12.2 Thermography

Many pathological processes in the human body are closely connected with local or general temperature change. In section 11.2 we considered thermal measurements at only one location at a time. This can be made rather precisely. In some cases, the temperature distribution over the body surface is also of medical interest. Such continuous mapping of thermal fields is known as **thermography**. The measuring detector may or may not be in contact with the body.

12.2.1 Contact thermography

This method of temperature mapping is based on application of **cholesteric liquid crystals**. These crystals have **thermooptical properties** consisting of changes of spatial arrangement of liquid crystal molecules depending on the temperature. The axes of liquid crystal molecules form a spiral-like structure. By increasing temperature, the distance between molecules decreases and vice versa. In this way, the steepness (slope) of the spiral as well as the wavelength of reflected light decreases. At the lowest temperature the colour image is characterised by the longest wavelength (red colour), by increasing temperature the colour image is shifted to shorter wavelengths (yellow - green - blue). Every hue corresponds to a temperature and represents the **isotherm** – a region of identical temperature. In medical practice, the contact thermography is now replaced by the contactless method.

12.2.2 The contactless thermography

The principle of the contactless **thermography** is detection of infrared radiation (IR) emitted from the body surface. Spectrum of the human body radiation is relatively broad with a maximum at about 9 μm and respective energy of 0,1 eV. The recording is done from distance by means of optoelectronic systems which transform the energetic IR map of the selected part of body surface in a grey or colour scale image. These systems are also denoted as **thermovision**.

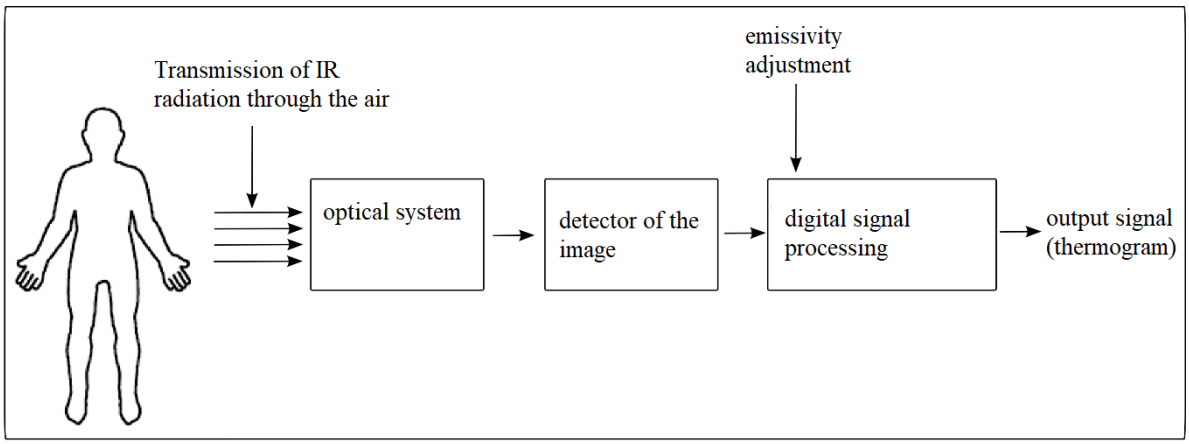
The thermographic system consists of four main parts: an optical system (objective), radiation detector, signal processing unit, and a display plus electronic memory (Fig. 12. 2. 2a). The IR image recording is very similar to the recording of visible image by means of a digital camera. First, the IR radiation propagates through the air, then is directed by objective lenses, filtered, and produces an image on the detector. Normal glass can be used only for IR light of very short wavelength which is emitted by very hot bodies. Therefore, the objective lenses are made of germanium or ZnSe.

The detector used in the IR camera is a transducer which transforms the IR radiation energy into electric signals. We can distinguish quantum detectors (so-called photonic, made of InSb or PbSe, for example). They are based on the photoelectric effect. They are accurate, very sensitive, and produce thermograms with high resolution (1344×784 pixels and more). However, the photonic detectors have these excellent properties only at low operational temperatures, and must be cooled, mostly by the Peltier effect. A little less accurate are the microbolometers which principle is close to thermistor principle. There is no need of cooling, are much cheaper but their sensitivity is not so high. These detectors have also problems with thermal stability. Their resolution is smaller (often only 320×240 pixels). Both quantum and microbolometric elements are organised in a matrix of detectors. The electric signals produced in detectors are consequently processed and displayed.

The display shows the temperature maps (thermograms) with different speed depending on the kind of the detector. In the quantum detectors it can be even thousands of images per second, in the microbolometric detectors it is only 30-60 images per second.

In the grey scale thermogram, the cold areas are dark, and the warm areas are white (Fig. 12.2.2b). In a coloured thermogram, each temperature is coded by certain colour which also represents an isotherm. The modern devices produce mostly the colour thermograms. They are able to show temperature profiles of the examined areas and perform simple image analysis. The recorded thermograms can be processed in the same way as any other image information by means of a computer software on-line or off-line (e.g., determination of the temperature of any depicted body surface point, calculation of areas of isotherms, different colour palette settings, adjustment to external conditions and statistical evaluation of the results).

A factor which complicates accurate measurement of the surface temperature by means of IR cameras is the surface **emissivity** or the so-called reflected temperature. The external medium and close heat sources can be mirrored by the surface of the examined object and thus influence the measured temperature of the object (the same laws of reflection and refraction are valid for infrared light as for the visible light). Emissivity is defined as the ratio of the radiant power of the absolutely black body radiating at given temperature, and the radiant power of the measured body. The infrared cameras are calibrated by means of the so-called black body since the black bodies have emissivity close to 1,000. It means that their "emitted" temperature is not influenced by the reflected radiation. Typical values of human skin emissivity (independent on skin colour) is 0,96 - 0,98. This value is valid for the skin without hairs, dry and without any bandages, ointments, lotions etc., which can diminish the emissivity values. In examination of a patient we also must consider the parameters of surrounding medium (optimum room temperature, humidity) and also long enough acclimatization of the patient or respective body surface part before examination.



Obr. 12.2.2a Scheme of IR radiation detection by means of a thermocamera

Obr. 12.2.2b Grey scale thermogram of a face. Temperature scale on the right side.

Diagnostic value of thermography

About fifty years ago, thermography was connected with great expectations in non-invasive screening of some oncologic diseases, namely breast cancer. However, this hope was not lived up to. Today we use thermography rather as a complementary imaging method in diseases which are connected with temperature changes of body surface also called **dynamic thermography**. We can admit that a substantial decrease of prices of thermographic equipment, higher resolution and detector sensitivity, as well as a possibility to record video sequences made this method attractive again for clinical medicine which is demonstrated mainly in the clinical research up to now.

The sensitivity of modern thermographic systems to temperature changes achieves about 0.025 K. However, in medical imaging, the sensitivity is influenced by localisation of heat sources. It is relatively high in superficial lesions or lesions just beneath the skin. The deeper is the lesion the lower the sensitivity. It is caused by different thermal conductivity of tissues between the skin area heated and the heat producing lesion. These tissues can carry the heat away or influence its transport in some other way so that the lesion projection on the body surface need not necessarily correspond to its localisation in depth.

Specificity of thermographic examination is low, in general, as we detect only the place with the increased or lowered temperature, which can be caused by various pathologic conditions – an inflammation, tumour, metabolic disorder, or abnormal blood supply. In most cases thermography itself is not able to differentiate between these causes. In spite of that the list of medical indications of thermographic examinations is quite extensive: ischemia of extremities (Fig. 12.2.2c), impairment of nerves, diabetic neuropathy and angiopathy, tissue healing after reconstructive surgery, inflammations of musculoskeletal system, or psychosomatic disorders. In clinical experiments it can be used for control of hyperthermia and cauterisation, some problems in sports and occupational medicine, in physiotherapy and also in fast fever screening of people in hospitals or airports or during epidemies. There is a lot of technical applications of thermography, which can have indirect importance for medical facilities for example checking heat lines and sources, electric power technologies, transformers, heaters, thermal leaks from buildings etc.

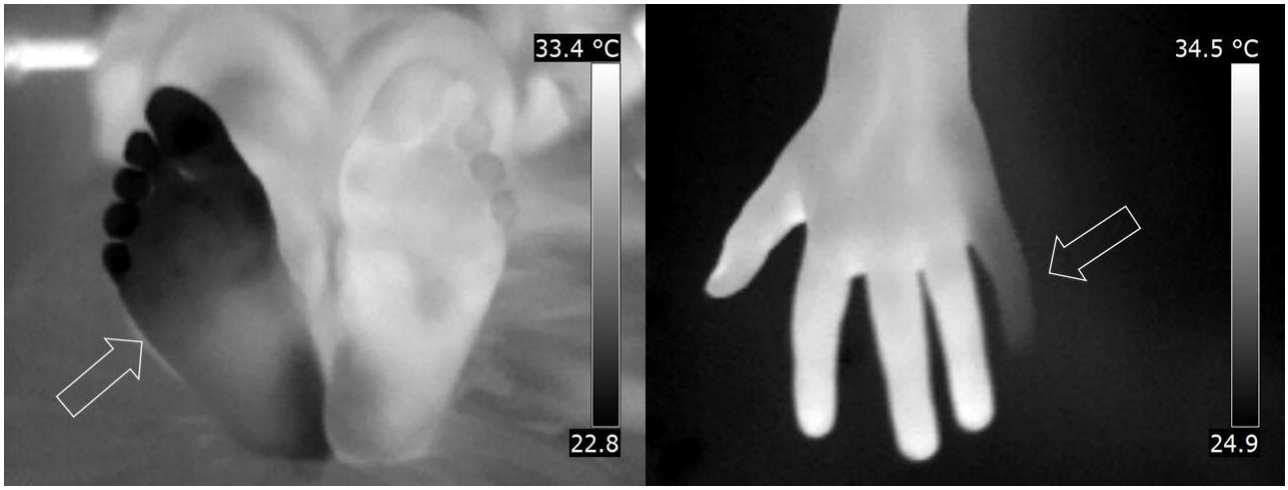


Fig. 12.2.2c Left: acute lower extremity ischaemia. Right: left upper extremity with *n. ulnaris* paresis, see lowered temperature of the little finger.

12.3 Ultrasound imaging and Doppler methods

12.3.1 Theoretical basis

Ultrasound is a mechanical wave motion, the frequencies of which are above the level of human hearing (20 000 Hz). Most diagnostic applications of ultrasound use frequencies in the range of 2 - 20 MHz. The energy of ultrasound travels through the medium as longitudinal, transverse and surface waves. Longitudinal waves are preferred for almost all biomedical applications. In such waves, the particles of the medium vibrate backwards and forwards about their mean position. This means that the energy is transferred parallel to the direction of wave propagation. An ultrasound wave in a given medium has a frequency *f*, wavelength λ and a propagation speed *c*, which are related by the equation:

$$\lambda = \frac{c}{f} \qquad (1)$$

The velocity of ultrasound passing through a liquid medium (in principle, most biological tissues) depends on the medium's elasticity and density. The velocity in most soft biological tissues varies between 1500 and 1600 m/s (velocity in water is approximately 1490 m/s).

Some characteristics of the transmission of ultrasound are similar to those of light, especially when the wavelength is short enough. The ultrasound wave can be directed as a beam with little scattering and can be focused by an acoustic lens. The ultrasound beam can be reflected and refracted on the interface of the media and is absorbed and scattered in the media. All these transmission properties depend on the **acoustic impedance** of the medium, which is defined as the product of the ultrasound velocity and the density of the medium. The characteristic acoustic impedances Z of some materials are given in the following table.

Medium	*Z* $[kg \cdot m^{-2} \cdot s^{-1} \cdot 10^6]$	*Medium*	*Z* $[kg \cdot m^{-2} \cdot s^{-1} \cdot 10^6]$
air	0.0004	brain	1.55 – 1.66
water	1.52	blood	1.62
lung	0.26	soft tissues	1.6 – 1.74
fat	1.35	bone	3.75 – 7.38

Ultrasound needs for its propagation an elastic medium. Reflection and refraction can occur when a beam of ultrasound reaches the interface of two media with different acoustical impedances. At the interface, a portion of the ultrasound energy will be transmitted into the second medium, and a part of the energy will be reflected. Assuming a zero angle of incidence of the beam, the fraction *R* of the incident energy that is reflected is given by the equation:

$$R = [(Z_2 - Z_1)/(Z_2 + Z_1)]^2, \qquad (2)$$

where Z_1, Z_2 are acoustic impedances of the two media.

Ultrasound will not travel an infinite distance through any medium without changes. A part of the ultrasonic energy will be lost due to attenuation in the transmitting medium. The attenuation of ultrasound in any specific medium depends on frequency. When frequency increases, attenuation increases too. This dependence is linear in the tissue. The attenuation generally includes absorption and scattering. The attenuation for a medium can be expressed in dB/cm or by using the half-value thickness, the distance in which the initial intensity is

reduced by one half. The **half-value thickness** for bone at a frequency of 2.5 MHz is 6.5 mm. For the brain, the liver and the kidney it varies between 15 - 30 mm.

At megahertz frequencies used in medical applications, ultrasound is generated and detected by probes utilising the **piezoelectric effect**. The probes, also called **transducers**, convert electrical signals into acoustical ones and vice versa. By applying an alternating voltage of the desired frequency, the piezoelectric transducer generates an ultrasound signal of that frequency. Conversely, when the transducer is periodically compressed by the reflected ultrasound, an oscillating electrical potential arises according to the magnitude and the direction of the deformation, and the same transducer becomes a receiver. The ultrasound is emitted in short impulses.

The main physical mechanism of diagnostic application of ultrasound is its reflection at acoustic boundaries in tissues. Ultrasound that is not reflected travels beyond the boundary and may be reflected at deeper boundaries. The maximum penetration is limited by the attenuation of the ultrasound passing through the given tissue. It is important to be aware that ultrasound is almost completely reflected at boundaries with gas. This restricts the investigation of gas-containing structures. For this reason, it is necessary to exclude air between the probe and the patient. This is done by using a special gel or water or another layer with closely similar acoustical impedance to the examined tissue.

