MUNI PHARM

Medical Imaging

Biophysics

1

Medical Imaging Methods

There are a variety of medical imaging methods based on the different principle:

- Use of optical properties (endoscopy)
- Evaluation of changes in acoustic properties (ultrasonography)
- Passage of ionizing radiation through tissues (X-ray, CT)
- The behaviour of substances in a magnetic field (MRI)
- Observation of the decay of radionuclides in tissues (PET)

2

Magnetic Resonance Imaging (MRI)

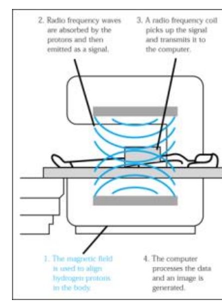
MRI is one of the most important imaging methods.
Originally known as nuclear magnetic resonance (NMR) imaging.

- 1920 W. Pauli predicted the phenomenon of nuclear magnetic resonance
- 1945 the first observation of NMR phenomena (two independent teams)
- 1952 Nobel Prize for physics (discovery of the NMR phenomenon); E.M. Purcell and F. Bloch
- 1950-1960 first NMR spectrometers able to determine the structure of molecules
- 1971 first tomographic images of the human body (MRI)

3

Magnetic Resonance Imaging (MRI)

- MRI uses powerful magnets to align hydrogen nuclei (i.e. single protons of water molecules) in human tissue.
- The MRI machine emits a radio frequency (RF) pulse at the resonant frequency of the hydrogen atoms on water molecules.
- The RF pulse is absorbed by protons. When the RF pulse is turned off, the protons "relax" and emit radio-waves in the process.
- This radio-frequency emission from the hydrogen-atoms on water is what is detected and reconstructed into an image.

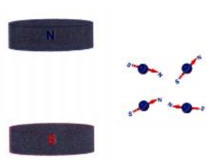


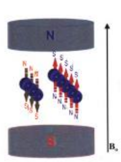
4

Magnetic Resonance Imaging (MRI)

The magnetic properties of nuclei:

- Protons that exhibit a magnetic moment (i.e. have a nonzero spin numbers I, manifested as miniature magnets) have a random orientation of magnetic moments
- External magnetic field causes a division into 2 populations (I = 1/2; ^{1}H) having the same or opposite magnetic moment relative to the external magnetic field
- A larger number of protons has a magnetic moment oriented in agreement with the external magnetic field (lower energy) – this property is the fundamental principle of MRI.



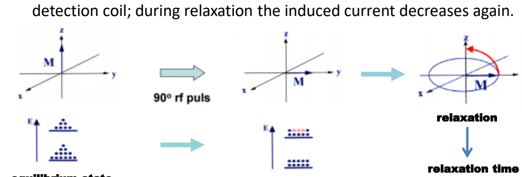


5

Magnetic Resonance Imaging (MRI)

The magnetic properties of nuclei:

- External RF pulse (radiation energy corresponds to the energy difference between the populations of protons) can excite the nuclei into a higher energy state.
- The energy of RF pulse (at angle of 90°) will flip the magnetization vector to the *x-y* plane. Consequently the protons relax (return to initial state). The relaxation rate is called relaxation time T_1.
- Flipping of the magnetization vector induces a current in the detection coil; during relaxation the induced current decreases again.

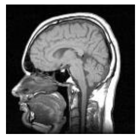


6

Magnetic Resonance Imaging (MRI)

The magnetic properties of nuclei:

- The faster is the relaxation of protons, the shorter is the T_1 and the stronger is the signal.
- The individual tissues have different biochemical structure; different representation of protons (^{1}H) influences the magnetic moment and relaxing time.
- Differences in T_1 are displayed as grayscale differences (solid tissues are displayed lighter than liquid).
- Application of contrast agents (paramagnetic) – accelerate the relaxation of protons and thus reduce T_1 => stronger signal.
- Classical method of measurement is long (tens of minutes). Nowadays devices utilize the magnetic field gradient (allows to select the plane of the cut) and addition of other magnetic fields (3D images).
- MRI is controlled by a computer (data processing).

