Artificial organs and implant devices

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Dimitrios I. Fotiadis

Professor of Biomedical Engineering

University of Ioannina

Substitutive Medicine

- Over the past 50 years, humanity has progressively discovered that an engineered device can substitute for most organs and body functions
- Fundamental tenet of substitutive medicine: beyond a certain stage of failure, it is more effective to remove and replace a malfunctioning organ than to seek in vain to cure it
- Hybrid artificial organs, or bioartificial organs, are more recent systems which include living elements (organelles, cells, or tissues) as part of a device made of synthetic materials.

Substitutive Medicine

- Depending upon medical needs and anticipated duration of use, artificial organs can be located:
  - outside of the body yet attached to it (paracorporeal prostheses or assist devices) or
  - implanted inside the body in a appropriate location (internal artificial organs or implants).
- The application of artificial organs may be temporary, (e.g., the heart-lung machine), or permanent organ replacement (e.g., left ventricular assist devices)

Implant devices

- An implant device is a medical device manufactured to:
  - replace a missing biological structure,
  - support a damaged biological structure,
  - or enhance an existing biological structure
- Medical implants are man-made devices, in contrast to a transplant, which is a transplanted biomedical tissue

Implant devices

- The surface of implants that contact the body might be made of a biomedical material such as titanium, silicone or apatite depending on what is the most functional
- In some cases implants contain electronics e.g. artificial pacemaker and cochlear implants
- Some implants are bioactive, such as subcutaneous drug delivery devices in the form of implantable pills or drug-eluting stents

Implant devices

- Implanted devices can act as either sensors or stimulators
- Sensors measure a biosignal from inside the body and transmit this information to an external device
- They can measure body temperature, blood pressure and glucose concentration, for example, and detect respiratory, cardiac and arterial wall movements, the contraction of blood vessels and cardiac pressure disorders

Artificial organs

- An artificial organ is a man-made device that is implanted or integrated into a human
- The aim is to replace a natural organ, for the purpose of restoring a specific function or a group of related functions so the patient may return to a normal life as soon as possible
- The replaced function doesn't necessarily have to be related to life support, but often is

Biomaterials

- Depending upon medical needs and anticipated duration of use, artificial organs can be located:
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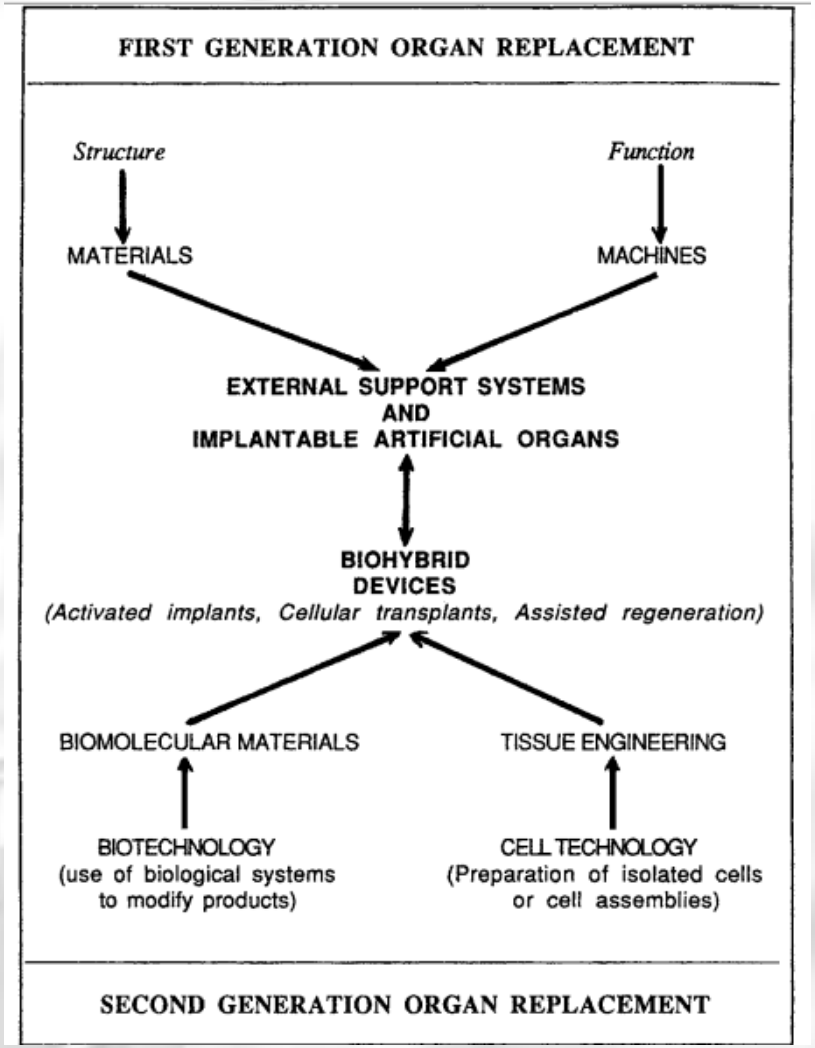
Outlook for Organ Replacement

- Schematic description of the advances in engineering, biologic, and medical technology which led to the first generation of artificial organs and the newer developments in body replacement parts



J.D.Bronzino , Biomedical Engineering Handbook, 2000

Design Considerations

- Defining specifications and constraints is the first step in the conceptualization of an artificial organ
- Once all considerations have been integrated, the next step is typically the construction of a prototype
- At this point, new experiments are needed to establish the reliability and effectiveness of the device (often in animal models)
- This is the stage of validation of the device

Design Considerations

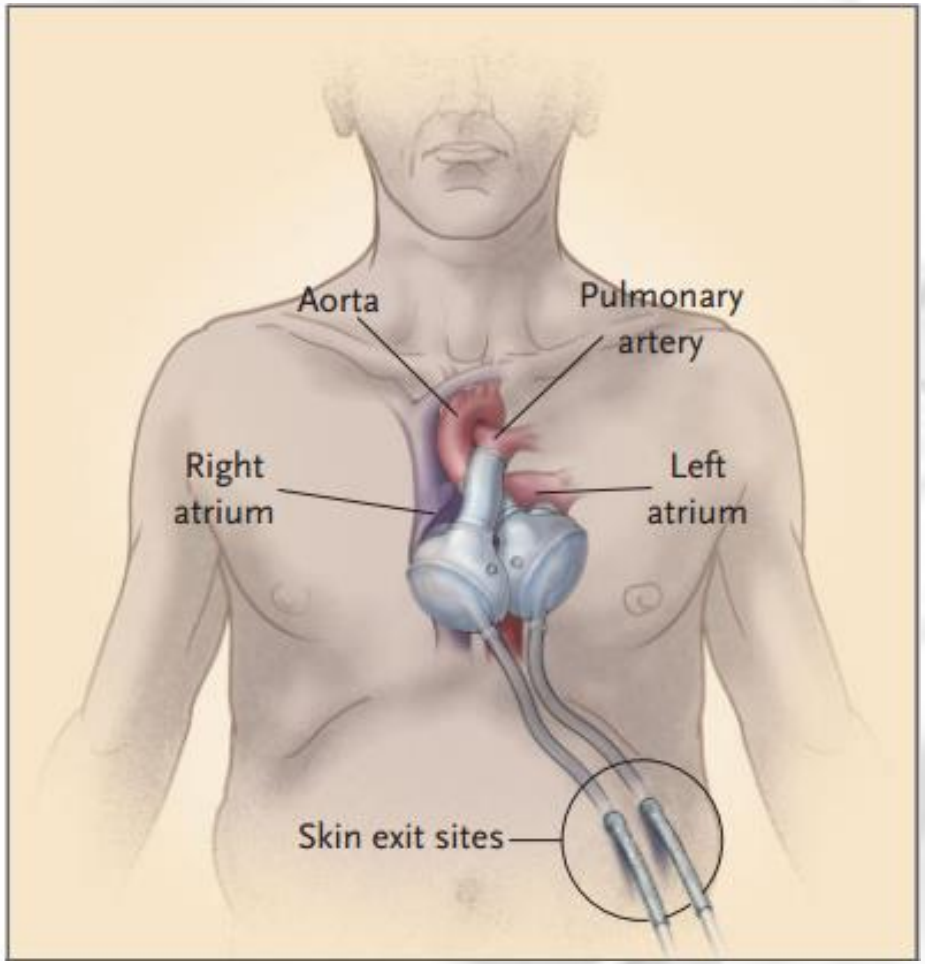
- The final stage of design, for many artificial organs, is individualization, i.e., the ability to fit the needs of diverse individuals
- In some cases, the prostheses must fit very strict dimensional criteria (human body size), which implies that they must be fabricated over an extended range of sizes (e.g., cardiac valves)
- In other cases, there is enough reserve function in the device that one pediatric model and one adult size model may suffice (e.g., blood oxygenator for cardiac surgery)

Evaluation Process

- The evaluation of an artificial organ typically is done in six phases:

1. *In vitro* bench testing
2. *Ex vivo* appraisal
3. *In vivo* studies with healthy experimental animals
4. *In vivo* studies with animal models of disease
5. Controlled clinical trials
6. General clinical use

Artificial Heart and Circulatory Assist Devices



Copeland et al., Cardiac Replacement with a Total Artificial Heart as a Bridge to Transplantation, N Engl J Med 2004

Artificial Heart and Circulatory Assist Devices

Engineering Design

- Problem Definition—Clarification of the Task
- Fit of the System
- Pump Performance
- Bicompatibility
- Reliability and Quality of Life
- Conceptual Design—Plan Treatment
- Detailed Design—Execute Plan

Artificial Heart and Circulatory Assist Devices

Problem Definition

- This step can best be accomplished by writing the detailed design requirement or specification for the device
- A general statement of the problem for a total artificial heart or assist device is “to develop a that when implanted in the human will provide a longer and better quality of life than conventional pharmacologic therapy
- In general, the devices will be assumed that they will be intended for long-term use (one year or longer) but may also be utilized for short-term applications

Artificial Heart and Circulatory Assist Devices

Fit of the System

- One must first decide who the device is intended for as it must first “fit” the patient
- Careful consideration must be given to the physical attributes of the system, i.e. the actual shape of the system in terms of sharp corners or edges that may damage tissue or organs
- The effect of device movement and vibration should be considered in the design specification

Artificial Heart and Circulatory Assist Devices

Fit of the System

- The acceptable sound levels at various frequencies must be specified.
- A device should meet existing standards for electromagnetic interference and susceptibility
- The use of any percutaneous tubes will require the choice of an exit site
- This site must not be in a location of constant or excessive movement or tissue breakdown will be experienced at the interface.

