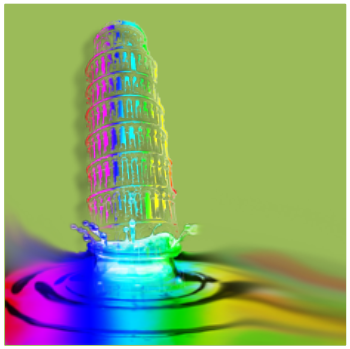
Centro E. Piaggio
bioengineering and robotics research center

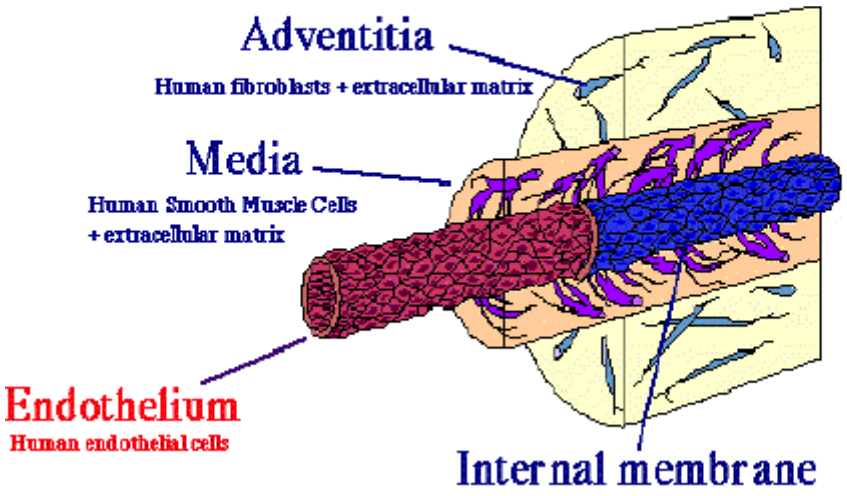


Protesi vascolari

Vascular prostheses

- Medical devices permanently implanted in order to restore the efficiency of a vascular duct that, for any reason, is not more able to transport the blood correctly.
- The vascular implants are arterial systems: it depends on the fact that venous pathologies are much less frequent and serious because the venous pressure is inferior to that arterial (this fact reduces the vascular damage) and usually collateral circulations are generated that allow to venous blood to flow.

Blood vessels



- **Intima**: lining of endothelial cells
- **Media**: smooth muscle cells and circularly aligned fiber of elastin
- **Adventizia**: fibroblasts and connective tissue

Blood vessels

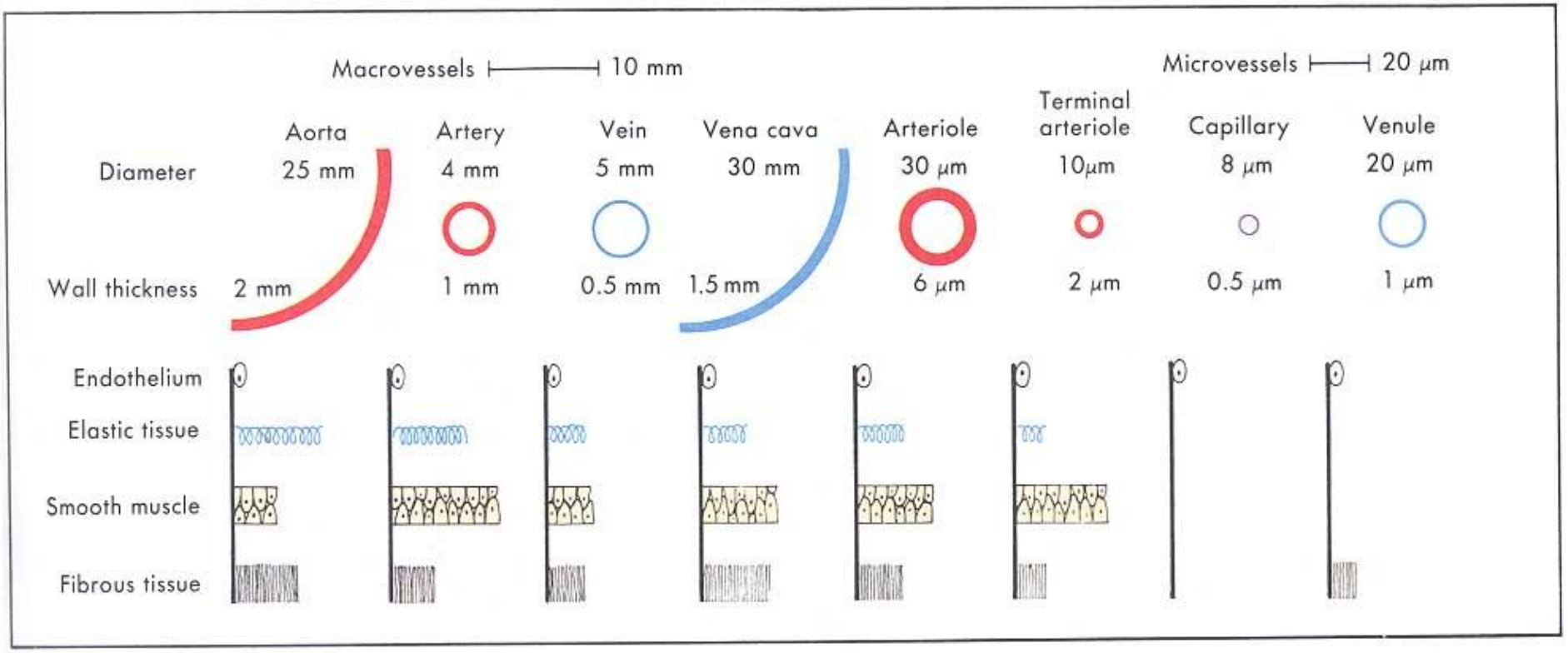
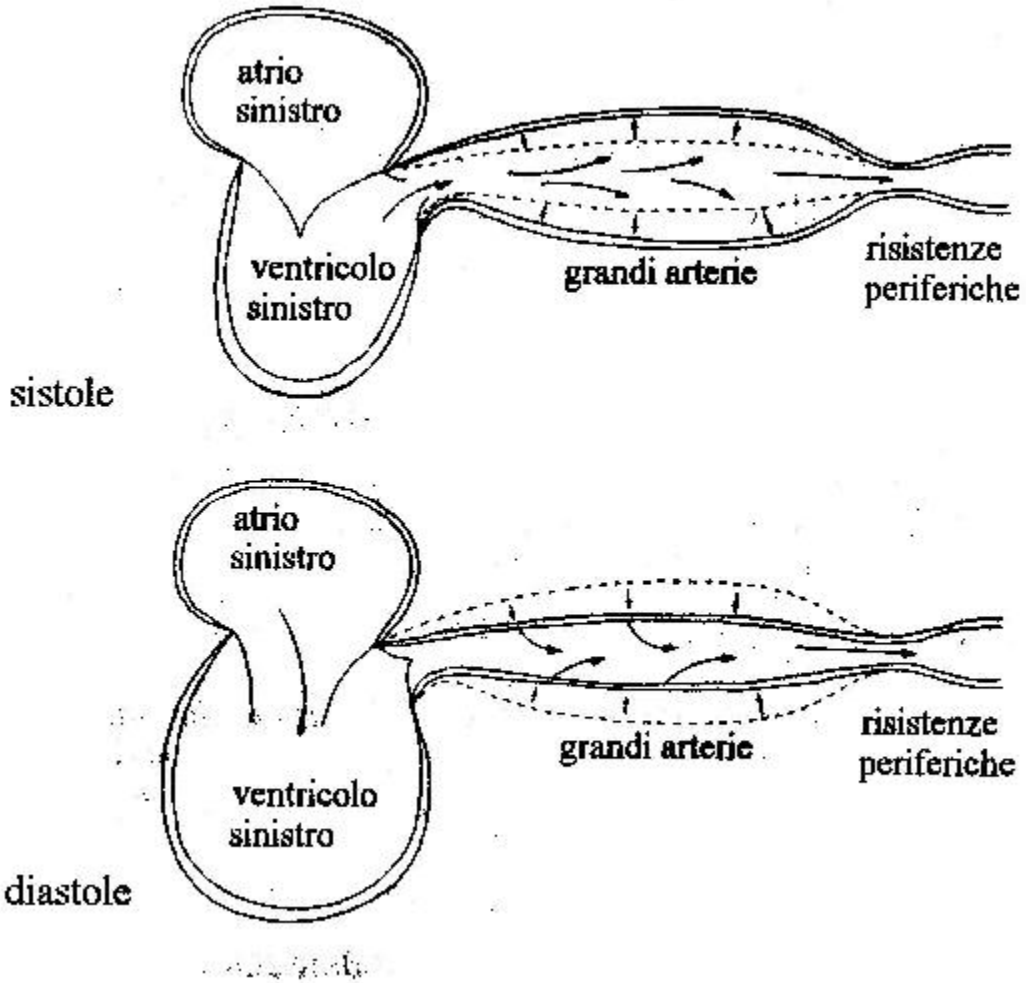


FIGURE 15-1 Internal diameter, wall thickness, and relative amounts of the principal components of the vessel walls of the various blood vessels that compose the circulatory system. Cross sections of the vessels are not drawn to scale because of the huge range from aorta and venae cavae to capillary. (Redrawn from Burton AC: Physiol Rev 34:619, 1954.)

Elastic behavior of arteries

- shading of blood pulse propagation



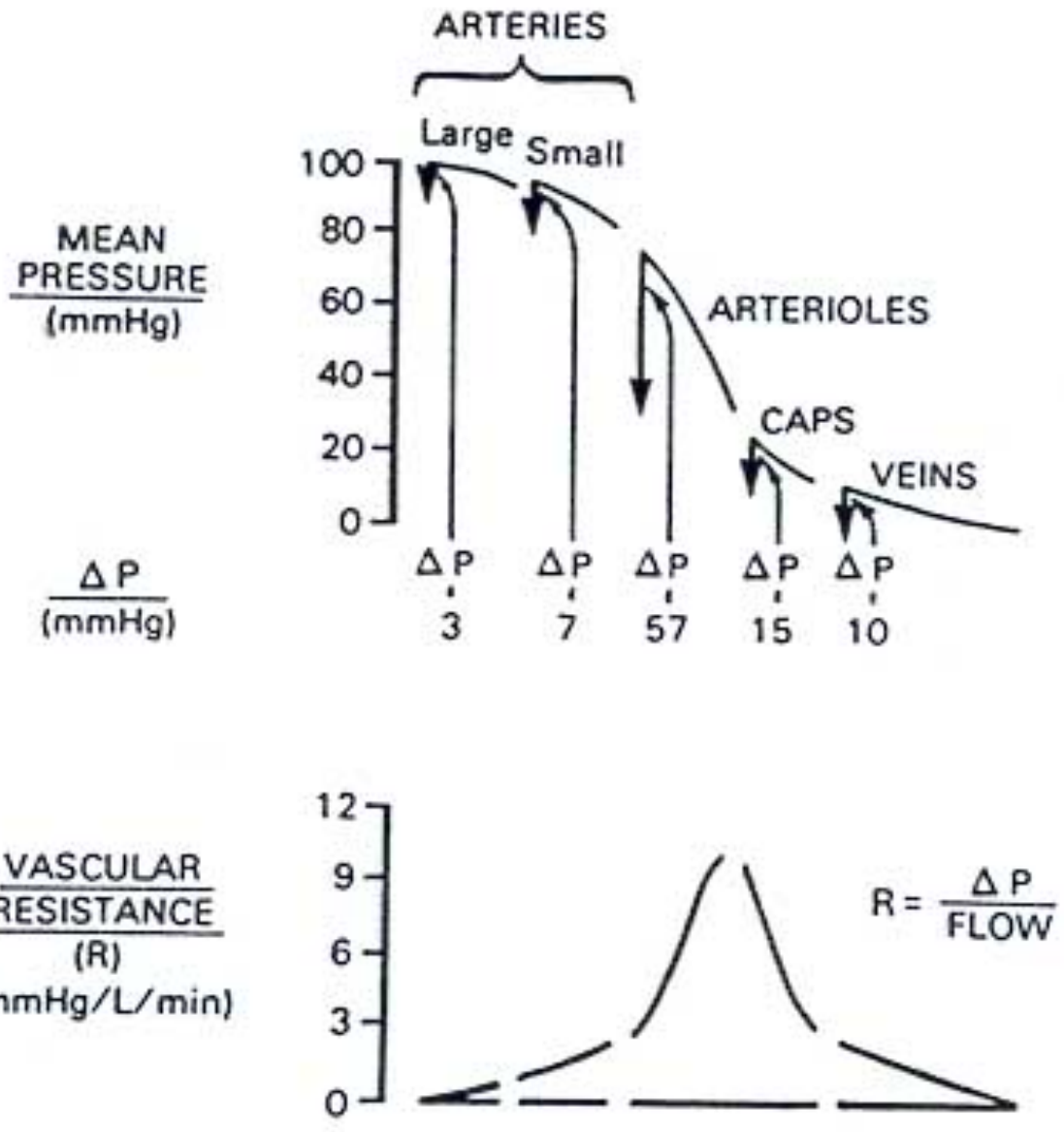
Important information

Table 3.1. Some properties of the circulation and blood

Number of red blood cells (mm^{-3})	5×10^6	Specific gravity	1.06
Number of white blood cells (mm^{-3})	10^4	Heart rate (min^{-1})	60–70
Blood volume (L)	5–6	Cardiac output (L min^{-1})	5–6
Viscosity of whole blood (mPa s; cP)	3–4*	Stroke volume (mL)	70

