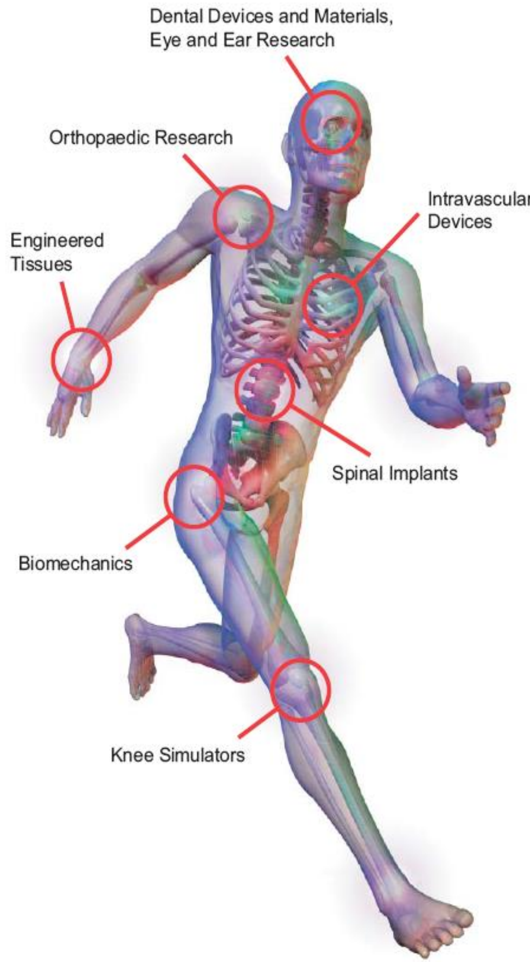
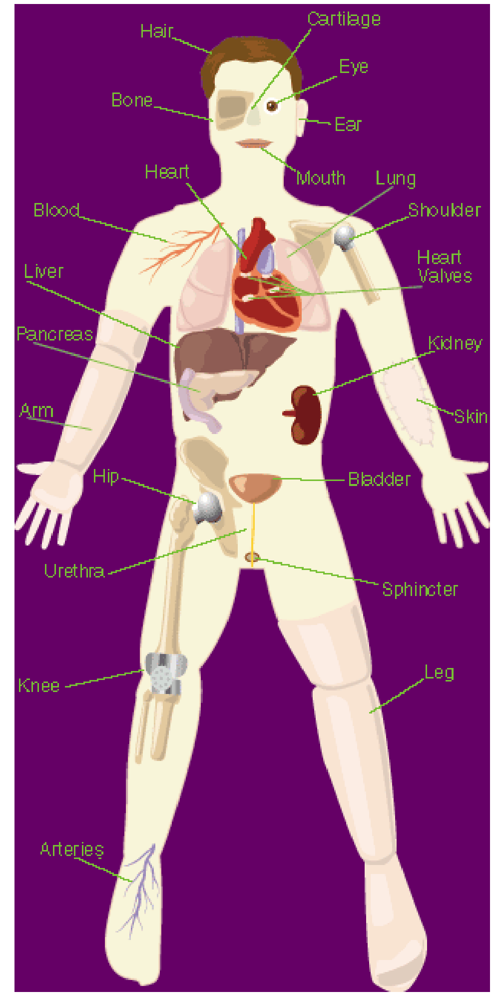
# ARTIFICIAL ORGANS

- Replacement of a hole or a part of an organ to achieve a more physiological function.
  - Active – passive systems.
- Organs in broad clinical use
  - Heart
  - Lungs
  - Kidney
  - Skin
  - Joints
- Organs under development
  - Sensing organs
  - Pancreas
  - Liver

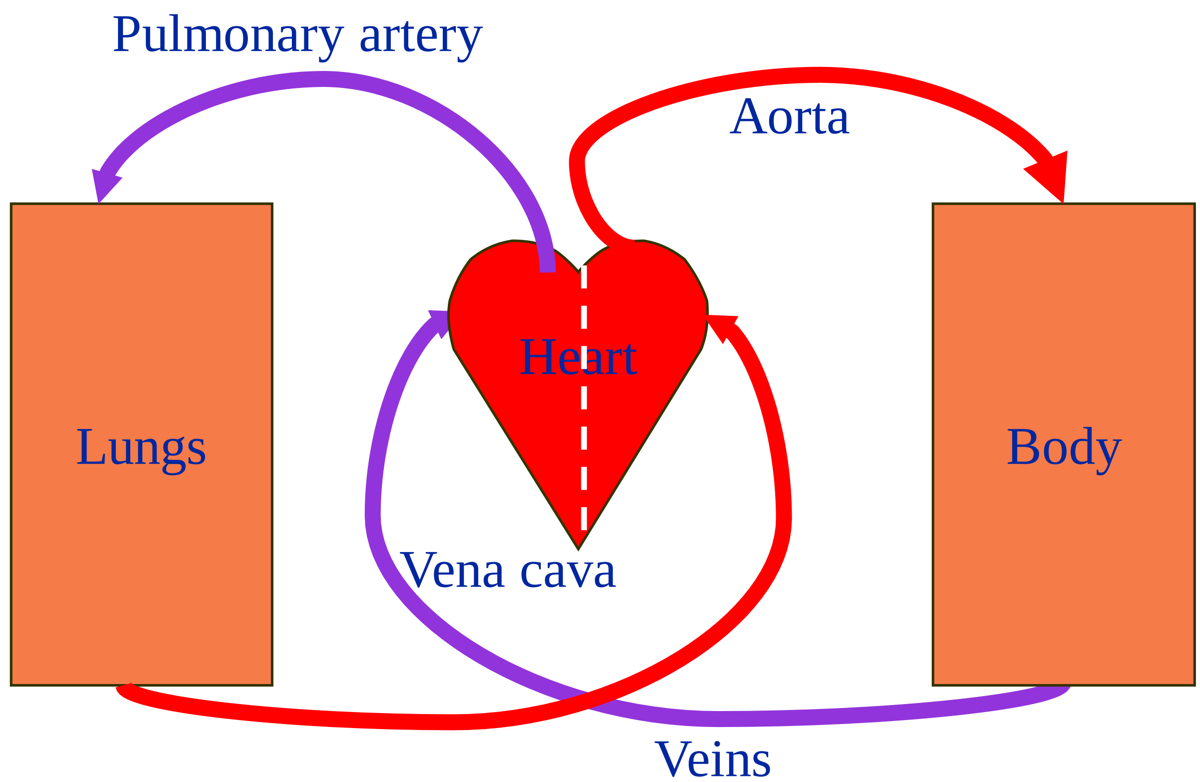


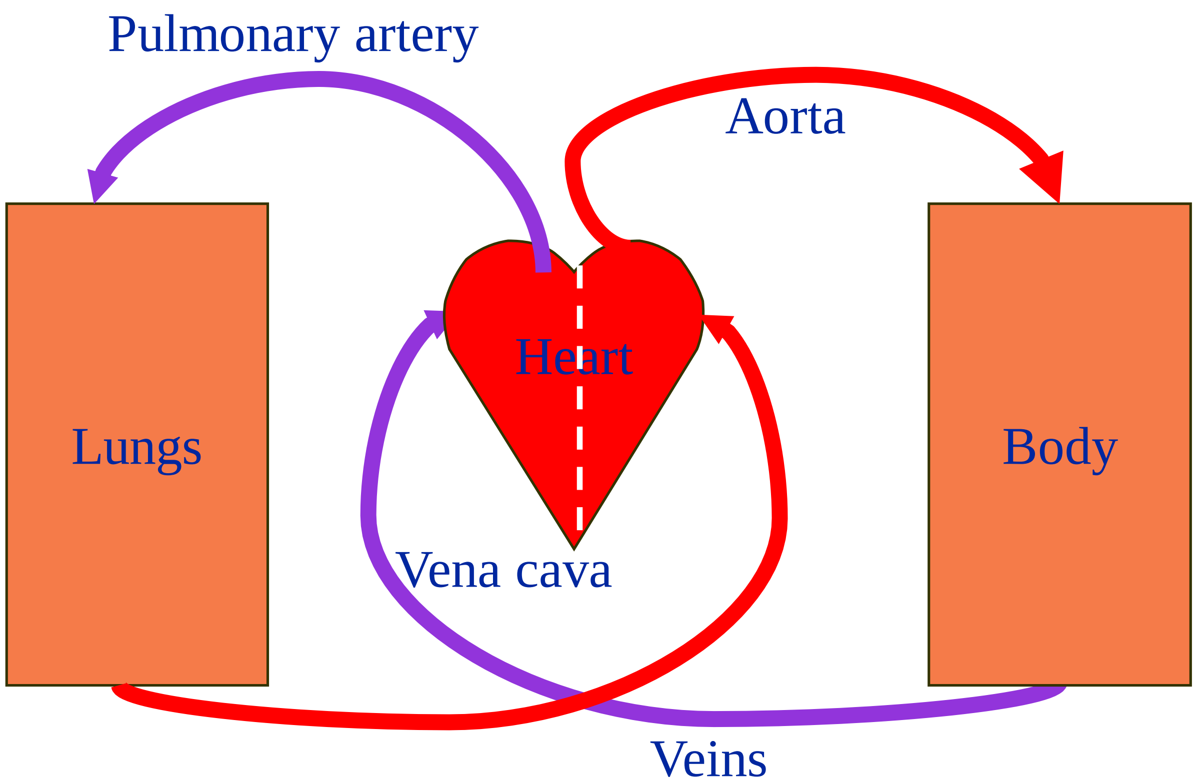
# Cardiovascular system

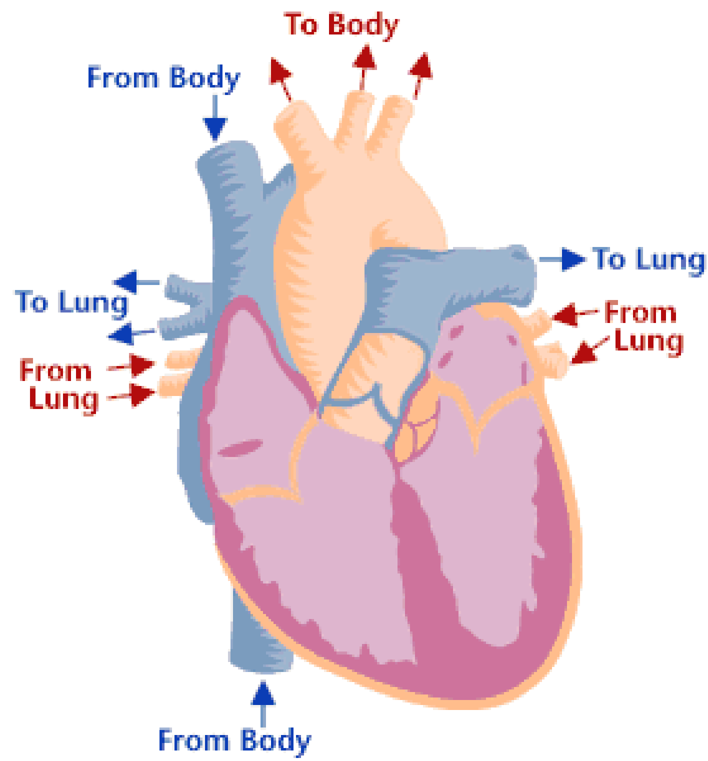
- Active systems
  - Total Artificial heart (TAH)
  - Ventricular assist devices (VAD)
    - » Right ventricle (RVAD)
    - » Left ventricle (LVAD)
  - Blood pumps
- Passive systems
  - Artificial heart valves
    - » Mechanical valves
    - » Biological valves
  - Artificial blood vessels
  - Vascular stents: Coronary – peripheral circulation

