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From Engineering to Medicine and Back: the Physiology of Mechanical Circulation
An artificial organ is a man-made device that is implanted or integrated into a human 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.

An engineer is a professional practitioner of engineering, concerned with applying scientific knowledge, mathematics, and ingenuity to develop solutions for technical, societal and commercial problems. Engineers design materials, structures, and systems while considering the limitations imposed by practicality, regulation, safety, and cost.[1][2] The word engineer is derived from the Latin words ingeniare ("to contrive, devise") and ingénium ("cleverness.")
Cardiovascular System Function

- Functional components of the cardiovascular system:
  - Heart
  - Blood Vessels
  - Blood

- General functions these provide
  - Transportation
    - Everything transported by the blood
  - Regulation
    - Of the cardiovascular system
      - Intrinsic v extrinsic
  - Protection
    - Against blood loss
  - Production/Synthesis

Comparison to some mechanical system: heart-pump, vessels - pipes, blood - fuel or power station - wires - electricity. But sewage also.

Total integration - no such comparison in mechanical world.

Self protection - infection.

Self sealing - unique?

This is the problem with mechanical alternatives.
Functional Anatomy of the Heart

Chambers

- 4 chambers
  - 2 Atria
  - 2 Ventricles

- 2 systems
  - Pulmonary
  - Systemic

Atria - compliance chambers
Ventricles - pumping chambers
Two chambers pump
Functional Anatomy of the Heart

Valves

- Function is to prevent backflow
  - Atrioventricular Valves
    - Prevent backflow to the atria
    - Prolapse is prevented by the chordae tendinae
      - Tensioned by the papillary muscles
  - Semilunar Valves
    - Prevent backflow into ventricles
One way valves
Cardiac Cycle - synchronous and repetitive movement

- Electrical Conduction Pathway

1. SA node depolarizes.
2. Electrical activity goes rapidly to AV node via internodal pathways.
3. Depolarization spreads more slowly across atria. Conduction slows through AV node.
4. Depolarization moves rapidly through ventricular conducting system to the apex of the heart.
5. Depolarization wave spreads upward from the apex.
Synchronous and repetitive movement
Mechanical properties of cardiovascular system

Closed circulation and transport system

- **Main parts:**
  - Heart muscle (myocardium)
  - Closed system of blood vessels
  - Blood

- **Main functions:**
  - Supplying cells by nutrients and oxygen,
  - Transport of hormones and other chemical signals,
  - Removal of waste and side products from cells (tissues)
  - Heat transfer - thermoregulation
Mechanical properties of blood

- **Laplace law** – mechanical stress of blood vessel walls is directly proportional to the pressure and \( r \), the vessel radius.

\[
T = r \cdot p
\]

### Tension \( T \) in walls of some blood vessels:

<table>
<thead>
<tr>
<th>vessel</th>
<th>( r(m) )</th>
<th>( p(kPa) )</th>
<th>( T(\text{N.m}^{-1}) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>aorta</td>
<td>0.012</td>
<td>13</td>
<td>156</td>
</tr>
<tr>
<td>artery</td>
<td>0.005</td>
<td>12</td>
<td>60</td>
</tr>
<tr>
<td>capillary</td>
<td>( 6 \times 10^{-6} )</td>
<td>4</td>
<td>0.024</td>
</tr>
<tr>
<td>vein</td>
<td>0.005</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>vena cava</td>
<td>0.015</td>
<td>1.3</td>
<td>20</td>
</tr>
</tbody>
</table>
Reynolds number

- **Blood flow**: laminar (ordered)
- turbulent (whirling)
- Reynolds (1883)

- Reynolds number (for a liquid flowing in a cylindrical tube): \( R_e = \frac{\rho \cdot v_m \cdot r}{\eta} \)
  
  - \( \rho \) - liquid density, \( v_m \) - mean flow rate, \( r \) - vessel radius, \( \eta \) - coefficient of dynamic viscosity

- Critical flow rate: \( v_m = 1000\eta/r\cdot\rho \)
The differences between theoretical and real flow rate profiles are given mainly by the fact that blood is a non-Newtonian liquid and is influenced by the distensibility and compliance of the vessel wall.
Peripheral impedance (resistance) of blood vessels

- Analogy of electrical impedance ($R = U/I$)
- Pressure $p$ is an analogy of voltage $U$
- Blood flow volume $Q$ is an analogy of electric current $I$
- $R = \frac{\Delta p}{Q}$
- Considering the Hagen-Poiseuille formula for flow volume ($m^3.s^{-1}$):

$$Q = \frac{\pi r^4 \Delta p}{8 \eta \Delta l} \Rightarrow \frac{\Delta p}{Q} = \frac{8 \eta \Delta l}{\pi r^4}$$
• Mechanical power of heart
  (for pulse rate 70 min\(^{-1}\)) ........ 1,3 W
• Total power of heart
  (at rest conditions) ......................13 W
• Total power of human organism
  (at rest conditions) .................................115 W