Vessels	Diameter (mm)	Length (cm)	Wall thickness (mm)	Contained volume (cm^3 or mL)	Mean pressure (mmHg)	Average velocity (cm s^{-1})	Reynolds number	
							Average	Maximum
Aorta	25.0	40.0	2.0	100	100(av.)	40(av.)	3000	8500
Arteries	15–0.15	15.0	0.8	350	90(av.)	40–10	500	1000
Arterioles	0.14–0.01	0.2	0.02	50	60	10–0.1	0.7	—
Capillaries	0.008	0.05	0.001	300	30–20	< 0.1	0.002	—
Venules	0.01–0.14	0.2	0.002	300	20	< 0.3	0.01	—
Veins	0.15–15	18.0	0.6	2500	15–10	0.3–5	150	—
Vena cava	30.0	40.0	1.5	300	10–5	5–30	3000	—

Important information



Important information

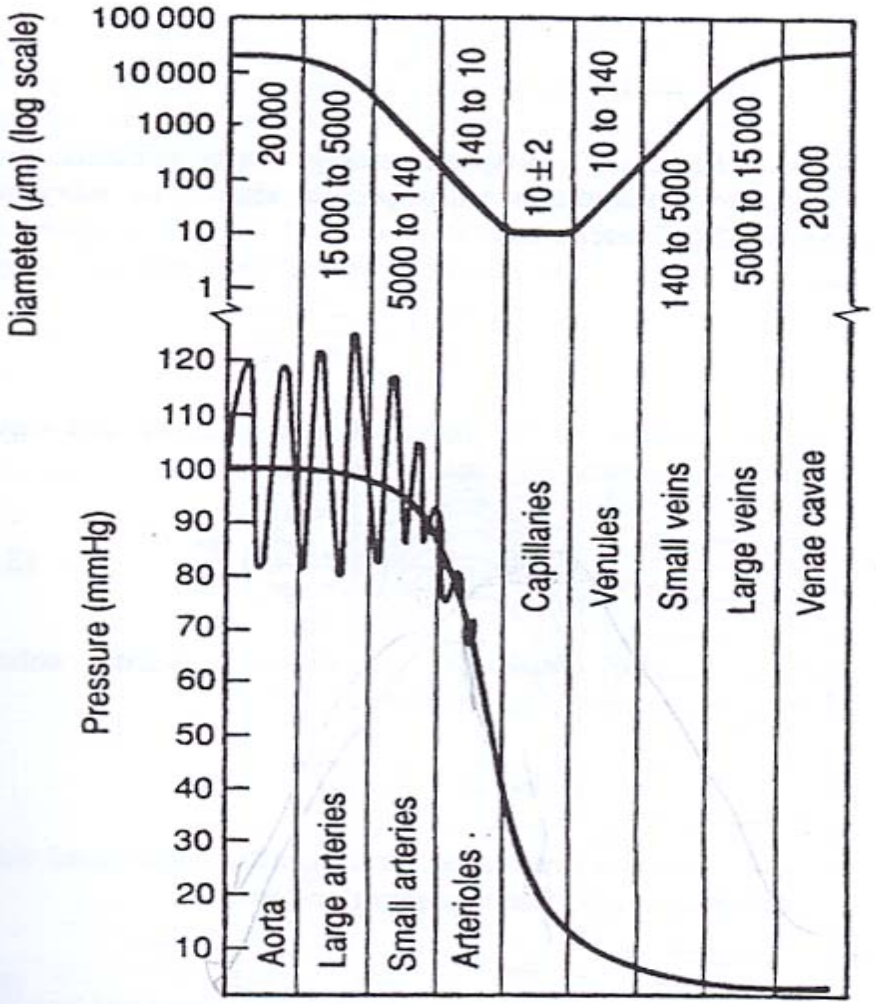


Fig. 3.4 Pressure variation in the systemic circulation.

Important information

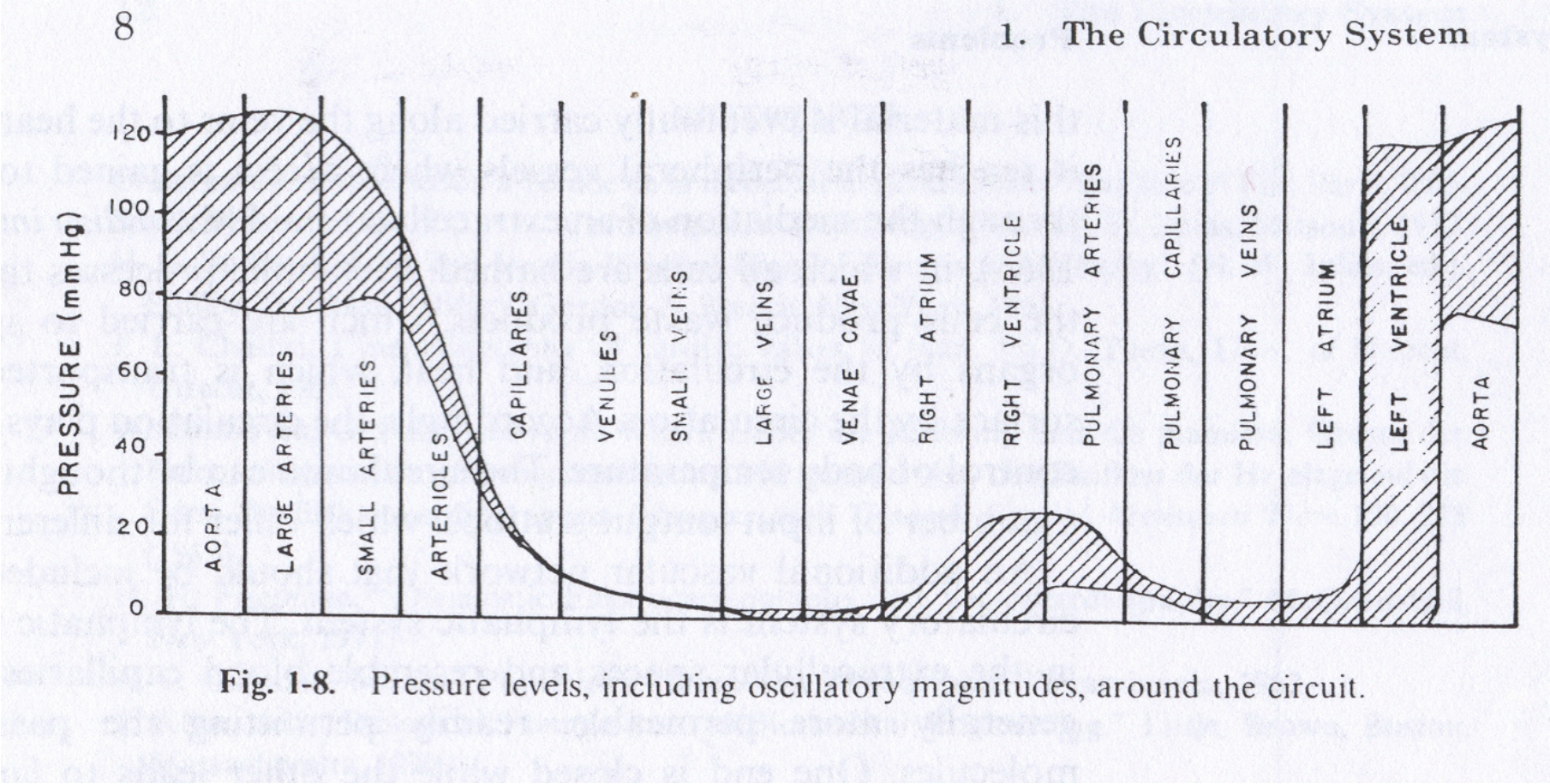
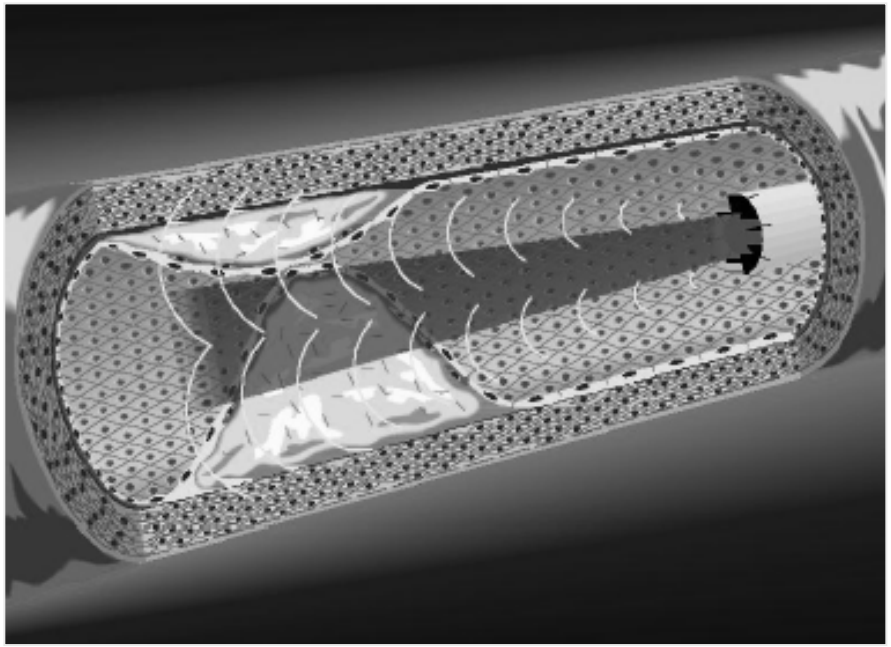
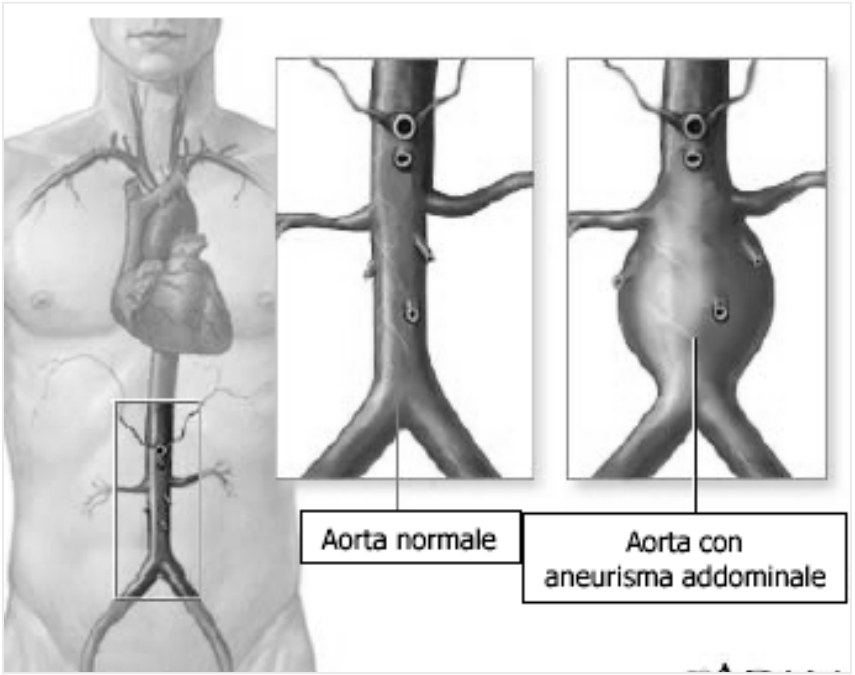


Fig. 1-8. Pressure levels, including oscillatory magnitudes, around the circuit.

Vascular prostheses

- Other than for trauma, vascular prostheses are used for artery pathologies:
  - STENOSIS
  - ANEURISM.



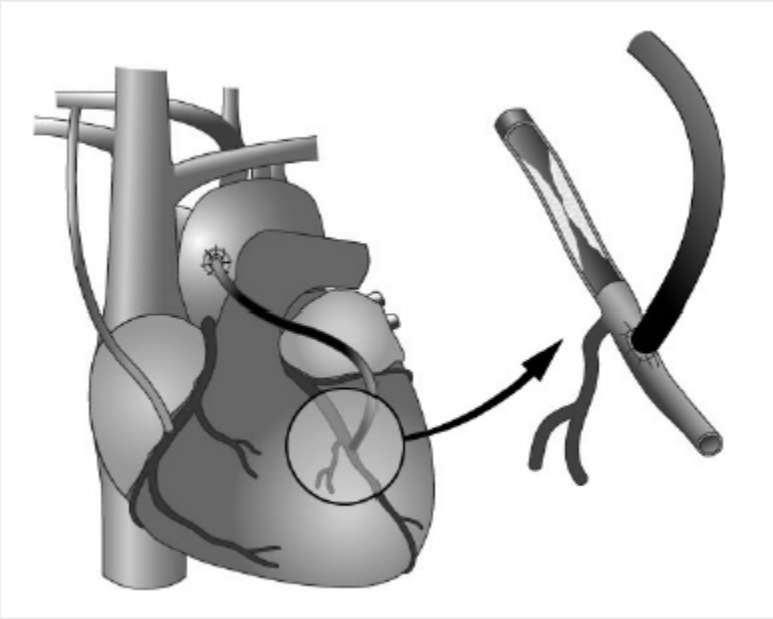


Stenosis

- Stenosis: narrowing of the diameter of the artery caused by the increase of the atherosclerotic plate or by the generation of a clot;
- A stenotic artery is not more able to transport the blood towards the more peripheral districts and when the stenosis is serious the tissues after it become ischaemic.
- The ischaemia reduces or cancels the oxygen contribution to the tissue with possible necrosis; in the organ hit by necrosis there is infarct, that it produces a partial or total loss of the function of the same organ.

