Scanning Technologies

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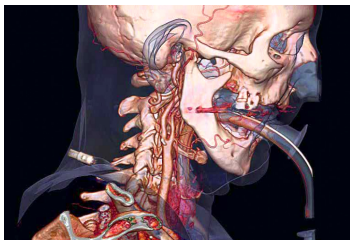

Figure 1: Latest dual-source CT technology introduced in 2008/11 [Siemens 2008]

Abstract

This article gives a basic understanding of the four most relevant scanning technologies in clinical diagnostics namely sonography, computed tomography, magnetic resonance tomography and positron emission tomography. The development of these highly sophisticated technologies required more than a century. They still offer new possibilities and ways to improve the scanning procedure. Today radiological and nuclear diagnostic is used in nearly every considerable clinical domain which makes an extensive description almost impossible. This article focuses on fundamentals necessary to facilitate classification and to understand how these technologies co-exist and complement in clinical context. Furthermore it describes recent enhancements and todays most relevant improvements as well as their future perspectives.

Keywords: sonography, computed tomography, magnetic resonance imaging, positron emission tomography, combinations, enhancements

1 Introduction

Improving clinical diagnostic in a way to avoid surgery diagnostics occupied mankind for very long time. Many researchers gave their life on experimenting with ionizing radiation and many volunteers may have suffered from long term consequences on testing new procedures. With the introduction of the first pioneering techniques clinical diagnosis performed a huge evolutionary step. Presurgical planning, disease monitoring and early-stage diagnoses are just a view of the new available possibilities. Continuous research lead to the introduction of a whole range of paradigms and an almost unmanageable amount of different architectures. The demand for non-invasive diagnostic methodologies advanced their development and lowered their price. Although, some of them are only available in specific research centers and require well trained personal or even technical physicists to ensure appropriate operation.

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Sonography is the simplest, safest and cheapest scanning method. It is applied in uncountable ways and already served reliable for decades. The use of absolute nonhazardous sound waves for image acquisition particularly established sonography in examinations on fetus. The sound signal attenuates in material which implies insufficient resolution for critical examinations. Computed tomography is able to handle this lack of resolution and provides very good anatomical information of all parts of the body. Today CT is available in many hospitals and is part of daily clinical routine. A major drawback was the ionizing radiation used to acquire structural information. Recently introduced architectures like Dual-Source CT reduce the radiation dose to a minimum of the yearly natural radiation exposure and deliver high quality images. CT acquires images by measuring the attenuation of density intensive matter. Due to that early architectures were hardly able to image soft tissue structures. Magnetic resonance image was a very good complement due to its ability to image hydrogen and hydrogen charged structures. Strong magnetic fields alter the direction of naturally magnetized protons. These alternations can be detected an generate images with various properties. In contrast to these anatomical diagnostic methods, functional technologies are able to track metabolic processes. Positron Emission Tomography delivers this kind information with the use of radioactive solubles injected the patients veins. These solubles accumulate in areas where matablic processes take place (e.g. brain, tumors, etc) and can be detected from outside the body.

Today these technologies offer many different applications and modified architectures. Hybrid systems for instance combine two image acquisition modalities and deliver both anatomical and functional information in one image. The combination complement in various ways like providing better attenuation correction using anatomical information for functional image construction. Without a doubt, Dual-Source CT was the most mentionable enhancement during the last few years. It requries less radiation dose and delivers very accurate images with temporal resolution below one second. These images are usable for investigating the constantly beating and moving heart without the application of any beta-blockers. Also MRI development constantly introduces new technologies. One of them is functional MRI which is able to image brain activities triggered by certain stimulations. It is used an various areas ranging from better understanding the brain functionalities to understanding diseases like Alzheimers, Parkinsons or Schizophrenia.

2 Technologies

2.1 Sonography

2.1.1 Introduction

Sonography is a very widespread technology. Its principles can be ascribed to the introduction of ultrasound by Spallazani and Lazarro in 1794 who described the acoustic orientation sense in bats. About 90 years later in 1881 the Curie brothers introduced the piezo-electric effect of the sound waves which can be considered as the fundament of ultrasound in medicine [Zmudzinska 2008]. During World War II electromagnetic waves were used to develop RADAR and its underwater ultrasound complement SONAR. The use of ultrasound waves allows large signal distances in comparison to electromagnetic radio waves. Especially underwater, sound waves are able to cover large distances without any noticeable attenuation.

Today ultrasound examination can be performed even in the smallest hospitals due to the relatively low acquisition and maintenance costs in comparison to other technologies like computed tomography. Because of the use of non-ionizing radiation ultrasound is free from any hazard to the patients. Hence 95% of the operators are non-radiologists. In clinical diagnostics ultrasound is considered to be a kind of an instant technology to get a quick overview. On the other hand it is also applied as a long term monitoring tool to trace the healing process of diseases [Kauffmann et al. 2006].

2.1.2 Principles

As already stated, ultrasound examination uses nonhazardous high-frequency sound waves for image generation. [Guy and ffytche 2000] describe the ultrasound waves as follows:

> An ultrasound wave, like all sound waves, is a propagating mechanical disturbance of the matter through which it passes. The sound wave creates pressure disturbances that accelerate and displace the atoms in its path.

Ultrasound diagnostics use these conditions to generate images by emitting sound waves and recording the reflected echo to calculate the distance and density of tissue just like several animals do to navigate or communicate in their environment (bats, whales). The so called transducer is responsible for both the creation of the sound wave as well as for the detection of the resulting echo. It sends a very short impulse which lasts for about 0.5μs and waits for incoming echoes (**pulse-echo principle**. For the generation of this ultrasound impulses it uses piezoelectric crystals. By applying alternating voltage, the crystals start a compression and expansion process which generates the ultrasound waves. The receiving process works the other way around. The reflected sound waves "'bump"' on the piezoelectric crystals. The deformation induces measurable electric current (see Figure 2). The propagation of sound is coupled to material. To improve the transmission of the waves between the transducer and the human body, clinical ultrasound uses gel with specific sound conducting properties [Lechner and Breitenseher 2003].

Difficulties

Dealing with the resulting echo is relatively complicated. Three main factors make this process difficult:

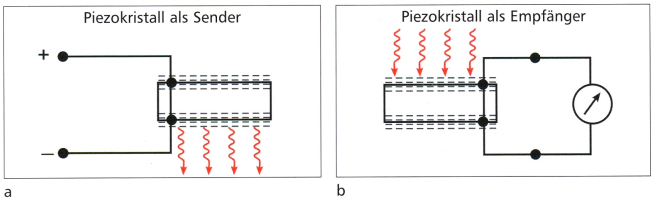


Figure 2: The transducer acts (a) like a transmitter and (b) like a receiver of sound waves using piezoelectric crystals. [Kauffmann et al. 2006].

- **The proximity** of the reflecting surface to the transmitter. Ultrasound in clinical diagnostics has to deal with very low distances between the transmitter and the detecting objects. As a consequence the examination of tissue close to the transmitter requires small piezoelectric crystals and higher frequencies whereas tissue far from the transmitter can be administrated with lower frequencies. The distance defining the boundary between "'near"' and "'far"' tissue depends on the size D of the transmitter and is defined as

$$d = \frac{D^2}{4\lambda}$$

- **The range of size** of reflecting objects in relation to the wavelength. In comparison to SONAR where the objects are relatively big and far away from the emitter, successful detection requires relatively low wavelengths. It is more easy to detect a huge underwater hill than very small gallstones within a relatively low distance.
- **The high level of absorption** of ultrasound in all types of tissue. With increasing signal propagation the attenuation also increases. As a consequence the resulting echo of surfaces with a high distance to the transducer reflect a weaker echo. The absorbed energy induces motion in the cellular structure and transforms into heat. In comparison to x-rays, ultrasound has a relatively high attenuation rate. That is why examinations on adipose people not always deliver the desired results.

Image resolution

The frequency of the emitted sound wave is also a very crucial parameter in ultrasound diagnostics. It ranges from 1-10MHz. In comparison: human hearing capabilities are limited to a range of 10 to 20,000Hz which implies that the ultrasound noise is above the bandwidth of human hearing. The high frequent waves are necessary to increase spatial resolution - the minimal distinction between two points. There are two means of resolution in ultrasound diagnostics: The **axial resolution** describes the minimum distinction between two points in the direction of the propagating sound also known as the resolution in depth. At a frequency of 7.5 MHz it provides a distinction of elements at the size of 0.25 mm. The **lateral resolution** describes the minimum distance of two points perpendicular to the sound propagation direction. It heavily depends on the width of the ultrasound signal as well as on the width of the transducer. At a frequency of 7.5 MHz, two points at about 0.8 mm may be distinguished. The lateral resolution is always lower than the axial resolution [Lechner and Breitenseher 2003].

Detection modes

A-Mode measurements use a one-dimensional signal. The emitted sound wave can be considered as a single beam. The returned echo is recorded by an oscilloscope and printed in a

coordinate system. The size of the amplitude describes the intensity and the wavelength describes the depth of the received echo.

B-Mode measurements allocate a two dimensional image typically for examinations in pregnancy. The transmitters use an array of single emitters. Unlike A-mode the description of the intensity uses different brightness levels (B). Fast image acquisition at a frequency at 20 times per second is known as **Real-Time Sonography** [Kauffmann et al. 2006].

2.1.3 Doppler sonography

The doppler sonography is based on the so called **doppler effect**. It concerns changes in wave frequency and wavelength caused by transmitter or receiver motion - remember the engine noise of a passing car (see Figure 3).

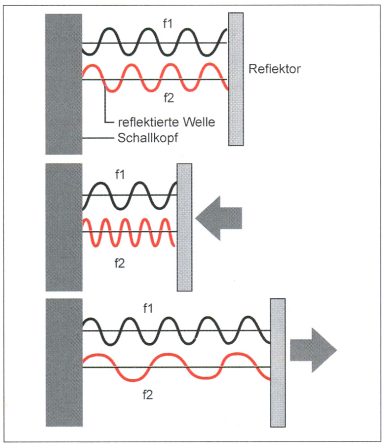


Figure 3: Approaching objects increase signal frequency (top), leaving objects decrease signal frequency [Lechner and Breitenseher 2003].

