SUMMARY OF THE COURSE
in master's programme Biomedical Engineering
Course 322.018 Cardiovascular System Dynamics

Summary of the complete lecture

Executed by: Daniela L.
Student ID number: -

Supervisor: Univ. Prof. DI Dr. Heinrich Schima

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TECHNISCHE UNIVERSITÄT WIEN

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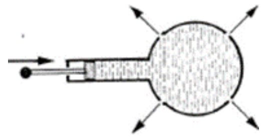
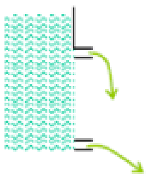
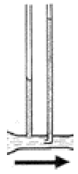
1.1 Basic Physics of the Circulation

Pressure in liquids

Table 1: The three possibilities of pressure of liquids

Designation	Cause	Picture
Hydrostatic pressure	Pressure is applied from outside (e.g. filling a pressure cylinder)	
Pressure caused by gravity = gravitational pressure	Is caused by the weight of the liquid (e.g. emptying water tank)	
Dynamic pressure	Is caused by acceleration (e.g. water pipe)	

Unit of pressure

The international unit for pressure is Pa (= Pascal).

$$P = \frac{F}{A}$$

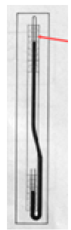
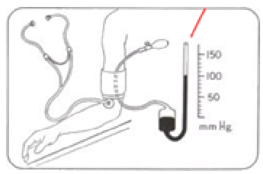
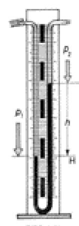
$P...Pressure\ [Pa]$
$F...Force\ [N]$
$A...Area\ [m^2]$

Table 2: Conversion table for different units

Pa	mmHg	meter water column	bar	Atm
100 000	**750**	**10.197**	**1**	-
133	**1**	0.0135	0.0013	0.0013
101 300	**760**	**10.33**	1.013	**1**

Pressure measurement Basic principle

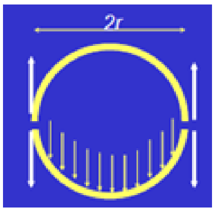
Table 3: Pressure gauges with liquid column (mercury or water)

Designation	Measuring device	Functionality	Picture
Absolute pressure	Barometer	At the top the glass cylinder is closed and at the bottom it is open. Due to gravity the liquid sinks to the bottom, the air pressure counteracts this via the open end.	
Relative pressure	Pressure gauge	U-tube pressure gauge. Due to the pressure difference on the two sides of the U, the pressure always shifts to the open side of the pipe until a balance of forces is restored.	
Differential pressure	Differential pressure indicator	Different pressures act on the liquid in the pipe from both openings of the measuring device. Where the pressure is higher, the liquid column is lower.	
-	Mechanical or electrical pressure measuring device	The fluid bends a membrane in the measuring device.	

Strain (*Druck*)

In veins, the vessel wall must exert a balancing force against the prevailing pressure. This causes tension in the wall. This tension is proportional to pressure, radius and wall thickness. The following formulas result from this.

Table 4: Rule according to Laplace

for cylindrical objects	for spherical objects	Definition	Picture
$\sigma = \frac{P \cdot r}{d}$	$\sigma = \frac{P \cdot r}{2 \cdot d}$	$\sigma ... wall\ stess\ []$ $P ... Pressure\ [Pa]$ $r ... radius\ [mm]$ $d ... wall\ thicknes\ [mm]$	

1. Stress: Force/area
2. Tension: Force per length
3. Strain: Relative change in length due to stress

The Laplace rule is important for the clinical treatment, not following it can result in various negative consequences for the patient. This is the most important one:

- at the same pressure the tension increases linearly with the diameter of the vein.
- the tension in the wall increases when the wall is thinned.

Due to the elastic properties of the vessel wall, increased stress leads to elongation (increase in vessel diameter). This relationship is highly non-linear, due to the effects of both the elastin and collagen components.

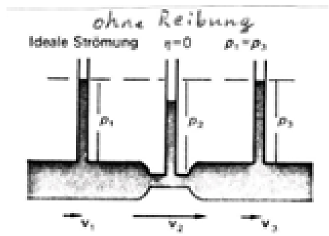
Flow, continuity equation

The following relationships apply to liquids. Of particular clinical interest is the fact that, in closed vessel systems, A*v=const. applies to every cross-section.

$$Q = A \cdot v$$
$$v_{mean} = \frac{Q}{A}$$
$$A \cdot v = const.$$

$Q ... Volume\ velocity\ [m^3/s]$
$A ... Area\ [m^2]$
$v_{mean} ... Flow\ rate\ [m/s]$

Table 5: Bernoulli equation without friction

Dynamic pressure	Gravity pressure	Static pressure	Definition
$P_{dyn} = \frac{1}{2} \cdot \rho \cdot v^2$	$P_{stat} = \rho \cdot g$	$P_{hydrost} = \frac{F}{A}$	$P_{dyn}...hydrodynamical\ pressure\ [Pa]$ $P_{stat}...hydrostatic\ gravity\ pressure\ [Pa]$ $P_{hydrost} hydrostatic\ pressure\ [Pa]$ $\rho...Density\ [kg/m^3]$ $v...Flow\ rate\ [m/s]$ $g...gravity\ [9.81\,m/s^2]$ $h...high\ [m]$ $F...Force\ [N]$ $A...Area\ [m^2]$
If the friction is zero, the sum of the pressures (=energy) also remains constant. $P_{hydostat} + P_{stat} + P_{dyn} = const.$			

Viscosity

Viscosity occurs because the liquid adheres to each other (adhesion) and to walls (cohesion). The resulting friction depends on the speed of the individual layers. This friction is also called shear rate.

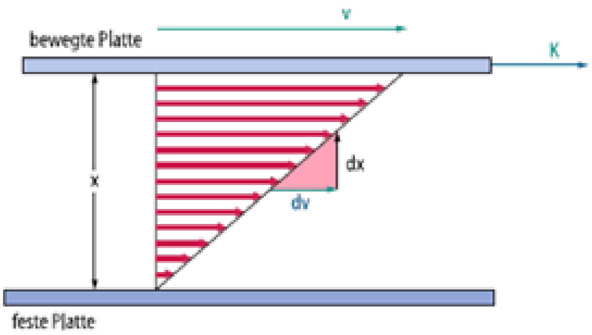


Figure 1: The fluid is sheared between fixed plate (bottom) and moving plate (top).

$$\dot{\gamma} = \frac{dv}{dx}$$

$$F = \eta \cdot A \cdot \frac{dv}{dx}$$

$\dot{\gamma}...shearrate\ [1/s]$

$dv ... difference\ in\ speed$ []
$dx ... distance\ of\ the\ plate$ []
$F ... Force\ [N]$
$\eta ... dynamic\ viscosity\ [Pa \cdot s]$
$A ... Area\ [m^2]$

A Newtonian fluid is a fluid with linear viscous flow behaviour. The shear rate is proportional to the shear stress. Non-Newtonian fluids do not behave linearly. Especially in multiphase fluids, fluids with long molecules or fluids with trapped particles, the interactions between the fluid components become very difficult. Blood is a non-Newtonian fluid.

Blood has a viscosity of 0.0035 - 0.0038 Pa*s in fast flowing vessels. This corresponds to a viscosity 3.5 times higher than that of water. As the flow rate decreases, the viscosity increases. In order to reduce the viscosity even in small capillaries and thus also the capillary resistance, the erythrocytes use various tricks such as the Fahraus-Lindqvist-Effect.

Liquids can also flow laminar or turbulent. The transition between these two types is very rapid and can be determined by the Reynolds number.

- 2000 - 2500 $\rightarrow$ Laminar
- $>$2500 $\rightarrow$ Turbulent

The Reynolds number is made up of

$$Re = \frac{Speed \cdot Diameter \cdot Density}{Viskosity}$$

Friction in pipes

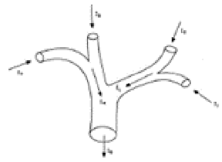
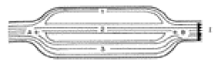
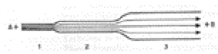
Hagen Poiseuille's law states that, due to friction on the wall and in the fluid, energy is converted into heat, and this loss of energy is reflected in a pressure drop between the beginning and the end of the pipe.

For laminar currents the following relationship exists: $\Delta P = \frac{8 \cdot Q \cdot \eta \cdot l}{\pi \cdot r^4}$

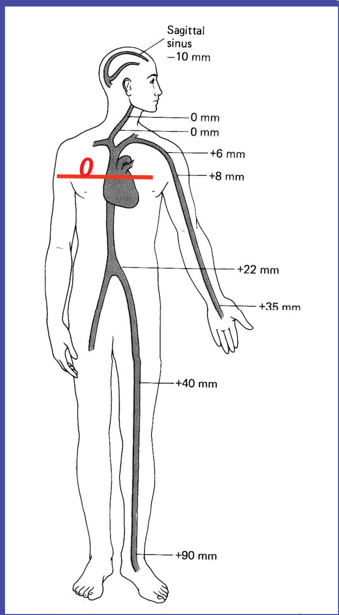
$\Delta P ... Pressure\ difference\ [Pa]$
$Q ... Volumen\ velocity\ [m^3/s]$
$\eta ... Absolute\ viscosity\ [Pa \cdot s]$
$l ... Length\ [m]$
$r ... Radius\ [m]$

Vasculature

Table 6: Kirchhoff has established several laws for incompressible liquids, all of which apply

Act	Formula	Definition	Picture
The sum of the incoming volume flows is equal to the sum of the outgoing volume flows	$I_{ges} = I_1 + I_2 + I_3$	$I ... Current\ [A]$	
With parallel pipes, the volume flows are inversely proportional to the resistance of the pipes	$I_{ges} = I_1 + I_2 + I_3 = \frac{\Delta P}{R_1} + \frac{\Delta P}{R_2} + \frac{\Delta P}{R_3}$	$I ... Current\ [A]$ $\Delta P ... Pressure\ differenve\ [Pa]$ $R ... Resistance\ [\Omega]$	
With serial combination of pipes the pressure drops add up to the cumulative pressure drop	$P = P_1 + P_2 + P_3$	$P ... Pressure\ [Pa]$	

Gravity Caused Pressure (I):



Pressure caused by the weight of the liquid column:

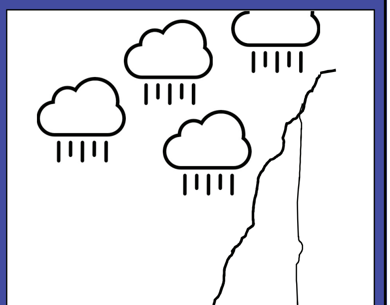
The pressure in the veins of the foot in a standing person is similar to that in the arteries at heart level!

The pressure in the veins of the head is negative – Danger of air embolism in patients with head trauma,
and in patients with catheters in the jugular vein !

The reference level is the level of the cardiac atria !

Gravity Caused Pressure (II): Counter-Intuitive Effects

Prevention of flood of the Danube in Wachau – Thin walls are sufficient!



Rainfall in mountain area with a small gap in the Swiss alps.....

1.2 Invasive Blood Pressure Measurement

Pressure Sensor

A pressure sensor converts the force caused by the pressure into a change in resistance by deforming a membrane.

The sensitivity of the sensors can be improved by a Wheatstone bridge in which the pressure influences the sensors both negatively and positively. In this way undesirable side effects can also be compensated.

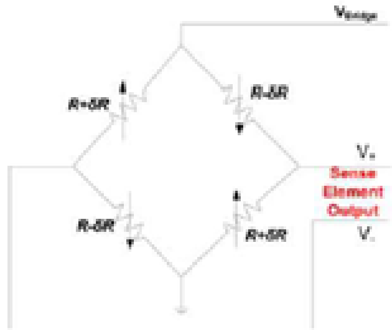


Figure 2: Wheatston Bridge.

Tip catheter

In tip catheters, the sensor is mounted in the tip of a catheter and therefore requires no mechanical transmission. This leads to an excellent frequency response. A problem is that zero calibration is not possible at the measurement location.