Stenosis

- The prosthesis can be used to serve to pass the pathological zone (stenosis) and in this case it becomes a parallel branch (by-pass)
- Anastomosis is the suture between the prosthesis and the natural vessel.

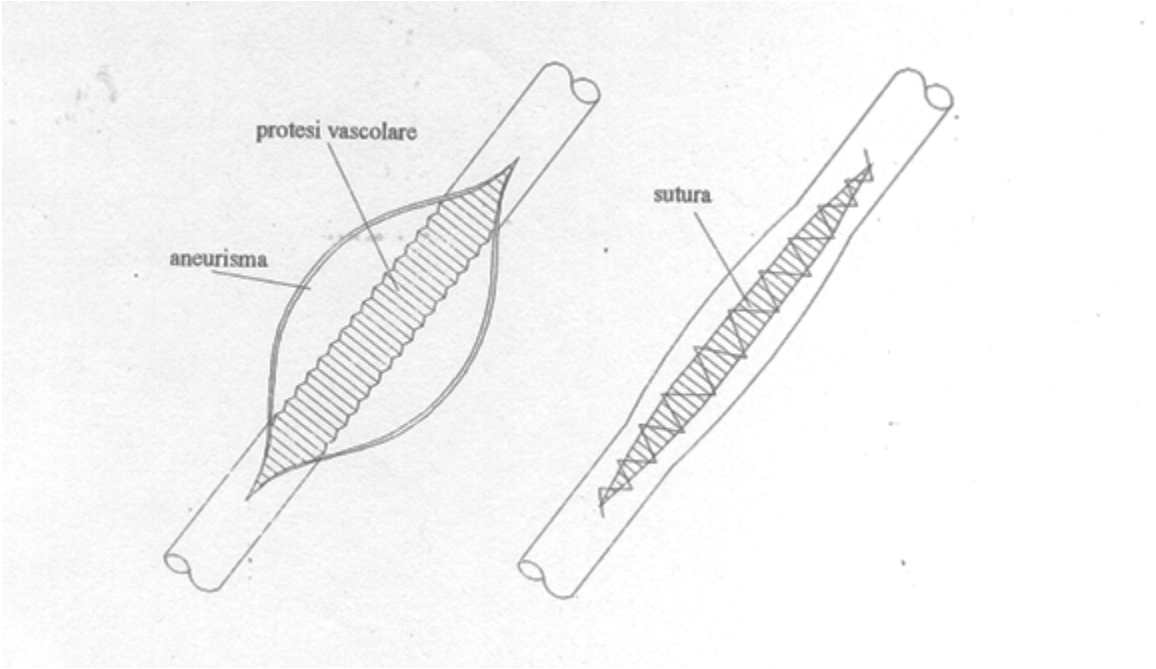


Aneurism

- Aneurism: increase of the artery diameter caused by a progressive yielding of the vascular wall.
- The wall can be broken off provoking an inner hemorrhage and does not transport more the blood.
- The aneurism causes moreover anomalous fluid-dynamic conditions, that can lead to the thrombosis of the expanded area.

Aneurism

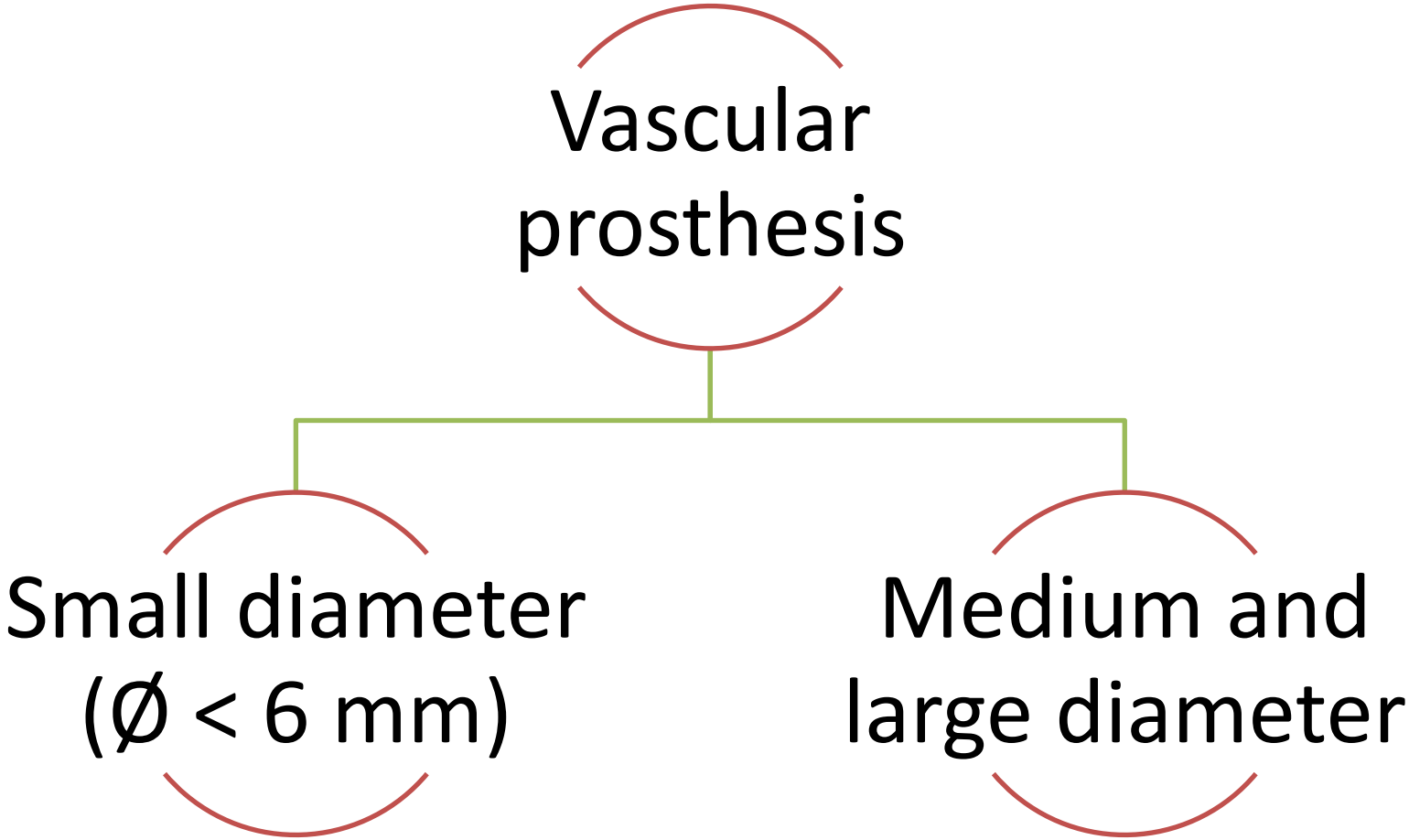
- In the case of an aneurism, the prosthesis is implanted in the blood vessel reducing its increasing
- The implant of a vascular prosthesis allows to restore the correct conditions of flow and so to reduce the risk of break of an aneurism.



Fate of vascular graft depends on:

- Patient:
  - Site of implant
  - Size and progress of pathology
  - presence of other pathologies (diabetes, hypertension, tumors, infections....)
  - Risk factors (smoke, problem with coagulation.....)
- Graft
  - Type and quality of material
  - Technological design of the graft
- Surgical procedure
  - Technical factor led to the implant of the graft

Vascular prosthesis



Characteristics of a graft

- The duration of the graft must be greater than the life expectancy of patient.
- The implant of the graft must not cause undesired reactions different from those the patient is able to contrast.

Characteristics of a graft

- **Non thrombogenic smooth surface with a low friction coefficient**

- The wall friction can produce local shear stresses that cause perturbations in the flow, and also turbulences, in proximity of the wall of the vessel.
- This can provoke the aggregation of plates and thrombosis. This process, than once primed is auto-spreading, is a serious problem more in prostheses with small diameter than in those to wide diameter:
  - the fluid layer closer to the wall (the boundary layer) is proportionally more thick in small diameter vessels;
  - the biological covering that shapes on the wall reduces the lumen and, in some small diameter vessel, acts as a stenosis.

Characteristics of a graft

- **Non thrombogenic smooth surface with a low friction coefficient**

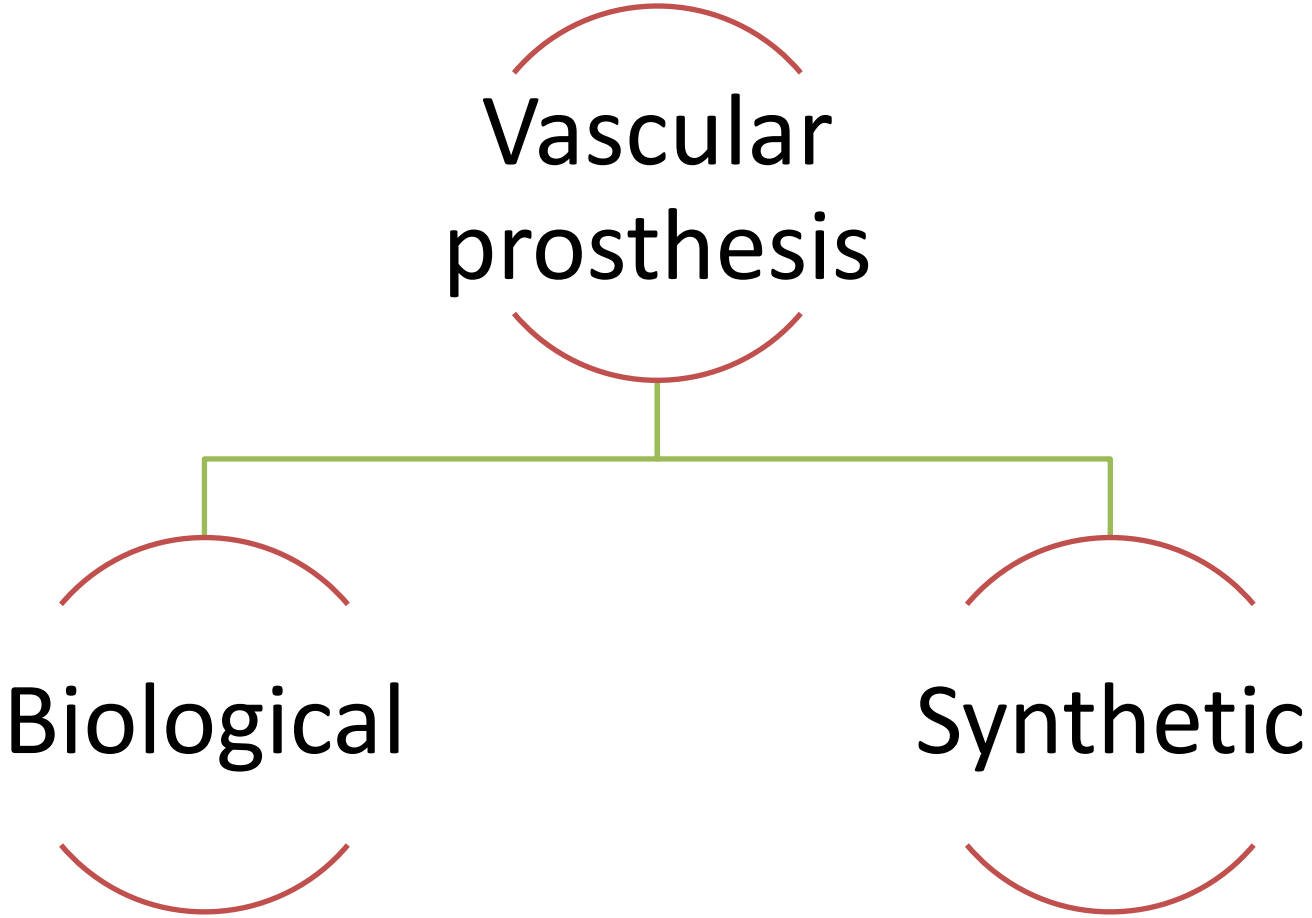
- Porous wall promotes the regeneration of a neo-intimae layer
  - haematic loss
  - hyperplasia of intimae
- Techniques of precoagulation
  - increase of thrombotic phenomenon
  - infections
- Inner coating made of inert material (pyrolitic carbon),
  - poor regenerative processes
- Bioactive coating (Heparin, Growth factors)
  - difficult to dose the activity and the quantity of drug
- Generation of a natural endothelium seeding endothelial cells inside the prosthesis (tissue engineering)
  - inability of cells to remain adhered to the surface of prosthesis and proliferate