Doppler sonography in clinical context focuses on the blood flow in vessels or on monitoring the activities of the heart. The angle θ between the transducer and the vessels is a crucial parameter which has to be considered by the clinical staff. At a 90° angle there would be no dopper shift. If the angle is to small, the reflection would arise from a length of vessel that contains an averaged value over multiple objects. In practice an angle of about 60° has proven best. The expression for the change in frequency is:

$$\Delta f = \frac{2 * f_0 * v * \cos(\theta)}{c}$$

f_0 describes the emitted frequency of the transmitter, v is the flow velocity of the blood and c is the specific speed of sound propagation in tissue (about 1540m/s) [Guy and ffytche 2000].

2.2 Computed Tomography, CT

2.2.1 History

The first step to modern CT was made by W.C. Roentgen in the year 1895 when he discovered x-rays. Over the next 80 years several inventions and improvements took place until G.N. Hounsfield and J. Ambrose introduced a number of first computed tomography examinations in 1972. One of them was the calculation of distribution of material or material property in an object layer along any number of lines passing through the same layer referring to fundamentals from J.H. Radon in 1917. The first experiments on calculating the absorption distribution in the human body where carried out by A.M. Cormack in 1963. He worked on displaying absorption differences in soft-tissue structures and never had occasion to put this into practice. Although his fundamental research awarded him the Nobel Prize in 1979 shared with Hounsfield who successfully implemented his postulations in 1973. Today Hounsfield is recognized as the inventor of CT.

After the introduction of the first clinical examination, CT was enthusiastically welcomed by the medical community. Later enhancements like spiral CT by W.A. Kalender in 1990 pushed the upward trend in clinical use. By the year 2000 over 30,000 installed devices proofed the success of this technology [Kalender 2006].

2.2.2 Principles

The main idea of the CT imaging process is to separate the scanned object into slices of 1-10mm. Theses slices are located in the x/y-plane (transversal image) of the imaginary coordinate system where the z-axis is adjusted parallel to the floor. A single slice can be perceived as a matrix where each single cell represents a discretized object density value. The cells are also referred to as voxels. Every voxel has a gray value. White represent high- and black represent low object density. This is one of the main differences between classical x-ray radiography and CT. Radiography images the attenuation of a x-ray beams. Thus, high density bone structure with a high attenuation contribution always covers soft tissue. In contrast, CT is able to "'look behind"' high density areas. Hence the resulting image contains density values of neighbored structures.

The first necessary operation in the CT scanning process is to determine the **attenuation coefficient** μ along a single beam. This is achieved by calculating the difference between the primary ray intensity I_0 and the recorded attenuated intensity I. In homogeneous structures this a relatively simple task because the intensity falls off exponentially and depends strongly on the absorber thickness d. If the absorber thickness is known, the attenuation coefficient μ can be calculated relatively easy (see Figure 4). This approach is not very different from traditional radiography.

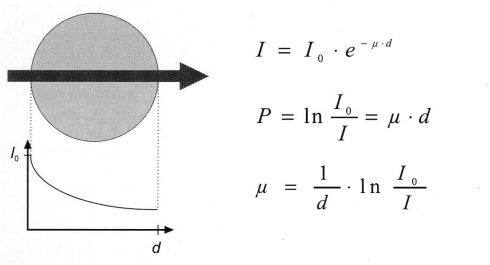
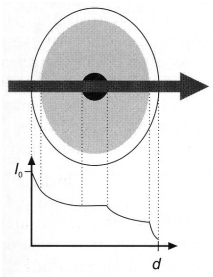


Figure 4: For homogeneous objects the attenuation coefficient μ along a x-ray beam can be calculated relatively easily and does not necessarily require tomographic imaging. [Kalender 2006].

The calculation turns out to be more complex in inhomogeneous objects where the attenuation changes within steps of d_i. The summation of all attenuations μ_i has to be carried out in small steps of d_i and is considered to be the integral over μ. Image quality increases with the number of line integrals acquired and with the steps of d_i (see Figure 5). Still, it is not possible to calculate μ_i at a single position along a line. This can be achieved by a combination

of attenuation profiles, also referred to as "'projections P"', imaged from different angles along the z-axis.



$$I = I_0 \cdot e^{-\mu_1 \cdot d_1 - \mu_2 \cdot d_2 - \mu_3 \cdot d_3 - \cdots} =$$

$$= I_0 \cdot e^{-\left[\sum_{i=1}^{n} \mu_i d_i\right]} = I_0 \cdot e^{-\int_0^d \mu \, ds}$$

$$P = \ln \frac{I_0}{I} = \sum \mu_i d_i$$

$$\mu_i = ?$$

Figure 5: In inhomogeneous objects a single measurement is not sufficient to calculate single μ_i values. [Kalender 2006].

So the x-ray tube emits radiation with specific intensity I_0 linearly along the object axis. The detectors located behind the scanned object measure the attenuated intensity I and generate a attenuation profile for the specific angle α_i. Once finished the x-ray tube and the detecting units turn along the z-axis to the next angle $\alpha_{(i+1)}$ and acquire the next angle specific attenuation profile. Image quality increases with the amount of linearly emitted x-ray beams and the steps of α_i. Ideally the system takes measurements over an angular range of 360°. For a representative image 180° are at least necessary. Modern CT systems apply a 360° rotation and take more than 1500 projections with each projection providing at least 1200 data points (μ values).

After the 360° turn the projections from different angles have to be combined to generate the distribution of μ(x,y) for the resulting image. The resulting image is described by a N x N matrix with N^2 values of μ. Several methods exist to achieve this combination. The most obvious one is to solve N_x independent equations in N_p, the number of projections and N_d the number of data points per projection (**algebraic reconstruction technique, ART**). This method induces a high amount of computation effort considering a scanning process with 1000 projections and 1000 data points. Thus, the system has to solve one million independent equations which for standard computing systems last far too long. A much more efficient reconstruction is the so called **convoluted-backprojection** which is usually utilized today. The simple backprojection uses a zero filled matrix and subsequently adds all projections according in the order of measurement. Applying a simple addition generates a blurred resulting image. Each detail does not only contribute to the desired area it also contributes to the whole image. To avoid this blurry artifact each projection has to be convoluted before added to the matrix. The projection is convoluted with the use of a convolution kernel which has a strong impact on the quality of the resulting image (e.g. smoothening, sharpening, ...). In fact, the convolution generates over- and undershoots at object boundaries and can be perceived as a high pass filter (see Figure 6). These kind of negative contributions even out the unintentional whole image contributions of single image details [Kalender 2006].

Hounsfield Scale

The attenuation value strongly depends on the primary applied intensity I_0. In fact different CT systems apply different values of I_0 and different convolution kernels. This makes the comparison of CT images very difficult and makes a qualitative image comparison nearly impossible. Therefore the attenuation value μ is transformed into so called CT values also referred to as Hounsfield units, HU. The transformation is performed by relating the measured attenuation μ_T value to the attenuation value of water μ_{water} which by

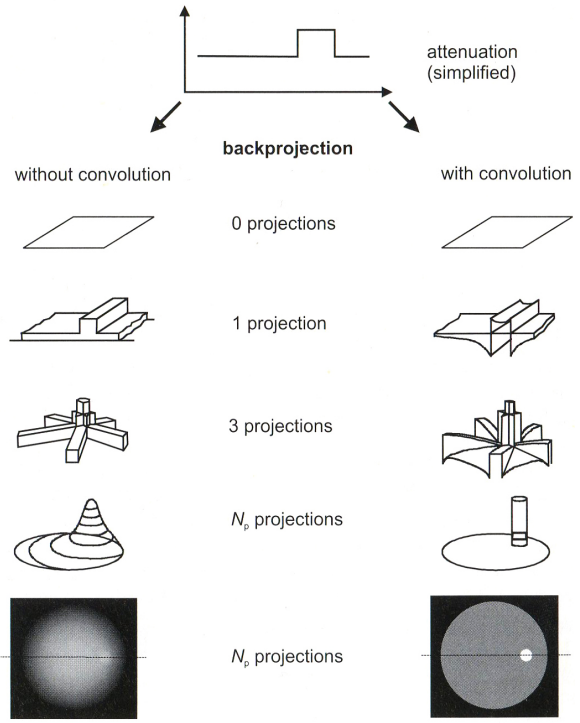


Figure 6: Direct backprojection creates unsharp images. A convolution of the profiles avoids unintended contributions and generates a representative image [Kalender 2006].

definition has a value of 0 HU [Kalender 2006].

$$CTvalue = \frac{(\mu_T - \mu_{water})}{\mu_{water}} * 1000HU$$

Every material has a specific HU value. CT makes use of this property and is able to put a focus on specified material. While compact bone has a specific HU value of at least 300 HU up to 1000 HU and higher the specific value of long tissue starts and -550 HU and goes down to -950 HU.

Dose

As already stated, CT is based on the classical radiography and therefore uses ionized radiation for image acquisition. Basically this kind of radiation is categorized as hazardous but the human organism can handle small and moderate doses which may not cause harmful side effects. The dose is also a crucial part in CT imaging because of its direct relation to the spatial resolution. The dose is proportional to the inverse fourth power of the spatial resolution. So if the resolution is improved from 1 mm to 0.5 mm the dose would increase by a factor of 16. The radiologist has to decide if the need for higher spatial resolution excuses the higher dose of radiation. Todays clinical CT systems operate with doses of 1-10 mSv which is 0.5-5 times higher than the yearly natural exposure and 50-500 times higher than the exposure in radiography. Small doses can cause non-specific nausea. Regularly overexposure with high amounts of ionizing radiation can cause a wide range of negative impacts like the stop of manufacturing new blood or gut cells or malignant tumors. Researchers keep developing new concepts and architectures which dramatically decrease the applied dose and increase image quality and accuracy. Unfortunately these designs

may require several years to find their ways into clinical practice [Guy and ffytche 2000].

Enhanced architecture

As stated above, the first CT systems used a single beam moving along a linear object axis to acquire projection values. After a turn of 1° the beam started again recording the next projection. This procedure was sensitive to patient movement and needed a about 5-10 min for a standard thorax image. The second CT generation offered a couple of parallel beams to improve scanning duration. The third generation introduced fan beams which only need a view seconds to generate a complete thorax image. Although patient movement and table motion produces image artifacts. The gantry rotation-interruption during the scans also needs a lot of time. **Spiral CT** improves the influence of patient movements by scanning the patient continuously in space and time. This is achieved by transporting the patient through the gantry along the z-axis while the scanning module keeps rotating, generating a continuous projection with a minimum data transfer rate of 2 MB/s (see Figure 7). The uninterrupted scanning process allows to image a 15 cm slice in 30 seconds with a table speed of 5 mm/s. Former systems acquired slices with the maximum of 3.75 mm in with.

