Chapter 9

Radiation used for diagnostic purposes

In this chapter we shall discuss the use of radiation of different kind for medical imaging. This include ordinary x-ray film, the use of contrast media, fluorescent screens, image intensifiers, CT and the use of digital technology to all x-ray systems. In the case of x-rays the source is on the outside of the patient and the detector is on the other side – unless in the case of backscattered x-rays.

We also intend to look in more detail into the use of radioactive isotopes for diagnostic purposes. When isotopes are used, it is always the γ-radiation that gives the information. Furthermore, the isotopes are inside the body – and it is the γ-photons coming out that yield the information. Two types of information are obtained; a). Information about where the isotopes are localized, b). Whether the distribution of activity deviates from normal in an organ or part of the body. We shall give the development of nuclear medicine including the PET-technique.

Both x-rays and isotopes will give a radiation dose to the patient. The doses are rather small, – and should not be of any concern – unless the LNT hypothesis and collective doses are used.

In order to complete the diagnostic field we shall mention a couple of other methods such as magnetic resonance (MR or MRI) and ultrasound. In the case of MR electromagnetic radiation is used in combination with a strong magnetic field. The electromagnetic radiation is within the radio frequency field and can not ionize.
Ultrasound is sound waves with a frequency above 20 kHz.
History of x-ray pictures

The first x-ray picture was taken three days before Christmas 1895 when C. W. Roentgen brought his wife into his laboratory, and they emerged with a photograph of the bones in her hand and of the ring on her finger (the picture is shown below).

Roentgen presented the news on the 28th of December 1895 and the discovery was spread rapidly around the world. About a month later, 23 January 1896, he gave a lecture on the new rays to the Physical Medical Society of Würzburg. During the meeting Roentgen took an X-ray photograph of the hand of the anatomist A. von Kölliker, who was in the audience (see picture below). After this had been done, von Kölliker proposed that the new rays should be called “Roentgen’s rays”, and this suggestion was approved with great enthusiasm by the audience. In Norway and some other countries we use that name.

The development from this first photo was rapid both with regard to technology and use. We shall give a short history of the development that resulted in sharper and much better pictures.

In an ordinary x-ray photo the object is placed between the x-ray source and the detector (for example film). The picture is based on the x-rays that penetrate the object and hit the detector – and yields the electron density in the object.

Here we present three pictures of a hand. The two of them are the two first and famous pictures of Mrs. Roentgen (left), von Kölleker (middle). The first one is taken 22. December 1895 and the second one 23 January 1896. You clearly see the improvements. The last one is observed using a digital filter to enhance the details and reduce the noise.
Nikola Tesla and his pictures – shadowgraphs

In the years before 1900 a number of other physicists worked with equipment similar to that of Roentgen. In particular we would like to mention the multigenius Nikola Tesla. He discovered what he called “shadowgraphs” – which in fact was x-ray pictures. The famous one of a foot and shoe is shown here.

Nikola Tesla was born in Croatia and emigrated to USA in 1884. He is frequently cited as one of the most important contributors to the birth of commercial electricity and is known for his many revolutionary developments in the field of electromagnetism in the late 19th and early 20th centuries. We can mention that he designed the first hydroelectric power plant in Niagara Falls in 1895.

Nikola Tesla invented his own vacuum tube which had only one electrode. Electrons were emitted and accelerated by the electrical field in his “Tesla coil”. When the electrons hit the glass walls, x-rays were produced. Tesla managed to obtain images of the human body with this radiation – the shadowgraphs.

He also sent some of his images to Roentgen shortly after Roentgen published his discovery. Tesla gave Roentgen full credit for the finding and never attempted to proclaim priority. Roentgen, on the other hand, congratulated Tesla for his sophisticated images.

In the magazine “Electrical Review” for 1896 some X-ray observations by Tesla were published. He described some clinical benefits of x-rays – for example; determination of foreign body position and detection of lung diseases. He noted that denser bodies were more opaque to the rays. Tesla even discovered reflected x-rays which recently has been used (see later).