# Circulatory system



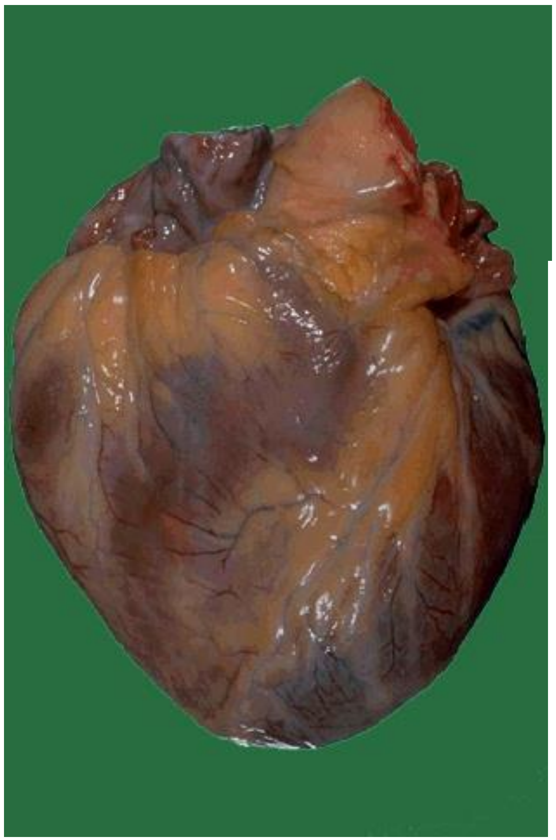
# Heart function

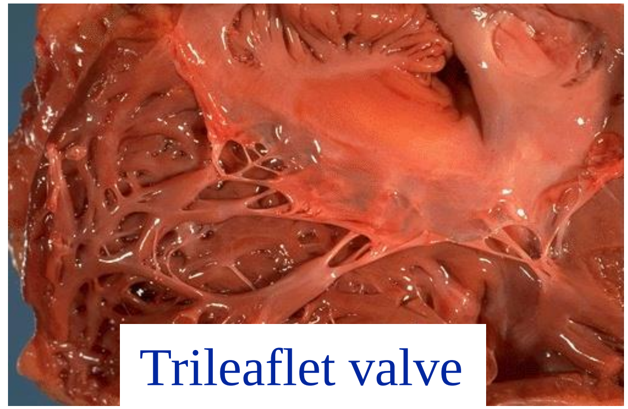


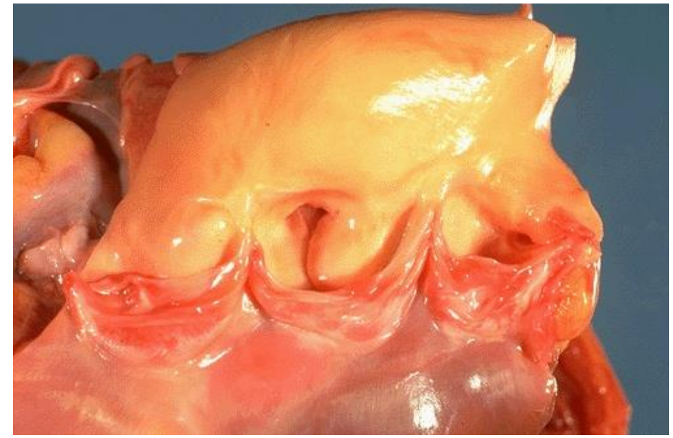
# The heart

Heart

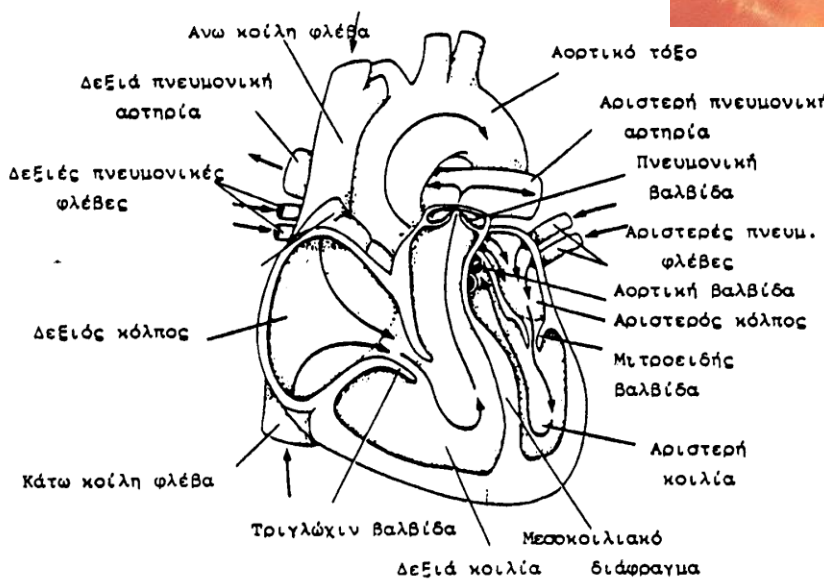




Trileaflet valve

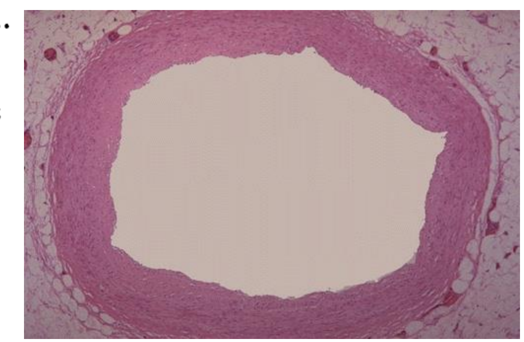


Aortic valve



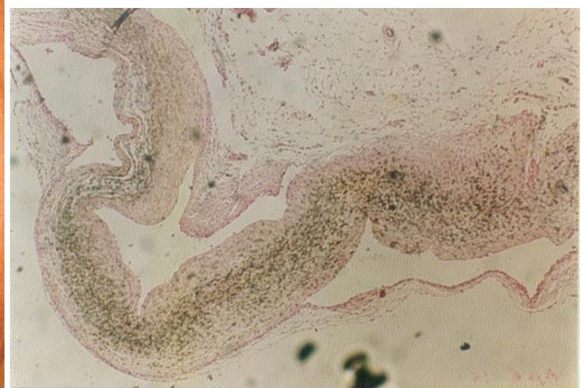

Σχ. 1 Αναπαράσταση της καρδιάς. Τα βέλη δείχνουν τη διαδρομή του αίματος στα διάφορα τμήματά της (Snell, R.S. 1984: Histology for medical students, Little, Brown and Comp. Boston).

Coronary artery



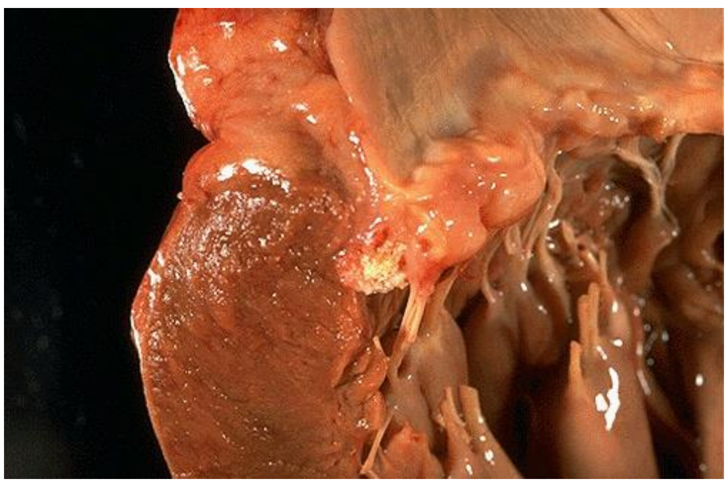
# Cardiovascular pathology

Aortic valve calcification

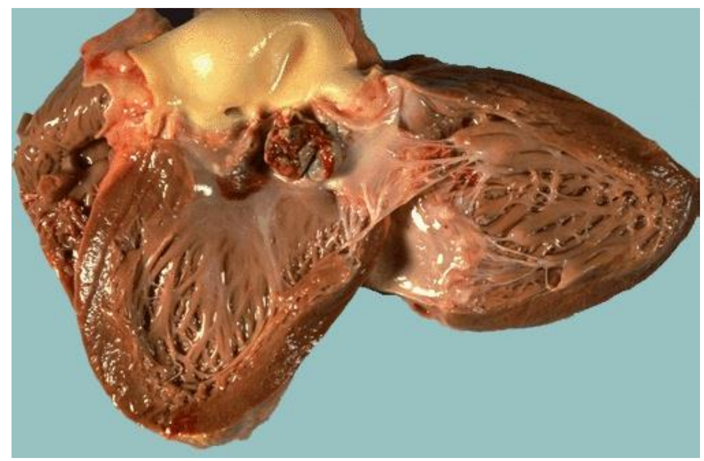


Bileaflet aortic valve-calcified

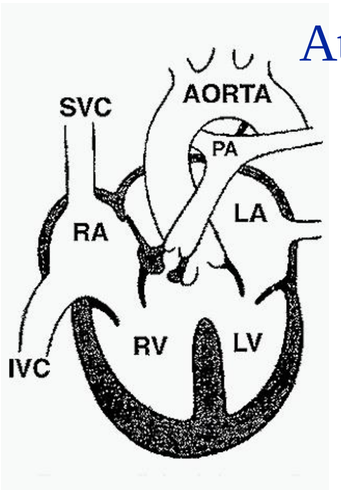
Mitral valve. Aortic ring calcification



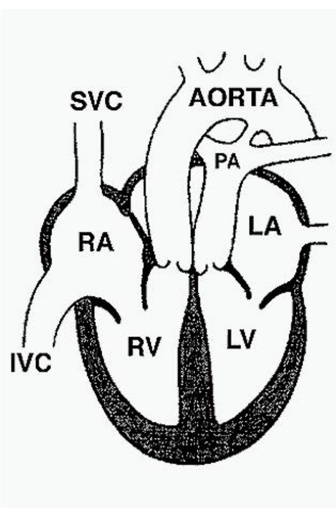
Infective endocarditis



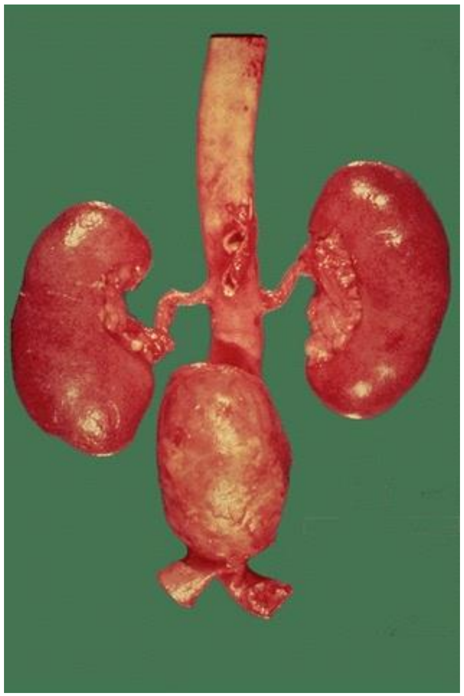
# Cardiovascular pathology




Congenital heart diseases

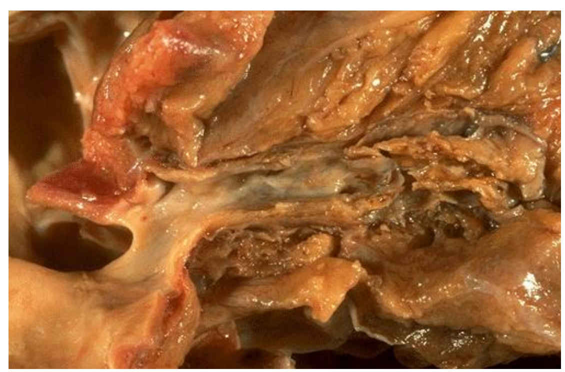


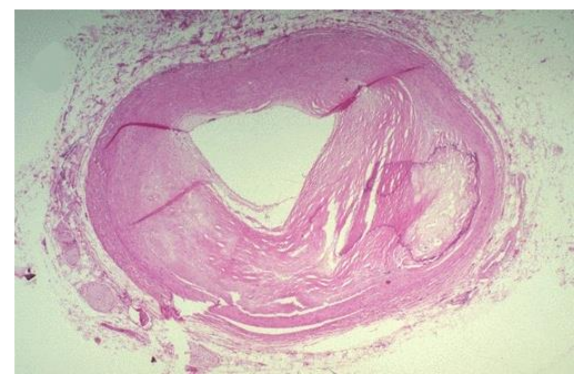

Atheromatic aneurism of abdominal aortaς



Aortic atheroma

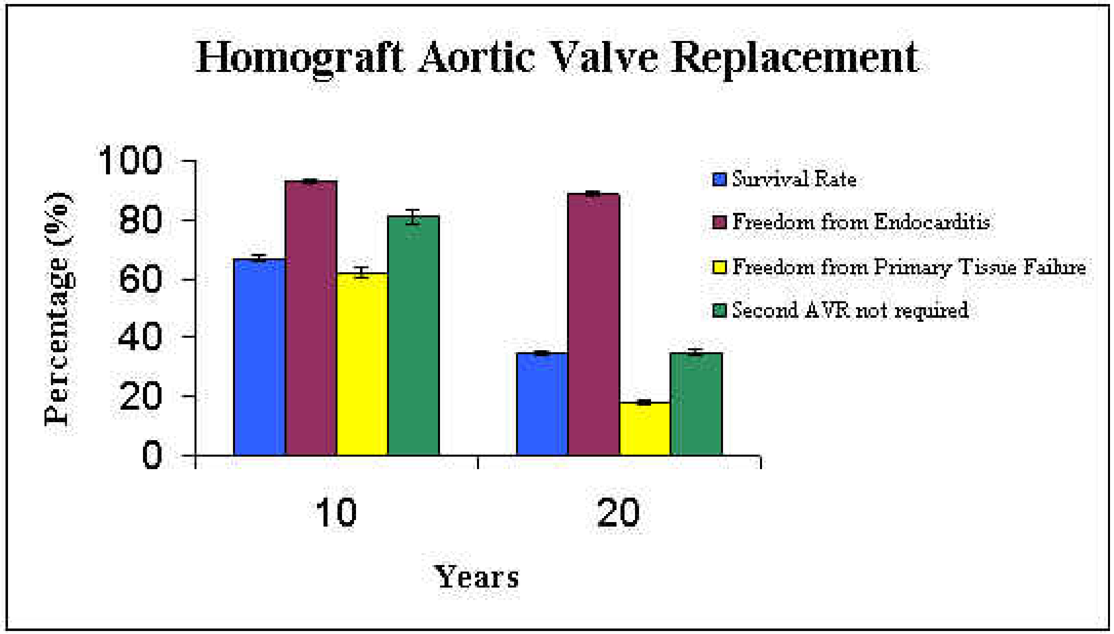
Atheroma of coronary artery



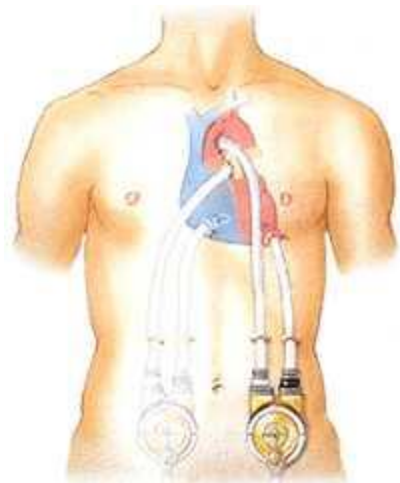


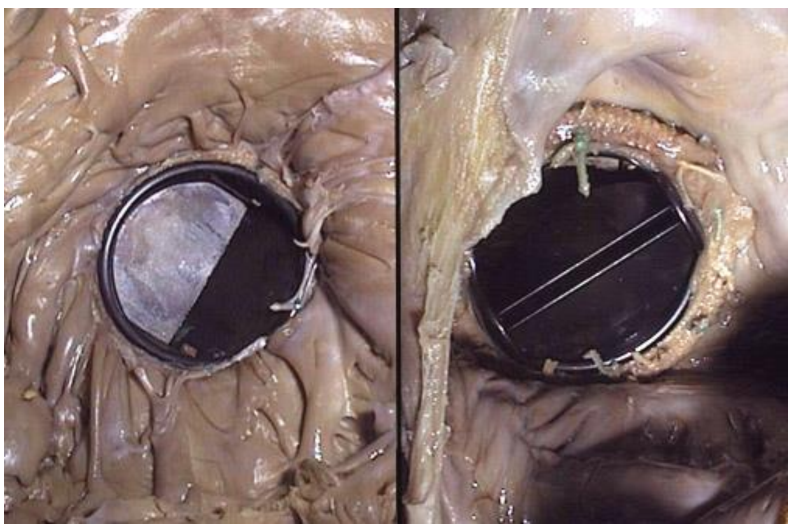
# Donor transplantation

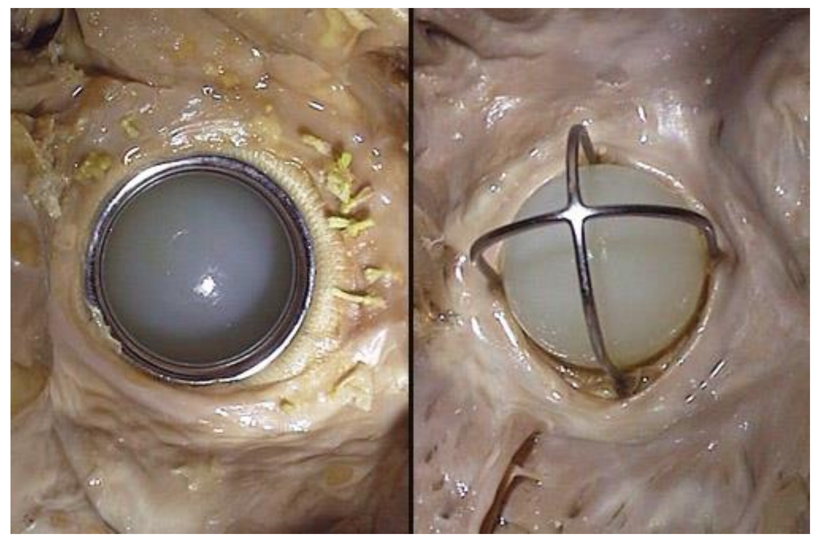
- Difficult to find donors
  - Availability - burrocracy
  - Conditions
  - Equipment – experience
  - Distance – transportation
  - Compatibility
  - ……….
- As a result, even ideally, less of 10% of clinical needs can be covered worldwide



