Measurement Basics

- Measuring is the experimental determination of a measured value by quantitative comparison of the measurand with a comparison value in a direct or indirect manner
- Measured value obtained by this procedure is given as a product of a numeric value and a dimensional unit
- It can be recorded continuously as a temporal variation of a physical value or discontinuously at particular moments
- Deviation of measured value from the measurand is the measurement error
  - Depends on measurement procedure, measurement device, and environmental effects
  - Systematic and random errors are distinguished

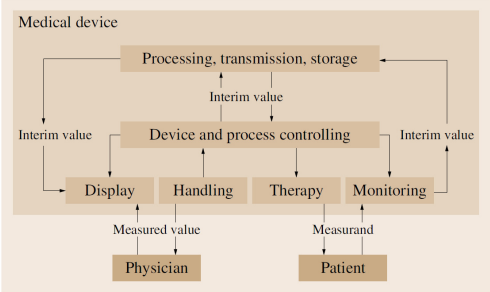
Measuring in Medicine

- Aim of measuring in medicine is objective description of state of patient who might possibly not be able to cooperate
- Goal is to help the physician to define the respective therapy and to evaluate the therapy process and assess the prognosis
- Long-term monitoring of physiological parameters is combined with an alarm function if preset limiting values are exceeded
- New developments include closed-loop systems which directly intervene in patient's state after analysis of measured values
- Unique in having inter-individual and intra-individual deviations for biological measurements, owing to biological variability
  - Measured values vary from patient to patient and within same patient

Objectives

- Metrological acquisition, conversion, processing and transmission of biological signals
- Measuring the reaction or the behavior of the biological object to an external stimulus
- Measurements during application of extra- or intracorporeal assist systems to support organ functions or as organ compensation, as well as manipulators for therapeutic means
- Application of substances, irradiation or waves and measurement of reflection, absorption, scattering, distribution or fluorescence to display structures and functions in the organism
- Extraction of body fluids, substances and tissues, as well as tests and analysis in clinical and chemical laboratories

Model



Unique Aspects

- Extent of inconvenience for patient and measurement procedure directly influences the reliability of measured values
- Biological sources of interference (biological artifacts with physiological origin) superimposing the measurand
- Measurement duration and the reproducibility of an examination are limited for most methods
- Wide variability of examined persons
  - Ranging from fetus, infants and trained athletes to aged people
- Include subjective methods requiring cooperation of patient
  - e.g., audiometry, vibration tests and temperature sensation

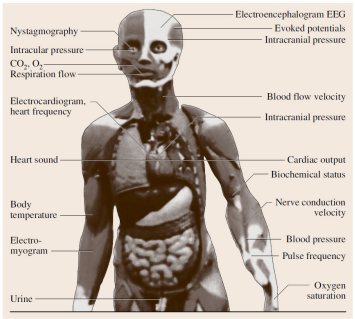
Biosignals

- Biosignals can be defined as phenomena to describe functional states and their variations in a living organism
  - Actual measurand that should be metrologically determined for diagnostic purposes
- Provide information about metabolic, morphological and functional changes, describe physiological and pathophysiological states as well as process dynamics
- To analyze them, generation locus and thus spatial and temporal correlation is significant
- Biosignals are acquired from living organisms, organs and organ parts down to single cells

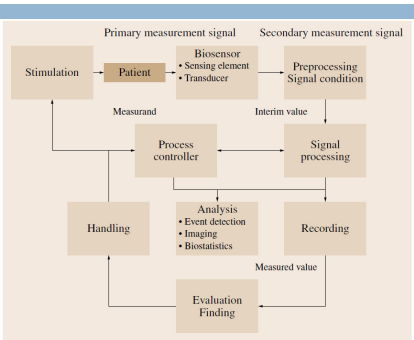
Biosignal Types

- Bioacoustic signals (heart sound, lung sounds, speech)
- Biochemical signals (substance compositions, concentrations)
- Bioelectric and biomagnetic signals (electric potentials, ion currents)
- Biomechanical signals (size, shape, movements, acceleration, flow)
- Biooptical signals (color, luminescence)
- Biothermal signals (body temperature)