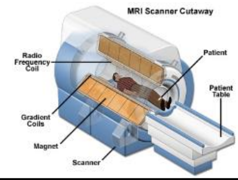


7

Magnetic Resonance Imaging (MRI)

Instrumentation:

- The patient is placed in a strong magnetic field (0.5-7 T).
- Around the patient there are a number of coils that serve to generate a radio frequency pulse and receive a signal.
- Final images are obtained by complicated mathematical data processing.
- Workplaces must be shielded (radio frequency interference): Faraday's cage (the walls of the room are insulated with non-magnetic steel mesh).



8

Magnetic Resonance Imaging (MRI)

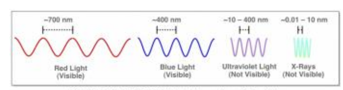
Application:

- ✓ Privileged position in diagnosis of neurodegenerative diseases, strokes, brain tumors.
- ✓ Diagnosis of cardiovascular diseases and musculoskeletal disorders.
- ✓ Allows easy differentiation of blood vessels from solid tissues (difference from CT).
- ✓ MRI does not use ionizing radiation.
- ✓ The action of the magnetic field is short and does not have biological effects.
- ▪ MR imaging can not be used in patients with pacemakers or magnetic materials (e.g. joint replacement).
- ▪ MRI examination is expensive.

9

Medical X-ray Imaging

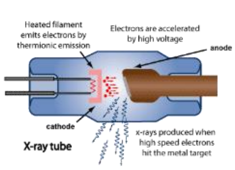
- 1895 Wilhelm Conrad Röntgen (discovery of X-rays)
- Very quick implementation in medicine
- 1901 Nobel Prize in Physics
- Establishment the new discipline: Radiology – Radio diagnostics
  – Radiotherapy
- X-rays are electromagnetic waves (is similar to that of gamma radiation)

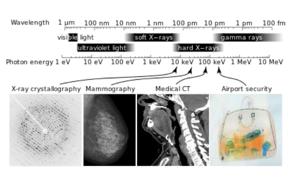


10

X-rays: Sources and characteristics

X-ray tube





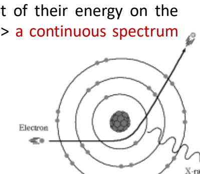
- Glass evacuated tube with heated filament (cathode) and metal target (anode).
- Heated cathode emits high speed electrons which hit the anode .
- The wavelength of X-rays depends on the voltage between cathode and anode (λ = 1.24/U [nm; kV]); U_{max} = 150 kV.

12

X-rays: Sources and characteristics

Braking X-ray radiation

- Is formed by transforming the kinetic energy (braking) of the electrons onto the anode
- During passage of electrons around the atomic nucleus of anode material is the trajectory deviates from a straight line
- Under the action of electrostatic forces the speed of the electron is dramatically reduced
- Part of the kinetic energy (which the electron lost) is converted into X-rays
- The incident electrons lose a different part of their energy on the outer electron layers of the anode atoms => a continuous spectrum (represented by different wavelengths)
- Braking X-ray radiation is used for diagnostic purposes

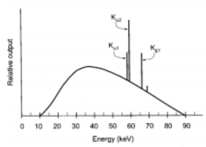


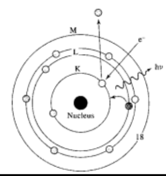
13

X-rays: Sources and characteristics

Characteristic X-ray

- When the incident electron strikes the target electron in a anode material, the target electron is ejected from the inner shell of the atom.
- Outer-shell electrons then fall into the inner shell, emitting X-ray photon.
- The energy of the emitted photon is equivalent to the energy difference between the electron levels.
- The wavelength of the characteristic X-ray depends on the anode material (line spectrum).
- Characteristic X-ray is used in the structural analysis of substances.