Nikola Tesla has been honoured by calling the SI unit for magnetic field (also known as “magnetic flux density) for “tesla” (abbreviated T). We shall meet this within the field of MR.

Nikola Tesla (1856 – 1943)

Nikola Tesla's famous picture.
Some of the highlights for x-ray diagnostic

We shall first mention some of the developments in chronological order.

1900

The use of chest x-ray made possible the early detection of tuberculosis. Furthermore, during the next 50 years x-ray pictures and fluoroscopy played an important role in the treatment of tuberculosis. In the period before streptomycin (1947) the only treatment was pneumothorax – an attempt to let the lung rest by accumulation of air in the pleural cavity – and the lung more or less collapsed. The air was absorbed within a couple of weeks and new air was filled in. In order to control this treatment fluoroscopy was used. The patient was x-rayed both before and after a filling. The treatment usually lasted for 2 – 3 years and the doses could be quite large. We can note that no dosimetry was carried out at the time – and the doses now quoted are very much speculations (see page 210).

1906 – 1912

X-ray contrast medium was introduced. The idea was to introduce elements that could absorb efficiently the x-rays and thus enhance the contrast. An x-ray picture yields the electron density of the exposed object. The main absorption mechanism is the photoelectric effect – which varies considerably with the atomic number (approximately as $Z^4$). In a complex mixture of elements like that found in the organs of a patient, the degree of attenuation varies with the average of the atomic number of all the atoms involved. If two organs have similar densities and similar average atomic numbers, it is not possible to distinguish them on a radiograph, because no natural contrast exists. This situation commonly occurs in diagnostic radiography. For example, it is not possible to identify blood vessels within an organ, or to demonstrate the internal structure of the kidney, without artificially altering the electron density and absorption. Consequently, contrast compounds were introduced.

Different iodine (iodine has atomic number 53) compounds have been used as well as BaSO$_4$ (barium has atomic number 56). Up to about 1950 Thorotrast (ThO$_2$) was used. Thorium has atomic number 90. Since Thorium is radioactive, ThO$_2$ was forbidden. In the period from 1931 until it was stopped 2 – 10 million patients worldwide have been treated with Thorotrast.

The first image using contrast was of the renal system (kidneys) in 1906. In 1910 barium sulfate was introduced as contrast agent for gastrointestinal diagnosis. In 1924 the first imaging of the gallbladder, bile duct and blood vessels took place.

1913

The single most important event in the progress of radiology was the invention made by William Coolidge in 1913 when he introduced the Coolidge x-ray tube.

This tube was superior to other tubes at the time because of; 1) its high vacuum and 2) a heated filament as the source for electrons.

The result was a more brilliant x-ray source.
1929
Cardiac catheterization was first performed by Werner Forssmann on himself. He was able to show that a narrow catheter could be advanced from a vein in the arm into the right atrium of the heart, a distance of almost two-thirds of a meter. Obviously, this constituted a remarkable advance – and could be visualized by contrast compounds. W. Forssmann was awarded the Nobel Prize for Physiology or Medicine in 1956.

Werner Forssmann
(1904 – 1979)

1955
The x-ray image intensifier was developed. It allowed the pick up and display of the x-ray movie using a TV camera and monitor. By the 1960’s, the fluorescent system was largely replaced by the image intensifier/TV combination. This opened the way for angiography which allowed the routine imaging of blood vessels and the heart.

1970
X-ray mammography finds widespread application in imaging the breasts. We shall return to this.

1972
Computed Tomography (CT) scanning was invented by Godfrey Hounsfield and Allan Cormack. In connection to this “break-through” in medical imaging we have to mention the forerunner of the technique called “planigraphy”.

In 1948 Marius Kolsrud at the University of Oslo presented a master thesis with the title;

*Røntgen-skikt-avbildning. Eksperimentelle og teoretiske undersøkelser.* Translated this is; “*X-ray tomography. Experimental and theoretical studies*”.