Artificial Heart and Circulatory Assist Devices

Pump Performance

- Pump performance must be specified in terms of cardiac output range
- Control of the device is critical and must be included in the design specification
- For the total artificial heart, the device must always maintain balance between the left and right pumps
- The device must respond to the patient's cardiac output requirements

Artificial Heart and Circulatory Assist Devices

Bicompatibility

- Bicompatibility has already been alluded to in the design requirements by saying that the device must not cause excessive damage to the biologic system
- Specifically, the device must be minimally thrombogenic and minimally hemolytic
- It should not promote infection, calcification, or tissue necrosis
- It should have a minimal effect on the immune system

Artificial Heart and Circulatory Assist Devices

Reliability

- The design specification must assign a target reliability for the device
- The design specification must state which components of the system could be changed if necessary
- The design specification must deal with any service that the device may require
- The reliability issue is very complex and involves moral, ethical, legal, and scientific issue

Artificial Heart and Circulatory Assist Devices

Quality of Life

- The designers must specify what is a satisfactory quality of life
- The design specification must state the weight of any external power supplies
- The designer must consider:
  - how much weight an older patient will be able to carry
  - how often will the energy source require a recharge?
- In many instances there are no right and wrong answers to these questions

Artificial Heart and Circulatory Assist Devices

Conceptual Design
Plan Treatment

- In the conceptual design phase, the designer must plan the treatment of the problem and consider various designs that meet the design specification
- In the design specification, it must be stated whether the blood pump is to be pulsatile or non-pulsatile
- Non-pulsatile devices include centrifugal pumps, axial flow pumps, shear flow pumps, and peristaltic pumps
- Pulsatile pumps have traditionally been sac- or diaphragm-type devices

Artificial Heart and Circulatory Assist Devices

Conceptual Design
Plan Treatment

- Careful consideration must be given to source of energy
- Sources that have been considered include electrical energy stored in batteries or derived from piezoelectric crystals, fuel cells, and thermal energy created either thermonuclearly or through thermal storage
- The performance of each of these energy sources must be considered in the conceptual design phase.

Artificial Heart and Circulatory Assist Devices

Conceptual Design
Plan Treatment

- Systems such as sac-type blood pumps have been described as having intrinsic automatic control
- These devices can run in a fill limited mode, and, as more blood is returned to the pump, it will increase its stroke volume
- Intrinsic control is desirable, but, unfortunately, this generally provides for only a limited control range

Artificial Heart and Circulatory Assist Devices

Conceptual Design
Plan Treatment

- Once a reliability goal has been established, the designer must ensure that this goal is met
- In the conceptual design phase, one must carefully weigh quality of life issues when evaluating solutions to the problem
- Careful consideration needs to be given to the traditional quality of life issues such as the patient's emotional, social, and physical well-being, as well as to the details of day-to-day use of the device

Artificial Heart and Circulatory Assist Devices

Detailed Design
Execute Plan

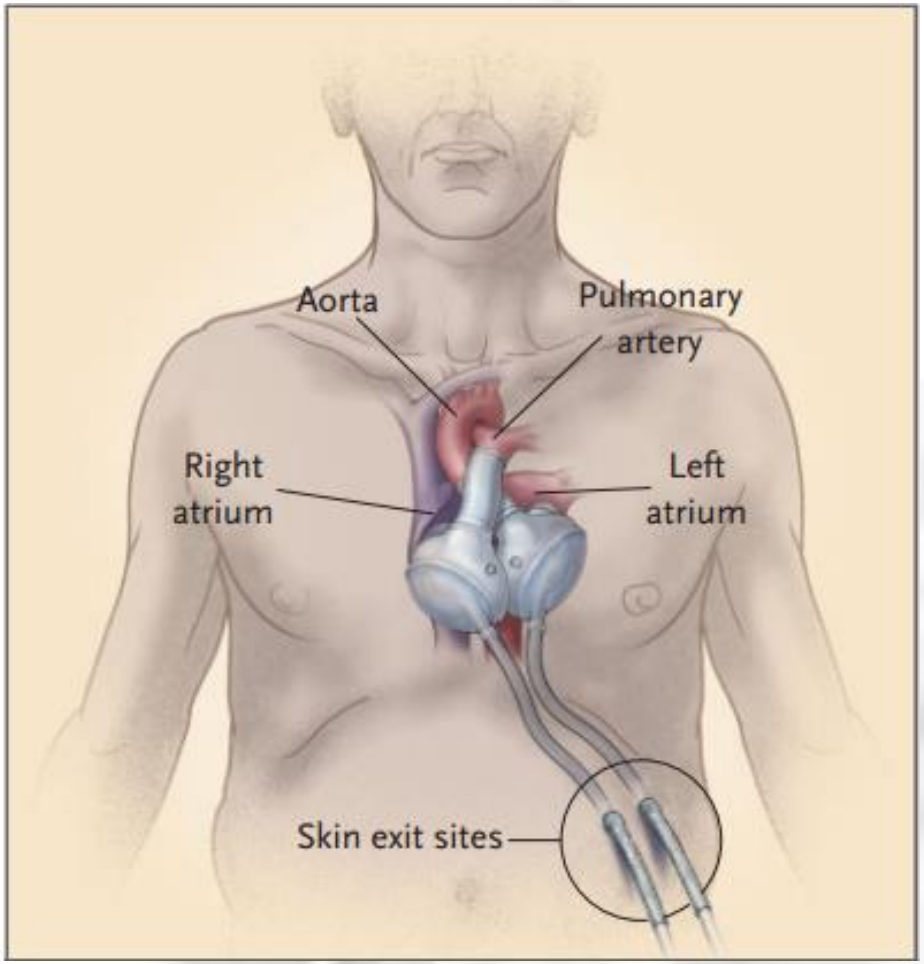
- This is the phase of engineering design where the designer and other members of the team must begin to do what is generally considered the designer's more traditional role, i.e., calculations and drawings
- This phase of design may require some initial prototyping and testing before the detailed design can be complete
- It is up to the designer to review current literature and determine what fundamental principles are applicable to his or her design

Artificial Heart and Circulatory Assist Devices

- The design of artificial hearts and circulatory assist devices is a very complex process involving many engineering disciplines along with medicine and other life science areas
- Social issues must enter into the design process
- The design of such devices requires sound engineering design principles and an interdisciplinary design team dedicated to the development and ultimate clinical application of these devices

Artificial Heart and Circulatory Assist Devices

- Two types of artificial hearts:
  - ✓ Ventricular Assist Devices (VAD's) and
  - ✓ Total Artificial Hearts (TAH's)



Copeland et al., Cardiac Replacement with a Total Artificial Heart as a Bridge to Transplantation, N Engl J Med 2004