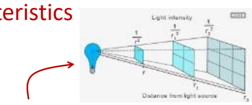




14

X-rays: Sources and characteristics

Interaction with matter



- The X-ray intensity decreases with the square of the distance
- X-ray penetrates all substances and is partially absorbed
- The ability of different compounds to absorb X-ray to different degrees is the basis for diagnostic use
- The quantity of transmitted X-rays depends on the atomic number (*Z*), density (ρ), the thickness (*d*) of absorbing material and the X-rays wavelength (λ)

$$I = I_0 * e^{-\mu * d}$$

I_0 – intensity of incident X-rays
I – intensity of transmitted X-rays
μ – absorption coefficient ($\mu = \rho * \lambda^3 * Z^4$)

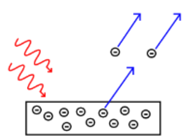
X-rays interact with matter in two main ways: photoelectric absorption (dominant interaction mechanism for the soft X-ray) and Compton scattering (dominant interaction mechanism for the hard X-ray).

16

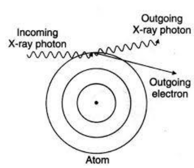
X-rays: Sources and characteristics

Interaction with matter

Photoelectric absorption – the incident X-ray photon interacts with an atom of the absorbing material, and the photon completely disappears; its energy is transferred to one of the electrons of the atom (electron is ejected at high velocity).



Compton scattering – the incident X-ray photon transfers only a part of its energy to the an electron (electron is ejected) and the remaining energy is emitted in a different direction from the original. This phenomenon reduces the contrast of X-rays imaging.

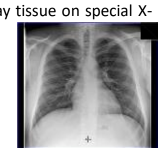


17

Medical X-ray Imaging

Projectional radiography

- is the practice of producing two-dimensional images using X-ray radiation.
- When the primary beam passes through the body, part of the radiation is absorbed, which allows us to display tissue on special X-ray films.
- Hard X-rays (U > 100 kV) enables short exposure, but the picture is less focused (eg. for the lung imaging)
- Soft X-rays (U < 45 kV) suitable for imaging of soft tissues (e.g. mammography)



Disadvantages: can not be used to study of organ function (show only the resulting situation). The image is two-dimensional recording of three-dimensional object.
Advantages: permanent document enabling studies and small details (resolution of film material is high).

18

Medical X-ray Imaging

Fluoroscopy

- is an imaging technique to obtain real-time moving images.
- A fluoroscope consists of an X-ray source and a fluorescent screen, between which a patient is placed.
- Modern improvements in flat-panel detectors (convert X-ray to electrical signal), digital image processing and image analysis allowed for increased image quality while minimizing the radiation dose to the patient.

Disadvantages: higher radiation dose and lower resolution compared to projectional radiography.

Advantages : the patient can rotate in different planes. It allows to monitor dynamic processes (eg. peristalsis of the stomach and intestines, pulsation of the heart, movement of the diaphragm).

19

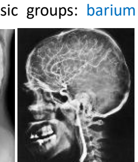
Medical X-ray Imaging

Radiocontrast agents

- are used to improve the visibility of the body's internal structures.

Negative contrast agents: absorb X-ray radiation less than the examined body part; on radiographs cause brightening. The most commonly used gaseous substances (air, CO_2). Use e.g. in the examination of the lungs (pneumothorax) or peritoneal cavity.

Positive contrast agents: absorb X-ray radiation more than the examined body part; on radiographs cause shadow. Two basic groups: barium sulfate (imaging of the digestive tract) or iodine organic compounds (to visualize vessels and changes in tissues).

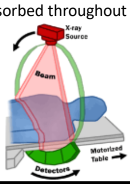


20

Medical X-ray Imaging

Computed tomography (CT)

- CT is a diagnostic imaging test used to create detailed images of internal organs, bones, soft tissue and blood vessels.
- The cross-sectional images generated during a CT scan can be reformatted in multiple planes, and can even generate three-dimensional images which can be viewed on a computer monitor, printed on film or transferred to electronic media.
- With CT scanning, X-ray source and a set of electronic X-ray detectors rotate around patient, measuring the amount of radiation being absorbed throughout patient body.