Kolsrud made equipment that made it possible to take x-ray pictures of a single plane in the object. The X-ray source and the film moved in opposite directions during the exposure. Consequently, structures in the focal plane appear sharper, while structures in other planes appear blurred. It is thus possible to select different focal planes which contain the structures of interest. Kolsrud made experiments with a sphere and a piece of barbed wire. This method was used for chest x-ray pictures in connection with tuberculosis for a number of years. Since a large number of pictures was necessary in order to scan through the lung, the total doses to the patients were rather large – larger than a CT scan.

Godfrey Hounsfield
(1919 – 2004)

Allan Cormack
(1924 – 1998)

Nobel prize in 1979

Marius Kolsrud
1919 – 2007
Prof. in theoretical physics at UiO
1976
Coronary angioplasty was introduced by surgeon Andreas Gruentzig at the University Hospital, Zurich, Switzerland. This technique uses x-ray fluoroscopy to guide the compression of plaques and minimize the dangerous constriction of the heart vessels.

1978
The start of digital radiography. The signal from the x-ray system is converted to a digital picture which can then be enhanced for clearer diagnosis and stored digitally for future review.

1984
Three-dimensional image processing using digital computers and CT or MR data, three dimensional images of bones and organs were first made.

The physical basis for an x-ray picture

The x-ray picture is a shadow picture of the part of the body that is between the x-ray tube and the film. Only the x-ray photons that penetrate the object and reach the film can give a signal or blackening of the film. We do not see the photons that are absorbed or scattered.

To see into the body we must have “something” that can penetrate the body – come out again – and give information. The figure below is an attempt to illustrate the main points for making an x-ray photo.
1. The x-ray source

On page 8 we described the basic principles for the formation of x-rays – or rather bremsstrahlung. When electrons with high energy smash into the “anticathode” – a tiny part of the energy is transformed into radiation. This implies that the x-ray photons formed, may have a number of different energies – in fact a whole spectrum is formed (the “Initial spectrum” in the figure below).

X-rays are usually described by their maximum energy, which is determined by the voltage between the electrodes. In x-ray diagnostic the maximum is in the range from 20 kV up to about 120 kV. The x-ray spectrum can be illustrated by the following figure.

![Initial spectrum](image)

Here is given some details of the radiation from an ordinary x-ray tube. The amount or fraction of the electron energy that is transformed into x-rays from the anode surface is only about a percent of the electron energy. This implies that most of the energy is dissipated as heat, and consequently the anode must be cooled. The probability for transferring the electron energy into radiation is proportional to $Z \cdot E^2$.

Here $Z$ is the atomic number of the anode and $E$ is the electron energy. The result is a spectrum – in the figure called “initial spectrum”.

In order to use the radiation it must get out of the X-ray tube. The window absorbs some radiation – mainly in the low energy part. The spectrum changes like that illustrated above – from the “initial spectrum” into the ”final spectrum”.

The absorption by the window depends on the composition of the window. For example, if low energy x-rays are needed, a beryllium window is used since this window has much lower density than a glass window.

The spectrum also contains characteristic x-rays from dislodging of K- and L-shell electrons from the target. This will not be further discussed when the x-rays are used for diagnostic purposes, but is important for x-ray crystallography.

The maximum energy can be changed according to the purpose. It is in the range from 20 – 120 keV.
A lot of technological improvements have been made with regard to the x-ray source – probably the most important by William Coolidge – which resulted in stronger (more brilliant) and stable sources.

We are not going to describe all the technological developments with regard to the control of the exposure time – and equipment for the different types of examinations. The maximum energy used, depends upon the type of examination. Thus, in the case of mammography the maximum energy is low (below 30 kV) whereas in skeletal and abdominal examinations the energy is larger, between 60 to 85 kV.

Another aspect is that the radiation dose in an examination should be kept as low as possible. Several developments – using intensifying screens have reduced the exposure (see below).

2. Absorption and scattering in the body

The x-ray picture is based on the radiation that penetrates the body and hit the detector (film). The details in the picture are due to those photons that are absorbed or scattered in the body. Since both the absorption and the scattering depend upon the electrons in the object (body) we can say that;

**“the x-ray picture is a shadow-picture of the electron density in the body.”**

On page 30 we discussed the mechanisms for the absorption of x- and γ-rays in matter. Since x-ray diagnostic uses low energy radiation only the “photoelectric effect” and the “Compton scattering” contribute to the absorption.