Biosignal Examples

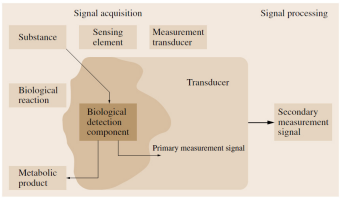


Biological Measuring Chain



Biosensor

- Biosensor is a probe to register biological events and morphological structures
- Often, it is directly connected to a transducer, or it transduces the primary measurement signal into a secondary signal itself

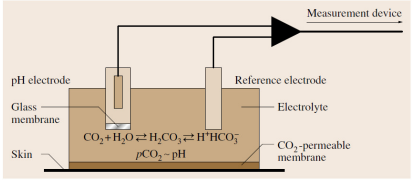


Biosensor Requirements

- Feedback-free registration of the signals
- Provide reproducible measurement results
- Transmission behavior has to remain constant for a long time
- Narrow production tolerances
- High biocompatibility
- Low stress to patient
- Small mass and small volume
- Application should be simple and manageable
- Allow cleaning, disinfection and possibly sterilization

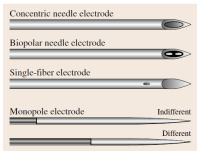
Chemoelectric Transducers

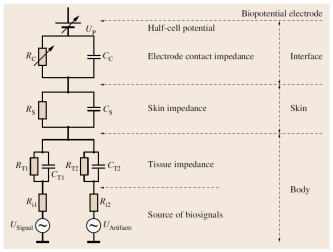
- Used for the measurement of individual chemical components in the blood, in body tissues, in the exhaled air or on the skin
  - Potentiometric sensors, based on the measurement of cell potential
  - Amperometric sensors, based on cell current
  - Conductometric sensors, based on admittance



Electric and Magnetic Transducers

- Transduce electric signal (ion current) into electric signal (electron current)
- Two groups: microelectrodes (metal microelectrodes) and macroelectrodes (surface electrodes)





Mechanoelectric Transducers

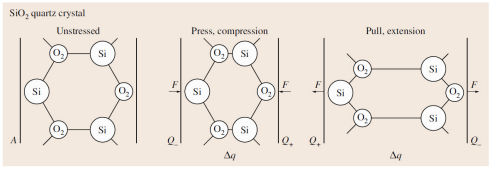
- Measure length changes, strains, pressure changes in tissue, body fluids and organs as well as for the measurement of sounds, microvibrations and blood flow
- Strain Gauge: R=ρL/A allows detecting changes in L
- Piezoresistive elements as strain gauge in a Wheatstone bridge
  - Changes in resistivity can be observed that are up to 100 times larger than the geometric effect yielding a more sensitive strain gauge
- Capacitive transducer: force applied to capacitor yielding a change in the distance between its two plates changes C

$$C_X = \varepsilon_0 \varepsilon_\gamma \frac{A}{x}$$

Mechanoelectric Transducers

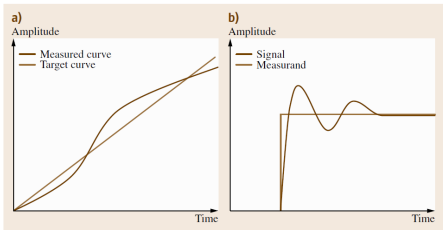
- Piezoelectric transducers: Mechanical stress in the direction of a polar electric axis causes the generation of electric charges due to a shift of the atoms, at very small deformations

$$\Delta q = k \Delta F$$



Dynamic Properties of Biosensors

- Ideal transmission behavior of a measuring chain is linear
  - In reality, relation is not linear, delayed and sometimes oscillating
- Signal processing is to correct for such problems



Bioacoustic Signals

- Includes sounds of the upper respiratory tracts (snoring, speech), lung sounds and heart sound
- Can be registered with a microphone or a stethoscope