Invasive blood pressure measurement

As tip catheters are very expensive and do not allow zero calibration, pressure measurements with liquid filled catheters are preferred as they transmit the pressure to a sensor. To avoid clotting at the tip of the catheter, a saline solution must be administered continuously. Additionally the signal is consumed due to the damped oscillating circuit.

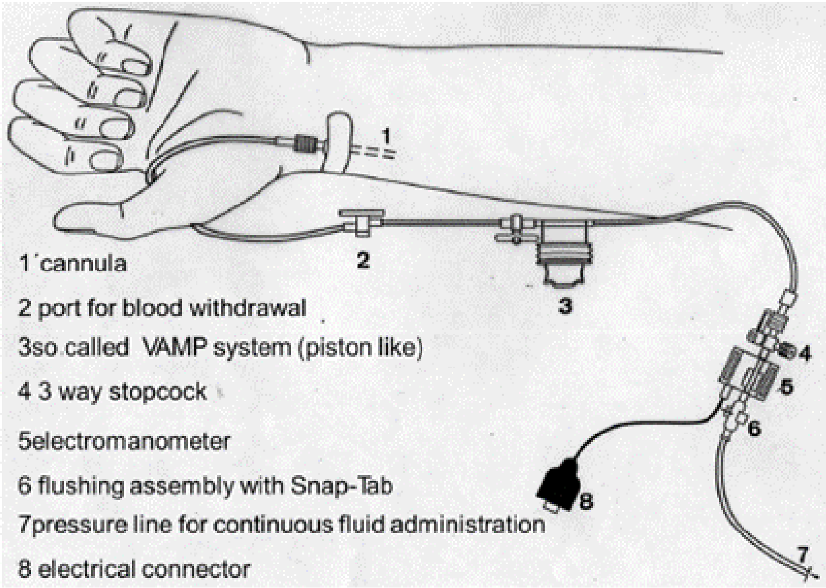


Figure 3: Setting an invasive measurement including flush.

Central venous catheter

The main tasks of a central venous catheter are

1. Evaluation of the central venous pressure
2. Evaluation of mixed oxygen saturation (vena cava superior and inferior)
3. Infusion
4. Acute dialysis or blood apheresis

Important! Each hose needs a clamp, otherwise air can be sucked in. If the insertion is not tight, bleeding can occur.

Depending on the position of the catheter tip (downstream or upstream), the dynamic pressure caused by the kinetic energy increases or decreases the measured pressure.

Blood Pressure (BP) Classification	Diastolic	Systolic	Treatment
Normal:	<80 mmHg	<120 mmHg	Normal
Prehypertension:	80–89 mmHg	120–139 mmHg	No antihypertensive drug
Hypertension Stage 1	90–99 mmHg	140–159 mmHg	ACE, ARB, β-blocker
Hypertension Stage 2	>100 mmHg	>160 mmHg	2-Drug combination

Figure 4: Classification and management of blood pressure.

Intracranial pressure measurement

Important for diagnostics and therapy monitoring in brain trauma.

Pulmonary artery catheter

This catheter has an inflatable balloon at its tip, which allows the inflow from the veins through the right ventricle into a side branch of the pulmonary artery.

Carbon monoxide (CO) determination by thermodilution

Cold saline solution is rapidly infused into the right atrium and the transport properties in the pulmonary artery are measured. This provides information for determining cardiac output.

1.3 Data acquisition of biosignals: The path from event to computer to reliable result

Sensors

Sensors convert physical and chemical quantities into electrical signals. In doing so, they should fulfil the following requirements:

1. high sensitivity
2. good biocompatibility
3. good dynamic behaviour
4. Robustness
5. etc.

To detect and display the signals without distortion, the following important points must be observed:

1. Selection of electrode/contact gel

2. Length, shielding and routing of the measuring cable

3. Amplification of all relevant frequencies

4. Filtering of disturbances

5. sufficient sampling rate (= acquisition time)

6. sufficiently good resolution

Accelerometers

An accelerometer consists of a spring-mass combination. The deflection of the mass, when the speed changes, is recorded. As the object oscillates there is a resonance frequency, signals near this frequency are displayed exaggerated.

In order to achieve a sufficiently good receptivity, a minimum size of the measurement dimensions is necessary. This additional weight can in turn influence the movement process.

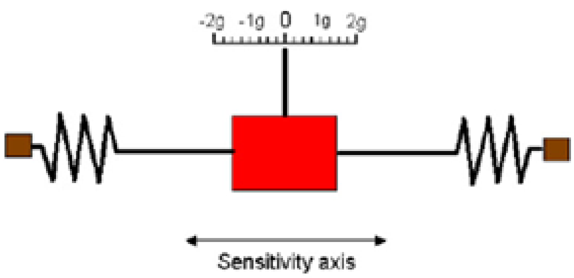
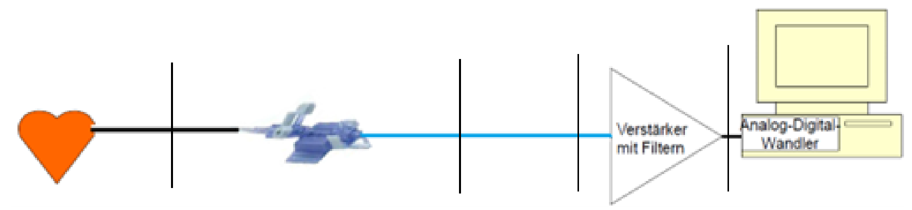


Figure 5: Schematic structure of an accelerometer.

Table 7: The three possibilities of pressure of liquids

Picture						
Designation	Vessel	Catheter	Pressure Sensor	Manag-ement	Amplifier with filter	Analoge-Digital (AD) con-verter
Function	Measuring object	Mechanical transmis-sion	electrical converter	Measuring line	Level adjust-ment and filtering	Signal conver-sion
Error	Influence of punc-ture pain on the patient	Air bub-bles or constric-tions in the catheter	Incorrect zero point ad-justment	electrical brum/noise	wrong fil-ter limits	too rarely read in; too rude gradation

A catheter works in such a way that the membrane in the pressure sensor is moved by the blood pressure in the blood vessel over the fluid column in the catheter. The friction in the catheter tube, the mass of the fluid column and the elasticity of the tube and membrane modify the original signal (resonant system). High frequencies (= rapid changes) are transmitted only poorly, while in the area of resonance of the column an increased transmission takes place.

It should also be noted that the errors and disturbances in the entire transmission chain should be kept as low as possible. Nevertheless it is possible to correct errors afterwards if you know which component causes which error. BUT once lost information cannot be recovered!

Signal level, signal-to-noise ratio

If the interfering signal is in a different frequency range than the wanted signal, it can be reduced by filtering. If the interference is randomly distributed, it can be reduced by repeated measurement or correlation.

Table 8: Comparison of the possible types of errors occurring during measurements

	Systematic measurement errors = methodological errors	Statistical measurement errors
Reason of origin	Error in or during operation of the measuring instrument	Random influences with each measurement, always occur with different values
Special feature	Can not be reduced by repeating the measurement. If the error is known, the result may be corrected.	Can be reduced by repeating the measurement and forming averages.
Examples	• Bent measuring pointer • too heavy transducer • wrong choice of filter frequencies • Incorrectly taught-in reading of the system	• Air pressure fluctuations between measurements • Noise • Non-correlated interference signals
Countermeasure	• Comparison measurements on known quantities/with other methods • Checking the measurement conditions • Modification of the measurement setup	• Repeated measurement • Mathematical correction

Measuring chain of an invasive blood pressure measurement

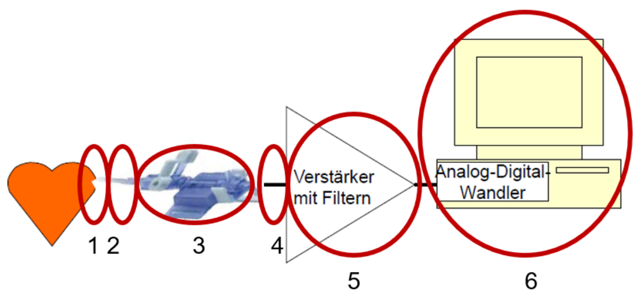


Figure 6: Structure of the measuring chain of an invasive blood pressure measurement with numbering of the individual influencing points which are explained in more detail

1. Catheter Tip Every measurement affects the object to be measured, therefore, care should be taken to ensure high biocompatibility in order to keep this interference as low as possible or not to damage the measuring device. The measurement procedure should be specific and sensitive to make it as insensitive to interference as possible.
   The catheter tip can exert the following influences on the test object:
   a) Catheter opening can be placed against the vessel wall

b) Catheter can fling through the pulsation

c) Blockage of the catheter due to blood clot

d) Catheter can irritate the vessel

2. Hose line The fluid column is influenced by the interaction of fluid inertia, elasticity of the tubing and sensor as well as mechanical/chemical transmission.
   The liquid can have the following effects:

   a) Transmission system can interfere with signal frequencies due to the natural frequency

   b) Faults can be coupled into the system

3. Sensor Depending on the measuring principle, the conversion of the measured variable into an electrical variable practically always has offset, gain and linearity errors.
   The errors are caused by:

   a) Pre-expansion of the membrane

   b) non-linear strain behaviour

   c) imprecise conversion of signals mechanical/electrical

   d) Wear and temperature

4. Management Cables can contribute to interference in the measurement signal due to electromagnetic effects:

   a) Brom,

   b) Radio frequency interference

   c) Crackling

5. Measuring amplifier The measuring amplifier should amplify, monitor (overrange alarm) and condition a precisely defined signal to such an extent that it can be used for further signal processing. Nevertheless, the user must always be aware of the signal properties that are passed on, as these are essential for the respective result.
   Possible measuring errors of the measuring amplifier:

   a) Incorrect gain setting

   b) Poor choice of filter limits

   c) Excessive load on the sensor

   d) Output load too high

6. AD converter For computer processing, the previously analog signal must be digitized. For this purpose, the signal is measured at specified intervals and converted into a digital value.
   The following characteristic values are of particular importance:

   a) Input voltage range: specifies the range in which the signal may be located; if a measured value is above/below this range, the lowest/highest value is assumed

   b) Resolution: indicates the number of steps into which the measuring range is divided ; indicated in 2n bit

c) Sampling rate = Sampling rate: specifies how often per second the measurement is performed; the sampling rate must be at least double the frequency of the highest in the signal the frequency of the frequency that occurs! (=sampled- theorem of Shannon); if the sampling theorem is not fulfilled, "aliasing" occurs

1.4 Noninvasive Blood Pressure Measurement

Pressure

The blood pressure in the human body can be influenced by two main factors:

- Gravity
- Age of the person

Hypertension (= increased blood pressure without a recognisable cause) can be caused by several factors which can be divided into two groups. Secondary hypertension is high blood pressure caused by another disease.

The pressure distribution depends on the vasoconstriction (= contraction of the vessels) in the arterioles.

Table 9: Factors for high blood pressure, only the most common ones are listed

Secondary hypertension	Risk factors
1. chronic kidney disease	1. Family burden
2. hormonal imbalance	2. Smoking
3. Atherosclerosis	3. Diabetes (Type I or II)
4. Stenosis of the renal arteries	4. Alcohol abuse
5. etc.	5. etc.