The photoelectric effect occur with bound electrons, whereas the Compton process occur with free or loosely bound electrons. Both processes vary with the radiation energy and the atomic number of the absorber.

**Photoelectric effect – variation with photon energy**

For the energy region in question – and for atoms like those found in tissue the photoelectric cross-section varies with $E^{-3}$. Thus, it is a rapid decrease with the energy in this region.

**Photoelectric effect – variation with atomic number**

The variation with the atomic number is quite complicated. For an energy above the absorption edge, the cross-section per atom varies as $Z^4$ (i.e. the cross-section per electron varies as $Z^3$). It can be noted that the K-shell energy for all atoms in the body (C, N, O, P, and Ca) is below 4 keV. Consequently, for the diagnostic purposes the absorption varies with $Z^4$ per atom.

**Compton effect – variation with photon energy**

For the energy range used for diagnostic purposes the Compton effect is rather constant – and decreases slightly with the energy. Compton scattering is most important for energies above 60 keV. For lower energies the photoelectric effect is by far the most important.

**Compton effect – variation with atomic number**

The Compton process increases with the electron density of the absorber. This implies that it is almost independent of the atomic number $Z$. 

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Conclusion

1. The absorption processes are the photoelectric effect and the Compton scattering.

2. Photoelectric effect depends strongly on the atomic number \((Z^4)\). This implies that the absorption in bones (with an effective atomic number of about 13) is much larger than that for tissue (with effective atomic number of about 7.5). For energies below about 30 keV the absorption is mainly by the photoelectric effect. In this energy region it is possible to see the small variations in electron density in normal and pathological tissue like that found in a breast.

It can be noted that due to the strong dependence of the photoelectric effect with the atomic number we find the key to the use of contrast compounds. Thus, compounds containing iodine \((Z = 53)\) or barium \((Z = 56)\) will absorb the low energy x-rays very efficiently. In angiography the arteries becomes visible when iodine compounds are used.

3. The Compton process varies slightly with the energy in this range – and is the dominating absorption process for energies above 50 keV.

4. In addition to the absorption processes some photons will be scattered, i.e. elastic scattering. In Rayleigh scattering the photon interacts with a bound electron and is scattered without loss of energy. The probability of this scattering process is proportional to \(Z^2/E\). In Thomson scattering the photon interacts with a free electron and the radiation is scattered in all directions. The two elastic scattering processes accounts for less than 10 % of the interactions in the diagnostic energy range.

The purpose for discussing these details about absorption and scattering is to give some background knowledge of the physics of the x-ray picture.

It is differential attenuation of photons in the body that produces the contrast which is responsible for the information. The attenuation of the radiation in the body depends upon; the density, the atomic number and the radiation quality. The absorption of x-rays decreases as the energy \((kV)\) increases.

In mammography one are interested in visualizing small differences in soft tissue – and we use low energy x-rays \((26 – 28 kV)\) to enhance the tissue details.

In the case of chest pictures the peak energy must be larger because the absorbing body is very much larger – and some radiation must penetrate the body and reach the detector.

It is the transmitted photons that reach the detector that are responsible for the picture.
3. The detector system

A number of different detectors (film, ionization chambers, luminescence and semiconductors) have been used since the beginning of x-ray diagnostic.

For a very long time film was used. The x-ray picture was created when the radiation was absorbed in the film emulsion consisting of silver halides (AgBr as well as AgCl and AgI). The emulsion was suspended on gelatin as the supporting medium.

In the usual morning meeting the doctors were often gathered in front of the “light box” to discuss the patients (see illustration).