# Organ replacement
# Artificial organs

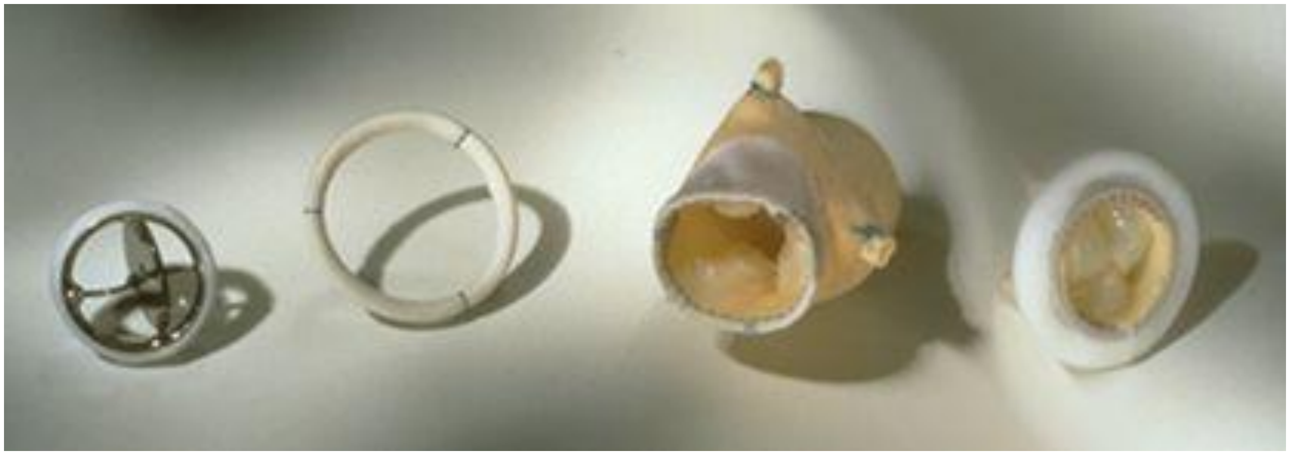




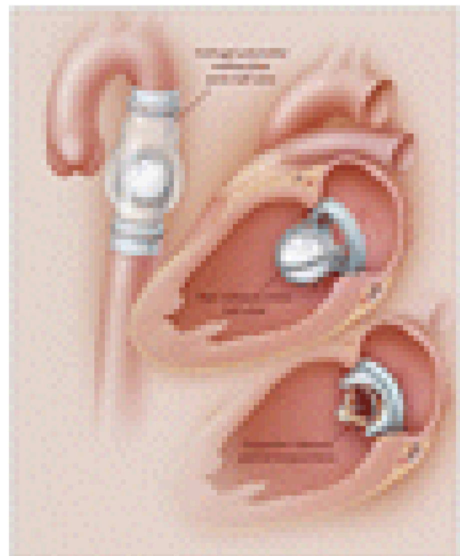
# Artificial heart valves

- Passive systems to secure quite physiological unidirectional blood flow
- Heart valve replacement according certain patients’ score indexes (e.g.  NYHA)
- Estimation of proper type (mechanical – biological), design, anatomical characteristics
- Post implantation (various techniques) short – mid – long time patient check up
- Short or for life drag therapy – support (e.g. anticoagulation)
- AS A RESULT: Patient never lives a normal life, even if physiological function is recovered.

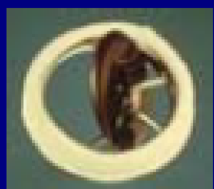


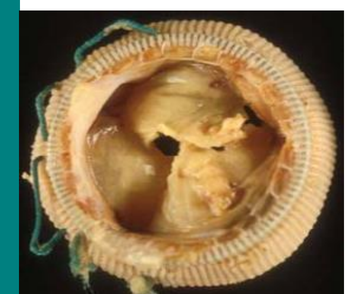
# Artificial valves: evolution

- 1952:First implantation (Charles Hufnagel) Plexiglass-Nylon_silicon. Descending aorta
- 1953: 1st open heart surgery: oxygenators, deaeration. New biomaterials
- 1955: 1st implantation in aortic anatomic position (Sheffield UK). Death after 14 hrs (ball movement)
- 1961: Starr-Edwards valve. Long term survival in 6 out of 8 patients
- End of 60s: Carpentier’s stent mounted bioprosthetic heart valve.



# Types of prosthetic valves

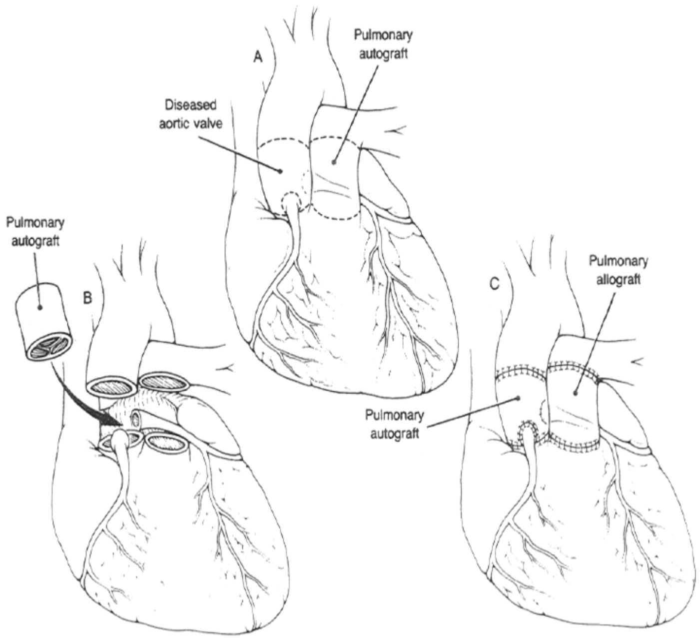
| Valve type | Advantages | Disadvantages |
|---|---|---|
| ***Mechanical***  | • Longevity<br>• Easy implantation<br>• Variety of size-designs<br>• Availability | • Non physiological geometry - hemodynamic<br>• Chronic anticoagulation therapy<br>• Risk of thromboembolism<br>• Regular medical examinations |
| ***Bioprosthetic***  | • Physiological anatomy - hemodynamic<br>• Minimize anticoagulation therapy<br>• Availability | • Tissue deterioration<br>• Calcification<br>• Undesirable host reactions |
| ***Living grafts*** | • Ideal anatomy - hemodynamic<br>• Physiological remodeling<br>• Minimal anticoagulation therapy | • Tissue deterioration<br>• Calcification<br>• Minimal availability<br>• Undesirable immunologic reactions |

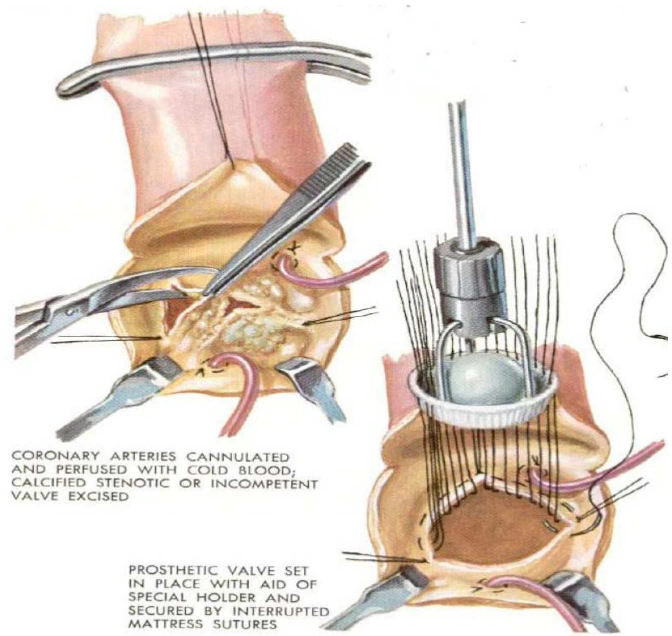


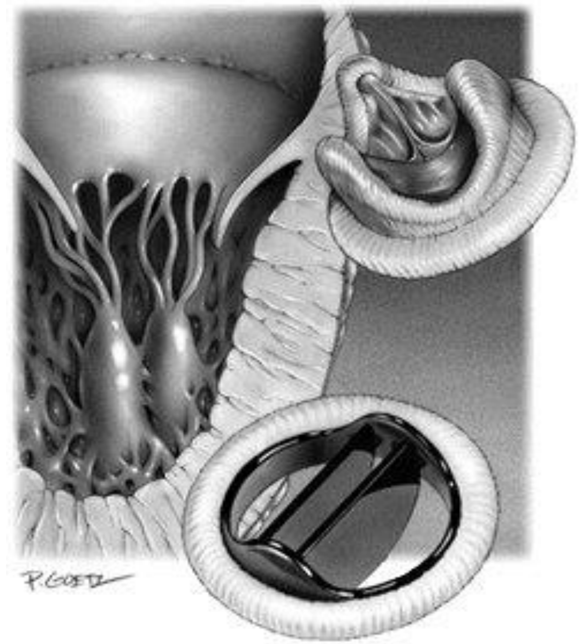
# Mechanical valves

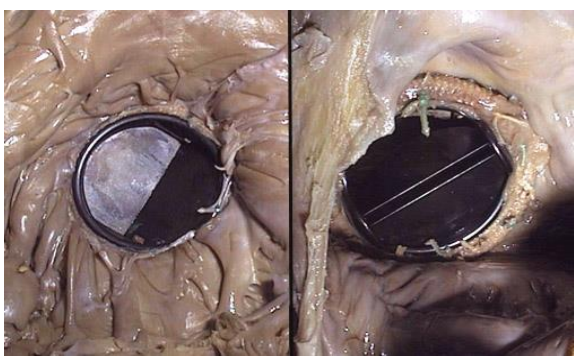
- Various designs regarding closing mechanism:
  - Caged ball
  - Caged disk
  - Tilting disk
  - Bileaflet (even trileaflet?)
- Anatomical position:
  - Aortic (LV)
  - Mitral (LV)
  - Pulmonary (RV)
  - Trileaflet (RV)

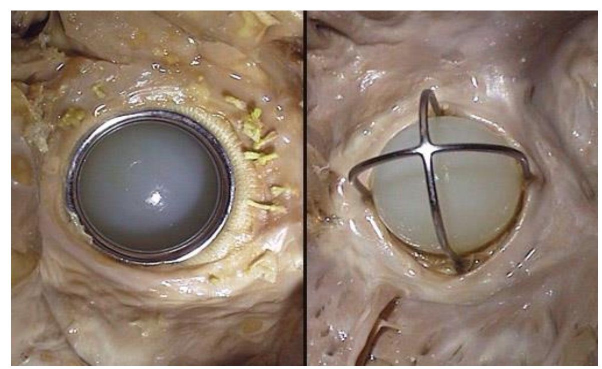
# Heart valve replacement techniques







# An ideal heart valve

- Non thromboembolism
- Chemical-biological inert*
- Low resistance
- Fast closing (<0,05sec)
- Good cooptation in closing position
- Stable physical – geometrical characteristics*
- Anatomic compatibility
- Permit stable strong suturing
- Non problems to receipt
- Easy – fast implantation (Harken D.E., 1962)

# Mechanical valves - evolution

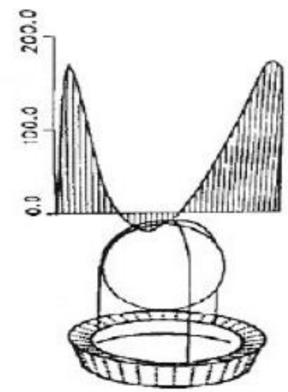
More than 30 different approaches from the first caged ball to recent trileaflet mechanical, including trileaflet polyurethane valves

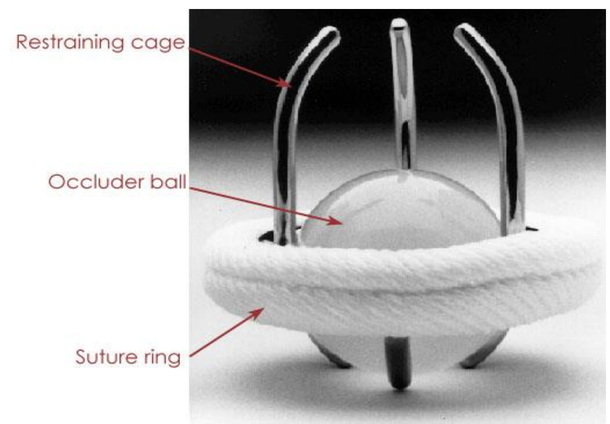
Main design topics:

- Centrally weighed blood flow
- Hemocompatible biomaterials (to reduce anticoagulation therapy)
- Better fatigue strength
- Reduction of wear (cracks - cavitation)

# Caged ball

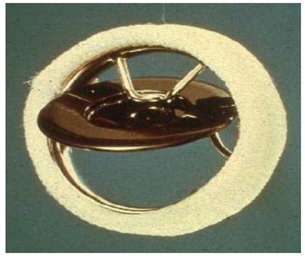
- Early design (1961: Starr-Edwards)
- Silicone ball (+), Cage wire stellate, titanium
- Suturing ring Teflon, polypropylene
- Peripheral flow – shear stresses near vascular wall
- Big heavy moving ball – excess myocardial work – caged disc
- Big trans-valvular pressure gradient
- Strong anticoagulation therapy (life long)
- Noise, remodeling of vascular walls

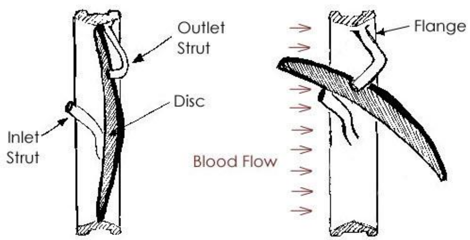


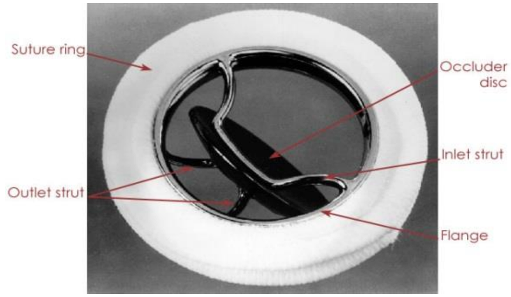



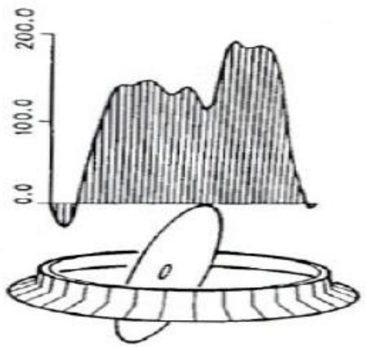
# Tilting disc

- From mid 60s, after a short presence of caged disk
- Disk in angle under a stable supporting element
- Disk material: Pyrolytic carbon
- Support: Haynes 25, titanium
- Suturing ring: Teflon
- More physiological flow
- Fast movement, no backflow
- Less anticoagulation therapy (but still for lifelong)
- A risk for fatigue fracture to the soldering of outlet support wire (Bjork-Shiley 1979-90: 600 cases, 2/3 to death).
- Monobloc titanium case