Ultrasound diagnostics involves two groups of methods:

- Imaging methods

- Doppler methods

12.3.2 The mechanism of ultrasound imaging

All ultrasound diagnostic methods are based on the detection of ultrasound waves that are **reflected** at boundaries between different tissues of the body. The magnitude of the reflected wave depends on the difference of acoustic impedances of tissues forming such a boundary. The very short ultrasound pulse (shorter than 1 μs) generated by the piezoelectric transducer and transmitted into the body (the mean repetition frequency is 1000 Hz) is reflected on the boundary between two media of different acoustical impedance and detected by the same probe. The time delay between the transmission of the pulse and the detection of its echo depends on the propagation speed and the path length. The propagation speeds in different soft tissues are so similar that a constant relationship between time and distance can usually be assumed. The intensity of the echo compared to that of the incident pulse is strongly diminished for two reasons:

1) The reflected part of ultrasound depends on the acoustical impedances of the tissues on the boundary according to equation (2).

2) The intensity of the ultrasound decreases exponentially with the depth of penetration according to the equation:

$$I = I_o \cdot e^{-\alpha \cdot d} \qquad (3)$$

where I_o is the initial intensity, α is an attenuation coefficient, d is the distance.

The attenuation due to the depth of penetration is compensated by special amplifiers. The frequency dependence of attenuation limits the choice of scanning frequency. Lower frequencies (2.5 - 6 MHz) are used for scanning of tissues located deep in the body, whereas higher frequencies (7 - 15 MHz) serve for scanning of superficial organs.

Depending on echo processing, several scanning systems which may be used:

A-mode (**A**mplitude modulated): This basic pulse-echo system is used for measuring the depth of echo-producing boundaries in one direction. The display on the monitor is called A-

scan and is characterised by deflections of the time base. The time delays between pulses correspond to the distances between the boundaries within the body (Fig. 12.3.1a-a). This one-dimensional imaging method is actually used for biometric measurements, especially in ophthalmology.

B-mode (**B**rightness modulated): The information obtained by the transducer can be processed and displayed on a brightness-modulated system so that the brightness increases or decreases with the echo amplitude. It is the basis for two-dimensional imaging called **B-scan**. The aim of B-scanning is the production of an image of a cross-section through the soft tissue structures of the body (Fig. 12.3.1a-b).

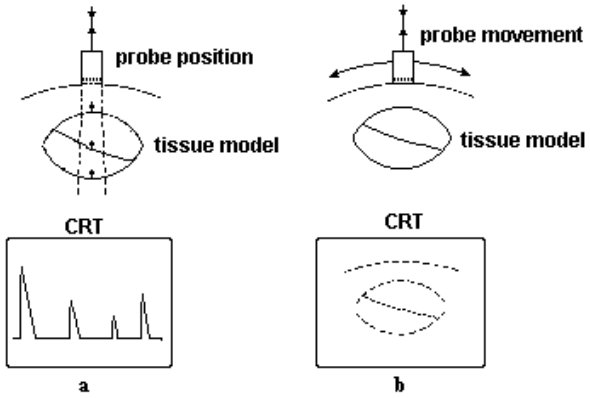


Fig. 12.3.1a. Principle of A-mode (a) and B-mode (b) imaging.

In the older approach, the mechanical system restricts the motion of the probe to a two-dimensional plane and links the direction and the position of a B-scope time base on monitor screen. This method is obsolete, the image on the monitor is not displayed in real time and thus the tracing of moving structures was not possible (Fig.12.3.1b).

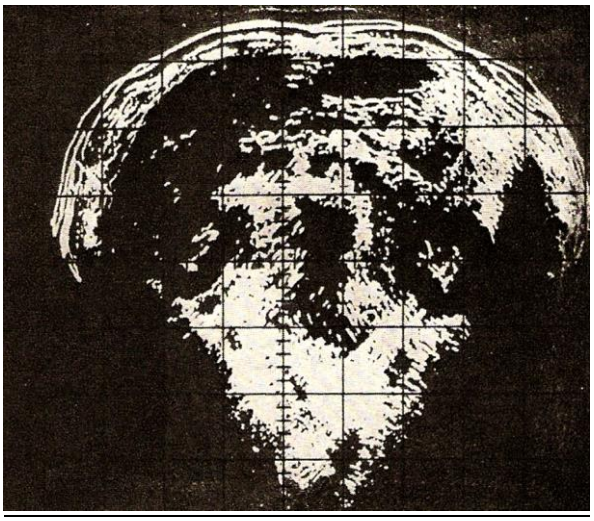


Fig. 12.3.1b Static B-scan of epigastrium

The current approach utilises a **real-time scanner** with multiple separate transducer elements (up to 128). The elementary transducers are synchronously switched. By this method, the need for mechanical motion of the probe is eliminated. The shape of the probe exactly defines its ultrasonic field and simultaneously the shape of the cross-section of the body that is momentarily displayed on the monitor. When the probe is moved over the surface of the body, you can see images corresponding to the cross-sections of the structures situated in the ultrasound field of the probe. Probes for **linear** and **sector scanning** are widely used (Fig 12.3.1c). When the frequency is increased, the image resolution improves, but penetration decreases. This problem is now solved by using multifrequency imaging probes. These probes scan the near field with higher frequencies and the far field with lower

frequencies. Probes differ according to the geometrical arrangement of elementary transducers and their electric driving (phased array, linear array, annular array probes). **Convex** probes are popular, the transducer arrangement on the convex area is almost linear, and the image, however, is similar to that of a sector probe.

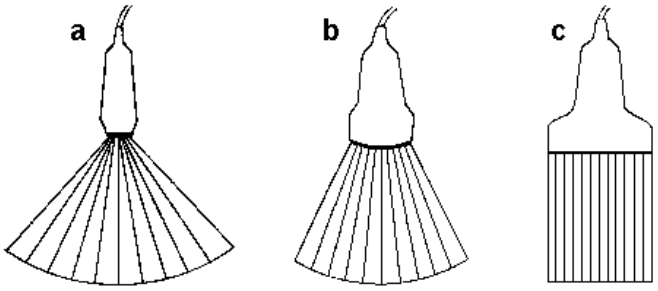


Fig. 12.3.1c. Imaging lines of a sector (a), convex (b) and linear transducer (c)

Sector and convex probes operating at lower frequencies are generally used to scanning deep structures (abdominal scanning) – Fig. 12.3.1d. Linear probes operating at higher frequencies are designed for examination of superficial organs.

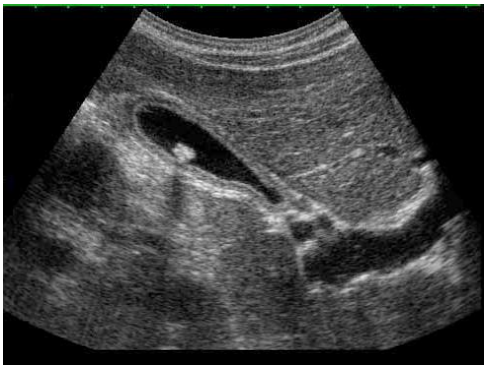


Fig. 12.3.1.d. convex image of liver region with gallbladder and a small gallstone. An acoustic shadow forms behind the stone.

M-mode recording (sometimes referred to as T-M mode). M-mode (motion-mode) is used to examination of moving boundaries (heart valves are the typical example). M-mode recording is composed of B-scans curves lying side by side. Every curve describes the motion of one boundary expanded in time (i.e., one axis is time; second axis is the shift of the boundary). Depending on the velocity of the movement and the depth of the examined structure, it is necessary to choose an appropriate repetition rate. On the one hand, the deeper the structure, the slower must be the repetition frequency; on the other hand, the faster the movement of the structure, the higher must be the frequency of repetition. This implies that it can be a problem to display fast and deep structures.

12.3.3 Doppler diagnostic methods

The measuring and imaging of moving structures is based on the **Doppler principle**. The frequency shift between incident and reflected waves depends on the velocity of the movement. If v is the velocity of the moving boundary, and c is the speed of propagation of ultrasound in the given medium, the Doppler frequency shift f_D in the reflected wave is given by the equation:

$$f_D = \frac{2v.f}{c}\cos\alpha\,, \qquad (4)$$

where α is the angle between the direction of the ultrasound beam and the direction of the moving structure.

Ultrasound Doppler methods are now widely used in the study of moving structures or in the measurement of the velocity of the blood flow in the vessels.

Continuous-wave Doppler (CWD) and **pulsed-wave Doppler (PWD)** systems, both produce Doppler shift signals which depend on the velocity of the movement. The continuous-wave system utilises separate transmitting and receiving transducers (Fig. 12.3.3a). This system can be used only for flow measurement in superficial vessels. The most **flowmeters** are directional, e.g., they can measure separately direct and reverse flow (Fig 12.3.3b). The signal processed can be displayed in the form of the velocity time-course on a monitor and simultaneously supplied to a loudspeaker.

The pulsed-wave system also provides information about the position of the examined moving structure. This system is able to measure blood flow in deeply located vessels independently on other moving structures in the surrounding. Recording of velocity curves is often designated as spectral Doppler.

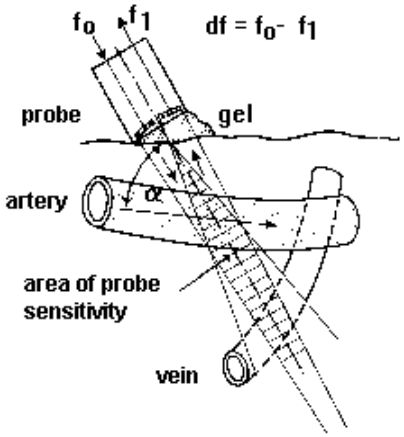


Fig. 12.3.3a. Velocity measurement using CW Doppler

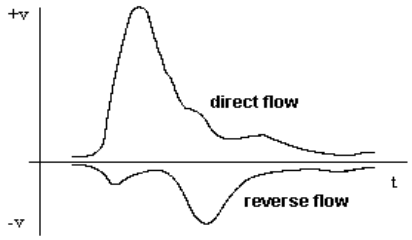


Fig. 12.3.3b. Velocity curves of a directional flowmeter

Most systems using the Doppler principle are combined with two-dimensional imaging. This combination is called **duplex method**. The vessel under examination is first identified using a two-dimensional scan and then the flow parameters are measured by the Doppler method. In more sophisticated systems it is possible to co-ordinate the colours to the defined range of velocities. This **colour flow mapping** (CFM) method enables us to improve the analysis of the moving structures. Combination of a two-dimensional B-scan, spectral Doppler and colour flow mapping represents a **triplex method** (Fig 12.3.3c,d). See also chapter 12.3.7.

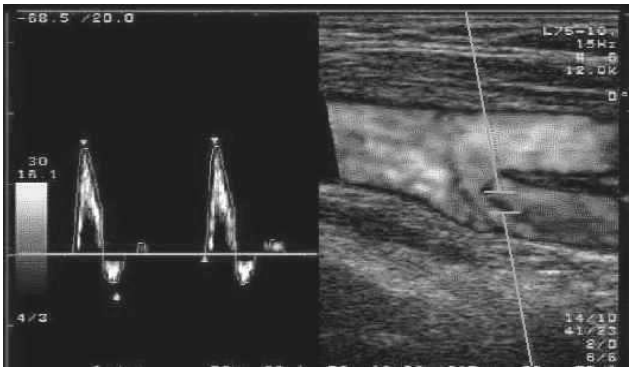


Fig. 12.3.3c. Duplex measurement of blood flow in lower limb - *a. profunda femoris* (high resistant curve)

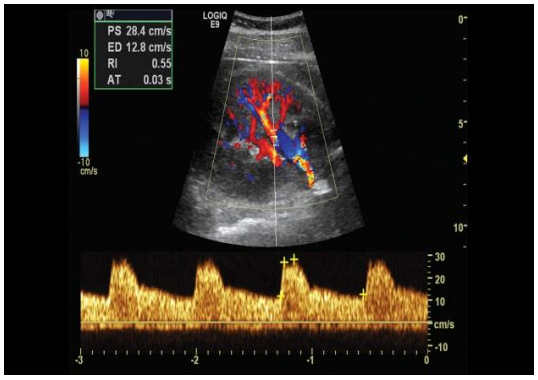


Fig. 12.3.3d Triplex measurement of blood flow in intrarenal artery (low resistant curve)

12.3.4 Ultrasound echo-contrast agents

Ultrasound contrast agents (echo-contrast or echo-enhancing agents) are air or gas microbubbles, free or encapsulated in a polymer cover. Echo enhancement made its first appearance in 1968 when an increase in ultrasound signal intensity was observed after a rapid intravenous injection of saline. However, the mechanism of this echogenic effect remained obscure until 1980 when it was proved that echo enhancement is due to microscopic air bubbles that scatter ultrasound energy in all directions. These bubbles have significantly lower acoustic impedance than the surrounding liquid medium. This higher difference in acoustic impedance can enhance the echogenicity of the body space in which they are introduced.

Short-lived bubble suspensions were first applied in echocardiography to enhance the echogenicity of the right side of the heart. However, none of them survived pulmonary transit to enter the left side of the heart and the systemic circulation. Therefore, efforts to produce longer-lasting enhancement have been directed towards the creation of stable suspensions of gas microbubbles that can pass through the pulmonary capillary bed. Three approaches have been used to produce stable contrast agents:

- gas-filled microspheres

- microparticle suspensions

- suspensions of free gas bubbles in pure liquid vehicle

The factors that determine bubble survival are the rate of diffusion of the gas from bubbles into the liquid, the viscosity of the fluid and their surface tension. Gas-filled microspheres are protected against gas loss by a shell (for example of serum albumin or other biopolymer). Water-soluble galactose microparticles originate gas microbubbles when they are mixed with an aqueous vehicle – Fig. 12.3.4. Palmitic acid of 0.1 % forms a flexible protective monolayer around the gas bubble and retards the diffusion of the gas into the surrounding medium.

The third approach is represented by a liquid in liquid dispersion in water that contains a liquid, sulphur hexafluoride (SonoVue), which converts into gas microbubbles at body temperature. The most gas bubbles in all types of contrast agents have a diameter of 2-5 μm.

