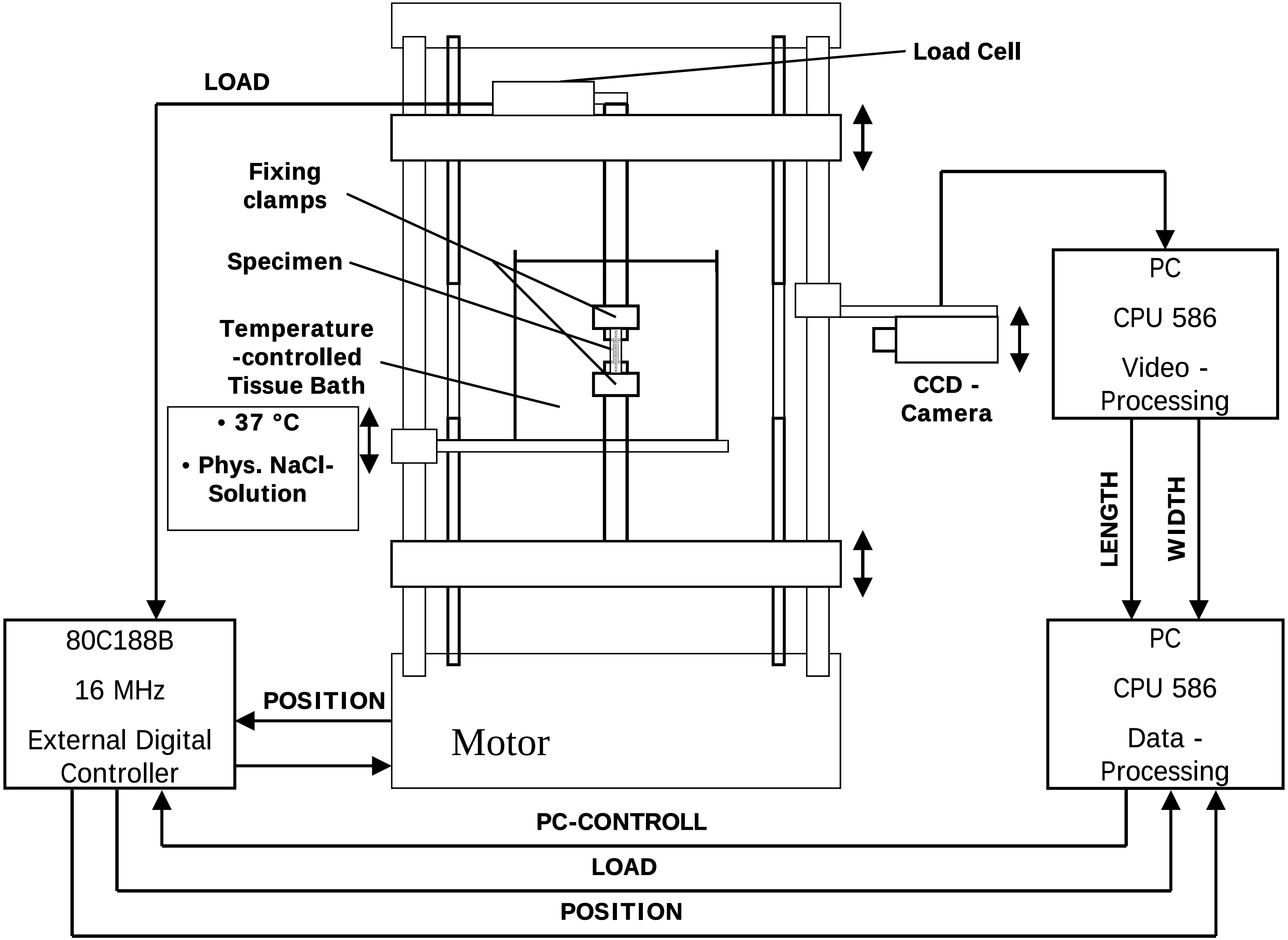
Functions of Arterial Layers

Adventitia **Media** **Intima**



Experimental methods
Left anterior descending coronary artery

Arterial Wall Mechanics



Autopsy

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Axial *In Situ* Stretch

↓

Layer Preparation

↓

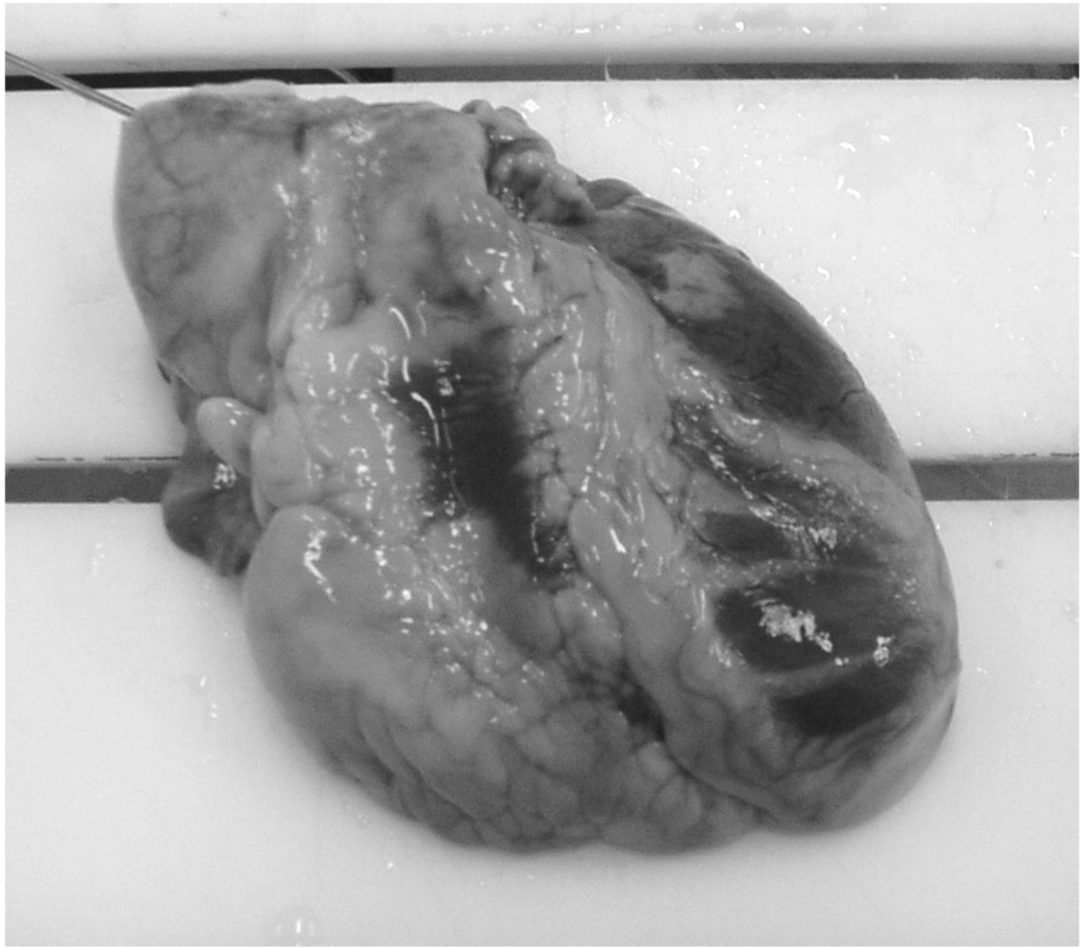
Mechanical Testing

↓

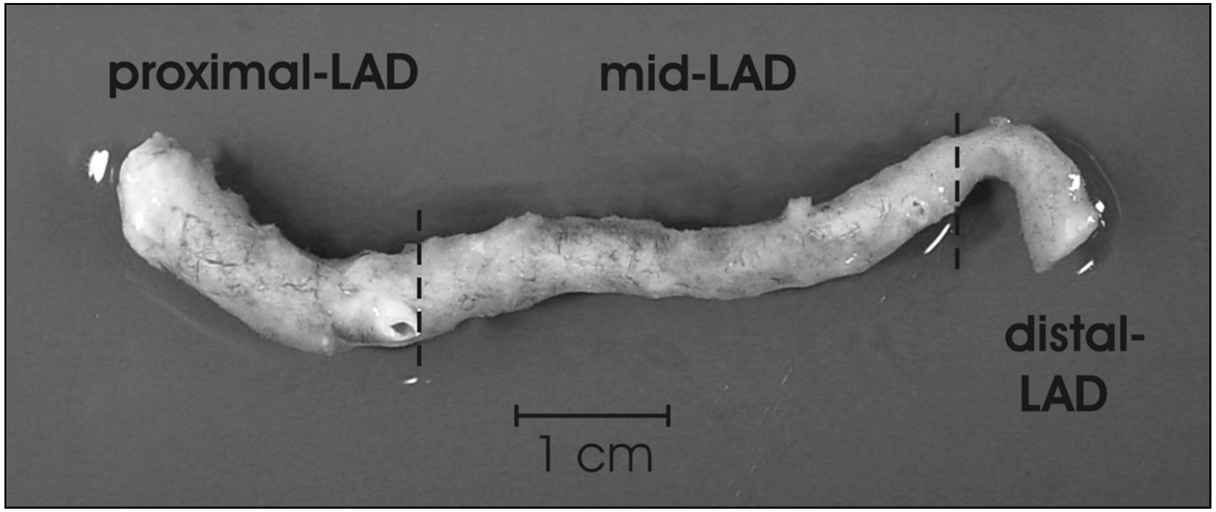
Ultimate Tensile Strength

↓

Histology



- Autopsy
- **Axial In Situ Stretch**
- Layer Preparation
- Mechanical Testing
- Ultimate Tensile Strength
- Histology



Arterial Wall Mechanics

Autopsy

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Axial *In Situ* Stretch

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Layer Preparation

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Mechanical Testing

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Ultimate Tensile Strength

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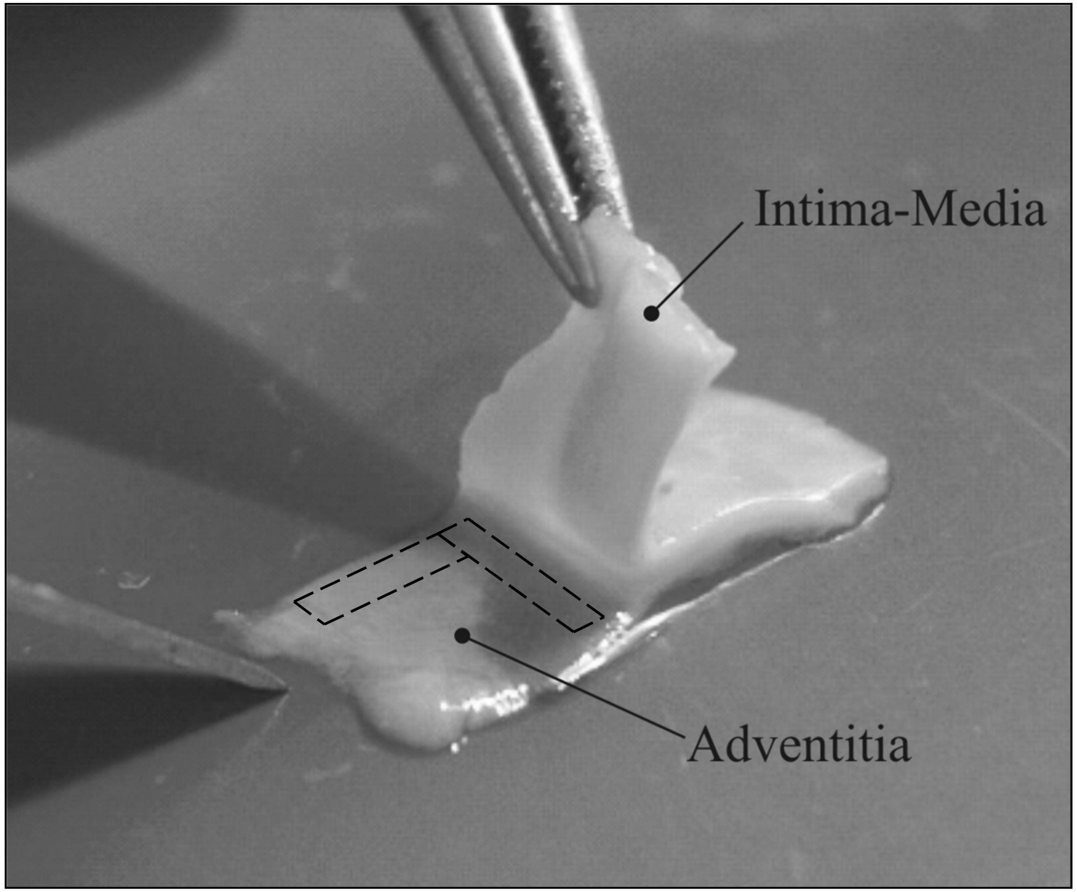
Histology