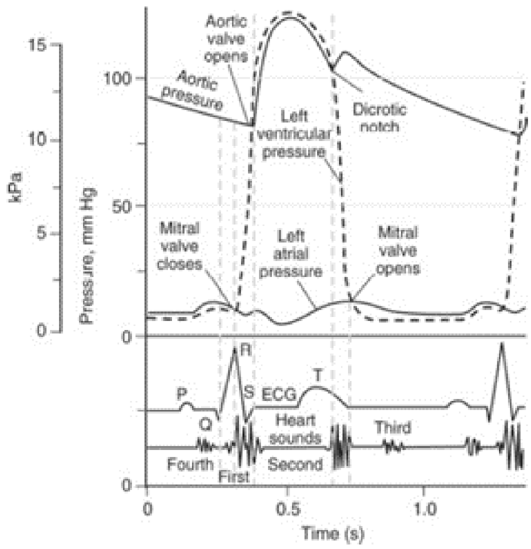


Figure 7: Above: Pressure in the left atrium, ventricle and aorta; Below: ECG and heart sounds

The average pulse rate is calculated using the formulas.
Heart near arteries:
$P_{mean} = P_{dia} + \frac{1}{2} \cdot (P_{sys} - P_{dia})$

Heart distant arteries:
$P_{mean} = P_{dia} + \frac{1}{3} \cdot (P_{sys} - P_{dia})$

$P_{mean}...mean\ arterial\ blood\ pressure\ [mmHg]$
$P_{dia}...diastolic\ blood\ pressure\ [mmHg]$
$P_{sys}...systolic\ blood\ pressure\ [mmHg]$

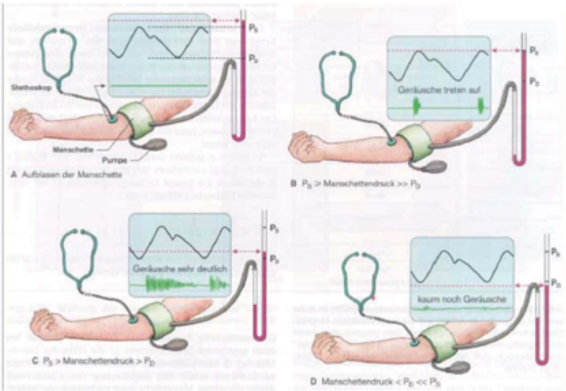


Figure 8: Blood pressure measurement according to Riva-Rocci with representation of the occurrence of the Korotkow sounds

Riva-Rocci invented the arm cuff. By reading the pressure on the manometer you can determine the systolic blood pressure. Korotkov improved this technique by adding a stethoscope. The Korotkow sounds indicate the systolic blood pressure by their appearance. You disappearing marks the diastolic blood pressure.

Although there are no precise guidelines for cuffs, it should be noted that the width should be 40% of the upper arm and the inflatable part 80% of the upper arm.

Instructions for non-invasive blood pressure measurement on the upper arm:

1. Inflate the cuff until the cuff pressure is approximately 30 mmHg higher than the systolic pressure.
2. Release the air in the cuff at a speed of approx. 2-3 mmHg/sec
3. Occurrence of knocking sounds (Korotkow sound) $\longrightarrow$ Systolic blood pressure
4. Decrease or disappearance of noise Auscultatory gap
5. Increasing the noise level
6. Abrupt start of damping
7. Disappearance of the sounds $\longrightarrow$ diastolic blood pressure

Penaz' method: continuous, non-invasive

In this method, the continuous vascular discharge is caused by a constant adjustment of the cuff pressure, this is done by a Proportional–integral–derivative (PID) control. The photoplethysmograph sends a feedback signal which adjusts the cuff pressure to maintain the vascular discharge.

Some Reasons for Hypertension

Frequently the causes for an higher than normal blood pressure cannot be found. This situation is named **Primarily increased blood pressure** or **Essential hypertension.** In most cases several risk factors are involved such as:

- Familiy history in respect to hypertension, stroke or heart attack;
- Life style such as overweight, smoking, alcohol or drug abuse, stress, low physiological activity

Secondary Hypertension can be caused by deseases such as

- Chronic renal disease or stenosis of renal arteries
- Disturbance of hormone level
- Atherosclerosis and elevated cholesterin levels
- - Ulcer, ...

1.5 Diagnostics in the Circulation: Measurement Methods for Flow, Flow Velocity and Fluid Volume

The complexity of flows

Pulsatility and eddies can cause complex, stationary local patterns that affect the accuracy of flow measurements.

Table 10: Methods for measuring blood flow and velocity

• Ultrasonic Doppler	• Electromagnetic flux probes
• Laser Doppler Perfusion Evaluation	• Ultrasonic transit time measurement
• Nuclear magnetic resonance	• Spirometric method (Fick's principle)
• Laser-t-Resonance	• Thermodilution (Swan-Gantz-Catheter)
• Optical plethysmography and oximetry	• Semiinvasive contour analysis
• Impedance Plethysmography	• Angiography, Scintigraphy

Ultrasonic Doppler

An ultrasonic beam with a certain diameter is directed into the vessel under examination. The movement of the particles causes the echo signal to be shifted in frequency. However, since there are many echoes that come back from different distances (and depths of tissue), there are different methods of analysis.

The ultrasound is produced with quartz crystals which have a dipole structure. By an electrical excitation these structures contract, the piezo mechanical effect is used for detection. If the transmitter transmission is stopped, the crystal can be used as a receiver.

Table 11: Speed of ultrasound in different types of tissue

Tissue	Speed [m/s]
Air	approx. 340
Water, fat, muscle, brain	1450-1550
Bones	approx. 3600
Steel	approx. 6000

Continuous Wave Doppler ("CW Doppler")

In this type of ultrasound two crystals are used where one always sends and one always receives. Due to the continuous signal, the time between transmission and reception, which would give information about the distance between sensor and target, is not known. Therefore the maximum frequency shift from the signal mixture is used to determine the maximum velocity within the volume covered by the ultrasonic beam. This type of measurement does not provide depth information but only maximum velocity information.

First the vessel is identified in B (= Brightness) mode, then the beam direction is defined and the CW echo is displayed in an fd time diagram.

$$f_d = 2 \cdot f_t \cdot \frac{v_{bloos}}{c} \cdot \cos\Theta$$

$f_d ...Doppler - shift\ [Hz]$
$f_t ...durch\ gelassener\ Strahl\ [Hz]$
$v_{bloos} ...Speed\ [m/s]$
$c...Speed\ of\ ultra\ sound\ [m/s]$
$\Theta...Winkel\ zwischen\ Ultraschallstrahl\ und\ Strmungsachse\ []$

Pulsed Doppler

Instead of continuous ultrasound, sound "packets" are emitted, each containing several oscillations of the carrier frequency. The time between transmission and reception of the signal provides information about the depth of the echo structure.

$$t_{laufzeit} = 2 \cdot \frac{d}{c}$$

$t_{laufzeit} ...[s]$
$d...Distance\ [Hz]$
$c...Speed\ of\ ultra\ sound\ [m/s]$

Aliasing

If the transmission pulses are transmitted in too close a sequence, echoes from previous pulses can be misinterpreted as if they were caused by a later pulse. This can lead to mixing and mirroring effects and must be corrected by choosing the correct pulse repetition rate and intensity.

Nuclear magnetic resonance (NMR)

During NMR imaging it is possible to determine local blood velocities by means of targeted magnetic marking and subsequent tracking of the marked particles, this is also possible in 3D format.

Laser Doppler Perfusion Measurement

A small sensor is positioned in a place with thin epidermis. The perfusion in the capillary bed can be estimated from the Doppler frequency shift of the light reflected from the capillary bed.

Transmission and reflex plethysmography

A cuff placed around the finger, which contains an infrared diode and a sensor, can measure how much oxygen is present in the blood based on adsorption. The absorption depends on the amount of blood and the change in colour of the erythrocytes due to oxygen saturation.

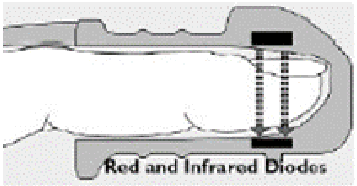


Figure 9: Image of the cuff for measuring oxygen in blood

Impedance Plethysmography

The fluid content of the vessels, heart and lungs, but also of intercellular and cellular water can be determined by changes in electrical resistance. For this purpose, 2 or 4 electrodes are positioned in the relevant area to measure the difference in resistance. This method is used to measure respiratory and heart rate.

Angiography

By injecting contrast agents during medical imaging using X-rays or CT, the vessels can be visualized including their filling times and possible stenoses or aneurysms.

Scintigraphy

In scintigraphy, radioactively labelled substances are tracked on their way into the tissue and according to the location of their accumulation. This is done with the help of gamma cameras.

Heart minute volume and oxygen transport

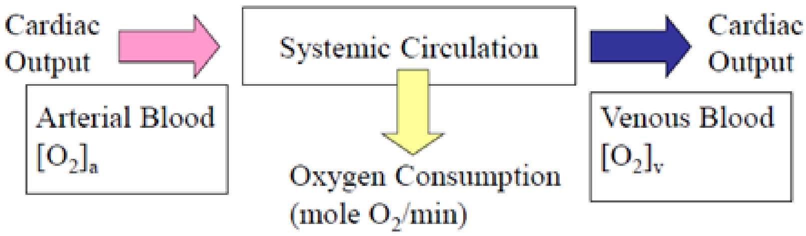


Figure 10: Spirometric CO determination

$$\left.\begin{array}{l} CO \cdot [O_2]_a - CO[O_2]_v = VO_2 \\ CO \cdot ([O_2]_a - CO[O_2]_v) = VO_2 \end{array}\right\} \quad \text{law of conservation of mass}$$

Pulmonary artery catheter

This catheter has an inflatable balloon at its tip, which allows the inflow from the veins through the right ventricle into a side branch of the pulmonary artery. It enables the measurement of central venous pressure, pulmonary artery pressure and pulmonary wedge pressure.

It can also be used to determine the CO content in the blood. For this purpose, cold saline solution is rapidly infused into the right atrium and the transport properties to the thermistor in the pulmonary artery are measured. This measuring method can only be used in a limited number of cases.

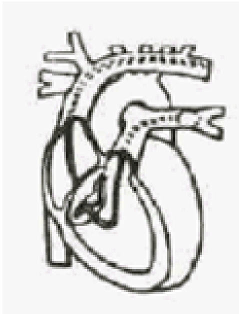


Figure 11: Pulmonary artery catheter in the heart

Invasive flow measurement with electromagnetic probes

If a conductor or a conductive liquid is moved through a magnetic field, an electrical voltage is built up transversely to the magnetic field and the direction of movement (law of induction). This voltage depends on the strength of the magnetic field, the geometry and the speed of the movement.

Due to its disadvantages, such as the sensor has to bypass the entire vessel, electrons have to touch the vessel, etc., this measuring method is hardly used in medicine anymore.

Ultrasonic transit time flow determination with invasive sensors

or accurate and uninterrupted measurement of the time-dependent flow, sensors are wrapped around the vessel based on the ultrasonic transit time effect. This effect is based on the fact that when the signal

- is directed towards an upstream current is slowed down.
- is directed towards a current flowing downstream is accelerated.

The system integrates the information of the local speeds, so an average value is obtained which then represents our signal. However, the accuracy depends on the hematocrit, temperature, vessel thickness and, in the case of tubes, the tube material.

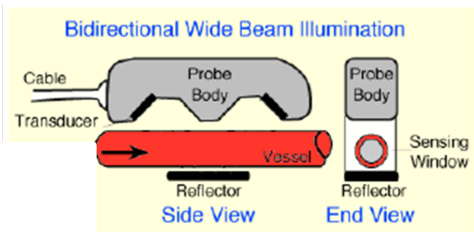
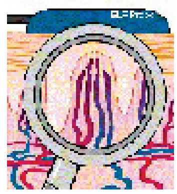


Figure 12: Sensor for flow determination

Laser-Doppler-Perfusion Measurement/Estimation:

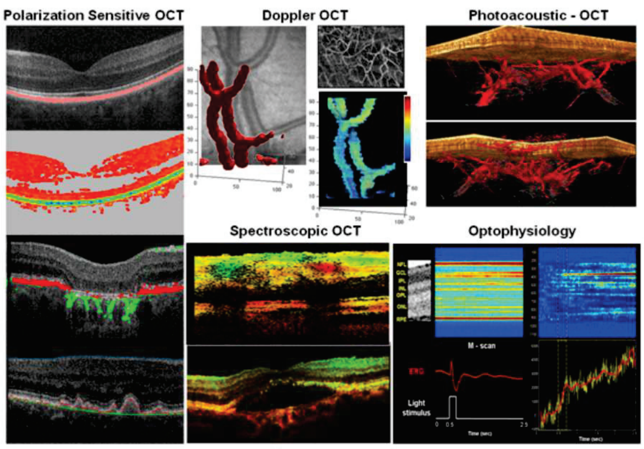
The perfusion in the capillary bed kan be estimated from the Doppler-Frequency shift of the reflected light from the capillary bed.
For this purpose a small sensor is positioned above a location with thin epidermis.
This technology allows a semi-quantitative estimation of alterations of perfusion during a measurment. A repeatability with replaced sensor is possible only very limited due to the high influence of the actual sensor position on the result.