The absorption in the thin film emulsion is very small. Consequently, in order to increase the sensitivity, intensifying screens were introduced. The screen is usually a phosphor scintillator that converts the x-ray photons to visible light that in turn expose the film. The introduction of intensifying screens was made already in 1896 by Thomas Alva Edison. He introduced the calcium tungstate screens which were dominating up to the 1970-ties. This material has now largely been replaced by rare-earth metal based screens. We do not intend to go through the technical details with regard to intensifying screens – nor to the many technological details within x-ray diagnostic. However, a few points should be mentioned.

Conventional radiography uses energies between 50 and 80 kV. In order to ensure that the photoelectric effect is dominant lower energies are used. Energies lower than 30 kV are used for mammography – which is very effective for seeing details in soft tissue. However, this energy range is only useful for tissue thicknesses of a few centimeter.

Mammography

In mammography the goal is to see the contrast between different density of soft tissue, fat and blood vessels without use of contrast media. The x-ray energy is between 25 and 30 kV in order to ensure that the photoelectric effect is dominant. This also result in absorption of radiation and an increase of the patient dose.

A typical situation is given in the illustration to the right.
Examples

It is sometimes very convincing to see a mammogram like that shown to the right. It is also amazing that we can see details like this in soft tissue without using contrast media to enhance the difference in electron density.

The next example is shown below. Here you see two mammograms of the same normal breast. The large differences are due to the technique used.

To the left is a modern digital picture whereas the other is a film-based mammography.

Implants

It is obvious, even for the layman, that the presence of breast implants does interfere and makes it more difficult to obtain good information with mammography.

The presence of implants affects the way mammograms are done, since additional views are needed during routine screening mammography to visualize all of the breast tissue. Implants also makes it more difficult to interpret in some cases. The lesson to learn from this is that implants could be an impediment to cancer detection.

We can conclude that you have to be well trained to give a good description.
Fluoroscopy

With the ordinary x-ray film it was impossible to see any movements. This became possible by using phosphor screens. The transmitted x-rays caused scintillations that was viewed directly. In order to reduce the dose to the doctors the fluorescent screen was backed by lead glass. The whole examination was performed in a dark room and with adapted eyes. The images were faint and low in contrast. This examination (in Norway known as “gjennomlysning”) was widely used in the treatment of lung tuberculosis and pneumothorax treatment.

The screens were outdated and “image intensifiers” were introduced (see figure). The x-rays were converted to light by using phosphors (CsI:Na) – and again to photoelectrons. They were accelerated and focused on a smaller fluorescent screen which in turn is coupled to a recorder system; for example a video camera or a film camera.

If the technique is coupled with the use of contrast media it is possible to follow the contrast when it is flowing through the blood vessels. It is thus possible to perform some type of treatment while viewing it.

Shoe-fitting fluoroscopy

Today it is almost unbelievable that x-rays was used to find the right pair of shoes. However, during the period 1930 – 1950 an x-ray fluoroscope like the one shown was used.

The system consisted of a vertical wooden cabinet with an opening near the bottom into which the feet were placed. When you looked through one of the three viewing ports on the top of the cabinet (e.g., one for the child being fitted, one for the child’s parent, and the third for the shoe salesman or saleswoman), you would see a fluorescent image of the bones of the feet and the outline of the shoes.
The machines generally used a 50 kV x-ray tube in the bottom of the cabinet. When you put your feet in the opening, you were standing on top of the x-ray tube. The only shielding was a one mm thick aluminum filter.

Measurements made in recent years indicate that the doses to the feet were in the range 0.07 – 0.14 Gy for a 20 second exposure. Doses to the pelvis ranged from 0.03 to 0.17 mGy.

**Digital imaging**

The technique with digital x-rays was introduced in the 1970’s. Analog to digital converters and computers were adapted to conventional fluoroscopic image intensifier systems. Angiographic procedures for looking at the blood vessels in the brain, kidneys, arms and legs, and the blood vessels of the heart all have benefited tremendously from the adaptation of digital technology.

It is reasonable to assume that all of the film systems will be replaced by digital x-ray detectors. The benefits of digital technology can be summarized as follows:

1. The x-ray dose can often be reduced to achieve the same high quality picture.
2. The digital x-ray images can be enhanced and manipulated with computers.
3. The digital images can be sent via network to other computers and hospitals.
4. The digital images can be archived onto compact disks and thus save storage space.
5. The digital images can be retrieved from an archive at any point in the future for reference.