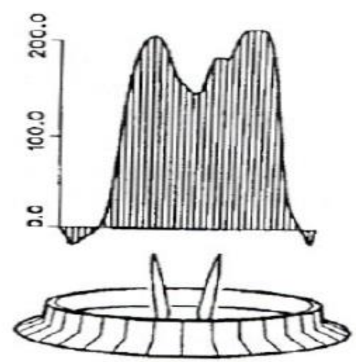



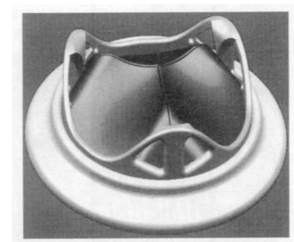



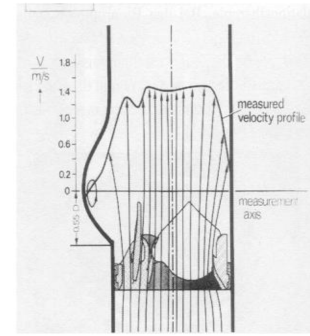
# Bileaflet

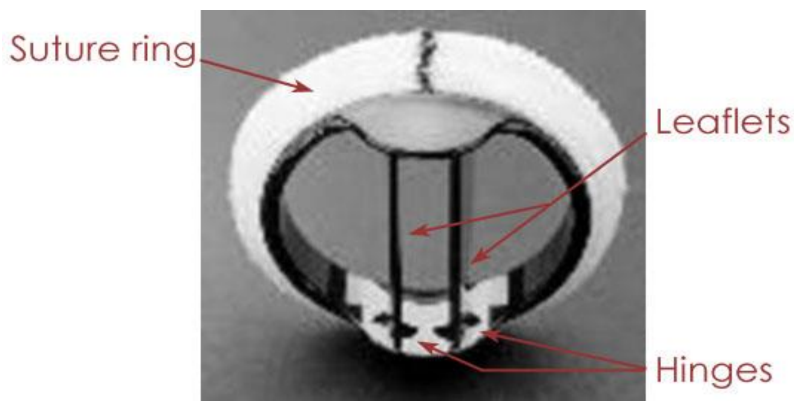
# Trileaflet

- Presence in 1979
- Twin half disks, support by hinges
- Disks, ring coating by pyrolytic carbon
- Suturing ring: Teflon, polyester
- Better central flow
- Faster leaflet movement
- Problems of cooptation in closing
- Potential disk movement restrictions by tissue hypertrophy into hinges - ring

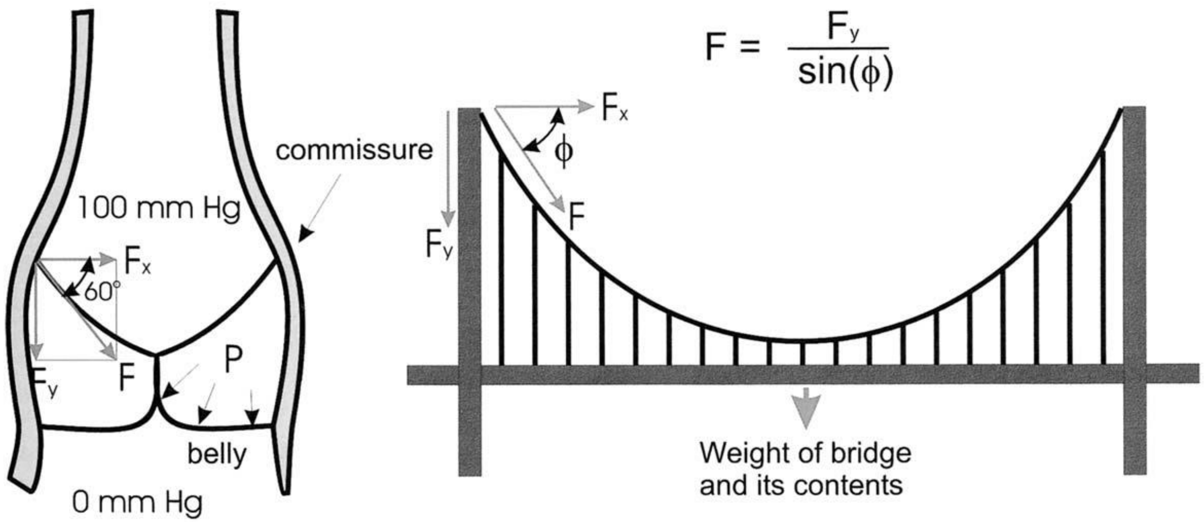




# Natural geometry
# Flexible leaflet valves

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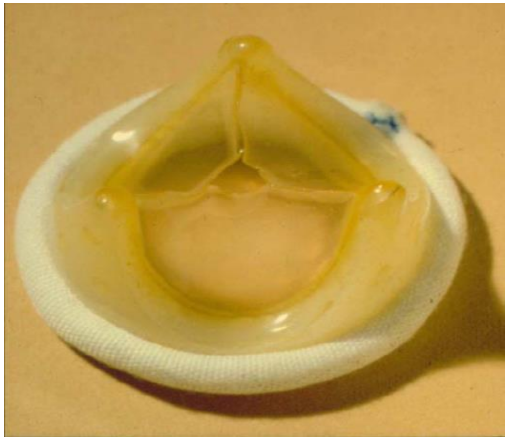
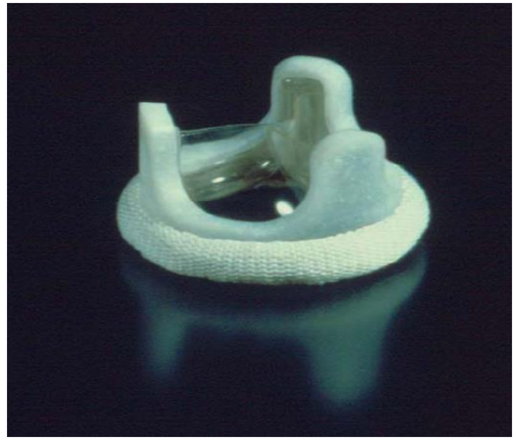
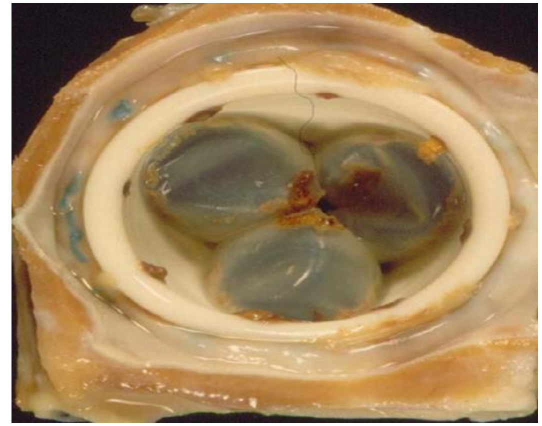
- Mechanical loading in systole – diastole
- Functional failure, fatigue
- Compatibility - calcification

# Polymeric valves

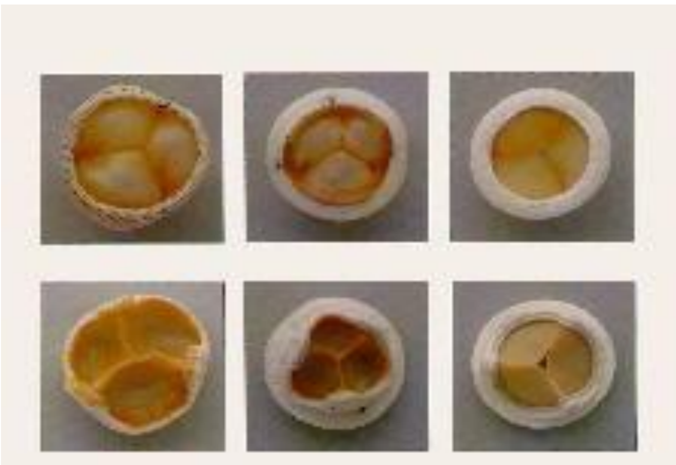




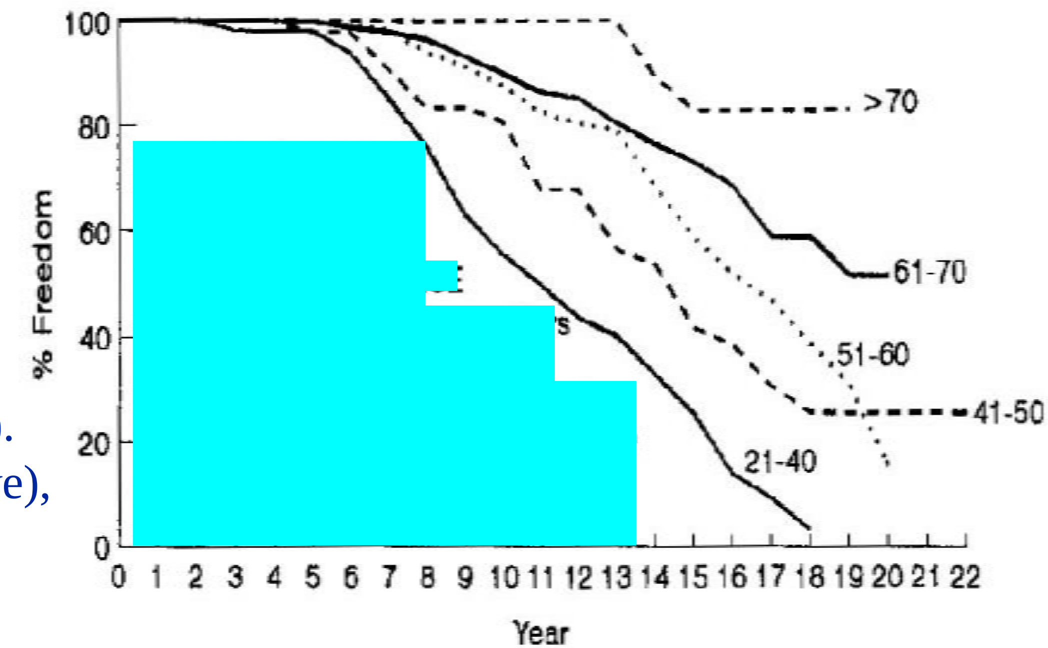


- Flexible elastomeric membranes (polyurethanes)
- Excellent hemodynamics
- Reduced functional strength
- Calcification
- Use in artificial heart devices

# Biological valves

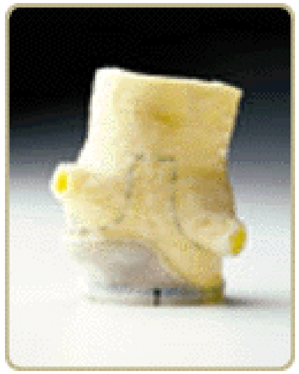


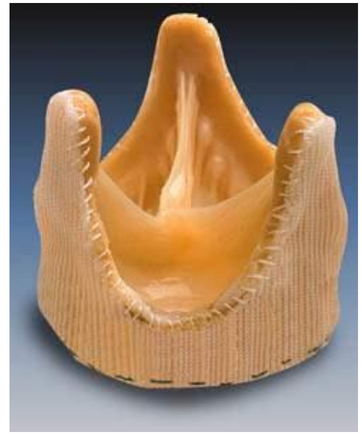
- Animal tissue (hole valve or constructed).
- Antigen neutralization (cell death -remove), crosslinking for proteolytic protection (Formaldehyde, glutaraldehyde ….)
- Excellent hemodynamics
- Reduced longevity
- Calcification
- Use in Elderly population, artificial heart devices



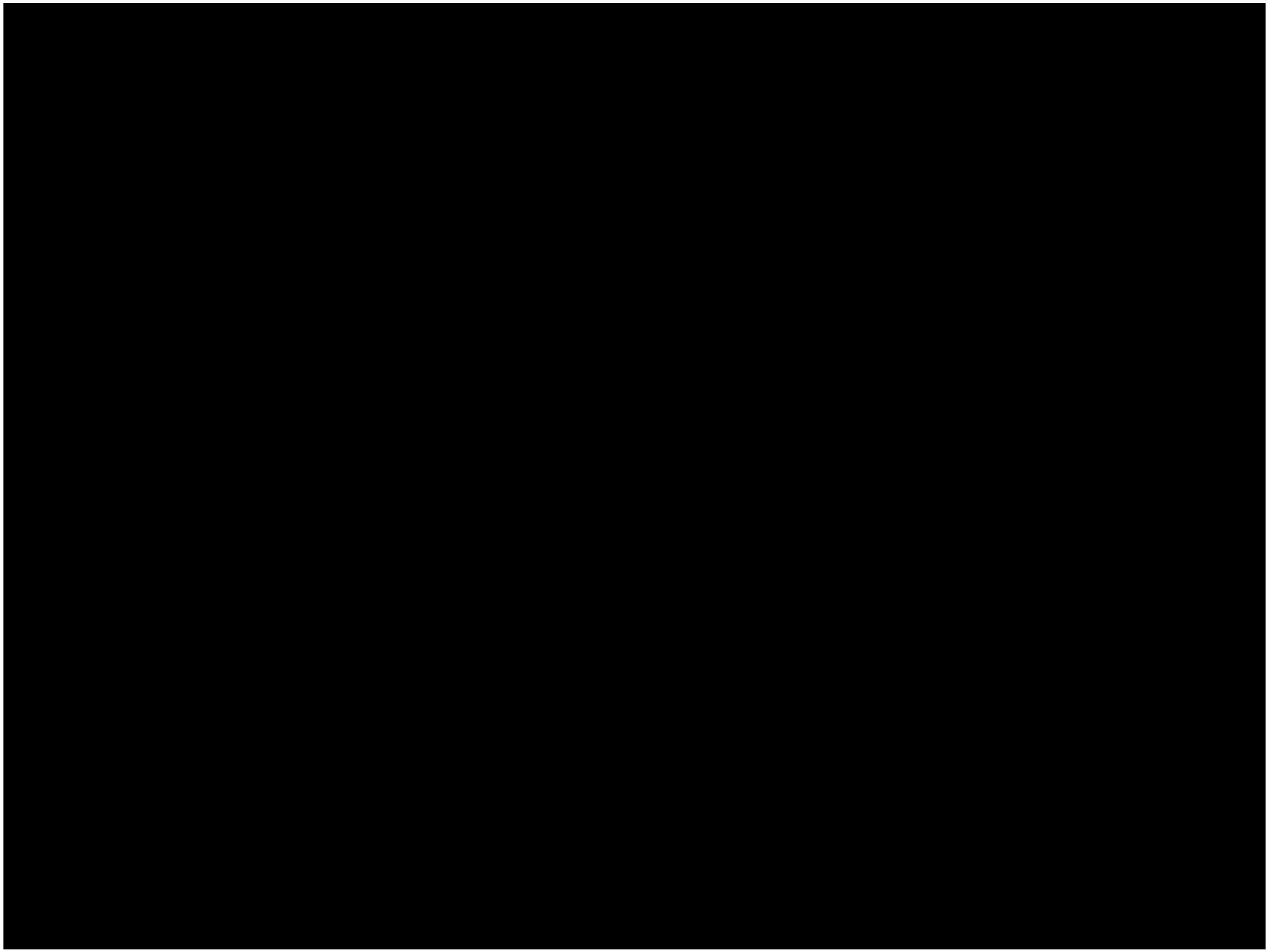

*Carpentier-Edwards standard porcine aortic valves, aortic site*
*WRE Jamieson et al -Ann Thor Surg 1998*