 H.Schima 22

Optical Laser Tomography and Doppler Measurement

With more sophisticated lasers, the superficial skin and also the retina can be investigated both with tomographic approaches and Doppler velocity ment. Several groups in our center are on the frontiers of this research. Details of the variety of methods would exceed this presentation.



In addition to the visualization of microscopic, cellular tissue morphology, extensions of OCT enable contrast enhanced imaging as well as detection of localized tissue function.

https://zmpbmt.meduniwien.ac.at/wissenschaft-forschung/optical-imaging/oct/ H.Schima 22

2 FH TW-WS2020-MHE

2.1 Biocompatibility and Blood compatibility
A short Overview

Definition of Biocompatibility

- Application time: From minutes to days, months and life time
- Durability (*Lebensdauer*): From resorb-ability (*Resorbierbarkeit*) to lifelong interia
- Mechanical Properties: Elasticity, Flexibility, Strength, etc.

Biocompatibility is the property of a material to archive an appropriate (*angemssene*) defensive reaction at a specific use.

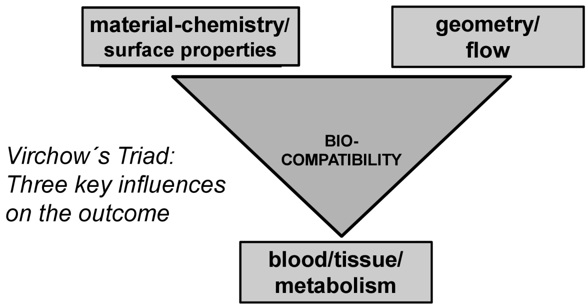


Figure 13: Virchow's Triad

Tensile stress test (*Zugprüfung*)

$$\sigma = \frac{F}{A}$$

$$\varepsilon = \frac{(l_1 - l_0)}{l_0} \cdot 100$$

$$E = \frac{\sigma}{\varepsilon}$$

$\sigma ... Tension\ (Zugspannung)\ [N/m^2]$
$F ... Force\ [N]$
$A ... Cross\ section\ area\ [m^2]$
$\varepsilon ... Strain\ (Dehnung)\ [\%]$
$l_1 ... Deformation\ length\ [mm]$
$l_0 ... Original\ length\ [mm]$
$E ... E - module (Elastizitätsmodul)\ [N/m^2]$

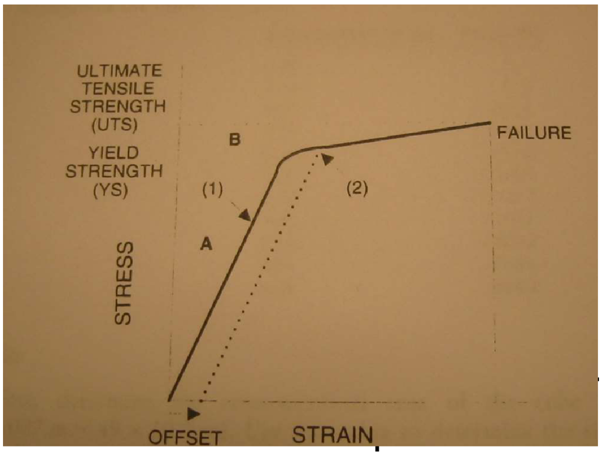


Figure 14: Tensile stress test; A elastic region, B plastic region

Yield point ($Streckgrenze$); where material begins to deform permanently.
Metall 0,2 %
Plastics 2 %
The peak stress which is attained at failure is called ultimate tensile strength ($Bruchfestigkeit$)
ductile ($dehnbar$)→stretches much
brittle ($spröde$)→not deform much

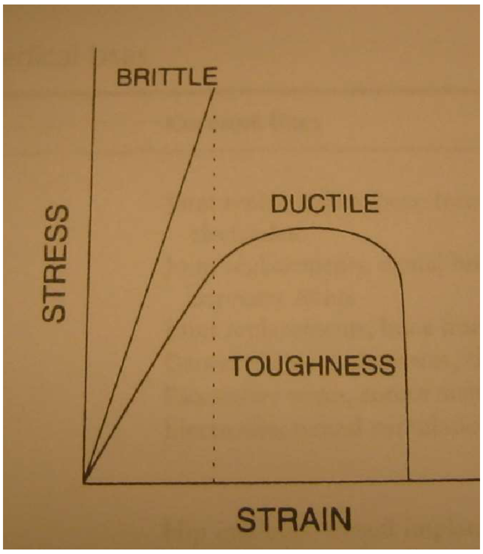


Figure 15: Yield point

Stress shielding is when the stress ($Belastung$) transfer between an implant and bone is not homogenous→different E-moduli. It can be came to an bone atrophy ($Knochenschwund$). To solve this problem you should take an material for the implant with the near same E-moduli as the bone is.

Materials used for implants: Metals

Table 12: List of different metals an there properties

Name	Properties	Disadvantages	Applications	Example
Stainless steel (*Edelstahl*)	strong, though, ductile	corrosion, high e-moduls, stress distribution (*Spannungs − verteilung*)	artificial hip, osteosynthesis, plants, screws	CrNiMo
Titanium	no corrosion		bone/joint, replacement, surgical instruments, etc.	TiAl6V4
Memory alloys (*Legierung*)	three different shapes		self-expanding stents	Nitinol
Magnesium			cardiovascular, orthopaedic	Mg

Materials used for implants: Ceramics

Table 13: Pro and con for ceramics

Advantages	Disadvantages
• inert (*reaktionsträge*) • low wear rates (*Verschleissrate*) • resistant to microbial attacks • strong in compression • do not conduct heat and electricity • direct bone bonding possible	• brittle (*spröde*) • potential to fail catastrophically • difficult to machine (*bearbeitung*) • very high melting point

Figure 16: Classification by chemical composition

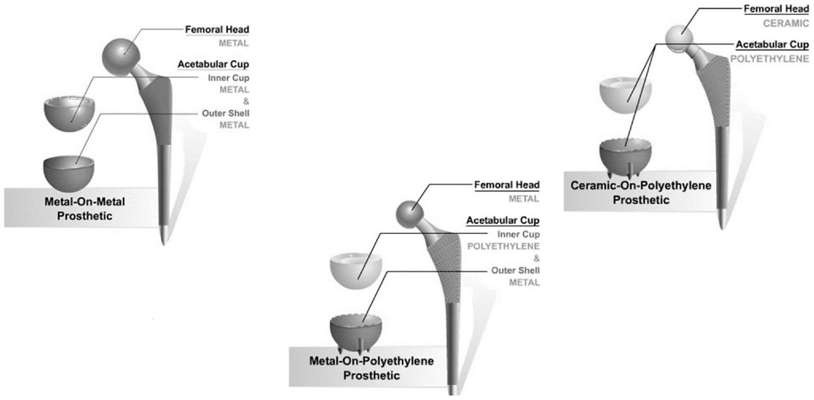


Figure 17: Can make of combination of metal, ceramics and plastics. Choice what are implant depends on the patient.

Materials used for implants: Plastics

- Synthetic Polymers e.g. Thermoplasts, Elastomers, Duromers, Thermoelastics
- Biological Polymers e.g. Collagen
- Accellularized Matrices

Table 14: Synthetic Polymers

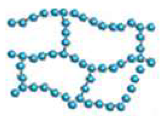
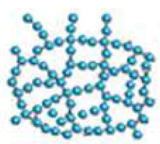
Name	View	Structure	Work
Thermoplastic		molecules linked by intermolecular forces	material softens, when it get heat and returns to original condition when it get cooled
Elastomer		molecules are joined ($verbunden$) by chemical bonds and are slightly crosslinked	high elongation ($Streckung$), flexibility elasticity thermoplastic elastomers melt when heated thermoset elastomers not
Thermoset		usually 3D networked and high degree of cross-linking	irreversibly solidifies insoluble ($unlöslich$)

Table 15: List of all polymers

Name	Type	Properties
Polycarbonate	Thermoplastic	good manufacturing properties, durable, limited strengh
Polymethylmethacrylate PMMA, Plexiglas	Thermoplastic	high stiffness, good manufacturing properties, sensible to alcohol contact
Polysiloxane Silicone	Elastomer	compatible to soft tissue, hemocompatibility, limited mechanical properties, lipoabsorption
Polyurethanes	Thermoplastic and Elastomer	broad spectrum of types low amount of diffusive solvents
PVC	Thermoplastic	excellent mechanical properties, the includes softeners are genotoxic
Polyamids	Thermoplastic	excellent strength, surgical sutures ($Nähte$)
Polyoxymethylen POM	Thermoplastic	high stiffness, high dimension stability
Polyethylene Terephatalate PET	Thermoplastic	
Polythetrafluoroethylenen PTFE	Thermoplastic	
ePTFE	Thermoplastic	porosity

Biofunctional and bioresorbale polymers

Biofunctional Polymers can be coated ($beschichtet$) with pharmacologically active materials e.g. Anticoagulants, Antibiotics, Growth factors. The coatings can be either catalytic or with a defined released time ($Freisetzungszeit$).

Biomimetric materials: Inclusion of functional groups (e.g. receptors, membranes) into biological materials.

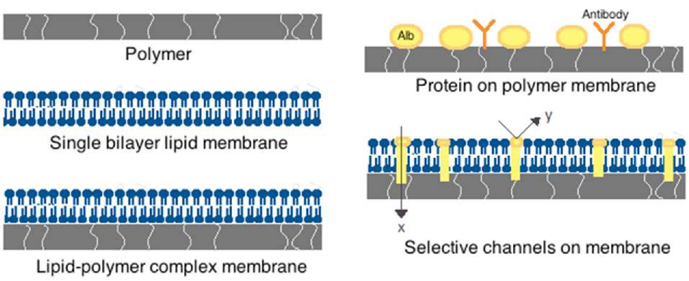


Figure 18: Biomimetric membranes

Nanostructured Materials

Cells are sensitive to the mechanical properties ($Eigenschaften$) of their environment ($Umgebung$), so it is necessary to create smaller structures to minimise this negative influence ($Einfluss$). The increase of the surface layer also helps to improve ($Verbesserung$) the pharmacological activity.

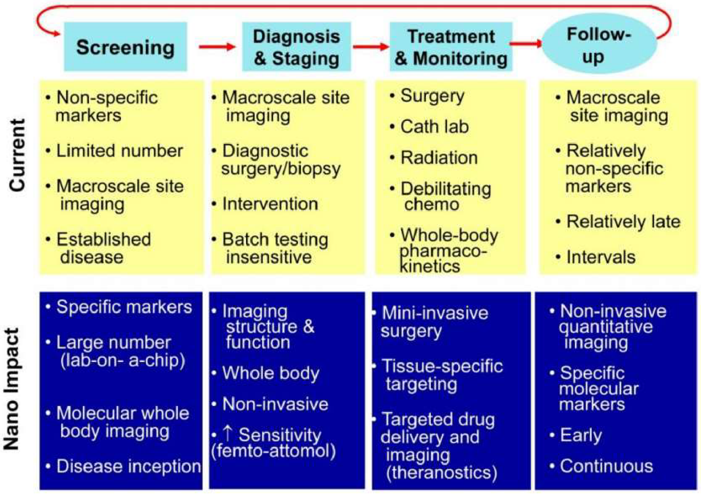


Figure 19: Proposed impact of nanotechnology

Methods for Nanostructuring

- Mixing with non solvable agents, to cause foam-like structures
- Lithography[1]
- Printing
- Electro-Spinning

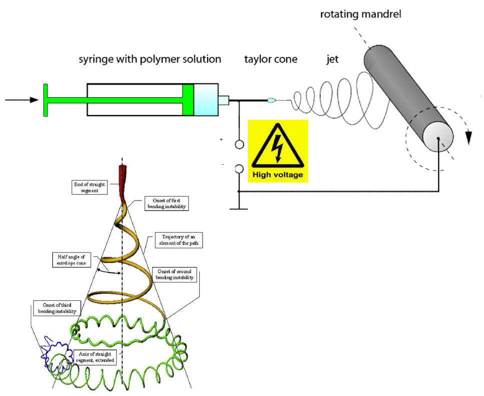


Figure 20: Electro-Spinning; By fast moving targets you control the porosity, fiber orientation and biomechanics

[1]Lithography = Buchdruck, Druckplatte auf Medium pressen

Table 16: Potential biomedical applications of some nanoparticles

Material	Applications	Comments
Quantum dots	Imaging and tracking by fluorescence	emitted wavelength depends on the size of the nanocrystal, can be coupled to antibodies
Iron oxide particles	Imaging and tracking by MRI	can be used to generate local heating and kill targeted tissue
Nanotubes	Biomolecular sensors	Cell tracking and MRI contrast agent
Gold shells	Biomolecular sensors	Electrocatalysis
Nanotubes	Drug and gene delivery	multifunctional agents
Liposomes	Drug delivery	Versatile biodegradable multifunctional paricles

Biocompatibility testing

Standard provided by

- Norming Institutes, e.g. ISO, EN
- Health Institutes, e.g. NIH, FDA
- Surface characterization with contact angle measurement. Provides information about protein adsorption.
- Surface characterization. Gas adsorption gives information on surface area in complex surfaces.
- In-vitro Testing
  in-vitro = in the glass
  in-vivo = animal/human testing

In-vitro do not reflect the whole spectrum of possible responses ($Reaktionen$).