**Examples**

We have already shown a couple of examples with digital technique.

On page 173 the picture of a hand is shown together with some old film-based pictures.

On page 182 you can see an example with mammography.

To the right is an example with dental x-rays. The image can be enlarged, which makes it easier to detect the problems.
CT – Computer tomography

On page 176 we mentioned that the forerunner to CT was called planigraphy – or linear tomography. Let us therefore look into this technique – which played a role in the treatment of tuberculosis in the 1950s and 1960s.

The technique was proposed early in the 1900s by the Italian radiologist Alessandro Vallebona. In Norway professor Marius Kolsrud constructed an equipment in 1948.

The idea is based on the simple principle of moving synchronously and in opposite directions the X-ray tube and the film. Consequently, structures in the focal plane appear sharper, while structures in other planes appear blurred. The lung was shown – slice by slice – and could yield information about the position and extent of the TB infection. In order to cover a lung about 20 x-ray pictures were required.

The next step was introduced by G. N. Hounsfield and A. M. Cormack in 1972. The CT or CAT scanner was successful since much smaller contrast differences can be observed. They replaced the x-ray film by a group of small detectors. The signals from the detectors were stored and analyzed mathematically in a computer. The computer rapidly reconstruct an image of the examined cross-section.

Scintillation detectors combined with photomultipliers or photo diodes have been used. We would also like to mention the gas detector. This is similar to the Geiger detector. In order to increase the sensitivity the gas detector is filled with pressurized xenon. Xenon is the heavy noble gas with atomic number 54. Consequently, the photoelectric effect is very efficient. An array of several hundred xenon detectors constitute the detection system. Since the detector yield analog voltage pulses they have to be digitized by an ADC converter.

This illustration, taken from Scientific American gives some of the main properties of a CT-scanner. The technique has been rapidly developed since the first scanner presented by Hounsfield in 1972. Both the x-ray tubes, the detector technique as well as the computer presentations with filters etc. have given amazing results.
A CT-scanner you can meet in the hospital

The above pictures – and a lot more – can be found on Internet. The examples show the power of this technique.
You can go to Internet and see a number of excellent pictures; for example see:

http://www.montclairradiology.com/
Backscattered X-rays – Compton scattering

On page 9 we presented a couple of cartoons from more than 100 years ago. These cartoons – given again below – represented a misunderstanding at that time and caused a big smile. The misunderstanding was that some people had the idea that it was possible to take x-ray pictures with reflected x-rays – which means that both the x-ray tube and the film was in the photographer’s box (like an ordinary camera). As a result of this some people feared that you could use an x-ray camera to watch people when they changed into swimming suits inside the small cabins on the beach. A London tailor company advertised therefore that they could make x-ray proof underclothing for ladies.

Today with the use of Compton backscattering technique all this is a reality – and in fact in use several places for security. Let us therefore give a short glimpse of the technique.

The old cartoons that caused a “big smile” 100 years ago. Today we know that it is possible to use reflected x-rays and see through cloths.

Compton scattering is the key

The Compton process is outlined by the figure. It is a reaction between the x-ray photon and a free or loosely bound electron. The scattered photon has a reduced energy. Since both the energy and momentum are conserved it can easily be shown that the energy of the scattered photon, $E_s$, can be given as a function of the scattering angle $\theta$ by the following expression;

$$E_s = \frac{E_\gamma}{1 + \frac{E_\gamma}{m_e c^2} (1 - \cos \theta)}$$
For backscattered photons the angle is approximately 180 degrees. Thus the energy of the backscattered photons is reduced by approximately 30%. The number of backscattered photons are given by the Klein and Nishina formula.

With the knowledge of backscattered Compton radiation, equipment have been developed for observing objects. The x-ray tube and the detector system is now on the same side of the object. The picture is formed by a pencil-shaped beam of x-rays that is sweeping the object. The energy used is approximately 100 keV (100 – 200 kV tubes) which ensures that the Compton process is dominating.