Arterial Wall Mechanics

Autopsy

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Axial *In Situ* Stretch

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Layer Preparation

↓

Mechanical Testing

↓

Ultimate Tensile Strength

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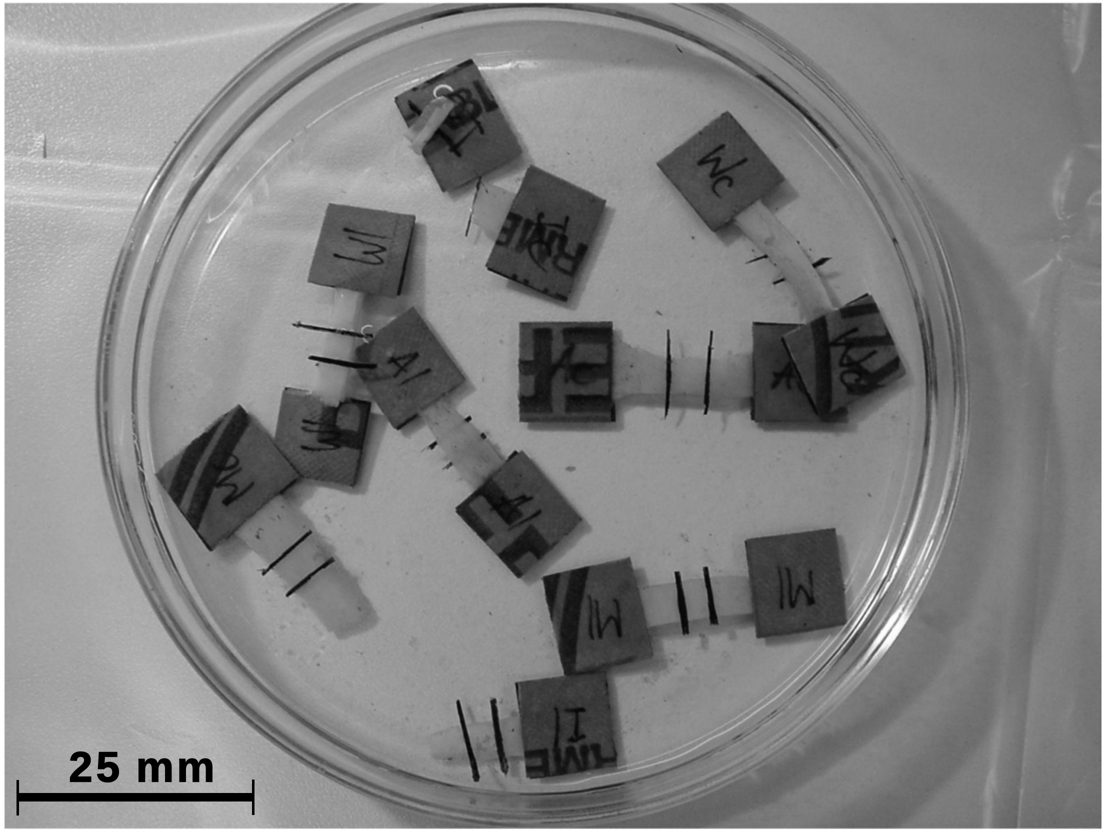
Histology



Arterial Wall Mechanics

Autopsy

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Axial *In Situ* Stretch

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Layer Preparation

↓

Mechanical Testing

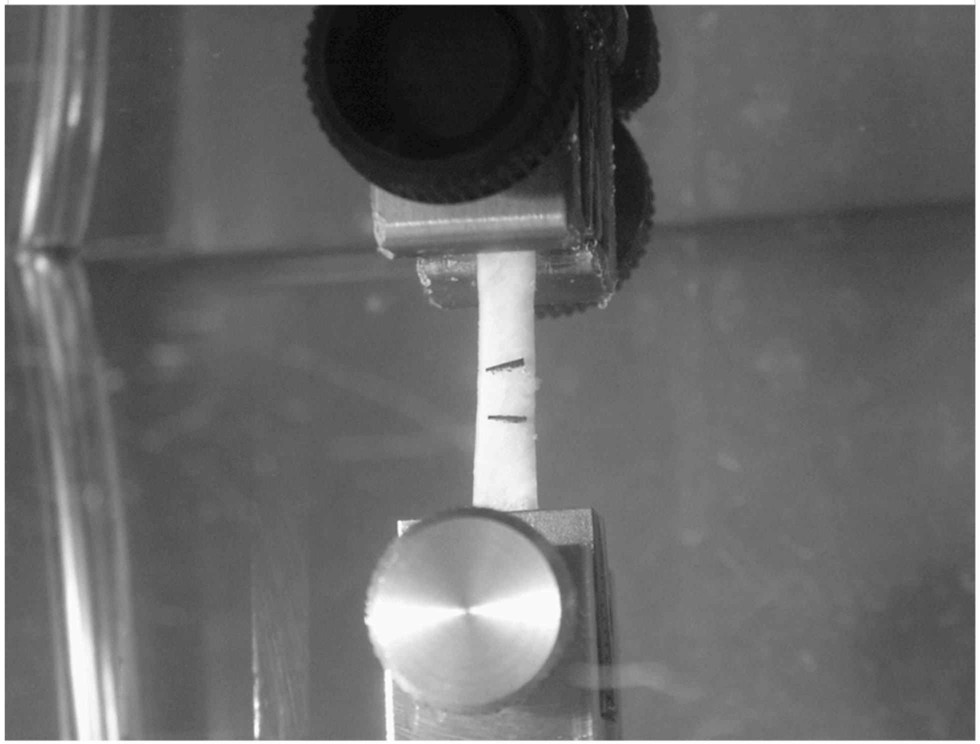
↓

Ultimate Tensile Strength

↓

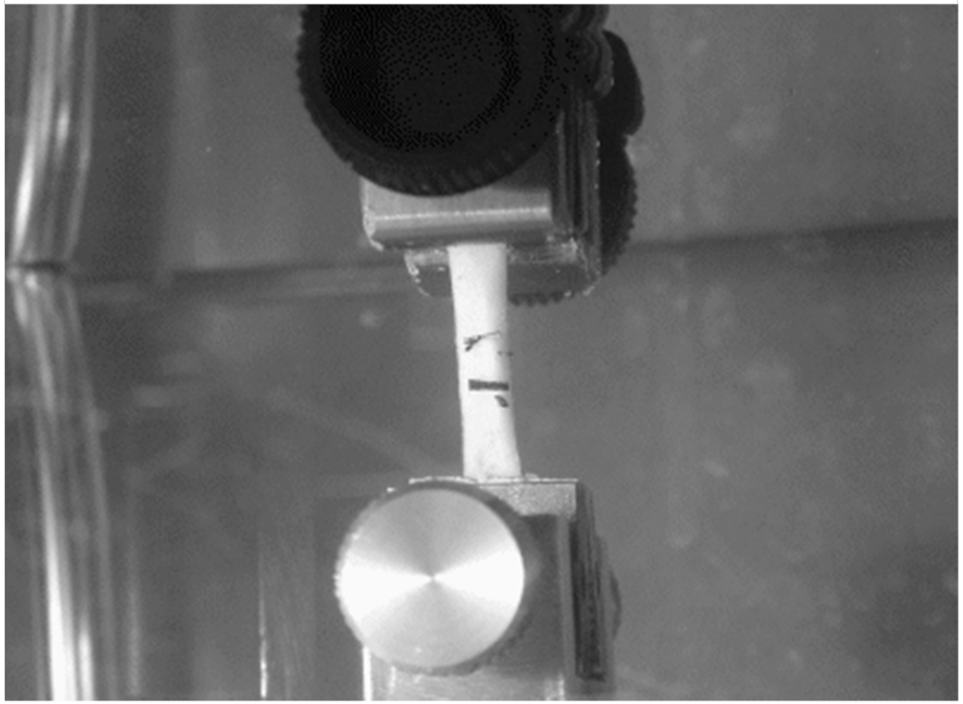
Histology

Strip Testing



- **Autopsy**
- **Axial *In Situ* Stretch**
- **Layer Preparation**
- **Mechanical Testing**
- **Ultimate Tensile Strength**
- **Histology**