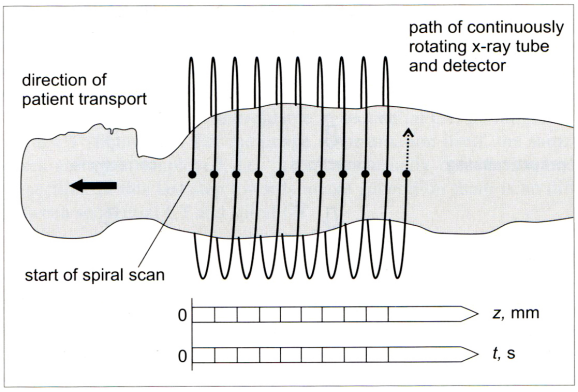


Figure 7: Geometry of spiral CT scanning process. The path of the x-ray beams looks like a spiral or a helix. [Fishman and Jr. 2000].

The image reconstruction in spiral CT requires an additional preprocessing step, the so called **z-interpolation**. A single 360° segment is due to the continuous movement not planar. The values at the end of the rotation are in fact slightly behind in z-orientation then the values at the begin. So in comparison to former CT systems, the coupling between the scan position and the image position does no longer exist. Spiral CT offers the possibility to choose image positions and slice thickness arbitrarily. Several approaches exist for z-interpolation to correct deviations and deliver a planar image.

The basic approach consists of a linear interpolation between the nearest measured data points before and after the chosen z-position Z_R. The resulting projection $P_Z(i,\alpha)$ at the projection angle α is computed as

$$P_Z(i,\alpha) = (1-w) * P_j(i,\alpha) + w * P_{j+1}(i,\alpha),$$

where w, the interpolation weight, depends on the distance of P_j and P_{j+1} to P_Z and i is the number of the selected channel. P_j represents the rotation at position j just behind the selected projection P_Z and P_{j+1} represents the next available projection just after P_Z. Other algorithms use redundancies and appropriate data sorting to improve the efficiency but the most commonly basically use the same concept shown above [Kalender 2006].

CT in practice

CT is a very complex and sophisticated issue. It offers many applications and improvements but still provides a high potential of enhancement. CT has a lot of advantages like the high spatial resolution, the relatively short scanning duration and the high availability. It also allows the application of contrast agents to focus on specific tissue or vessel structures. A major drawback is the use of ionized radiation which for instance normally excludes children from CT examinations due to their low radiation decomposition capabilities. CT is used in preliminary examination to get a basic overview and determine further examination steps. It is also used in acute examinations after accidents, as in this situation the medical staff needs to know about the patients injuries very quickly [Lechner and Breitenseher 2003].

2.2.3 Future

CT established well in clinical diagnostics and is yet indispensable. In comparison to other scanning technologies like Magnetic Resonance Imaging (MRI) or Positron Emission Tomography (PET) it provides a high economic efficiency. The wide spread use allowed vendors to build various types, sold at prices from several million dollar down to 250.000 dollars which makes CT also affordable for smaller hospitals. Concerns like these as well as increasing scanning time, increasing the applied radiation dose and increasing accuracy are the most important factors of CS's future success. Rather unpopular CT options like functional or molecular imaging may also advance and play a decisive role in future applications like tissue perfusion measurements or blood volume tests. However, the latest enhancement referred to as Dual-Source CT exactly provides these characteristics but still needs time to find its way in clinical diagnosis (see Section 4.1).

2.3 Magnetic Resonance Imaging, MRI

2.3.1 History

The origin of MRI as we know it today can be found in the year 1930 when Isidor Rabin discovered fundamentals on magnetic behavior of protons for which he was awarded the Nobel Prize for Physics in 1944. Short after World War II two American scientists, Felix Bloch and Edward Purcell, used Rabin's work and discovered the magnetic behavior of protons and their ability to resonate in magnetic fields. They found that special nuclei placed in a magnetic field are able to absorb energy from radiofrequent range. By absorbing energy the nucleus change their orientaion and flip back to their original orientation by re-emitting the energy. Magnetic scanners are able to detect the emitted energy and trace it back to produce images of the scanned materials. For the development of this process called nuclear magnetic resonance (NMR) also both of whom were awarded the Nobel Prize in Physics in 1952 [Guy and ffytche 2000].

Between 1950 and 1970 NMR was primarily used for chemical and physical molecular analysis. Later people like Raymond Damadian experimented with tissue and encouraged the scientific community to use the technology for the detection of diseases.

Another important person in the development process of MRI was Paul Lauterbur. He published his achievements on being the first to image a human finger by using the magnetic field gradients to

determine orientation and localization of tissue in 1973. The first attempt to publish his latest acquisitions was rejected by Nature because according to the referees his idea may not be sufficient enough and there may be no need for further applications. In the next ten years several enhancements like the phase and frequency encoding of images by Richard Ernst or diverse attempts to speed up the scanning process or increase image resolution. The imaging component turned out to be a major application so the term nuclear magnetic resonance changed to magnetic resonance imaging. Today only natural sciences use the synonym NMR while especially in the medical sector the imaging part became very significant [Aziz and Uetani 2002].

2.3.2 Principles

As the name of the technology implies the scanning process uses magnetic fields and radio waves to acquire images. In comparison to CT it does not use any x-rays and is therefore innocuous. As already stated,in 2.3.1, the MRI process uses atoms with a very high magnetic moment. Because of its nucleus consisting of exactly one proton, hydrogen is the most important atom for magnetic imaging. Like every elementary particle the proton has a characteristic spin which means that it is turning around its own axis without any outside interaction. A mentionable feature of the spin is that there is no need for any outside forces to keep it - the spin always exists and will not decrease or dissolve. It offers two important effects on elementary particles [Koechli and Marincek 1998]:

1. The rotation induces an angular momentum M. In analogy to the gyroscope, spinning particles like the nucleus may not change their orientation along the rotational axis unless a force from outside the system uses them to.
2. In the same way rotating electric charge also generates a magnetic moment μ and can therefore be considered as a magnetic dipole (see Figure 8).

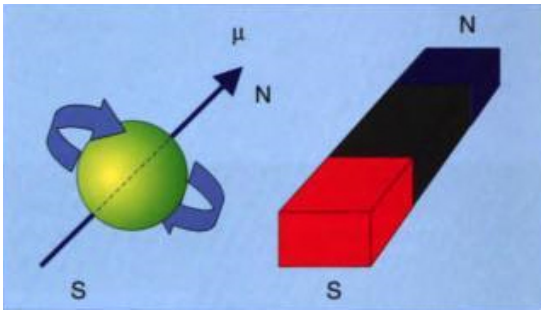


Figure 8: A charged spinning particle generates a magnetic moment μ and can be described as a magnetic dipole [Rinck and Bjrnerud 2001].

Under normal conditions the hydrogen atoms are oriented almost randomly. In a strong magnetic field, due to their magnetic behavior, they align themselves in the direction of the applied magnetic field. The functionality of a compass uses the same principle. The compass needle is a very low charged magnet. In the very weak terrestrial magnetic field, the needle always tries to align according to this field and therefore always points in the same direction. To apply this behavior on protons the magnetic field has to be much stronger. In comparison: the earth's magnetic field is about 24-66μ T while in MRI field strengths start at 0.5-1.5T [BGS].

So the first step of the MRI process is to apply a strong magnetic field on the object of investigation (e.g. tissue) to align the hydrogen atoms in one direction. Depending on their previous energy level, some atoms my align in the opposite direction of the applied magnetic field. Atoms with a low energy level are pointing in the same direction, protons with high energy level in the opposite direction. The number of low energy atoms is always slightly greater. For a successful scanning process it is necessary for all protons to point in the same direction. This can be ensured by a very strong applied magnetic field. In this case the low level atoms acquire additional energy from the magnetic field an switch their direction. The required additional energy is called the Larmor energy. At a 1.5 Tesla field, five out of a million atoms are not able to switch their energy level, which is definitely enough to get a representative image [Markisz and Aquilia 1996].

As long as the magnetic field is active all atoms will hold their aligned position. The alignment of almost all atoms in one direction is a fundamental requirement and the base of all further operations. The actual detection of the atoms and furthermore the image is accomplished with coils which detect induced current by moving atoms. Remember that the spinning atoms can be perceived as little magnets and that coils have the ability to generate electric current if a magnet moves next to it. This process acts analogue to a dynamo. So in the next step of the scanning process it is necessary to move the atoms or at least alter their pointing direction. Therefore another characteristic element of the spinning proton is relevant:

Applying a magnetic field an atom, makes the protons precess around the field direction.

In a given magnetic field all protons precess at the same speed which is called the **Larmor frequency**. The frequency can be determined with the use of the **Larmor equation**:

$$\mu = \gamma * B_0$$

γ is a constant called the gyromagnetic ratio which is 42.58 MHz/T for hydrogen and B_0 is the applied field strength in Tesla. In a scanner with a magnetic field of 1.5 T the corresponding Larmor frequency is about 64MHz. Now this is the point where the term **resonance** becomes important because the best way to move the precessing atoms is to apply an electromagnetic signal in form of radio waves which have the same frequency as the precessing atoms. The atoms now absorb energy and due to that change their direction in the magnetic field for 90°. As long as the signal is up they stay perpendicular to the magnetic field. If the radio signal is turned off, the atoms try to recover equilibrium and emit the absorbed energy. Turning back, which is also called **relaxation**, into original and parallel orientation induces electric current in the receiver coils which produces a signal used to generate the MRI image. The time the atoms need to recover the original orientation is referred to as **T1 relaxation time** .

Simultaneously to T1 relaxation another sort of relaxation takes place. It is referred to as **T2 relaxation**. While T1 relaxation lasts from 200 to 1000 ms, T2 is much faster and needs about 50 to 150 ms. After the appliance of the radiofrequent signal the atoms, as stated before, changed their direction and precess at the same speed. This produces an electromagnetic vector pointing in one direction. Interference between neighbored atoms causes interchanges of energy between the atoms, which bit by bit brings the atoms out of balance and causes the single strong vector being split up until many weak vectors pointing in random directions. So a synchronous precession of all atoms produces a strong electromagnetic signal while randomly precessing atoms neutralize each other until no signal can be perceived any more. Thus T2 is the time it takes for the signal produced by the synchronous precession to disappear [Markisz and Aquilia 1996].