Artificial Heart and Circulatory Assist Devices

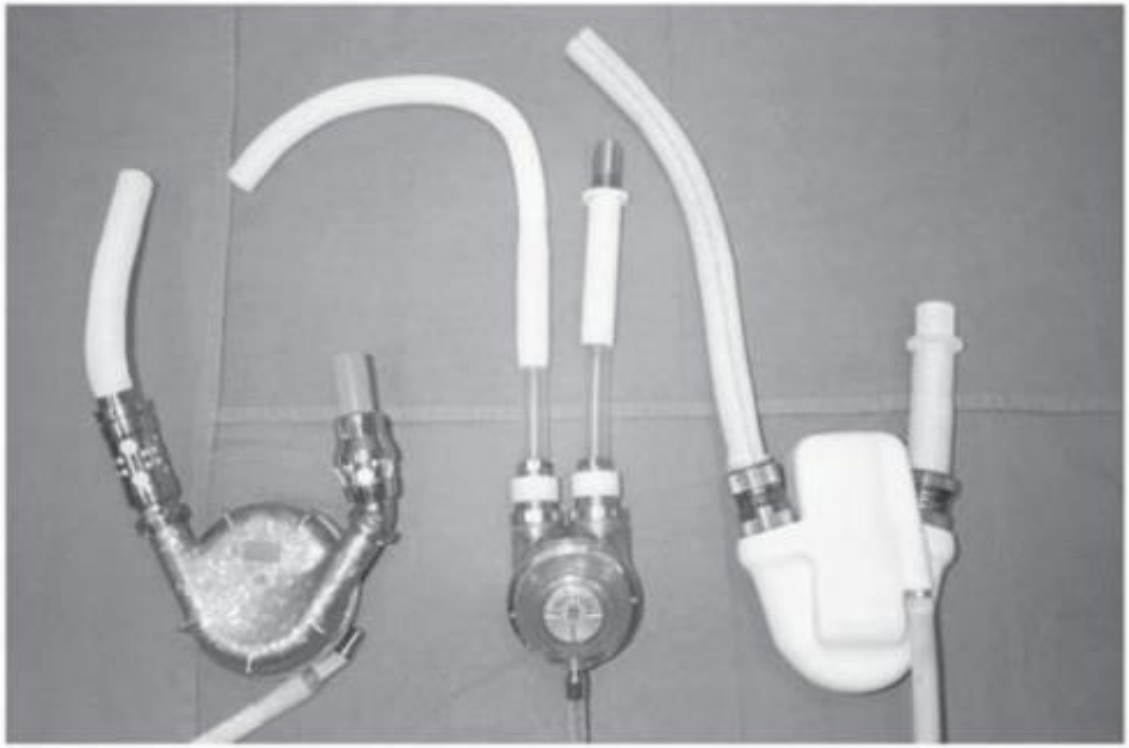
VAD's

- Does not replace heart and it works along side it
- VAD is a mechanical pump which is surgically implanted next to heart
- Runs on power from a battery pack that you carry at your side, constantly helping your heart to pump blood
- Attached to left ventricle and to aorta
- Works by helping heart pump blood from left ventricle into aorta

Artificial Heart and Circulatory Assist Devices

VAD's

- First-generation VADs deliver pulsatile blood flow and are mainly positive-displacement pumps



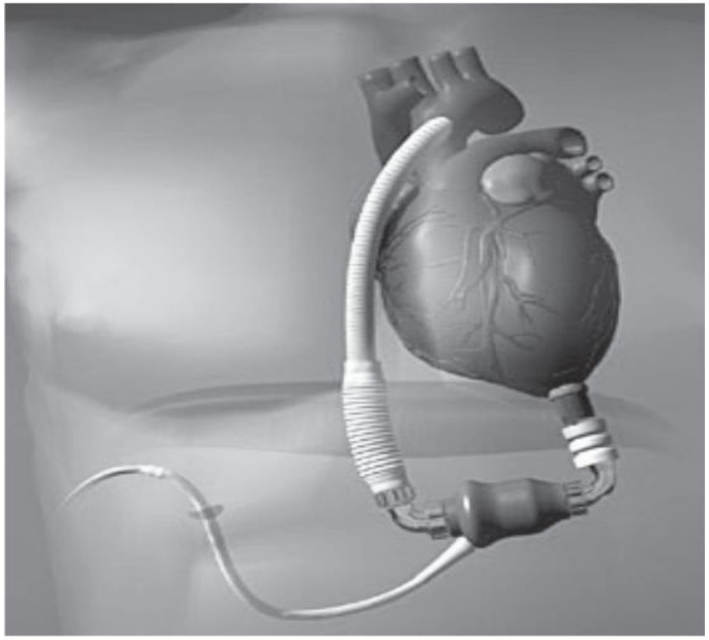
Lahpor , State of the art: implantable ventricular assist devices. Curr Opin Org Transp ,2009

Artificial Heart and Circulatory Assist Devices

VAD's

- Second-generation pumps are mostly rotary axial flow pumps with bearings immersed in blood or that can deliver diminished pulsatile or continuous blood flow.

- These devices are in different stages of development, testing and clinical use



Kozik et al., Mechanical circulatory support, Organogenesis,2011

Artificial Heart and Circulatory Assist Devices

VAD's

- Third-generation devices make use of magnetic levitation technology
- A rotating impeller is magnetically suspended within a column of blood, obviating the need for contact-bearing moving parts
- This provides the theoretical advantage of enhanced long-term durability

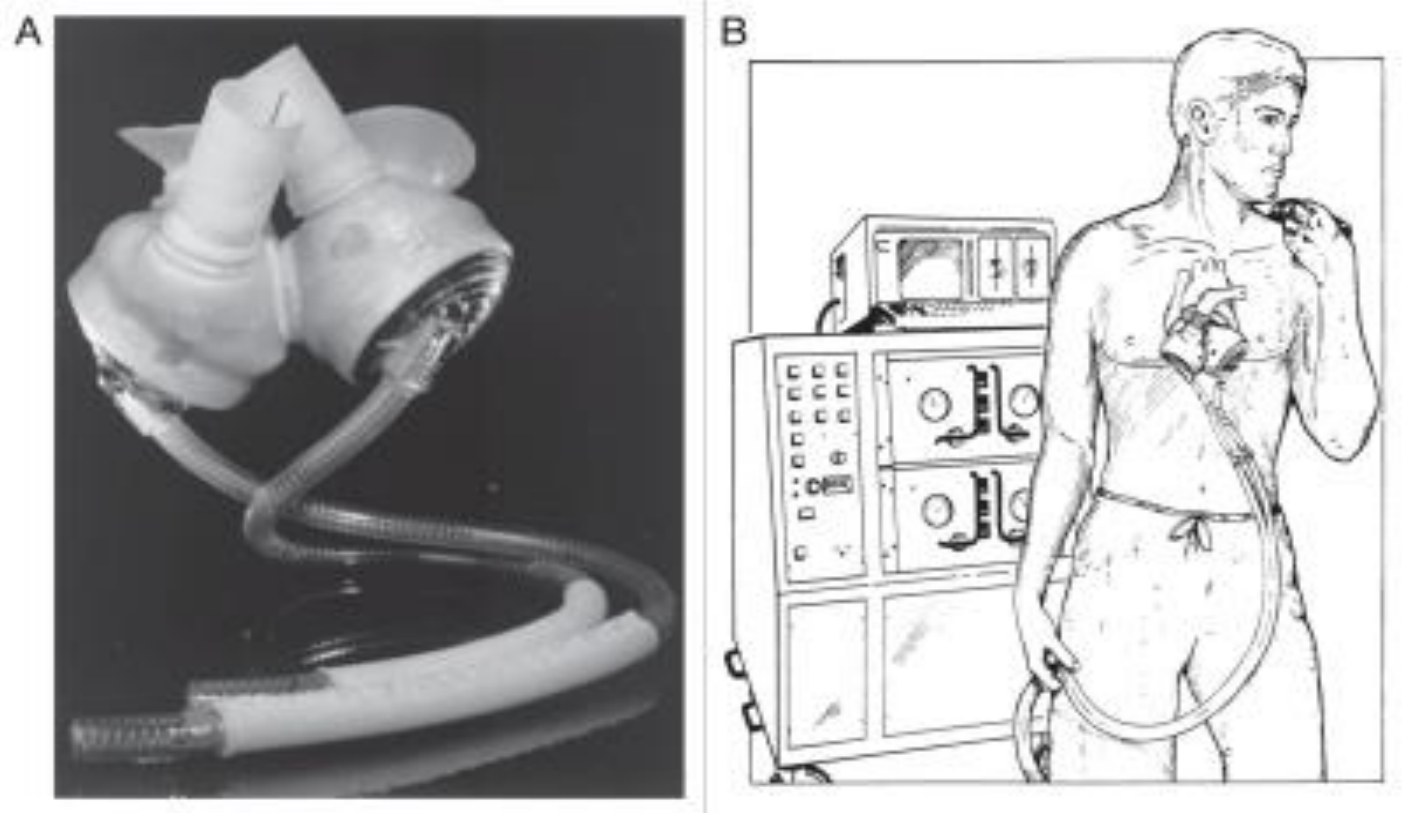
Artificial Heart and Circulatory Assist Devices

TAH

- Device that replaces the two lower chambers of the heart (the ventricles)
- TAH is attached to hearts upper chambers (Atria)
- Between the TAH and Atria are mechanical valves that work like the hearts own valves
- These control the flow of blood in the heart
- Two types of TAH's: CardioWest and AbioCor

Artificial Heart and Circulatory Assist Devices

TAH



(A) CardioWest total artificial heart. (B) Implanted with Console

Arabia et. Al, Implantation technique for the CardioWest total artificial heart.,Ann Thorac Surg, 1999

Cardiac Valve Prostheses

- The first clinical use of a cardiac valvular prosthesis took place in 1952, when Dr. Charles Hufnagel implanted the first artificial caged ball valve for aortic insufficiency
- The first implant of a replacement valve in the anatomic position took place in 1960, with the advent of cardiopulmonary bypass
- More than 50 different cardiac valves have been introduced over the past 35 years.
- Unfortunately, after many years of experience and problems associated with heart valve prostheses have not been eliminated