Characteristics of a graft

- **Dimensions and mechanical properties of grafts similar to natural vessels.**

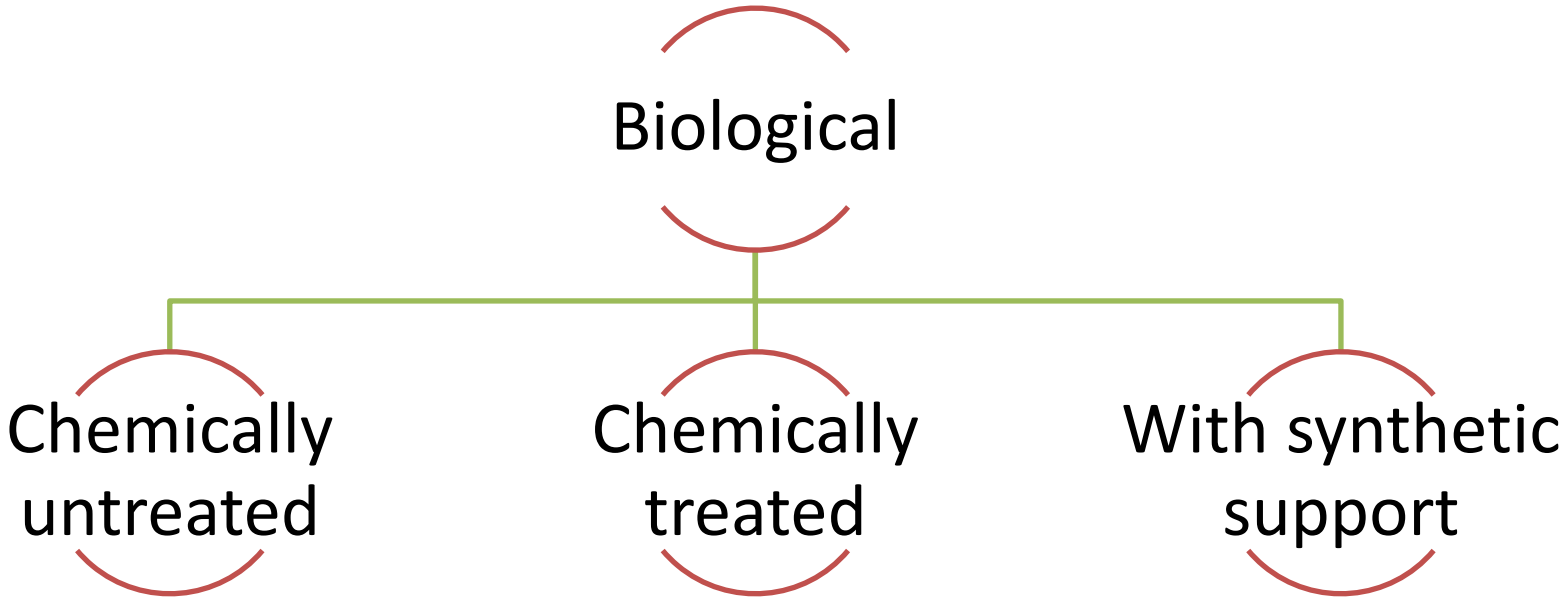
- In order to reduce disturbs in the flow the dimensions of prostheses and natural artery should be equal, and for an optimal transfer of pulsate energy also the elastic properties should be the same.
- A bad anastomotic connection is inefficient and inefficiency in vivo is aggravated because each graft has two anastomoses.
- The problem of prostheses is the compliance. The vascular prostheses are not compliant, and they do not simulate the mechanical behaviour of natural vessels.

Vascular prosthesis



BIOLOGICAL PROSTHESIS

Biological vascular prosthesis

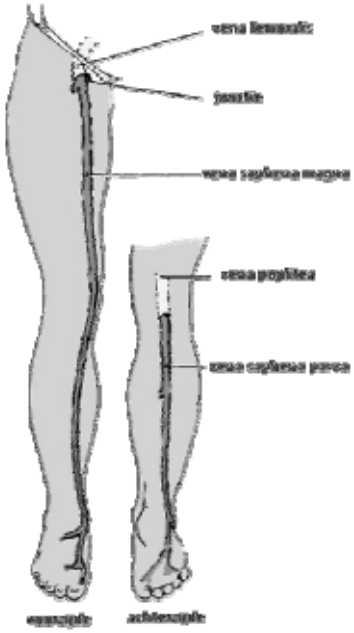


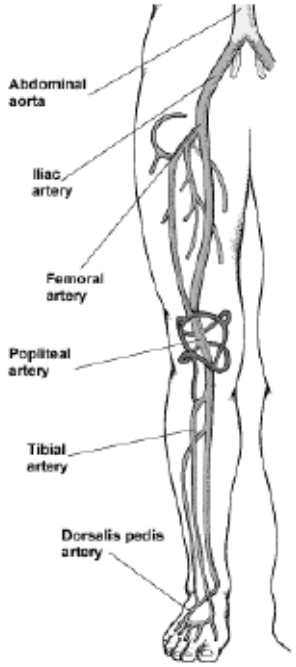
Biological chemically untreated vessels and tissues

- Today the autologous safena vein is optimal for arterial by-pass of diameter < 6mm, included distal arteries and the coronaries, while the autologous arteries (internal and external iliac artery, femoral artery, internal mammalian artery) are ideal for the bypass of the cardiac arteries and the peripheral arteries. Both systems introduce the disadvantage of the limited availability of donors.

Autologous Safena vein

- Advantages:
  - Presence of **a lining of endothelial cells**
  - Mechanical properties similar to those of natural arteries
  - Absence of bacteria colonisation
- the first bypass in 1948,
- bypass in situ for the revascularisation of the lower limbs in 1962 (leave the safena in its place, reducing therefore the ischemic and surgical damage due to the removal of the vein and extending the short and long term permeability)





Autologous Safena Vein

- Failure: 25-40%:
  - premature (within 30 days) for technical problems
  - intermediate (30gg-24 months) as consequence of technical errors, fibrosis of the valves, hyperplasia
  - late (> 24 months), secondary to progressing of atherosclerotic pathology.
- The safena vein is not available as graft in the 20-30% of the patients who need bypass of the inferior extremities. Many bypass are distally anastomosed for the recovery of the limbs, only the autologous grafts are considered efficient in these areas and some surgeons do not use synthetic grafts for distal bypass but sometimes they prefer arrange more than an autologous vein in order to construct composed graft.

Homologous veins

- The use of venous allografts is tried in order to repair peripheral arteries, in aorto-coronaric bypass and as secondary haematic access during the haemodialysis.
- The results are controversial: the method of conservation of the vein is charged to influence negatively its long term permeability and there is the problem of the rejection associated to the antigenic answer, also the criopreservation does not eliminate the immunological reaction mediated by cells. Homologous vein grafts should maintain their permeability only if their diameter is at least around 5 millimeters, because under this value there is the stenosis due to progressive thickening of the intimae wall and to the fibrotic reaction of adventitia wall.
- The immunotherapy can help, however its effects on biostability of grafts are not known. The greater problem of the use of these graft is the variability and the unprectability of their physical and mechanical properties.

Autologous arteries

- They are ideal substitutes of arteries, with good characteristics of long term healing.
  - internal and external iliac artery
  - femoral arteries
  - internal mammalian artery

- Advantages:
  - ideal substitutes of arteries
  - good characteristics of long term healing
  - flexibility, vitality, stability
- Disadvantages:
  - not idoneous dimensions
  - limited availability of donors

Homologous arteries

- They have been firstly used to the beginning of the vascular surgery. They are taken by corpses and criopreserved. But they have been abandoned for the degenerative phenomena to which they had. The interest towards their use in case of infection of prostheses in the peripheral circulation has renewed (Bahnini, J.Vasc.Surg., 14, 98, 1991).
- The idea is to take several arterial homografts by a donor of organs and to conserve them for a period of days or weeks to 4°C; in this way the graft would be available in order to replace an infected arterial prosthesis.

Biological chemically treated substitutes (Bioprosthesis)

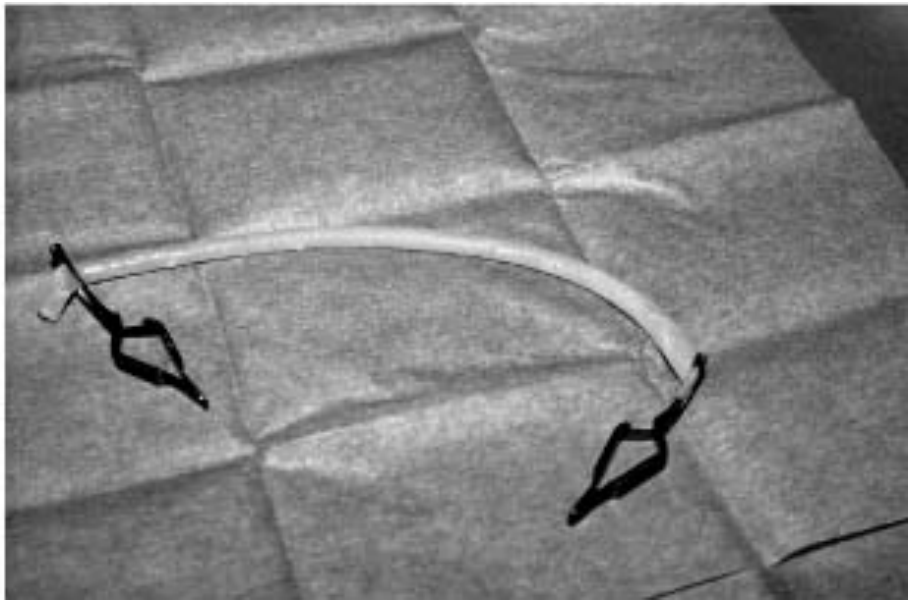
- The treatment consists in the “cross-linking" with gluteraldehyde (chemical cross-linking of collagen molecules).
- The treatment eliminates the antigenicity and increases the tensile strength, but also the embrittlement.
- The bioprostheses are not vital, and the endothelium lining is absent. The limiting factors are therefore the absence of reparative potentialities (healing) and structural embrittlement of the collagen wall.

Biological chemically treated substitutes (Bioprosthesis)

- Bovine Eterograft:
  - Calf carotid
  - Internal bovine mammary arteries
- The principal complications are expansion, biodegradation (calcification, disintegration), infection and formation of cysts.
- These graft are reserved to the patients that need procedures of secondary haematic access in haemodialysis, plasmaferesis and/or chemotherapy.

Biological chemically treated substitutes (Bioprosthesis)

Umbilical Vein
Bovine Carotid



Bovine Pericardium

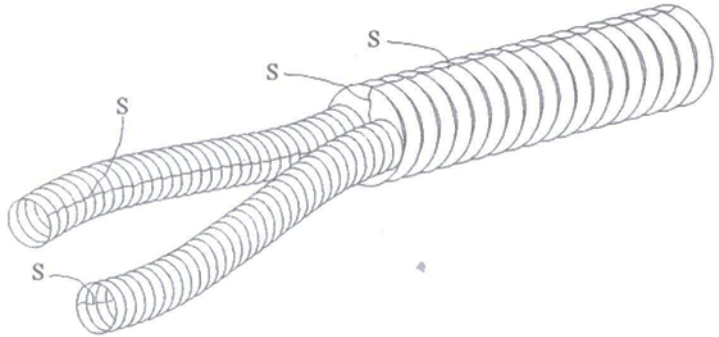


Figura 8.5 *Protesi vascolare in pericardio bovino trattato chimicamente e corrugato. Con S sono indicate le suture necessarie per realizzare la protesi.*

Human Umbilical Vein (HUV)

- It is prepared cross-linking the collagen with glutaraldehyde.
- In order to increase the stability and to reduce the probability of expansions of collagen tube it is reinforced with a knitted polyester fabric (Dacron).
- Defects: biodegradation of collagen, with progressive expansion and, in some cases, formation of aneurisms and bacterial colonization. There are problems associated to the lipid absorption that can favour the biodegradation process. The indications for the HUV are limited to their use as devices for haematic access and bypass of the inferior limbs when autologous vein is not available (alternatively to safena vein in patients with insufficient life expectancy).

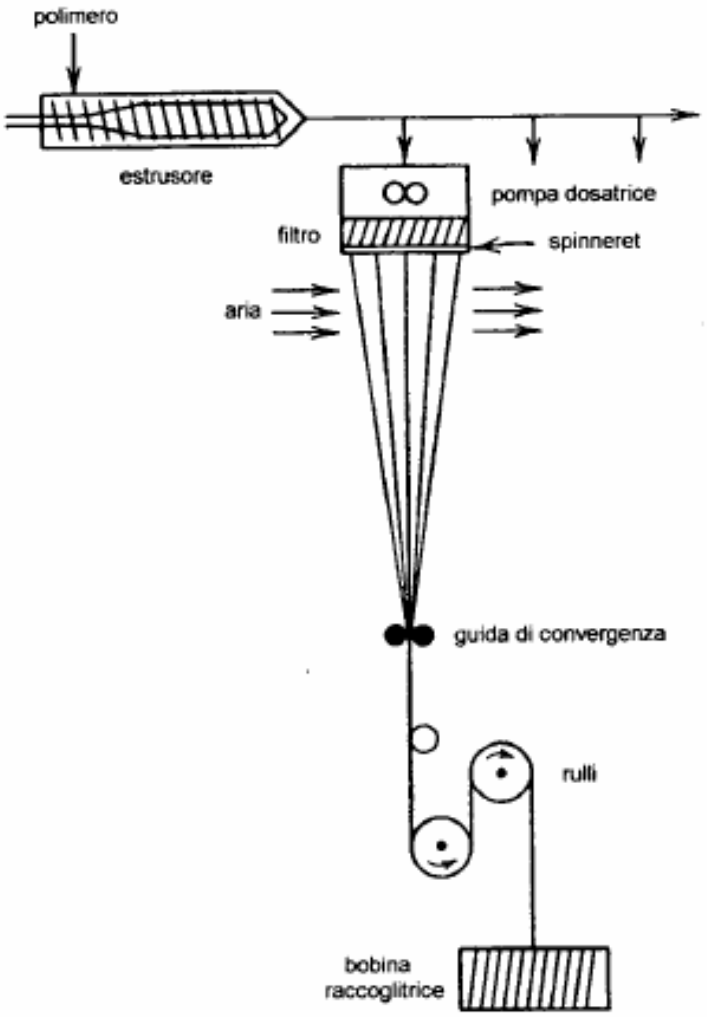
SYNTHETIC PROSTHESIS

Synthetic vascular prosthesis

- Tube-shaped prosthesis made of synthetic polymer fibers
  - Vinyon, Ivalon, Orlon
  - PTFE
  - PET
  - PUs
  - Silicones
  - ...