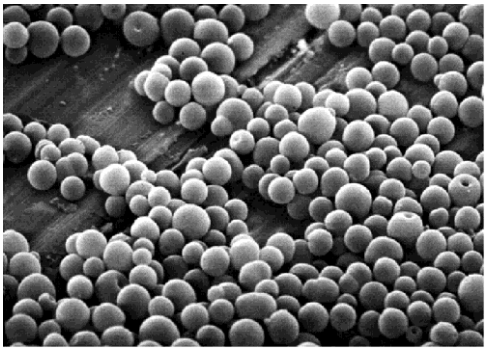


Fig. 12.3.4. Electron-micrograph (SEM) of an echo-contrast agent

Clinical applications example:

- **Local application** - hysterosalpingo-contrast ultrasonography. Intrauterine injection of a contrast agent improves visualisation of the Fallopian tubes.

- **Systematic use** in Doppler ultrasonography. Intravenous injection of contrast agent dramatically improves the amplitude of the Doppler signal. This application is particularly useful in transcranial examinations, echocardiographic examinations, imaging of carotid artery diseases and imaging of metastases of malignant tumours.

The improvement of image quality increases diagnostic confidence, leads to better treatment decision, saves time, and reduces the need for invasive procedures.

12.3.5 Additional forms of ultrasound imaging

Harmonic imaging. About 15–20 % of patients seem poorly examinable by conventional ultrasound imaging. To achieve a well evaluable image, it is necessary to increase acoustic power of ultrasound impulses and the time of examination is also longer. A significant increase of image quality in these patients and better contrast resolution in all other patients can be achieved even without echo-contrast agents by means of a **natural harmonic imaging** (THI, tissue harmonic imaging).

Principle of this method is very simple in first approximation: An ultrasound impulse with fundamental (first harmonic) frequency f_0 is transmitted in the body part. However, the probe does not receive the reflections of the fundamental frequency but the second harmonic signals with frequency $2f_0$. These oscillations are consequently processed. Unlike of the echo-contrast harmonic imaging (when using the echo-contrast agents), the harmonic frequencies originate directly in tissue structures as a result of so-called non-linear ultrasound propagation. However, the technical realization of the measurement is not simple as the second harmonic frequency is relatively weak. □

Panoramic imaging. This imaging modality enables a continuous recording of the tissue image across a broad area in desired direction. Hence an elongated view is produced for better assessment of dimensions and morphology of the whole examined area (Fig. 12.3.5a). This method is complementary to the conventional imaging which in most cases gives only partial view on the examined body part.

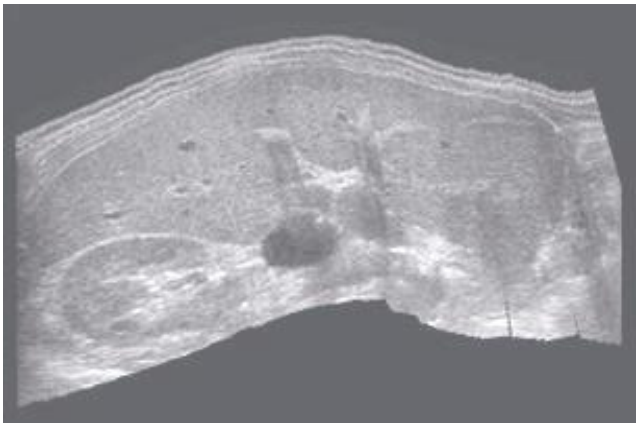


Fig. 12.3.5a Panoramic image of epigastrium (from left: liver, right kidney, gall bladder, spleen)

Endoluminal imaging. It is a method of interventional radiology: miniaturised transducers working at high frequency (20 - 40 MHz) are inserted into the blood vessels or hollow organs. Their high-resolution ability allows detection of small pathological changes in the vessel walls or some other organs. Fig. 12.3.5b.

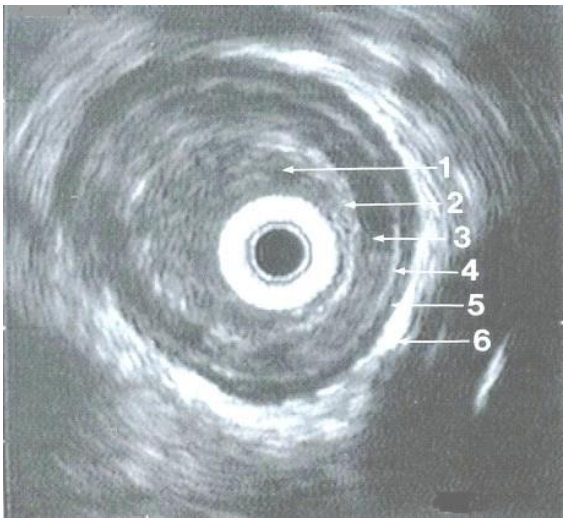


Fig. 12.3.5b Endoluminal imaging: Transversal section of oesophagus. The numbers denote individual layers of the oesophagus wall.

12.3.6 Ultrasound elastography

Elastography is a new imaging modality which is an emulation of the palpation. The basic idea is that pathologic changes of tissues are manifested by their changed mechanical properties, first of all rigidity. Malignant lesions are mostly more rigid in comparison with benign lesion of healthy tissues.

The method provides images of tissue structures based on the measurement of the response of the soft tissues on defined compression of the adjacent body surface. These properties depend on molecular structure of individual tissue components (fat, collagen) and their spatial organisation. Moreover, the tissues have also some viscoelastic and poroelastic properties (poroelasticity is the specific elasticity of porous materials which pores are filled by a liquid).

It is not possible to obtain elastic properties of tissue from a simple ultrasound image. Therefore, during last almost three decades several ultrasonic elastographic methods were elaborated:

Static compression elastography or *Strain-Stress Elastography*, where the deformation of the tissue is evoked by the pressure of examination probe (Fig. 12.3.6a).

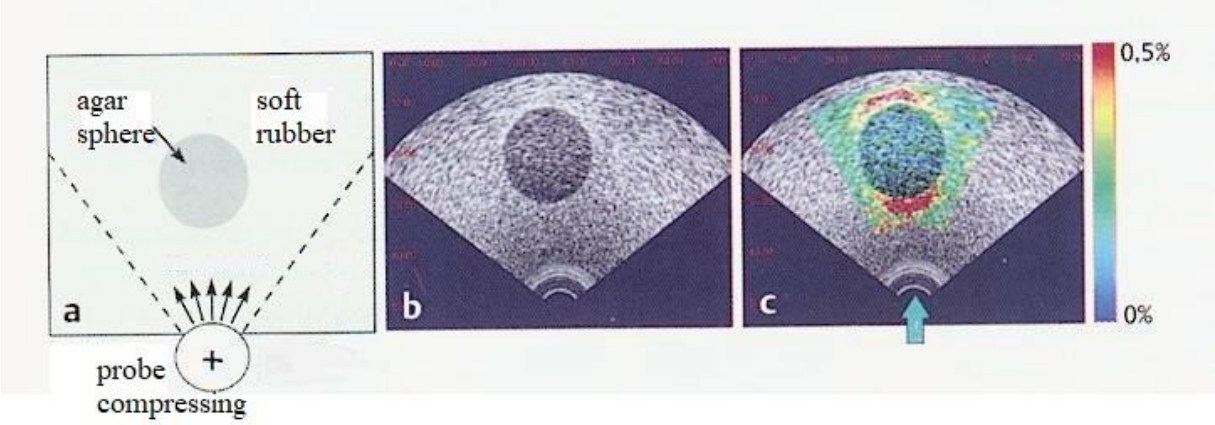


Fig. 12.3.6a Static elastography of a phantom: a – scheme of the phantom, b- ultrasonogram, c- elastogram.

In the *Acoustic Radiation Forced Impulse Elastography* the pressure is evoked by a strong impulse of radiation force.

Transient elastography is a single-purpose method for diagnostics of the degree of fibrosis in liver. Its typical technical component is a vibrator which produces mechanical middle-amplitude oscillations at a frequency of 50 Hz.

In present time, the SWE – *Shear Wave Elastography* has a dominant position in this field of examination. Instead of pressure action of the probe, this method exploits the so-called radiation force of the ultrasound waves. The acoustic compression is achieved by means of relatively long repeated focused impulses along the imaging line, which produce acoustic shear (transverse) waves. These waves propagate much slower than the longitudinal acoustic waves and their speed is proportional to the elasticity of the tissue (Young modulus). The particles of elastic medium move with amplitude of only micrometres. Imaging of such movement needs a special imaging mode denoted as supersonic imaging with very fast image processing (5000–20000 images per second). In contrary to the previous method the information about tissue elasticity is quantitative and the colour scale is calibrated in kPa.

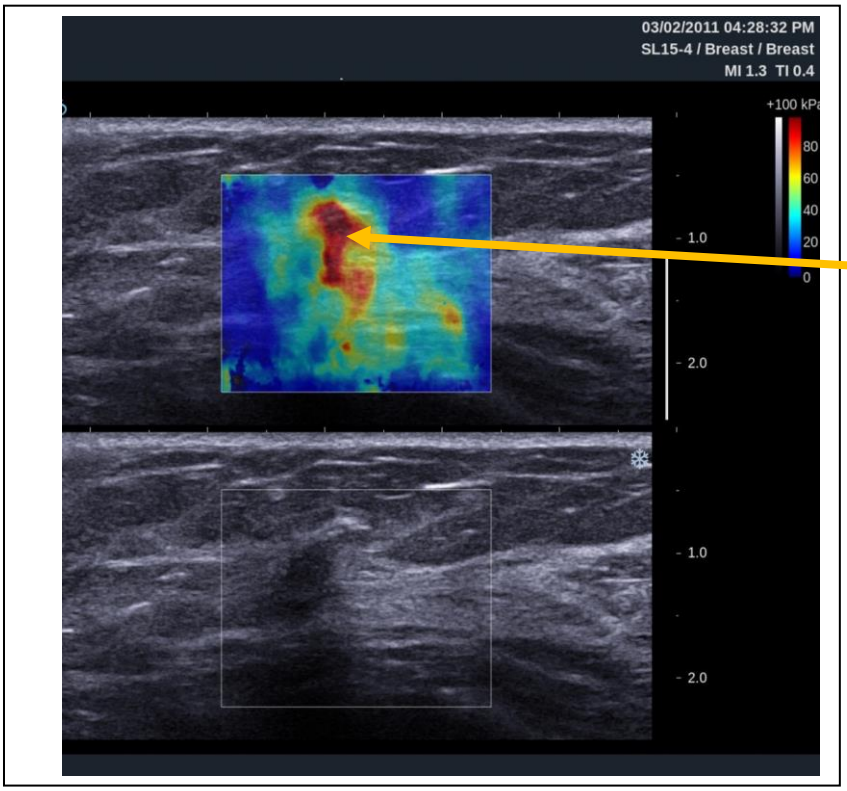


Fig. 12.3.6b SWE of the ductal carcinoma of the breast. Stiffness 105 kPa

12.3.7 Special methods of Doppler imaging

Power Doppler (PD). The limitations of colour Doppler imaging are mostly removed in the technology of the colour Doppler signal imaging denoted as "Power Doppler" or "Power angio". This method differs from the conventional blood flow imaging in utilisation of all energy of the Doppler signal.

The advantages of this technology can be summarised as follows:

- Detection of the blood flow only little depends on the so-called Doppler angle and enables us the flow imaging even at almost perpendicular incidence of the ultrasound beam on the examined vessel.

- There is no aliasing effect.

- The method can be used also for very slow flows hence it is “predetermined” for imaging of organ of tissue blood perfusion (Fig. 12.3.7a).

Disadvantage: Missing information about the flow direction. Only one colour (mostly orange) is used for flow coding. This disadvantage tries to remove a new method called *Directional Power Doppler*.

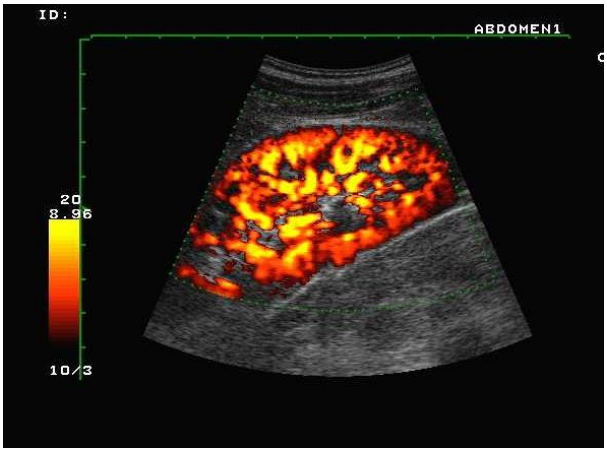
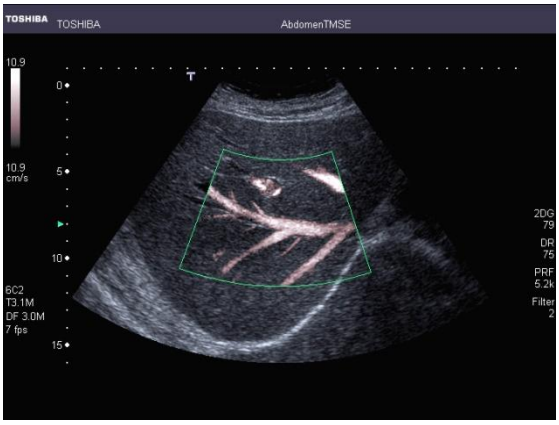


Fig. 12.3.7a. Perfusion image of kidney obtained by Power Doppler. The bright areas are orange in original picture.

B – flow. It is a new ultrasound diagnostic method based on combination of blood flow and tissue structure imaging in real time. It is not Doppler method thus we obtain no information about the blood flow speed. However, there is no worsening of spatial and time resolution in comparison with conventional colour Doppler.

The B – flow method depicts blood flow similarly to static structures in grey scale. The digitally encoded broad-band impulses reflect from the moving erythrocytes. The reflected echoes are again decoded and filtered in order to increase the detection sensitivity. The main advantage of this method is a correct imaging of the boundary between the blood vessel wall and streaming blood. (Fig. 12.3.7b). In the conventional colour Doppler, the colour area often overlaps the vessel walls. In superficially located vessels, e.g., carotids, this method can show the position and extent of atheromatous plaques more precisely in comparison with colour Doppler. Similarly, in the venous system we can see better small thrombi. The only limiting factor of this method is the ultrasound attenuation which makes difficult imaging of deep vessels.



Obr. 12.3.7.b Hepatic veins.

