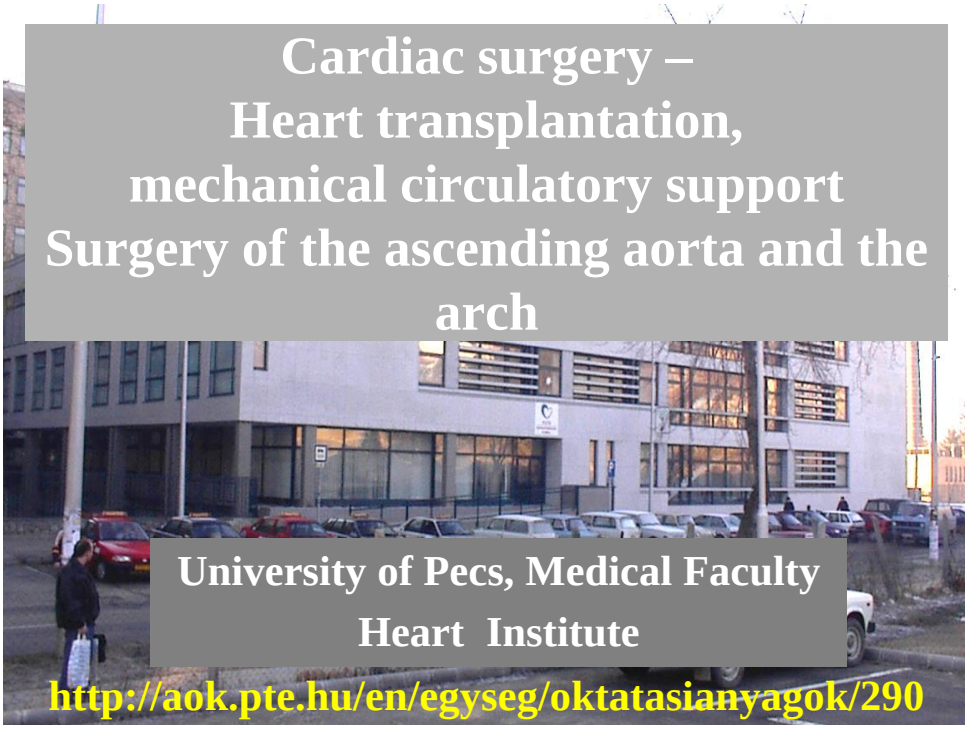
Cardiac surgery – Heart transplantation, mechanical circulatory support Surgery of the ascending aorta and the arch



University of Pecs, Medical Faculty

Heart Institute

http://aok.pte.hu/en/egyseg/oktatasianyagok/290

Treatment for heart failure

Medical:
inotrops, digitalis, diuretics, beta-blocker...

CRT, multisite pacing

Conventional surgical or interventional treatment of CAD, valvular disease

Acute mechanical circulatory support (<2 weeks)
Permanent mechanical circulatory support (>2 weeks)

„bridge to transplantation", „bridge to recovery", „bridge to bridge", „destination therapy"

Heart transplantation

Mechanical circulatory support

<u>Indication:</u> serious reversible or irreversible heart failure in spite of maximal conventional therapy

<u>Aims:</u>

Reversible: 1. assuring adequate tissue perfusion
2. unloading the heart until recovery

Irreversible: assuring adequate perfusion until HTX

Short range (<2 weeks) ⟷ Long-range (>2 weeks)

Extracorporal ⟷ Intracorporal

TAH ⟷ VAD (LVAD, RVAD, BiVAD)

Pulsatile ⟷ Continuous flow

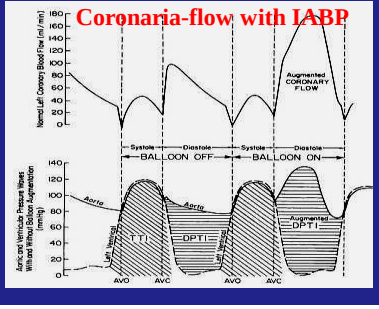
(TAH – total artificial heart, VAD – ventricular assist device)

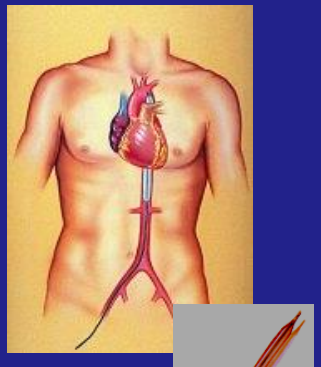
Acute mechanical circulatory support

<u>Intraaortic balloon pump</u> (IABP)

- failure of inotropic treatment
- threatening! cardiogenic shock

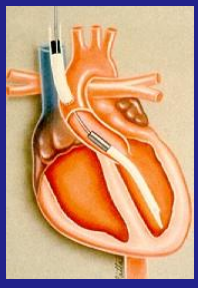
➢ improving coronary perfusion
➢ (reducing afterload)





Acute mechanical circulatory support

Hemopump



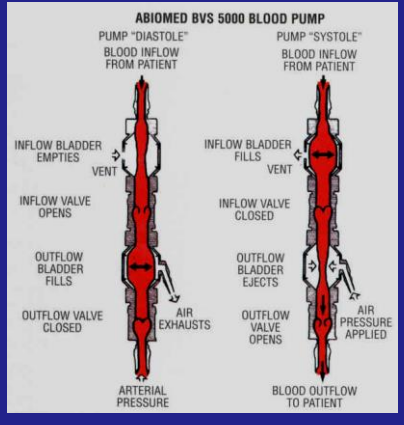
Hemopump device inserted into the left ventricle through the ascending aorta and the portable control unit.

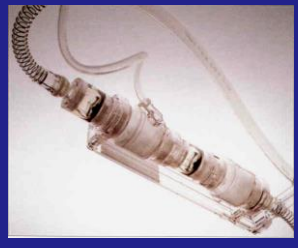
The 24-Fr version is capable to maintain the total minute volume, therefore the heart can be arrested medically without the background of ECC.

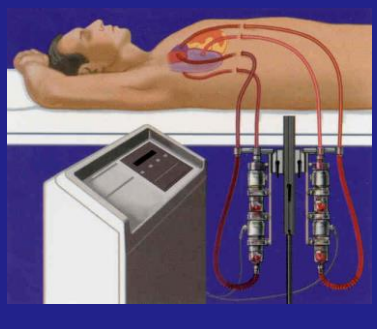
Acute mechanical circulatory support

Abiomed BVS 5000

Univentricular or biventricular assist.