Types of in-vitro, measure the initial reaction, necrotic and toxic reactions at implant side.

- Cytotoxicity tests. Various typs of cells are used.
  - Elution, cells in culture
  - Agar overlay
  - direct contact tests
- Mutagenicity and Genotoxicity tests
  Mutagens are those materials that modify the genome of the host →genotoxic. Ames-Tests use a mutant bacterial cell line when the bacteria grow you can see that you material is genotoxic.

- Hypersensitivity Tests
  for Leukocyte migration inhibition, lymphocyte transformation tests and testing individuals about there genetic sensitivity to specific materials.

- Haemocompatibility Tests
  for testing of cardiovascular prostheses
  - Simple tests with blood
  - Mock circulation tests
  - ex vivo tests

Blood tests are usually performed by comparison with control samples.

Special aspects about blood biocompatibility

Blood has to

- Transport gas
- Immunoresponse
- "Sealing" ($Abdichtung$) of the vascular system

Erythrocytes = Red blood cells (oxygen transport) by chemical binding of haemoglobin. View discs. By mechanical shear exposure the erythrocytes can be deformed and destroyed. When this the haemoglobin becomes free. For kidney and liver to much haemoglobin (> 30 mg/dl) is toxic. The allowable shear stress depends on amount ($Höhe$), duration ($Dauer$) and type (Art) of shear stress ($Scherspannung$).

Leukocytes = White blood cells
Immunoresponse, inflammatory response ($entzüngliche\ Reaktion$), phagocytosis, wound healing. View ball.

Bacteria, which can sit on surface from prothesis, deliver a complex slime which can not be attacked effectively by the leucocytes or antibiotics.

Blood platelets, Blood coagulation ($Blutgerinnung$), together with fibrin building of blood clots ($Blutgerinnseln$) for sealing defective vessels.

Blood plasma, Transport, balancing of osmotic properties, tuning ($abstimmung$) of fluidie properties 55-65% of blood volume.

Blood is a non-Newtonian fluid. The viscosity depends on the shear rate. Money roll formation of erythrocytes in slow flow.

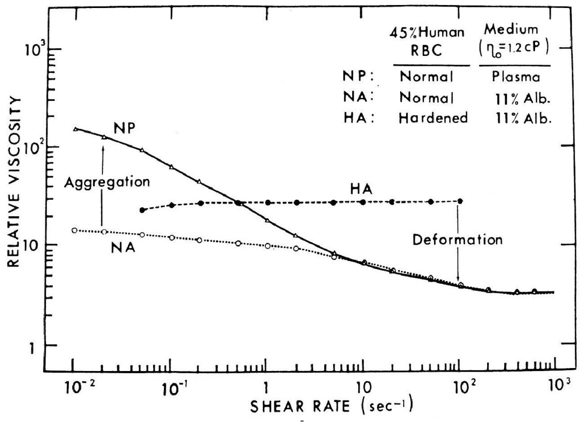


Figure 21: ↑(Zunahme) Share, ↓(dünn flüssiger) Viscosity

In the healthy organism, the clot-demanding ($Gerinungsfördernd$) and clot-inhibiting ($Gerinnungshemmend$) mechanisms are balanced so that blood clotting or haemostasis should occur. Blood clots consist of a combination of fibrin threads and platelets, with trapped erythrocytes and leukocytes involved in inflammatory reactions.

Vascular prostheses are used to replace vessels or to bypass them. The materials used are Dakron and PTFE. Due to limited biocompatibility, intimal hyperplasia[2] often occurs at the suture ($Nähte$) site.

Stents are used to reconstruct dilated vessels and to widen narrowings. They are most frequently used for coronary diseases. There is also a risk of hyperplasia here.

Damage to the heart valve can lead to stenosis[3] or insufficiency[4]. In these cases, the valve should be replaced with an artificial heart valve. Artificial valves cause a higher pressure drop.
mechanical = hard heart valve
Homograft = from donor ($Spender$)

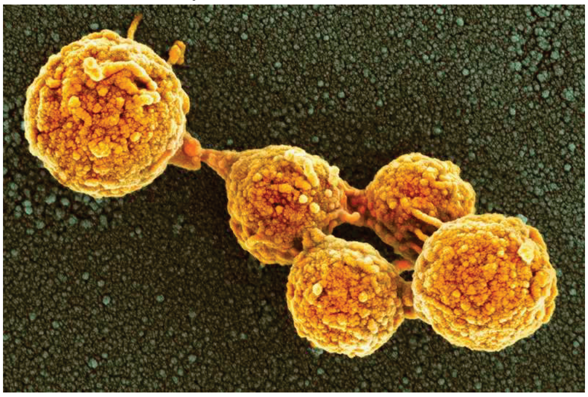
Donor valves are fixed with dehyd, which ensures that no rejection reaction is triggered. The problem with these valves is that they have a limited shelf life.

Important requirements for valve prostheses

- Low pressure drop with pressure flow (valve diameter!)
- tightness against backflow
- low blood destruction
- No formation of clots ($Gerinnung$) (mechanical valves thrombus danger - anticoagulant)
- durability

[2]Intimal hyperplasia = Unregelmäßige Bildung von Zellansammlungen
[3]Stenose = Verschluss/Verengung
[4]Insufficiency = Schäche

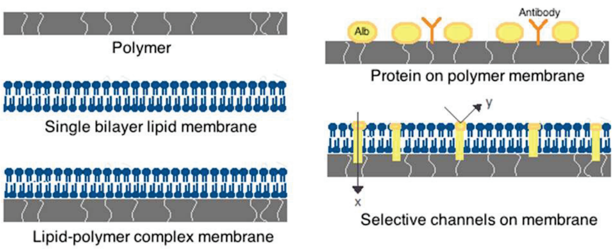
A hot topic in current research with questionable consequences:
"Artificial life made in lab can grow and divide like natural bacteria" (New Scientist 29.03.2021)



Some of the first synthetic Mycoplasma bacteria produced by Craig Venter and his colleagues

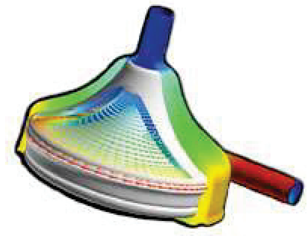
Biomimetic membranes (I):

Membranes can be designed in different complexity, thus allowing also complex functions (ideally such as cell membranes)



Source

Rotary Pumps for short term Assist: Biomedicus® since ca. 1980



The discs forward the blood by adhesion and centrifugal force: CFD of shear stress *(Simulation Keyhani et al., after 2000)*

This pump superseded in the clinical application completely already available impeller pumps.

Amazing experimental findings in our Lab in 1987 ....

Rotors with disks (such as Biomedicus were considered less traumatic, because they avoided vanes "crashing" through the blood.

But in in-vitro experiments with bovine blood rotors with vanes showed a better performance.

The best performers where those with simple straight vanes ?!?!

The group was confused, and a young unexperienced researcher discussed the his unexplainable findings with an expert from USA/Japan....

Rotor Type	Number of experiments	delta fHb/Hb (mg%)	Std. dev.
IRS6	4	5.4	7.5
IRS9	6	3.6	6.4
IRF6	10	26.9	46.7

Table 1: Increase of plasma free hemoglobin in-vitro after 3 hours of pumping:

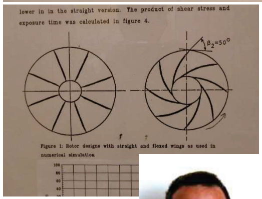
... and a stunning explanation in our coffee room from a hydrodynamic specialist from Athens in December 1988!

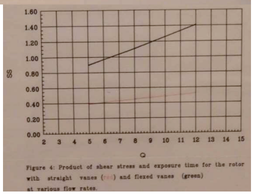
Dr. Dimitris Papantonis from the TU Athens did the -to my knowledge very first numerical simulation of blood flow in a rotary pump.

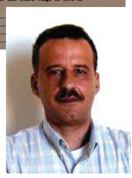
This simulation was 2-dimensional, on a small (even for those times) computer.

He explained the experimental finding with the **product of shear stress and exposure time**: This was high for vaneless rotors with discs, and lowest for the straight-vaned rotors with few inclination: In these rotors a short peak at the vane entrance accelerated the blood rapidly, afterwards not much shear was necessary to transport the blood.

IN VITRO-TESTS AND NUMERICAL STUDIES OF DIFFERENT IMPELLER DESIGNS FOR CENTRIFUGAL BLOOD PUMPS
H. Schima, D. Papantonis *), A. Wohlfahrt, G. Wieselthaler, D. Croba *), M.R. Müller, H. Thoma
Boltzmann-Institute of Cardiac Surgery, 2nd. Dept. of Surgery, Univ. of Vienna, Austria
*) Hydrodynamic Laboratory, Techn. Univ. of Athens, Greece







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The Problem of Mathematic Models of Blood Trauma

Up to now, the problem of experimental determination of blood trauma has not been solved: Blood components should be exposed to well defined shear stress for a very short time, measuring a very low percentage of blood destruction or even sublethal damage. As seen in the old example, extrapolation and ignorance of shear levels can lead to large errors.

Today, it is generally accepted, that there is a relation of shear amount and exposure time (usually modelled in a product with exponents and a sreshhold), but the absolute values, and the questions of repeated shear stress and the effects of laminar versus turbulent shear are still under discussion.

Recently, the FDA stimulated Robin-Rounds of multiple research teams to push such models forward (Malinauskas et al. ASAIO J 2017)

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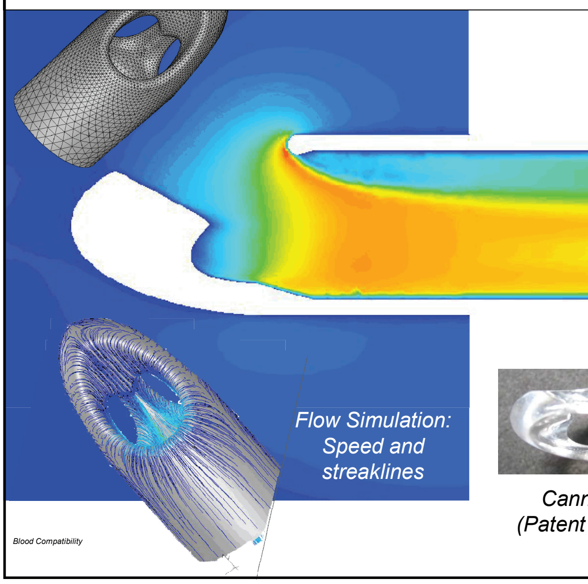
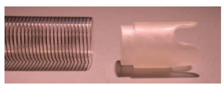
Appendix:
Some examples of cardiovascular implants
(Sorry, some explanations are in German)

Inflow cannula for a minimal invasively implanted LVAD

Requirements:
- Avoid deadwater areas
- Smooth transitions
- Limited shearstress
- Long term biocompatible material





Cannula tip
(Patent pending)

Cannula with
Heartware MVAD-Pump

Three generations of Rotary Blood Pumps

First Generation:

Mechanical bearings, with sealing or working in the bloodstream; High shear forces at the bearing rim, heat generation, flow stagnation. A "controlled" thrombus formation may in some be accepted.