Cardiac Valve Prostheses

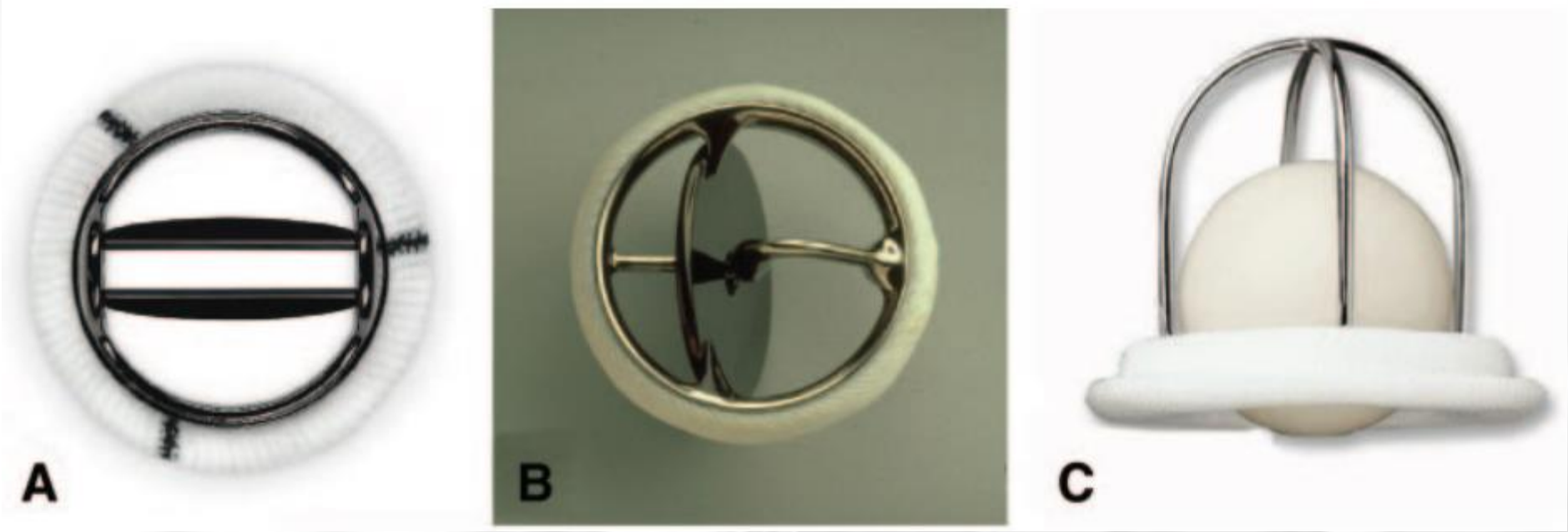
- The most serious problems and are:
  - Thrombosis and thromboembolism
  - Anticoagulant-related hemorrhage
  - Tissue overgrowth
  - Infection
  - Paravalvular leaks due to healing defects, and
  - Valve failure due to material fatigue or chemical change

Cardiac Valve Prostheses

- The ideal valve substitute should mimic the characteristics of a normal native valve
- It should have excellent hemodynamics, long durability, high thromboresistance, and excellent implantability
- Unfortunately, this ideal valve substitute does not exist, and each of the currently available prosthetic valves has inherent limitations
- Two types of Prosthetic Heart Valve exist: Mechanical and Bioprosthetic valves

Cardiac Valve Prostheses

- Three basic types of **mechanical valve** design exist: bileaflet, monoleaflet, and caged ball valves



A) Bileaflet mechanical valve (St Jude). B) monoleaflet mechanical valve (Medtronic Hall). C) caged ball valve (Starr-Edwards).

Pibarot et. Al, Valvular Heart Disease: Changing Concepts in Disease Management, Circulation, 2009

Cardiac Valve Prostheses

- *Caged ball valves*, which consist of a silastic ball with a circular sewing ring and a cage formed by 3 metal arches, are no longer implanted
- However, several thousands of patients still have caged ball valves, and these patients require follow-up
- *Monoleaflet valves* are composed of a single disk secured by lateral or central metal struts
- The opening angle of the disk relative to valve annulus ranges from 60° to 80°, resulting in 2 distinct orifices of different sizes

Cardiac Valve Prostheses

- *Bileaflet valves* are made of 2 semilunar disks attached to a rigid valve ring by small hinges
- The opening angle of the leaflets relative to the annulus plane ranges from 75° to 90°
- The open valve consists of 3 orifices: a small, slit-like central orifice between the 2 open leaflets and 2 larger semicircular orifices laterally.

Cardiac Valve Prostheses

- Three basic types of **bioprosthetic valve** design exist: stented bioprostheses, stentless bioprostheses, and percutaneous bioprostheses

E) Stented pericardial bioprosthesis (Carpentier-Edwards Magna). F) stentless porcine bioprosthesis (Medtronic Freestyle) . G) percutaneous bioprosthesis expanded over a balloon (Edwards Sapien).

Pibarot et. Al, Valvular Heart Disease: Changing Concepts in Disease Management, Circulation, 2009

Cardiac Valve Prostheses

- The design of *stented bioprostheses* purports to mimic the anatomy of the native aortic valve
- Porcine bioprosthetic valves consist of 3 porcine aortic valve leaflets crosslinked with glutaraldehyde and mounted on a metallic or polymer supporting stent
- Pericardial valves are fabricated from sheets of bovine pericardium mounted nside or outside a supporting stent
- In an effort to improve valve hemodynamics and durability, several types of *stentless bioprosthetic* valves have been developed

Cardiac Valve Prostheses

- *Stentless bioprostheses* are manufactured from whole porcine aortic valves or fabricated from bovine pericardium

- *Percutaneous* aortic valve implantation is emerging as an alternative to standard aortic valve replacement in patients with symptomatic aortic stenosis considered to be at high or prohibitive operative risk

- At present, the procedure appears promising, but it remains experimental and is currently undergoing further investigation

Cardiac Valve Prostheses

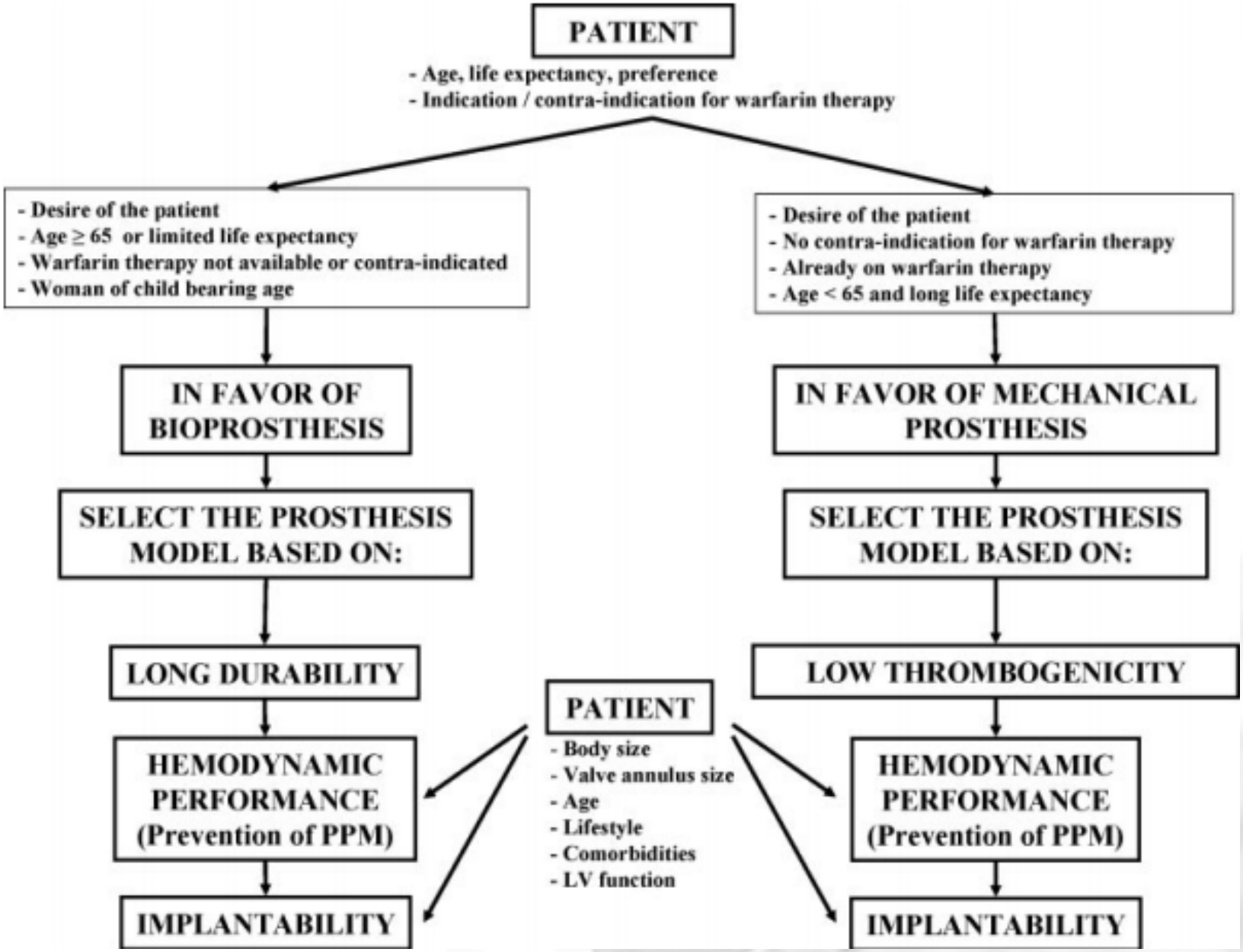
Engineering Concerns

- In terms of considerations related to heart valve design, the basic engineering concerns are:
  - Hydrodynamics/hemodynamics
  - Durability (structural mechanics and materials)
  - Biologic response to the prosthetic implant