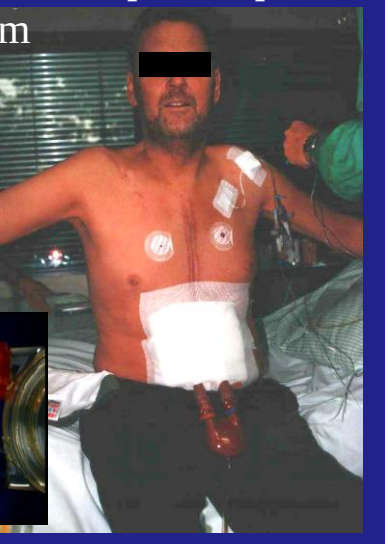






Mechanical circulatory support

Pulsatile flow, paracorporal, mid-term

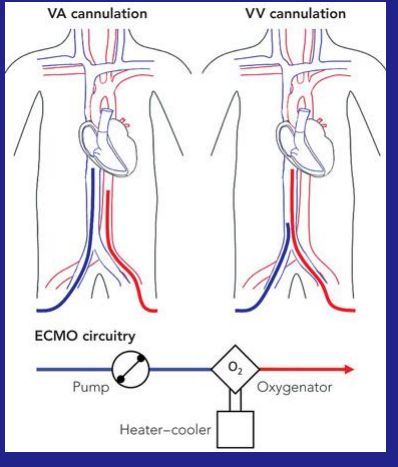


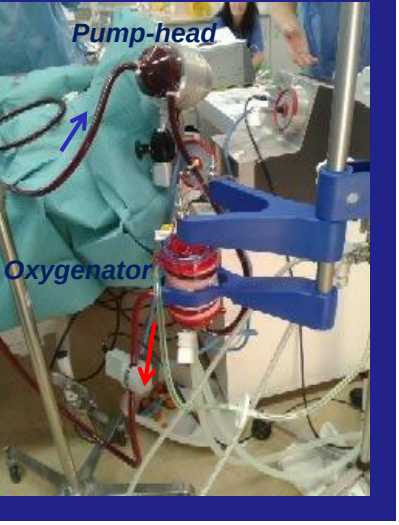
RVAD LVAD
BiVAD

MEDOS Medizintechnik AG

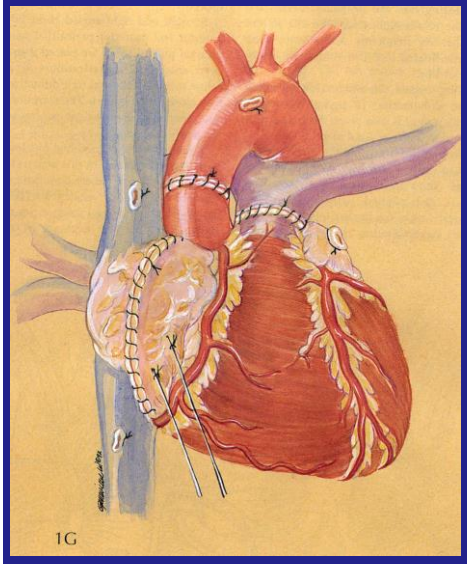
ECMO – extracorporal membrane oxygenator

Respiratory, cardiorespiratory insufficiency





The evolution of HTX



1905. Carrel, Guthrie
vascular suture, organ tx
1960. Lower, Shumway
present technique, cooling
1964. Hardy et al.
chimpanzee heart to human
1967. Barnard
human to human
1980s
cyclosporin

Admission to the HTX program

Indications:

- **NYHA IV in spite of maximal iv inotrop therapy**
- **Max. VO2 < 10ml/kg/min (<14, relative indic.)**
- **syncope, ventricular ectopies**
- **bad quality of life, complaints limiting everyday activity**
- **high risk for cardiac mortality within 1 year**

Contraindications:

- **> 65 years**
- **active infection, or GI ulcer, diabetes mellitus, serious peripheral vascular disease, pulmonary disease, malignancy**
- **elevated pulmonary vascular resistance (>5 Wood, >3.5 rel)**
- **psychical instability, alcohol or drug abuse**
- **loss of compliance, impossible follow-up**

Donor selection

- brain death
- matching ABO with the recipient
- age possibly less than 40-45 years
- similar body weight (size) to the recipient
- loss of cardiovascular disease
- loss of pulmonary disease
- no malignancy (except brain tumor)
- no infection (HIV, CMV, Hepatitis)
- no sepsis
- expected ischemic time < 4-6 hours

Immunosuppression after HTX

- MMF (mycophenolate mofetil, *Cellcept*)
- tacrolimus (calcineurine inhibitor)
- corticosteroid (prednisolone)
- /cyclosporine (earlier)/

Rejection:

- corticosteroid
- ATG (anti-thymocyte-globuline)
- ALG (anti-lymphocyte-globuline)

Regular endomyocardial biopsy

Special complications of HTX

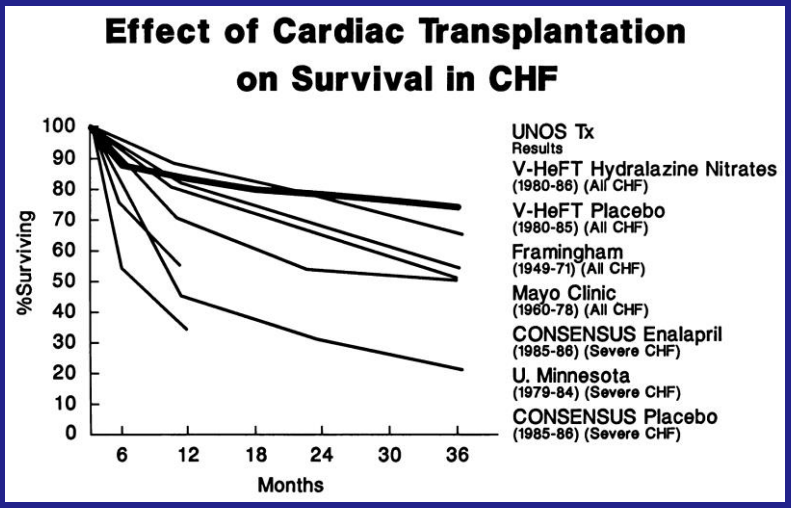
- infection (transmission, susceptibility)
- rejection
- vasoplegia syndrome
- graft coronariasclerosis
- secondary malignancies (lymphomas)
- nefrotoxicity (of cyclosporin)
- death

Problems of HTX

- complications → new immunosuppressives
- donor shortage → networks (UNOS, Eurotransplant), alternatives
- ethical concerns (abating)
- legal concerns (abating) (definition of brain death, need for consent)
- expenses

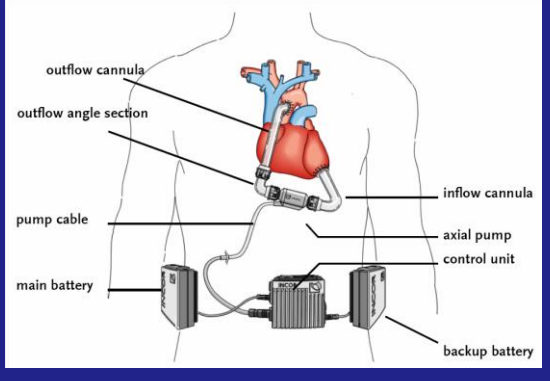
90 % one-year and 50 % 10-year survival, annually about 3500 HTX all over the word, whereas emerging need for several ten-thousand

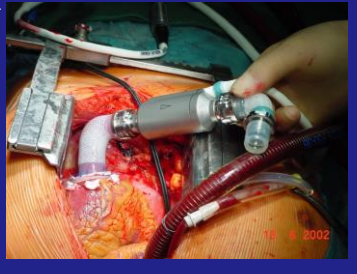
Comparing survival after HTX or medical treatment

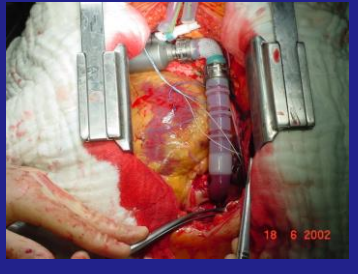


Berlin Heart Incor (LVAD)

- **Intracorporal, continuous flow, permanent**
- **INR: 2,8-3,2**
- **APTI: 70-90 s**
- **Efficient anti-TCT therapy**