• Mechanical work of heart muscle:
  Some very small work \(dW\) is done against external pressure \(p\)
during ejection of very small blood volume \(dV\):
  \[dW = p.dV\]
The whole work during a systole:
  \[W = \int p.dV\]
  Very small part of this work is transformed into kinetic energy of
  blood ejected.
Estimation of heart work during one systole

- \( p = \text{const.} \Rightarrow W = p_m \Delta V \),

- \( p_m \) is mean blood pressure at the beginning of aorta

- **Left ventricle**
  - \( p_m = 13.3 \text{ kPa} \)
  - \( \Delta V = 70 \text{ ml} \)
  - \( W = 0.93 \text{ J} \)

- **Right ventricle**
  - \( p_m = 2.7 \text{ kPa} \)
  - \( \Delta V = 70 \text{ ml} \)
  - \( W = 0.19 \text{ J} \)

- Mechanical energy of ejected blood volume \( W_k \):
  - \( W_k = 0.009 \text{ J} \)
  - \( W_k = 0.0018 \text{ J} \)

\( W_k = \frac{1}{2} \rho v_m^2 \Delta V \),

\( r = 1.06 \times 10^3 \text{ kg.m}^{-3} \),

\( v_m = 0.3 \text{ m.s}^{-1} \),

resp. \( 0.22 \text{ m.s}^{-1} \) in pulmonary artery)
Work and efficiency of myocardium

- Energy necessary to maintain tonus of myocardium:
  \[ \alpha \int T \, dt \]

- T - mechanical tension of heart walls (tonus) [N.m\(^{-1}\)], t - time

- Total energy necessary:
  \[ E_c = \int p \, dV + \alpha \int T \, dt \]

- Mechanical efficiency: \( W/E_c \) (max. 10 %)
Conclusion

- Heart is a marginally efficient low flow dual chamber pulsatile pump
- Therefore, it could easily be replaced (e.g. engineered by cleverness) with the more efficient mechanical alternative
Why heart can not easily be replaced by a mechanical pump?

- Blood is a non-Newtonian fluid
- Blood has auto-sealing properties (e.g. coagulation)
- Biological surfaces have auto-protection features (inflammation, infection etc.)
- Non-biological surfaces cause damage to blood elements
Why heart could not be replaced by a mechanical pump?

- Heart has self-recharging energy source
- The resistance to fatigue is far bigger than with any artificial material
- Auto-regulatory mechanism of the flow control cannot be matched by its electronic alternative
Mechanical circulatory pump

- Pumping (e.g. method of transferring mechanical energy of the pump to blood movement)
- Driving (e.g. method of utilization of external energy)
- Biocompatibility
The principal dilemma

Pulsatile  vs  Non Pulsatile
CONTINOUS VS REPETITIVE MOVEMENT

- BIRDS FLY BY REPETITIVE MOVEMENT
- MOVEMENT IS COMPLEX
- THRUST IS THRUST (WHATEVER SOURCE)
- CONTINOUS MOVEMENT IS MUCH MORE FEASIBLE FROM THE MECHANICAL POINT OF VIEW
- FATIGUE W. REPETITIVE MOVEMENT
- VIBRATIONS?
- SO WE CONVERT THE REPETITIVE MOVEMENT OF THE PISTON ENGINE TO CONTINOUS MOVEMENT OF THE AXLE SHAFT AND OF THE PROPELLER
- THE THRUST GENERATED IS EQUALLY VALUABLE !!!!
CONTINOUS VS REPETITIVE MOVEMENT

IS THIS THE CASE IN BLOOD PUMPING
Pulsatile

- Ventricle-like pumping sac device.
  - Blood enters via the inflow cannula and fills a flexible pumping chamber.
  - Electric motor or pneumatic (air) pressure collapses the chamber and forces blood into systemic circulation via the outflow cannula.

- Can be LVAD, RVAD, or BiVAD

- First-generation devices (in use since early 1980s)

- Patients will have a palpable pulse and a measurable blood pressure. Both are generated from the VAD output flow.
Pulsatile VAD Key Parameters can be measured by usual medical methods

- **Pump Rate:**
  - How fast the pump is pumping (filling & emptying)
  - Can be set at a fixed rate or can automatically adjust
  - Pulsatile pumps are loud and the rate can be assessed by listening

- **Output:**
  - The amount of blood ejected from the pump
  - Measured is liters per minute
  - Is dependent upon preload, afterload, and pump rate
Non-Pulsatile

- Continuous-flow devices
  - Impeller (spinning turbine-like rotor blade) propels blood continuously forward into systemic circulation.
  - Axial flow: blood leaves impeller blades in the same direction as it enters (think fan or boat motor propeller).

- Most implanted devices are LVADs only

- Are quiet and cannot be heard outside of the patient’s body. Assess VAD status by auscultation over the apex of the LV. The VAD should have a continuous, smooth humming sound.

- The Patient may have a weak, irregular, or non-palpable pulse

- The Patient may have a narrow pulse pressure and may not be measurable with automated blood pressure monitors. This is due to the continuous forward outflow from the VAD.