Cardiac Valve Prostheses

Engineering Concerns

- The ideal heart valve design from the hemodynamic point of view should:
  - Produce minimal pressure gradient
  - Yield relatively small regurgitation
  - Minimize production of turbulence
  - Not induce regions of high shear stress
  - Contain no stagnation or separation regions in its flow field, especially adjacent to the valve superstructure



Algorithm for the selection of the optimal prosthesis in the individual patient

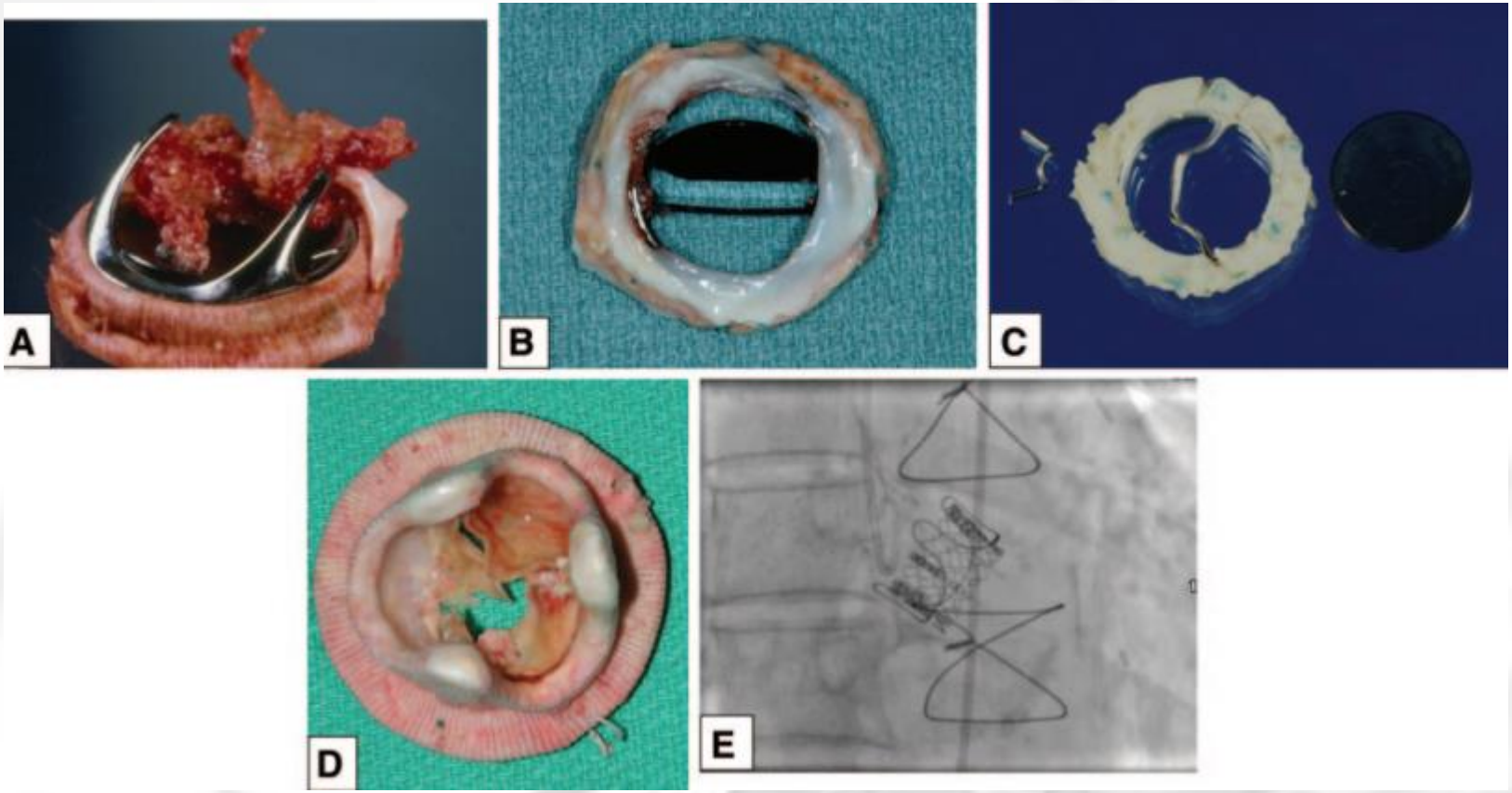
Pibarot et. Al, Valvular Heart Disease: Changing Concepts in Disease Management, Circulation, 2009

Cardiac Valve Prostheses

Long-Term Complications

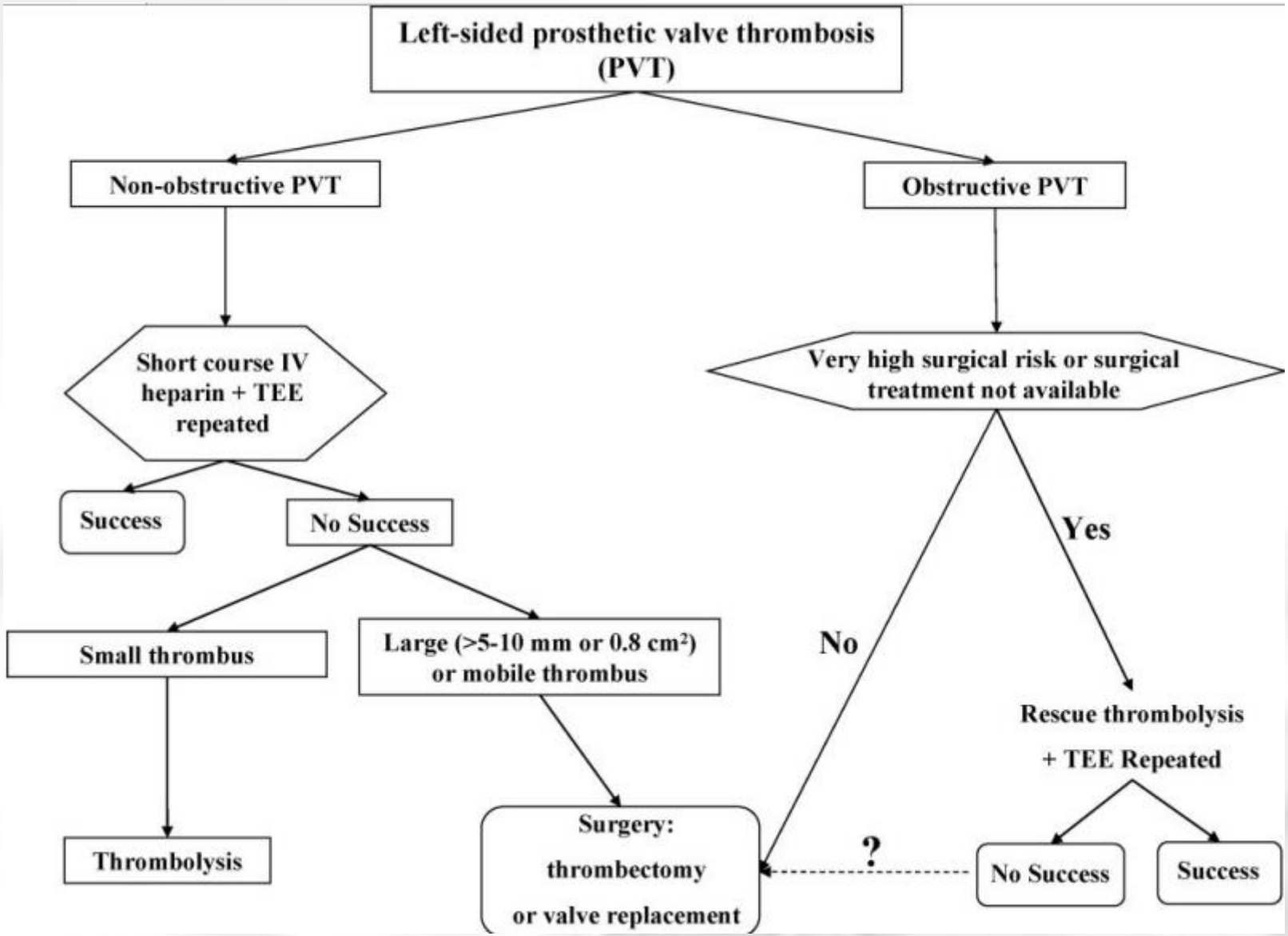
- Mechanical valves have a substantial risk of thromboemboli and thrombotic obstruction
- They require long-term anticoagulation therapy
- Nonetheless, contemporary mechanical valves have excellent durability.
- In contrast, bioprosthetic valves have a low risk of thromboembolism without anticoagulation, but their durability is limited by calcific or noncalcific tissue deterioration

Cardiac Valve Prostheses



A) Obstructive thrombosis of a Lillehei-Kaster prosthesis. B) Pannus ingrowth interacting with leaflet opening in a St Jude Medical bileaflet valve. C) Rupture of the outlet strut and leaflet escape in a BjörkShiley prosthesis. D) Leaflet calcific degeneration and tear in a porcine bioprosthesis. E) One of the first in-human valve-in-valve cases.