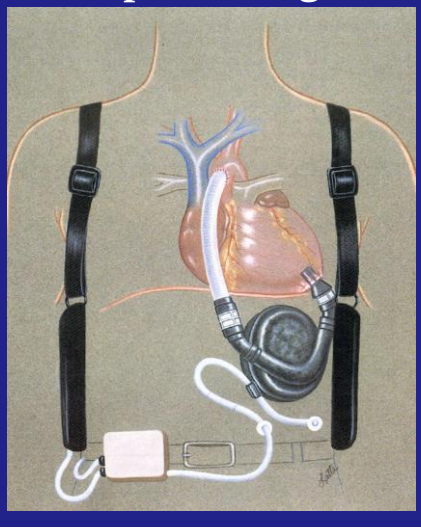


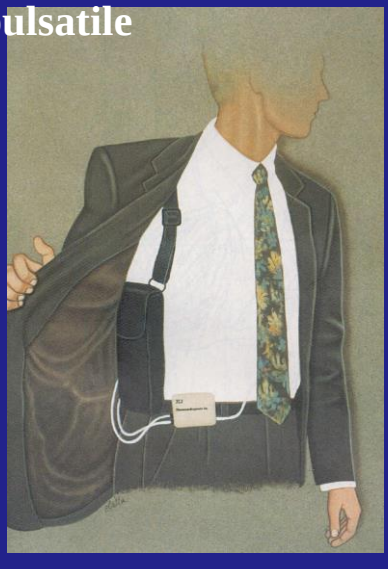




Mechanical circulatory support - Univentricular assist

Intracorporal, long-term, pulsatile





Mechanical circulatory support - Univentricular assist

1963. M. DeBakey – first human application

Draining blood from the apex of the left ventricle, pumped into the ascending or descending aorta. (applicable also in the right heart)
Since the 80s mainly in the US several hundred devices were implanted as a bridge to transplantation. Recognized the reverse remodeling as an effect of unloading the heart. Many patients were removed from HTX program because of their improvement. The future?

Artificial heart, xenotransplantation

Artificial heart: human application in experimental phase

1959. S. H. Norton, T. Akutsu, W. Kolff

1969. D. A. Cooley (Liotta pneumatic heart) as a bridge to transplantation

1982. DeVries (Jarvik-7) as a final therapy

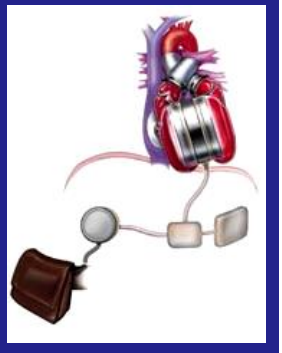
***Now:* Texas (Abiocor), Cleveland, Pittsburg**

***Problems:* thromboembolism, power supply, safety of operation, infection, haemolysis, adaptation to needs**

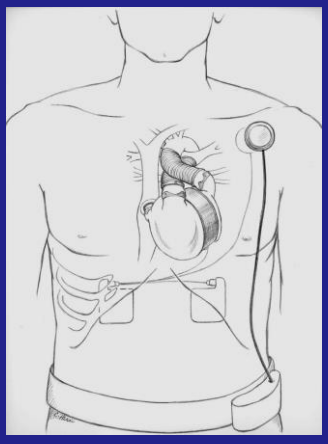
Xenotransplantation: animal experiments (swine)

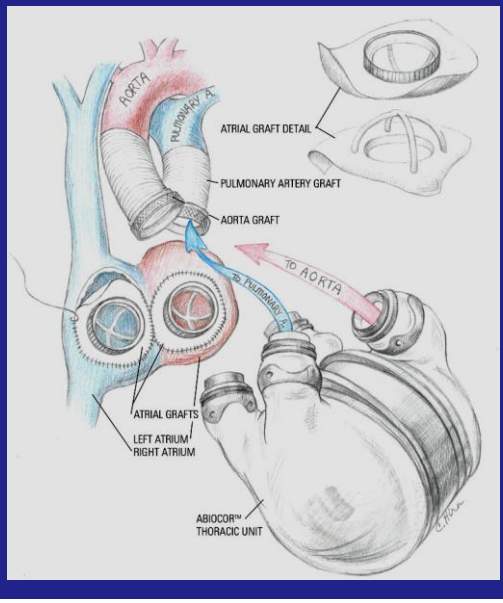
Preventing rejection with modified surface antigenes

Artificial heart – the Abiocor

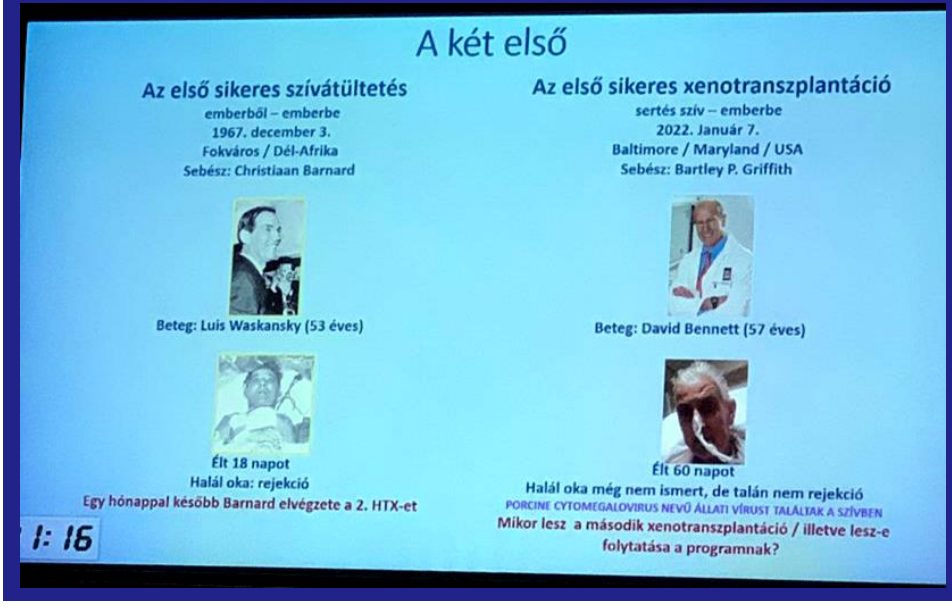


Artificial heart – the Abiocor





Xenotransplantation



Sensation: xenotransplantation

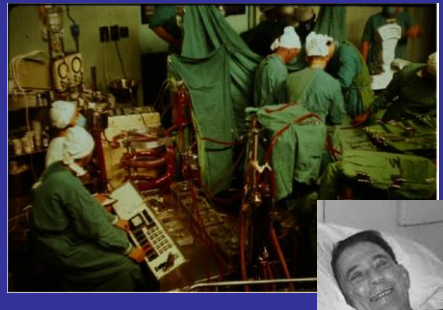
On January 7, 2022, David Bennett became the first person to live with a pig's heart beating inside his chest. (JACC)

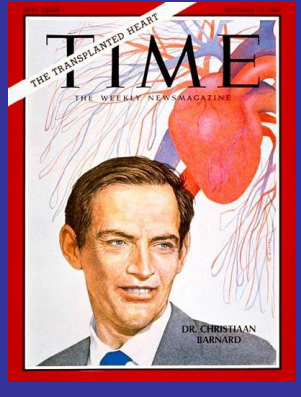
- too ill to undergo human-donor HTX
- arrhythmias → poor candidate for VAD
- a history of disregarding medical advice

Pig heart recipient **David Bennett** Sr. with his transplant doctor, **Bartley Griffith, MD** of the University of Maryland.