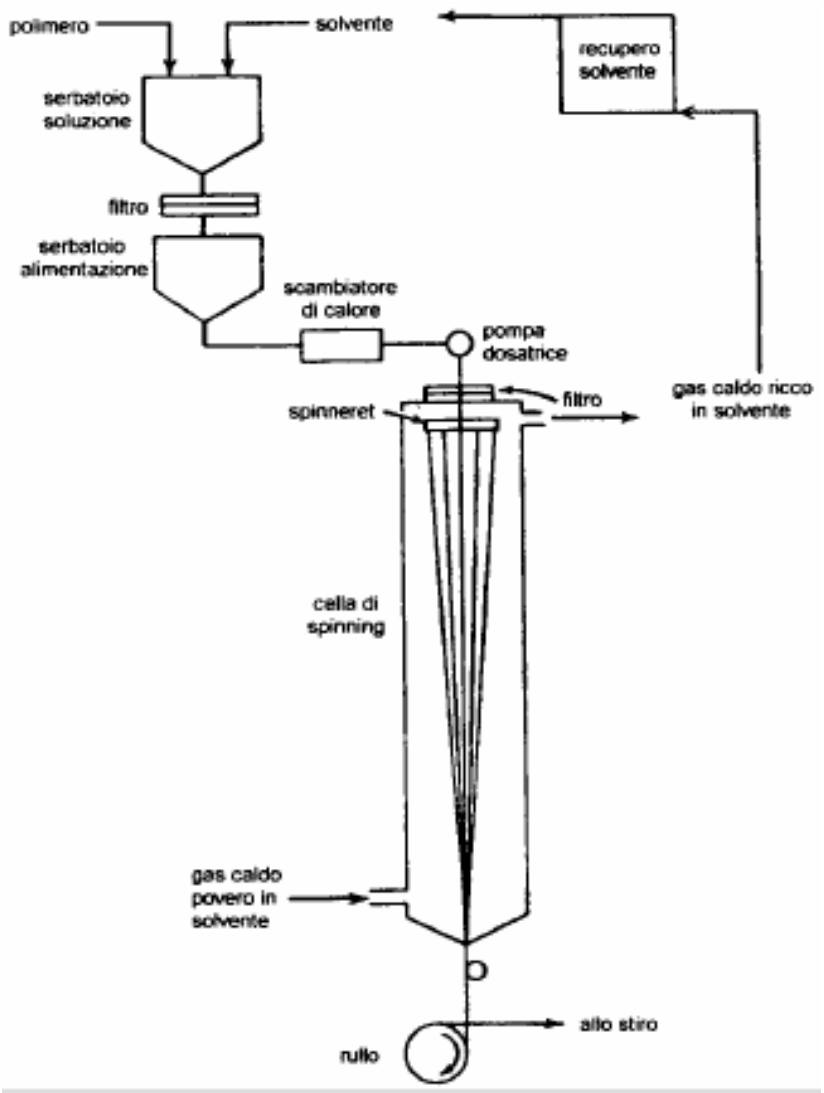
How to make fibers

Melt spinning



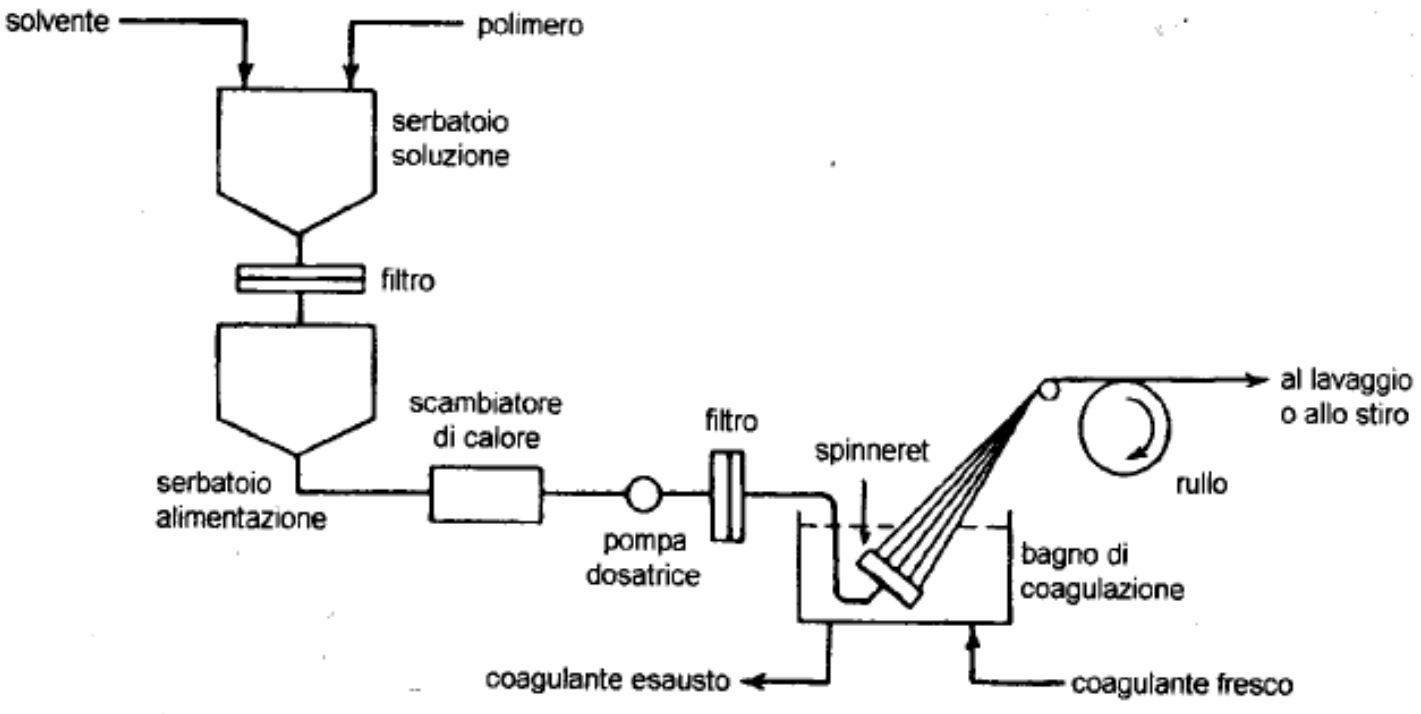
How to make fibers

Dry spinning



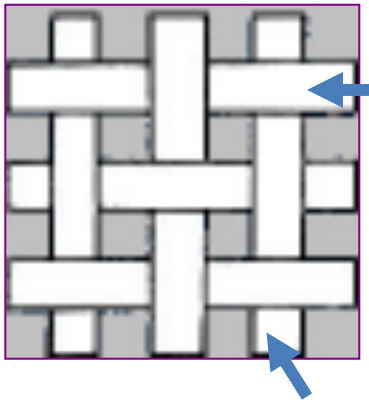
How to make fibers

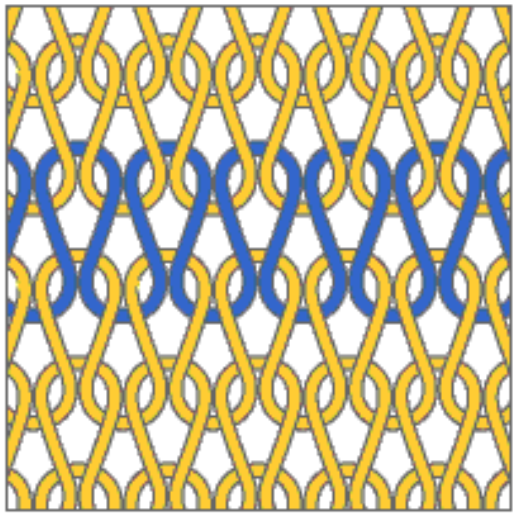
Wet spinning



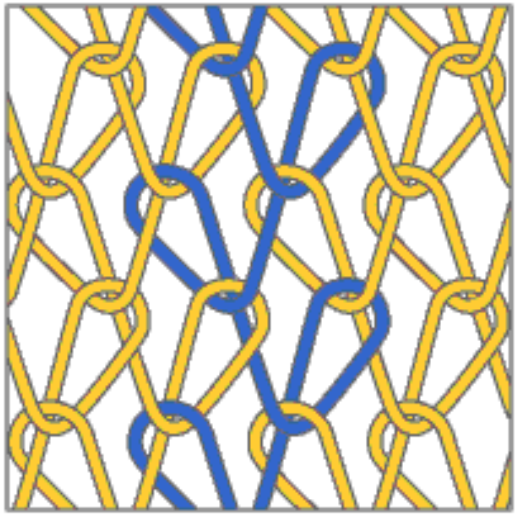
Prosthesis fabrication

Woven





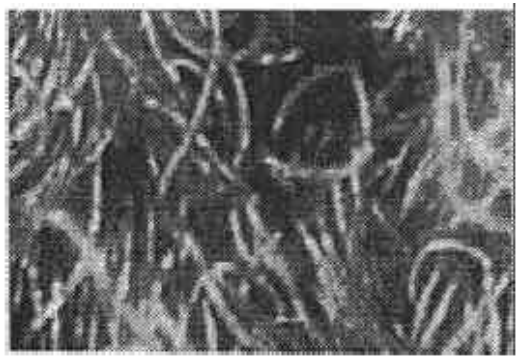
Weft knitting



Warp knitting

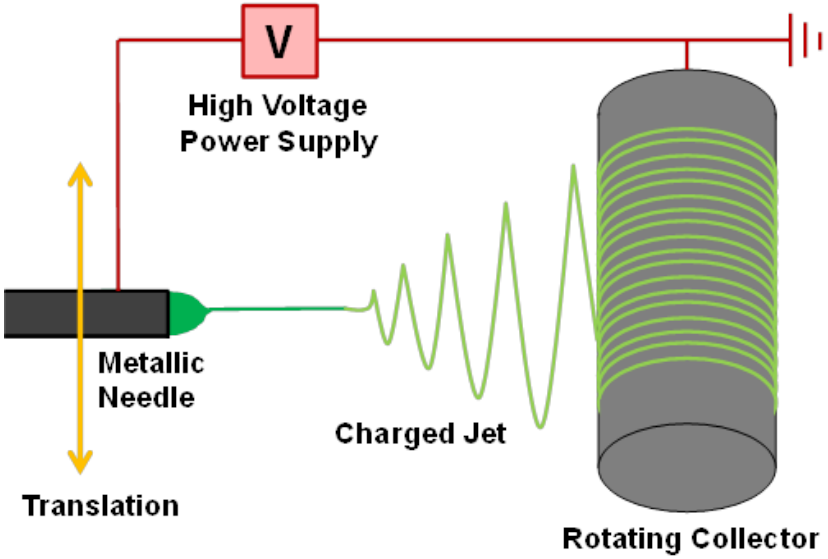
Prosthesis fabrication

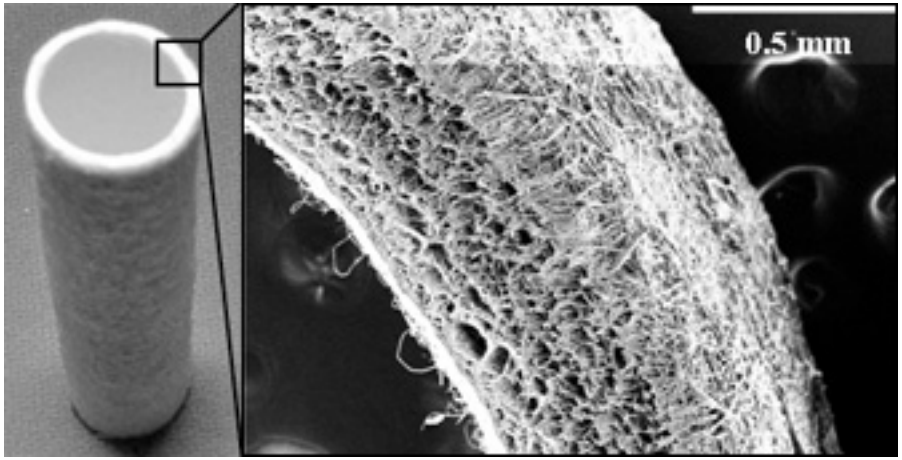
- Additional Technology:
  - **Velour graft,** composed of many filaments anchored to the surface of woven or knitted graft. I graft can be planar, with or without velour, or present internal, external or both velour.
  - **Electrospun graft**, fabricated via electrospinning over rotating cylindrical collector



Prosthesis fabrication

- Electrospinning





First used materials

- VINYON N = copolymer PVC/acrylonitryle
- IVALON = polyvinilphormale
- ORLON = polyacrylonitryle
- First synthetic grafts do not incorporate themself in host tissues and produce thrombosis and generation of emboli.