2.3.3 Image Contrast

As explained in the previous section, the MRI image acquisition is based on the electromagnetic stimulation and movement of hydrogen atoms. So it is obvious that objects, composed at a high degree of hydrogen atoms, offer a more intensive signal than objects with a low hydrogen share. This means that greater differences in hydrogen occurrence imply a higher image contrast and consequently a better and more comfortable way to interpret the resulting image. So image contrast is a very important artefact. Therefore MRI provides three major parameters to control the image contrast [Koechli and Marincek 1998]:

1. **density-weighted images:** By keeping the influence of T1 and T2 relaxation low, the entire contrast is acquired by the amount of hydrogen atoms. The higher the hydrogen density, the more contrast can be offered.

2. **T1-weighted images:** The T1 relaxation time (see 2.3.2) determines the period of time needed for hydrogen atoms to recover their original alignment in the magnetic field after the radiofrequent waves changed their orientation. T1 time is not constant, rather it is a characteristic attribute of different materials. A typical material providing a short T1 time is fat. So if the image focuses on that the receiving coils stop their signal recognition after a short period of time to perceive fat - providing a short T1 time - and cut off those with long T1 times. Figure 9 shows the coherence between signal-strength and repetition time for materials providing short as well as long T1 times. The repetition time determines the time taken between two radiofrequent signals being applied (time between two MR signal recordings).

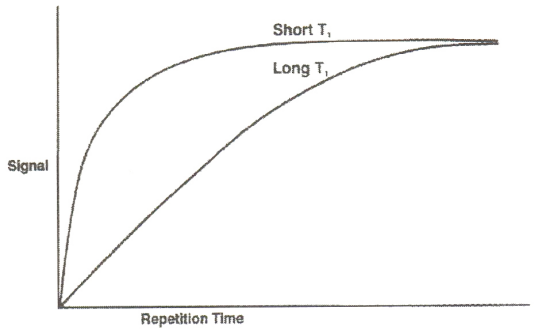


Figure 9: Tissue with short T1 values produces a higher signal in shorter times [Markisz and Aquilia 1996].

3. **T2-weighted images:** T2 time (see 2.3.2) determines how fast a MR signal disappears after a radio wave impulse. Similar to T1 different materials provide different T2 times. To acquire contrast from that kind of material (e.g. tumor) the focus on recording the MR signal is set on T2 times. In complement to the T1 time-curves in Figure 9 the T2 time-curves seen in Figure 10 start at a high signal value (atoms are precessing synchronous) and decrease until the signal is almost zero (atoms precess in different frequencies or phases). The time on the abscissa is referred to as echo time. It specifies the time elapsed until the MR signal is recorded.

Figure 11 shows two MR images from the cranium. The image on the left-hand side is T1 weighted where liquor provides a low signal (hypointense). The image on the right-hand side is T2 weighted. Here liquor offers a high signal thus it offers a high contrast (hyperintense).

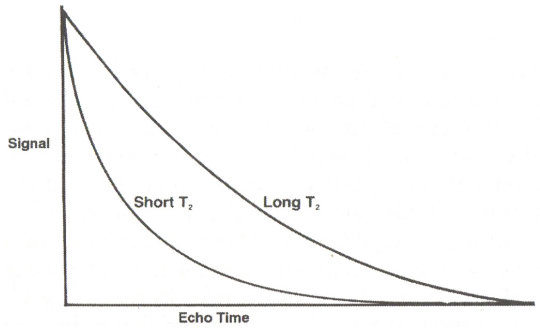
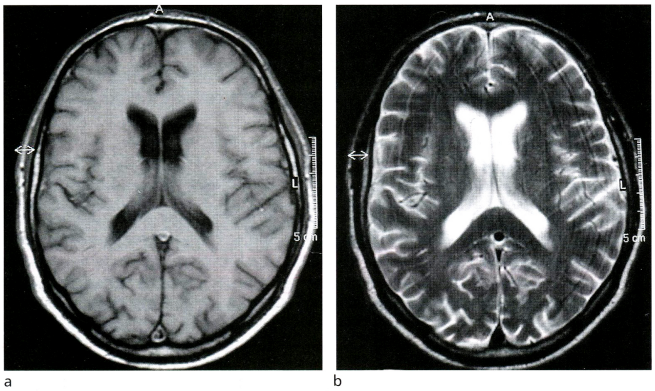


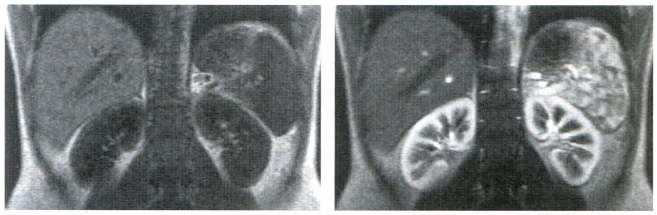
Figure 10: Tissue with short T2 values looses signal more rapidly than those with higher T2 values [Markisz and Aquilia 1996].



a b

Figure 11: Transversal MR image of the head; T1 weighted (left) and T2 weighted (right). Notice the lack of contrast in (a) compared to (b) [Lechner and Breitenseher 2003].

The focus on particular parts of the body (e.g. articular cartilage) or particular tissue (e.g. tumors) scanning steps with different calibration in T1 and T2 relaxation times can be combined. The computer synthesizes several MR images and extracts the information needed in an extra MR image. This process is referred to as **Sequencing**. In some examinations sequencing can not deliver the desired result. Alternatively, **contrast agents** can be used to change the appearance of certain tissue and enhance their contrast. The agents either change the distribution of hydrogen or alter the T1 or T2 relaxation time by taking influence on their magnetic behavior. Nearly all common contrast agents contain the paramagnetic element gadolinium. Like all paramagnetic materials gadolinium decreases the T1 relaxation time of infiltrated tissue which therefore will be displayed brighter. The contrast agent has to be prepared in a way that it is able to bind to a carrier substance which accumulates in the specified tissue. The most frequently used substances have a half-life of approximately 20min. So contrast agents are applied short before the MR scan [Markisz and Aquilia 1996].



a b

Figure 12: T1 weighted slice (a) before and (b) after the application of gadolinium. In (b) the contrast agent has accumulated in the kidney and parts of the spleen [Lechner and Breitenseher 2003].

2.3.4 MRI in practice

Magnetic fields

Clinical MRI with magnetic fields below 3.0 T are considered safe for humans. Until now no hazardous side effects have been monitored it is now accepted that there is no evidence of any risks like the alternation of the human DNA because MRI does not use any ionizing radiation like x-rays or gamma rays. In the MRI research sector, the magnetic fields have to be very strong. As a consequence also the induced current is more intense. This is why some patients claim dizziness or headaches at fields above 2.0 T. Patients even recognize flashes of light if small amounts of current induce in their optical nerve. An evident side effect is the accumulation of heat. Much of the harmless radiofrequent radiation re-emits and produce the MRI signal. A part of the energy simply stays in the body tissue and turns into heat (specific absorption rate, SAR). In clinical MRI it is considered normal if the body temperature raises up to 0.5° Celsius. The magnets are closely monitored and observe the SAR limits. Still the higher magnetic fields (above 3.0 T) in research basis have not been cleared of potential risks.

The strong fields also require safety guidelines in MRI rooms. All kinds of metallic items must be removed. Persons who enter the room have to be checked for metallic items like pens, keys or stethoscopes. The attraction of the magnetic field might pull those items out of pockets and makes them fly through the air as if they were missiles which is very dangerous for patients lying in the bore of the scanner. As a consequence, people having surgically implanted metallic devices have to be excluded from MRI analysis.

Pregnancy

Concerning fetal imaging, sonography is the first choice imaging method. Although it is widespread availability and low cost, it raises some disadvantages like the small field of view, beam attenuation by adipose tissue or the relatively poor image quality. To compensate these payoffs fetal MRI is a very efficient supplement. It offers a higher resolution by using array multicoils. Fetal MRI is concerned safe for both mother and fetus because it does not use any kind of ionizing radiation. So in clinical practice no complication or trouble has been monitored, although safety has not been established sufficiently. As a consequence fetal MRI will not be applied during the first trimester of pregnancy. In some cases the diagnostic benefit is more crucial than the possible related risks [Coakley 2003].

Noise

The induced current at the gradient coils produces a large force which tends to try to make the heavy coil move. This process produces the MRI typical very loud knocking and banging noise which is about 90db. In comparison: an elevated city train at a distance of 7 m produces the same decibel level. New enhancements like the spin-echo technology minimize the decibel level but it is still very displeased. Even anti-noise systems which produce an identical noise in the opposite phase to cancel the original noise out have been introduced. The noise increases anxiety, headaches and even temporary hearing losses. [Brummet 1988] reported that 43% of people, scanned without ear protection, suffered from temporary hearing loss. So today every patient is suggested to use ear plugs [Markisz and Aquilia 1996].

Prearrangement

Before patients undergo the MRI examination, clinical staff has to inform them about the scanning process in detail. Several circumstances like the loud noise or the narrow bore makes the patients feel very uncomfortable or even anxious which might lead to abortion of the scanning process once it started [Markisz and Aquilia 1996].

2.3.5 State of the Art

Researchers at the University of Aberdeen, UK, who strongly contributed knowledge in designing the first available MRI systems, developed a new procedure which adds new visible features to the MRI image. In contrast to traditional MRI where the magnetic field is held constant, the so called fast field-cycling MRI (FFC MRI) method switches the magnetic field rapidly during image acquisition. This allows to gain information about how molecules behave in a spectrum of fields. Also samples of T_1 and T_2 relaxation times are recorded over time to acquire new information. In first examinations a clearer vision of proteins and free radicals which are involved in diseases like Alzheimer's, Parkinson's and Multiple Sclerosis was achieved which may lead to earlier diagnosis and even new treatments. In the future FFC MRI may also be applied in other sectors like the food industry or in sport sciences for non-invasive muscle mass measurements or for recovery tracking after injury. FFC MRI requires special, power supplies as well as adapted software and is yet limited to only a few laboratories until further investigations and research results allow clinical application [Lurie et al. 2008; ABDN 2007];

2.4 Positron Emission Tomography, PET

2.4.1 History

Emission and transmission tomography was introduced in the 1950s. Due to the use of annihilating radiation, Gordon L. Brownell constructed the first clinical positron imaging device in 1952. After some refinements this was used to be the first version of commercially available PET scanners. In 1962 scanners making use of two rows of nine detectors increased the sensitivity and allowed a three-dimensional estimation of the actual signal origin. About a decade later in 1971 rotational and translational detector banks and adapted interpolation algorithms improved the sampling and image quality. In the early 1970s the comprehension of the so called filtered back-projection allowed to add the word **tomography** which stands for imaging by sectioning or slicening.