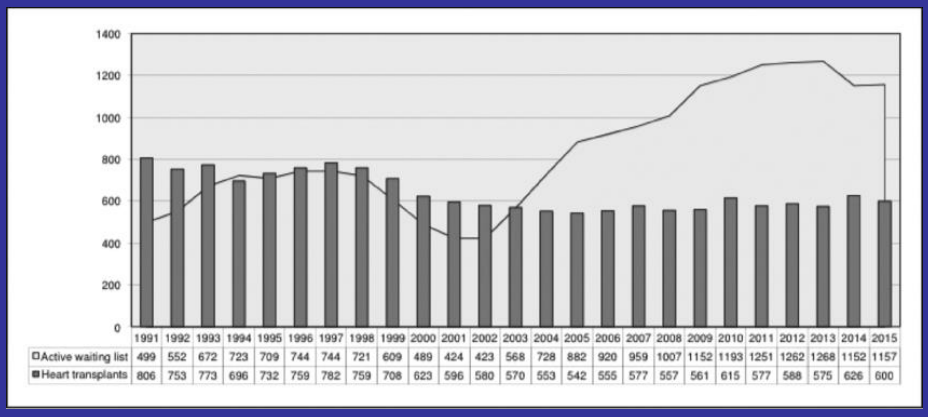
C. Barnard 1967. first human-human HTX

1967. Dec 3. Mr. Louis Washansky, died after only **18 days**, Barnard soon carried out a second transplant, and this patient led an active life **for almost 19 months**.





Human donor << end-stage heart failure pts.



	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Active waiting list	499	552	672	723	709	744	744	721	609	489	424	423	568	728	882	920	959	1007	1152	1193	1251	1262	1268	1152	1157
Heart transplants	806	753	773	696	732	759	782	759	708	623	596	580	570	553	542	555	577	557	561	615	577	588	575	626	600

eurotransplant.org

The xenotransplantation delays…

• **Human donor:** legal-ethical problems, poor survival in the 1960's and 70's

• **Optimal species:** primate vs. pig (immunological difference, infection transmission, size, expenses)

• Pig is ideal – morally acceptable, grows up within 6 months, but visuses! and rejection!

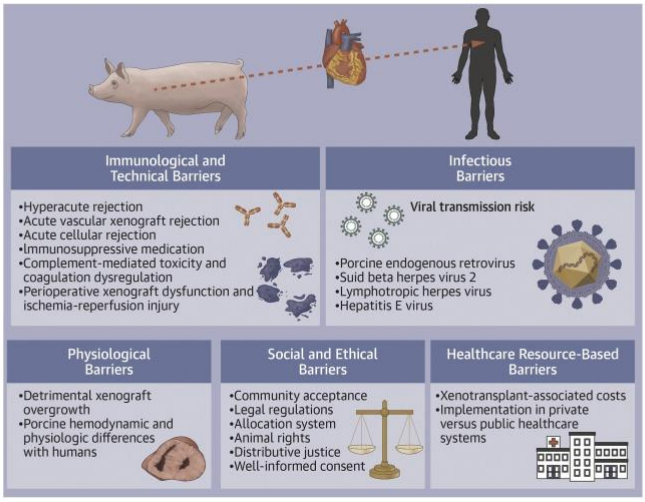
• **ciklosporin** from the 80's, clear legal background (definition of brain death), excellent results with human-to-human HTX.

• other alternatives: dynamic development of mechanical circulatory support

• Abiocor by AbioMed: the first TET-based TAH, **2001.** Jul. 2., 15 patients, survival of **151 – 512 days**

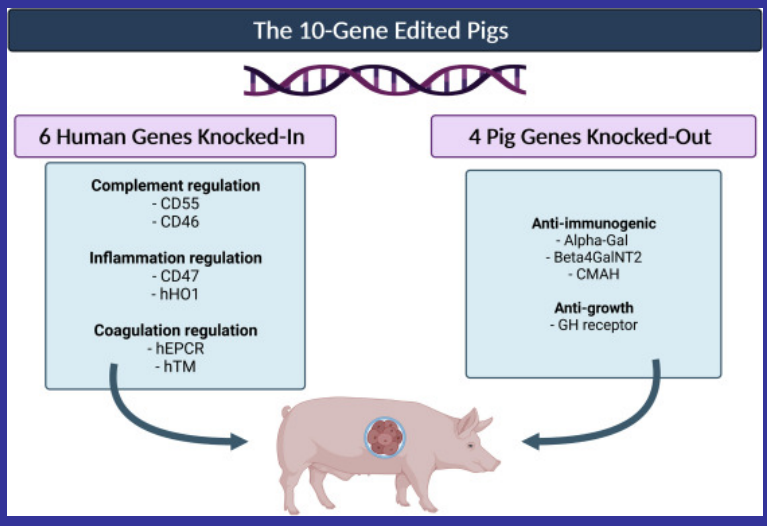
Difficulties in XTR

CENTRAL ILLUSTRATION The Barriers to Xenotransplantation Translation Into the Clinical Realm

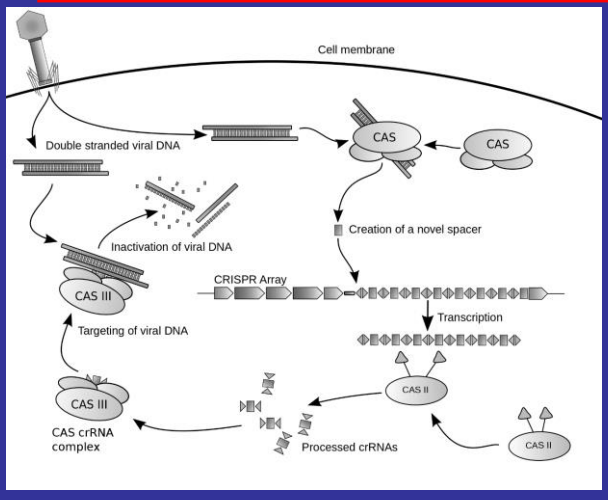


Boulet J, et al. J Am Coll Cardiol Basic Trans Science. 2022;7(7):716-729.

Genetically modified pigs



CRISPR/Cas9: bacterial „immun system”



2020 Nobel-prize in chemistry:
J Doudna, E Charpentier

Restriction endonuclease Palindroms:
„madam”
„race car”
„A man, a plan, a canal – Panama”

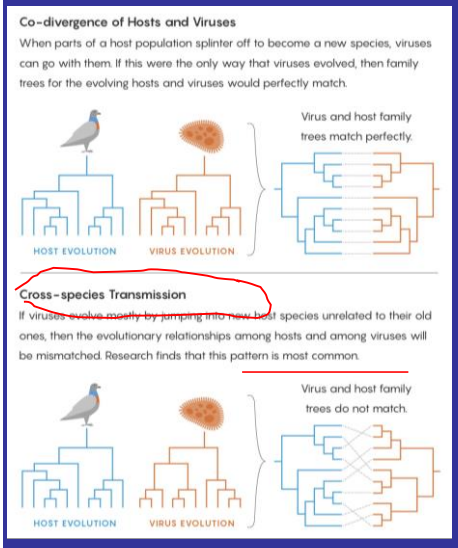
CRISPR = *clustered regularly interspaced short palindromic repeats (bact DNA)*

„Meet the pigs that could solve the human organ transplant crisis”