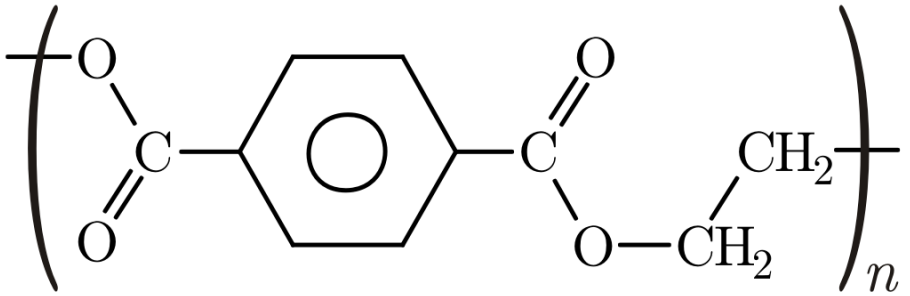
Synthetic used materials

- DACRON® (polyethylentereftalate)
- Results: Long term success in 90% of implants in large vessels (⦸>8mm)

- PTFE (polytetraphluoroethylene)
- Results: Long term permeability in medium vessels (⦸=6-7mm), as second choose respect to biological substitutes

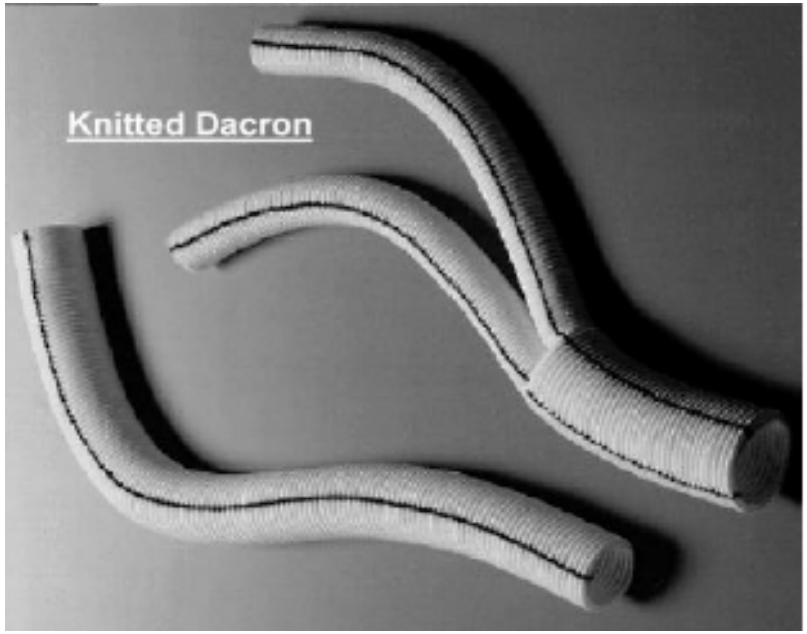
Polyethylentereftalate (PET)

Dacron®

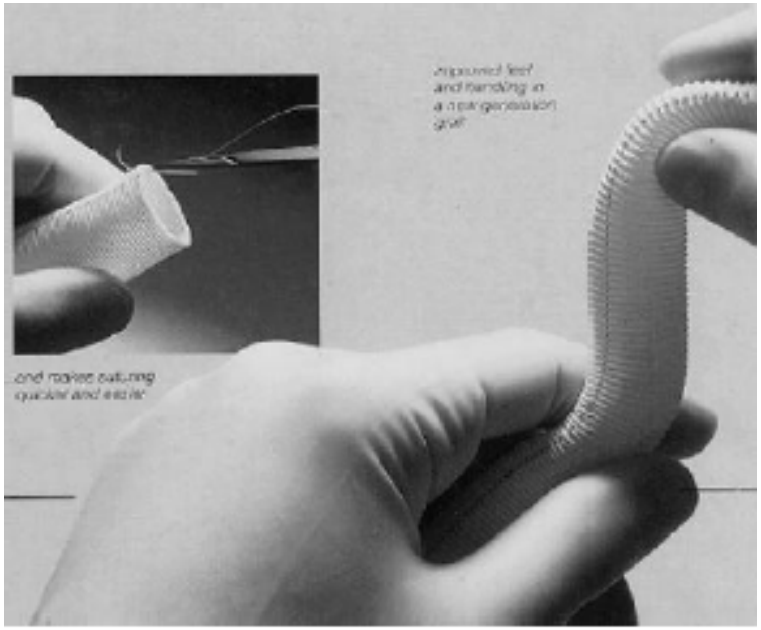


- WOVEN
- KNITTED
  - Warp: fabricated in longitudinal direction, denser than weft, it resists to the unthreading.
  - Weft: fabricated in radial direction, more flexible and stretchable than warp; it need precoagulation and it is more subject to expansion.
- It must be avoided that woven of graft, once cut unthreads with worsening in the site of anastomosis.
- The woven prostheses are less porous. Low porosity produces an elevated rigidity, with consequent facility of calcification. There is a bad connection between the synthetic graft and the natural vessel. The failure at anastomosis is easier.
- Results: Long term success in 90% of implants in large vessels

Dacron® prostheses



Knitted Dacron

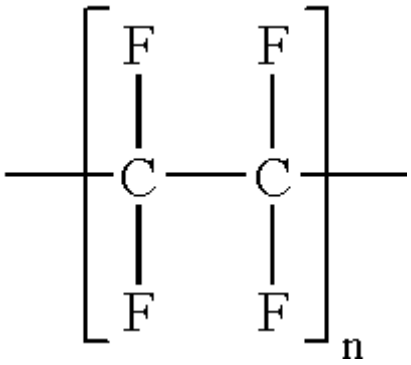


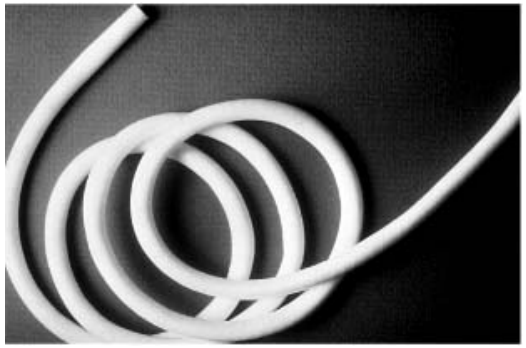
Woven Dacron

Polytetrafluoroethylene (PTFE)

Teflon®

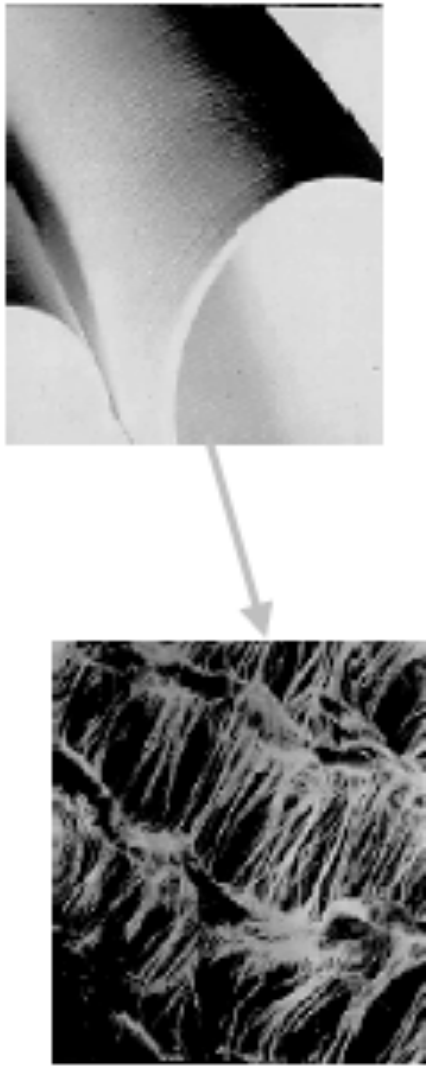
- The PTFE or Teflon prostheses have been designed with woven structure, that but it has been discarded because charged of haemorrhages and formation of false aneurisms to the anastomosis. Some Authors (Couture, Guidoin ET To, Can.J.Surg., 27, 575, 1984) think that the use of suture in silk has contributed to these effects.
- The Woven Teflon has given less satisfactory results than the knitted Teflon. The in-vivo and clinical tests has marked the absence of regeneration of the neo-intimae in woven graft, and not in that knitted graft. As the long term stability of the Teflon is better than whichever synthetic or biological material or biological.
- Some researchers think that the fabrication of PTFE warp-knitted prothesis should take in serious consideration that are able do not unthreat at cut point.



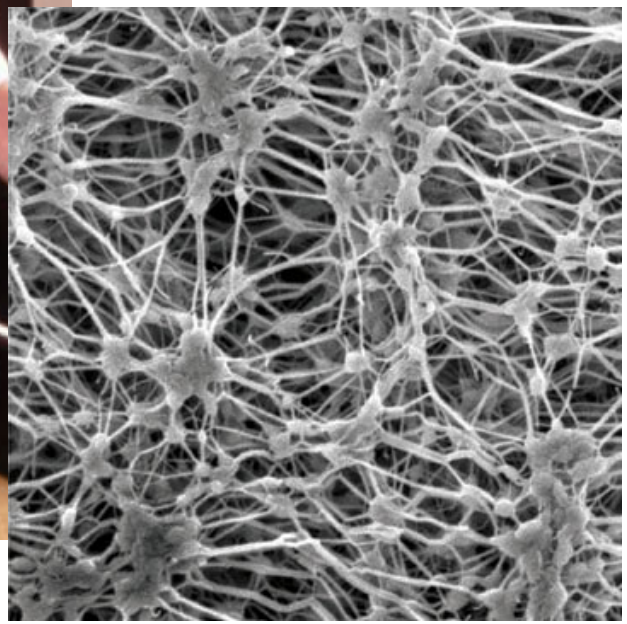


Foam PTFE

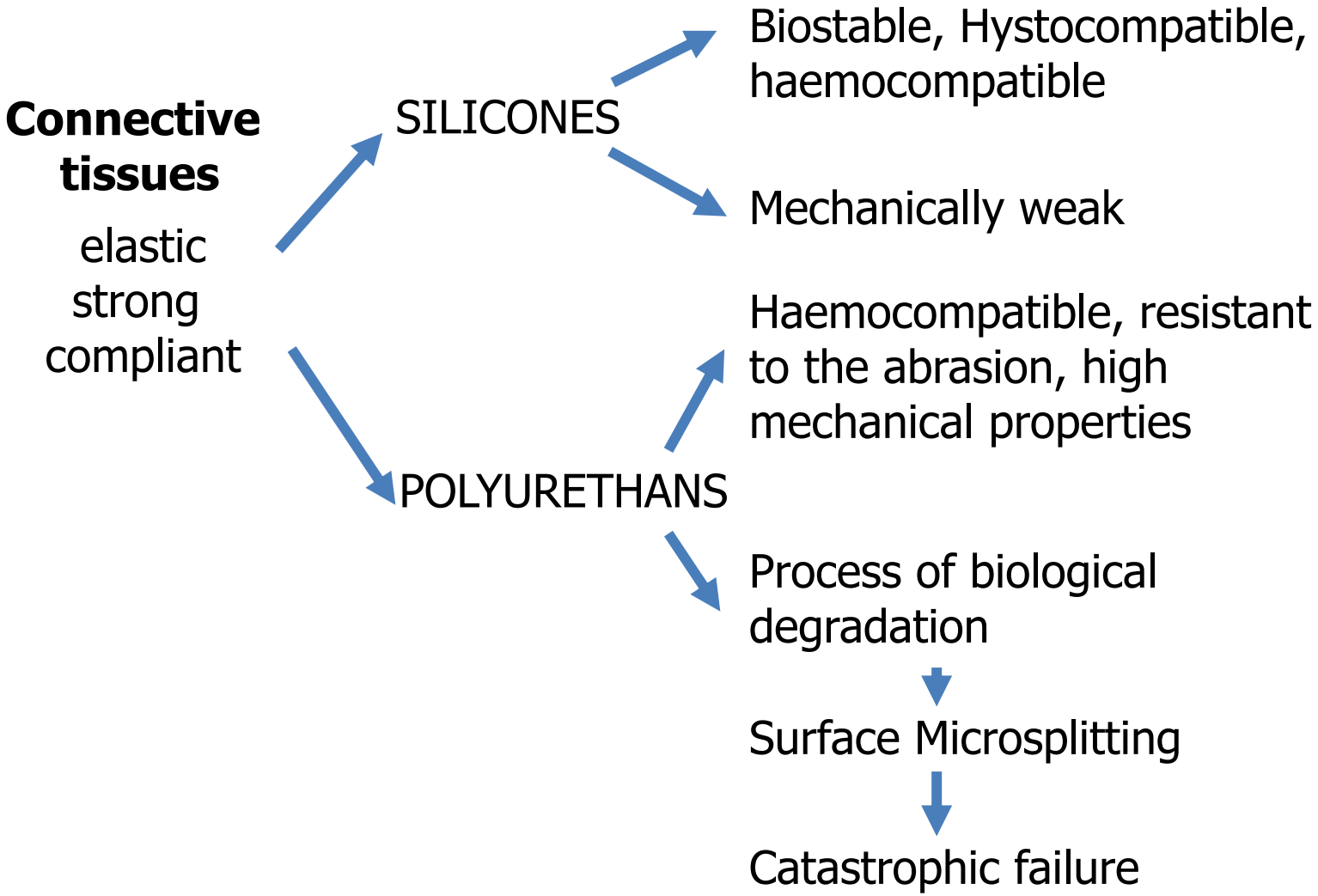
- Impra®, Gore-Tex®, Vitagraft®
- It is produced with a stretching process at high temperature that produces PTFE nodules interconnected with highly aligned fibres.
- Goretex graft has an external additional cover circularly aligned in order to increase the mechanical resistance, but this characteristic decreases the permeability of wall of the graft.
- Poor compliance
- Thrombogenic without surface modification
- High stable