Second Generation:

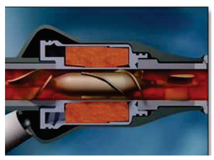
Levitated Rotor with actively controlled electromagnets; Reduced shear stress, but complex and energy-consuming.

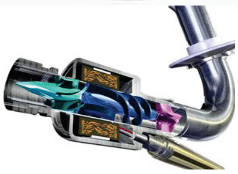
Third Generation:

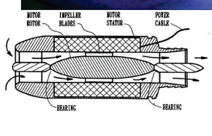
Hemodynamic bearings with passive magnets. Rotor is sliding in blood; Controlled, elevated shear.

1. Mechanical Bearings

Eva-Heart







Jarvik 2000

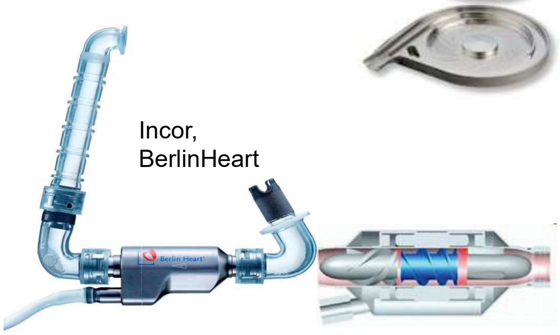
Thoratec HeartMate II

37

Actively Magnetically Suspended Impellers

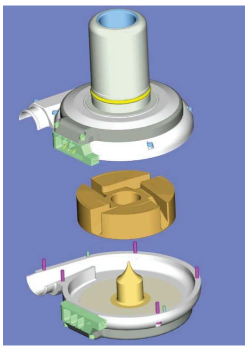
DuraHeart,
Terumo

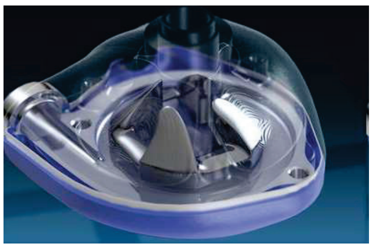
Incor,
BerlinHeart



3. Hydrodynamic Bearings

HVAD,
HeartWare





VentrAssist, Ventracor

2.2 Heart lung machine and Oxygenators

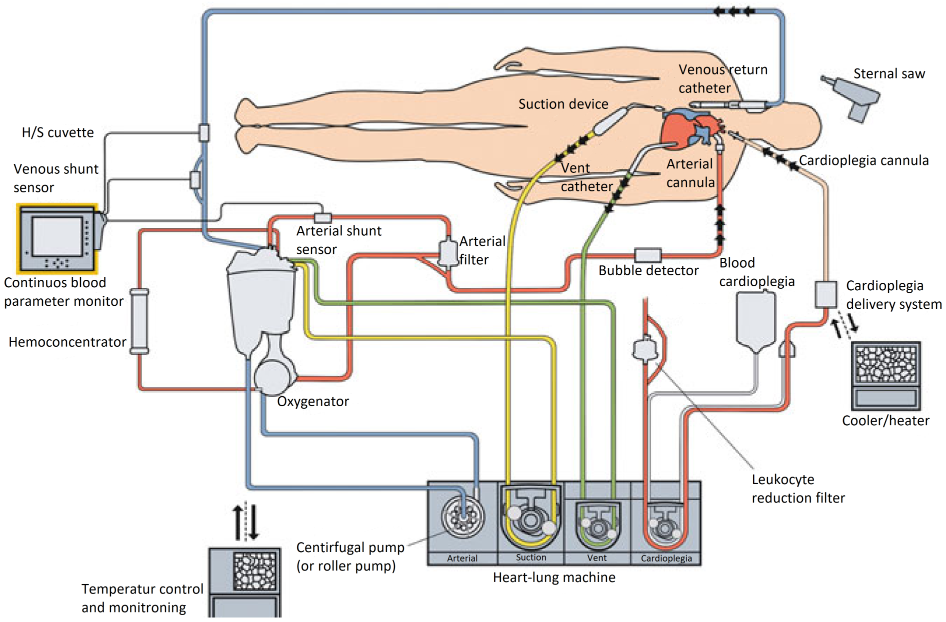


Figure 22: HLM

This system can substitute the pumping function of the heart and the gas-exchange function of the lung over several hours.

It has to provide:

- appropriate $(angemessene)$ blood removal $(abnahme)$ and blood pressure before returning to the patient
- appropriate oxygenation and CO_2-removal
- filtering
- warming/cooling
- uptake of spilled $(verschütteten)$ blood
- monitoring of vital parameters
- safety alarms and blockades

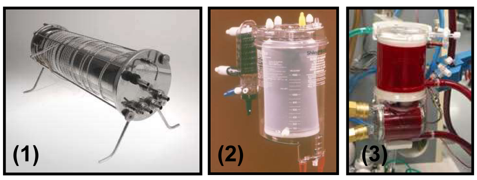


Figure 23: 1 Film oxygenators, 2 bubble oxygenators, 3 membrane oxygenators

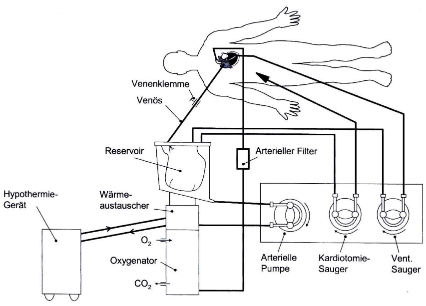
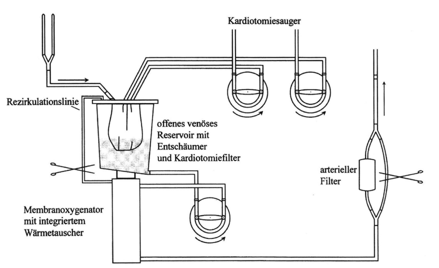
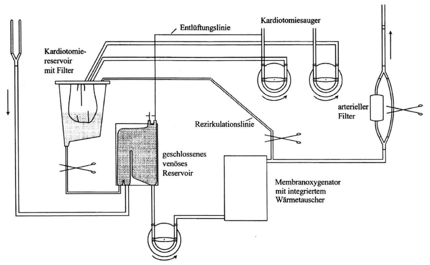
Image	Pro	Con
 Basic scheme		
 HLM open system, reservoir is open	higher priming volume, easier to manage	more blood trauma
 HLM closed system	avoids (*vermeidet*) air contact, need no defoaming (*entschäumung*)	higher complexity in components and handling

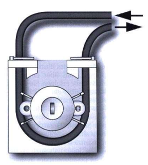
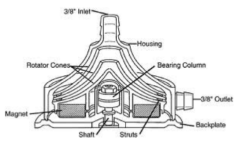
Table 17: Different HLM; Where the scissors is is the place of emergency care when the system e.g. artery filter fails

Open and closed denote (*kennzeichnet*) the possibility of venting (*entlüften*) the reservoir during operation. Open venous reservoirs are mostly constructed as hard shell reservoirs with a defoamer (*Entschäumer*). Closed venous reservoirs, on the other hand, are flexible, collapsible (*kollabierbare*) bags. Air collects at the upper end of the bag and can be removed through a valve (*Ventil*).

Components of a HLM

1. Pumps

Table 18: Different pump types which are used in heart-lung machines

Pumps	Image	Advantages	Disadvantages
Roller pumps		• cheap • flow proportional to speed • no leak at still stand	• blood trauma • spallation of tubing particles • limit durability $(Haltbarkeit)$ of tube
Centrifugal pumps		• low blood trauma • longer application time	• leak at still stand • thrombus formation • expensive

2. Oxygenators

Fick's Law: $VO_2 = \dfrac{P_1 - P_2}{L} \cdot K \cdot F$

$VO_2 ... Oxygen\ perfusion\ per\ time$
$P_1 - P_2 ... partial\ oxygen\ pressure\ difference$
$L ... Layer\ thicknes$
$K ... diffudion\ constant$
$F ... Surface$

Oxygen delivery to tissue: $DO_2 = CO \cdot CaO_2$

Oxygen consumption: $VO_2 = CO \cdot (CaO_2 - CVO_2)$

$DO_2 ... Oxygen\ delivered\ to\ tissue$
$CO ... Cardiac\ output$
$CaO_2 ... Arterial\ oxygen\ content$
$VO_2 ... Oxygen\ consumption$
$VCO_2 ... Mixed\ venous\ oxygen\ content$

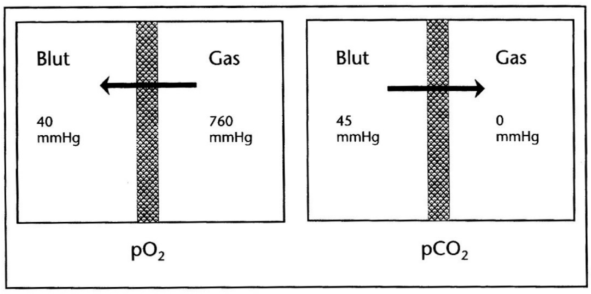


Figure 24: Pressure difference

Gas exchange can be improved by increasing partial pressure difference, turbulence, surface and decreasing blood thickness layer. Plasma should not be transfer through the membrane orifices to the gas phase.

3. Heat exchange
Nowadays he is integrate in the oxygenator. The water in the heat exchanger must not exceed 42℃.

4. Sensors and alarmsystems
Monitorong includes:

- Pressure
- Flow
- Level monitoring
- Bubble sensors
- Temperature
- Oxygen/CO_2 venous and arterial
- Hematocrit
- Timers

5. Tubings
Tubing diameters are shown in inch. For connection to pressure lines, sample removal and drug application you use Luer-Lock system.

6. Cannulas
What cannula are use depends on the inflow and outflow. The masses also in inch. After ventilation, various physiological damages can occur, such as red cell damage, memory problems, etc.

7. Reservoirs and filters
-

Table 19: Factors for O_2 in blood and CO_2 elimination

O_2	CO_2
• Thickness of the blood • Membrane material and thickness • Time of red cells in gas exchange area • Haemoglobin concentration • Inlet saturation	• Membrane long geometry • Flow rate of sweep gas • Surface area • Blood pCO_2 • Blood flow • Membrane lung ventilation flow

2.3 Cardiac Assist and Replacement An Overview

A blood pump has to:

- generate sufficient blood flow
- treat the blood particles gently ($schonendeBehandlung$)
- avoid ($vermeiden$) thrombus formation
- minimal traumatization during and after implant

It gives the following principles of blood pumps. The classification can done in tree types.

Applicaton: Total artificial heart and ventricular assist

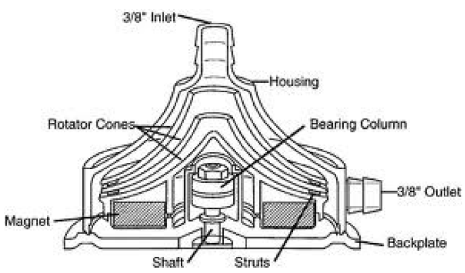
Pump type: Pulsatile pumps and Rotary pumps

Duration: short term, bride and long therm

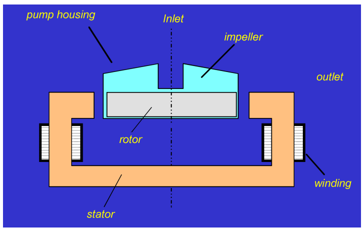
By rotary blood pumps is the bearing ($lagerung$) of the rotors important for blood trauma and thrombus formation. Mechanical bearings include areas of high shear stress, heat and low washout. These factors contribute to blood trauma and thrombus formation. Rotary blood pumps should be simple and small, but you should also have a good biocompatibility.