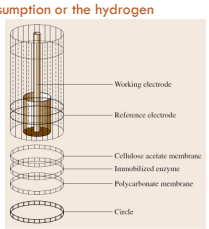
Signal	Specification	Frequency (Hz)
Heart sound	Adults	15–1000
	Fetus	15–150
Lung		0.2–10

Biochemical Signals: Glucose

- Can be determined *in vivo* or *in vitro*
- They can be registered directly or indirectly by reaction
- Example: Glucose identification
  - Amperometrically detected by the O_2 consumption or the hydrogen peroxide formation

$$\text{Glucose} + O_2 \xrightarrow{\text{GOD}} \text{Gluconolactone} + H_2O$$

$$\xrightarrow{H_2O_2} \text{Gluconic acid} + H_2O_2$$

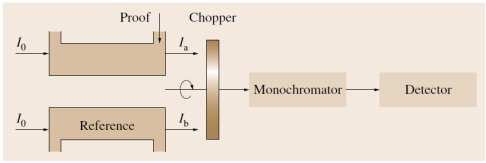


Biochemical Signals: Concentration

- Infrared spectrometers measure the intensity attenuation of infrared radiation after passing a measuring cuvette and compare it with a reference

$$I_a = I_0 e^{-kcl}$$

  - I_a :output intensity, I_0 :input intensity, c :concentration, l :layer thickness, and k :constant of proportionality



Bioelectric and Biomagnetic Signals

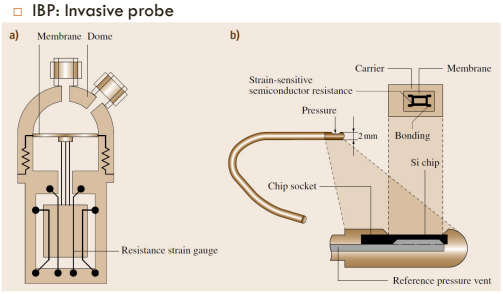
Signal	Frequency (Hz)	Amplitude (mV)
ECG (heart)	0.2–200	0.1–10
EEG (brain)	0.5–100	2–1000 μV
EMG (muscle)	10–10 000	0.05–1
EGG (stomach)	0.02–0.2	0.2–1
EUG (uterus)	0–200	0.1–8
ERG (retina)	0.2–200	0.005–10
EOG (eye)	0–100	0.01–5
FAEP (brain stem)	100–3000	0.5–10 μV
SEP (somatosensory system)	2–3000	0.5–10 μV
VEP (visual system)	1–300	1–20 μV

Biomechanical Signals

Signal	Spezification	Amplitude	Conversion
Pulse (rate)		720–200 min^{-1}	
Breathing (rate)		5–60 min^{-1}	
Blood pressure (arterial)	Systole	8–33 kPa	60–250 mmHg
	Diastole	5–20 kPa	40–150 mmHg
Blood pressure (venous)		0–4 kPa	0–30 mmHg
Intraocular pressure		0–7 kPa	0–50 mmHg
Blood flow		0.05–51/min	
Blood flow velocity		0.05–40 cm/s	
Respiratory flow velocity		20–120 cm/s	
Cardiac output		3–8 l/min	
Respiratory volume		200–2000 ml/gasp	
Muscle work		10–500 W	
Blood volume	Adults	7000 ml	
Amount of urine	Adults	1500 ml/d	
Nerve conduction velocity	Median nerve	50–60 m/s	