# Types of biological valves





# Isolation of aortic conduit from a porcine valve
# Video





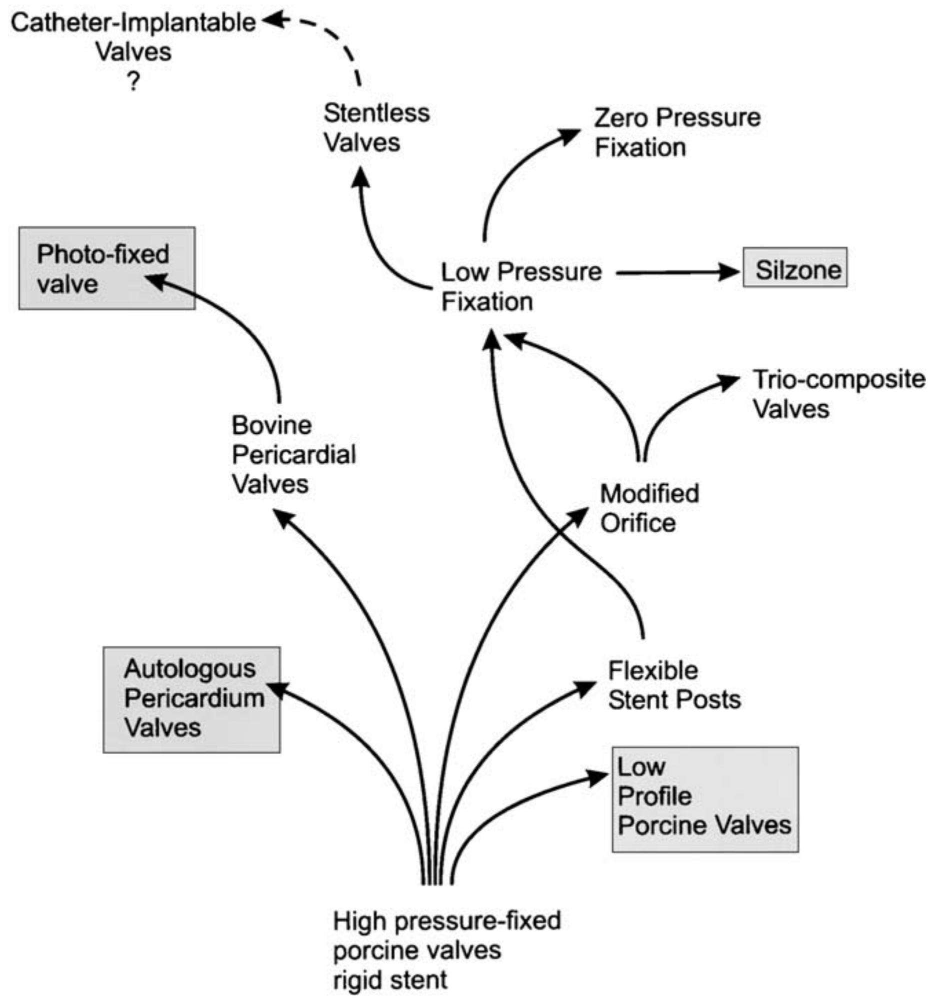
# Photos



# Fixation with glutaraldehyde

# Evolution of bioprosthetic valves

- Glutaralgehyde croslinking: Apply pressure for valve leaflet closing
- High-low support profile
- From total porcine to structured pericardial valve
- Rigid-flexible supporting stent, stent less
- Postfixation anticalcification treatments

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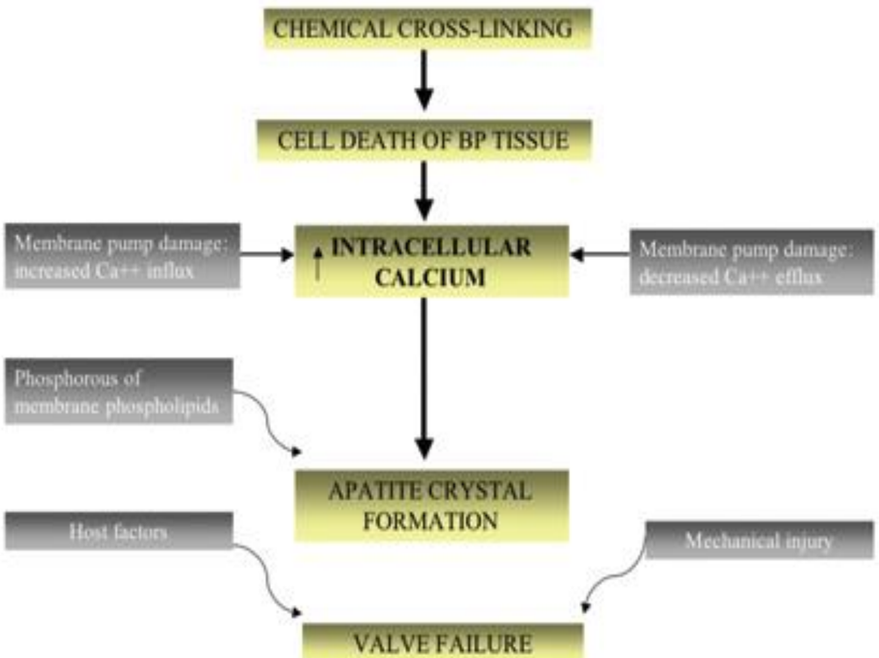
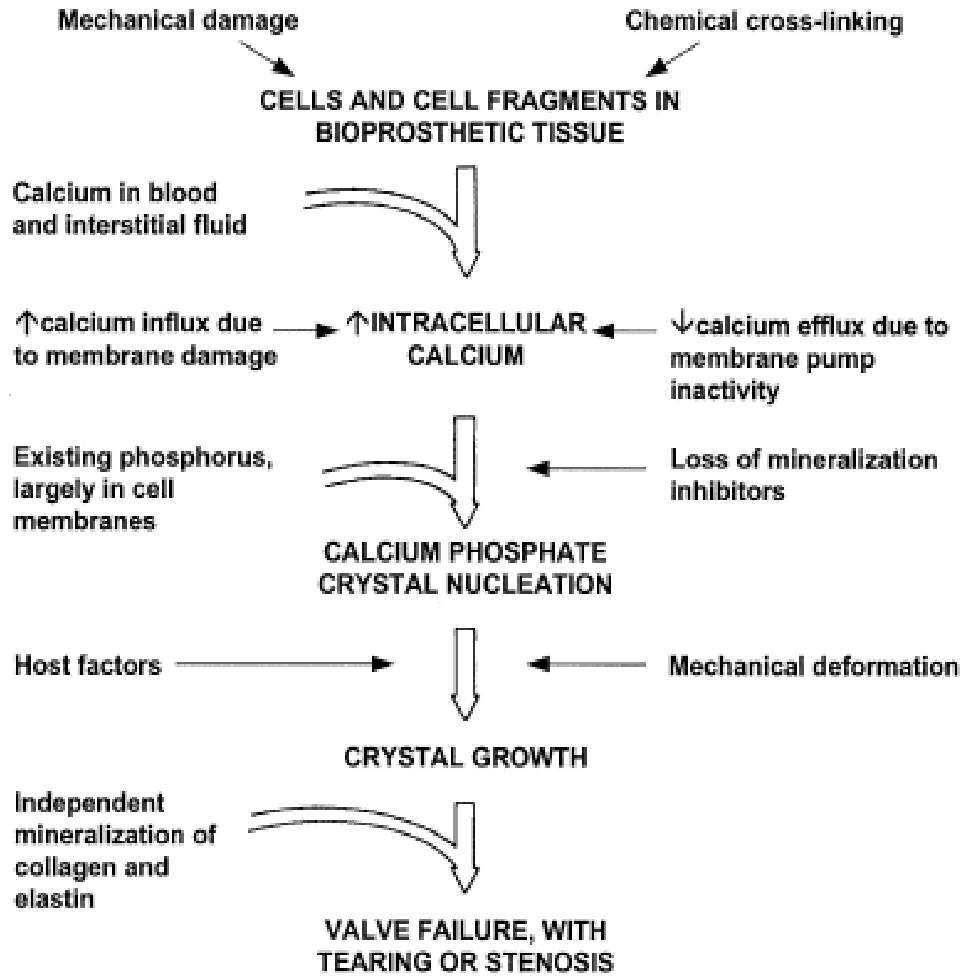
# Calcification mechanisms, solutions

- Much is written, a few are proved
- Crystal nucleation Ca-$PO_4$ (+ sodium, magnesium, carbonates) in regions with high mass concentration-activation
- Necrotic cells, cell remnants – decellularization
- Phospholipids-alkaline phosphatase - hydrolysis , ethanol removing
- Failure of collagen fibers (fatigue, denaturation). Better fixation
- Lipids - removal
- Free aldehydes in treated-fixed tissue. Deactivation-masking

# Proposed mechanisms

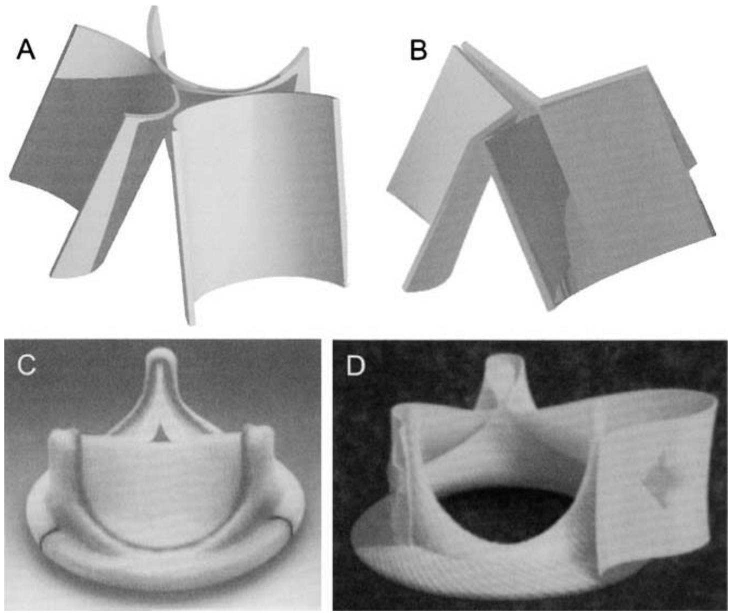



Thiene – Valente, 2004




Schoen et Al., 2005

# Pericardial bioprostheses

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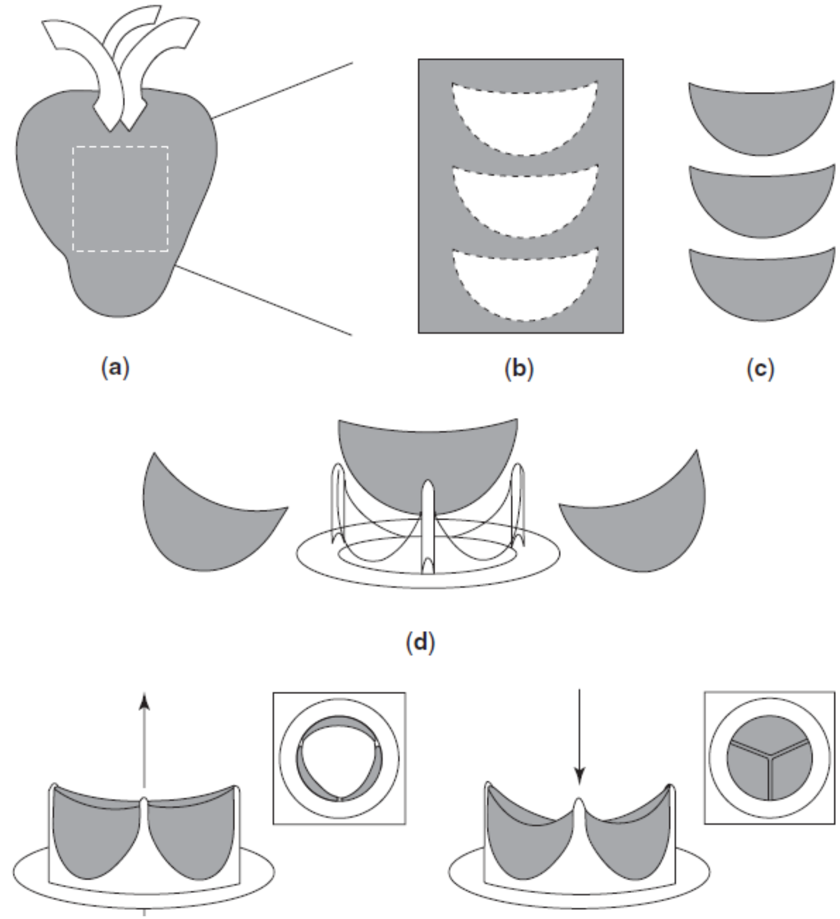
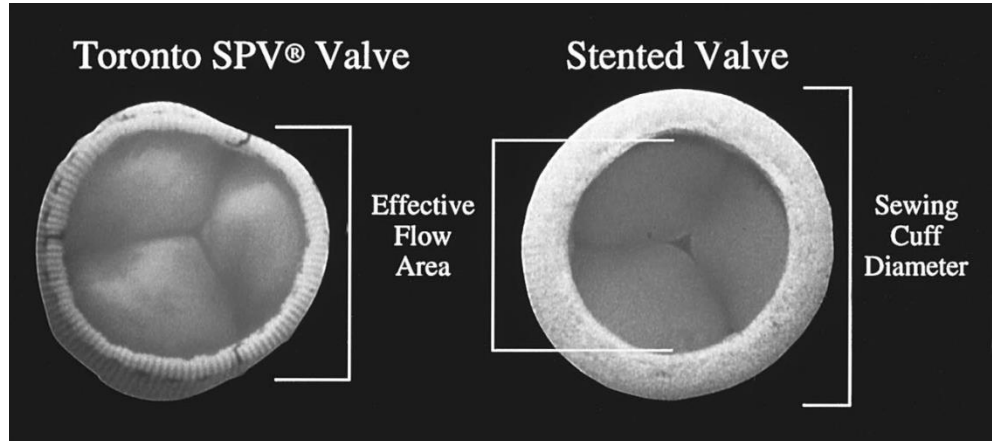


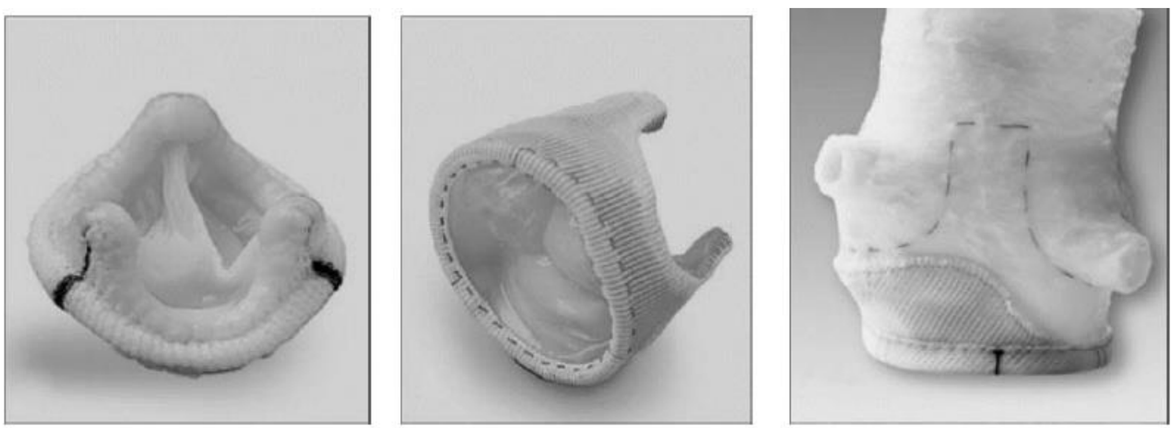

DAN T. SIMIONESCU
*Wiley Encyclopedia of Biomedical Engineering*, Copyright © 2006