Developing radiopharmaceuticals to provide specific examinations ever was a crucial task in emission and transmission tomography. With the introduction of radiopharmaceutical ^{18}F labeled 2-flourodeoxy-D-glucose (2FDG), the scope of PET imaging was largely expanded and the technology gained acceptance in the scientific community. With a nearly optimal half-life time for positron imaging, ^{18}F could give precise values of energy metabolism in brain, heart and other organs. The next logical step was taken in the early 1980s when the planar scanning cameras were replaced by the first detector rings. Several hardware improvements lead to the PET scanners as we use them today in clinical everyday life. Currently the attention of research in nuclear medicine concentrates on providing higher image resolution and primarily developing and enhancing the properties of radiopharmaceuticals [Brownell 1999].

2.4.2 Principles

The majority of all nuclear medical diagnostic technologies require the administration of a soluble carrier substance which is labeled by a radioactive nuclide. The applied rate of the substance is very low so that it is harmless for the human organism. Once administrated either by injection or orally the blood distributes the solution throughout the body until it concentrates in the preferred target organ or around a particular disease process. As it is a radioactive substance it emits gamma-rays. Outside the body a so called gamma camera collimates and counts the rays to finally generate a map of distribution which allows localization of the administrated substance. Unlike radiological applications like MRI or CT the nuclear approach delivers functional not anatomic information (see Figure 13). So these different diagnostic paradigms are not strictly comparable to each other.

A functional image offers poor spatial resolution and a high signal to noise ratio (SNR). These artifacts partly result from the small concentration of the radioactive substance. If the dose is higher, scattering and absorption of the human body might be omitted but a higher rate also implies an overexposed image and aside from that could be hazardous for patients as well as for clinical personal. Due to the tracking of intensive metabolic processes, functional imaging is widely used in oncology to discover tumors. Three main types of nuclear imaging have established today [Guy and ffytche 2000]:

- planar imaging similar to x-ray radiography
- single photon emission tomography (SPECT)
- positron emission tomography (PET)

Planar imaging and SPECT use one or more large area gamma cameras to record radiation. The camera consists of mainly three parts:

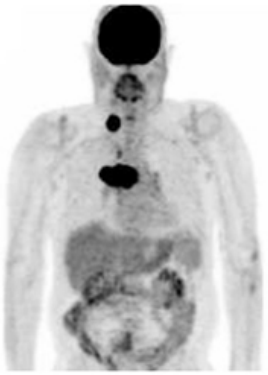


Figure 13: Typical functional image retrieved from PET in a patient with non-small cell lung cancer of the right lung. [UAMS].

a collimator, a crystal scintillator and a positron sensitive photon counting unit. The collimator obtains a line of sight to achieve a parallel projection perpendicular to its face. It filters out obliquely angled photons to provide a planar image. Perpendicular oriented γ-rays pass the collimator and produce low energy scintillation photons in the thallium activated sodium iodide, $NaI(Tl)$, crystal. A photomultipler finally detects and counts the scintillations and forwards its data to the logical unit to generate an accumulated image.

Due to transmission losses for every million γ-rays emitted by the radioactive substance only about 10 are actually counted. Although planar imaging provides a representative and usable result. While planar techniques use a fix mounted gamma camera, SPECT tilts it with respect to the patient thus a collection of 2D projections can be obtained. A combination of theses projections (**backprojection**) delivers the desired tomographic images. As the collimator determines the line of sight, with increasing depth the gamma count rate decreases and the signal turns lower. Scanning the patient with two gamma cameras compensates the effect but still restricts the spatial resolution to 8-15 mm [Guy and ffytche 2000].

Positron Emission Tomography uses a fairly different architecture which makes spatial resolution of 4-6 mm possible [Lechner and Breitenseher 2003]. Theoretically resolutions below are even possible but in practice never achieved. Non-influencable factors like inaccuracy concerning the collinearity of the emitted photons after the annihilation process (see below) or the movement of the patient during the examination actually worsen the resolution. Nonetheless PET has established in nuclear diagnostics and in comparison to SPECT delivers precise images. It makes use of a fact that has not been discussed yet. The tracer introduced into the patient, is a positron emitter. When a positron annihilates with an electron provided by biological tissue, gamma radiation in the form of actually **two photons** emerges (see Figure 14 (a); Note: any radiation including gamma radiation is quantized by photons). PET is able to make use of both emitted photons by changing the planar gamma cameras against a detector ring. Placing the patient in the center of the about 10 cm broad ring allows constant 360° imaging. The scintillation crystals are placed in the inner side of the ring next to each other. If a single crystal detects a photon another crystal on the opposite waits for about 5-10 ns to receive the second photon. An appropriate registration of the gathered lines between two detected photons inside of the ring gives information about the location of the radiotracer. As previously stated the photons do not propagate exactly within a 180° angle due to scattering and deflection which contributes negatively to the image quality.

So PET is a wholly tomographic procedure. It collects much infor-

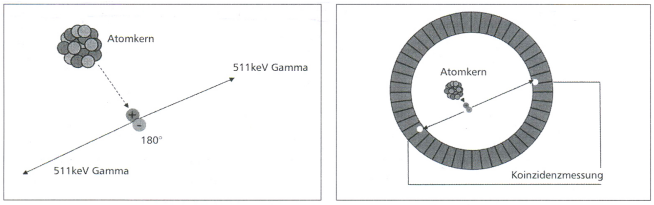


Figure 14: When a positron annihilates with an electron γ-rays in the form of two photons emerge. These photons propagate in opposite directions of 180° with the energy of exact 511 keV (a). The scintillation detectors are arranged in form of a ring. When a crystal detects a positron the scanner waits for the second to collide in the opposite crystal (b). A subsequent combination of the coincident lines between two detected photons gives information about the annihilation origin. Improved detectors even calculate the time difference between two coincident detections to exactly calculate the origin and provide better spatial resolution. [Lechner and Breitenseher 2003].

mation which finally can be combined to reconstruct a 2D or 3D image of isotope concentration. Whereas SPECT looses precision with increasing scanning depth due to the collimator field of view (the line source-response function LSRF increases), PET achieves a relatively constant LSRF (see Figure 15).

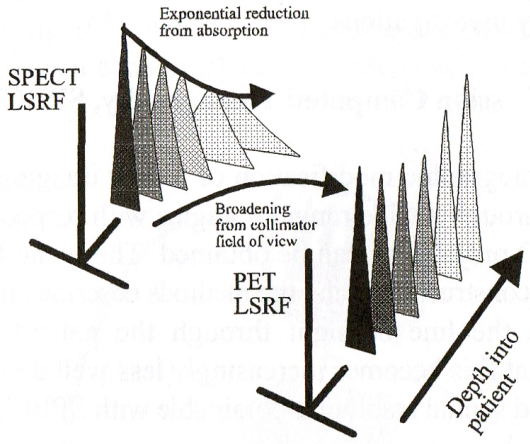


Figure 15: Comparing SPECT and PET accuracy. Increasing depth also increases the field of view which leads to inaccuracy. The accuracy of PET remains relatively constant with increased depth. [Guy and ffytche 2000].

The coincidence of the captured photon pares is crucial for the success of PET. If no further software correction is applied two completely unrelated photons which arrive at the same time may count as a successful photon detection. Also scattered photons may cause counted detections by mistake. One approach to get rid of those events is to shorten the time window waiting for the second photon to be detected. Preventing scattered detections requires software correction algorithms. Before the actual PET scan starts a separated scan process calculates an empirical attenuation factor with respect to the position of the initial annihilation process. This correction factor is comprised within the actual scanning process. If a perception of two single photons exceeds the attenuation factor it can either be corrected useing the correction factors or skipped to avoid any negative artifacts.

2.4.3 Radiopharamaceuticals

The design of suitable radiopharmaceuticals is crucial for the success of functional imaging. Radiopharamaceuticals are substances that can take part in metabolism and are labeled with gamma radioactive elements for diagnostic reasons. Optimally the radionuclide is its own carrier substance like ^{123}I-Iodid which takes its own way to the destined organ - in this case the thyroid. For the majority of the applications the radionuclide needs to be bound to a organ specific molecule. Several methods can be applied to perform this chemical reactions (e.g. molecular exchange, chemical syntheses, etc.) [Kauffmann et al. 2006]. The clinical choice of a particular pharmaceutical has its own constraints and always depends on the application. The far most widely used nuclide is the gamma isotope Technetium ^{99m}TC. The production takes place in clinical context on demand by a chemical separation of the longer lived precursor molybdenum ^{99}MO. MO is a product of central reactor facilities and has a half-life of 67 hours. TC offers a half-life time of 6 hours and a nearly constant γ-ray energy of 140keV which is very convenient for gamma ray imaging [Guy and ffytche 2000]. An overview of some frequently used radionuclides is given in Table 1.

Nuclide	Half Life	Energy	Production
Molybdenum ^{99}MO	66h	740 γ	Fission
Iodine ^{99}MO	66h	740 γ	Fission
Cesium ^{137}Cs	30 y	662 γ	Fission
Oxygen ^{15}O	2.07min	511 β^+	Cyclotron
Fluorine ^{18}F	109min	511 β^+	Cyclotron
Technetium ^{99m}T	6h	140 γ	chemical generator
Gallium ^{68}Ga	68min	511 β^+	chemical generator

Table 1: Selection of frequently used isotopes. The energy specifies the photon energy in keV.

2.4.4 Recent enhancement

Nuclear imaging technologies like PET do not offer high spatial resolution in comparison to technologies like CT. Researchers from Hokkaido University in Sapporo, Japan, compensated this little drawback by building a PET system based on semiconductor detectors in 2008 which provides better SNR and improves spatial resolution. This is mainly due to the size of the detectors. Their thinness facilitates the arrangement and allows more detectors to be placed next to each other with less space in between. The prototype scanner already demonstrated better characterization of epilepsy as well as nasapharyngeal cancer (developes at the top of the throat). The researchers predict better early-stage diagnoses of cancer in general, better detection of neurological disorders as well as patients' responses to therapies and several other applications where high spatial resolution claims high importance. The prototype installed at the Hokkaido University Hospital delivered mentionable results and is feasible for clinical use [SNM 2008]. For more information see also [Morimoto et al. 2008].