Biomechanical Signals: Pressure

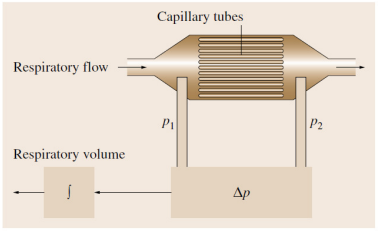
- IBP: Invasive probe



Biomechanical Signals: Volume

$$\dot{V} = \frac{\pi r^4 \Delta p}{8 l \eta}$$

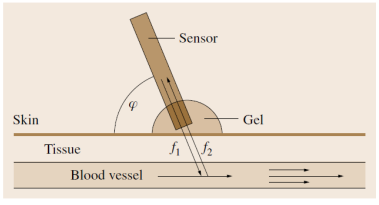
$$V = \int_0^t \dot{V}\, dt$$



Biomechanical Signals: Flow Velocity

- Doppler effect

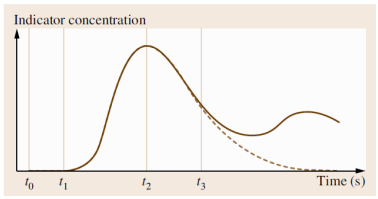
$$\Delta f = f_1 - f_2 = f_1 \frac{2v \cos\varphi}{c}$$



Biomechanical Signals: Cardiac Output

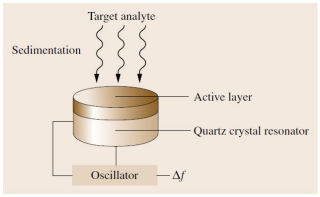
- Indicator-Dilution method

$$CO = \frac{m_0}{\int_{t_0}^{\infty} c(t)\,dt}$$



Biomechanical Signals: Mass

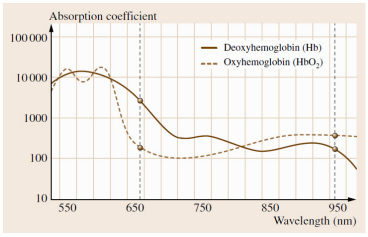
- Quartz microbalance
  - measurement is based on resonance frequency shift of an oscillating crystal due to deposition of substances on the crystal surface



$$\Delta f = \frac{2.3 \times 10^6 f_0^2 \Delta m}{A}$$

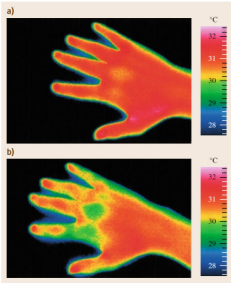
Biooptical Signals: O_2 Saturation

- Evaluation of color (skin)
- Evaluation of O_2 saturation based on the different absorption characteristics of oxygenated and deoxygenated hemoglobin



Biothermal Signals: Thermography

- The Most important biothermal signal is the body temperature
- Using thermography, temperature distribution on a skin area can be determined.
- Pathological changes can be detected from distribution relative to normal areas
  - Example: reduction of blood flow due to smoking

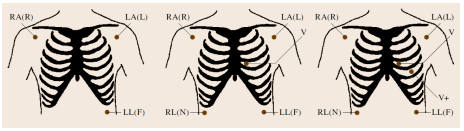


Introduction

- Cardiovascular monitoring covers monitoring of heart and circulatory functions
- It makes it possible to commence interventions quickly in the event of any impairment
- Measurements are used to assess the condition of the patient, reach a diagnosis, decide on therapy, and monitor therapy
- Covers cardiac function in the form of electrical phenomenon (ECG) and its mechanical effects including pressure build-up and volume delivery, contractility, preload, and afterload

Electrocardiogram (ECG)

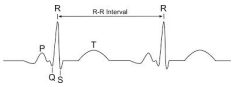
- ECG provides information about heart rate and rhythm, excitation, conduction, and repolarization and disturbances in these functions
- ECG does NOT provide any direct information about the pumping capacity of the heart (i.e. mechanical cardiac function)



Lead Wire Color Code:
- IEC2 (US): RA: white, LA: black, LL: red, RL: green, V: brown, V+: gray/brown
- IEC1 (Europe): R: red, L: yellow, F: green, N: black, V: white, V+: gray/white

Heart Rate (HR)

- Heart rate (typical measuring range of 15–300 beats/min) is determined as a moving average over a specific time (e.g. 10s), or a specified number of QRS complexes
- An alternative to ECG that can be used when there are interferences in ECG, e.g. during cauterization in the OT)
- Can be computed in the form of pulse rate from the arterial blood pressure or pulse curve from the SpO_2 signal
- Basis of heart rate measurement is safe detection of QRS complexes in ECG and assessment of RR intervals