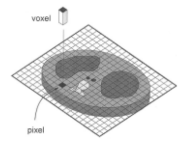


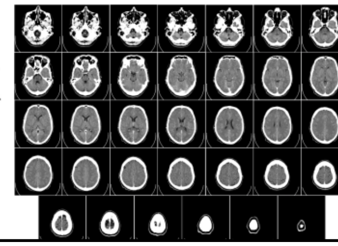
21

Medical X-ray Imaging

Computed tomography (CT)

- A special computer program processes this large volume of data to create two-dimensional cross-sectional images of patient body, which are then displayed on a monitor.
- A CT scan exposes the patient to much higher radiation dose than with classical X-ray imaging (dose is higher 50 × to 500 ×).





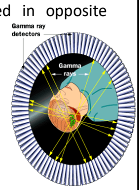
22

Gamma Scintigraphy

- **A source of ionizing radiation is in the patient's body** (administration of radionuclides)

Positron emission tomography (PET)

- Imaging of the **function** of organ or metabolic activity of a body part, not its anatomical structure (MRI, CT).
- Using radionuclides emitting positron (radiopharmaceuticals).
- Positron passes through the tissues (distance not exceeding a few mm) and as a result of interaction with the electrons it will annihilate to form two gamma photons (emitted in opposite directions at an angle of 180°).
- Detectors register pair of annihilation photons in time. The information is further processed, allowing reconstruction of the position where the positron annihilated. A picture of the spatial distribution of the radiopharmaceutical in the organism is obtained.

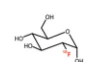


23

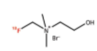
Gamma Scintigraphy

Positron emission tomography (PET)

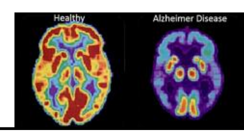
- The radionuclide is bounded to suitable carrier (biologically active molecules) which are involved in the biological processes.
- Radionuclides used in PET scanning are typically isotopes with short half-lives such as ^{11}C (~20 min), $^{13}N_2$ (~10 min), $^{15}O_2$ (~2 min), ^{18}F (~110 min).
- PET is the most sensitive and the most selective imaging technique => imaging of metabolic functions.
- PET is used heavily in clinical oncology (medical imaging of tumors and the search for metastases), and for clinical diagnosis of certain diffuse brain diseases such as those causing various types of dementias.



fluorodeoxyglucose



fluorocholine

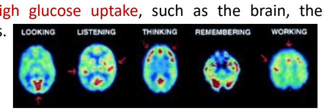


24

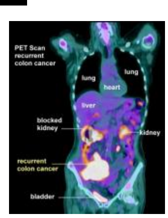
Gamma Scintigraphy

Positron emission tomography (PET)

- Using fluorodeoxyglucose results in intense radiolabeling of tissues with high glucose uptake, such as the brain, the liver, and most cancers.



- Pharmacokinetics: In pre-clinical trials, it is possible to radiolabel a new drug and inject it into animals. Such scans are referred to as biodistribution studies. Drug absorption, tissue distribution and elimination can be monitored much faster than conventional procedures involving the killing of animals and tissue analysis.



25

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Thermic

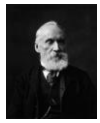
Biophysics

27

Heat, temperature, fundamentals of thermodynamics

Thermics - macroscopic approach; studying the system as a whole (simplifies the description of thermal processes).

Thermodynamics - concerned with heat and temperature and their relation to energy and work.



The Lord Kelvin

Heat is a form of energy, **temperature** state of a system.

The relationship between the change in temperature of the system and the amount of supplied / removed thermal energy: **$\Delta Q = m * c * \Delta T$**

ΔQ (J) heat change, ΔT (K) temperature change, m (kg) weight, c (J/kg.K) specific heat capacity.

Thermodynamic temperature: Kelvin (K), the SI unit. In medicine Celsius scale (°C). USA: Fahrenheit (0°C = 32°F; 100°C = 212°F).