Tissue Doppler imaging. Originally, the movements of tissues, e.g., heart or vessel walls or peristalsis of digestive tract could be observed and assessed only in a grey-scale image. The Doppler imaging modality which is called *Tissue Doppler Imaging* (TDI), invented in 1994, makes possible to get colour information about the speed and direction of tissue movement. This method was invented for cardiologic purposes (detection of pathologic changes in cardiac wall movement). However, today is used also in other areas of ultrasound diagnostics, mainly in sonoangiology.

Basic principle: The ultrasound echoes reflected from moving tissues are relatively strong, but the speed of the tissues is very small. On the other hand, the reflections from moving erythrocytes are weak but the speed of blood is high. In the colour imaging of streaming blood, the colour images of vessel walls and surrounding tissues are an interfering effect, a colour artefact which is removed by filtration. In TDI are the signals caused by high speed of streaming blood supressed, but the image is showing low speed movements (of heart or vessel walls) in the range of 1 – 10 mm/s.

TDI given information mainly about diseases of coronary arteries, ventricular arrhythmias, heart infarction etc. In angiology it enables more precise assessment of vessel wall elastic properties connected with atherosclerosis. Other applications can be expected.

Advantages of colour duplex and triplex methods. The main advantage of these methods is an **easy and fast identification** of a vessel in comparison with another part of the body filled by a liquid. The tone colour, which brightness is a function of the streaming blood velocity makes easier to find a stenosis and assess its degree. It makes also easier diagnostics of pathologic changes of deeper vessels. In peripheral vessels, it makes the diagnosis more precise, and in many cases can substitute X-ray angiography which endangers the patient by ionising radiation.

A disadvantage of conventional colour mapping of blood flow is relatively small sensitivity to slow streaming and a tendency to colour image artefacts which is caused by additional movements (probe shifts, breathing or peristalsis movements) or by transmission of arterial pulsation on the surrounding tissues. These colour artefacts can be removed or limited by correct manipulation with the probe or by frequency filtering. Since these methods can produce colour images of only mean stream flow it is possible that the maximal velocities can be underestimated. Therefore, we must pay attention to the right setting of velocity range and the record of velocity spectrum should be also added.

The general disadvantage of all colour methods is a relatively long-time interval necessary for the production of the colour image (50 - 150 ms). It decreases the image frequency in comparison with the grey scale image frequency. For example, if we need 65 ms to obtain a colour image it means that the image frequency is only 15 frames per second. The quality of colour image is also influenced by the size of the colour image window which is overlapping the grey scale picture.

Many of these disadvantages or limitations can be removed by the new technologies of image processing (e.g., power Doppler or B – flow method).

12.3.8 Principles of three-dimensional imaging (3D/4D)

The loss of one dimension, i.e., reduction of information about the volume element into a planar two-dimensional image is a general disadvantage of all imaging methods. In ultrasonography, an effort to remove this disadvantage by changing the image plane during the examination appears recently. It can be done by means of **probe movement** during the image acquisition. The probe can be shifted linearly, can be tilted, or rotated. The data about reflectivity in individual planes are stored in memory of a computer which performs

mathematical reconstruction of the 3D-image based on sequence of planar images (Fig. 12.3.8a). Special probes for 3D imaging can be also used.

There are two basic algorithms for acquisition of 3D-image:

3D surface mode. It is based on identification of structure surfaces with sufficiently big contrast to the surrounding tissues. The reconstruction is fast, but its information value is relatively small. Imaging of foetus structural surfaces can be a good example (Fig. 12.3.8b)

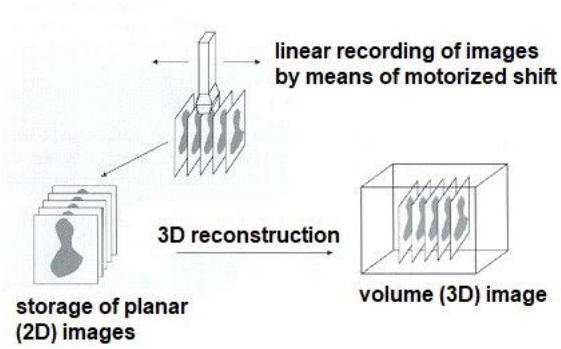


Fig. 12.3.8a Reconstruction of 3D-image from a sequence of planar images.

3D volume mode is based on the vector spatial imaging of all the reflection points of the examined structure which leads to formation of voxels. The position of each reflection point is accurately specified in the image volume. An advantage of the volume image is a possibility of its cross-section and rotation (Fig. 12.3.8c).

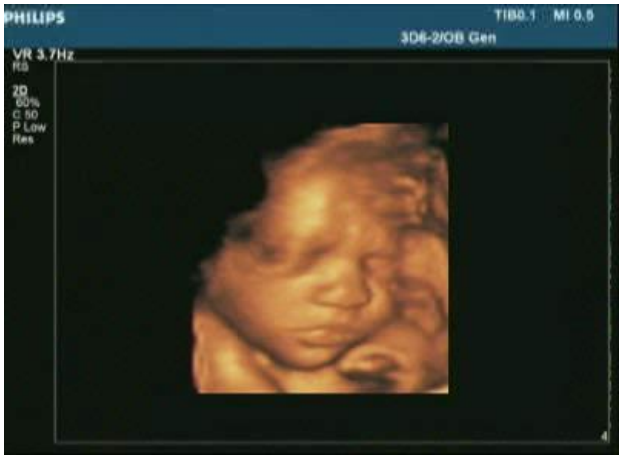


Fig. 12.3.8b 3D image of the foetus head

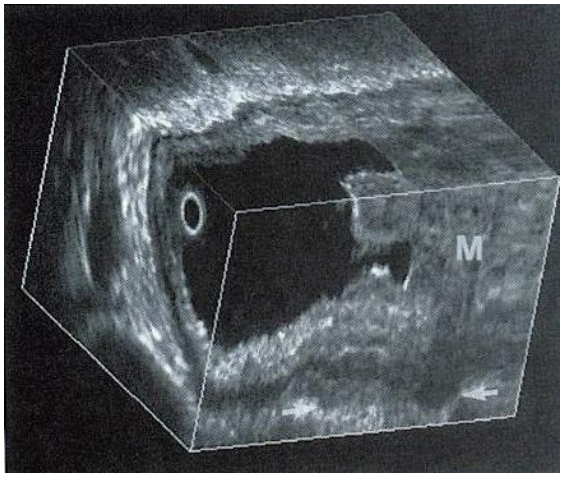


Fig. 12.3.8c 3D image of a tumour in oesophagus (dark area)

3D ultrasound multiplanar analysis could be the most accurate method for a correct assessment of examined organs morphology. A digitalised 3D spatial image (Fig. 12.3.8d) can be sent via suitable network to any chosen office or department.

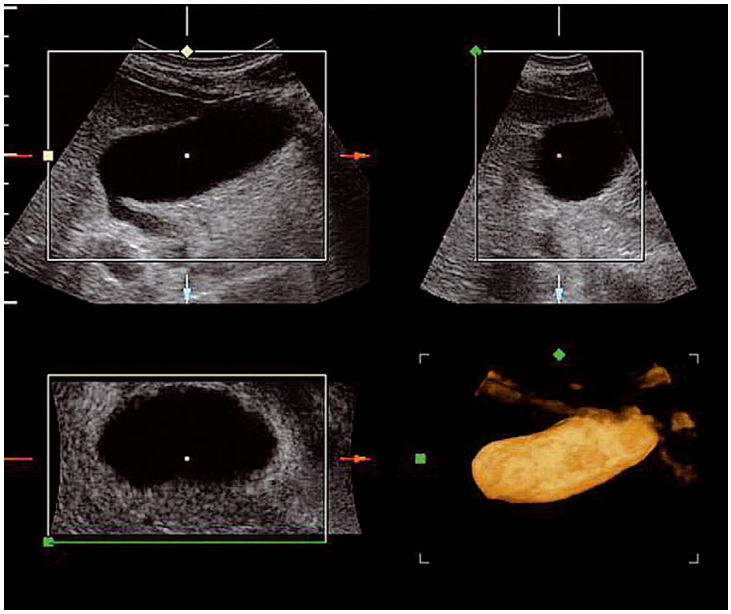


Fig. 12.3.8d The multiplanar image of gall bladder region (from left to right: longitudinal, transverse and coronal cross-sections plus volume reconstruction of the gall bladder)

The term 4D is used for systems which can process the volume image in real time. The advantage of this kind of imaging is its complexness, the disadvantage is its relatively difficult interpretation.

12.3.9 Safety of ultrasound diagnostic procedures

The interaction of ultrasound with biological tissues depends on its intensity. At sufficiently high intensities so-called **active interactions** take place. These interactions are used in physical therapy, surgery and in different laboratory experimental methods. **Passive interactions** take place at low ultrasound intensities. These interactions form the basis of ultrasound diagnostics.

Ultrasound of relatively low intensity has no ionising ability and its direct action on biological system is effectuated by means of three main mechanisms:

- **Heating** due to the absorption of acoustic energy in tissues and its conversion into heat.
- **Mechanical effects** due to the radiation force and radiation torque in the vicinity of cell and tissue interfaces.
- **Cavitation** meaning the production and dynamic behaviour of gas microbubbles formed in a liquid medium during the underpressure phase of an acoustic wave. Bubble oscillation and collapse cause microscopic shock waves capable of damaging surrounding cells and forming free radicals.

From the practical point of view, the damage of tissues due to heating is more likely to occur than that due to cavitation. For clinical practice, introduction of two on-screen indices

(i.e., numbers), the **thermal** (TI) and the **mechanical** (MI), is recommended. These indices should warn the physician of potential risk.

12.3.10 Clinical value of ultrasonography

During the last sixty years, ultrasonography became the most widespread imaging diagnostic tool in many branches of medicine. Ultrasonic examination forms mostly the first step in the diagnostic imaging algorithm because of its accessibility and cost-effectiveness. The basis of ultrasonography forms the dynamic (real time) B-mode imaging, enabling detection of solid and/or cystic lesions in soft tissues. Only ophthalmology uses the one-dimensional A-mode imaging for precise biometric measurement. Very good results have been achieved in applying ultrasound examination in cardiology, gastroenterology, obstetrics and gynaecology and endocrinology. Musculoskeletal ultrasound is in the stage of rapid development.

For assessment of haemodynamics and functional state of moving organs, sophisticated duplex and triplex methods have been developed. These methods represent a combination of dynamic B-mode imaging with spectral and colour Doppler methods. Several new methods, such as intraoperative and interventional ultrasound, 3-D imaging, and harmonic imaging are in the stage of technical development. These advancements should ensure that ultrasound remains the preferred diagnostic imaging modality of the near future.

12.4 Endoscopic methods

Endoscopes comprise a group of optical devices used for viewing internal body cavities, based on the reflection and refraction of optical beams. The endoscope is introduced in the cavity under examination either by its natural orifice (nose and oral cavity, larynx, trachea and bronchi, bladder, vagina, rectum) or by openings created surgically (thorax, abdominal cavity, joint etc.).

Endoscopes can be classified according to their complexity, form of illumination and mode of observation.

According to their complexity, endoscopes can be classified in three groups:

a) endoscopic mirrors,

b) endoscopes with rigid tubes,

c) fibroscopes and videoendoscopes, capsule endoscopy.

The source of light can be external or internal. Mirror endoscopes have external illumination. In rigid tubes, the source of light forms an integral part of the device. The source can be introduced within the tube in the cavity (distal illumination) or the light beam is introduced in the cavity from outside (proximal illumination).

Observation of the cavity be can direct or indirect. In direct observation, the examiner looks directly into the optical system of the device. In indirect observation, the image of the cavity is scanned by a microcamera and displayed on the screen.

12.4.1 Endoscopic mirrors

Simple endoscopes are flat, convex, or specially shaped specular (mirroring) surfaces. The curved surface focuses the light on the region of interest. The most frequently used endoscopic mirrors are following:

The **laryngoscope** is a small flat mirror forming on a holder at an angle of 60°. It is designed for examining the larynx and the (naso)pharynx.

The **otoscope** is a cone shaped mirror for visual examination of the external auditory canal and the eardrum. It is equipped often by light source and magnifying glass.

The **ophthalmoscope** permits the physician to examine the interior of the eye. Bright light is projected into the subject's eye, and the light reflected from the retina can be focused by the examiner. The lens system of the patient's eye acts as a built-in magnifier (Fig. 12.4.1).

The **vaginal speculum** is a double spoon-shaped instrument with a mirroring part used in gynaecology for examination of the vagina and the cervix uteri. Today it is a component of the **colposcope** together with a camera and some mechanical parts.

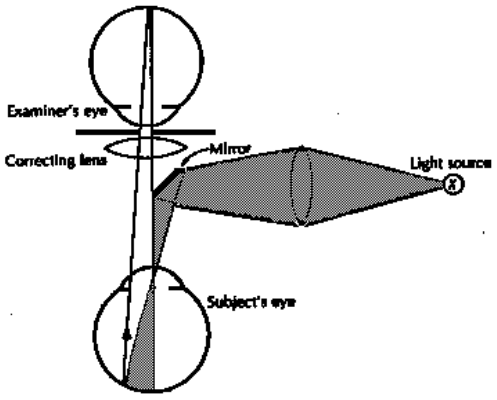


Fig. 12.4.1. Principle of an ophthalmoscope

12.4.2 Endoscopes with rigid tubes

These types of endoscopes have been developed prior to the discovery of fibre-optic techniques (*Adolf Kussmaul*, 1868). They consist of metallic tube of different length with a light source. Many of them are equipped with optical attachments to magnify the tissue being studied (Fig. 12.4.2). Through the tube, special surgical instruments can be introduced for taking tissue samples or other minor surgery.

Rigid tube endoscopes have two main disadvantages:

- The rigidity of the endoscope body represents a certain discomfort for the patient.
- The light transmission is connected with great losses of light energy.

Endoscopes often have names indicating their purpose:

Bronchoscopes for examining the air ways in the lungs.
Gastroscopes for examining the stomach.
Cystoscopes for examining the urinary bladder.
Rectoscopes (proctoscopes) for examining the rectum.
Laparoscopes for examining the abdominal cavity.
Arthroscopes for examining the articular cavities.
Many of these rigid endoscopes have been replaced by flexible ones.