Hemodynamics

- Hemodynamics is the study of flow of blood in circulatory system
  - This flow is driven by pressure generated by heart
- Since the pressure in the vascular system is highly dependent on activity and the position of the body (hydrostatic pressure), blood pressure measurements are always taken at rest and are based on height of the heart (right atrium)
- Vascular system is functionally divided into low-pressure system (small, pulmonary circuit) and high-pressure system (large, systemic circuit), connected by the heart as driving element

Hemodynamics

- Heart generates pressure in its contraction phase (systole), by means of which stroke volume (SV) is expelled from the ventricle into arterial vascular system
  - Every stroke volume conveyed generates a pulse wave
- Peak pressure during expulsion of stroke volume from ventricle is systolic blood pressure (highest point of pressure curve)
- Pressure at end of relaxation phase (diastole) is referred to as diastolic blood pressure (lowest point of pressure curve)
- Difference between systolic and diastolic pressure is blood pressure amplitude

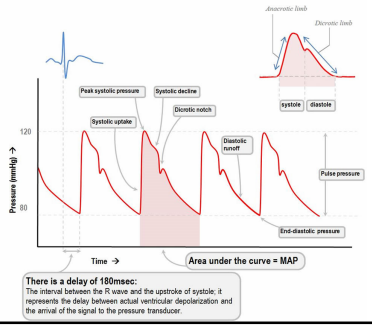
Hemodynamics

- Pressure that maintains blood flow in vascular system and act as driving force of perfusion is mean pressure
  - In systemic circuit mean arterial pressure is termed APm (also MAP)
  - In pulmonary circuit mean pulmonary artery pressure is termed PAPm
- Stroke volume depends on preload, contractility of myocardium and afterload
- Preload is stretching of myocardium brought about by passive filling of ventricles at end of diastole and is best described by end-diastolic volume
- Afterload is force exerted by cardiac muscles to overcome resistance in outflow tract of left ventricle and peripheral circuit
  - Mean arterial pressure and vascular resistance are measures of afterload

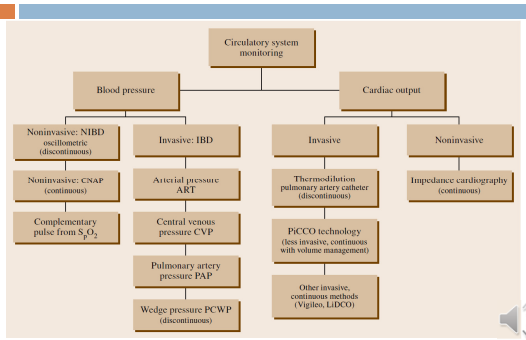
Hemodynamics

- Factors that also determine blood pressure behavior include elasticity of vascular system components, circulating blood volume and peripheral vascular resistance
  - Influenced by wall tension of vessels (vessel tone) controlled by sympathetic nervous system
- Delivery volume of blood per minute is known as the cardiac output (CO) and is the product of stroke volume and heart rate
- Control mechanisms in the body regulate circulation with aim of adjusting cardiac output to circulation required to supply oxygen to the organism and eliminate CO_2, keeping the blood pressure largely constant and adjusting the circulation in the individual organs and tissues to the functional state in each case

Hemodynamics

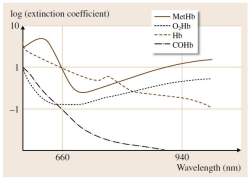


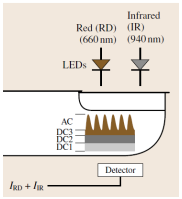
Hemodynamic Monitoring



Pulse Monitoring

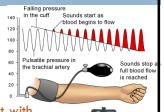
- Pulse monitoring is performed either invasively from the arterial pressure curve or noninvasively from the plethysmogram of pulse oximetry
  - Pulse monitoring has particular importance as a safety measure in such condition as monitoring pacemaker patients