Ultimate Tensile Stress and Stretch



Arterial Wall Mechanics

Autopsy

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Axial *In Situ* Stretch

↓

Layer Preparation

↓

Mechanical Testing

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Ultimate Tensile Strength

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Histology

- Confirm Correct Layer Separation
- Histostructural Homogeneity

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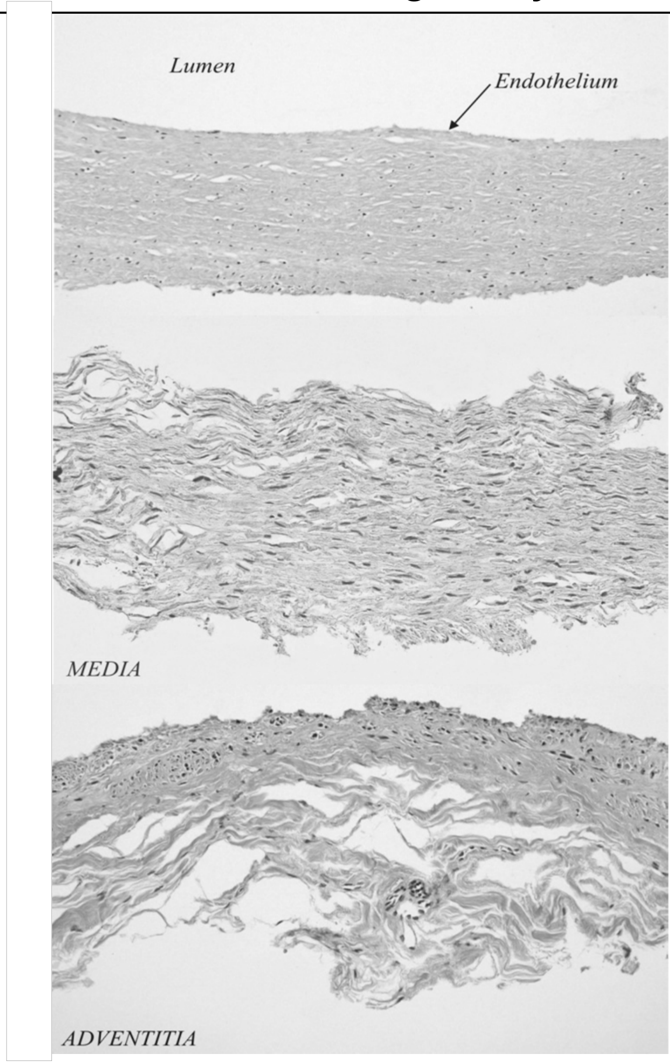
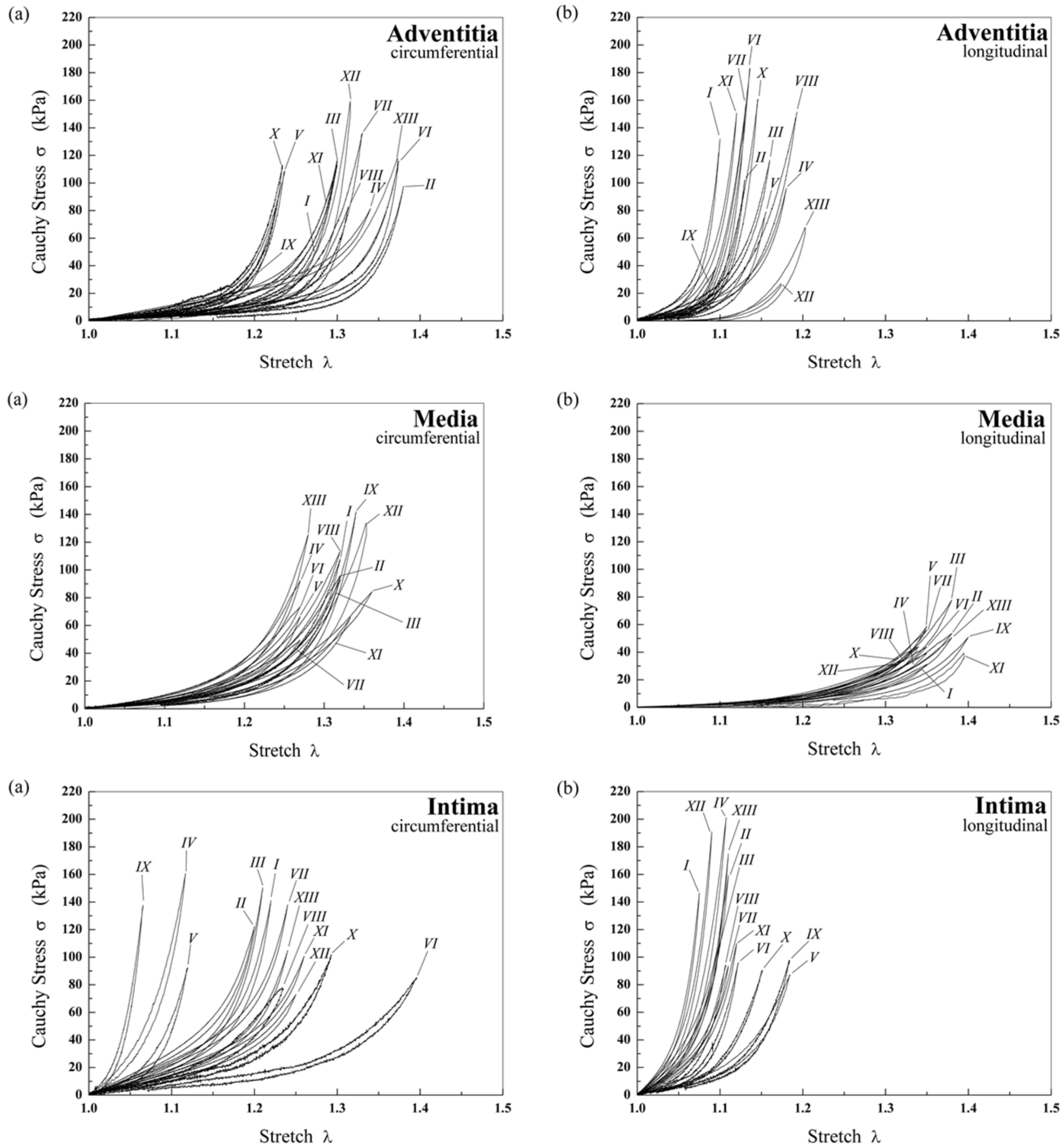
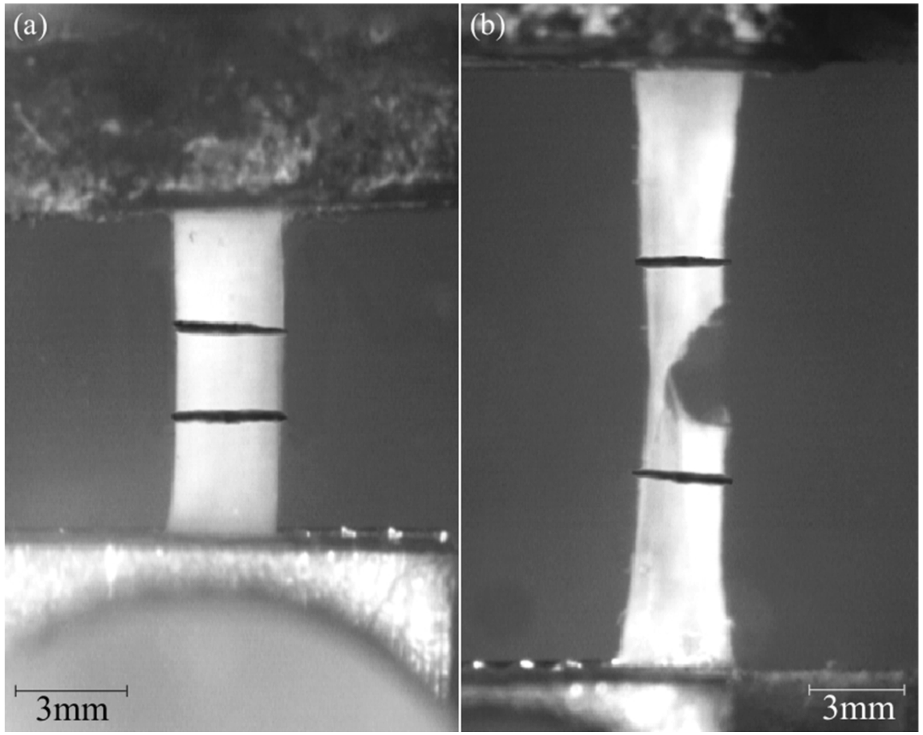


Mechanical Behavior of the LAD (circ. and axial)

- Nonlinear and anisotropic
- Layer-specific differences
- Media showed less stiffness



Results: Ultimate Tensile Stress and Stretch



	Arterial Layer and Orientation					
	Adventitia		Media		Intima	
	AC (n = 5)	AL (n = 6)	MC (n = 9)	ML (n = 7)	IC (n = 6)	IL (n = 7)
$\bar{\sigma}_{\text{ult}}$, kPa	1430.0±604.0	1300.0±692.0	446.0±194.0	419.0±188.0	394.0±223.0	391.0±144.0
λ_{ult}	1.66±0.24	1.87±0.38	1.81±0.37	1.74±0.28	1.60±0.29	1.55±0.40

Circ. and long. ultimate tensile stresses of adventitia **> 1.3 MPa**

Summary

Intima demonstrates remarkable thickness, load-bearing capacities and mechanical strength

Non-stenotic aged coronary arteries needs to be modeled as a structure composed of 3 solid mechanically relevant layers

Wall overstretch and rupture is strongly restricted by adventitial strength

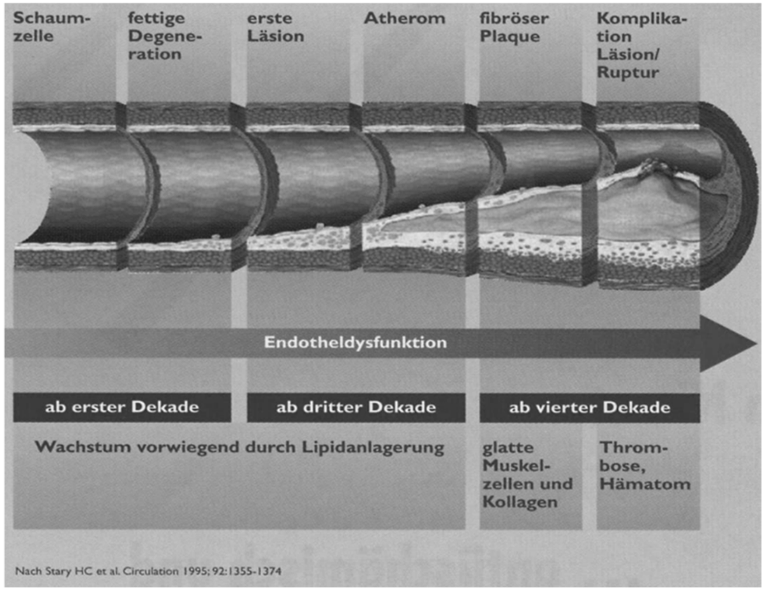
Aging and Pathology

Aging and Pathology

• The arterial wall reveals a stiffening with increasing age. Histological investigation shows an increase of collagen fibers and a fragmentation of elastin fibers (Riede, 1995). This alteration is called arteriosclerosis (Arteriosklerose). Arteriosclerosis is a general term describing any hardening (and loss of elasticity) of arteries.

• Atherosclerosis is the condition in which an artery wall thickens and stiffens as the result of a build up of fatty materials such as cholesterol.

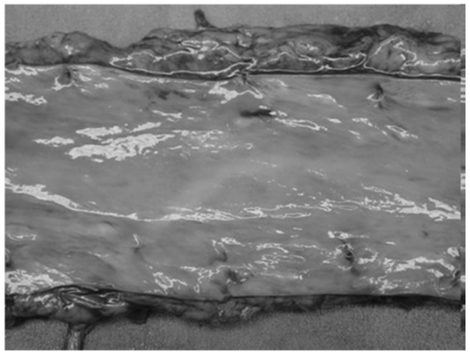
• Atherosclerosis starts in the childhood with forming of so-called “fatty streaks” (Stary, 1990).



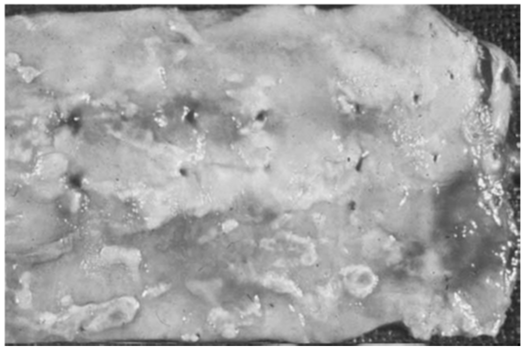
Aging and Pathology

• Atherosclerotic lesions (plaques) show different stages during development (Stary, 1995).