T [K] = t [°C] + 273.15

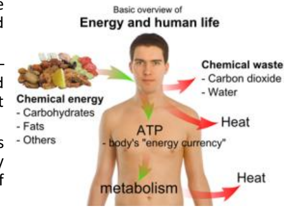
28

Heat balance of chemical reactions in the body

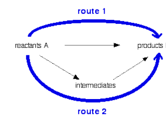
In a living organism take place two thermodynamically opposed processes :

a) **irreversible processes** – degradation of energy and entropy increase (nutrient conversion to CO_2 and water)

b) **open systems** – life processes prevents increase of entropy (they increase the entropy of their environment)



Nutrient conversion to CO_2 and water takes place via a series of reactions. The enthalpy (the maximum amount of heat) of a chemical process is independent of the path taken from the initial to the final state (**Hess's law**).



30

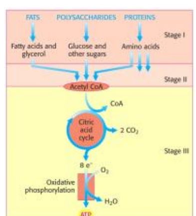
Heat balance of chemical reactions in the body

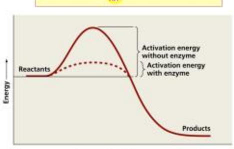
The maximum amount of energy that can be converted into work during a chemical reactions:

$\Delta G = R * T * \ln K$

K (equilibrium constant) = *[products] / [reactants]*

- $\Delta G < 0$ for spontaneous reaction; releases energy into the surroundings.
- When removing reaction products (open system), remains $\Delta G < 0$.
- Spontaneous reaction can be very slow (thermodynamics does not expresses rate). Metabolism of nutrients (carbohydrates, lipids, proteins) occurs only in the presence of enzymes.





31

Thermoregulation

The temperature is crucial for the metabolism - a highly temperature sensitive enzymes.

The average body temperature in humans ranges from 36.5 °C to 37.3 °C. Skin temperature ranges from 31 °C to 35 °C.

Heat production:

The relative share of heat production at rest: about 56% internal organs and 18% muscles and skin (during physical work, it grows up to 90%).

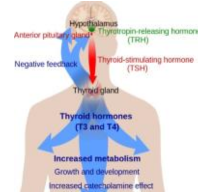
a) Basal metabolism

– energy from nutrients is converted mainly into heat

b) Increased metabolism

– muscular work (eg. goosebumps, tremor from cold, digestion)

– regulatory action of hormones (thyroxine, noradrenaline)



32

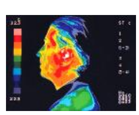
Mechanisms of heat loss

Direct heat loss: radiation, conduction, convection.

Indirect heat loss: evaporation (evaporation from the lungs; perspiration)

Radiation

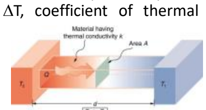
Represents up to 60% of total heat loss (depending on ambient temperature). Every body that is in an environment of lower temperature radiates heat as infrared radiation (5-20 μm).



Conduction

Liquids are well thermally conductive: blood transfers heat from inside the body to the skin.

The amount of transferred energy at time between two points depends on the difference in their temperatures ΔT, coefficient of thermal conductivity and surface area.

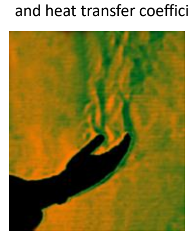


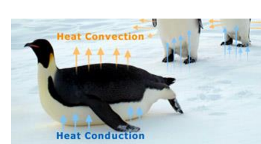
33

Mechanisms of heat loss

Convection

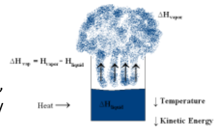
- is the transfer of heat from one place to another by the movement of fluids (liquids or gases). The heat transfer over time depends on the air fow rate (for example, frostbite occurs at low temperatures faster in the wind than in no wind), surface area, difference in temperatures ΔT and heat transfer coefficient.