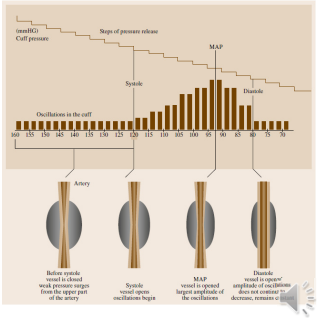
Discontinuous Noninvasive Blood Pressure (NIBP): Auscultatory Method

- Sphygmomanometer
  - Riva Rocci: Systolic blood pressure measurement
  - Korotkoff: Diastolic blood pressure
- Auscultatory Method
  - Cuff placed on exposed upper arm at the level of heart with middle of rubber bladder positioned over brachial artery
  - After palpating the brachial artery, the cuff is inflated to≈ 30mmHg above the pressure at which the pulse can no longer be detected
  - Stethoscope is placed against the brachial artery and the cuff pressure is slowly released.
  - Pulsation that then begins causes knocking noises (Korotkoff sounds phase 1): systolic blood pressure is read off from the manometer
  - Sounds change until sound can no longer be heard (phase 5) and is measured as the diastolic pressure



Discontinuous Noninvasive Blood Pressure (NIBP): Oscillometric Method

- When cuff pressure is released once the systolic pressure has been reached, the vessel walls begin to oscillate and maintain this behavior until the vessel is no longer occluded
- Oscillations are transmitted to air in cuff and are read on the manometer
- Today, oscillations are measured electronically using pressure sensors



Continuous Noninvasive Arterial Blood Pressure Measurement (CNAP)

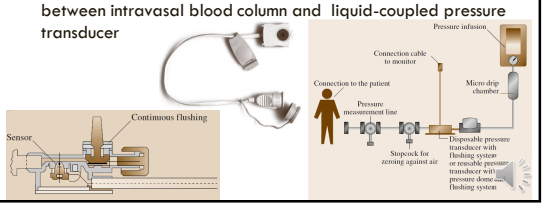
- Blood pressure is not always constant but can change within a matter of seconds
  - In particular, during anesthesia and its induction, variations in blood pressure can arise and require immediate medical attention
- Noninvasive technique of relaxed arterial wall (vascular unloading technique or volume clamp method) uses optical sensor in small cuff around finger to measure volume pulses due to each heart beat
  - Pressure in the cuff is regulated by means of feedback such that the optical measuring path always remains constant
- When a pulse occurs, cuff pressure is increased accordingly, and when the pulse subsides the cuff pressure is reduced.
  - Cuff pressure reflects the pressure occurring in the enclosed finger artery with high degree of accuracy

Continuous Noninvasive Arterial Blood Pressure Measurement (CNAP)

- CNAP uses pairs of sensor cuffs, which are placed on adjacent fingers
  - Only one cuff is used for measurement at any time, and after no longer than half an hour continuous measurement is automatically switched
- Venous stasis that naturally occurs during measurement on finger very quickly decreases once more after the switch
- Great advantage of this method is calibration of continuous measurement with the normal NIBP measurement, so that correct values are displayed even when the fingers are not level with the heart
  - Advantages of both NIBP and CNAP

Invasive Pressure Measurement in High-Pressure System

- Continuous availability of measurement signal (pressure curve) and pressure values
  - Provides possibility of triggering an alarm if predefined limit values violated and of further signal processing of measurement data
- Connection is set up by means of an intra-arterial catheter between intravasal blood column and liquid-coupled pressure transducer



Invasive Pressure Measurement in Low-Pressure System

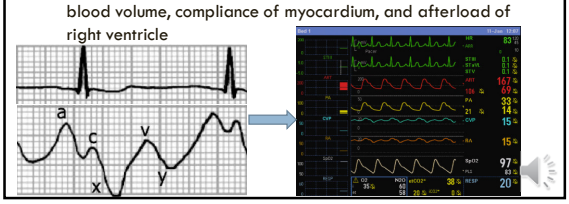
- Aim is to obtain information about right ventricular function, pulmonary circuit, and filling of vascular system
  - Central Venous Pressure (CVP)
  - Pulmonary Artery Pressure (PAP)
  - Pulmonary Capillary Wedge Pressure (PCWP)