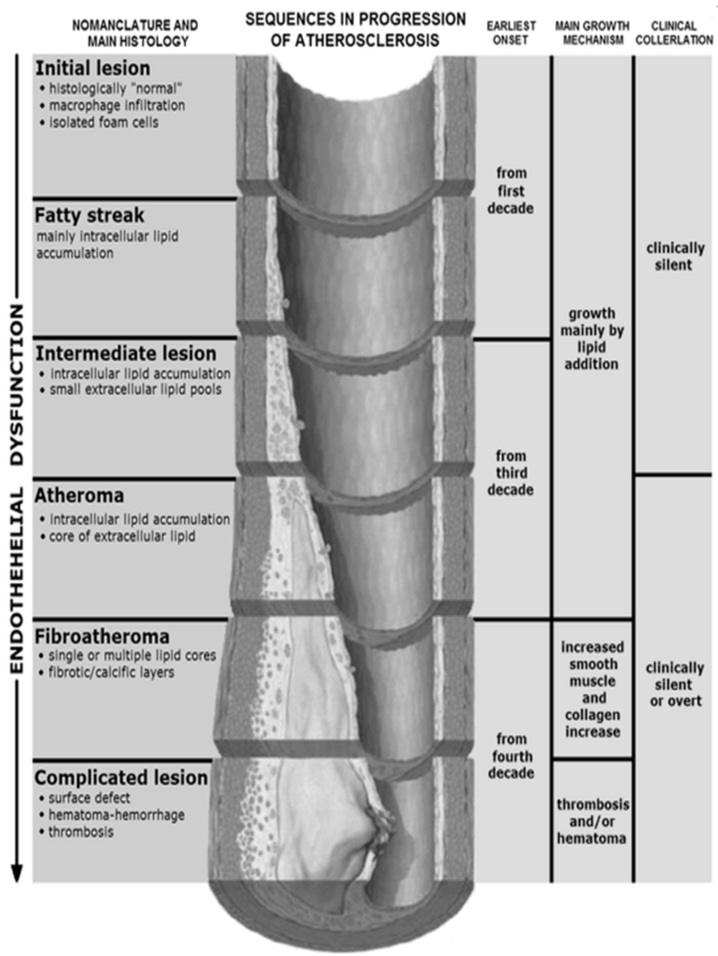
• They start with small thickening of the intima (initial lesion, fatty streaks), over “atheroma” (lipid accumulation and forming of a lipid core), until to the so-called “complicated lesions” which can lead to clinical events (heart attack, stroke, acute peripheral occlusive disease).



http://www.kgu.de/zmorph/histopatho/patho/pub/data/cm/s002_a.jpg



http://www.pathology.vcu.edu/education/dental2/images/lab7.jpg



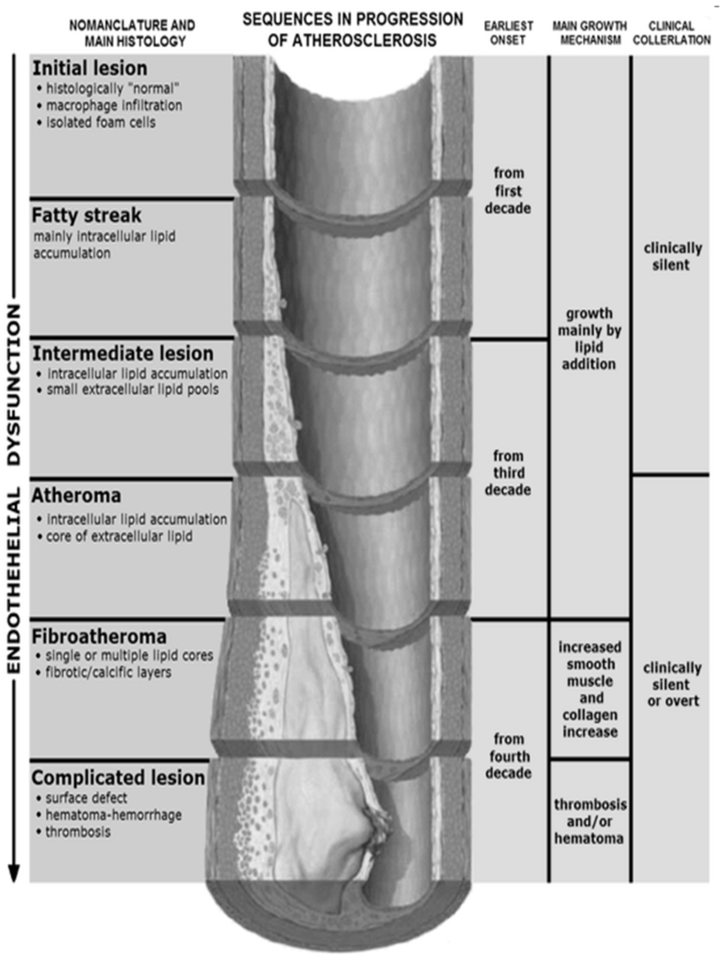
http://scienceblogs.com/denialism/images/atherosclerosis.jpg

Aging and Pathology

• The geometry and the histological composition of plaques are highly complex and vary strongly from lesion to lesion.

• The mechanical behavior of different plaque components are highly variable and due to testing methodical problems poorly investigated.

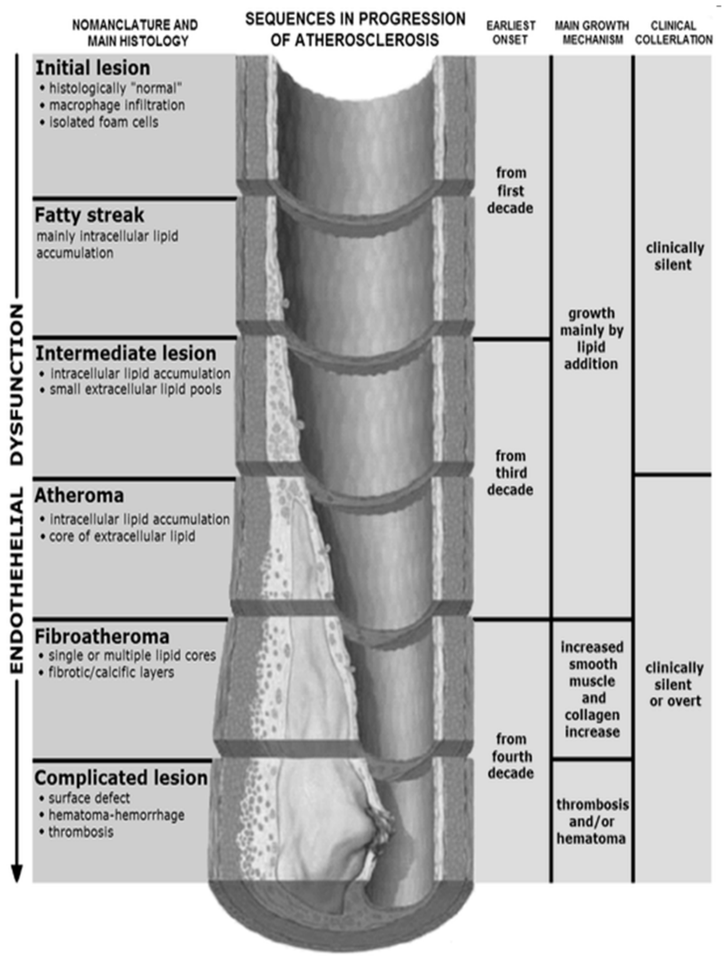
• Lipid pools show behavior like viscous fluids, fibrous tissues show strong direction-dependent nonlinear properties, and calcified tissues have very high Young's modulus and are brittle.



http://scienceblogs.com/denialism/images/atherosclerosis.jpg

Aging and Pathology

• For the testing of the mechanical behavior of human arterial walls it important to document for existing cardio-vascular diseases, risk factors, gender, and the general condition of the vascular system in regard to atherosclerosis.



http://scienceblogs.com/denialism/images/atherosclerosis.jpg

Experimental methods
Aging and Pathology

Arterial Wall Mechanics

Autopsy

↓

hr MRI Examination

↓

Histology

↓

Tissue Preparation

↓

Mechanical Testing

↓

Ultimate Tensile Strength

Autopsy

↓

hr MRI Examination

↓

Histology

↓

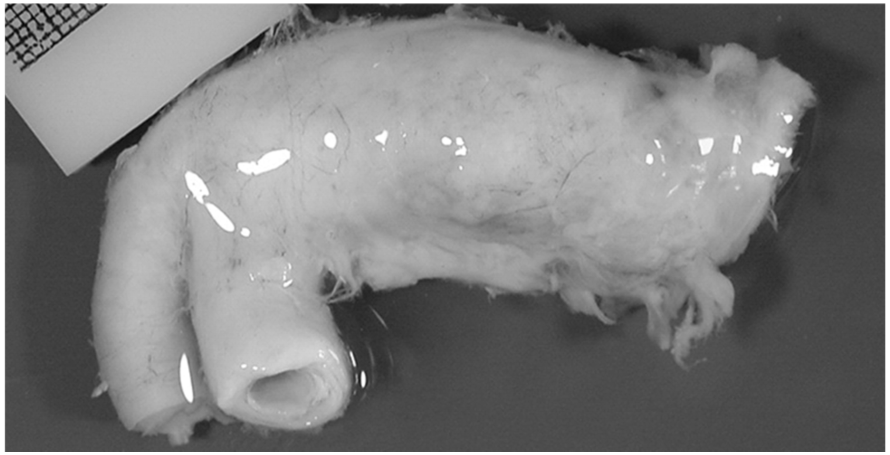
Tissue Preparation

↓

Mechanical Testing

↓

Ultimate Tensile Strength



Specimens

- Iliac arteries
- N = 9
- Atherosclerotic lesion of Type V or higher (Stary 2003) were required
- 7 Different Tissue Types
- Age: (74.9 ± 12.5 yrs, mean ± SD; range 60 to 90)
- Female : male = 6 : 3