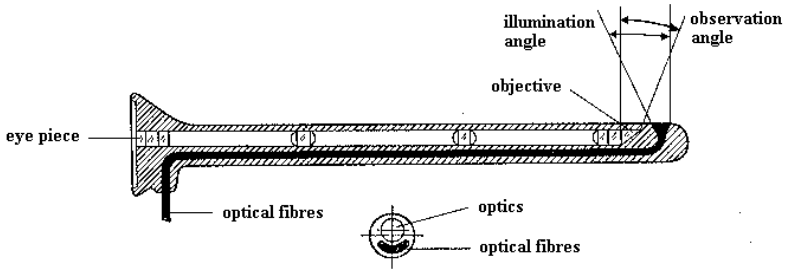


Fig. 12.4.2. Longitudinal section of a rigid endoscope

12.4.3 Fibre-optic endoscopes and other endoscopic systems

The development of fibre-optic technique permitted the construction of **flexible endoscope**s. These instruments can be used to obtain visual information from regions of the body that cannot be examined with rigid endoscopes, such as the small and large intestine. The light is conducted by optical fibre with minimal losses using the principle of the **total reflection**.

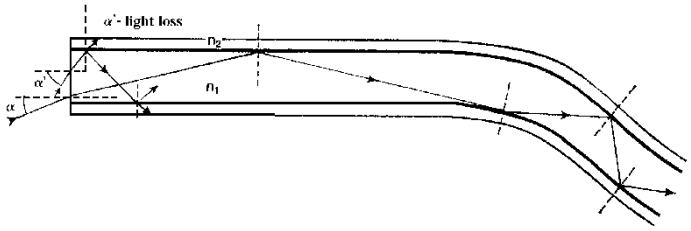


Fig. 12.4.3a. Schematic picture of an optic fibre

An optical fibre is usually formed by two layers (Fig 12.4.3a). The core of the fibre has a higher refraction index ~~of~~ n_1 than the outward packing n_2. Exploitation of the total reflection depends on the angle α, under which the light beam enters the fibre. Total reflection takes place if the following condition is fulfilled: $\sin\alpha < (n_1^2 - n_2^2)^{1/2}$, meaning that the angle of the incident beam must be greater than the critical angle. Separate fibres for illumination and for

image transmission form great bundles. In the image-transmitting bundle, the position of single fibres on the input and output must be the same. Losses of light energy in optical fibres are very low. The attenuation does not exceed 0.001 - 0.005 dB/m.

In the body of a fibre-optic endoscope, there are several channels: two optical channels (light and viewing channels), water or air channel and a biopsy channel permitting passage of devices to take tissue samples (Fig. 12.4.3b). On the distal end of the viewing channel is a viewing objective. On the proximal end, there is a viewing ocular and a mechanical control of the endoscope distal part. A halogen or LED source of light forms an integral part of the endoscope.

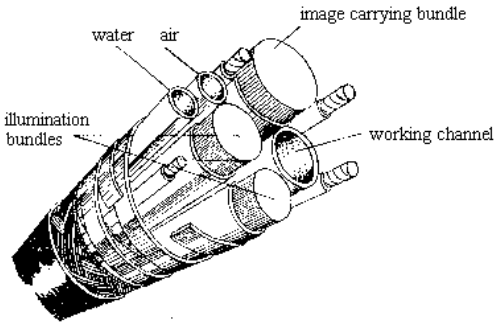


Fig. 12.4.3b. Cross-section of a fibre-optic endoscope

Videoendoscope represents a more sophisticated version of fibre-optic endoscopes. In this instrument the viewing objective is replaced by a micro-camera and the image of the examined cavity is displayed on the TV screen (Fig. 12.4.3c).

The **capsule endoscopes** are small independent probes which can be swallowed. During their passage through the digestive tract, they repeatedly record images and transmit them to the external part which is connected with the monitor and storage unit. These devices are disposable. Their independent part consists of a small battery, light source, camera, and transmitter electronics.

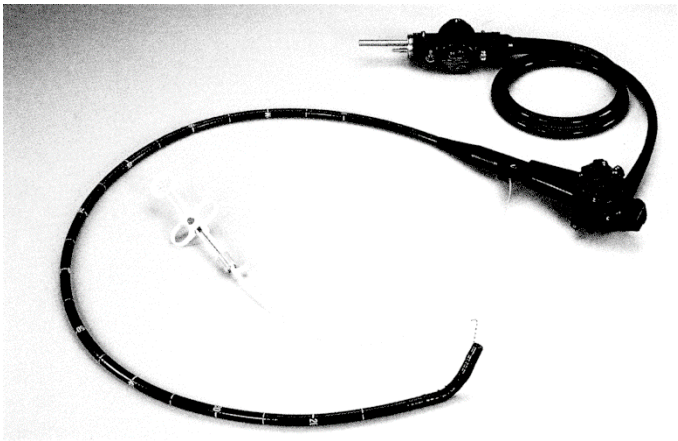


Fig. 12.4.3c. Duodenovideoscope (Olympus)

12.5 X-ray imaging methods

X-ray diagnostics began more than one hundred years ago with the epochal discovery of German physicist *Wilhelm Conrad Roentgen* (in 1895), who obtained the first radiograph of a part of human body, the famous picture of his wife's hand. In recent decades, the X-ray examinations were partly replaced by ultrasound or radionuclide examinations, but X-ray imaging nevertheless remains a commonly used diagnostic modality. Relatively low costs, facility and precision are the advantages of the X-ray images. Exposing patients to ionising radiation is the main disadvantage. Nevertheless, X-ray diagnostics still remain one of the most important imaging diagnostic methods in most branches of medicine.

X-ray imaging methods are based on the principle of different absorption and scattering of X-rays in different body tissues. Attenuation (i.e. absorption plus scattering) of a transmitted beam of radiation can be expressed by the term

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

where I_0 is the original intensity of radiation, I is the final intensity of transmitted radiation, d is the thickness of the absorbing layer, and μ is the **attenuation coefficient**. This coefficient depends mainly on the effective proton number of the absorbing medium, which is given by the mean proton number of elements present, considering their relative proportions. The attenuation coefficient also depends on the energy of transmitted radiation, and the kind of interaction of photons with matter (the photoelectric phenomenon, Compton scattering and electron-positron pair production).

The so-called **densitometry** is based on the mere measurement of the attenuation of x- or gamma-rays in bones. The method serves for determination of the degree of bone tissue calcification. It is also called DEXA – dual X-ray absorptiometry.

12.5.1 Principal scheme of an X-ray device

In general, each X-ray diagnostic apparatus consists of several basic parts. Electrical parts include a source of direct high voltage, X-ray tube, control panel and image detector. There are also some mechanical parts, which change the position of the patient relatively the X-ray tube and give mechanical support to the whole system.

The **source of high voltage** for feeding the X-ray tube (correctly, Coolidge type tube, see below) consists mainly of a transformer, rectifier, and the circuit for smoothing the pulsating direct current which is supplied by the rectifier. The **transformer** changes the relatively low mains voltage (230 or 380 V) to the very high voltage necessary for feeding the X-ray tube (roughly up to 150 kV). The output voltage of the transformer is continuously adjustable, and its high values result in high values of the X-ray photon energy. This high voltage could be led directly to the X-ray tube, but it is alternating, so that only each second half-period of the alternating current could be utilised for production of the X-rays. Electrons can pass through the X-ray tube in only one direction, i.e. from the hot filament (cathode) to the anode. Therefore, the alternating current is changed into direct current by means of a **rectifier**. However, the rectifier gives a pulsating current consisting of sinusoidal half-waves. The changing voltage of these half-waves could cause unwanted production of photons of low energy. That is why this pulsating current must be **smoothed**. The pulsation is almost fully removed in this way.

Besides changing the voltage led to the X-ray tube, we can also change the intensity of the current through the X-ray tube by changing of filament heating. The intensity of current

through the X-ray tube (the "amperage") influences the intensity of the X-ray beam, but not the energy (i.e. the penetration ability) of individual photons.

The control panel (control unit) of the instrument is equipped by different control elements and meters, mainly a voltmeter and ammeter to check the voltage and current across the tube. There is also an ammeter for checking the heating current, time switches etc. Other control elements serve for positioning of the patient and the instrument. In modern instruments, most of these functions are controlled by means of a computer and its software. In most cases, the control unit is placed outside the examination room, or behind a shield made of lead glass, so that the useless and endangering exposure of the physicians and other medical staff is avoided.

The main mechanical part of the instrument is a stand which holds the X-ray tube and its shielding housing. The stand is usually mechanically connected with the examination table on which the patient lies. The so-called Bucky grid (see Fig 12.5.2.1) is built in the table, along with a plane of the image detector (see Fig. 12.5.3.1). If not necessary, the grid can be removed. The table with the patient is moved manually or by means of servomechanisms.

While the electrical parts of X-ray instruments are fairly uniform, the mechanical parts vary greatly depending on the use of the instrument. For example, movable instruments have no examination table, but can be used directly in surgery or hospital rooms.

12.5.2 Origin of the X-ray image

X-rays are an electromagnetic radiation originating in atomic electron shells. They are photons of very high energy (higher than the energy of ultraviolet light photons). They are produced in X-ray tubes (Fig. 12.5.2), glassy evacuated tubes involving two electrodes: the anode and the cathode. The construction of modern X-ray tubes differs from the Roentgen's original. The modern tubes are often called **Coolidge tubes.**

Electrons are intensely accelerated by a very high electric voltage in the space between the **hot cathode,** also called the **filament,** and the anode. The energy of electrons incident upon the anode is given by the term $U \cdot e$. The electrons are suddenly decelerated in a tungsten target which is a part of the anode. A small part of the liberated energy (kinetic energy of the electrons decreases during deceleration) is transformed into high-energy photons - the X-rays. Only seldom can happen that all the energy of electrons is transformed into energy of photons.

$$U \cdot e = h \cdot f_{\max} = \frac{h \cdot c}{\lambda_{\min}},$$

where $h \cdot f_{max}$ is the maximum energy of the liberated photon (under the condition that all the kinetic energy of the electron is transformed into photon energy). Such photons are of the maximum possible frequency f_{max} or of the shortest possible wavelength λ_{min}. The spectrum of these X-rays is continuous. The X-rays arising in this way are also called "**Bremsstrahlung**" (i.e. deceleration radiation in German). Photons of X-rays can also originate by jumps of electrons between the innermost electron shells of heavy atoms, if there is a free place formed by incident electrons. Their energetic spectrum consists of lines. This is the so-called **characteristic radiation.**

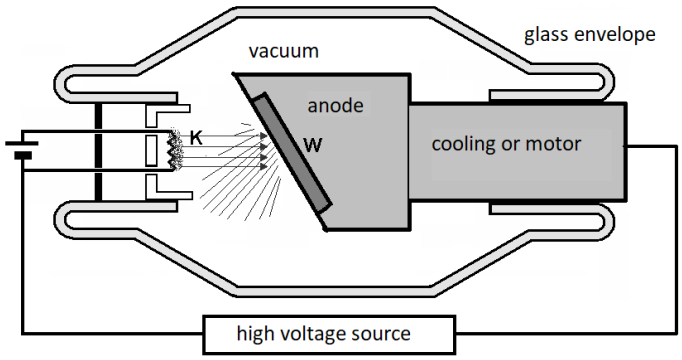


Fig. 12.5.2. The X-ray tube. K – cathode with hot filament (main part of the cathode, the whole cathode is often denoted as filament), W - tungsten target.

12.5.2.1 Course of X-rays

X-rays are emitted from a very small area on the anode surface which is bombarded by the electron beam coming from the cathode. This small area is called the **focus**. Thus, it is not a point source of radiation. The X-rays propagate in straight lines in the surroundings of the X-ray tube. The relatively narrow beam of radiation necessary for formation of the image on the detector is delimited by the movable aperture cylinders and **cones**, usually made of lead. The rays pass then through the body and hit the detector (or fluorescent screen or the radiographic film). There they form electric signal or visible light image or a latent photographic image as a consequence of unequal attenuation of the radiation beam by different parts of the patient's body. The X-ray image is analogous to a shadow behind a three-dimensional, semitransparent and optically non-homogeneous body placed in the path of a light beam coming from an almost point source. The formation of an image depends on different absorption (attenuation) coefficients and thicknesses of inner body structures. We will describe the passage of X-rays through the body in more detail.

X-rays originating on the anode pass through the glass wall of the X-ray tube. Some photons are absorbed there. Low-energy photons are then absorbed in the **primary filter,** which is made of, e.g. aluminium plate of 3 mm in thickness. This filter absorbs mainly photons which could not contribute to the image formation but could cause damage to the patient's skin and subcutaneous tissues, where they are absorbed. The remaining, higher energy X-rays are transmitted through the targeted body part, in which absorption and scattering occurs. In many cases the so-called Bucky grid, (Fig. 12.5.2.1), which is near the screen or film, is used.

The **Bucky grid** absorbs photons which were scattered in the body and no longer travel parallel to the original bundle. The grid is made of parallel-layered lead strips, amongst which material is nearly transparent to X-rays. The gaps between strips are so oriented that only rays propagating in their original direction can pass through them. To avoid creating shadows of the strips on the detector, they must be very fine, or they must move during the exposure. The Bucky grid increases the patient's exposure about two to six times, but also absorbs 80 - 90 % of the scattered X-rays.

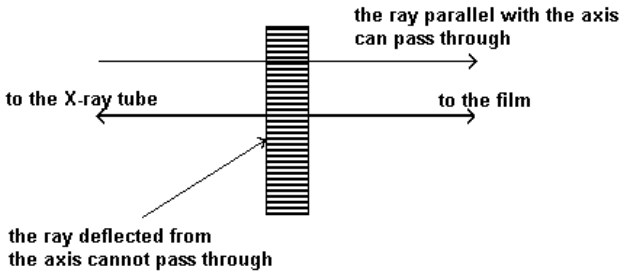


Fig. 12.5.2.1. Principle of the Bucky grid

The bundle of the X-rays finally comes to the place where the image is formed. If a fluorescence screen is used for direct observation of the image, the imaging method is then called **fluoroscopy**. Stable images, radiographs, usually took the form of a photo negative on a developed photographic film. This method is called (general or plain film) **radiography**. The blackening could be achieved directly by the X-rays, but by attaching fluorescent foils (intensifying foils) to the film we can achieve a substantial enhancement of the blackening. This way of image acquisition becomes obsolete. Modern digital technologies are based on planar semiconductor detectors (usually called flat panel detectors). We can obtain both fluoroscopic records and radiographic images using this type of detectors. There are two main approaches of conversion of X-ray photons to electric signal in these flat panel detectors – direct and indirect conversion. **Direct conversion** detector utilizes photoconductors, such as amorphous selenium, to capture and convert incident x-ray photons directly into free electric charge. Signal is then typically read out by a thin-film transistor array. This setting provides high spatial resolution sensitivity for low energy photons, motivate the use of this detector especially for mammography. **Indirect detectors** additionally contain a layer of scintillator material, which converts the x-rays into visible light. The photoelectric converter is based on amorphous silicon photodiode.