Pibarot et. Al, Valvular Heart Disease: Changing Concepts in Disease Management, Circulation, 2009



Algorithm for the management of patients with left-sided prosthetic valve thrombosis

Pibarot et. Al, Valvular Heart Disease: Changing Concepts in Disease Management, Circulation, 2009

Artificial Lungs and Blood-Gas Exchange Devices

- The natural lung is the organ in which blood exchanges oxygen and carbon dioxide with the body environment
- In turn, blood brings oxygen to all body tissues, so as to oxidize the nutrients needed to sustain life
- The challenge of replacing the function of the natural lungs by an exchange device allowing continuous blood flow and continuous blood arterialization was first outlined by physiologists at the end of the 19th century but could not be met reliably until the 1950s

Artificial Lungs and Blood-Gas Exchange Devices

- As is the case for most artificial organs, artificial lungs may be called upon to replace entirely the pulmonary gas exchange function
- An artificial lung (AL) is a prosthetic device that provides oxygenation of blood and removal of carbon dioxide from blood
- A successful artificial lung could be used as a support device following transplant or as supplemental support to mechanical ventilation

Artificial Lungs and Blood-Gas Exchange Devices

- Artificial lung technology initially has been limited to its use in cardiopulmonary bypass and extracorporeal membrane oxygenation (ECMO)
- CMO, however, is very time-consuming, needing large amounts of monitoring and personnel, and the device itself consists of tubes and cannulae that can rupture and lead to fatal results
- For these reasons, the latest advances have diverted from ECMO therapy

Artificial Lungs and Blood-Gas Exchange Devices

- The intravascular oxygenator, IVOX, is an alternative technology
- Gas enters and leaves the system via conduits outside a small skin incision
- The device, a membrane oxygenator, is placed in the vena cava and a vacuum pump pulls oxygen through the device fibers
- Another version has replaced the vacuum pump with a pulsating balloon that allows for optimal blood mixing across the gas exchange fibers

Artificial Lungs and Blood-Gas Exchange Devices

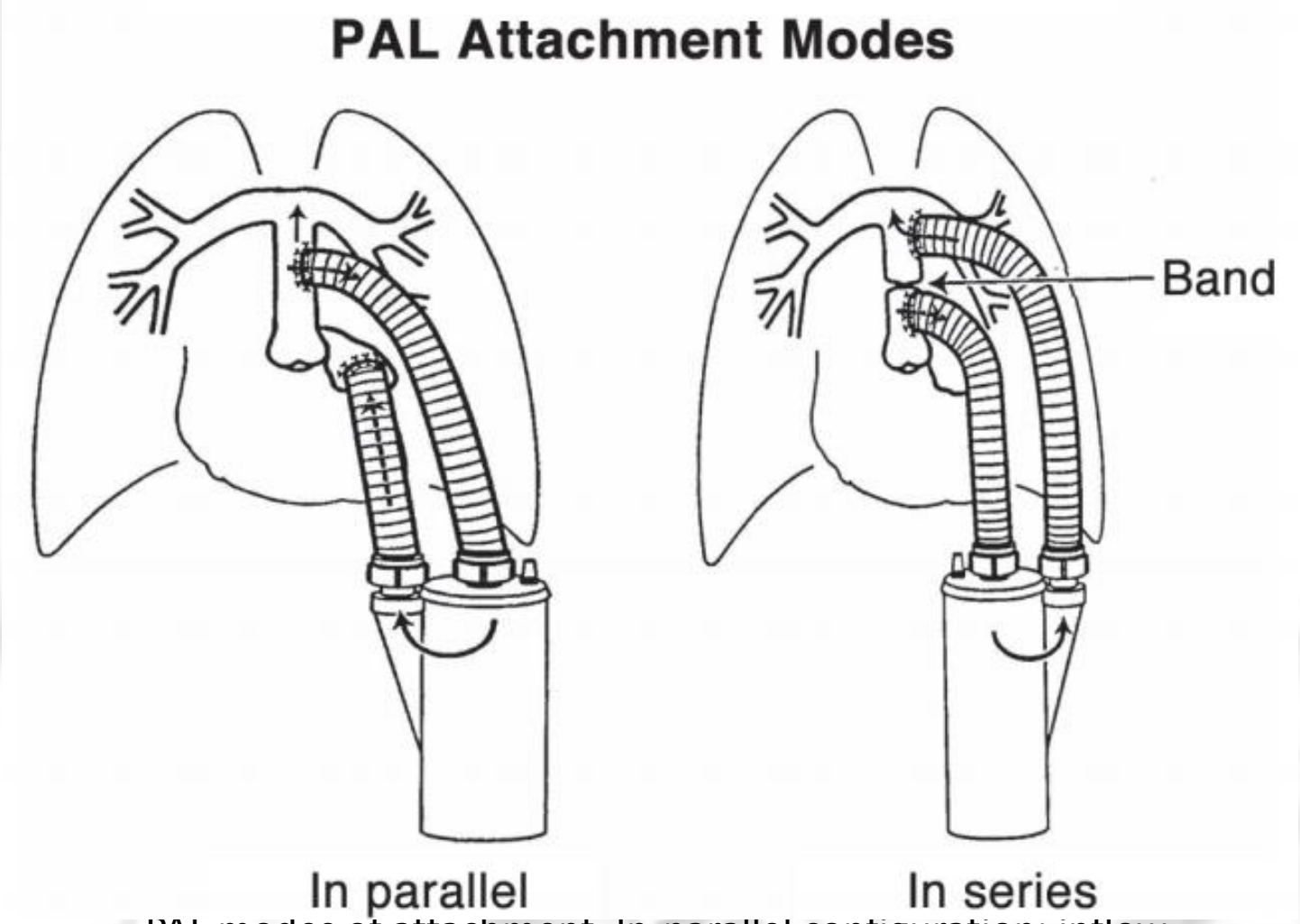
- Another alternative choice is a high-flow cannula placed in the femoral artery and vein that creates a pumpless shunt
- This method, deemed interventional lung assist, allows for complete CO^2 removal and due to the device's location in the peripheral vasculature the natural lung can still provide oxygenation within its capabilities
- Conversely, the device will receive only partial cardiac output, which will limit its effectiveness, as both adequate cardiac output and arterial pressure are necessary

An experimental sheep standing freely and eating/drinking normally with dark black blood out of drainage lumen in clear contrast against the vivid red blood in the infusion lumen

Nolan et. Al, Artificial lung basics, Organogenesis, 2011

Artificial Lungs and Blood-Gas Exchange Devices

- The placement of the device is crucial to its function
- Currently two modes of placement predominate, in-series and in-parallel, although alternative configurations have also been considered
- A third configuration has recently shown great promise, combining the in-series method through the venous system
- There are advantages and disadvantages to each, with the patient and his/her disease state being the ultimate deciding factor



PAL modes of attachment. In-parallel configuration: inflow attached to pulmonary artery and outflow attached to left atrium. Inseries configuration: inflow attached to proximal pulmonary artery and outflow attached to distal pulmonary artery (pulmonary artery ligated with band between inflow and outflow cannulae

Zwischenberger et. Al, Artificial lungs: A new inspiration, Perfusion, 2002

Artificial Lungs and Blood-Gas Exchange Devices

- For the in-parallel configuration, the blood inlet to the artificial lung is anastomosed surgically to the pulmonary artery
- The blood outlet of the artificial lung is then similarly connected to the left atrium
- The blood will flow into the device as a result of the high resistance in the patient's own pulmonary system and a much lower resistance in the artificial lung pathw
- The in-parallel configuration is the least stressful for the right ventricle

Artificial Lungs and Blood-Gas Exchange Devices

- Problems with the in-parallel configuration stem from the complete bypass of the native lungs
- Providing more than just gas exchange, the lungs also perform metabolic functions within the body and act as a blood filter
- Currently there are no attempts to duplicate these functions in an artificial lung device
- In addition to its role in the metabolic pathway, the native lung also acts as a filter, capturing small emboli and preventing them from entering systemic circulation

Artificial Lungs and Blood-Gas Exchange Devices

- For the in-series configuration, the blood inlet of the artificial lung is again anastomosed to the pulmonary artery
- The blood outlet, however, is also anastomosed to the pulmonary artery distal from the blood inlet anastomosis
- A band is placed between the two anastomoses in order to direct blood flow from the proximal pulmonary artery into the artificial lung and back to the distal pulmonary artery

Artificial Lungs and Blood-Gas Exchange Devices

- The in-series configuration is not without its problems
- The aforementioned right heart stress, despite alleviating design alterations, is still an important consideration for researchers
- Another complication to this setup is the short pulmonary artery in humans
- Placement is limited, and the outflow graft competes for space in the mediastinum with the superior vena cava and the curve of the ascending aorta

Artificial Kidney

- The key separation functions of the kidney are:

  1. To eliminate the water-soluble nitrogenous end-products of protein metabolism

  2. To maintain electrolyte balance in body fluids and get rid of the excess electrolytes

  3. To contribute to obligatory water loss and discharge excess water in the urine

  4. To maintain acid-base balance in body fluids and tissues

Artificial Kidney

- Kidney function is served by two major mechanisms:
  - ultrafiltration, which results in the separation of large amounts of extracellular fluid through plasma filtration in the glomeruli, and
  - a combination of passive and active tubular transportof electrolytes and other solutes, together with the water in which they are dissolved, in the complex system provided in the rest of the nephron

Artificial Kidney

- Functionally, an artificial kidney is a device in which water and solutes are transported from one moving fluid stream to another
- One fluid stream is blood; the other is dialysate: a human-made solution of electrolytes, buffers, and nutrients
- The solute concentration as well as the hydrostatic and osmotic pressures of the dialysate are adjusted to achieve transport in the desired direction (e.g., to remove urea and potassium ions while adding glucose or bicarbonate to the bloodstream)