Arterial Wall Mechanics

Autopsy

↓

hr MRI Examination

↓

Histology

↓

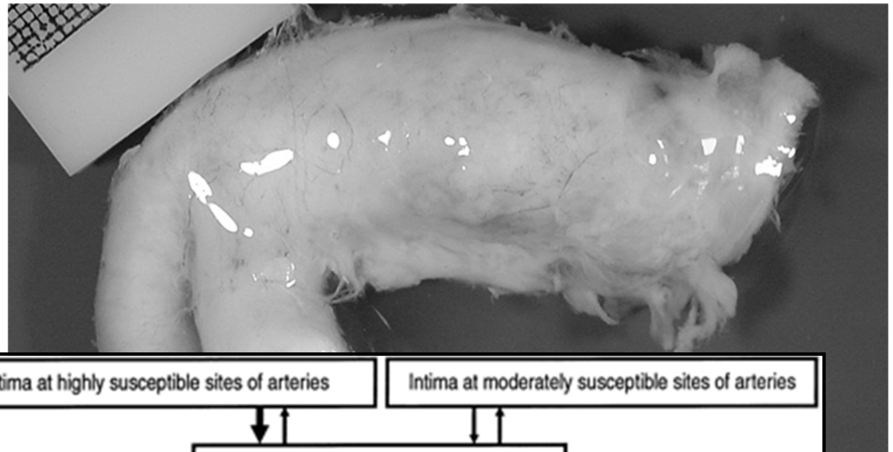
Tissue Preparation

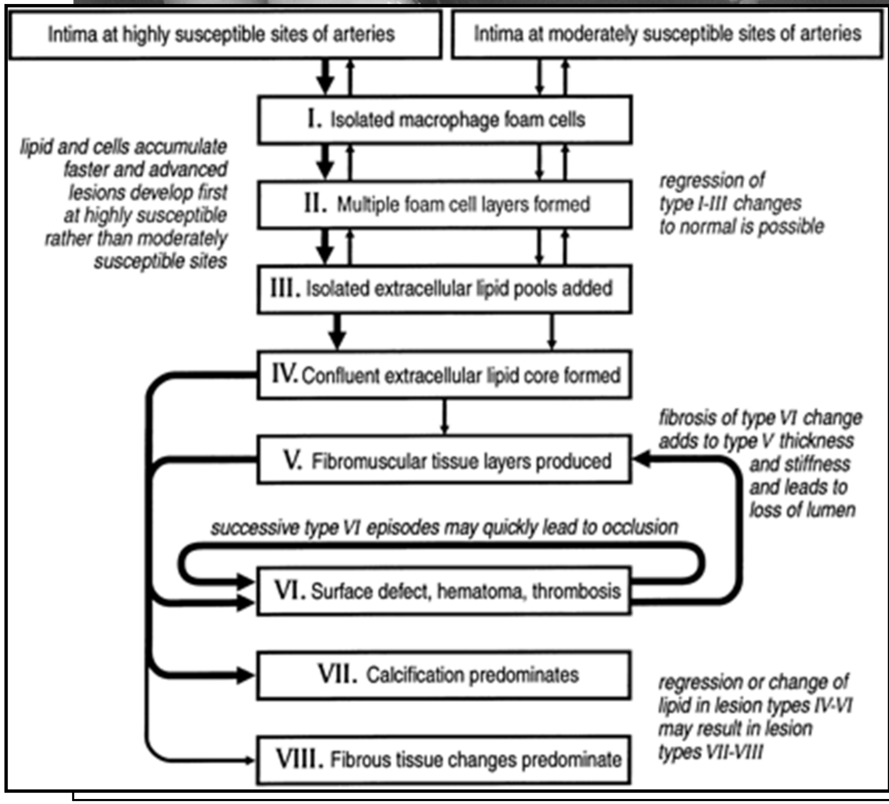
↓

Mechanical Testing

↓

Ultimate Tensile Strength





/ or higher

SD; range

Arterial Wall Mechanics

Autop

hr MF Examina

Histolo

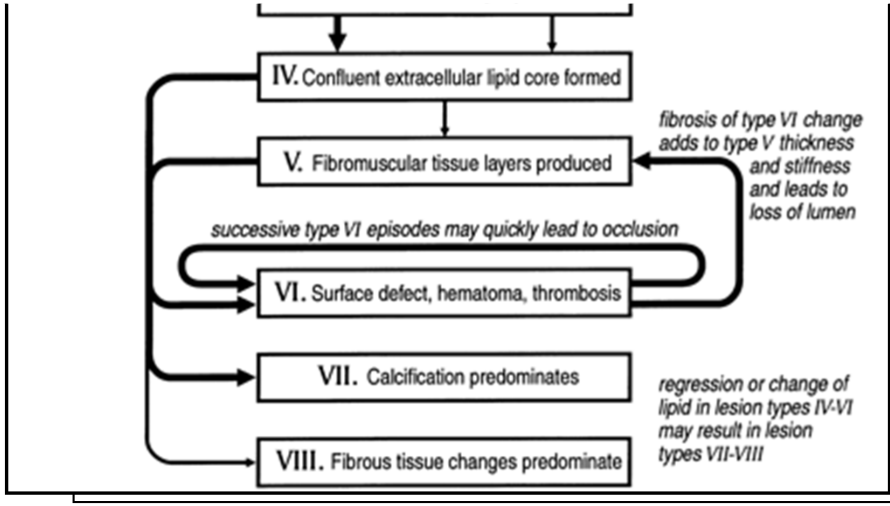
Tissu Prepara

Mechanical Testing

Ultimate Tensile Strength

Table 1 Anamnesis: CIA, common iliac artery; EIA, external iliac artery; IIA, internal iliac artery; AH, antihypertensives; AS, atherosclerosis; BP, bronchopneumonia; BS, bypass surgery; CS, coronary sclerosis; GHD, global heart dilation; GS, generally atherosclerosis; MI, myocardial infarction. Types of atherosclerotic lesions are according to Stary et al. [22]. Assessment of atherosclerosis is based on autopsy reports (y, medium or high grade; n, no or low grade).

Specimen Type of iliac artery	I EIA	II CIA	III IIA	IV CIA	V CIA	VI IIA	VII CIA	VIII IIA	IX CIA
Age (yrs)	65	90	80	64	81	60	60	87	87
Sex	f	m	f	f	f	m	m	f	f
Primary disease	CS	GS	AS	CS	CS	CS	AS	GS	GS
Cause of death	MI	MI	BP	MI	MI	GHD	MI	BP	BP
Atherosclerosis									
Type of atherosclerotic lesions [22]	*V*	*VII*	*V*	*VIII*	*VII*	*VII*	*VII*	*VII*	*VIII*
Adjoining vessels	y	y	y	y	y	n	y	y	y
Peripheral	y	y	y	y	y	n	y	y	y
Coronary	y	y	y	y	y	y	y	y	y
Cerebral	y	y	n	n	y	n	n	y	y
Renal	y	y	y	n	y	n	n	y	y
Cardiovascular treatments	n	AH	n	BS	n	n	n	n	n