Classification of rotary blood pumps depend on the baring ($Lager$) technology:

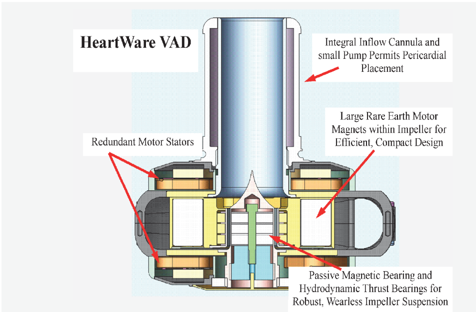
1. mechanical bearing



2. magnetic bearing



3. magnetic bearing combined with hydrodynamic stabilization



Rotary pumps for long clinical use bring many questions:

- physiological compability of "pulseless" flow
- implant technique
- optimal pump adjustment and postoperative magnet
- etc.

By rotary pumps you must adjust the flow speed cartful. Because when the speed is to high the patient can become an heart collapse. The wall of the heart are collapse ($einfallen$).

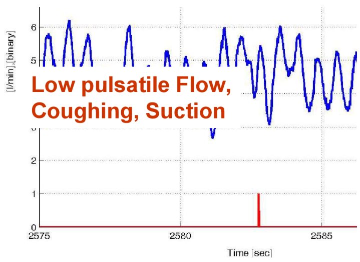


Figure 25: Continuous flow $\neq$ non-pulsatile flow

Pump flow stays somewhat ($aufgrund$) pulsatile due to remaining heart contractility. But the patient has mostly no pulse because the pump rotate so there is no thing who makes the pulse.

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Data Reported by Home Patients:

Hemodynamics: * AoP
* Heart frequency

Pump: # Performance (flow, power, speed)
+ Alarms (caused by pump and handling)

Anticoagulation: & INR (either home or laboratory data)

Others: * Body temperature (indicator for infection)
* Body weight (indicator for fluid balance)
& Subjective feeling (ranking 1-5)

* Noted twice daily; & daily; + On demand; # by E-Mail

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Do we still need physiologically responsive control ?

Yes, we do :

-to adapt to changes in aortic pressure,

- to adapt to changes in fluid balance and circardian rhythm,

- to adapt to sudden changes in homeostasis (sitting up, standing up, coughing, Valsalva-Maneuver),

- to maximize available flow in case of impaired right heart contractility, without impeding the right heart functionality,

- to react to persistent suction, which may not only damage blood and the intra-ventricular wall, but additionally cause right heart failure due to septum shift and subsequent tricuspid insufficiency.

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A control system has to provide :

- proper adaptation to venous return and physical activity;

-safe and robust performance,

- adaptation to special conditions in the pathologic patient (such as arrythmia, collapsible septum),

- minimal sensor requirements, limited to long-term stable signals,

- minimal and simple settings by the physician to adapt to individual patients should be necessary.

We chose an approach, which is based on determination of venous return and on heart rate. Additionally, a very reliable detection system for eventual suction was developed.

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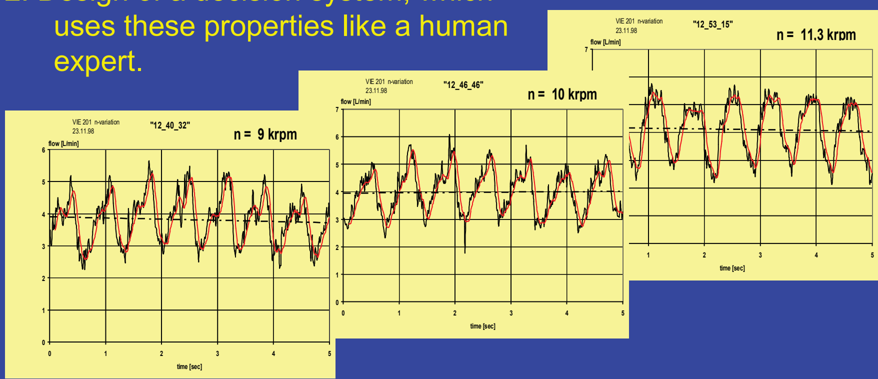
Analysis of flow patterns for eventual suction:

1. Extraction of pattern properties in the time domain;

2. Design of a decision system, which uses these properties like a human expert.



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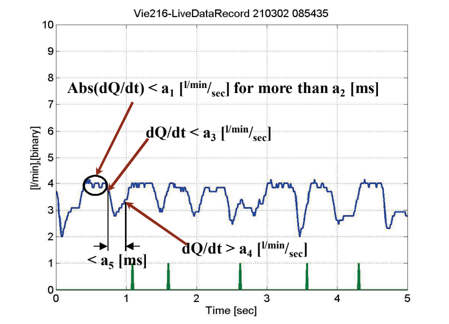
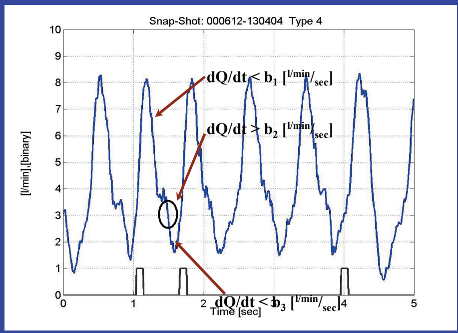


Plateau Criteria

A flow decrease after a plateau situated at the top of a flow peak will be detected as suction if a consecutive increase in pump flow can be observed



Saddle Criteria

A significant flow decrease followed by a phase of low flow changes will be assessed as suction if a consecutive flow decrease occurs

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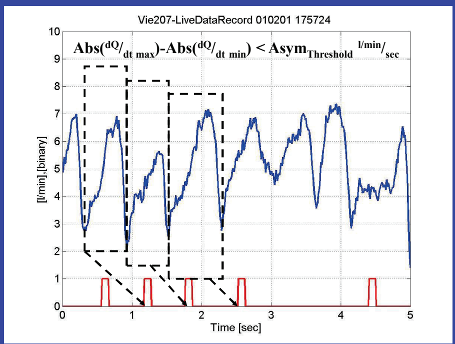
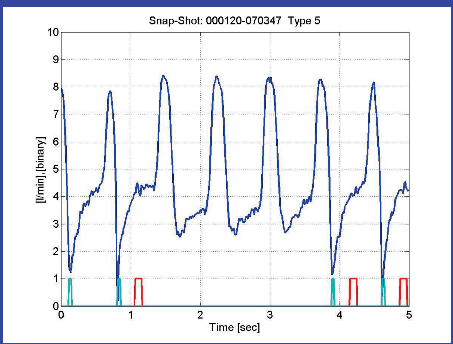


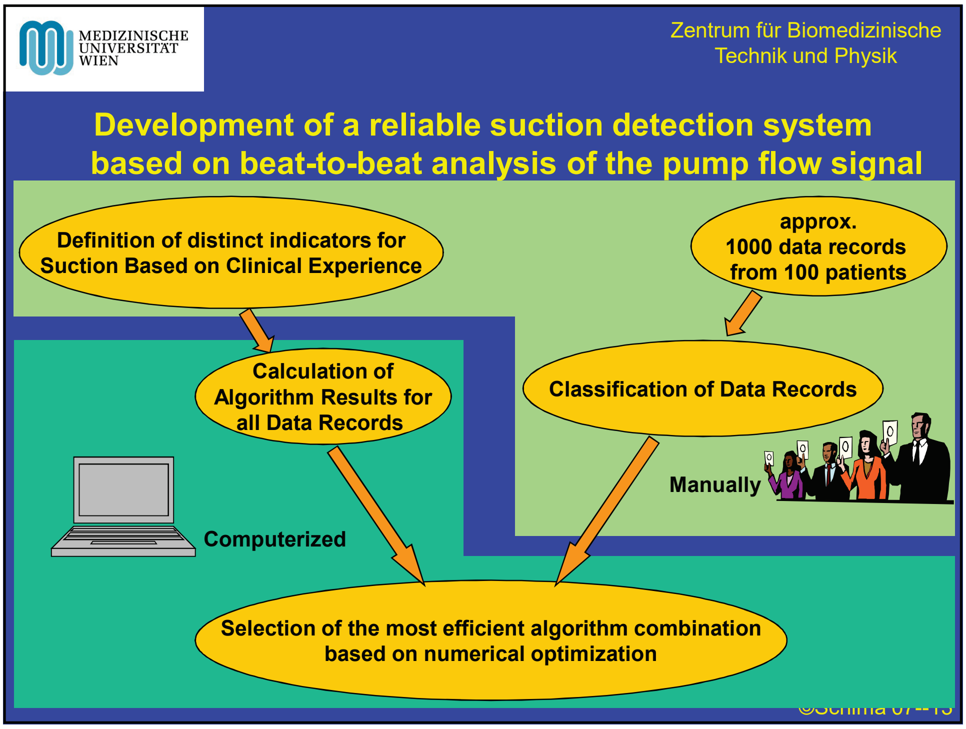
Asymmetry Criteria

The calculation of the asymmetry criteria is based on the determination of local flow minima. Suction will be assessed if the falling arch of one flow peak is much steeper than the rising one.

SlewRate Criteria

Suction is assumed if the slew rate of a falling edge exceed a threshold level of 60 l/min/sec. Certainly the slew rate criteria and the asymmetry criteria yield to the same result.





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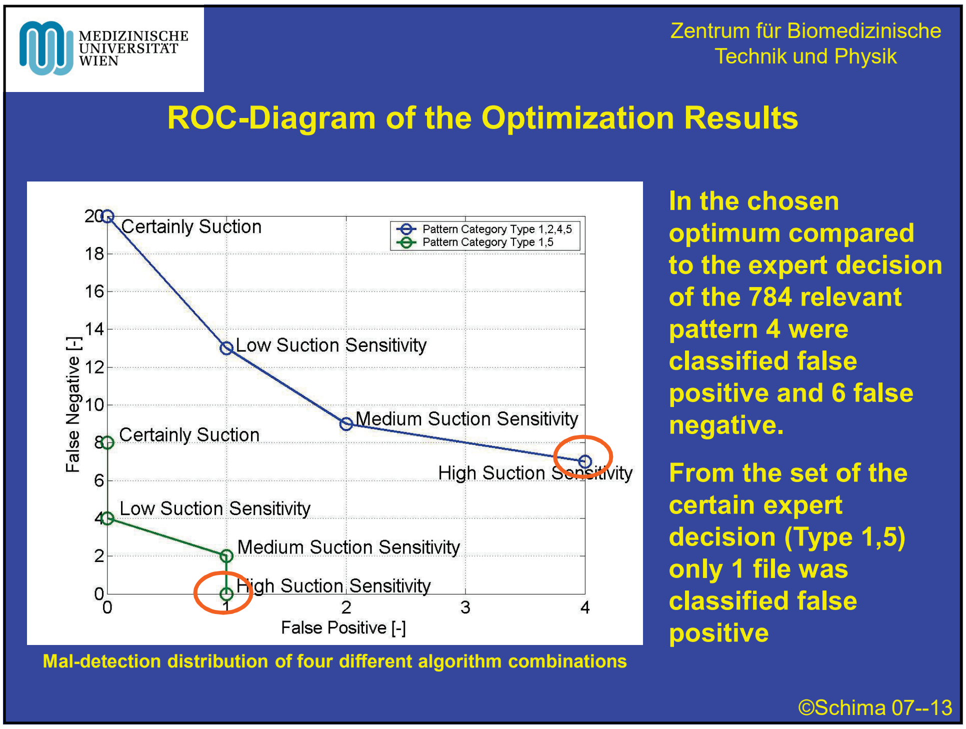
Development of a reliable suction detection system based on beat-to-beat analysis of the pump flow signal
Definition of distinct indicators for Suction Based on Clinical Experience
approx. 1000 data records from 100 patients
Calculation of Algorithm Results for all Data Records
Classification of Data Records
Manually
Computerized
Selection of the most efficient algorithm combination based on numerical optimization



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ROC-Diagram of the Optimization Results
Pattern Category Type 1,2,4,5
Pattern Category Type 1,5
Certainly Suction
Low Suction Sensitivity
Medium Suction Sensitivity
High Suction Sensitivity
Certainly Suction
Low Suction Sensitivity
Medium Suction Sensitivity
High Suction Sensitivity
False Negative [-]
False Positive [-]
0
2
4
6
8
10
12
14
16
18
20
0
1
2
3
4
Mal-detection distribution of four different algorithm combinations
In the chosen optimum compared to the expert decision of the 784 relevant pattern 4 were classified false positive and 6 false negative.
From the set of the certain expert decision (Type 1,5) only 1 file was classified false positive
©Schima 07--13