Flat panel detectors are directly connected to the X-ray device enabling automatic **optimalisation** of exposition parameters. Direct digital radiography should not be confused with **computed radiography**, which uses cassettes with photostimulable phosphor plates. The plate is exposed to x-ray radiation exciting the phosphor, excited electrons are trapped in the lattice until they are stimulated by the second round of illumination. Analog to digital conversion is performed in separate machine, where the radiography plate is exposed to a small, high-intensity laser resulting in the previously trapped electrons to return to their respective valence bands, emitting light. This light is subsequently converted into an electric signal.

12.5.2.2 Unsharpness of the image

Even a very good radiograph is not absolutely sharp. The boundaries between projections of different inner structures of the body exhibit a continuous change of grey shades, even if the boundaries themselves are well defined (for example, boundaries between the bone and soft tissue). There are many reasons of this **unsharpness**.

(1) **Movements of the patient**. For example, tremor, movements by small children, breathing movements, tissue shifts caused by pulse waves or heart action. This negative factor can be limited by shortening the exposure time, but we need, of course, more intensive radiation for that.

(2) The so-called **geometric penumbra** is caused by the non-zero area of the anode focus. The source of radiation is not a point source. Therefore, the rays are incident onto the boundaries of differently absorbing media under different angles, which causes unsharpness (blurring) of their images. See Fig. 12.5.2.2.

The geometric penumbra can be limited by:

- Diminishing the focus area. This increases the need of anode surface cooling.
- Shortening the distance between the patient and the detector,
- Increasing the distance between the X-ray tube and the patient,
- Improvement of the Bucky grid function.

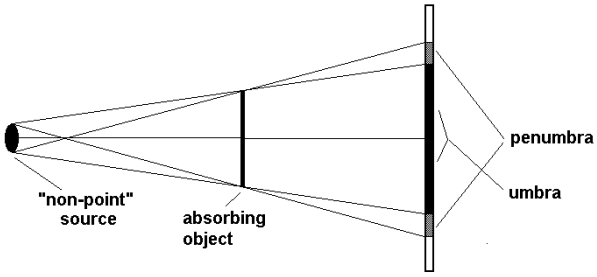


Fig. 12.5.2.2. The origin of geometric penumbra - unsharpness of the X-ray image.

(3) **Diffraction** and **scattering** under small angles occur (e.g. the Rayleigh scattering). Most scattered rays are absorbed by the Bucky grid, but not all of them, so that they can cause the unsharpness.

(4) Light emitted by the luminescent layer on the surface of the detector illuminates not only the nearest parts of the detector, but to a certain extent also the neighbouring parts (light propagates in all directions).

12.5.2.3 Usage of contrast agents

Soft tissues exhibit relatively small differences in the magnitude of their attenuation coefficients, and therefore are almost indistinguishable in the plain radiograph. For that reason, **contrast agents** were introduced, mainly for visualisation of various cavities, blood vessels, ducts etc. The contrast can be positive or negative, i.e., the attenuation of the X-rays can be increased or lowered. **Positive contrast** can be achieved by substances containing heavy atoms. For example, the suspension of barium sulphate ($BaSO_4$, the atomic mass of barium equals 137.33), denoted also as "barium meal", is used for imaging and functional examination of the gastrointestinal tract. This substance can be administered *per os* or *per rectum*. Substances containing **iodine** atoms are used for contrast imaging of blood vessels, bile ducts and urinary system.

Some hollow inner organs can be examined by means of **negative contrast**, using air or some other gases, namely carbon dioxide because of its high solubility in body fluids and fast removal by breathing. The cavities are inflated by the gas, so that they can be depicted as structures of very low X-ray absorption.

12.5.3 The most important methods in X-ray diagnostics

We can mention only some of the most important and commonly used radiographic methods in this chapter. Radiography can be encountered in almost any clinical branch of medicine. Very complex apparatuses are used, for example, in angiology (diagnostics of blood vessels), cardiology or urology. The most modern instruments use digital processing to achieve better resolution, contrast, contouring etc.

Digital subtraction angiography (DSA) is a classic example of these methods. The principle of this method is simple but demands precise technology. Two radiographs of the same region are recorded, which differ only by the presence or absence of a contrast agent. A contrast agent in the blood highlights the respective blood vessels or the surrounding tissue if there is internal bleeding. The two images are then digitally subtracted. In the resulting image, we can see only the structures in which the two original images differ - an image of the blood vessels, haematomas etc.

A specific method of X-ray diagnostics is the **mammography** which is extremely important for screening of breast cancer. Elderly women should regularly visit the examination centres. Besides the mechanical parts of the device which can compress the examined body part, the method exploits also softer X-rays. (Acceleration voltage about 30

kV, molybdenum anode, often also molybdenum primary filter is used. The molybdenum filter removes photons of *higher* energies hence the imaging is done by means of photons of low energy around 20 keV.)

12.5.3.1 Image intensifier

Conventional fluoroscopy, i.e., the direct observation of the image formed on the fluorescent screen, was a classical method of X-ray diagnostics. It was, of course, always connected with certain risk for the patients as well as the medical staff because of large absorbed doses of X-rays. That is why **image intensifiers** were introduced in practice. See Fig. 12.5.3.1.

Image intensifiers are large vacuum electronic tubes which contain the primary fluorescent screen, the photocathode, anode, anodic (secondary) fluorescent screen and the electron optics. Photons of X-rays pass through the patient's body and form a visible light image on the fluorescent screen. Emitted photons of visible light cause the photoelectric phenomenon in the photocathode. The ejected electrons are accelerated by the voltage across the photocathode and anode (15 - 22 kV) and directed by electron optics on the (secondary) fluorescent screen. There they form a small, inverted, but about 10,000-times brighter image, compared to the image of the primary fluorescent screen. This small picture can be observed by a camera and seen on a monitor. The monitor is usually placed in another room. Thus, the medical staff is almost absolutely protected against unwanted exposure. The considerable increase in image brightness enables us to also lower the patient's absorbed dose to one tenth of the value of a conventional fluoroscopy.

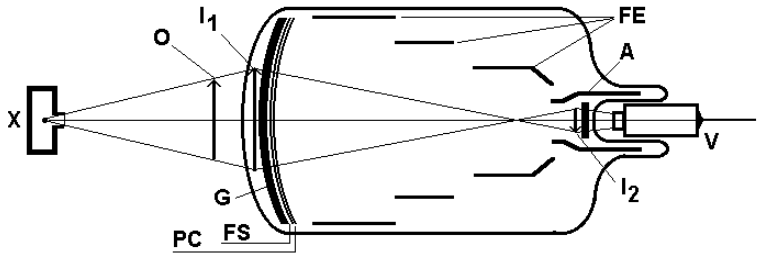


Fig. 12.5.3.1. Scheme of the image intensifier. X - X-ray tube, O - imaged object, I1 - primary image on fluorescent screen, G - glass support, FS - fluorescent screen, PC - photocathode, FE - focusing electrodes (electron optics), A - anode, I2 - secondary image on the anodic screen, V - camcorder. The individual parts are not proportionally depicted.

The image recorded by the camcorder can easily be digitised and stored in computer memory. Image intensifiers are used by surgeons to introduce catheters or other tools and objects inside patients, and to check the surgeon's work in orthopaedics, traumatology etc. In the late 1990s image intensifiers began being replaced with flat panel detectors (FPDs) on fluoroscopy machines

12.5.3.2 X-ray apparatuses used in dentistry

Most X-ray apparatuses used in dentistry are very simple. They work with low-intensity and relatively soft X-rays. They consist of a stand bearing the shielded X-ray tube and a control unit. The X-ray tube must be placed close to the examined site, and the patients themselves often use their fingers to keep a small piece of the film or a digital detector in place. The digital detectors are connected by means of cables or wireless to a computer which is able to process and display the image.

More sophisticated devices called **orthopantomographs (OPG)** give **panoramic images** of maxillary or mandibular sets of teeth. The principle of imaging is very similar to layer tomography.

In the last decade, an adapted cone CT system is also used in dentistry – see below.

12.5.3.3 Classical (layer) tomography

The classical or layer tomography was used relatively often in the past, but it is used only exceptionally today, except of a very similar method in dentistry. It provides images of thin body layers, which were very suitable for assessment of the position and shape of various lesions. In the simplest case, linear tomography, the X-ray tube and the film cassette moved in parallel planes in opposite directions. Thus, the points lying in a plane were projected on the same sites of the film. Only this single plane was sharply depicted. Structures lying outside

this plane were blurred. See Fig. 12.5.3.4.

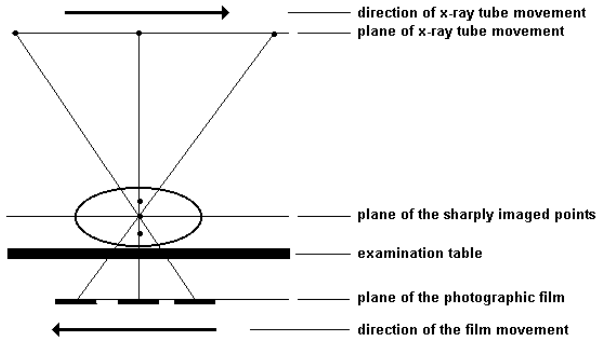


Fig. 12.5.3.4. Scheme of the classical layer tomography

The larger the angular displacements of the X-ray tube and the film (measured away the normal passing through patient's body), the thinner was the sharply imaged layer (and the higher were the demands of the whole system accuracy.

12.5.4 Computed tomography (CT)

Another X-ray imaging method - **computed tomography (CT)** - is one of the most important imaging methods in medicine. The first patient was examined by this method in London in 1971. The instrument was proposed by the English physicist *G. N. Hounsfield*, who was awarded the Nobel Prize for medicine in 1979, together with the American physicist A. *M. Cormack* who had proposed a similar principle (utilising gamma-rays) in the 1960's.

The principle of this method substantially differs from conventional X-ray imaging. The image is not a "shadow" cast on a screen. It is a mathematical reconstruction by computer of a transversal cross-section through the patient's body. CT-scanners of the first generation passed a single narrow beam of X-rays through the body from the X-ray tube to a suitable detector (scintillation or proportional counter) in the frame opposite (see Fig. 12.5.4).

The whole source-detector system moved linearly during the examination, so that the beam passed gradually through a cross-section of the patient's body. After each such movement (a **scan**), the system rotated by a small angle and a new scan was done. In the second generation of CT-scanners, the narrow beam was made fan-like and able to hit an array of detectors. The scanning movement and consequent rotation of the system was maintained. In the third generation of CT-scanners, the detectors are arranged into an arc and the whole system continuously rotates around the patient. Finally, in the fourth generation, the detectors circle the patient. Only the X-ray tube moves. The further development can be derived more likely from the third generation. Differences between the individual generations of CT-scanners are shown in Fig. 12.5.4.

The time intervals much shorter than one second are today sufficient to obtain the picture of one single cross-section. Despite of this fact, namely in connection with the 3D imaging, the X-ray tubes used in the CT scanners must provide high power for relatively long time. It results in strong heating of the anode which must have small focus, moreover. Therefore, it must rotate and be quite massive. The imaging process can be accelerated (below 0.1 s) when using two X-ray tubes, which beams are oriented in right angle. If these tubes work at different voltages, it can be utilised for identification of materials of different composition, e.g., to distinguish between the bone and the iodine contrast agent. This modification of CT technology using two X-ray energy spectrums is called **dual-energy CT**. There are other more possible ways how to construct dual-energy CT, e.g. rapid kV switching on X-ray tube, dual layer of detector for “soft” and “hard” X-ray photons. Another evolution step in CT material decomposition is photon-counting computed tomography. A photon-counting

detector registers the interactions of individual photons keeping track of the deposited energy in each interaction.

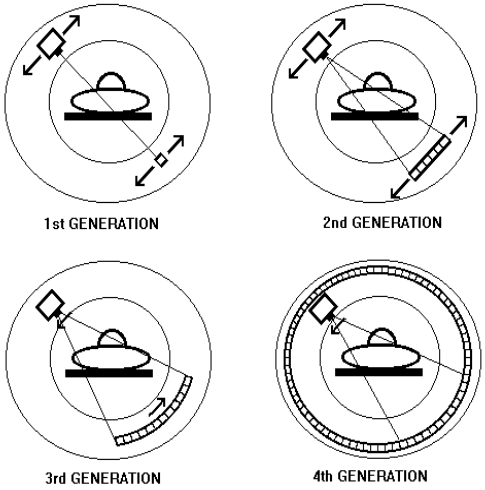


Fig. 12.5.4. The four generations of CT-scanners.

The development towards 3D imaging took place mainly in nineties. It was conditioned also by the progress in computer technology.

Spiral or **helical CT scanners** operate similarly to the systems of third or fourth generation but there is additional shift of the patient's body which enables the 3D reconstruction of his or her body parts. We can imagine it as a layering of many 2D tomograms hence we can speak about multiplanar imaging. Exposure time is up to tens of seconds.

Similar results can be obtained by means of the devices equipped by detector systems made of many parallel arcs. The number or arcs can by 128 or 254. In this way the exposure time necessary for acquisition of a 3D image can be much shorter. The patient is irradiated by an X-ray beam in the shape of a flattened cone to exploit all the arcs of detectors. This method commonly called **multi-slice CT** or **cone beam CT** (because of the conical shape of the beam. Some systems of this kind can work with lower resolution in the *fluoroscopic* mode making so possible some interventions (catheterisation, punctures etc.). Of course, the doses of radiation absorbed by patient's body are considerably high and the time of the procedure is limited.

A common problem of all CT systems providing 3D images are relatively high doses of radiation, Therefore, the **justification** of this examination is very important.