/ or higher

SD; range

Arterial Wall Mechanics

Autopsy

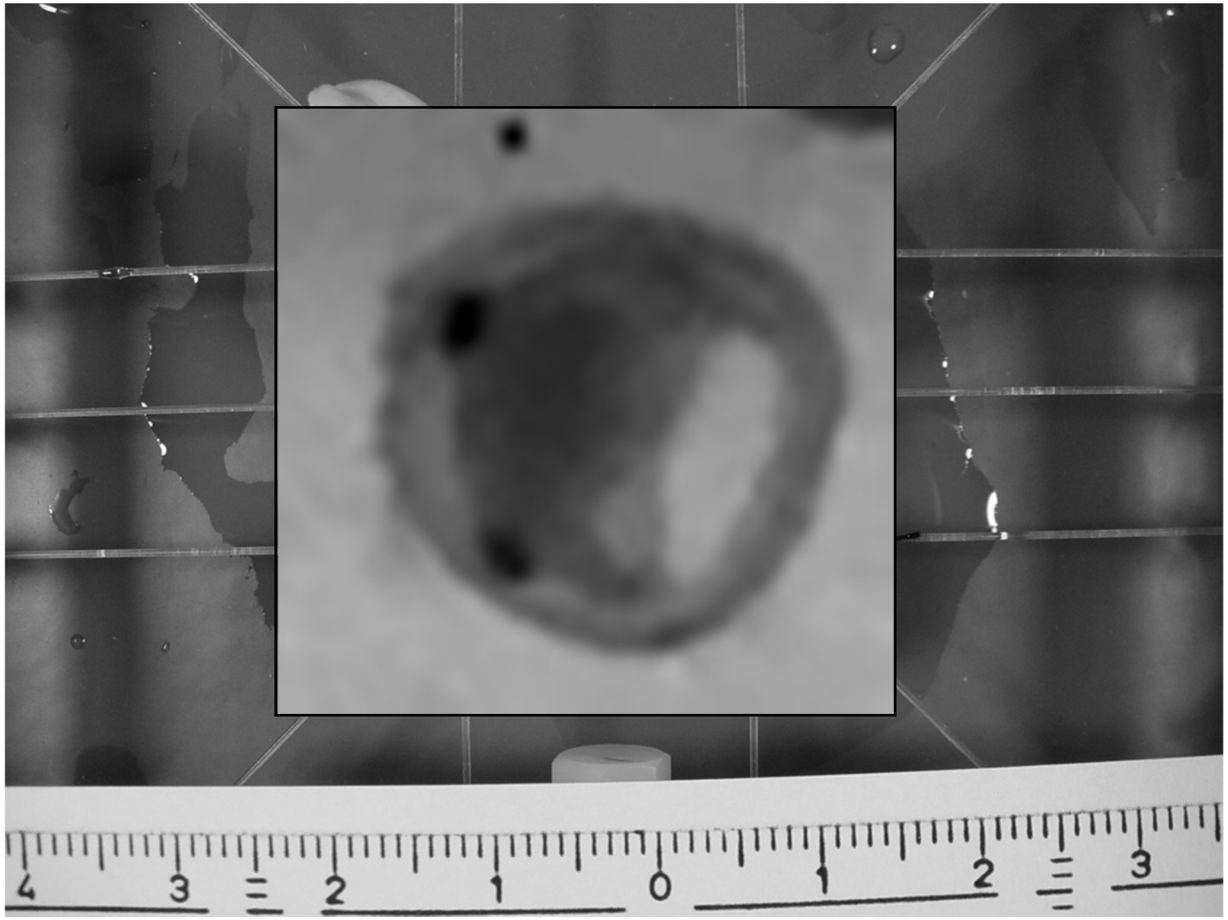
hr MRI Examination

Histology

Tissue Preparation

Mechanical Testing

Ultimate Tensile Strength



Arterial Wall Mechanics

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hr MRI Examination

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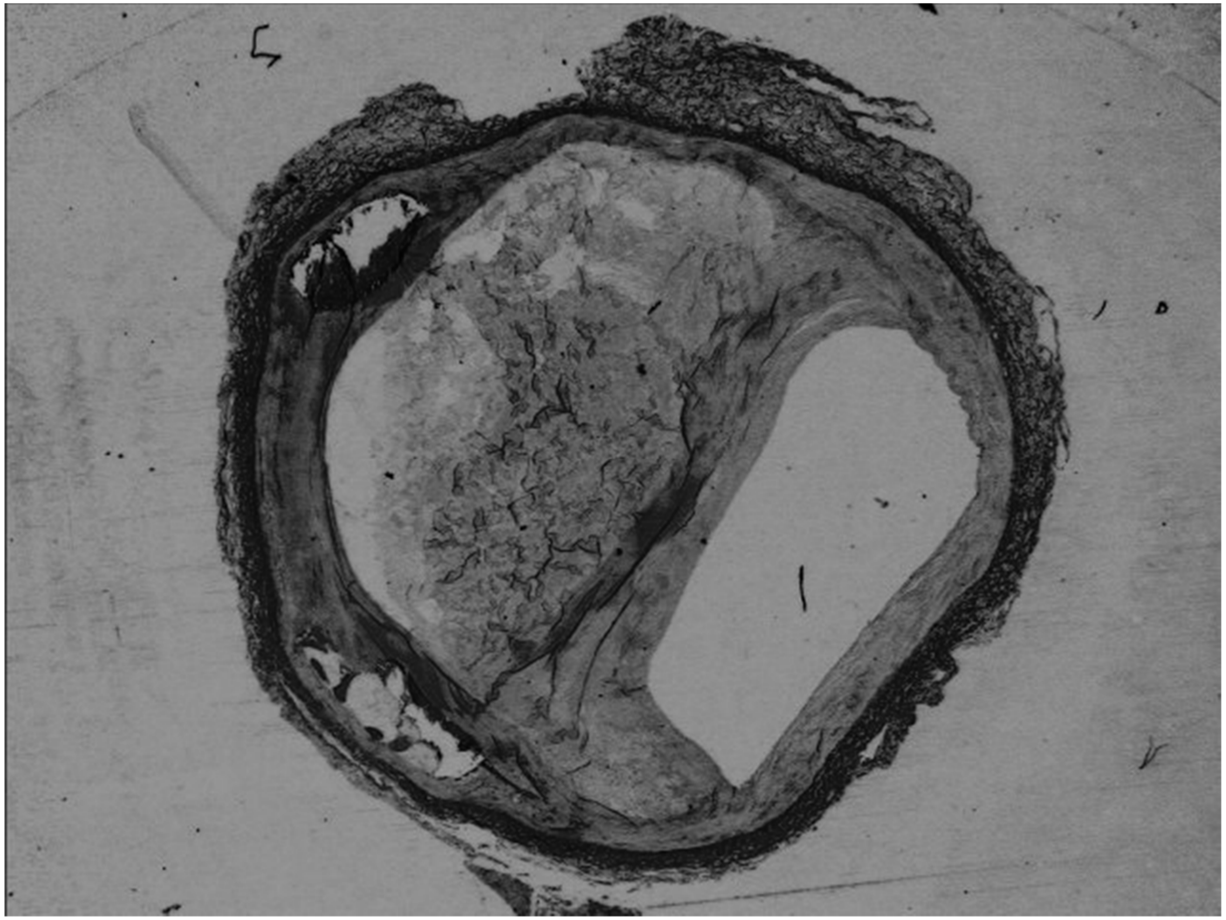
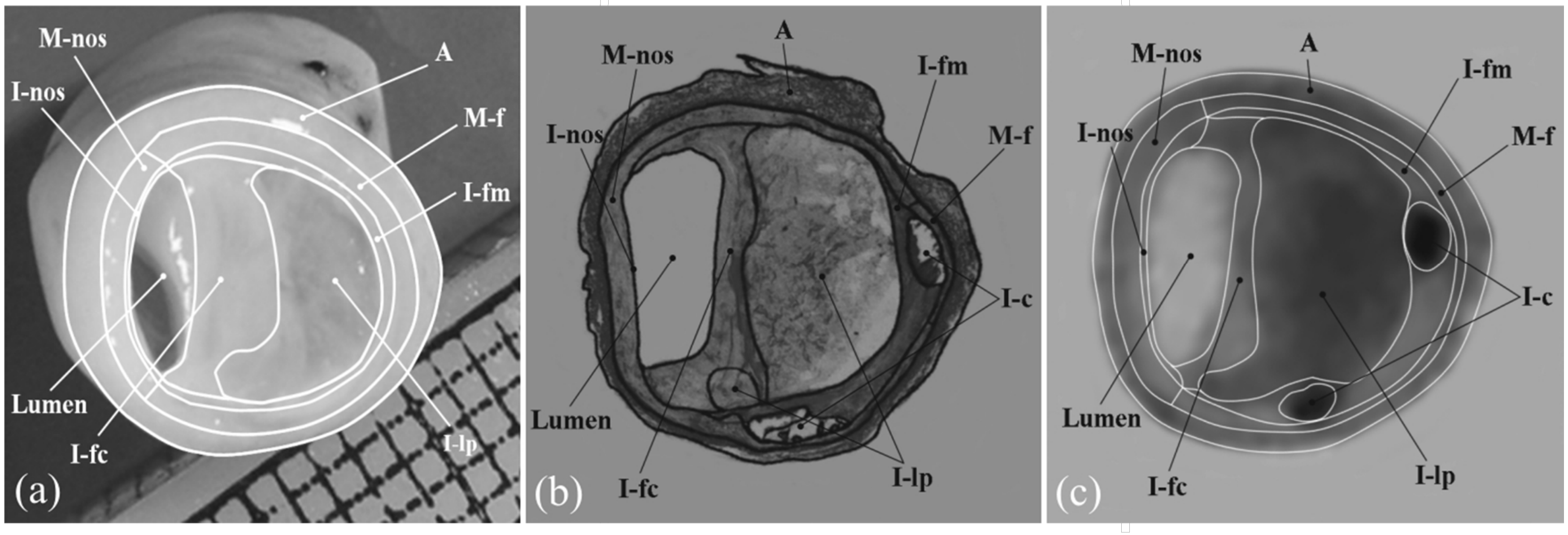
Ultimate Tensile Strength



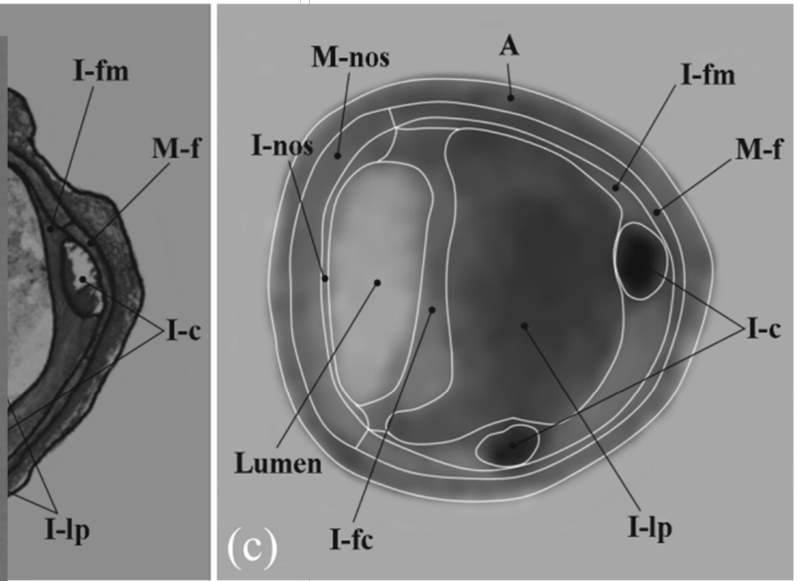
Tissue types of a high-stenotic Human External Iliac Artery



Macrocopic View Histological Section Hr-MRI Image

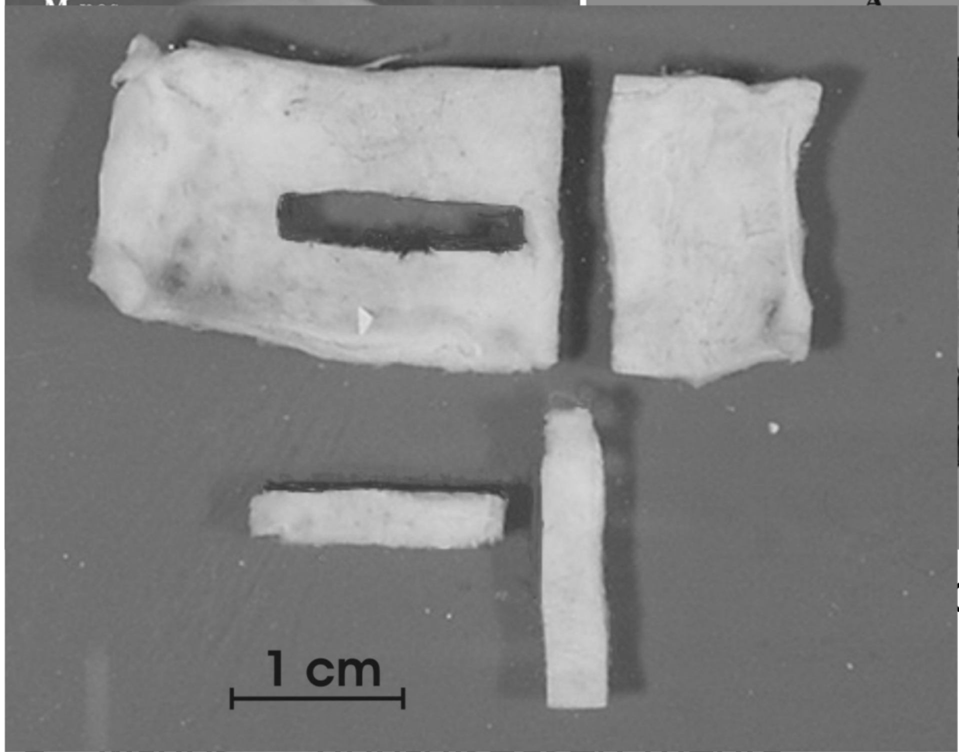
- A ... adventitia
- M-nos ... non-diseased media
- M-f ... diseased fibrotic media
- I-nos ... non-diseased intima
- I-fc ... fibrous cap
- I-fm ... fibrotic intima at medial border
- I-c ... calcification
- I-lp ... lipid pool

Tissue types of a high-stenotic Human External Iliac Artery



cal Section

Hr-MRI Image



- M-nos ... non-diseased media
- M-f ... diseased fibrotic media
- I-nos ... non-diseased intima

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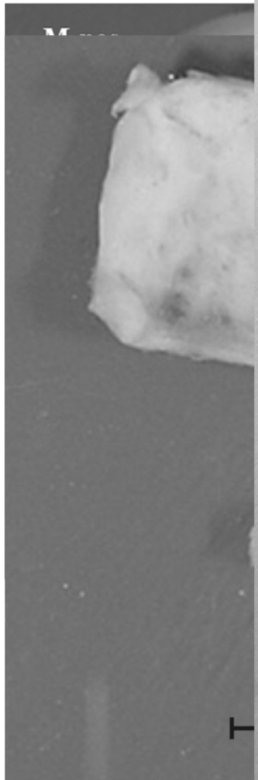
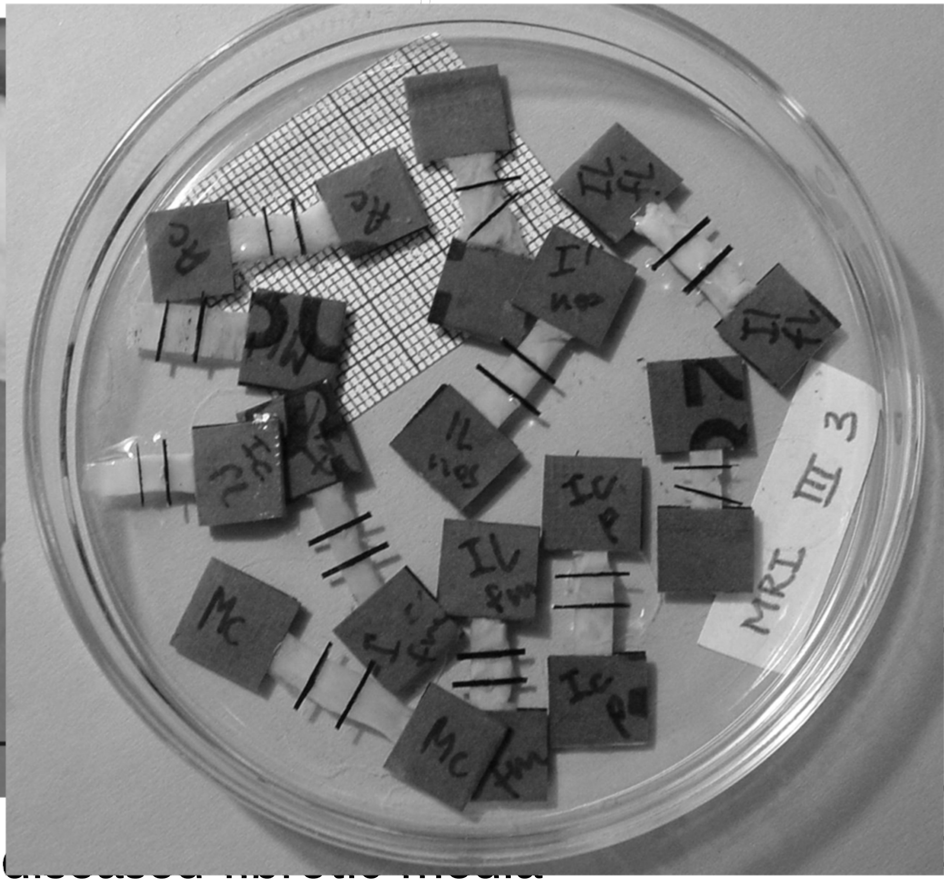
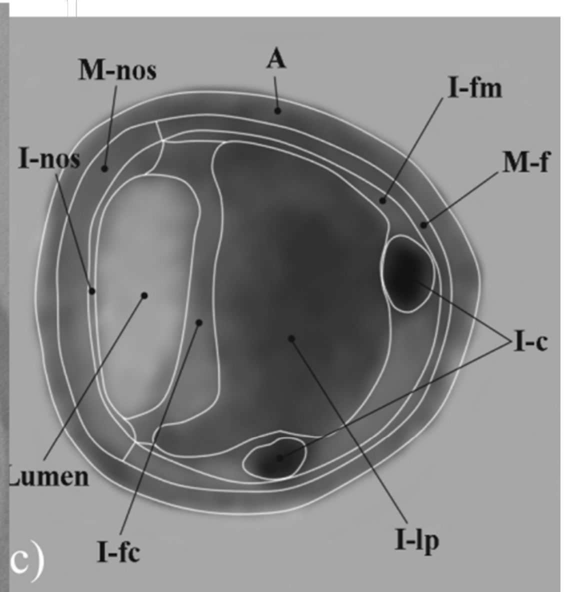
Tissue types of a high-stenotic Human External Iliac Artery