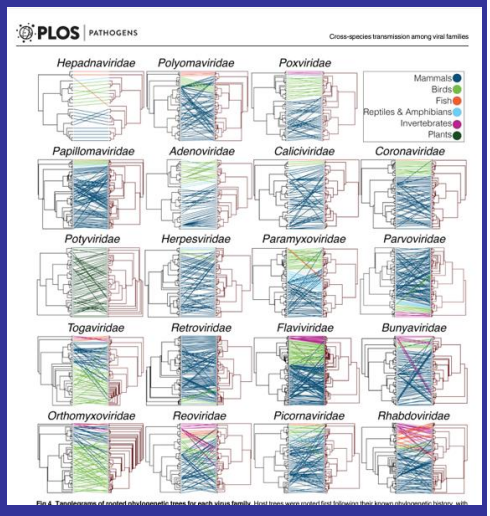
- „cesarean section”
- sterile keeping
- personnel locking (all clothes, watches, jewel left behind), shower with hair wash, scrub gown, cap
- irradiated vegan feeding
- the pig free from pathogenes
- HEPA filter air treatment

2018. Munich: pig heart to baboon (**>**180-195 days) („overgrowth” like in a 250kg pig)
SUNY, UAB: genetically modified pig heart into brain death patients in 2021
China: Langerhans-isle transplant into human
Korea: cornea transplant into human
Massachusetts: skin transplant to human

Interspecies spreading of viruses (jump)



Filogenetical trees of host and viruses:



PLOSPathogens|DOI:10.1371/journal.ppat.1006215 February 8, 2017

The first human xenotransplantation

D. Benett Sr. Day 40 napon has worsened, he lived **2 months** with pig heart**.** The transmitted CMV infection contributet his death.

- „The pig CMV (PCMV) cannot infect human cells”
- Pig organs transplanted into baboon, the PCMV decreased survival: large number of viruses in the myocardium (immunosuppression, the swine immun cells are not present in the human controlling the PCMV)
- more sensitive testing is needed!
- „Bennet was already very, very weak”
- Hundreds of swine DNA, bacteria and viruses are monitorized
- Day 40: fever, cytokine storm, septic symptoms
- Treatment of a human infected with swine virus??: cidofovir (no FDA licence), ***IVIG*** *(no anti-PCMV)*

Future possibilities

Molecular cardiomyoplasty: Fibroblasts in the infarction scar are "infected" with MyoD-gene resulted in muscular differentiation.

Cellular cardiomyoplasty: infiltrating the scar with myoblasts (satellite-cells) or stem cells from skeletal muscle, those can differentiate into heart muscle

Embryonal correction of the gene responsible for the cardiomyopathy

Induction of angioneogenesis by growth factors

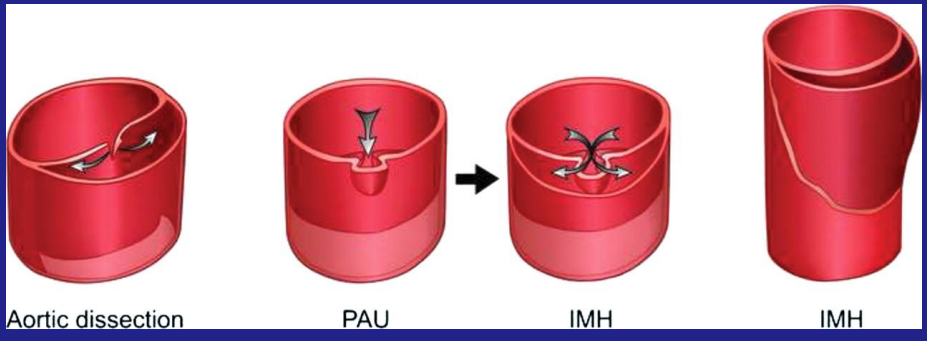
Summary

- **HTX – gold standard**
- **Efficient mechanical circulatory support avail.**
- **The timing of mechanical assist is crucial !**
- **Choosing the appropriate device (availabilities)**
- **Bridge to HTX reduces mortality and costs**
- **Fast technical development – future ?**
- **Expenses**

Aortic diseases

- Atherosclerosis
- Aneurysm (saccular, fusiform, ≥150% normal diam.)
- Dissection: intimal tear, flap, helical pseudo lumen (acute<2weeks, subacute, chronic>6weeks)
- Transsection (traumatic, due to deceleration, prox. DA, dist. AA)
- Rupture: bleeding to mediastinum, bronchi, pleura, pericardium (tamponade!)
- Aortitis (S. aureus, Salmonella, syphilis, Takayashu, Giant cell)
- Penetrating atherosclerotic ulcer (PAU)
- Intramural haematoma (IMH, from vasa vasorum)
- Acute aortic syndrome (acute dissection, PAU, IMH)
- Aortic regurg. (annular dilation, rupture, dissection)

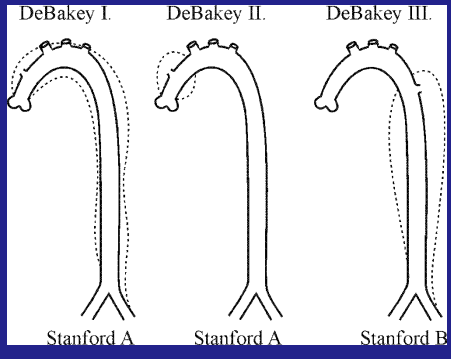
Acute Aortic Syndrome

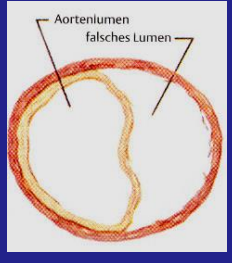


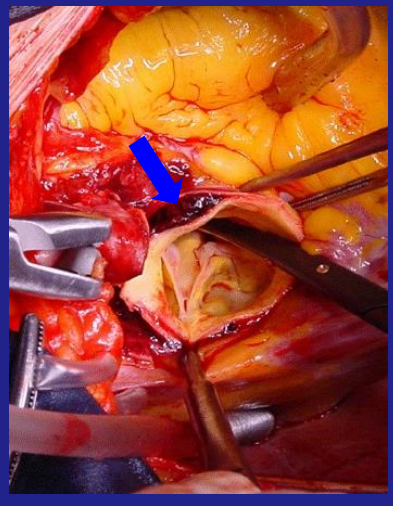
Acute aortic dissection

- 2-3.5 cases/100 000 persons/year
- Symptoms: chest pain, hoarseness, focal ischaemia, bleeding, hypovolaemia, shock, tamponade, AI→pulm. Edema, embol.
- Diagnosis: Echo, CT, MRI, TEE, D-dimer (?!)
- Spontaneous mortality:
  asc. included: 35% at 1 day, 50% at 2 days, 70% at 1 week
  desc.: 90% survival at 1 month
- Treatment:
  initial medical: (dP/dt↓, SBP<100-120mmHg, pulse:60-80/min)
  β-blocker, nitrate, opiate
  acute ascending – emergency operation
  desc – medical treatment unless ischaemic signs / bleeding occur

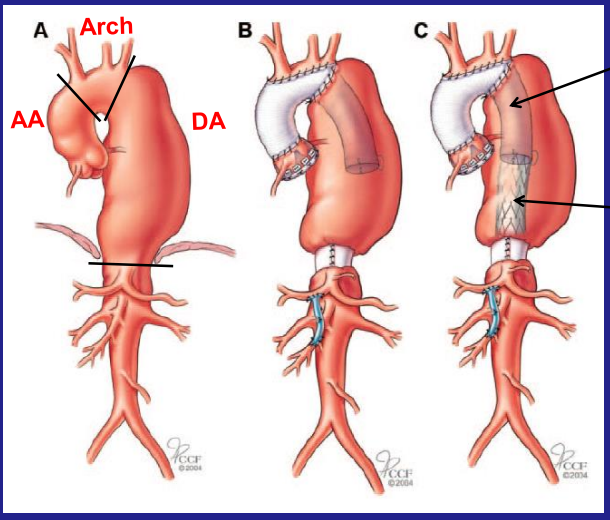
Aortic dissection







Extensive aortic aneurysm



Elephant trunk (Borst)

Stent graft

Recommendations for Asymptomatic Patients With Ascending Aortic Aneurysm

1. Asymptomatic patients with degenerative thoracic aneurysm, chronic aortic dissection, intramural hematoma, penetrating atherosclerotic ulcer, mycotic aneurysm, or pseudoaneurysm, who are otherwise suitable candidates and for whom the ascending aorta or aortic sinus diameter is **5.5 cm** or greater should be evaluated for surgery

2. Patients with Marfan syndrome or other genetically mediated disorders (vascular Ehlers-Danlos syndrome, Turner syndrome, bicuspid aortic valve, or familial thoracic aortic aneurysm and dissection) should undergo elective operation at smaller diameters (**4.0 to 5.0 cm** depending on the condition; see Section 5) to avoid acute dissection or rupture.