It holds in all generations of CT-scanners, that a single X-ray beam passes through the body, and its intensity decreases according to the mean attenuation coefficient of the passed-through tissues. The **absorption profiles** are recorded during the source-detector movement, or simultaneously from the detector array. The detector data (absorption profiles) are digitised and mathematically processed by the computer and displayed as a cross-sectional image, which is actually the "map" of the X-ray attenuation at each point of the cross-section. This map actually consist of matrix of voxels (volume matrix elements), usually with 512×512 definition. Computer processing reveals half-per-cent differences in attenuation values, which is impossible in the conventional X-ray imaging. Soft tissues and their pathological changes can be examined very well. Large demands on computer equipment are made by the three-dimensional image reconstruction in spiral CT-scanners.

The image (scan) on a computer screen is composed of points of different grey shades which represent tissue attenuation coefficients converted into **Hounsfield units** (HU):

$$\mathrm{HU} = \frac{\mu_T - \mu_W}{\mu_W} . k,$$

where μ_T is the attenuation coefficient of a medium (tissue), μ_W is the attenuation coefficient of water, and k is the constant of numerical value of 1000. It follows from this definition that water has a value of zero in the HU scale and air about -1000, because the attenuation of X-rays in air is negligible. The HU value for compact bone is about +1000. Therefore, we have a range of 2000 HU available. It makes no sense to represent this whole scale by individual grey shades because the human eye is able to distinguish only about 250 grey shades. Virtual colours can be used, but it is usually not necessary, as most tissues exhibit HU values from zero to +100. In such an absorption window, a grey scale is sufficient (see Table 12.5.4).

It is very important that the HU values **do not depend on the energy** of X-photons (given by acceleration voltage) so we can compare images obtained in different CT systems.

Very good resolution of soft tissues, including tumours, is the main advantage of CT imaging. The method also is very convenient for planning surgery and radiotherapy of tumours. The resolution can be improved by means of the contrast agents. The disadvantage is the approx. ten-time higher absorbed dose of radiation in comparison with conventional radiography. CT-scanners are also expensive, and they must be operated by highly trained and specialised staff.

Tissue or material	*Attenuation coefficient μ [cm^{-1}]*	*HU*
water	0.22	0
fresh blood	0.23	47
blood coagula	0.24	62
erythrocytes	0.24	76
blood plasma	0.22	11
white brain matter	0.23	30
grey brain matter	0.23	34
white matter oedema	0.23	25
bone (cranial)	0.38	706
neutral fat	0.21	-70
cerebrospinal fluid	0.22	5

Table 12.5.4. Attenuation coefficients and values of Hounsfield units for selected tissues.

12.6 Radionuclide imaging and other diagnostic methods

Radioactive elements, radionuclides, can be used in medicine in many ways. This chapter will deal with only some of them which need special instrumental technology. In some cases, the simple detectors (see section 11.8) are sufficient.

We can define the following main regions of radionuclide utilisation in biomedical sciences:

- tracing
- radioimmunoassay
- examination of physiology of body organs
- imaging of body organs or parts

In principle, only physiological examinations and imaging methods need special instruments (gamma-cameras, the PET- and SPECT-scanners).

12.6.1 Tracing and radioimmunoassay

Radionuclide **tracing** is often used to calculate compartment volumes, such as the volume of body water, circulating blood, or fat tissue. A known amount (known activity) of the radionuclide is introduced into the organism, either orally or by injection. Then sufficient time is allowed for the radionuclide to distribute evenly (i.e., reach equilibrium concentration) in the whole compartment. By taking a small sample volume and measuring its radioactivity, it is possible to calculate the total compartment volume. A similar condition must be also fulfilled in some organ examinations and imaging methods. It is also possible to start with activity measurement in the respective organ immediately after administration of the radionuclide in the so-called dynamic examination. The diagnostic value is different, of course.

Radioimmunoassay (RIA) is used in clinical biochemistry and haematology. It is used for determination of trace amounts of substances, notably hormones, in blood samples taken from patients. An interaction of antigen-antibody type is studied in vitro. The antibody is labelled by a radionuclide.

In RIA and tracing, beta-emitters are mainly used (tritium, iodine-125, iron-59 etc.), because the detector can be positioned close to the radioactive sample (we do not need penetrating radiation).

12.6.2 Scintillation counters

The **scintillation counter** is, in principle, a relatively simple instrument consisting of a scintillation detector, i.e. the counter proper (see Section 11.8.3), the mechanical part and the lead collimator which is connected with the lead shielding of the detector. The collimator makes it possible to detect radiation only from certain, relatively narrow, and sharply delimited solid (spatial) angle. Therefore, other radioactive sources present in the body or in its surroundings cannot influence the measurement results. Voltage pulses generated by the scintillation detector represent individual photons of gamma-radiation. They are amplified, counted, and recorded by joined computer. The examination by means of simple scintillation counters can be performed in two ways, in principle:

(1) The **detector is stable**. It measures the rate of storage or capture of a radionuclide bound to a suitable metabolite in a given place. Thus, this kind of examination gives information about the time-course of local metabolic activity.

(2) The **detector moves** in lines or scans ("zigzags") above the patient's body part. Such an instrument was denoted as a **rectilinear scanner**. So a "map" of the radionuclide

distribution could be obtained. At present, rectilinear scanners are replaced by more accurate imaging radionuclide methods.

12.6.3 Anger gamma-camera

The gamma-camera, invented by *Anger* in 1958, is a special kind of scintillation detector. The scintillation occurs in a large scintillator, a crystal of sodium iodide in the form of a square or a disc up to 40 cm in diameter. Numerous photomultipliers or other detectors (up to 50) are placed on one side of the scintillator. Detected signal is digitised and processed by a computer.

The positions of scintillation events, which reflect the distribution of a radionuclide inside the body, can be determined by means of computer processing of the signal coming from photomultipliers. However, a very important condition must be fulfilled to obtain an image: a defined point in the scintillator must represent a defined point in the body. (Let us imagine the plane of the scintillator as parallel with the plane in which the scintillator "sees" the projection of a body part. The defined points lie in these two planes.) Such condition can be fulfilled only using **collimators**. See Fig 12.6.3. So-called "pin-hole" (radiation passes through a small hole in conical lead shield placed in front of the scintillator) or absorption collimators are most often used. Absorption collimators are made of lead lamellas similarly to the Bucky grid in conventional radiography.

Anger cameras are very effective diagnostic tools because they show the distribution of a radionuclide inside the body very quickly. Therefore, they can be used also for imaging of relatively fast processes, e.g., the passage of blood through coronary arteries. These cameras can also move along the body axis, so we can quickly obtain an image of the radionuclide distribution in the whole body. Metabolic pathways can be studied in this way. It is also possible to search for cancer metastases if they are able to capture a substance containing a gamma-emitter: today technetium-99m or iodine-123. The technetium radionuclide exhibits a short half-life (6 hours in comparison with 8 days in the originally used iodine-131), so it must be prepared directly in departments of nuclear medicine in **technetium generators**. These generators are containers with radioactive molybdenum which decays to form technetium-99m, which is obtained from the container by a chemical process. Both radionuclides give radiation of relatively low energy, which is not able to evoke secondary radioactivity.

In the examination of the thyroid gland, radioactive iodine-123 (its half-life is 13,22 hours) is used in the form of sodium iodide. The kidneys are examined by the technetium-99m labelled compounds. Technetium-99m is not easily available, but it is almost an ideal radionuclide because of its fast excretion from the body, the short half-life and emission of almost pure gamma-radiation. The product of the Tc-99m decay is also little radioactive.

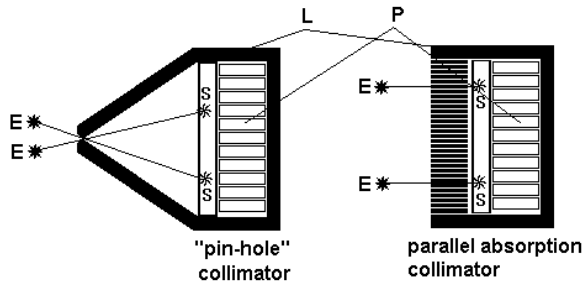


Fig. 12.6.3. Schematic drawing of Anger cameras with different kinds of collimators. E - emitters, P - photomultipliers, S - scintillation events (flashes), L - lead shielding of the collimator.

12.6.4 SPECT and PET

SPECT (single photon emission computed tomography) and **PET** (positron emission

tomography) are the most advanced diagnostic methods which utilise radionuclides. In computed (X-ray) tomography, the source of radiation is outside the body. In SPECT and PET, it is directly inside the body, but the way of image reconstruction is analogous.

In SPECT a source of gamma-radiation, i.e., the radionuclide, is introduced into the body in a labelled compound, which can be captured and stored in some organs, or quickly eliminated from the body (mainly with urine). Individual photons are counted by multiple scintillation counters.

The counting is done stepwise from different directions, which allows the two-dimensional reconstruction of a body cross-section. The structures seen in this cross-section are points or small volumes emitting the radiation.

The following detector arrangements and kinds of their motion are or were utilised for SPECT:

a) A simple scintillation detector equipped by a collimator scanned and circled around the body, similarly to the X-ray tube and the detector in the first generation of CT scanners. This method is obsolete.

b) More scintillation detectors are arranged into a circle or a square around the body. The whole system can rotate around the patient and move along his or her body axis. Also this method became obsolete.

c) The Anger camera with one, two or three "heads" circles around the examined patient. This way of image acquisition in used today.

SPECT uses the common sources of gamma-radiation (iodine-123 and technetium-99m) but PET must use positron emitters. These are radionuclides of biologically most important elements produced by bombardment of atomic nuclei by high-energy beams of accelerated particles. The half-lives of these radionuclides are very short, 109,7 min. in fluorine-18, 20 min. in the carbon-11, or even shorter in some other radionuclides. The construction and operation of the accelerators are very expensive. Because of the relatively long half-life of F-18, it became the most often used radioisotope which can be transported by a car up to about 150 km from the producer's accelerator (cyclotron).

The scintillation detectors are arranged in circles around the patient without the need of a lead collimator. The band of detector circles is about 25 cm broad in the cranio-caudal direction. Positrons can travel only very short paths in a liquid or solid (dense) medium because they annihilate immediately when colliding with an electron, forming two photons of gamma-radiation (E = 0.51 MeV) – see Section 2.1.3.3. These photons propagate in opposite directions from the place of their creation. Such an annihilation event can be detected by two detectors in so-called **coincidence circuit**, i.e., by detectors on opposite sides of the place of annihilation. The impulse is counted and processed only if the photons are detected by an opposed pair of detectors at the same time. (Photons propagate at the speed of light, so we can neglect small differences in distance - annihilation always occurs closer to the first or second detector). The principle of PET can be seen in Fig. 12.6.4a.

The resolving power of PET can be twice higher than SPECT.

The positron emitters can be bound in the metabolites, e.g., glucose derivatives, so it is possible to obtain not morphologic but functional information. PET-scans of the oncological patients are most frequent. However, we can also reveal brain centres which are actually active, i.e. have an increased uptake of a glucose derivative. Along with the EEG, PET is one of few methods by which it is possible to follow objectively the superior nervous activity of brain centres.

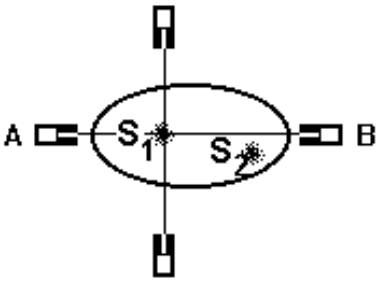


Fig. 12.6.4a. The basic principle of the PET. The opposing detectors are connected into a coincidental circuit. The radiation source S can be detected only when lying on the connecting line of the two detectors. The detector A can be hit from the source S_2, but not the detector B, because the source S_2 lies outside its detection angle. In SPECT, the signal coming from source S_2 would be overlapped by the signal coming from the source S_1. It explains the high resolving power of PET.

12.7 Magnetic resonance imaging

12.7.1 Nuclear magnetic resonance

Magnetic resonance imaging (**MRI**) which is based on the spatial analysis of the phenomenon of nuclear magnetic resonance (**NMR**) in human organism is probably the most advanced diagnostic imaging method in present time. The first MRI scan (of a human chest) was obtained by *Damadian* in 1977, but many other scientists took a part in the construction of first devices during seventies. The physico-mathematical description of this phenomenon and method is very complex and cannot be introduced here without unacceptable simplification. This description will be mostly qualitative. The approaches of classical and quantum mechanics will be also combined.

Each atomic nucleus with an odd number of nucleons (or even number of nucleons at an odd number of protons) exhibits a certain **magnetic moment** μ, which can be imagined as a consequence of the rotation of electrical charges of elementary particles forming the atom nucleus - their spin. (In classical physics, the magnetic moment is defined as the product of current intensity in a conductor loop, and the area delimited by this loop. It is a vector perpendicular to the plane of the loop. It determines the torque acting on the loop in the magnetic field of magnetic flux density *B*.) In practice, the light atomic nuclei with an **odd number of nucleons** are the most interesting, with spin values of $\pm$ 1/2. The proton (atomic nucleus of hydrogen), phosphorus P-31, carbon C-13, fluorine F-19 and sodium Na-23 are of considerable medical importance. It should be noted that there is a direct proportionality between the magnetic moment of nucleus μ and its angular momentum *S*:

$$\mu = \gamma.S,$$

where γ is the so-called **gyromagnetic ratio**. The magnetic moment of nucleus as well as the angular momentum of nucleus is vector with a direction identical with the axis of nuclear rotation (nuclear spin). In the absence of an external magnetic field, the nuclear magnetic moments are randomly oriented. Their vector sum per unit volume - the vector of **magnetisation** - is zero.