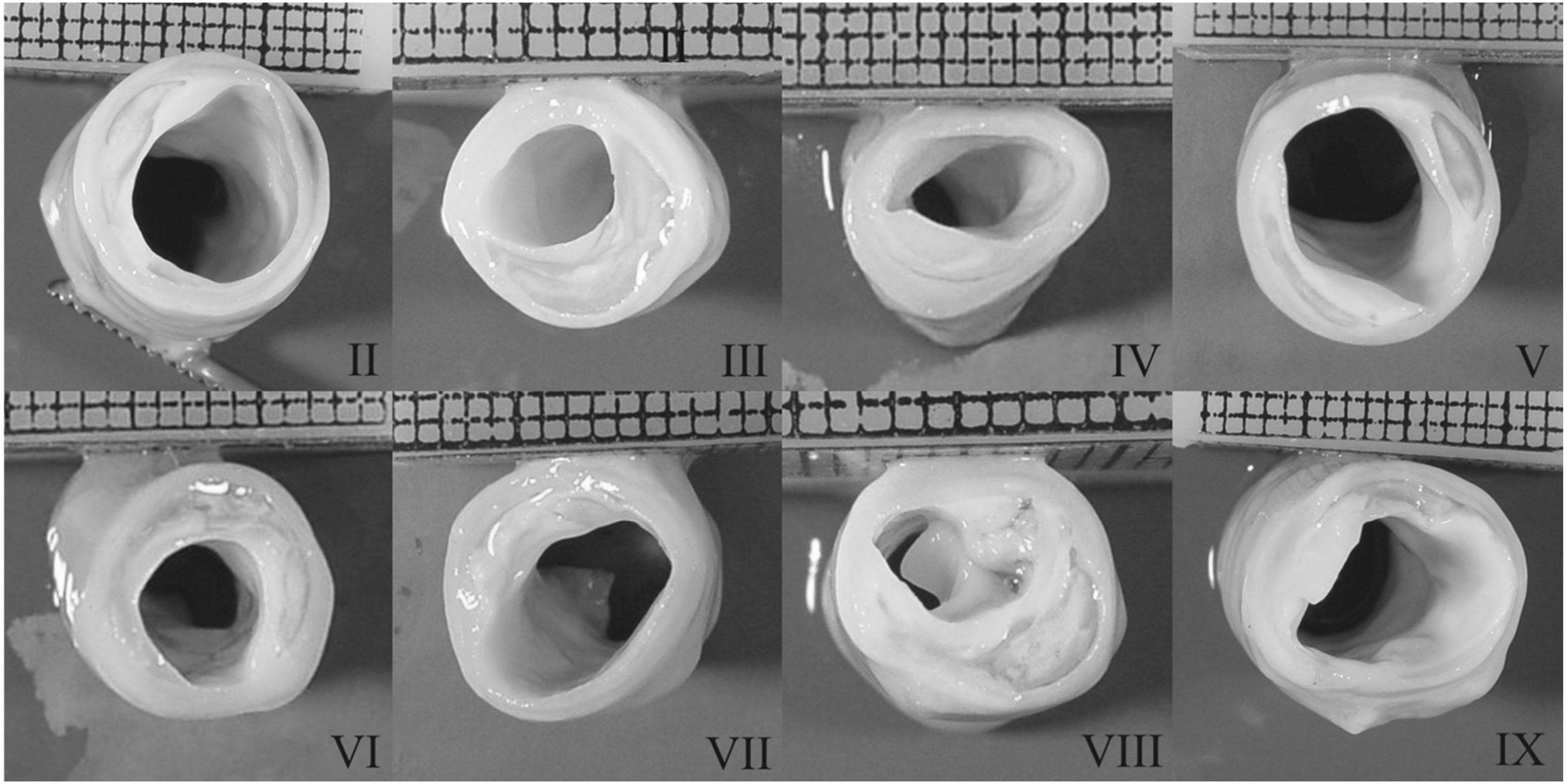


Hr-MRI Image

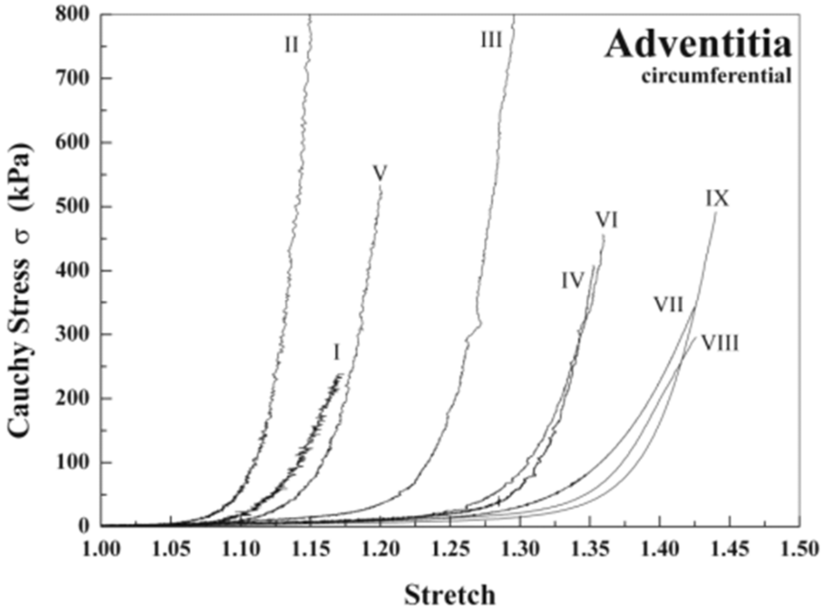
- M-nos
- M-f
- I-nos ... non-diseased intima
- ... fibrous cap
- ... fibrotic intima at medial ...der
- I-c ... calcification
- I-lp ... lipid pool

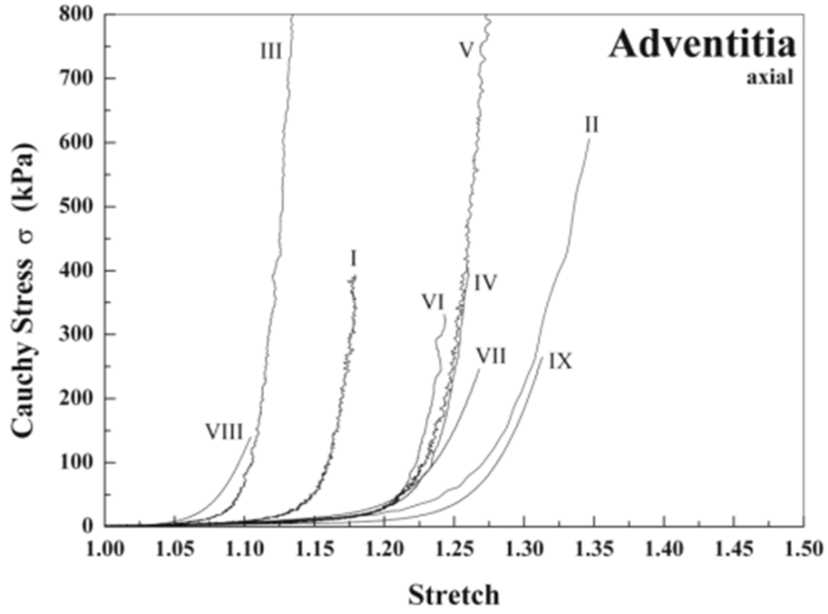
Macroscopic view of eight human stenotic iliac arteries

(Top ruler scale: one side of a square characterizes 1 mm)