Invention of Gore-Tex



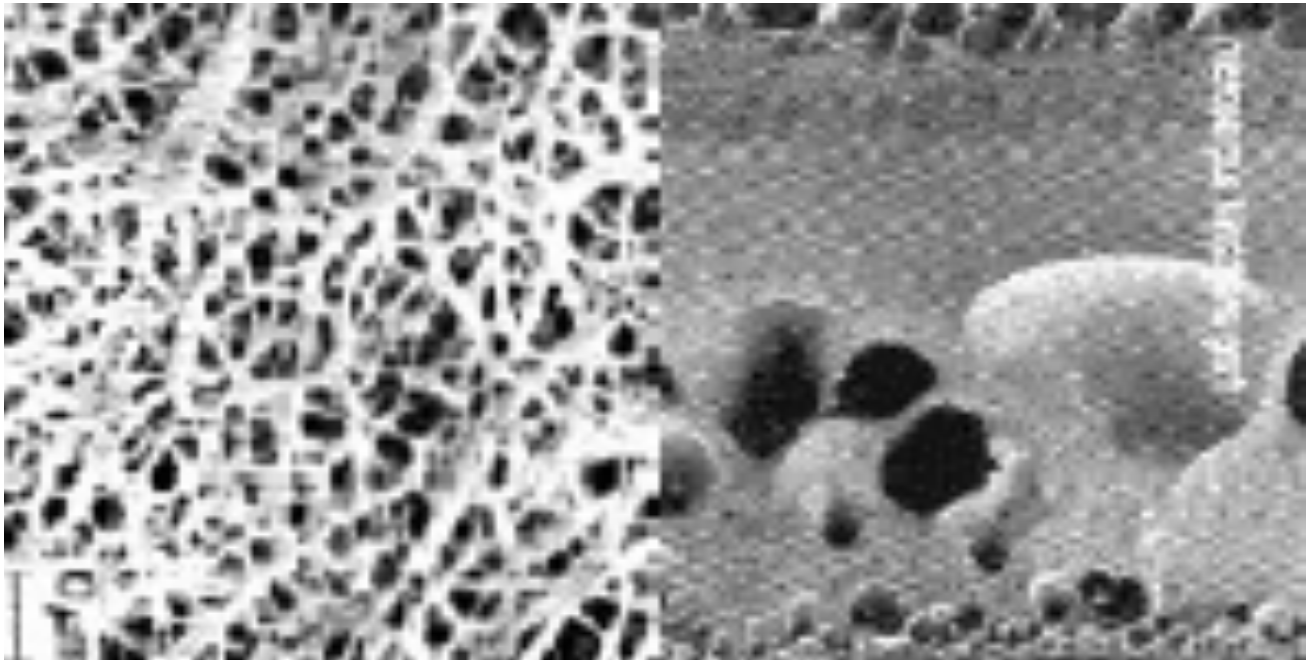
Alternative Materials: POLYURETHANS AND SILICONS



PolyUrethans (PUs)

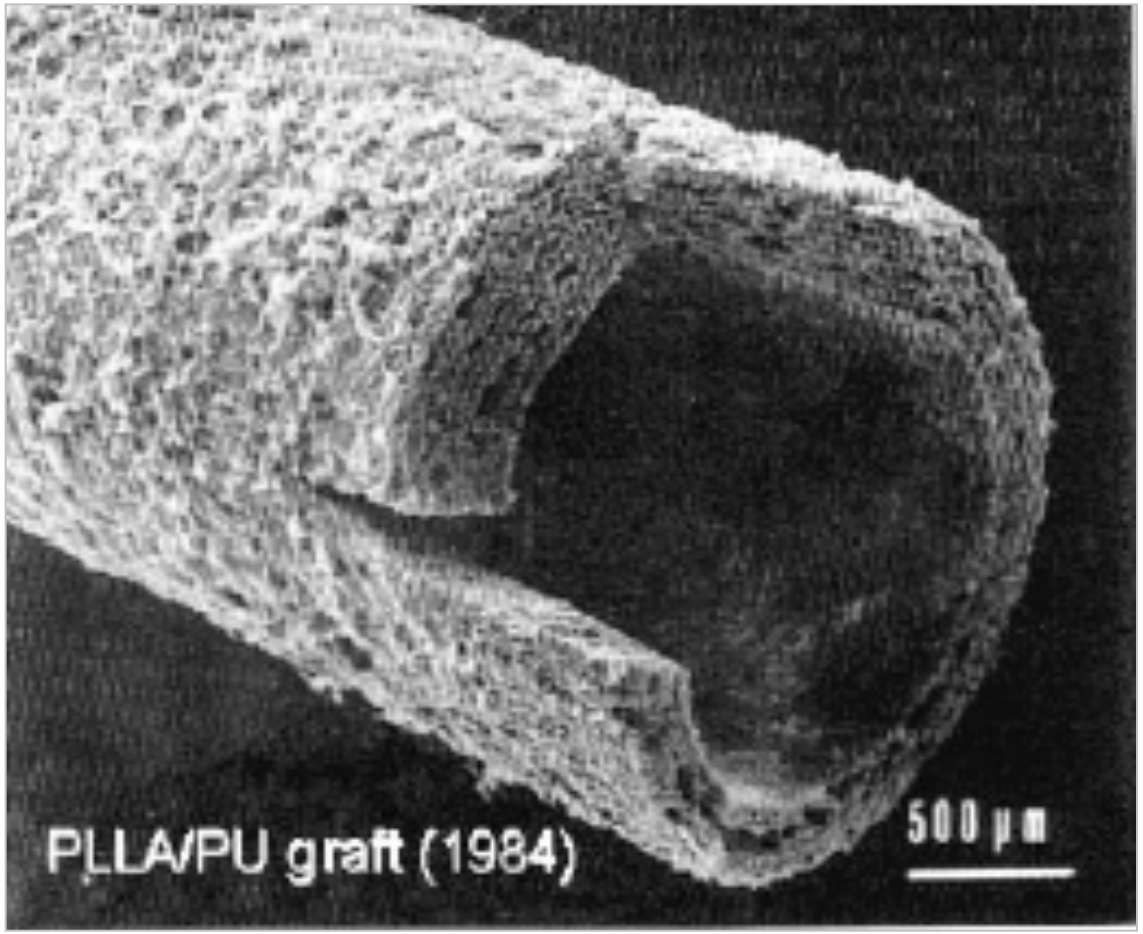
- Great structural versatility
- Easiness of manufacturing
- Elastomeric properties
- PUs allows to construct tubular small-calibre grafts with modulated and opportune chemical-physical characteristics of radial compliance and haemocompatibility.
- Soft foam, fibres, tenacious and rigid covers can be produced. Grafts with better compliance can be constructed with several techniques
  - filament winding,
  - solvent casting,
  - depositions with technical spray,
- On the basis of initial reagents polyurethanes more or less hydrophilic can be fabricated, or equipped of a surface that join hydrophobicity with hydrophilicity in order to encourage the specific protein absorption, or graftable with active molecules as heparin, polypeptides, etc, and with opportune physical property, compliance and stability.

PolyUrethanes (PUs)



Wall with variable porosity obtained by filament winding

Small diameter prosthesis made of POLYLACTIC ACID/ POLYURETHAN



Bioresorbable Graft

- The principle is to fabricate a graft that after the implant starts to degrade and simultaneously is replaced by natural tissue of the patient. The prosthesis developed at Groningen (Cell Tissue Res., 242, 569, 1985) was made of a blend of polyurethane-polylactic acid. It was microporous, compliant and bioresorbable.
- However the application of a bioresorbable prosthesis implies that the cells are able to reconstruct a new artery and this seems at least problematic because the cells pertain to a sick artery. The research in this area is still a lot and the way towards the clinical application is still along

Prosthesis characterization

- The characterization of the following parameters:
  - compliance,
  - permeability
  - porosity,
  - resistance to tensile stress,
  - resistance to burst
  - Duration (fatigue)

Compliance

$$\frac{\Delta V}{V} = \frac{\pi(R+\Delta R)^2 L - \pi R^2 L}{\pi R^2 L}$$

Expanding and simplifying, we get

$$\frac{\Delta V}{V} = \frac{2R\Delta R + \Delta R^2}{R^2}$$

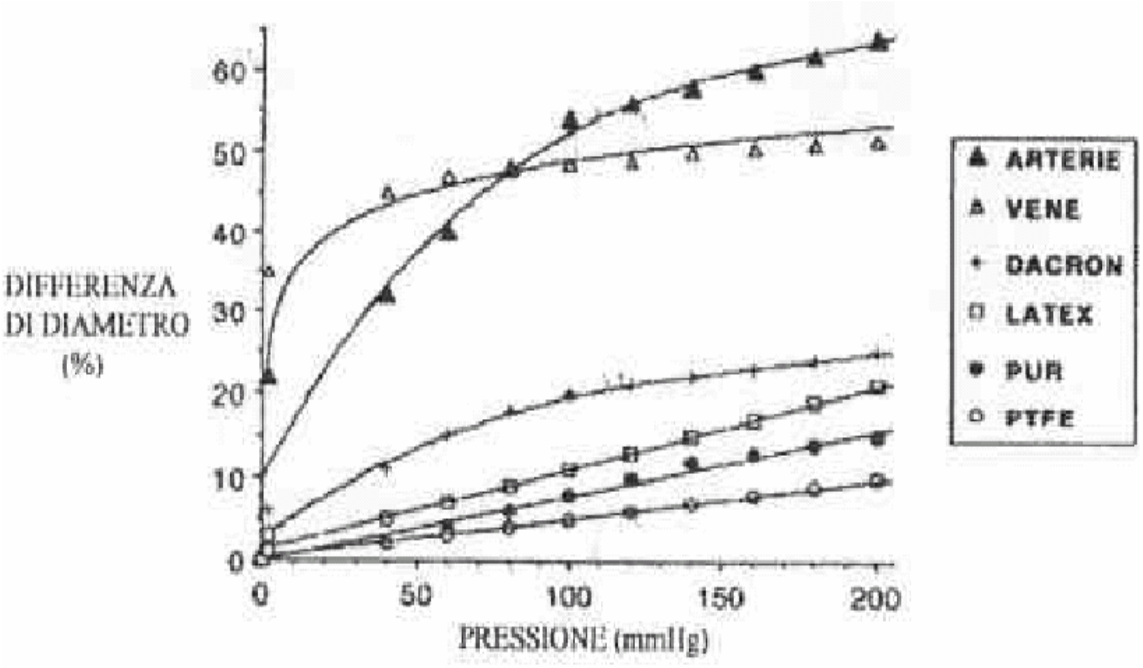
Since Δa is small, the higher power term can be neglected and hence, the volumetric strain will be given by the relationship

$$\frac{\Delta V}{V} = \frac{2\Delta R}{R}$$

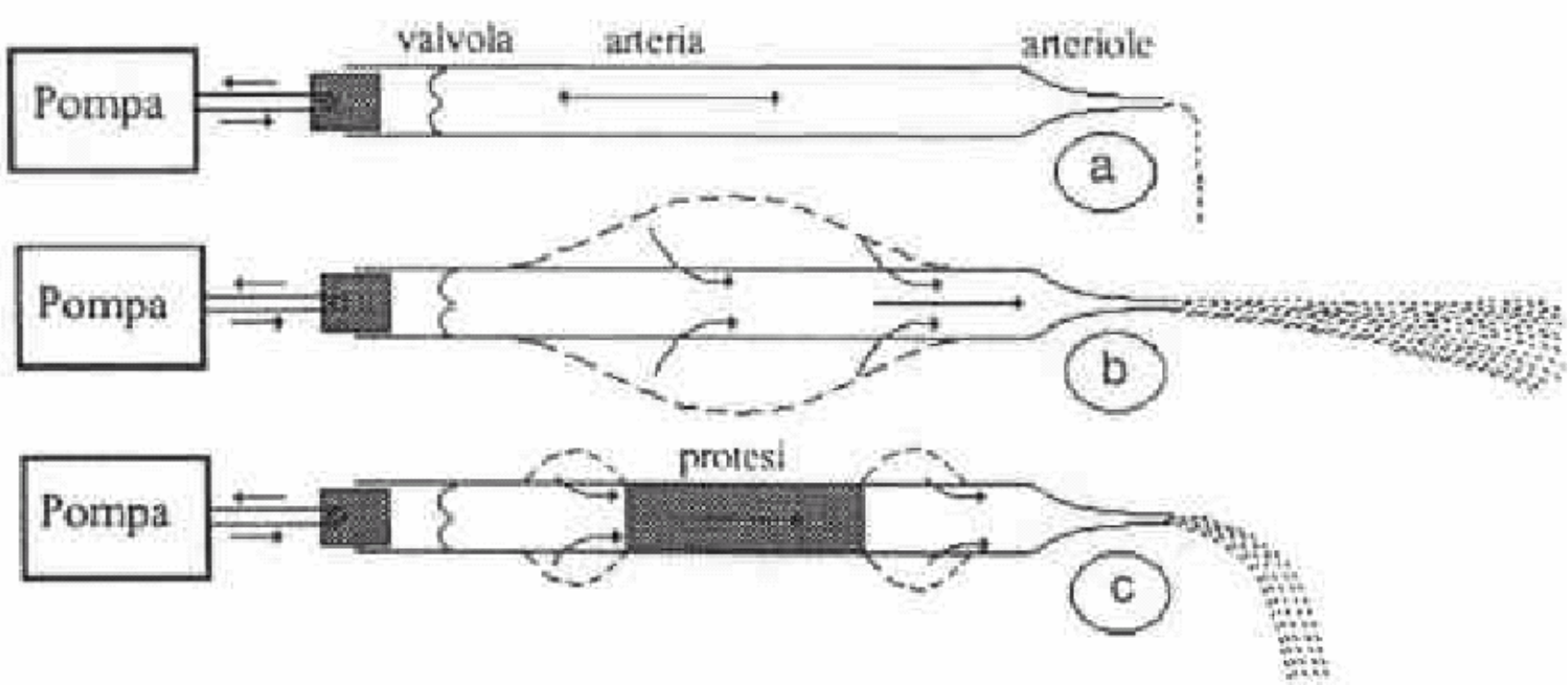
Neglecting the factor 2, the compliance can be written as