2.4.5 Future

Today PET is firmly established in nuclear diagnostics but for several reasons could not find a widespread use in clinical context. This is mainly due to the nearby required cyclotron to produce suitable positron emitting isotopes with acceptable half-life times and the relatively high costs. PET in comparison to SPECT has basically two advantages: the first is the spatial resolution which is at least

twice as good and the second is the use of biologically interesting radionuclides (e.g. ^{123}I). Although this facts are not sufficient for daily clinical use. The already stated drawbacks may keep PET in specialist centers where it is regarded as a research tool operated by well trained personal. These institutions mainly use the technology for investigating tumors, heart and brain function. Nonetheless, research continuously improves the technology and makes new ways of usage applicable. Single standalone PET scanners may phase out in the near future. Functional imaging technologies, especially PET, are more and more combined with anatomic imaging systems like CT (see Section 3.2.1). The latest combination was introduced in November 2008 and is referred to as Positron Emission Mammography (PEM). Standard x-ray systems are now able to provide additional functional information in standard breast examinations [Naviscan 2008]. Future PET research and nuclear diagnostic in general has to focus two major aims. First, to speed up the image generation process to shorten the examination time and avoid image artifacts as well as indirectly improve spatial resolution. The second major aim is to develop more and better radiopharamaceuticals to simplify the scanning process in clinical use as well as to increase the field of applications [Guy and ffytche 2000].

3 Dual-Modality Imaging

Single scanning technologies have proven reliable over the past 30 or even 50 years and offer high sophisticated applications. Although development has not finished yet and further research may cover new capabilities and opportunities. In the past two decades research also took a combination of both anatomical and functional imaging into account (see Figure 16). Single functional modalities often suffer from spatial resolution. So the allocation of certain diseases is a very hard or even impossible task for clinical personal without any anatomical information. A mental comparison of two individually generated images without any further processes involved is in fact possible but provides a lot of inaccuracies. Furthermore it requires a lot of time to image patients using different equipment in different places. Temporally differences between scans also induces changes in the patients positioning [Townsend 2008]. Mental comparison is in fact possible but turns out to be problematic due to differences in slice width and slice positioning. The application of high specific tracers sometimes generates images without any structural information. In this case the lack of similarities makes mental comparison nearly impossible [Lemke et al. 2004].

Still image comparison is possible but requires additional effort especially in cost and time. This effort naturally raises the question concerning the necessity of image fusion which in practice has to be answered in each individual case. The intention of image fusion is to gain additional information. Experience shows that this is possible in some cases. In literature the data concerning the factor of success varies from 20-45% [Lemke et al. 2004]. That is why image fusion still is a controversial subject.

Basically, clinical image fusion provides two approaches the **retrospective** and the **proscriptive** approach. The retrospective approach is also referred to as the software approach and was introduced in the early 1980s [Bybel et al. 2008]. The software uses functional and structural images for input, applies correlation algorithms and outputs the resulting combination. This process is also called registration (see 3.1). The major advantage of this approach is that it does not require any specific hardware. The separated imaging process though has a negative impact on the result. The circumstances in the proscriptive approach are contrary. Here, the functional (e.g. SPECT, PET) and the structural (e.g. CT, MRI) devices are combined in one device. So there is no need for patient movement between the two examinations. This is why the image fusion offers higher accuracy. The additional hardware implies higher costs which in practice allows only low availability. The process of image registration however is evident in both approaches. Therefore accurate algorithms are a major key to success in image fusion.

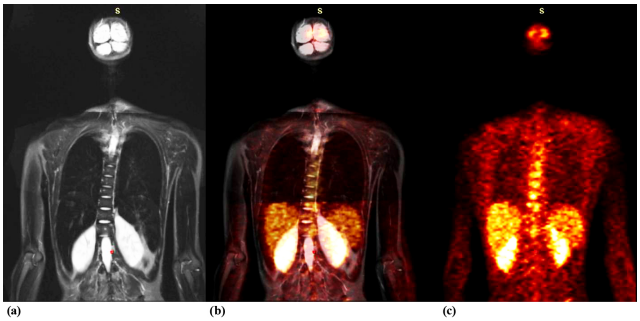


Figure 16: Illustrates the fusion (b) of a CT structural (a) and a T1 weighted MRI functional (c) image. [SIP 2007].

3.1 Image registration

Image registration adjusts two or more similar images in a way to become congruent after fusion. The adjustment can either be in location, size, angle, shear and even shape. [Tang et al.] provide a short definition of image registration:

> Image registration is a process in which a series of spatial transformations T is being applied to one image m until it aligns with another image f. To evaluate how well the transformation has mapped m onto f, a similarity metric $S(f,T,(m))$ is used.

So the process of image registration consists of two parts. First the images have to be rearranged in multiple domains. Concerning images of the brain, simple rigid-body transformations and spatial transformation corrections are adequate but things turn more complex in other body areas like the thorax. In the next step these changes have to be evaluated by so called similarity metrics. A frequently used technique is the so called mutual information metric which measures the statistical intensity relationship between images. The rearrangement uses landmarks or fiducial marks in order to obtain image alignment followed by a proper image transformation. More complex algorithms also involve shearing operations as well as nonlinear transformations which optimize the image metric, based on intensity values. These concepts work well concerning the combination of brain images acquired from CT, PET, SPECT and MRI but still have not proven success in other parts of the body. In clinical context software registration started in 2001 and was primarily used for radiotherapy treatment planning. Fusions in individual examinations only offered little for most patients [Lemke et al. 2004].

Today the improvement of algorithms is an important factor of success. Former algorithms were restricted to the fusion of brain and cranial images due to very good positioning reconstruction because of low uncontrolled movements. Enhanced algorithms are able to handle low variations, hence expand the field of applications (e.g. abdomen, pelvis, etc.). That is why the success of retrospective image fusion not only depends on the quality of the input images but also highly depends on the efficiency of the reconstruction al-

gorithms. Therefore, research concerning this subject continues in both the academic and the commercial domain [Townsend 2008].

3.2 Hybrid systems

Traditionally, functional and structural information was acquired sequentially using two different devices. In the early 1990s a completely new approach was considered to improve image fusion. It combines functional and structural image acquisition in one device. So the fusion problem is solved through accurate hardware architecture rather than highly sophisticated software algorithms (see Figure 17). Leaving the patients positioning unchanged is a major advantage and minimizes temporal and spatial differences. This effect can further be encouraged by using anatomical information to apply attenuation correction (see section 3.2.1). Still todays hardware combination still require axial bed translation. In fact, hardware combination places the anatomical and functional devices in tandem rather than providing a "'real"' combination without any patient movement. Thus, hardware combination basically reduces the space and time between two still separated scanning procedures. Nonetheless the resulting images provide high accuracy and low extra effort like labor-intensive software fusion. The system routinely generates a set of co-registered images with different configuration immediately after the scan. In contrast, retrospective fusion after the scanning procedures needs an extra amount of time to deliver accurate results.

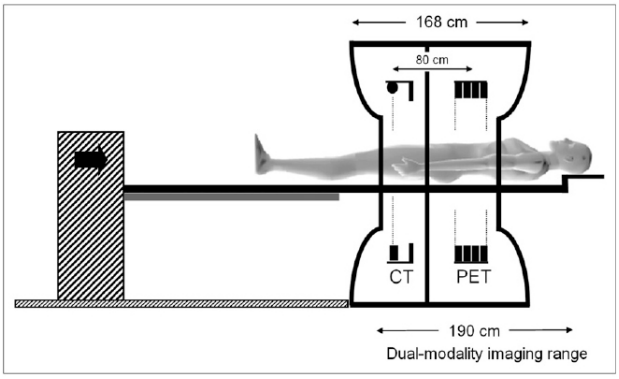


Figure 17: Schematic illustration of a standard PET/CT scanner. CT positioned in front of the PET scanner. The centers of the imaging field may not exceed 80 cm in distance to assure proper image registration [Kalender 2006].

So hardware fusion offers a lot of advantages; it is more convenient for the patient as well as the clinical personal; it requires less time and improves registration accuracy. Dual modality imaging in one device has established well today. The combination of PET and CT systems has proven reliable so single PET scanners tend to phase out. The majority of modern functional scanners offer an additional anatomic component today.

3.2.1 PET/CT

The first clinical PET/CT scanner was introduced in 1998. The image acquisition and reconstruction components were not integrated and every modality had to be controlled by its own console. After the scanning process the CT data had to be transfered to the PET console via Ethernet to perform attenuation correction. Although PET/CT turned out to be very useful and development continued. Components like the fixed complete PET rings and multi-slice CT have been upgraded. Also the patient handling system was improved in a way that it eliminates vertical deflection as it moves through the tunnel. The acquisition and reconstruction though was still performed on separated hardware. Additional workstations providing fusion and display software were added to review the studies. [Townsend et al. 2004].

Attenuation correction, AC

Today a whole body scan can be performed in less than 30 min. Former versions required 45 min for 100 cm. This improvement can be ascribed to the anatomic based attenuation correction. Standalone PET systems require a lot of time to generate attenuation maps (see section 2.4.2). In hybrid systems, CT data can be acquired in less than a minute for 100 cm and hence used for PET attenuation correction. The so called **attenuation correction factors (ACFs)** generated by CT data not only reduce the scan time by up to 40% they also provide more accuracy than PET generated ACFs. Before the actual correction process, the CT correction factors with a mean photon energy of 70 keV have to be scaled to the PET energy of 511 keV due to the energy dependent attenuation in CT. The scale factor is mainly determined by elemental composition. So theoretically different tissue composition requires a different attenuation value. In practice an appropriate threshold in the Hounsfield scale distinguishes regions of bone between regions of nonbone and the scale factors are linearly interpolated to the minimum and maximum of the Hounsfield scale which anyway delivers good results.