Artificial Kidney

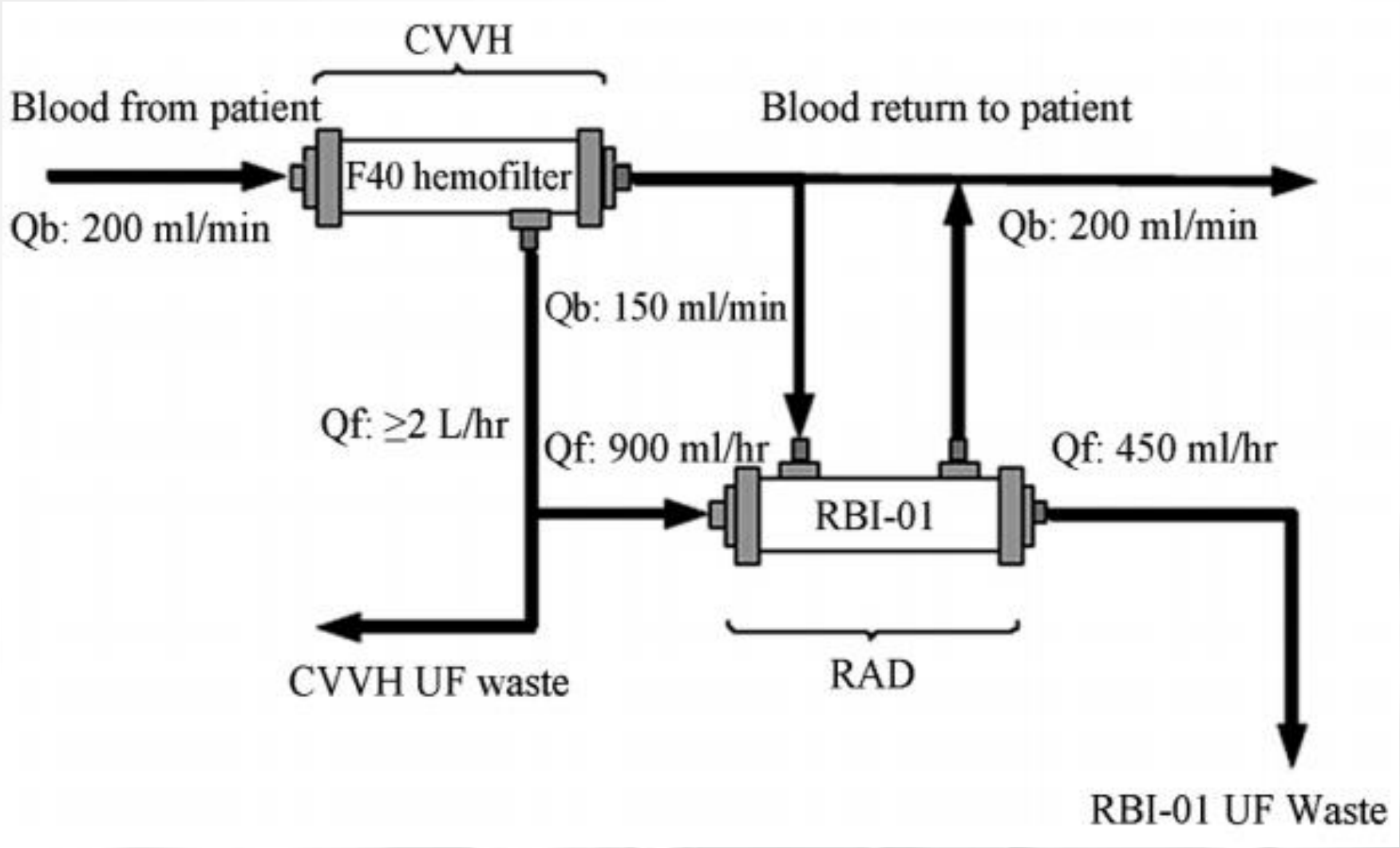
- In artificial kidneys, the removal of water and solutes from the blood stream is achieved by

  1. Solute diffusion in response to concentration gradients

  2. Water ultrafiltration and solute convection in response to hydrostatic and osmotic pressure gradients

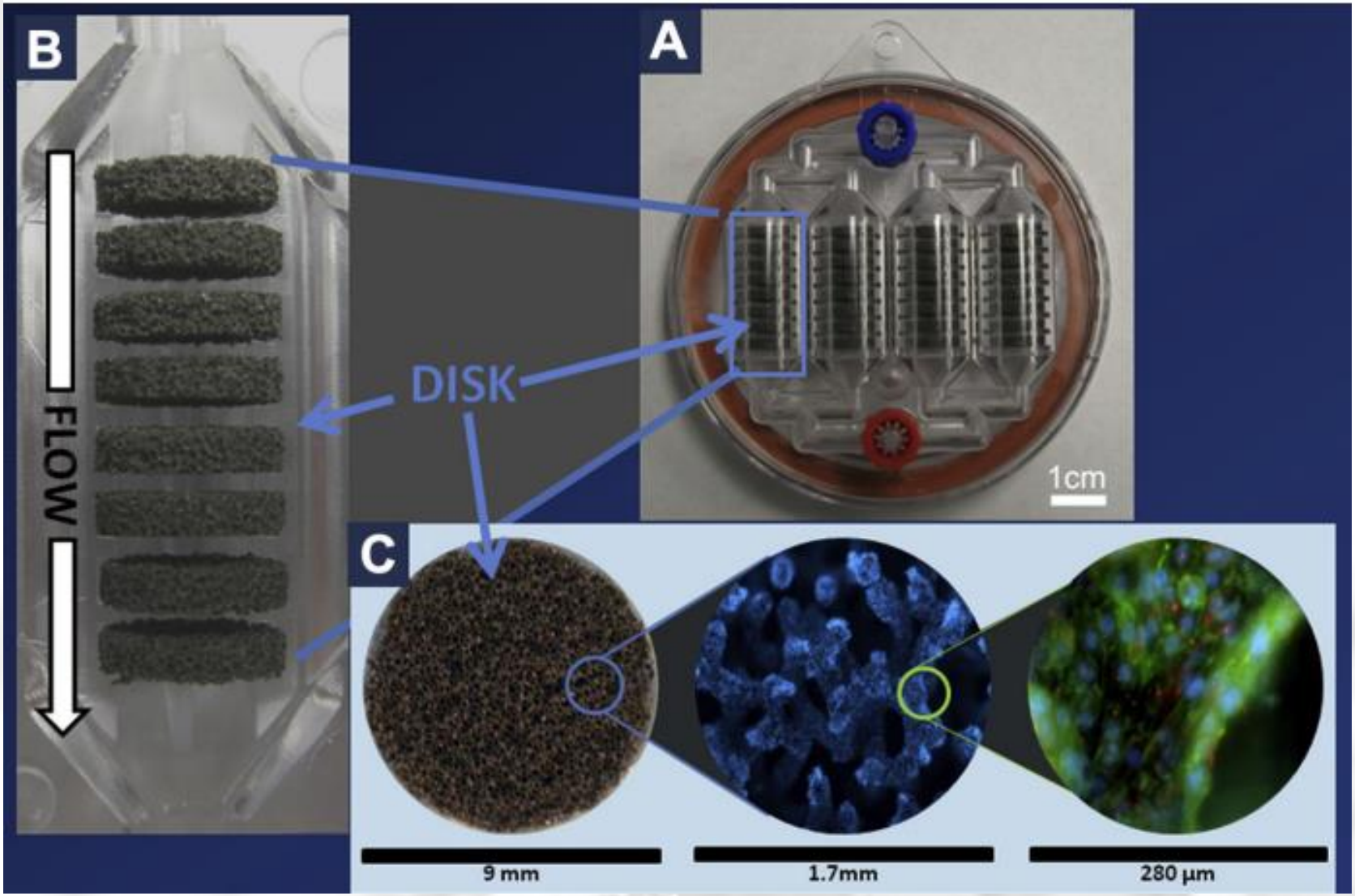
  3. Water migration in response to osmotic gradients

- In most cases, these processes occur simultaneously and in the same exchange device



Schematic circuit for extracorporeal perfusion system using the hemofilter and the renal tubule cell assist device

Tumlin, J. et al. , Efficacy and Safety of Renal Tubule Cell Therapy for Acute Renal Failure, J Am Soc Nephrol. 2008