$$C = \frac{\Delta a}{a \Delta p}$$

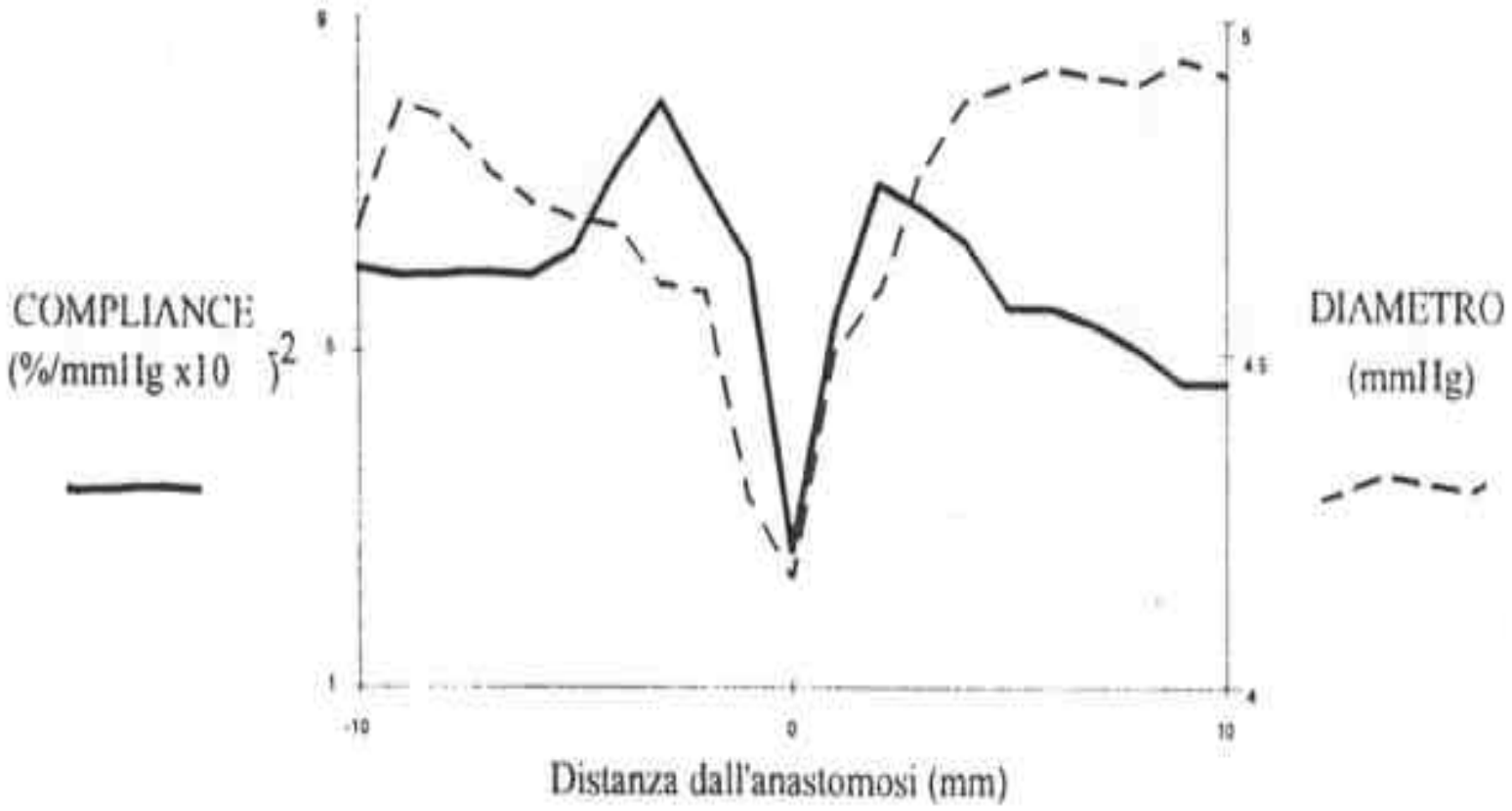
Compliance


DIFFERENZA
DI DIAMETRO
(%)
60
50
40
30
20
10
0
0
50
100
150
200
PRESSIONE (mmHg)
ARTERIE
VENE
DACRON
LATEX
PUR
PTFE

Compliance



Compliance


COMPLIANCE
(%/mmHg x10)2
DIAMETRO
(mmHg)
-10
0
10
Distanza dall'anastomosi (mm)

Permeability

- P = Q/A
  - Q= flow (ml/min)
  - A= area (cm^2)
- An high permeability favours the healing process but increase the risk of emorragy

Dacron	Permeabilità [ml/min*cm^2]	Precoagulazione
Protesi a rete	50÷200	No
Protesi a maglia	2000 (media)	Sì
Protesi con velour	1300 (uniforme)	Sì

Porosity

- Porosity = void space/total volume
  - Planar porosity (imaging)
  - Gravimetric porosity

Mechanical properties

- Effect of wrinkling
- Porosity, compliance

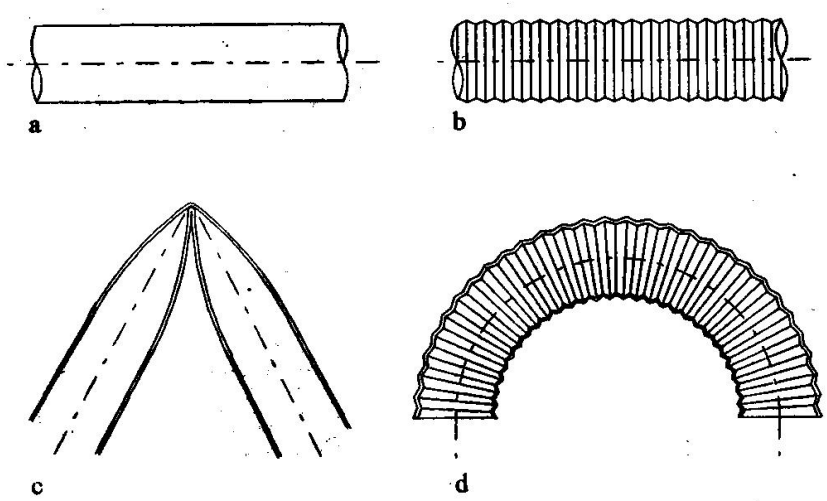
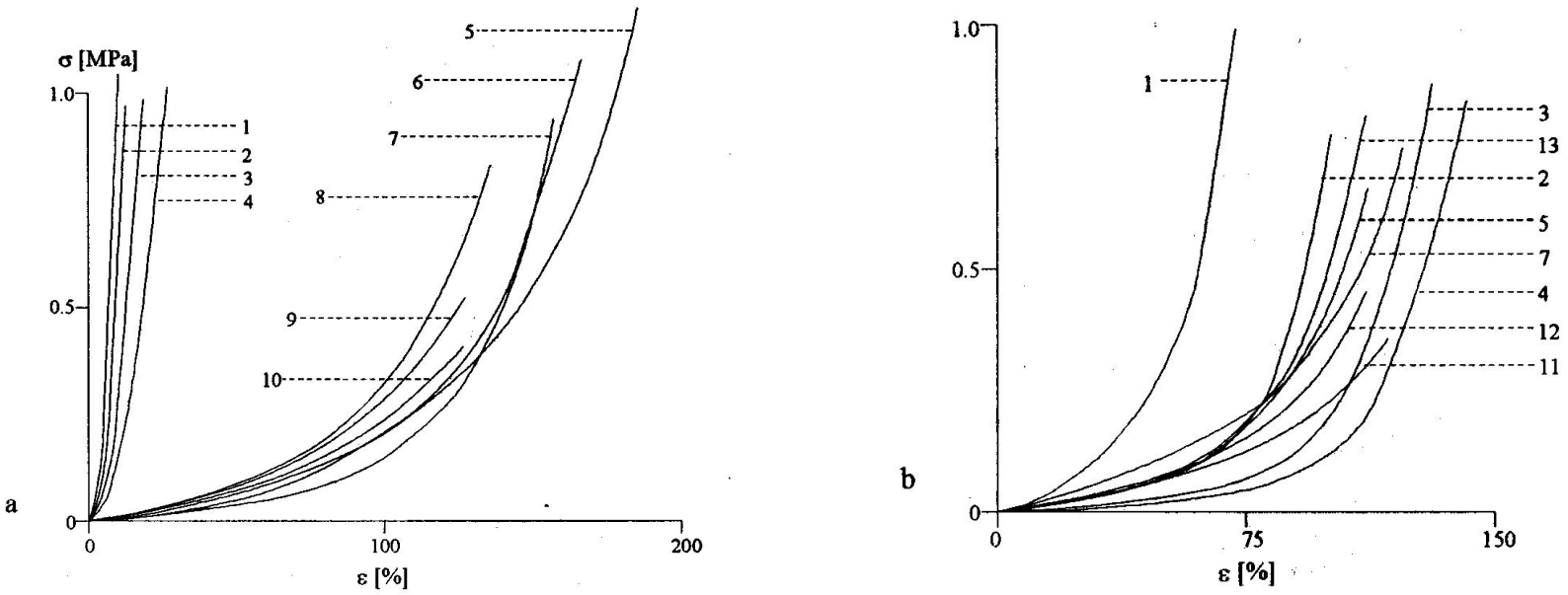


Figura 8.12 *Effetto del corrugamento della protesi vascolare sulla sua flessibilità. La protesi non corrugata (a) tende ad occludersi quando viene curvata (c) mentre la protesi corrugata (b) consente curvature senza occlusione del lume (d).*

Tensile mechanical behaviour

Circumferential

Longitudinal



Comportamento meccanico di protesi vascolari e, per confronto, di tratti di arterie. a: curve sforzo-deformazione in direzione circonferenziale; b: curve sforzo-deformazione in direzione longitudinale. 1: protesi in PET woven; 2: protesi in PTFE woven; 3: protesi in PET knitted; 4: protesi in PTFE knitted; 5: arteria iliaca; 6: aorta addominale distale; 7: arteria femorale; 8: aorta addominale prossimale; 9: aorta toracica distale; 10: aorta toracica prossimale; 11: aorta ascendente; 12: aorta toracica; 13: aorta addominale (da: M Hasegawa e T Azuma 'Mechanical Properties of Synthetic Arterial Grafts', J. Biomechanics, 12, pp. 509-517, 1979).

Problems

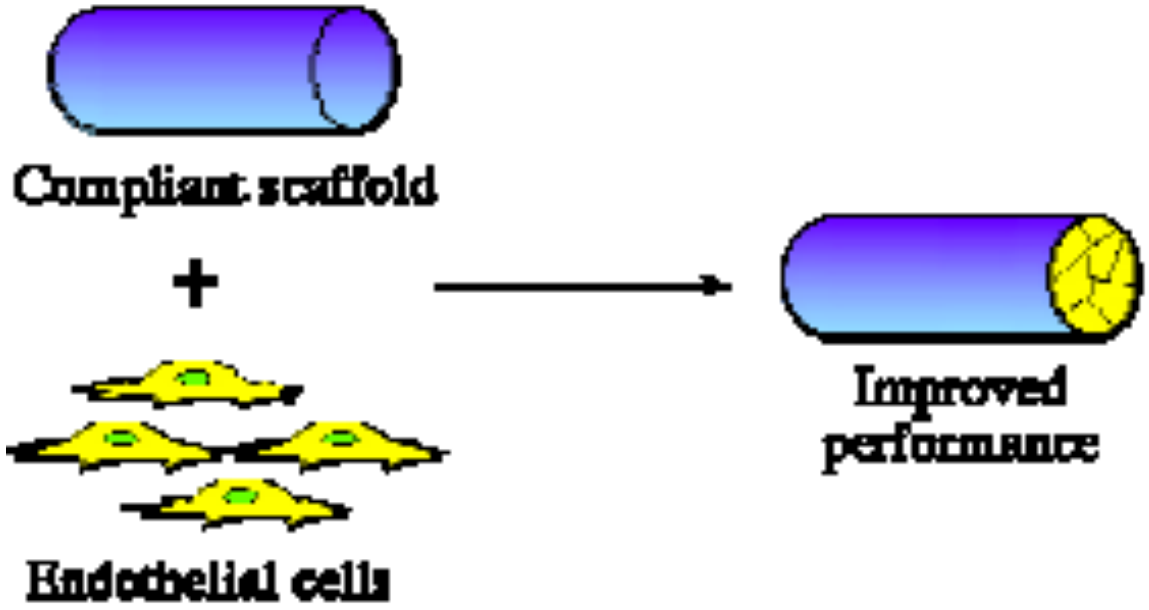
BIOLOGICAL Prostheses
- Rapid aging (Hyperplasia, sclerosis, calcification)
- Degradation
- Infections

SYNTHETIC Prostheses
- Thrombogenicits of internal surface
- Hyperplasia close to the anastomoses
- Difference of compliance in comparison to the natural vessel
- Absence of lining of endothelial cells around lumen of vessels

Engineered vascular substitutes, ideal characteristics:
- Properties similar to vascular vessels
- Presence of anti-thrombogenic endothelial lining

Tissue engineering

- Engineering blood vessels using cells and scaffolds



Tissue engieered blood vessels

Collagen tubular scaffold seeded with smooth muscle cells and endothelial cells