Central Venous Pressure (CVP)

- Measurement of the central venous pressure is by means of a liquid manometer or a pressure sensor using central venous catheter (CVC) placed in superior vena cava at the entrance to the right atrium
- Pressure transducers have the advantage that measurement information is available continuously and certain signal characteristics of the CVP curve are additionally available
- Because of the small pressure values, it is important that pressure measurement system is situated level with the heart (correct zero point positioning) in order to avoid errors
  - Hydrostatic pressure difference can cause incorrect measurements

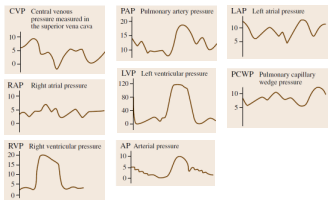
Central Venous Pressure (CVP)

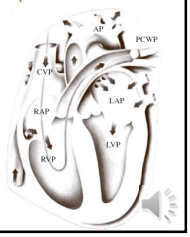
- Progression of CVP curve shows:
  - Atrial contraction (a-wave)
  - Beginning of the ventricular contraction (c-wave)
  - Relaxation phase (v-wave)
- Influenced by capacity of vascular system, cardiac output, blood volume, compliance of myocardium, and afterload of right ventricle



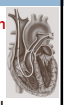
Pulmonary Artery Pressure (PAP) and Pulmonary Capillary Wedge Pressure (PCWP)

- To monitor hemodynamics of right ventricle, balloon catheter is pushed through venous system into right atrium, right ventricle, and then through pulmonary valve into arteria pulmonalis
  - Path of catheter is followed from different typical pressure curves





Pulmonary Artery Pressure (PAP) and Pulmonary Capillary Wedge Pressure (PCWP)



- Correct catheter position is reached once in wedge position
  - That is, once the inflated balloon of the catheter blocks off the pulmonary artery branch
- If tip of catheter rests against wall of pulmonary artery (pseudo-wedge), this causes damping of pressure curves when balloon is filled and there is continuous rise in pressure
- Although catheter is in right ventricle, in the wedge position pressure in left atrium can be inferred via the distal lumen
  - PCWP value corresponds in first approximation to the left atrial pressure (LAP) and thus to the end-diastolic filling pressure in the left ventricle
  - Left atrium, pulmonary capillaries, and pulmonary artery under normal conditions form a common pressure connection during diastole.

Balloon Catheters

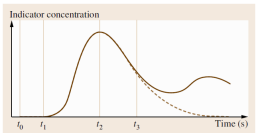
- Using balloon catheters (so-called flow-directed catheters, pulmonary artery catheters, or Swan–Ganz catheters) with different length and thickness, number of lumina, position of lumen exit sites, and other characteristics; CVP, PAP, and core body temperature can be measured simultaneously, and the PCWP and CO can be measured intermittently
- Specialized balloon catheters provide additional possibilities such as intracardial ECG measurement, supraventricular and ventricular stimulation, measurement of mixed venous oxygen saturation SvO_2 with integration of fiber optics, transluminal stimulation probe, or additional infusion lumina
- Balloon catheters are not free of risk and can cause complications such as:
  - Supraventricular and ventricular arrhythmias
  - Ventricular tachycardia or ventricular fibrillation (rarely)
  - Venous thrombosis (particularly with a low CO)
  - Sepsis (risk rises as the duration of catheterization increases)
  - Pulmonary infarction (due to catheter occlusion of peripheral pulmonary artery)
  - Pulmonary artery rupture (by balloon inflation or the catheter tip).