3. Patients with a growth rate of more than **0.5 cm/y** in an aorta that is less than 5.5 cm in diameter should be considered for operation.

4. Patients undergoing aortic valve repair or replacement and who have an ascending aorta or aortic root of greater than **4.5 cm** should be considered for concomitant repair of the aortic root or replacement of the ascending aorta.

Recommendation for Symptomatic Patients With Thoracic Aortic Aneurysm

1. Patients with symptoms suggestive of expansion of a thoracic aneurysm should be evaluated for prompt surgical intervention unless life expectancy from comorbid conditions is limited or quality of life is substantially impaired

- **TEE (semiinvasive)**
- **CT (ECG-gated)**
- **MRI (ECG gated)**

Recommendations for Aortic Arch Aneurysms

1. For thoracic aortic aneurysms also involving the proximal aortic arch, partial arch replacement together with ascending aorta repair using right subclavian/ axillary artery inflow and hypothermic circulatory arrest is reasonable.

2. Replacement of the entire aortic arch is reasonable for acute dissection when the arch is aneurysmal or there is extensive aortic arch destruction and leakage.

3. Replacement of the entire aortic arch is reasonable for aneurysms of the entire arch, for chronic dissection when the arch is enlarged, and for distal arch aneurysms that also involve the proximal descending thoracic aorta, usually with the elephant trunk procedure.

4. For patients with low operative risk in whom an isolated degenerative or atherosclerotic aneurysm of the aortic arch is present, operative treatment is reasonable for asymptomatic patients when the diameter of the arch exceeds **5.5 cm**.

5. For patients with isolated aortic arch aneurysms **less than 4.0 cm** in diameter, it is reasonable to reimage using computed tomographic imaging or magnetic resonance imaging, at **12-month** intervals, to detect enlargement of the aneurysm.

6. For patients with isolated aortic arch aneurysms **4.0 cm or greate**r in diameter, it is reasonable to reimage using computed tomographic imaging or magnetic resonance imaging, at **6-month** intervals, to detect enlargement of the aneurysm.

Recommendations for Descending Thoracic Aorta and Thoracoabdominal Aortic Aneurysms

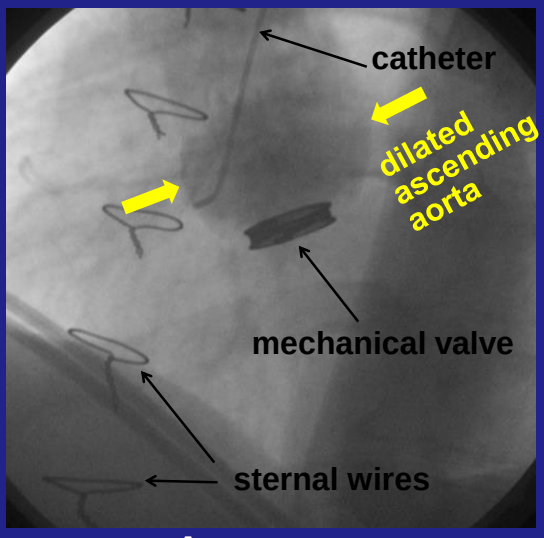
1. For patients with chronic dissection, particularly if associated with a connective tissue disorder, but without significant comorbid disease, and a descending thoracic aortic diameter exceeding **5.5 cm**, **open repair** is recommended.

2. For patients with degenerative or traumatic aneurysms of the descending thoracic aorta exceeding **5.5 cm**, saccular aneurysms, or postoperative pseudoaneurysms, **endovascular stent grafting** should be strongly considered when feasible.

3. For patients with thoracoabdominal aneurysms, in whom endovascular stent graft options are limited and surgical morbidity is elevated, elective surgery is recommended if the aortic diameter exceeds **6.0 cm**, or less if a connective tissue disorder such as Marfan or Loeys- Dietz syndrome is present.

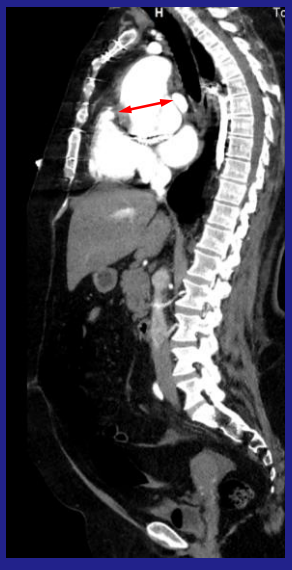
4. For patients with thoracoabdominal aneurysms and with end-organ ischemia or significant stenosis from atherosclerotic visceral artery disease, an additional revascularization procedure is recommended.

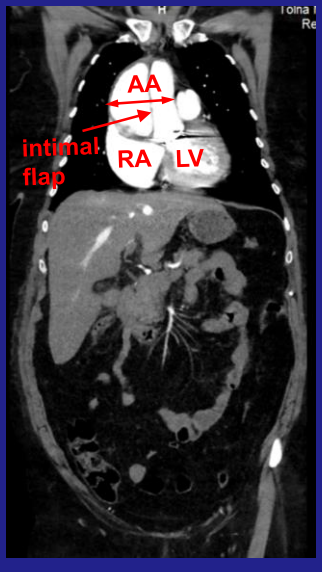
Dilated ascending aorta with artef. valve



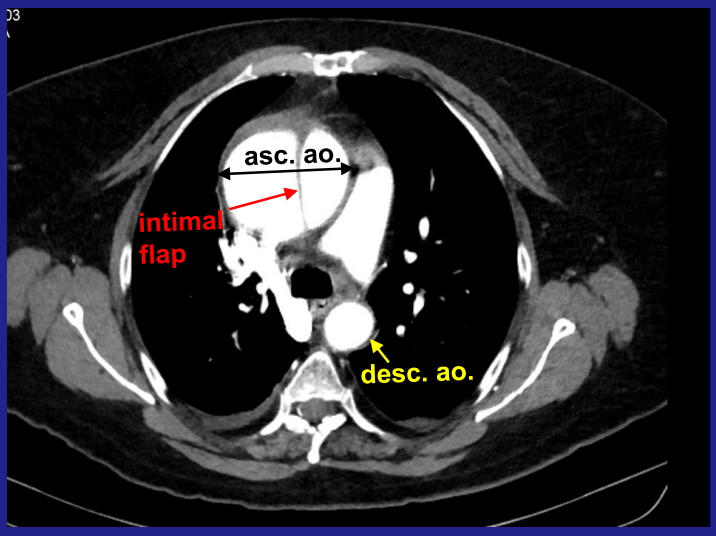
Aortogram

Chronic dissection on ascending aorta



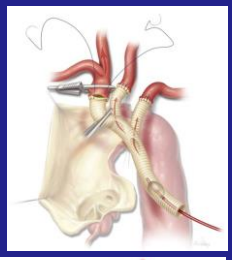


Chronic dissection on ascending aorta



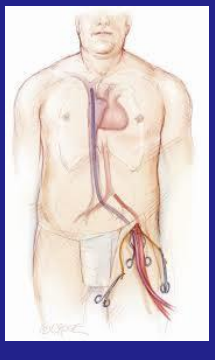
Hypothermia, cerebral protection

- Extracorporal circulation (heparinization)
- Decreasing metabolic demand by cooling (profound≤14°C, deep≤20°C, moderate ≤28°C, mild ≤34°C hypothermia)
- Circulatory arrest (at 20°C: 30-40 min)
- Selective brain perfusion (**ante**, retro)
- Selective visceral perfusion (thoracoabd.)
- Ice around the head
- Deep anaesthesia, barbiturate
- Room temperature set at 20°C