34

Mechanisms of heat loss



Evaporation

Due to the high specific heat of vaporization, evaporation of water makes up 25% of body heat loss (depending on the air humidity).

Evaporation of sweat from the skin surface has a cooling effect due to evaporative cooling.

Breathing – exhaled air is almost saturated with water vapor.

Perspiration

a) *unnoticeable* (spontaneous diffusion of water through the skin, without the participation of sweat glands); average loss of water 660 ml/day.

b) *noticeable* (via the sweat glands); loss of water to 1.5 l/h. Regulated by the organism; efficiency depends on the environment (e.g. humidity).

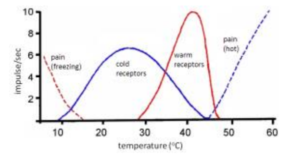
Noticeable perspiration is significantly applied when the surrounding temperature is high (> 36 °C) and other mechanisms can not be applied.

35

Thermoregulation

Warm-blooded animals maintain temperature using thermoregulatory mechanisms. The main regulatory mechanism is the **negative feedback** – a comparison of the desired temperature (hypothalamus) with the actual body temperature.

- Temperature changes are detected by the thermoreceptors in the skin, in the hypothalamus and also in some organs and vessels.
- In the epidermis are receptors for cold; in the upper part of the corium (dermis) are receptors for heat.



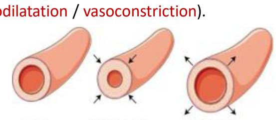
37

Thermoregulation

The organism produces heat => they need to control heat loss.

Skin and its importance in thermoregulation:

- Skin with subcutaneous fat is a good insulator => small removal of heat by conduction.
- **For thermoregulation is important blood flow from the organs to the periphery (skin)** => The efficiency of heat removal depends on blood supply to the skin (vasodilatation / vasoconstriction).



- Skin sweat glands regulates the body temperature (heat is removed by evaporation).

38

Temperature measurement (thermometry)

The temperature as a physical quantity describes the state of the organism as the biological system and is a significant and easily identifiable symptom of a large group of diseases.

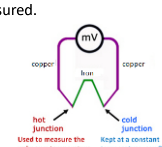
The temperature is NOT measured directly, but uses the known physical phenomena that show temperature dependence

Thermometers based on thermal expansion (eg. volume expansion).

Resistance thermometers: The electrical resistance of metals depends on the temperature.

Radiation thermometers: non-contact temperature sensors that measure the temperature from the amount of thermal electromagnetic radiation (e.g. infrared) emitted from the subject being measured.

Thermocouple thermometry: Thermocouple convert the heat directly into electricity at the junction of different types of wire. Miniaturization - Invasive temperature measurement in medicine (accuracy 0.05-0.01 °C).



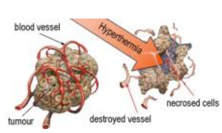
42

The use of thermal energy in medicine

Hyperthermia

It uses the thermal effect of microwave radiation, ultrasonic waves or laser in combination treatment of cancer.

High hyperthermic effect is achieved in tissues with low blood flow (less cooling) - tumor cells.



Used temperatures 42.5-45 °C (so that no damage to surrounding tissue) for 45-60 min.

Hyperthermia is most often used with radiation therapy (synergy effect).

Complicated computer processing of the absorbed dose and evaluation of the temperature profile limits the use of hyperthermia.

43

Cryotherapy

- **Use of cold to relieve pain** (ca 5 °C): vasoconstriction and subsequent vasodilation; Reduced transmission of nerve impulses and subsequent release of muscle spasm.
- Temperature reduction in **heart surgery**: reduce the risk of brain damage (at 30 °C oxygen consumption decreases to ½; at 20 °C to 1/10 compared to 37 °C).
- **Short-term conservation** of blood, serum, organs, etc.: a temperature about 4 °C.
- **Cryosurgery**: destruction of pathological tissues by a freezing probe.
- **Tissue fixation by freezing**: histological examination of the tissue removed during surgery (the result is known during the surgical procedure).

45