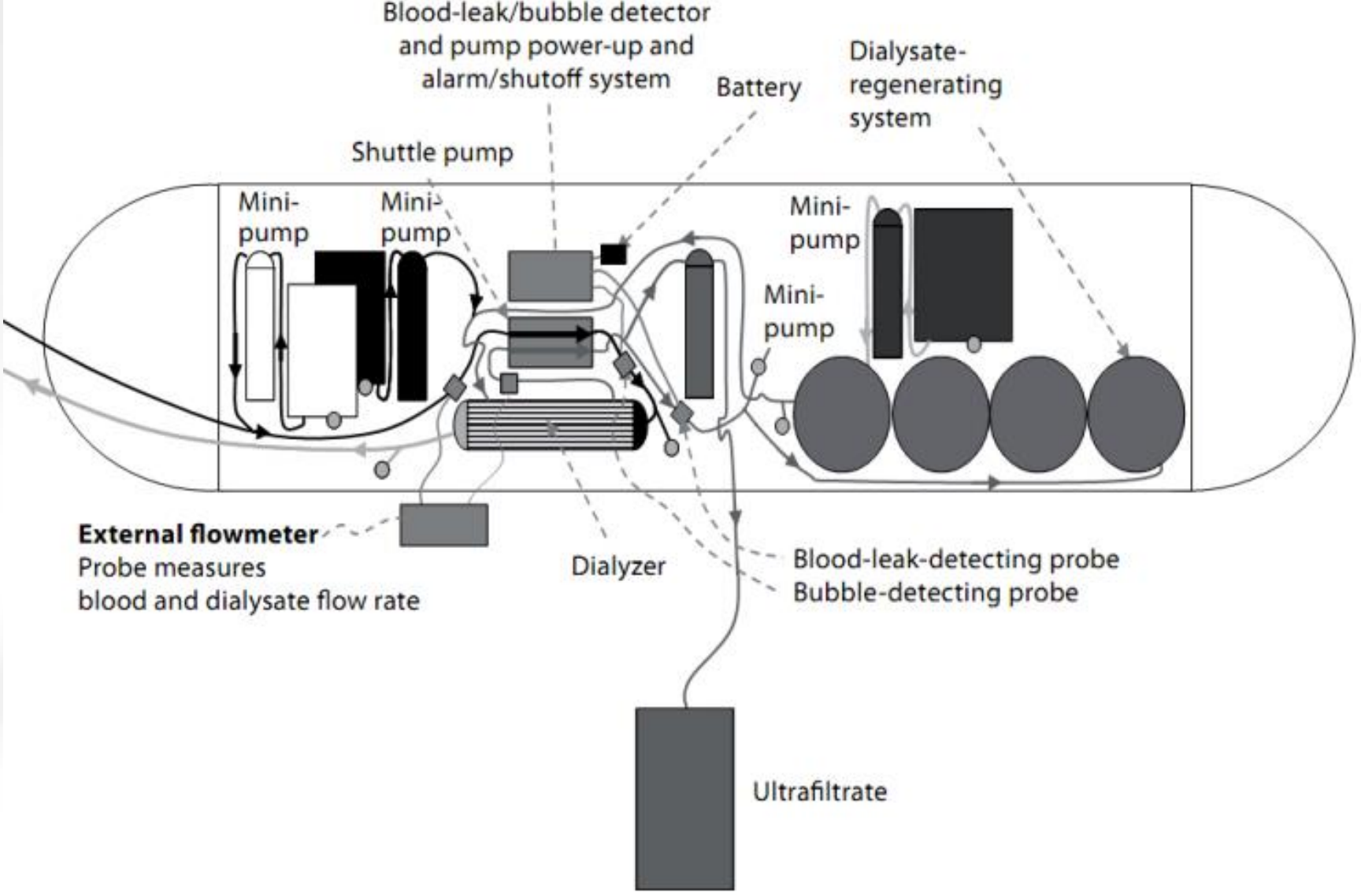


(A–C) The compact, freezable bioartificial renal epithelial cell system (BRECS) design

Humes et. Al, The bioartificial kidney, Pediatr Nephrol , 2014

Artificial Kidney

- To overcome shortcomings of today's dialysis system via technical breakthroughs, wearable dialysis devices have been developed
- Theoretically, wearable dialysis devices should function without cessation similar to native human kidney but, all of them show strengths and weaknesses
- The key of wearable hemodialysis system is mini-pump that can generate continuous countercurrent blood and dialysate flows and efficient battery which should be very small, lightweight and lasting for at least 24 hours

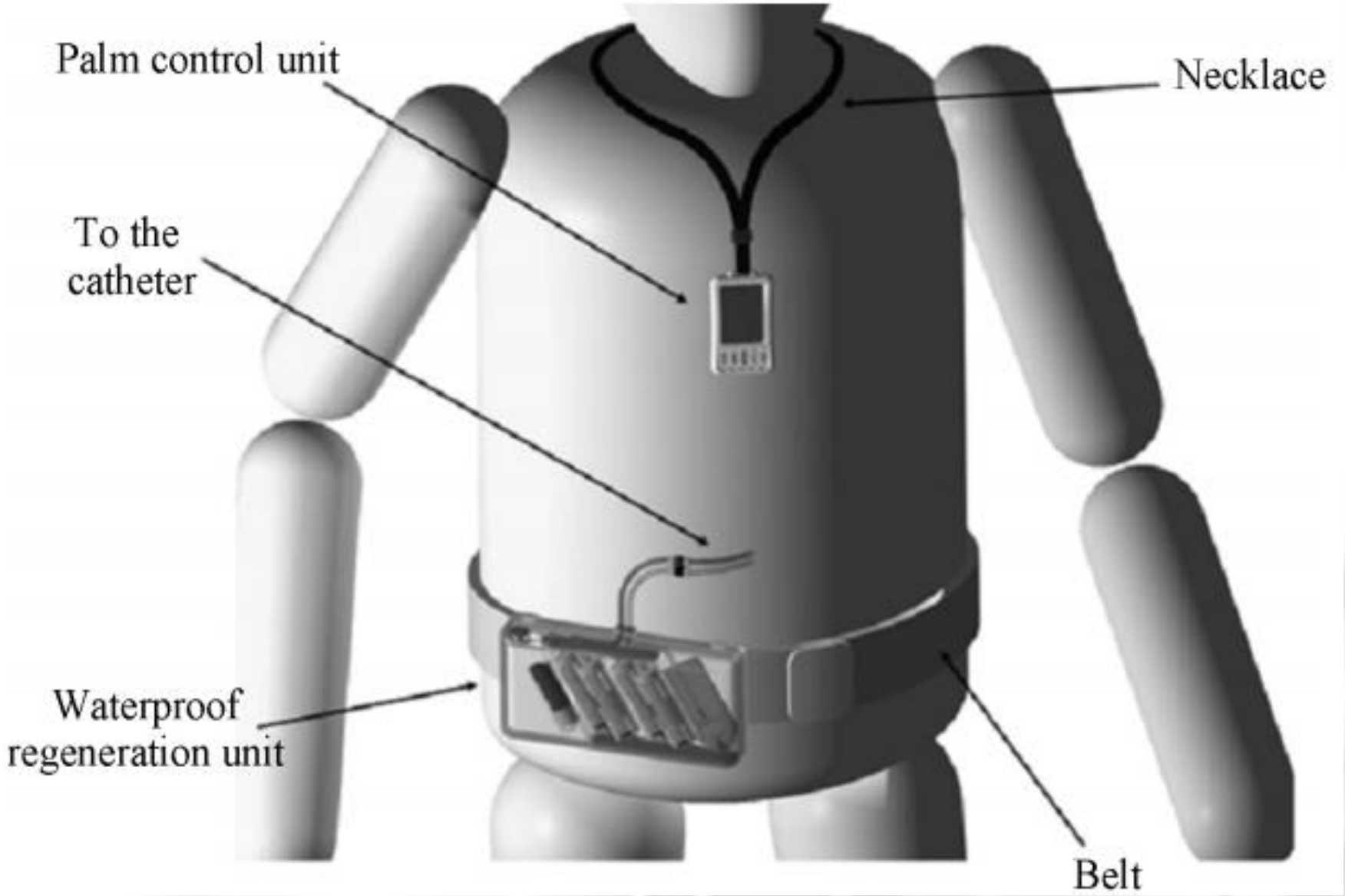


Circuit design of the wearable artificial kidney v 1.2 demonstrating 4 minipumps to control infusion of heparin, bicarbonate and electrolytes for regeneration of dialysate and ultrafiltration (US Patent No. 6,960,179)

Ronco, C. and Rosner, Hemodialysis: New Methods and Future Technology, M.H. Contrib Nephrol, 2011

Artificial Kidney

- Wearable artificial kidneys are feasible in modern technology
  - First, will it be convenient all day long, especially during sleeping time? Are there no problems in device weight and operation time without recharging the batteries?
  - Second, is method for blood access reliable and safe?
  - Third, will it be safe in emergent situation such as the risk of mitigation and technical system error?
  - Forth, is there no interference with the new technical device electromagnetically?



Schematic design of a wearable peritoneal dialysis system

Davenport et al., Portable and wearable dialysis: where are we now, Hemodialysis International , 2010

References

- Davenport et al., Portable and wearable dialysis: where are we now, Hemodialysis International , 2010
- Ronco, C. and Rosner, Hemodialysis: New Methods and Future Technology, M.H. Contrib Nephrol, 2011
- Humes et. Al, The bioartificial kidney, Pediatr Nephrol , 2014
- Zwischenberger et. Al, Artificial lungs: A new inspiration, Perfusion, 2002
- Nolan et. Al, Artificial lung basics, Organogenesis, 2011
- Pibarot et. Al, Valvular Heart Disease: Changing Concepts in Disease Management, Circulation, 2009

References

- J.D. Bronzino , Biomedical Engineering Handbook, 2000
- Copeland et al., Cardiac Replacement with a Total Artificial Heart as a Bridge to Transplantation, N Engl J Med, 2004
- Lahpor , State of the art: implantable ventricular assist devices. Curr Opin Org Transp , 2009
- Kozik et al., Mechanical circulatory support, Organogenesis, 2011
- A Kiourti, Biomedical telemetry: communication between implanted devices and the external world, Opticon1826, 2010