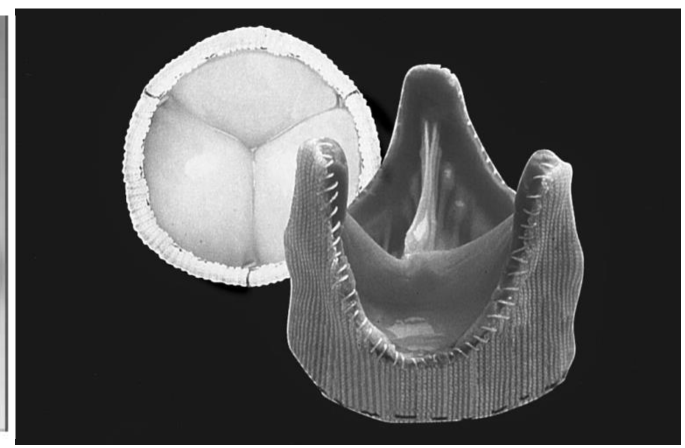
- Selection criteria - treatment
- Design – cut of leaflet
- Leaflet suturing on stents: Continuous-separate

# Stent less porcine valves

- Optimization on leaflet flexibility
- Gain in dimensions
- Changes for better hemodynamics



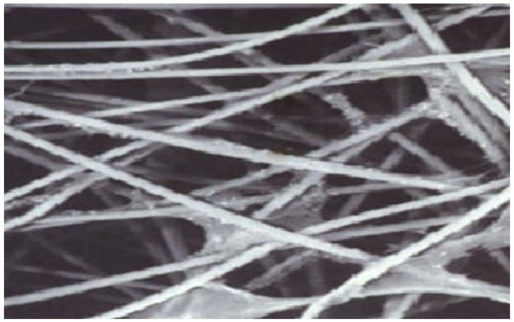



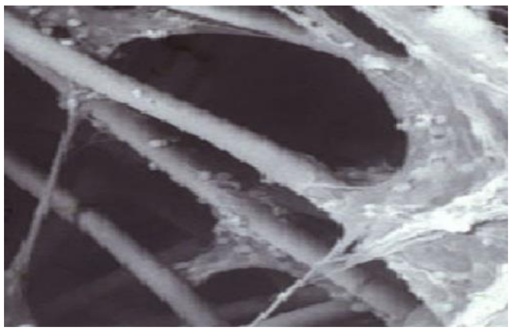


Dan Simionescu,
*Wiley Encyclopedia of Biomedical Engineering*, Copyright © 2006

Opin Cardiol 2000, 15:74–81 © 2000

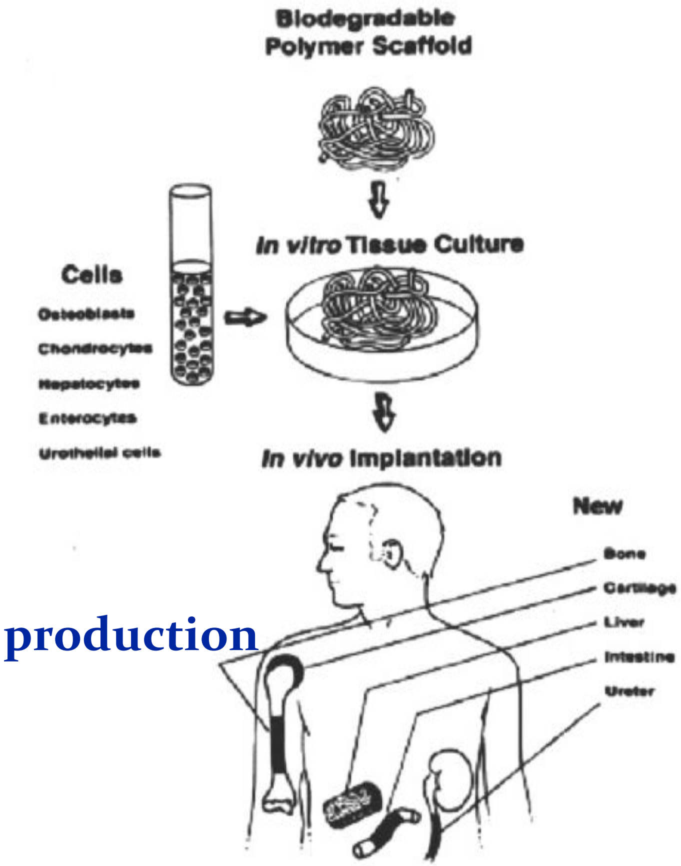
# Regenerative valves
# Tissue engineered scaffolds



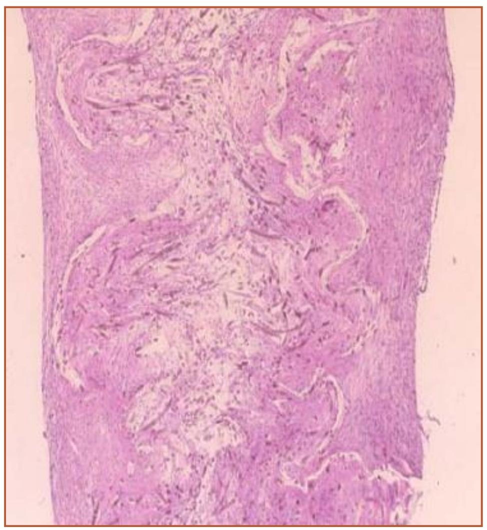


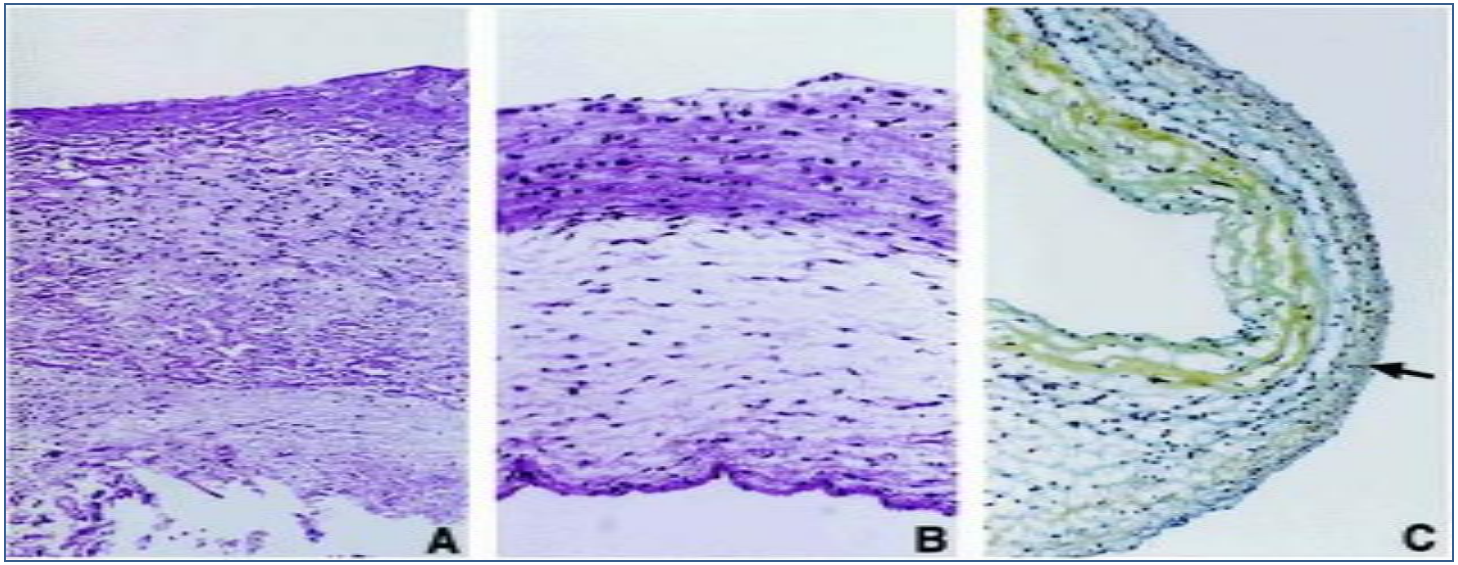
**Important factors**

- **Mechanical performance**
- **Cell proliferation/spreading**
- **Changes in cell phenotypes**
- **Extracellular matrix (tissue) production from cell**
- **Vascularization**
- **Biodegradation of scaffolds**
- **Regeneration/growth**



# Tissue engineered heart valves I






## Weeks *in vivo A*=6, B=16, C=20

Scaffold: PGA, prime cells from vascular wall
Sheep implantation

*In vitro*: 21 days

*SP Hoerstrup et al –CIRCULATION, 20006*

Bioreactor (2 step procedure)

# Mechanical heart valves
# Design characteristics

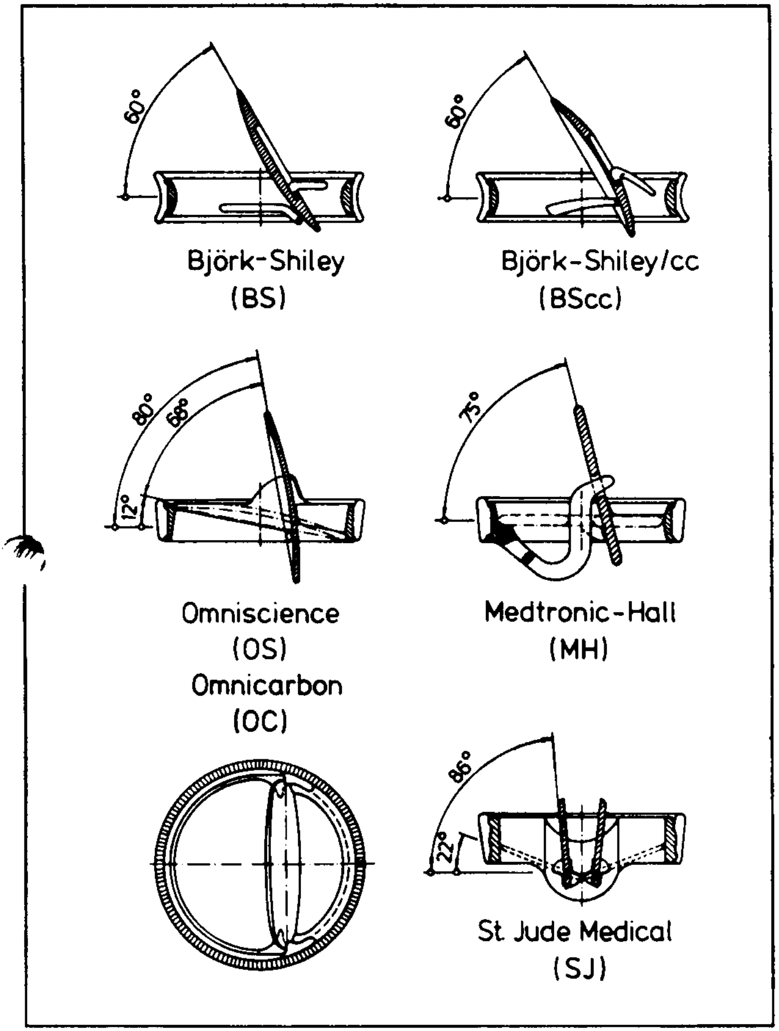



**Fig. 1** - *Technical (mechanical) heart valve prostheses.*

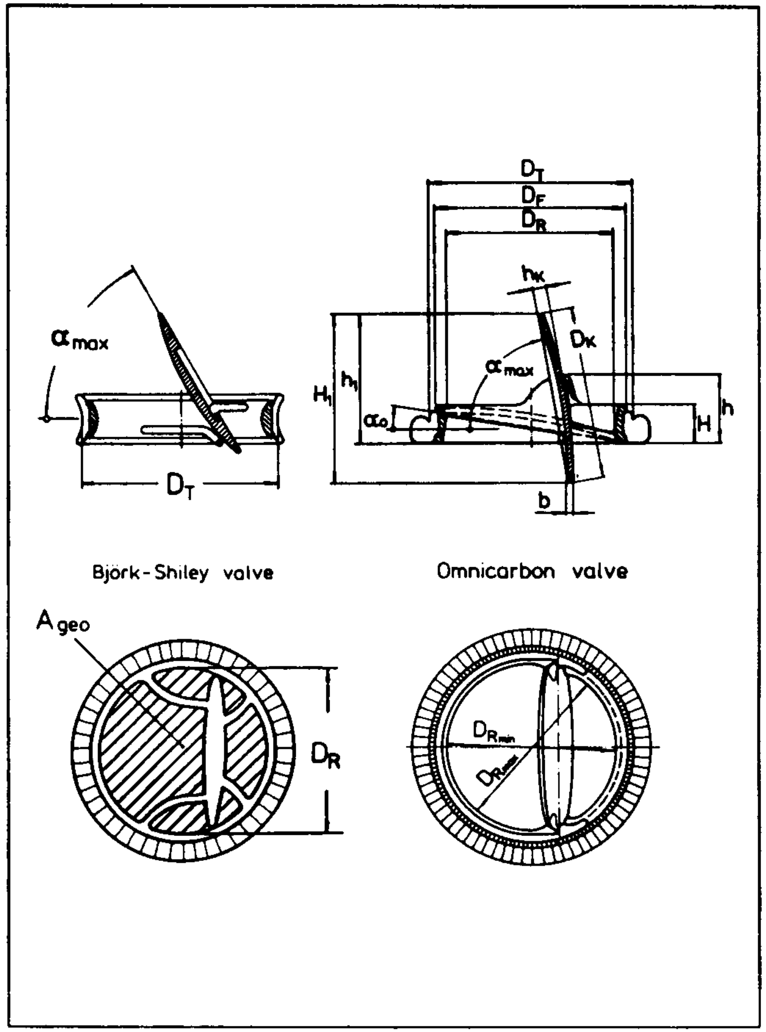
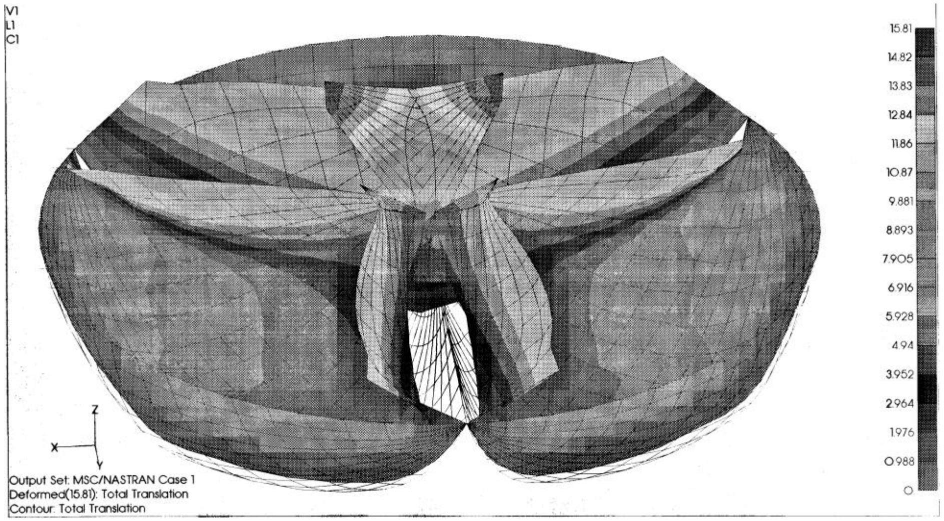
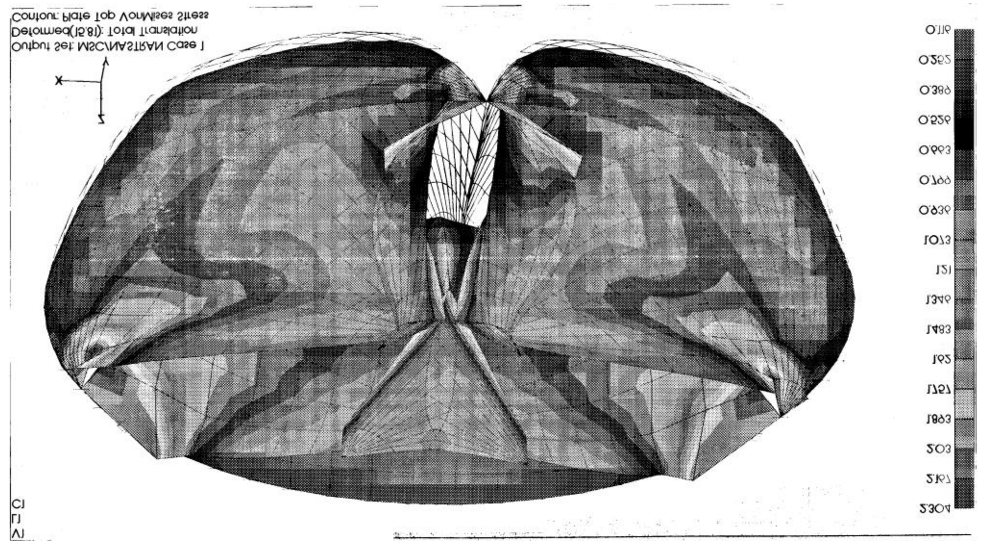
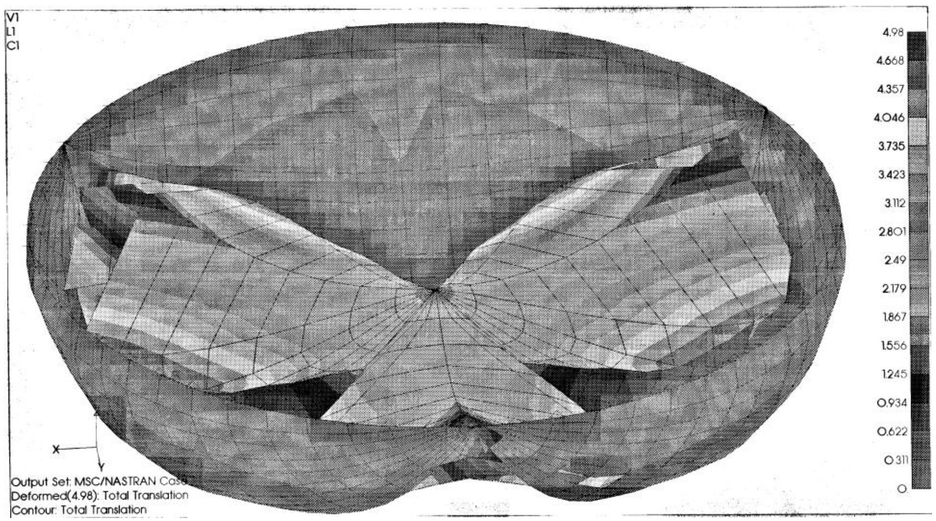