Determining the Cardiac Output (CO)

- Cardiac output is volume of blood conveyed per minute (l/min)
- Classical way of determining CO is by Fick's principle
  - Calculation is based quite simply on the law of conservation of mass
- CO is the quotient from oxygen consumption (VO_2) in the body and difference in oxygen content ($avDO_2$) between arterial blood flowing to the body and mixed venous blood returning from the body: $CO = VO_2/avDO_2$
  - Unfortunately, under routine conditions oxygen consumption cannot be measured with sufficient accuracy in the clinical environment

Dilution Methods to Measure CO

- Development of fundamental work of Stewart and Hamilton to determine CO by means of dye dilution (1920s)
  - Implemented with dye, cold, ions, radioisotopes dilution methods
- Introduction of thermistor catheter by Swan and Ganz (1970s) made thermodilution by means of a pulmonary artery catheter established as leading method for clinical use



Thermodilution Method

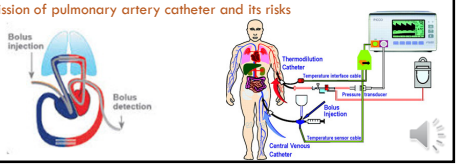
- Defined amount of saline solution at a temperature of 0–25 °C (the lower the temperature, the more accurate the measurement) is injected into the right atrium via proximal port of the multilumen pulmonary artery catheter
- Because injected fluid is mixed with warm flowing blood (37 °C) and is therefore diluted, change in temperature in blood stream can be measured by thermistor situated close to tip of catheter
- Shape and area of dilution curve change with cardiac output
- With known temperature of injected fluid and blood as well as known volume of injected fluid, measuring system determines CO from the area of thermodilution curve

Thermodilution Disadvantages

- Need for the pulmonary artery catheter, the indication of which is viewed particularly critically
  - Connors *et al.* (JAMA, 1996): "RHC is associated with increased mortality and increased utilization of resources"!
- Discontinuity of measurements
  - This was overcome by emitting heat pulses to the blood using a special pulmonary artery catheter and by evaluating their dilution curve
  - Since heat pulses can be applied at very short intervals (30–60 s), this virtually provides continuous measurement

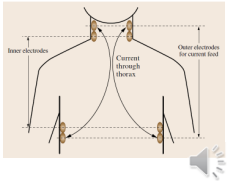
PiCCO Technology

- Thermodilution can, in principle, be done transpulmonarily
  - Cold bolus passes through lungs with thermistor placed in arterial system
- Cold bolus is injected into right atrium as in normal thermodilution except with normal central venous catheter (more common)
- Temperature profile is measured in arteria femoralis
- Advantage of this method is that it is less invasive
  - Omission of pulmonary artery catheter and its risks



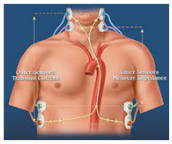
Impedance Cardiography

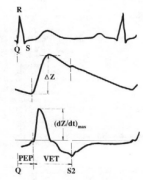
- It has long been known that blood volume expelled with each heart beat (stroke volume) leads to measurable variations in the thoracic impedance
  - Attempts to determine the stroke volume and CO from the variations in thoracic electrical bioimpedance (TEB)
- Offers several advantages
  - Completely noninvasive and low risk
  - Continuous beat-to-beat measurement
  - Easy to apply
- Cannot be used in some cases
  - Example: septic shock patients
  - PiCCO is used more due to that



Impedance Cardiography

- Weak high-frequency constant current (e.g. 2.5mA, 70 kHz) is passed through thorax by means of external ring electrodes (or special double electrodes) arranged on neck and thorax
- Current seeks path of least resistance, which is essentially blood-conducting aorta and voltage drop is measured by inner measuring electrodes





Calculation of Hemodynamic Variables

- Total Peripheral Resistance (TPR), also called Systemic Vascular Resistance (SVR), is resistance of systemic circuit, computed as quotient of propulsive pressure difference (Mean Arterial Pressure APm - Central Venous Pressure CVP) and flow (CO)

$$SVR = (APm - CVP)/CO \quad \text{dyn s/cm}^5$$

- Pressure difference in small circuit is Mean Pulmonary Pressure minus Wedge Pressure PCWP (as a measure of the left atrial pressure). The Pulmonary Vascular Resistance (PVR) is given as:

$$PVR = (PAPm - PCWP)/CO \quad \text{dyn s/cm}^5$$