While CT acquires the ACFs, patients are required to hold breath in order to avoid mismatches in the transformation process. Serious artifacts may also arise with the application of contrast agents in CT. The higher intensity in anatomic data may cause unintended overcorrection in the functional image. Hence, the contrast-enhanced CT pixels have to be separated and to remove the effect to avoid incorrect scaling. This can by done by first identifying bones with a threshold greater than 1500 HU and region-growing algorithms. All structure left with a CT value greater than 150 HU which this is well above any soft tissue value, can by identified as contrast enhanced tissue. These values can be corrected to standard tissue values and may no longer influence the PET attenuation correction. The importance of attenuation correction is demonstrated in figure 18. Today anatomical based attenuation correction is by default used in all hybrid systems and is jointly responsible for the continuing establishment of PET/CT in clinical diagnostics [Townsend et al. 2004; Kinahan 2005].

Future

Due to the high demand PET/CT development continues and may improve all kinds of components like the electronics, the computing power or scintillators. The use of lutetium oxyorthosilicate (LSO) scintillator crystals for instance allows a higher crystal density with lower space in between. They also allow panel design in the size of 52 x 36 cm. A mean thorax scan is then performed within one lateral patient table movement [Townsend et al. 2004]. Another interesting feature is the design of a gantry which fully integrates the hardware of both the CT and PET components. The big challenge is to develop shared detector systems which are able to measure both x-ray CT photons and annihilation PET photons. This may avoid any patient movement and therefore generate high quality images. There was also a demand for devices offering less performance concerning the anatomical spatial resolution to achieve cost savings. Certainly, the main costs can be ascribed to the PET components and therefore low resolution CT may not achieve the desired cost

savings [Kalender 2006].

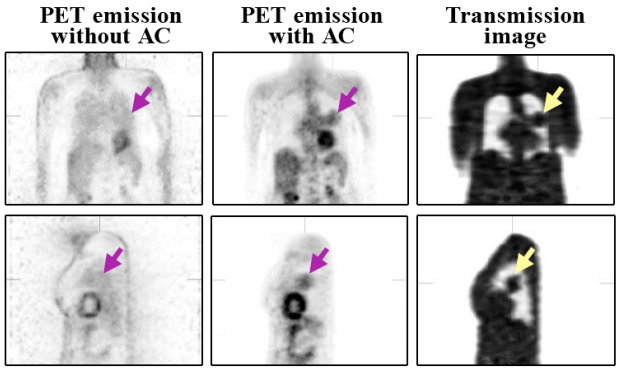


Figure 18: Shows the PET emission without (left) and with (center) attenuation correction. The harmatoma (arrowhead) may have not been identified without appropriate attenuation correction [Kinahan 2005].

3.2.2 PET/MRI

Successfully operating PET/MRI systems were first introduced in the year 2006 and are still not available for clinical diagnostics. First attempts to combine PET and MRI in one device where already made in the year 1996. This undertaking turned out to be very tricky because of the mutual interference between PET and MRI which at least lead to image distortion. The high magnetic field caused electromagnetic interferences (EMI) with the PET photomultiplier tubes (PMT) which are very sensitive to magnetic influence. On the other hand the electrical and radiofrequency components in PET significantly disturbed the homogeneous magnetic field which also lead to artifacts in the anatomic image. The first approach was to split the PMT from the scintillators and get them out of MRI's magnetic field. The two components where positioned in two separated rooms and linked with an optical fiber cable to transport the photon signal. Hybrid imaging indeed was possible but the PMT received a 50-70% weaker signal which was very weak compared to scintillation light standalone PET systems. Also the complex and bulky architecture due to the high amount of fiber cable may not have been practicable in clinical use [Harvey 2008].

Acalance technology

After a stop in research for several years, development continued in the year 2003 when the Acalance technology emerged and silicon-based Avalanche photodiod detectors have been deployed. These photodiodes are magnetic field-insensitive and therefore could be placed next to the scintillator crystals still connected wire optical fiber cable and with respect to MRI radiofrequency and gradient coils to minimize magnetic field inhomogeneities. The optical cable still reduces the PET generated light signal in a small amount. Attempts to place the photodiodes directly on the crystals, induced inhomogeneities in MRI's magnetic fields why the short distance between the photodiodes and the crystals is indispensable. Although, PET/MRI hybrid systems proved reliable in magnetic fields up to 9.4 Tesla. The system architecture is illustrated in figure 19. PET/MRI although offers some drawbacks. One of them is its small field of view of about 12 mm which makes whole body scans on humans hardly possible due to patient and uncontrollable body movement [Catana et al. 2008].

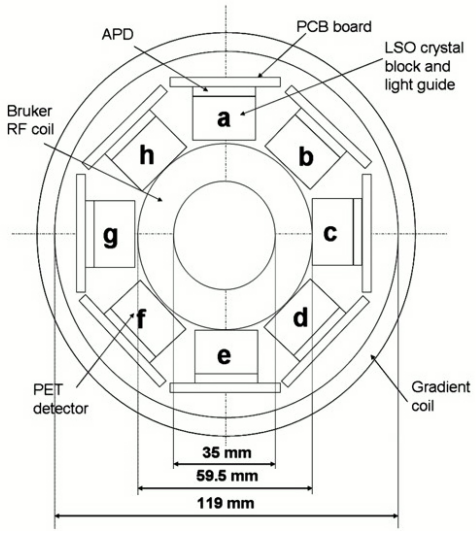


Figure 19: The PET detectors are mounted between radiofrequency and gradient coils to achieve simultaneous imaging. [Pichler et al. 2006].

Future

The new technology, still only available in research laboratories, achieved success in tracing the distribution of drugs in animal organisms. This for instance may help carry new drug therapies. Brain research may also benefit from new achievements concerning Alzheimers disease, Parkinsons disease, Schizophrenia or Epilepsy. So PET/MRI is very valuable where aspects which change with time. These dynamic image techniques may not be possible in PET/CT due to the long time radiation impact. This is why vendors are busy working on PET/MRI to facilitate commercial use. The market launch is dated to the remote future. Although, Siemens distributes hybrid systems in the US for research purposes [Harvey 2008].

4 Enhancements

4.1 Dual-Source CT

Spiral and multi-slice CT systems offer very good spatial and temporal resolutions for most applications. In some cases even better resolutions are required to generate clear and expressive images. Cardiac examinations for instance suffer from image quality due to the constant movement of the heart muscle which arouses artifacts impossible to correct by the use of software image registration. Nonetheless, especially in this domain very small image details are necessary to image the winding vessels that supply the heart to characterize calcified plaques in the coronary arteries.

Principles

The first attempts of multi-slice systems provided a temporal resolution of 250 ms which is barely enough to generate motion-free images in the mid- to end-diastolic phase at slow heart rates (65 bpm). Still motion artifacts and limited spatial resolution was a problem scanning patients with higher heart rates. Apart from that, the multi-slice scans needed patients to hold breath for more then 40

s to avoid motion artifacts which is unacceptable for patients with manifest heart disease. Even the administration of beta-blockers to decrease the heart rate was not able to deliver the desired results and was not practicable in every case. As a consequence, vendors tried to increase the gantry rotation speed. To provide temporal resolution less than 100 ms the mean gantry speed has to be less than 0.2 s. This rotation speed induces mechanical forces of more than 75 G which is beyond today's limits.

An alternative promising concept was introduced in 2005. The new scanner design makes use of two x-ray sources and two corresponding detectors and increased both temporal and spatial resolution. This architecture is also referred to as dual-source CT, DSCT. The two detecting units are mounted in an angular offset of 90°. One detector covers the entire field of view (FOV) while the other is restricted to a smaller field due to space limitations in the gantry (see Figure 20). By appropriately combining the two subsequent 32-slice readings to one 64-slice projection with a sampling distance of 0.3 mm each detector virtually acquires 64 overlapping 0.6 mm slices per rotation. Consequently temporal resolution of a quarter of the gantry rotation time is possible. This exquisite improvement makes the use of reconstruction algorithms and multi-segment reconstruction techniques obsolete. [Flohr et al. 2006] evaluated the performance of DSCT in an experiment and assessed the temporal and spatial resolution with different heart beat rates. The phantom dummy used in the experiments consisted of three contrast-filled lucite tubes with a diameter of 4 mm and two of them containing artery stents. A computer controlled robot arm simulated hard beat by continuously moving the phantom. With a simulated heart beat rate of 90 bpm DSCT was able to achieve **temporal resolution of 83 ms**; in comparison, single-source CT achieved 160 ms. Figure 21 compares the results. Due to the increased spatial resolution the scanning duration of a 120 mm slice decreased to between 5 s and 9 s depending on the patients heart rate. The spatial resolution examined is about 0.6-0.7 mm which can be improved to 0.5 mm by applying a sharp convolution kernel for the evaluation of stents or calcified coronary arteries.

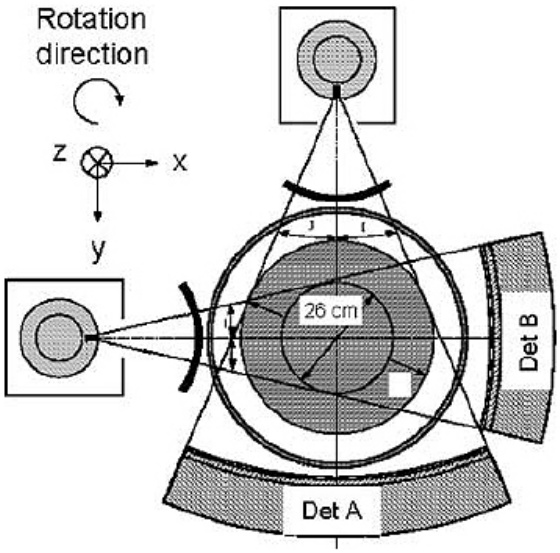


Figure 20: Illustrates the dual-source CT architecture. Detector (A) covers a FOV with a diameter of 50cm. Detector (B) is restricted to a FOV of 26 cm [Flohr et al. 2006].

DSCT is also applicable for general radiology purposes. The two detectors allow separated operation and independent imaging. By the use of one detector the DSCT is fully equivalent to a standard 64-slice spiral single-source CT. The independent x-ray tubes can be operated in different kV and mA which allows dual-energy data acquisition. In the near future this feature may differentiate between tissue which changes attenuation properties proportional to varying kV-values. A possible application may separate bones and iodine-filled vessels in CT angiography. With decreasing voltage the CT value of iodine disproportionate increases in comparison to the other CT values which allows the separation of vessels and bone. Figure 22 shows the result of an experiment where a contrast field tube was separated from the surrounding pig bone. Additionally stents and metal pieces where inserted and the 80 kv/140 kV scan delivered mentionable results. [Flohr et al. 2006].