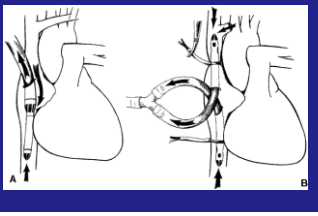


Cannulation techniques

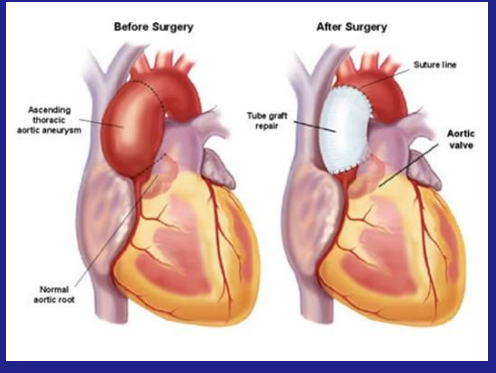
Arterial access:
- Ascending aorta
- Anonymous artery
- Proximal arch
- Axillary artery
- Femoral artery
- Carotid artery
- Vascular graft
- Lig. arteriosum
- Any other…

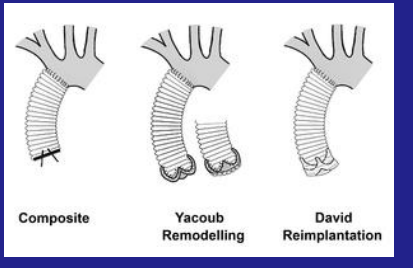


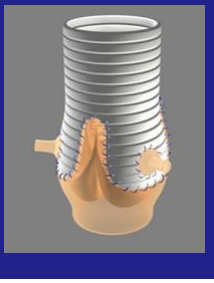
Venous access:
- Right atrium
  - -two stage
  - -bicaval
- Femoral vein

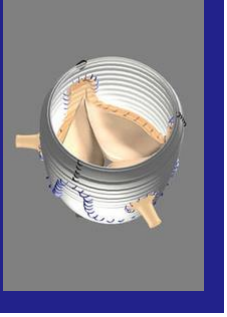


Isolated ascending, valve sparing





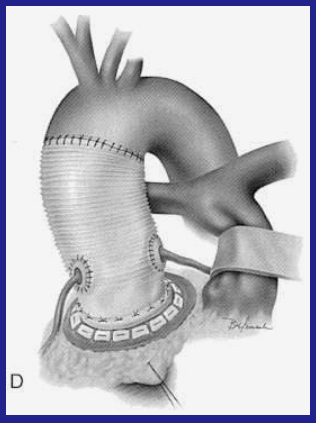




Bentall-procedure (valve+graft)