- The Mean Arterial Pressure is the key in monitoring hemodynamics. Ideal range is 65-90 mmHg.
Non Pulsatile Pumps Key Parameters

- The device parameters are displayed numerically on the VAD console or Controller

- Will vary with each individual patient and VAD device
Biocompatibility

- Not to interfere to the coagulation cascade
- Not to attract infection
- To have low shear stress
Coagulation pathway & endotelial lining
Equation of failure

High shear stress $\times$ non-biocompatibility = thrombosis
Thrombosis, thrombosis, thrombosis.....
Source of power

Cardiac Muscle

Striated, aerobic, interwoven, autorhythmic

Intercalated discs - gap junctions, strong junctional complex (desmosomes)
FIG. 5. The NHU atomic heart functioning in a calf. The device consists of a converter (fueled by plutonium-238) attached via hydraulic drive lines to the Model VIII heart assist pump, which in turn connects to the natural heart. (Source: John C. Norman et al., "An Implantable Nuclear-Fueled Circulatory Support System," Annals of Surgery 176, no. 4 [October 1972]: 500. Reprinted with permission.)
External power source with the driveline

Not self rechargeable so far
Process regulation
Resistance to wear
Evolution of the mankind made a natural heart as a perfect machine

- Internal and self rechargeable energy source
- Bio compatible with blood
- Self repairable (to some extent)
- Fully automated with several feedback loops
- Very resistant to wear
- Very resistant to foreign organism invasion (e.g. Infection)

.... and after eventually being worn out, it should be replaced with at least non-inferior artificial alternative

Well, good luck!
But, there is no alternative .... as heart failure is epidemic

- Prevalence in Europe: 2 %
- Prevalence > 65 yrs: 10 %
- 1st year mortality: 30 - 40 %
- 5 year mortality: 60 - 70 %
Deadly also...
Refractory Heart Failure - Definition

Persistence of symptoms that limit daily life (functional class III or IV of the New York Heart Association [NYHA]) despite optimal previous treatment with drugs of proven efficacy for the condition, i.e. ACE inhibitors, angiotensin II receptor antagonists (ARB), diuretics, digoxin, beta-blockers and nitrate-hydralazine (esp. in blacks)

Refactory Heart Failure - Definition

• Corresponds to stage D heart failure
  - refers to patients with advanced structural heart disease and severe signs of HF at rest who are candidates in the absence of contraindications for other specialized interventions such as –
  • heart transplantation
  • MCS
  • ventricular remodeling
  • intravenous inotropic drugs
Solutions in terminal/end stage heart failure

- Biological replacement - HTx efficient, limited availability, expensive
- Mechanical replacement - MCS efficient, always available, very expensive
- Death efficient, less expensive*, always available, unpleasant

* repeated hospitalizations can be also expensive
The Major Reason for Heart Failure Hospitalizations

- Worsening chronic heart failure (75%)
- De novo heart failure (23%)
- Advanced/ end-stage heart failure (2%)

Fonarow GC. Rev Cardiovasc Med. 2003; 4 (Suppl. 7): 21
Cleland JG et al. Eur Heart J. 2003; 24: 442
Potential medical need

- In Europe: \(500,000,000 \times 0.02 \times 0.02 = 200,000\)
- In Croatia: \(4,300,000 \times 0.02 \times 0.02 = 1720\)
- In Romania: \(22,000,000 \times 0.02 \times 0.02 = 8800\)
- In Turkey: \(78,000,000 \times 0.02 \times 0.02 = 31200\)
- In Montenegro: \(600,000 \times 0.02 \times 0.02 = 240\)
- In Italy: \(63,000,000 \times 0.02 \times 0.02 = 25200\)
- On Sicily: \(5,300,000 \times 0.02 \times 0.02 = 2120\)
But there is some hope...

Group 1: INTERMACS 1- death pending within hours
Group 2: INTERMACS 2–3- death pending within hours to weeks
Group 3: INTERMACS 4–7- heart failure
Therefore …

- Heart failure physicians have to adopt hybrid physiology
- They must gather clinical data from both patient and from machine
- Must be able to integrate such data into clinical decision
- Must be able to incorporate “mechanical patophysiology” into their mental pattern
Outpatient Blood Pressure Management

Continuous flow LVADs such as the HeartMate II represent an entirely new physiology

- Patients that have diminished pulse pressure frequently require a doppler
- Goal is to maintain mean arterial BP of 70-80 mmHg, not to exceed 90 mmHg
- Use of Doppler for measurements has improved
- Managing blood pressure will optimize cardiac support and may reduce hypertension-related stroke

Hybrid patophysiology cannula gradient on ECMO
VA: Venoarterial access via the neck vessels
VA: Venoarterial access via the femoral vessels
VAV: Venoarterial access with some venous RA return
Veno-venous ECLS with a double lumen cannula
Looks difficult?
But it is certainly rewarding....
April 22nd, platelet count 64, CRP 248

ECLS flow 5.5 l/min at 4420 RPM,
FIO2 70%, 6L/min
Art O2 18.55 kPa
SO2 98.4%
SIMV FiO2 0.4
ECLS FiO2 0.7