Let us place the nuclei exhibiting a non-zero magnetic moment into a strong external stationary and homogeneous magnetic field *B*. The nuclear magnetic moments will "try" to

orient in (or against) the direction of vector *B*. It is useful to identify this direction with the z-axis. This orientation change will evoke a torque which will be demonstrated by the so-called **precession** of nuclei - see Figs. 12.7.1a and 12.7.1b. The axis of nuclear rotation, more precisely the vector of their angular momentum and hence the vector of magnetic moment, will start to move like a flywheel (gyroscope), with its axis deflected from its original direction by an external force. The vectors of magnetic moments of nuclei will start to circumscribe the surface of a cone with its axis directed parallel to the vector B. The frequency f of this precession motion, the Larmor precession, is denoted as the **Larmor frequency**, and given by the formula

$$f = \gamma.B/2\pi.$$

The nuclear magnetic moment is the "quantised" quantity. For nuclei with typically an odd number of nucleons placed in an external magnetic field, only two energetic quantum states are possible. The state with the spin value of +1/2 (μ, more precisely its projection into the z-axis, and vector B are of the same orientation) is of slightly lower energy than the state with the spin value -1/2 (z-projection of μ and vector B are of the opposite orientation). Therefore, in a given assembly of nuclei, the states characterised by spin value +1/2 are slightly prevalent after reaching thermal equilibrium. The vector of magnetisation (its z-component) will not equal zero in this case.

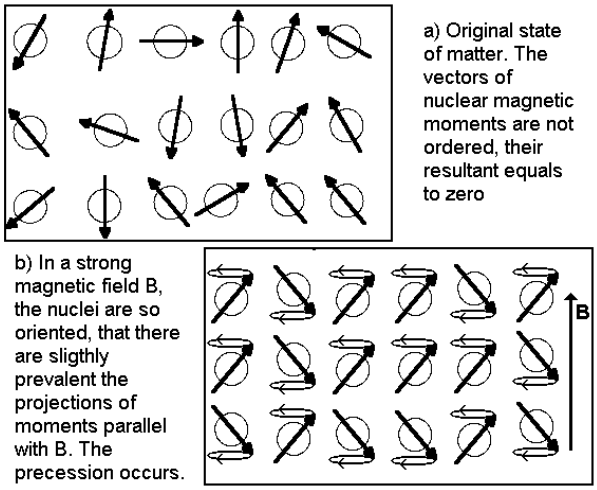


Fig. 12.7.1a. States of atomic nuclei with an odd number of nucleons before and after placement in a magnetic field.

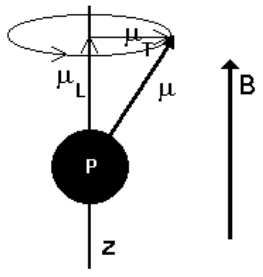


Fig. 12.7.1b. Precession of resonating nuclei. P - hydrogen nucleus (proton), *B* - magnetic field vector (density of magnetic flux), z - axis identified with the axis of precession (parallel with *B*), μ - magnetic moment of nucleus, μ_L - projection of the nuclear magnetic moment in the direction of z-axis (their vector sum in unit volume is called "vector of longitudinal magnetisation"), μ_T - projection of the magnetic moment into the plane xy (their vector sum in unit volume is called "vector of transversal magnetisation").

The precessing nuclei can absorb a quantum of electromagnetic radiation (a photon) of **frequency equal to the Larmor precession**, and jump into a higher energetic state. That is why the application of a radiofrequency pulse of such a frequency results in an increase of the number of higher energy states in the whole "population". The vector of magnetisation will not equal zero. Its z-component (the longitudinal magnetisation) will be oriented in opposite direction. The precession motion will also be simultaneously harmonised in phase, and in the

xy-plane rotating component of magnetisation (the transversal magnetisation) will appear. We could imagine that the vector of magnetisation will be also brought in precession motion. The return to the low-energy ground state (relaxation) is possible in two ways: by relaxation which is not connected with emission of electromagnetic radiation, and by emission of quanta of electromagnetic energy, the **NMR signal**.

We can speak about two **relaxation times**. The first of them, the **longitudinal relaxation time T_1** is the time necessary for the return of nuclear population into the original state with a slight prevalence of the direction of longitudinal magnetisation identical with the orientation of vector B. It is not the time of full return, which is measurable only with difficulty, but the return of 63 % of the nuclei to the original ground state. This time is strongly influenced by the interaction of magnetic moments with fluctuating magnetic fields of neighbour nuclei, so that we speak about spin-lattice relaxation. T_1 has values ranging from 300 to 2000 ms in biological media. The **transversal relaxation time T_2** is two- to ten-times shorter than the time T_1.

During the transition of the nuclear population into the higher energy state, the harmonisation in phase (coherence) is manifested by the non-zero value of transversal magnetisation. The transversal or spin-spin relaxation time (T_2) is the time necessary for "dephasing" of precession and the renewal of the original zero value of transversal magnetisation. Correctly, it is the time necessary for the decrease of transversal magnetisation to 37 % of the maximal value achieved.

The relaxation times represent information additional which can be obtained from the time-course (decay) of the NMR signal just after the radiofrequency pulse, and also from the MRI scans described below. The intensity and also the repetition frequency of applied radiofrequency pulses, in relation to the values of relaxation times, determine whether the NMR signal will carry information about the spatial distribution of protons or about the time T_1 or T_2. More detailed analysis of these problems is out of scope of this text. The presence of paramagnetic atoms, for example gadolinium, considerably reduces the relaxation time T_1, which causes amplification of the signal. This is the basis for the utilisation of gadolinium and some metals as **contrast agents** for MRI. Gadolinium compounds differ according to the body part examined.

The Larmor precession of nuclei in magnetic field can be measurably shifted by their chemical surrounding. This **chemical shift** is expressed in parts per million (ppm) of the value of a chemical standard. For example, there is a considerable difference in chemical shifts of protons bound in =CH- or -CH_2- groups, and the effect of their more distant surroundings is measurable. The measurement of chemical shifts is an important tool of structural analysis in chemistry, and, as shown further, it is also of medical interest. The method of chemical analysis based on the measurement of chemical shift is called **NMR-spectroscopy**.

12.7.2 The principle of image formation

The phenomenon of nuclear magnetic resonance can be induced and measured, in principle, in two ways. In the first case, we can have an external magnetic field of constant B and search for the energy (frequency) of electromagnetic oscillations able to cause nuclear resonance. In the second case, which is easier to achieve we can work with a constant energy (frequency) of electromagnetic oscillations and search for a value of B, at which resonance occurs. In this case we change the Larmor precession frequency. This second possibility is also exploited in **magnetic resonance imaging – MRI**.

When placing the examined body part in the homogeneous magnetic field, the radiofrequency pulse will produce an NMR-signal in the whole of the examined part, and the information about local characteristics of resonance will be lost. The situation is different in a

non-homogeneous magnetic field. When creating, for example, a field gradient in the direction of z-axis (identified with the body axis, in practice), the resonance condition will be fulfilled only in a thin slice of the examined part lying in the xy-plane - the signal will be produced only by nuclei present in this slice. We can also create a field gradient in the direction of x- or y-axis, forming so in the slice a thin stripe parallel with the x- or y-axis, or identifying a point, respectively - see also Fig 12.7.2. The setting of these gradients is done in various pulse regimens, and it is different in different variants of MRI or instruments. However, in each case, it is possible to obtain spatially specific information about the magnitude of a resonance signal, which is among other things proportional to the number of resonating nuclei in a given part of space. Two- or three-dimensional information about the distribution of resonating nuclei can be obtained by means of algorithms used in CT-method, or based on the Fourier transform.

Not only differences in the amplitude of resonance signal, but also differences in relaxation times can be depicted. We can also determine the chemical shift of resonating nuclei in chosen parts of the image.

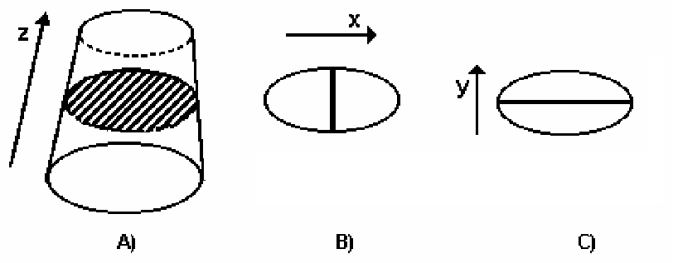


Fig. 12.7.2. The function of magnetic field gradients in image acquisition. A) the plane of section (the slice) is obtained by application of the magnetic field gradient, i.e. the setting of resonance value of *B* (and the Larmor frequency) in the direction of z-axis, i.e. the patient's body axis. B) We can delimit a column (stripe) by the gradient applied in the direction of x-axis in this slice. C) The same done in direction of y-axis allows resolving another stripe.

Let us note some technical aspects of MRI instruments. It is necessary to work with magnetic fields B which range from 0.1 to 3.0 tesla (T) to obtain the MRI scans. Devices equipped by giant permanent magnets weighing even tens of tons can achieve B values up to 0.3 T. These devices were relatively cheap and had low operational costs, but their resolution power was also relatively low, and they are not used more. Devices equipped by electromagnets can reach rather higher B values and also better resolution, but the winding of electromagnets must be cooled, and they consume a lot of expensive electric energy. Devices with superconducting magnets have the best resolution, but they need liquid helium and hence their operational costs are very high. These devices allow us to perform chemical analyses on the basis of chemical shift determination.

The necessary gradients of magnetic field are achieved by means of additional (gradient) coils, which disturb the homogeneity of the external magnetic field (its *B* is about 1 T, while the typical values of *B* gradients are several mT per meter). Near the patient are transmitting and receiving coils, i.e. the radiofrequency pulse source and receiver of NMR-signal of the same frequency (tens of MHz).

MRI devices generate strong magnetic fields and disturbing electromagnetic signals. That is why the coils and the electromagnet windings are maximally shielded. Despite this shielding, the gantry (tunnel) of the device is a source of such a strong field that ferromagnetic objects (e.g. small medical tools) can be pulled inside the gantry at very high speed and injure the patient or damage the device. No microelectronics or vacuum electronics (CRT screens),

magnetic memory media, including magnetic paying cards, etc., can be placed within many metres around the device. The shielding requirements are given by hygienic norms for these devices. Conversely, the examination can be disturbed by external magnetic or electromagnetic fields. Therefore, the examination rooms must be shielded (Faraday cage).

12.7.3 Clinical value of MRI

The MRI scan, i.e. the depiction of the tissue section, is a spatial reconstruction of resonating nuclei density. In contrast to computed tomography, these sections need not be only transversal, but can also be sagittal or frontal. The method gives very high contrast resolution of soft tissues (with maximum resolution in order of tenths of millimetre) due to the different densities of protons (hydrogen nuclei) in various body tissues. See Fig. 12.7.3.

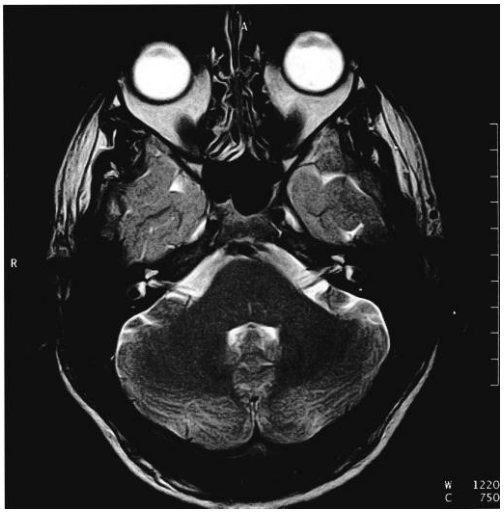


Fig. 12.7.3. „T_2 weighted“ image of transversal section of head in the level of cochlea. (Siemens)

In contrast to other tomographic methods, MRI does not utilise the ionising radiation, which is a large advantage. No biological effects of applied strong magnetic fields or radiofrequency pulses have been observed up to now, at least at the application times used in standard MRI examination. For this reason it is possible to use MRI in children, and if necessary in pregnant women, except during the first trimester of pregnancy.

There are, however, some potential problems for patients. They can be disturbed by the considerable noise which accompanies the examination. Of course, no ferromagnetic materials (old steel implants, iron splinters from war injuries etc.) or electronics (pacemakers with no guarantee that they can be used in MRI under certain circumstances) can be present in the bodies of examined patients. Problems can also be caused by some cosmetic preparations or jewellery. In some devices, and in sensitive patients, the fear of closed space (claustrophobia) can appear. However, it can be moderated by sedatives.

Some parameters of NMR-signal depend on temperature, for example, relaxation times or the chemical shift of protons present in water molecules. (It depends on the state of hydrogen bridges which are influenced by temperature.) It is possible to create an examination algorithm which leads to the tomographic depiction of temperature values distribution. A unique tool is obtained in this way, which enables us to measure directly and non-invasively the changes of tissue temperature during, e.g. ultrasonic or laser tissue heating.

The NMR-signal is also sensitive to the movement of resonating nuclei. For example, in a given site the nuclei present in streaming blood and "prepared" are always replaced by "unprepared" nuclei, i.e. nuclei which do not have the required value of Larmor frequency. We speak about a "washout effect" in this case. The analysis of signals coming from

structures in motion allows us to measure their velocity, e.g. the velocity of the blood stream (magnetic resonance angiography).

The movement of depicted structures also causes, however, some unwanted artefacts, so that the synchronisation with breathing or heart rate is necessary in some MRI examinations.

MRI can also be used for the study of metabolism, e.g. the metabolism of ATP. ATP contains phosphorus P. The phosphorus chemical shift varies during the hydrolysis of ATP to ADP + phosphate. The chemical shift of the free phosphate is also different. This information can be obtained from individual small volumes of the examined body part, and the metabolic activity, during which the ratio of ATP/ADP changes can be so visualised.

We already mentioned (Section 12.7.1) the use of gadolinium as an MRI contrast agent. Gaseous microbubbles used as a contrast agent in ultrasonography are also a suitable MRI contrast agent. (The pressure influences the bubble size and consequently medium density. Therefore, the NMR signal depends considerably on the ambient pressure.) In future, it may be possible to exploit these microbubbles for non-invasive MRI determination of actual blood pressure anywhere in circulation.

As mentioned, MRI is the most advanced diagnostic method available. The development of this technology was not finished. We may see the first real-time examinations, analogous to dynamic ultrasonography, already.

However, the very high price and high operational costs limit the use of MRI. That is why other imaging methods will remain in use for a very long time, e.g. conventional X-ray diagnostics and CT mainly in examination of tissues with low content of water; in cases, in which the MRI is contraindicated, ultrasonography, for its operative use in real-time and its relatively low costs; and radionuclide methods, for their considerable ability to follow the fate of metabolites in our bodies. Each of these methods also gives a different kind of information.