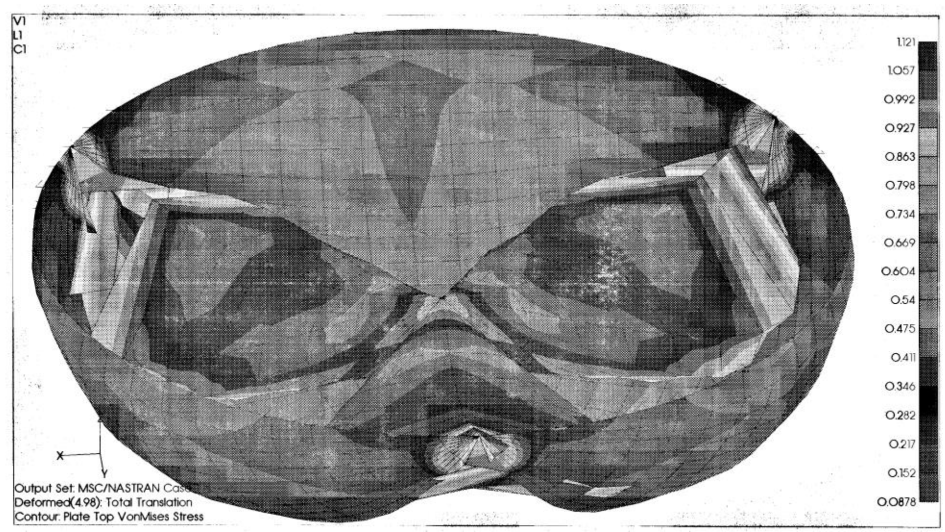

**Fig. 2** - *Geometrical parameters of technical heart valve prostheses.*

# Modelling finite elements
# S. Antoniadis, D. Mavrilas

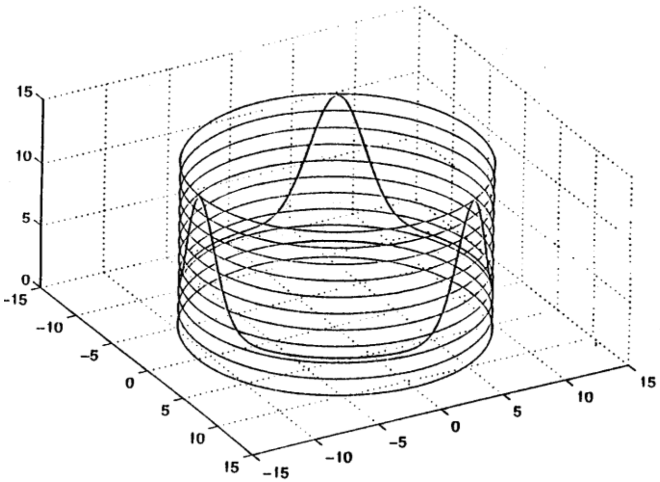


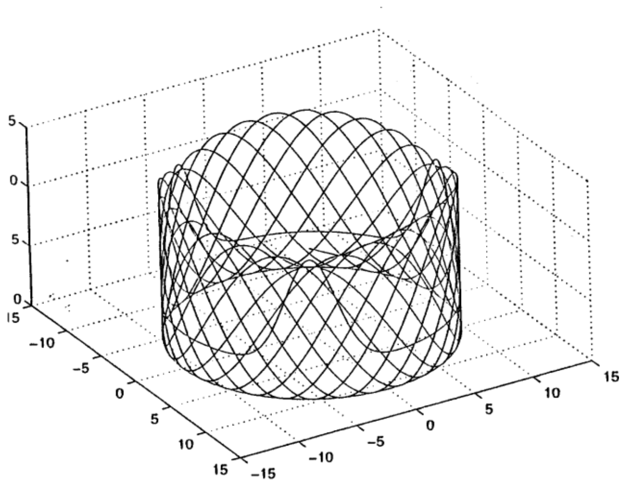



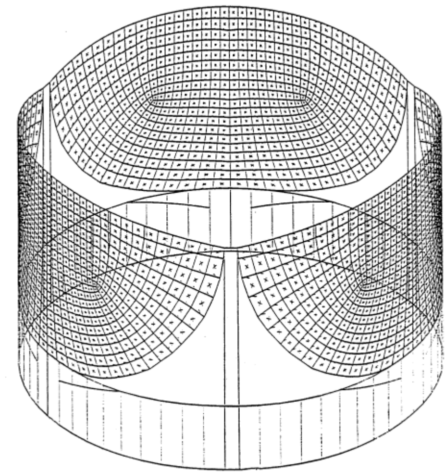


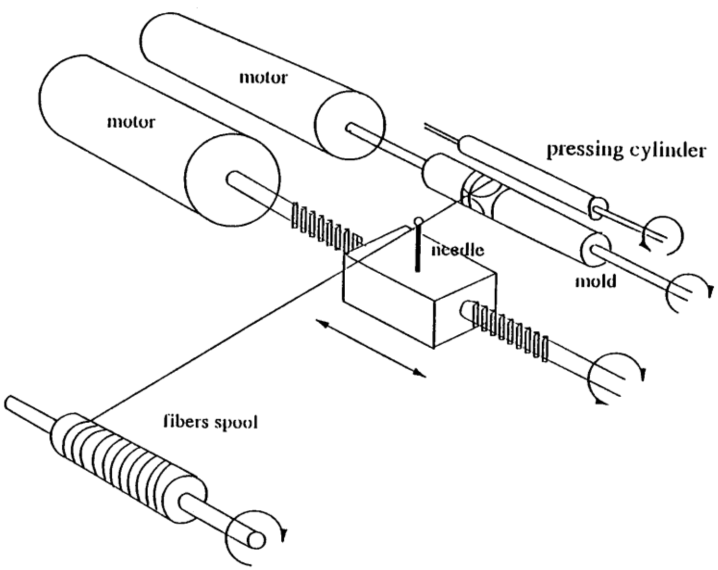



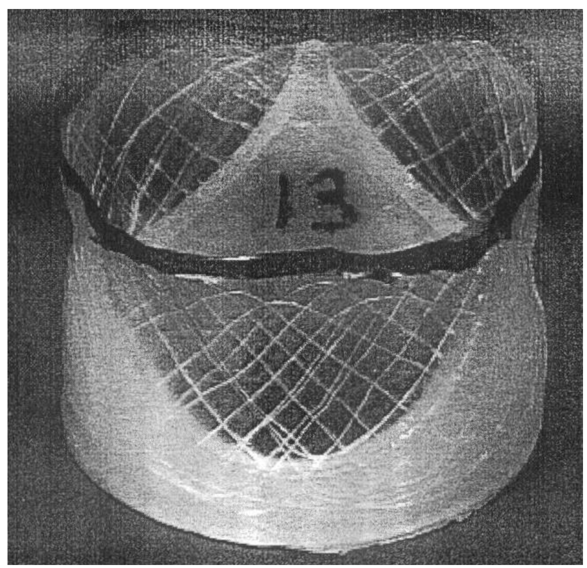
# Design of a polymeric valve
# G. Gacciola *et al*.

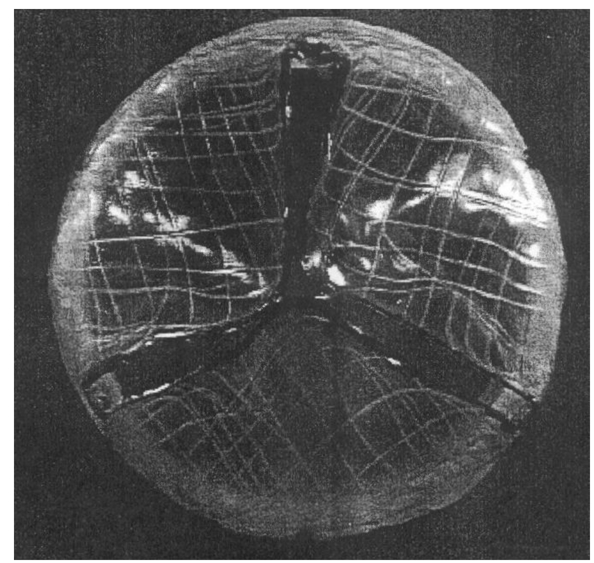




# Design of artificial valves
# Standardization of testing

CEN
European Committee for Standardization
Comité Européen de Normalisation
Europäisches Komitee für Normung

Netherlands
telephone: + 31 15 690390
telefax: + 31 15 690190
telex: 38144 nni nl
telegrams: Normalisatie Delft

doc. nr.

item nr. | supersedes document

CEN/TC 285 WG3 TF1
Title: Cardiac Valves

English version

"Non active surgical implants
Particular requirements for cardiac and vascular implants
Part 1: cardiac valves - March 1994

INTERNATIONAL STANDARD

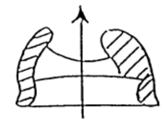
ISO 5840

Second edition
1989-12-01

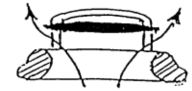
**Cardiovascular implants — Cardiac valve prostheses**

*Implants cardiovasculaires — Prothèses valvulaires*

CAGED BALL

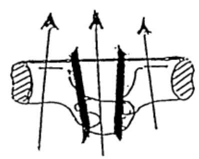


TISSUE



CAGED DISK

*DRAFT*
Replacement Heart Valve Guidance



BILEAFLET

TILTING DISK

Division of Cardiovascular, Respiratory, and Neurological Devices
October 14, 1994

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Devices and Radiological Health

# European standardization

ELSEVIER

European Journal of Cardio-thoracic Surgery 32 (2007) 690—695

EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY

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## Update of the European standards for inactive surgical implants in the area of heart valve prostheses

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Received 11 April 2007; received in revised form 10 August 2007; accepted 15 August 2007; Available online 17 September 2007

**Abstract**

**Objective:** The approval of a heart valve for the European market takes place in accordance with European and international standards. A new version of the EN Standards was published in June 2006, which responded to different technical innovations in the area of heart valve technology. This work outlines the differences between the new EN ISO 5840 (2005) and the old EN 12006-1 (1999). **Methods:** We compared the 'new' EN ISO 5840 (2005) and the 'old' EN 12006-1 (1999). **Results:** The following aspects have been updated in the new EN ISO 5840:

- Size designation of biological and mechanical heart valve prostheses in accordance with the patient annulus
- Differentiation of the annular implantation position (intra-annular, intra-supra-annular, supra-annular)
- Table for the description of the components of a heart valve prosthesis
- Use of compliance chambers for the hydrodynamic testing of prostheses without scaffold
- Determination of the minimum requirement for heart valve prostheses in hydrodynamic tests and specification of reference values with regard to prosthesis-related complications in clinical studies
- Definition of the requirements for clinical long-term studies (patient number, length)
- Introduction of an obligatory post-observation timeframe of 5 years for mechanical heart valves and of 10 years for biological heart valves.

**Conclusions:** The update in the new EN ISO 5840 gives consideration to the technologic evolution of heart valve development. Several changes in the new standard will improve safety for the patient and ensure high quality in the field of heart valve technology.

# Standardization
# Criteria for valves-results

Table 3
Minimum performance requirements (ISO 5840) [1]

| Position | Aortic | | | | | | | Mitral | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Size | 19 | 21 | 23 | 25 | 27 | 29 | 31 | 25 | 27 | 29 | 31 |
| EOA ($cm^2$) | 0.70 | 0.85 | 1.00 | 1.20 | 1.40 | 1.60 | 1.80 | 1.20 | 1.40 | 1.60 | 1.80 |
| Regurgitant fraction (%) | 10 | 10 | 10 | 15 | 15 | 20 | 20 | 15 | 15 | 20 | 20 |

EOA, effective orifice area (effective opening area of the prosthesis).