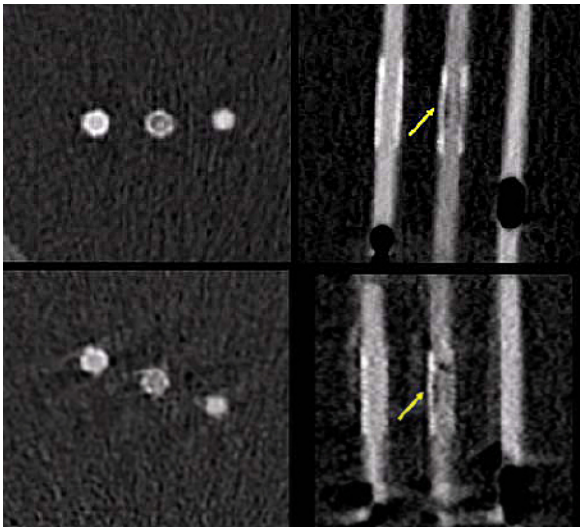


Figure 21: DSCT (top) compared with a 64-slice single-source CT system (bottom) at 90 bpm with a gantry rotation speed of 0.33 s. The single-source CT images clearly show blurring artifacts and the implanted stent hardly visible (arrow) [Flohr et al. 2006].

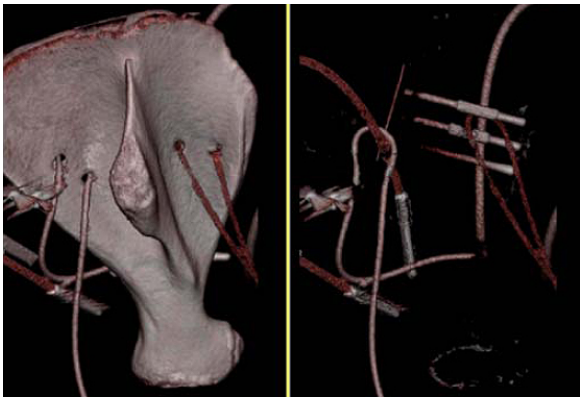


Figure 22: This comparison illustrates the dual-energy separation mode. Tubes filled with contrast agent were wrapped arround a bone in a piece of pork (left). In the resulting image (right) the bone was successfully removed even in critical anatomical situations where the tubes pass through the bone or are adjacent to it. [Flohr et al. 2006].

Dose

In general, the application of two separated detectors doubles the applied dose. Several strategies allow a significant dose reduction thus, the use of two detectors emitting ionized radiation does not necessarily induce a higher ionization dose in comparison to single detector systems. Single-source multi-slice CT systems require a slower pitch[1] to provide anatomic images without interpolation artifacts after the multi-segment reconstruction process. Thus, the slower pitch induces a higher patient dose over time. DSCT is able to operate heart rate independent and therefore allows a higher pitch which reduces the radiation dose. Other strategies apply ECG-pulsing protocols to decrease the applied current with respect to the heart beat ratio. In cardiac CT it is also possible to apply filter to the radiation beam which concentrate the radiation in the center of the scanned object, i.e. the heart. This approach in fact limits the peripheral image quality but decreases the total radiation dose. As a consequence, for ECG-gated coronary CT angiography DSCT doses are at least equal or even lower than that of multi-detector row CT depending on the patients heart rate [Stolzmann et al. 2008].

State of the Art

In November 2008 the latest generation of DSCT scanner was introduced at the 94th Scientific Assembly of the Radiological Society of North America (RSNA). It provides temporal resolution of 75 ms or 43 cm/s which does patients no longer require to hold breath during cardiological examinations (see Figure 1). This makes CT more applicable for examinations involving elderly as well es emergency patients. The improved speed can be lead back to the increased gantry rotation speed of 0.28 s and allows high quality 4D imaging (3D as a function of time). At the same time, it reduces the radiation dose for a spiral heart scan to less than 1 mSv. Former DSCT architectures at least required about 8 msV in comparable examinations. The low radiation rate is achieved by selectively reducing the dose when radiation is exposed to dose-sensitive areas like the female breast. This is done by switching the x-ray tubes off if these sensitive regions may be directly exposed to the radiation. Furthermore irrelevant prespiral and postspiral radiation is blocked by the use of dynamic diaphragms. The new architecture will be commercially available in the first quarter of 2009 [Siemens 2008].

Future

The most reasonable application of dual-source CT may be found in the characterization of calcium (e.g. renal stones, calcified plaques in vessels) as stated before. Another application may also allow tissue characterization where it might be possible to, e.g., detect tumors in the liver. The application of dual-energy CT in clinical diagnosis promises new image standards but all these possibilities require more research to determine the relevance in clinical context.

4.2 Functional Magnetic Resonance Imaging, fMRI

fMRI is a relatively young enhancement of classical MRI. Basically, it provides a map of activated brain regions while the patient is exposed a certain stimulus. The generated map is comparable to a PET image and allows the establish a relationship between the stimulus and the associated active brain region. Furthermore, this relationship is not only quantitative but also qualitative quantifiable which means that the amount of brain reaction can also be measured. In the majority of the examinations the patient stimulus is arranged in a visual or tactile way. So in fact, fMRI measures the induced local brain activity.

Principles

The desire to measure brain activity has occupied scientists for a long period of time. Michael Faraday used to study the magnetic characteristics of anhydrous blood. In 1936 these characteristics were lead back to hemoglobin which turns diamagnetic when it is bound to oxygen molecules, oxyhemoglobin, and paramagnetic without bound oxygen molecules, deoxyhemoglobin. Deoxyhemoglobin induces local magnetic field inhomogeneities which affect the T_2^* values[2]. fMRI images are therefore considered to be T_2^*-weighted to achieve a maximum of contrast. This effect occurs during changes in neuronal activity which generate a local increase in the amount of blood oxygen in these areas. In 1990 Ogawa et al. were able to use deoxyhaemoglobin as an endogenous contrast agent and detected these changes with the use of MRI. The so called blood oxygenation level dependent (BOLD) contrast can be perceived as an endogenous very sensitive MRI marker of neuronal activity [Dolan 2008; Raichle 1998].

In practice the BOLD contrast is generated by continuously blocks of sensory stimulation of about 30 s. These blocks are interrupted by phases without any stimulation to acquire images without any BOLD influence. After several repetitions the resting images are subtracted from the images influenced by the stimulation. The remaining areas represent the reduction in deoxyheamoglobin concentration which can also be perceived as the stimulated brain areas [Howseman and Bowtell 1999]. Figure 23 illustrates an example of a successfully applied fMRI scan.

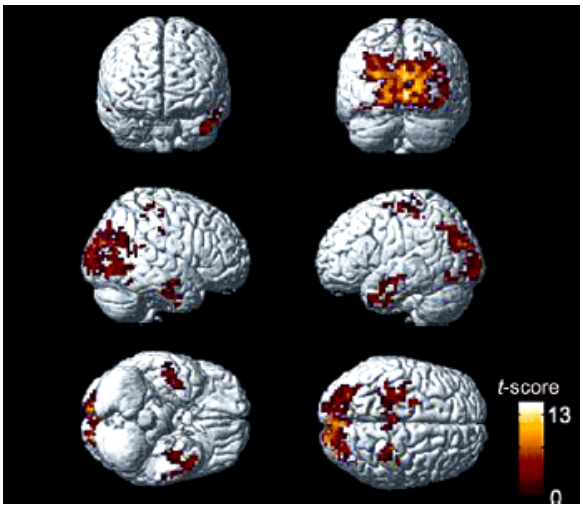


Figure 23: Illustrates the neural network with spontaneous activity in the primary visual areas. [Wang et al. 2007].

fMRI primarily was used to study brain function in the fields of vision, motor, language, memory, emotion or pain. Later great success in the fields of stroke, presurgical planning, epilepsy and several psychiatric disorders like schizophrenia. Before the introduction of fMRI, PET was used to detect cognitive processes and image brain activity. In fact fMRI turned out to be the preferred methodology due to its non-invasiveness, the absence of the potential hazards associated with radioactive tracers and its better spatial, less than 3 mm, and temporal resolution; less than 5

[1] Table translation speed (mm) with respect to the gantry rotation speed (rpm)

[2] T_2^* in contrast to T_2, considers disruptive factors which accelerate the signal decay.

s for the whole human brain [Howseman and Bowtell 1999].

Limitations

An immanent problem of fMRI imaging are the macroscopic field inhomogeneities found in several regions of the brain as well as in tissue, air and bone interfaces. These inhomogeneities operate over several voxels in the image and cover inhomogeneities induced by the BOLD effect. This leads to signal drop-out or even complete image distortion. Other potential limitations is the necessity of patient-side co-operation concerning the stimulation phases as well as the avoidance of patient-movement. Providing adequate patient stimulation requires additional effort. Especially visual stimulation requires certain equipment to operate in the strong magnetic field. Scanning rooms providing these modality have to be modified and requires additional investment. Nonetheless, fMRI offers a big advantage in comparison to PET. It does not make use of ionizing radiation. This allows repeated measurements, facilitating studies over time (4D) [Howseman and Bowtell 1999].

Future

This new tool was used to answer the question of how distributed brain regions interact while performing a psychological task especially how they interact after the manipulation i.e. monitor some kind of learning process. Currently two conceptual trends seem to emerge withing neuronal imaging. The first is a normative and descriptive approach which is based on classical, experimental manipulation and data analysis. This paradigm is used in the majority of all examinations. The other emerging approach is based on computational neuroscience as well as some kind of engineering and uses to answer questions like, how the human brain works. In general, these and other new approaches not only try to answer the question of where several signals and activities occur, they furthermore try to answer how these activities emerge and interact. Current investigations, e.g., focus on the a way of rebuilding brain function with mechanical exercises of the right hand or try to visualize vowels of people suffering from the locked-in syndrome. From todays point of view functional neuroimaging has a lot more to offer and requires continuous research concerning the technology itself as well as neuroscience and psychology. Its high potential to provide more sophisticated characterizations of processes in psychiatric disorders assures the increasing importance in the future. Apart from that, no comparable technology offering the same advantages may evolve in the near future. So fMRI will be the first choice concerning functional brain imaging [Dolan 2008].

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