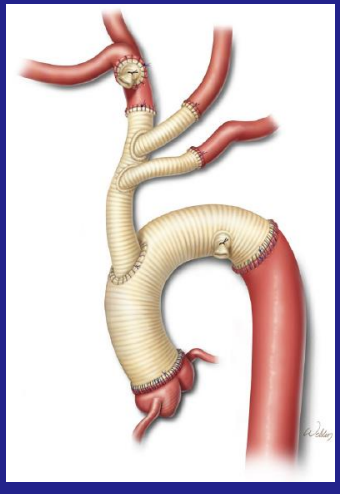
Conduit with valve

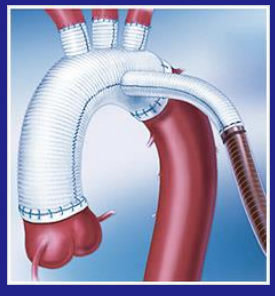
Valvular conduit in situ

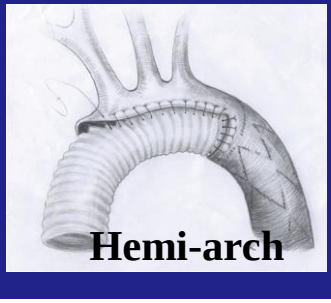


Prostheses – aortic arch

Total arch

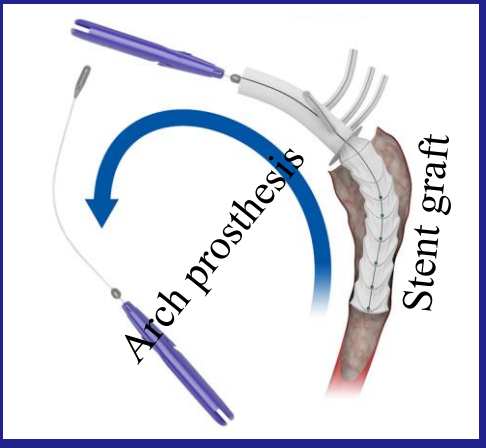


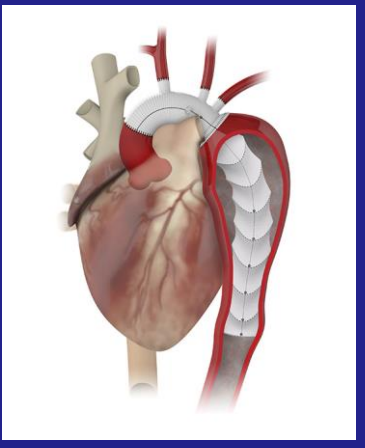




Hemi-arch

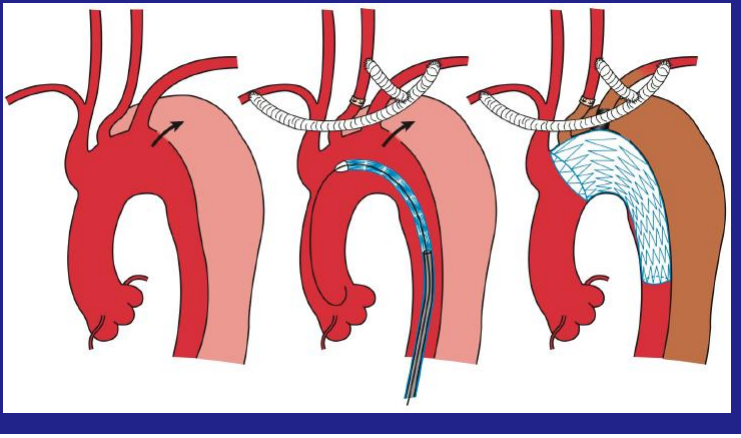
Prostheses – frozen elephant trunk



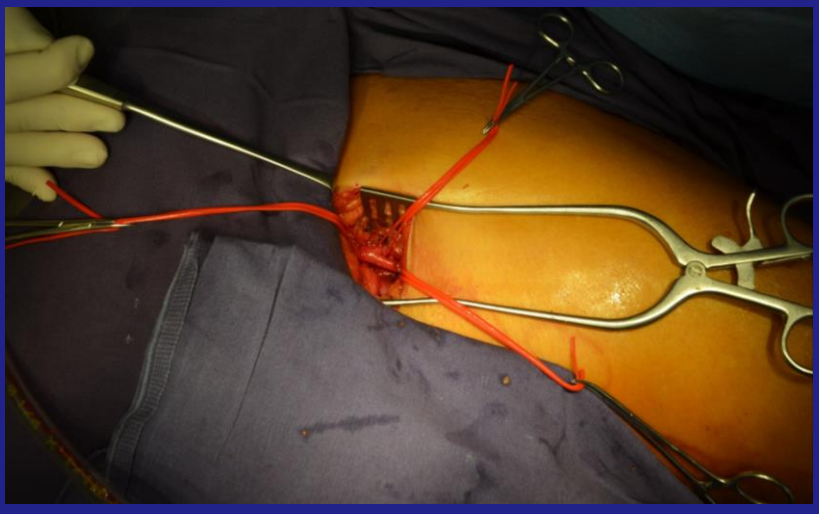


Stentgrafting (endovascular repair)

- Ascending: coronaries, valve, motion, aortic occlusion, brain damage (embolization, ischemia)
- Arch – crossover bypass (subclavian-carotid)

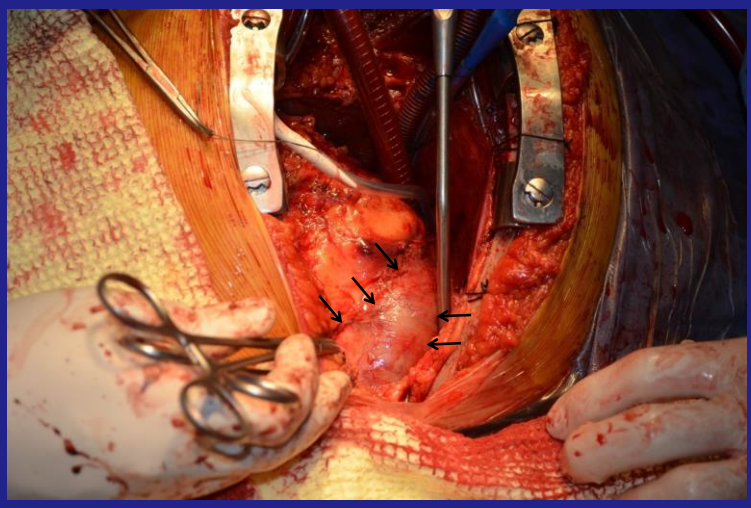


Exposing left femoral artery

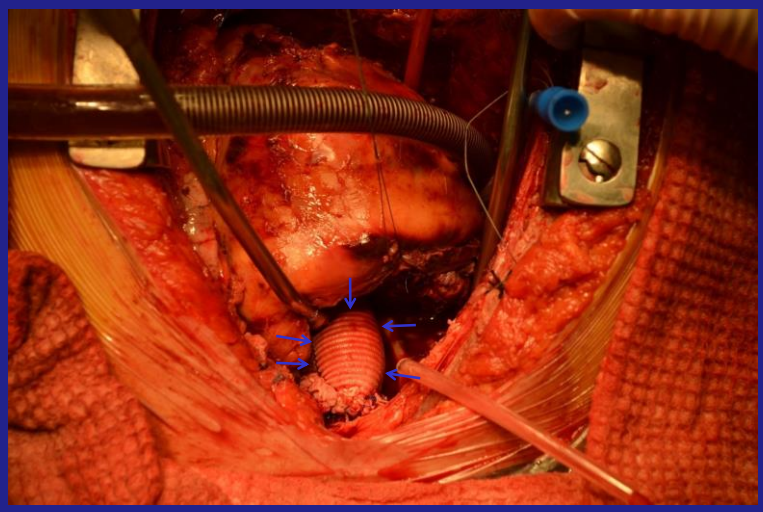


Femoral venous cannula

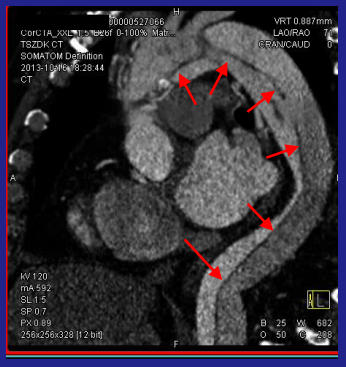
Chronic ascending dissection

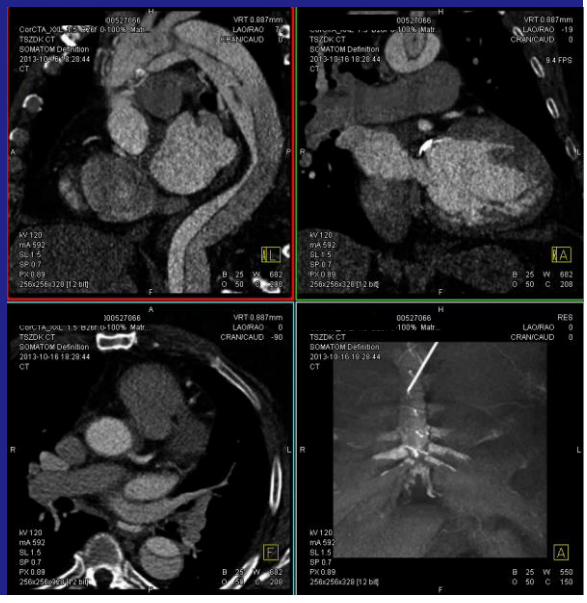


Ascending conduit in situ



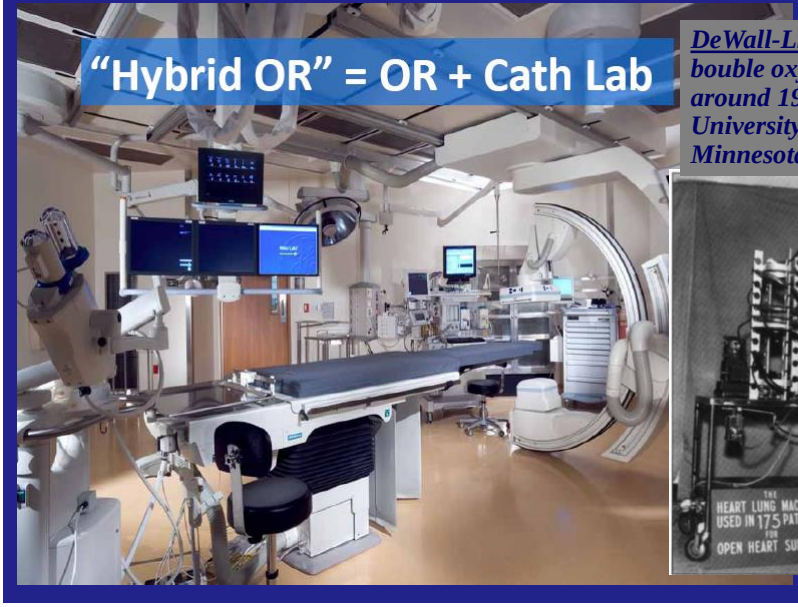
Residual arch and descending dissection after Bentall





Thx to Dr. Sandor Szukits,
PTE Radiology

Thank you for your attention !



DeWall-Lillehei bouble oxygenator around 1955-56, University of Minnesota