Table 6
Reference values of 1-year data (incidence in %)

| | Aortic valve (flexible) | Aortic valve (rigid) | Mitral valve (flexible) | Mitral valve (rigid) |
|---|---|---|---|---|
| Structural valve deterioration | 0.03 | 0.00 | 0.12 | 0.00 |
| Thromboembolism (major, RIND) | 2.06 | 2.78 | 2.48 | 2.63 |
| Valve thrombosis | 0.10 | 0.00 | 0.19 | 0.61 |
| Anticoagulant hemorrhage | 0.45 | 2.44 | 0.80 | 1.95 |
| Prosthetic valve endocarditis | 0.59 | 0.93 | 0.68 | 0.54 |
| Non-structural valve dysfunction/paravalvular leak | 0.38 | 0.84 | 1.05 | 1.75 |
| Reoperation | 0.77 | 1.09 | 1.05 | 1.95 |

# Testing of valve function

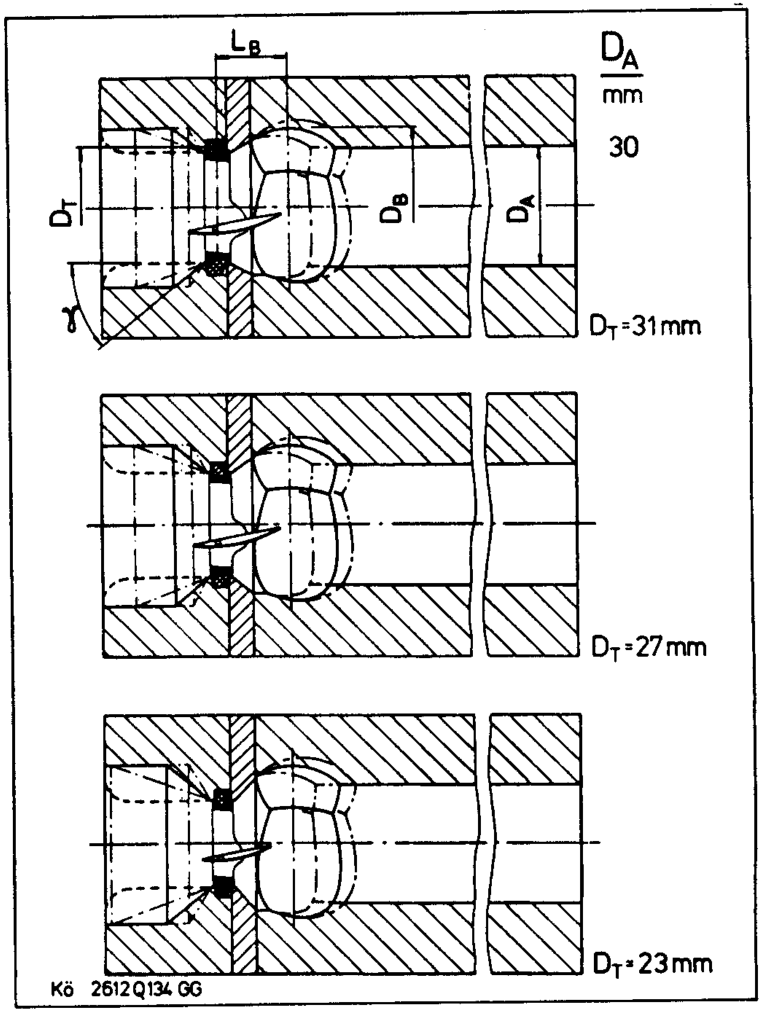



**Fig. 3** - *Geometry of standardized aortic models.*

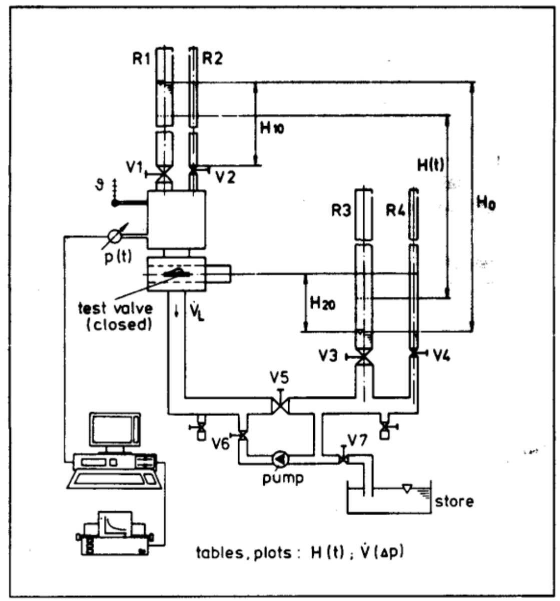



**Fig. 6** - *Leakage quick tester for quasi-steady flow.*

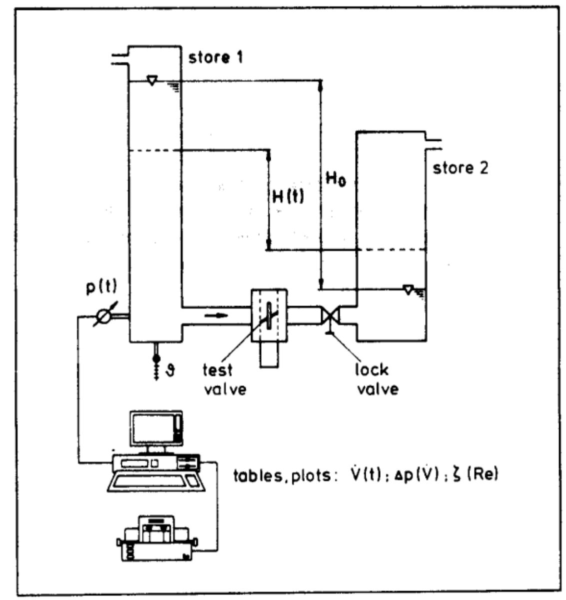



**Fig. 7** - *Pressure loss quick tester for quasi-steady flow.*

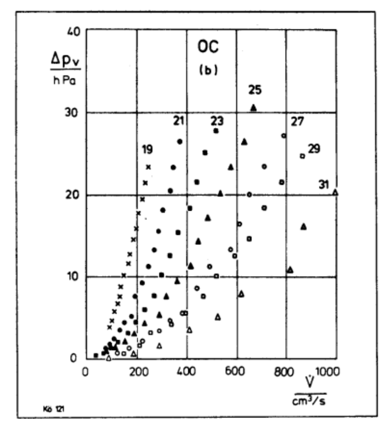
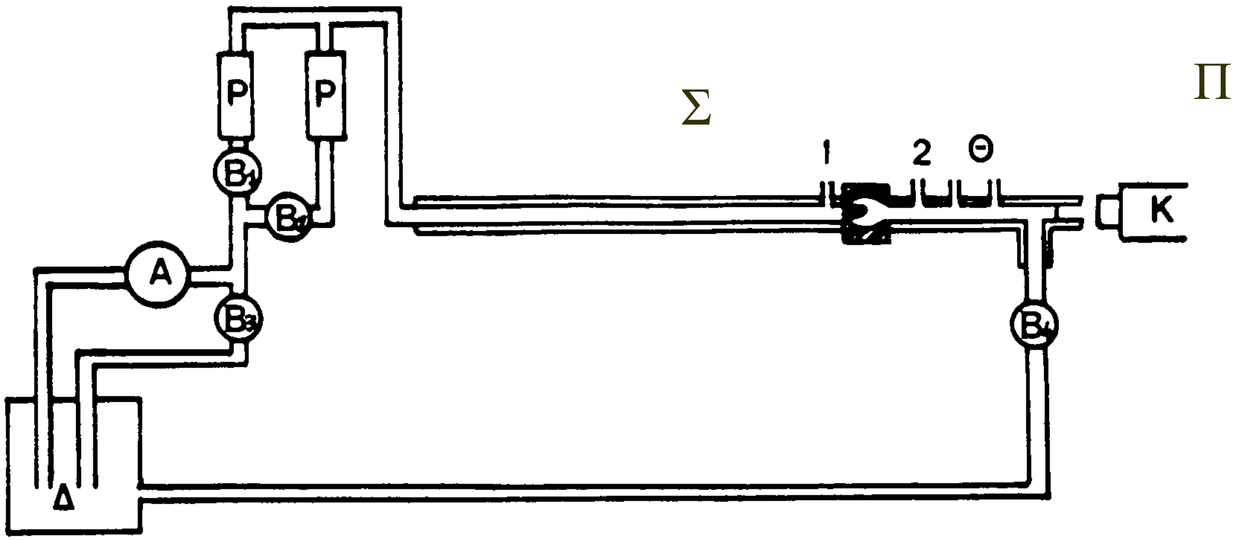


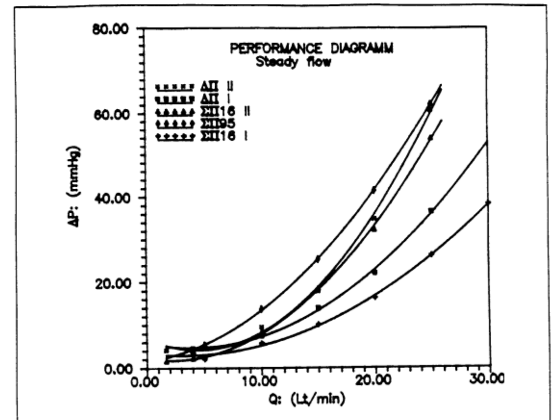

**Fig. 8** - *Pressure loss of a series of the Omnicarbon Valve depending on the volume flow measured in the pressure loss quick tester.*

# Testing of valve function. Steady flow




Σχ. 23 Παραστατικό διάγραμμα της πειραματικής διάταξης μόνιμης ροής. (A) Φυγοκεντρική αντλία, ($B_1$), ($B_2$), ($B_3$) και ($B_4$) βάνες ρύθμισης της ροής, ($P_1$) και ($P_2$) ροόμετρα, (Σ) σωλήνας εισόδου, (Θ) αορτικός θάλαμος, (1) και (2) στόμια μέτρησης της πίεσης, (Π) οπτικό παράθυρο, (Κ) βιντεοκάμερα και (Δ) δεξαμενή τροφοδοσίας.

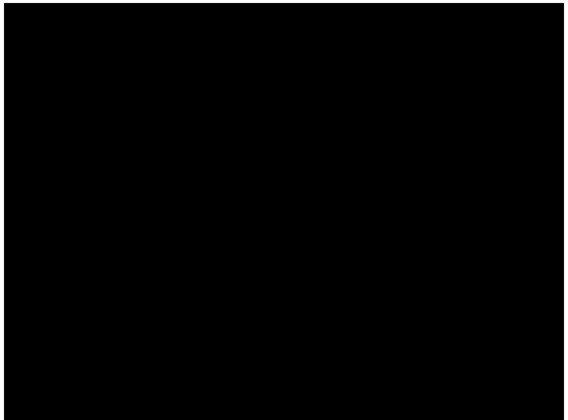
Transvalvular pressure gradient
$DP \approx KQ^2/2(EOA)^2$

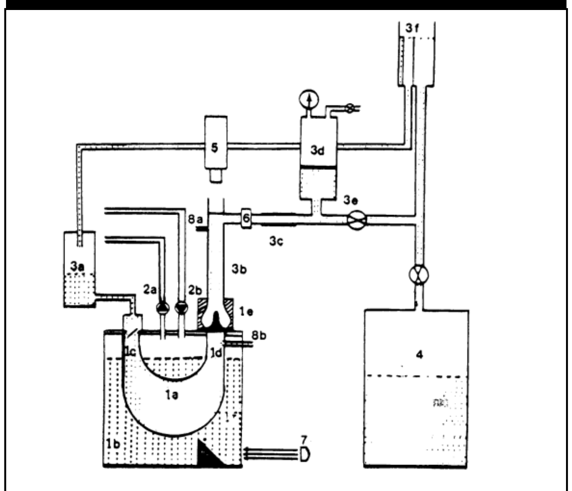



Σχ. 25 Διάγραμμα πτώσης πίεσης - ροής όλων των βαλβίδων γιά μόνιμη ροή.

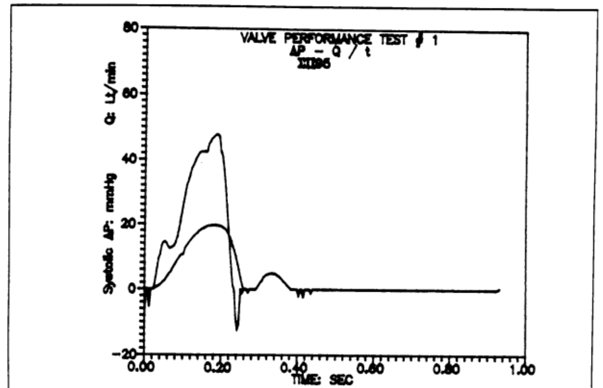
From
D. Mavrilas, PhD Thesis, 1991

# Testing of valve function. Pulsatile flow



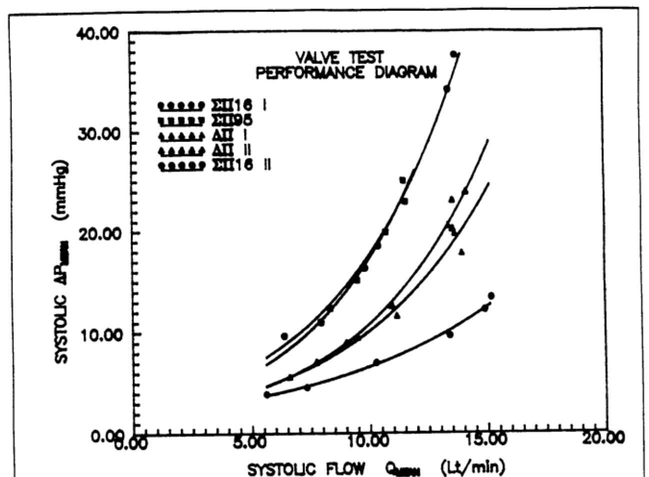



Σχ. 24 Παραστατικό διάγραμμα του προσομοιωτή παλμών (Pulse Duplicator).
(1a) Ελαστικός σάκος, (1b) δοχείο πλεξιγκλάς, (1c) μιτροειδής βαλβίδα, (1d) αορτική βαλβίδα, (1e) μοντέλο αορτικής ρίζας με τρεις κοιλότητες (κόλποι του Valsalva) υπό γωνία $120^0$.
(2a) και (2b) Ηλεκτροβάνες εξόδου και εισόδου του πεπιεσμένου αέρα.
(3a) Αριστερός κόλπος, (3b) ανιούσα αορτή, (3c) χαρ. ενδο-τικότητα αορτής, (3d) μεταβλητή περιφερειακή ενδοτικότητα, (3e) μεταβλητή περ. αντίσταση, (3f) δεξαμενή υπερχείλισης.
(4) Δεξαμενή τροφοδοσίας, (5) βιντεοκάμερα, (6) ηλεκτρομαγνητικός μεταλλάκτης ροής, (7) Φωτιστικός προβολέας και κάτοπτρο $45^0$.




Σχ. 27 Διάγραμμα συστολικής ΔP και Q σαν συνάρτηση του χρόνου t γιά έναν πλήρη καρδιακό κύκλο. Βαλβίδα ΣΠ95. Η Κ.Ε. ήταν 3.5 Lt/min.

Transvalvular pressure gradient
$DP \approx KQ^2/2(EOA)^2$




Σχ. 28(α) Διάγραμμα της μέσης συστολικής πίεσης $\Delta P_{mean}$ ως προς τη μέση συστολική ροή $Q_{mean}$.

Effective Orifice Area
$EOA \propto Q_{rms}/D_{mean}^{1/2}$

From
D. Mavrilas, PhD Thesis, 1991