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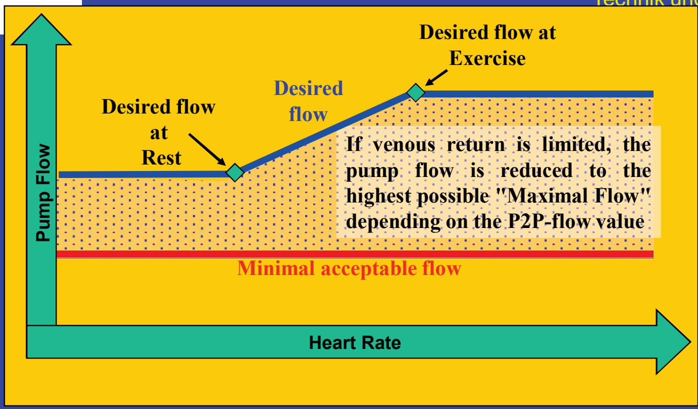
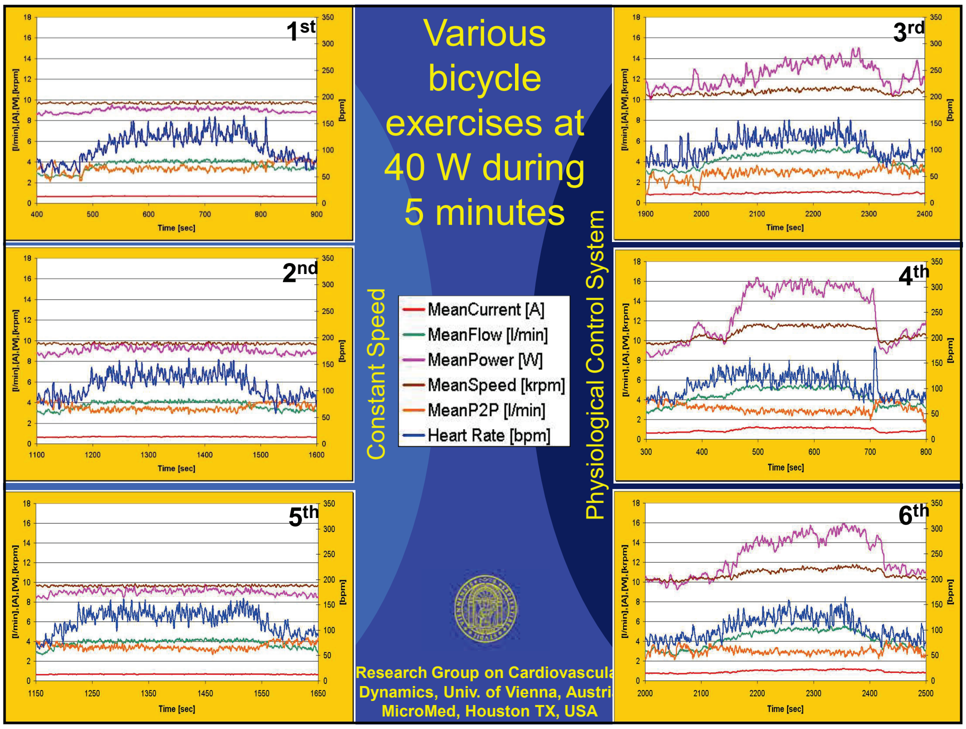


-Adjusts speed to obtain a desired flow;
- In case of sufficient venous return, a target desired flow depending on heart rate is achieved;
- In case of lack of venous return (suction indicated, too low flow P2P-amplitude), the maximal possible flow is achieved.
- If the maximal possible flow falls below a certain level, a fail-safe mode is activated.



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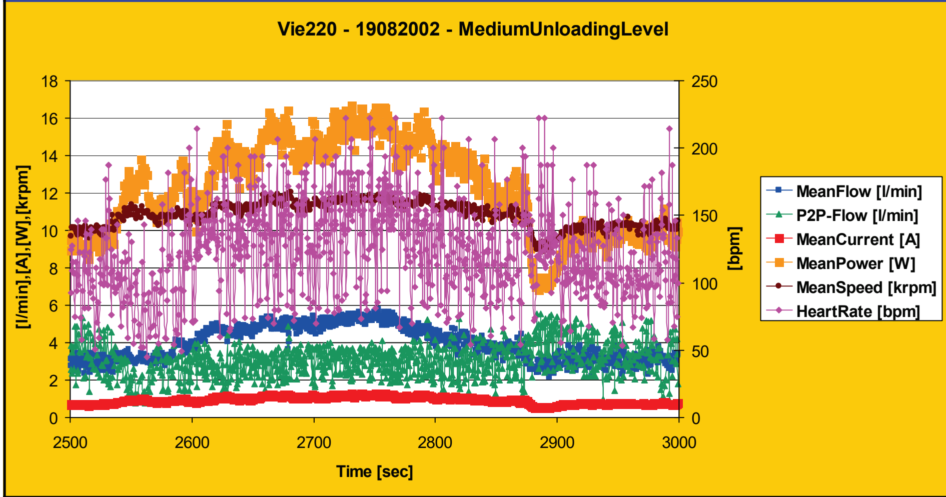
Nonfiltered data at arrythmia:



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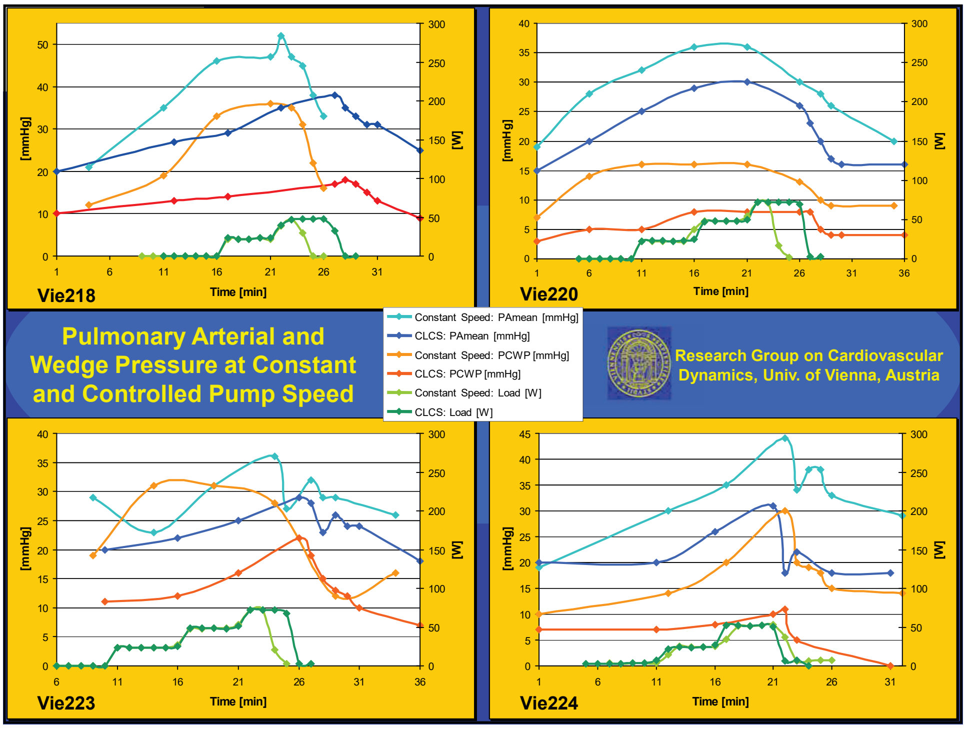
Test Protocol, Catheter Ergometry

Four patients received right heart chaTwo exercise tests, one in constant speed mode and one in controlled mode with a break of 45 minutes between:

1) **Preparation for exercise and recording of baseline parameters**
2) **Warm up: 5 minutes bicycling without load**
3) **Exercise: 5 minute steps of 25 Watt, 50 Watt, 75 Watt, until Respiratory Quotient RQ ≥ 1.1**
4) **Cool down: 2 minutes bicycling without load**
5) **Recording of final haemodynamic values at rest after 5 minutes**



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Conclusions:

- The algorithm proved safety, reliability, stability and functionality also in patients with massive arrythmia, very thin septal wall, and intensive care conditions;
- The system did properly react to physical exercise, with a massive increase of flow, compared to the low intrinsic flow increase at constant speed.
- In catheter-ergometry, pulmonary arterial (mean -26%) and wedge pressure (mean -50%) could be significantly reduced.
- In catheter-ergometry, the control system could increase the physical capacity up to 17% (mean 10%)
- In first blinded tests (which already exceeded the feasibility scope of the study) patients did report some subjective increase of wellness even in short exercise periods.

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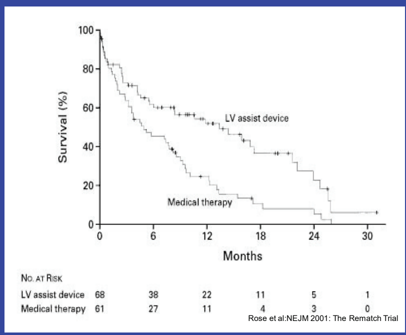
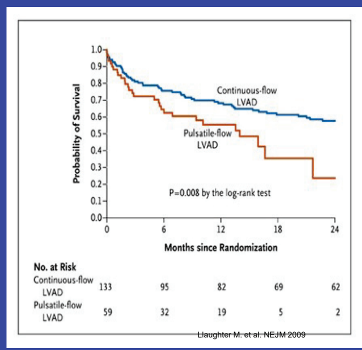
Anstieg der Überlebenszeit von 2001 to 2009:



2001: Pulsatiles System
vs. Pharma-Therapie



2009: Rotationspumpen
vs. pulsatile Pumpen

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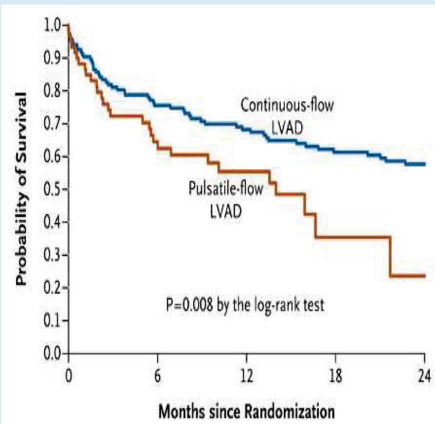
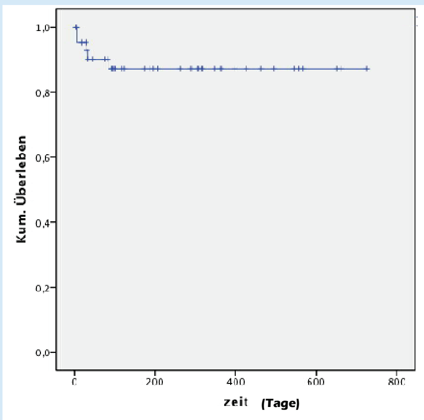
Dept. for Cardiac Surgery,
Center for Med. Physics and Biomed. Eng.
L-Boltzmann-Cluster for Cardiovasc. Research

Ludwig Boltzmann Cluster
kardiovaskuläre Forschung

Life expectancy of VAD-Patients:
After survival, also comfort gets an Issue



Slaughter et al, NEJM 2009, n=192



Vienna, yet unpublished data, n=44

The Vienna VAD Group (Dirs. G. Wieselthaler, H Schima) Oct 2010

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List of Figures

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List of Abbreviations

AD Analoge-Digital

APD Automated peritoneal dialysis

AV Arteriovenous

CAPD Continuous ambulatory perioneal

CCPD Continuous cyclical peritoneal dialysis

CO Carbon monoxide

CT Computed tomography

CVC Central venous catheter

DAPD Daytime ambulantory peritoneal dialysis

ECG Electrocardiogram

EEG Electroencephalography

EMG Electromyography

FI Fehlerstrom-Schutzschalter = Residual Current operated Circuit-Breaker

GFR Glomerular filtration rate

HLM Heart-Lung-machine

IPD Intermittent peritoneal dialysis

MARS Molecular absorbents recirculating system

NIPD ight intermittent peritoneal dialysis

NMR Nuclear magnetic resonance

PID Proportional–integral–derivative