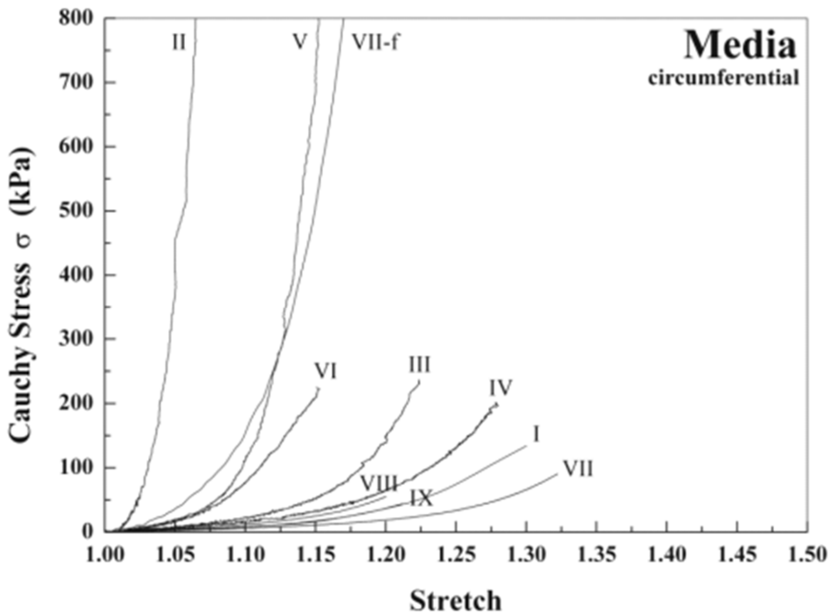


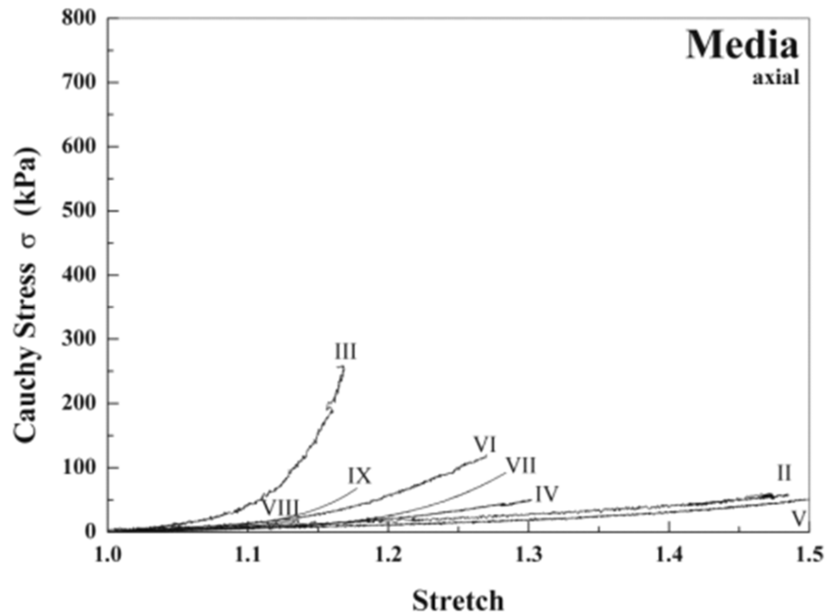
Results: Mechanical Behavior
ADVENTITIA





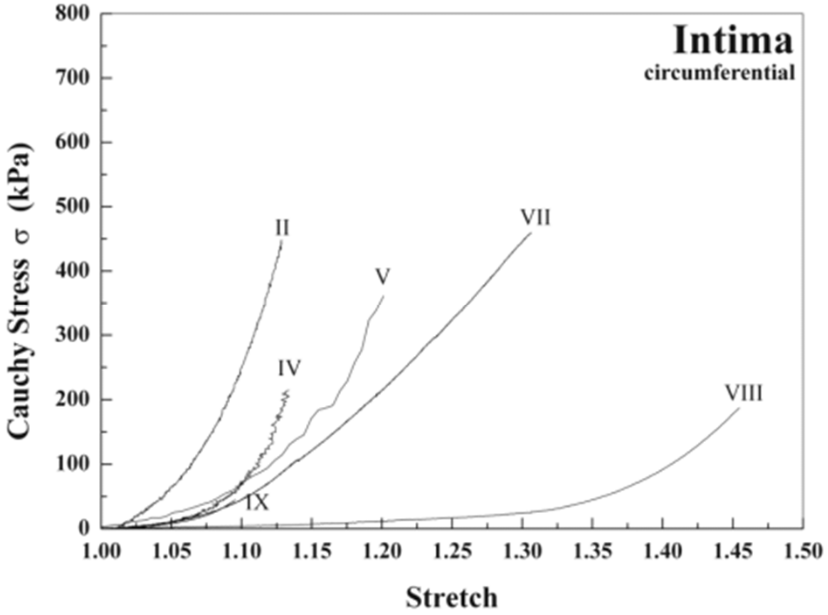
Results: Mechanical Behavior
MEDIA

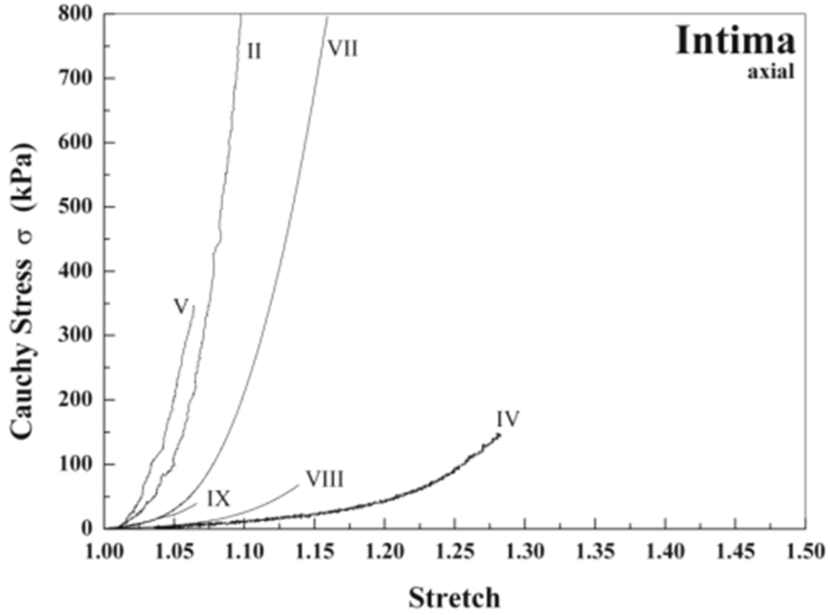




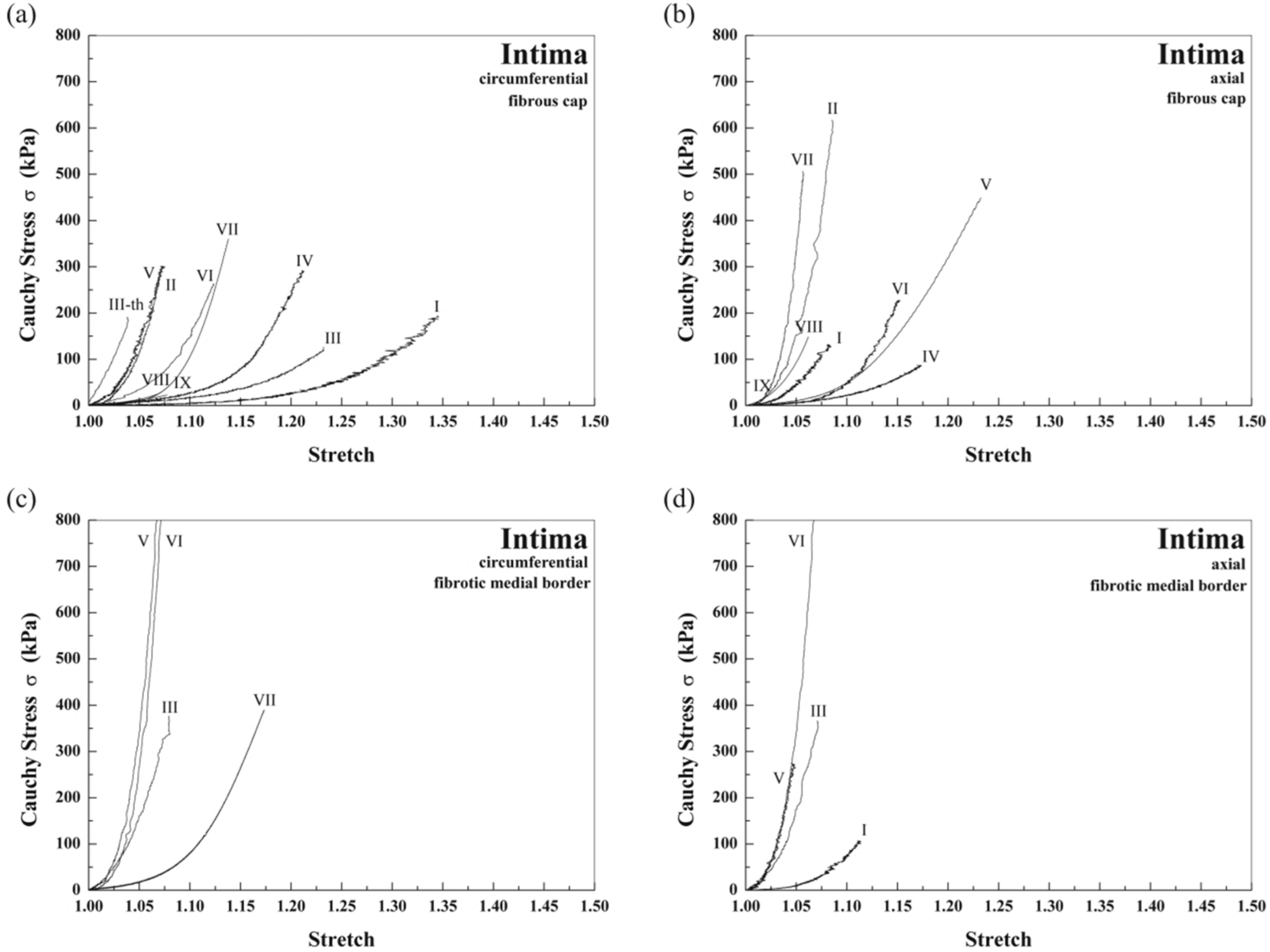
Results: Mechanical Behavior

INTIMA

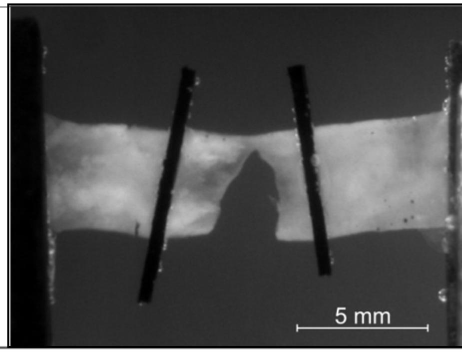




Results: Mechanical Behavior Diseased INTIMA



Results: Ultimate Tensile Stresses



		Tissue type											
		A		M-nos		I-nos		I-fc		I-fm		M-f	
Specimen		*c*	*a*	*c*	*a*	*c*	*a*	*c*	*a*	*c*	*a*	*c*	*a*
I	σ_{ult}	618.5	737.6	261.5	183.7			205.6	509.8		171.8	1278.1	181.5
	λ_{ult}	1.243	1.223	1.156	1.863			1.374	1.121		1.135	1.076	1.797
II	σ_{ult}	832.3	667.6	212.9	128.4	435.2	1321.9	299.3	617.5				
	λ_{ult}	1.173	1.392	1.409	2.005	1.129	1.117	1.073	1.068				
III	σ_{ult}	1188.3	1276.6	229.7	261.6			126.4			366.5		
	λ_{ult}	1.479	1.157	1.249	1.169			1.232			1.071		
IV	σ_{ult}	845.4	886.6	201.6				292.2					
	λ_{ult}	1.424	1.299	1.280				1.213					
V	σ_{ult}		990.7		432.7	356.4		301.3		941.1	294.3		
	λ_{ult}		1.282		1.830	1.201		1.076		1.071	1.057		
VI	σ_{ult}	802.3		298.2	121.8			287.9	506.1	999.2			
	λ_{ult}	1.413		1.177	1.283			1.126	1.058	1.078			
VII	σ_{ult}	1479.5		108.9	92.5	473.9	796.2	360.1	449.2	390.1		869.0	
	λ_{ult}	1.676		1.323	1.284	1.320	1.159	1.138	1.232	1.173		1.154	
VIII	σ_{ult}	1090.1	1005.3	93.7	141.3	368.2	703.8		402.3				193.2
	λ_{ult}	1.458	1.458	1.260	1.583	1.648	1.435		1.121				1.176
IX	σ_{ult}	1396	1097.9	209.9	148.1	809.1	952.9	165.8	326.9				
	λ_{ult}	1.652	1.658	1.313	1.267	1.357	1.309	1.222	1.208				
mean	$\bar{\sigma}_{ult}$	1031.6	951.8	202.0	188.8	488.6	943.7	254.8	468.6	776.8	277.5	1073.6	187.4
SD		306.8	209.0	69.8	110.9	185.6	272.3	79.8	100.1	336.2	98.4	289.3	8.3
mean	$\bar{\lambda}_{ult}$	1.440	1.353	1.270	1.536	1.331	1.255	1.182	1.135	1.107	1.088	1.115	1.487
SD		0.175	0.168	0.081	0.327	0.199	0.146	0.100	0.071	0.057	0.042	0.055	0.439

Summary

Novel direction-dependent stress-stretch data and fracture stresses of 7 tissue types of human atherosclerotic arteries

All tissue components indicate highly nonlinear and anisotropic properties

The present study shows the need for anisotropic models and may help to perform computational analyses of plaques during balloon angioplasty and stenting with higher accuracy