The resolution is (so far) not as good as for ordinary x-rays, but you can easily see objects with an atomic number different from that for tissue. The technique is worked out for security purposes on airports and other places. It is possible to use the technique to see the contents of a closed container through the container walls.

Below is a few examples taken from Internet.

On Internet you can find a number of backscattered x-ray pictures. The technique is excellent for observing hidden objects on people or the cargo in containers – objects that is not possible to observe with the usual metal detectors.

To the left is a famous picture given in combination with control at airports.

Below is shown an example of control of the cargo in a big truck.
The use of radioactive isotopes
Nuclear medicine

Radioactive isotopes have been used for more than 100 years in medicine – both for radiation therapy (will be discussed in the next chapter) and for diagnostic purposes. About 90% of the medical use of isotopes are for diagnosis. The most common radioisotope used in diagnosis is technetium-99, but a large number of other isotopes are in use. The thyroid, bones, heart, liver and many other organs can be easily imaged, and disorders in their function revealed.

Diagnosis

For diagnostic purposes we use radioactive tracers which emit gamma rays from within the body. The isotopes are generally short-lived and linked to chemical compounds which permit specific physiological processes to be studied. They can be given by injection, inhalation or orally.

For a number of years the $\gamma$-radiation was observed using a so-called gamma camera. The camera builds up an image from the points from which radiation is emitted. The image can be enhanced by a computer and abnormal conditions can be observed.

A more recent development is Positron Emission Tomography (PET) which is a more precise and sophisticated technique. It is based on positron-emitting nuclides – usually made in a cyclotron. When this nuclide decays, it emits a positron, which promptly combines with a nearby electron resulting in the simultaneous emission of two $\gamma$-photons in opposite directions. The detection gives a very precise indication of their origin. With the isotope F-18 as the tracer, it has proven to be the most accurate noninvasive method of detecting and evaluating most cancers. The reason for this is that F-18 can be added to glucose – and the tumors have an increased rate of glucose metabolism compared to benign cells. PET is also used in cardiac and brain imaging.

Isotopes for diagnosis

Let us point out a couple of important requirements for the use of radioactive isotopes:

1. Only $\gamma$-radiation is used for diagnostic purposes. For other purposes i.e. in tracer work, isotopes emitting $\beta$-particles can readily be used.

2. The isotopes should have a short half-life for safety reasons and handling. Short in this context is up to a few days.

Due to the requirement of a short half-life mainly or solely artificially made isotopes comes into question. This implies that the nuclear medicine started when equipment like the cyclotron and neutron sources like the reactor become available in the 1930s and 1940s.
Some of the highlights in the history of nuclear medicine

We shall first mention some of the developments in chronological order.

1924
This year can be considered as the start point for using radioisotopes as tracers and for biological studies. Georg de Hevesy and coworkers used Pb-210 (one of the isotopes in the Uranium-radium-series) and studied the absorption and elimination of lead, bismuth and thallium salts by animal organisms.
After the start of making radioisotopes in the 1930s O. Chievitz and Georg de Hevesy administered phosphate labeled with P–32 to rats and demonstrated the renewal of the mineral constituents of bone.
George de Hevesy was awarded the Nobel prize in chemistry for his pioneering work with radioactive tracers.

1930s in Berkeley
The University of California in Berkeley has played a significant role in the start and growth of nuclear medicine. In the front of the work carried out in Berkeley are the two Lawrence brothers (Ernest and John) and Glen Seaborg. The Lawrence brothers are of Norwegian heritage and Seaborg is coming from Sweden.

1936
John H. Lawrence, the brother of Ernest, made the first clinical therapeutic application of an artificial radionuclide when he used phosphorus-32 to treat leukemia. Also Joseph Gilbert Hamilton and Robert Spencer Stone administered sodium-24 to a leukemia patient.

1937
John Livingood, Fred Fairbrother and Glenn Seaborg discovered Fe-59 with a half-life of 45 days.

1938
Glenn Seaborg and coworkers discovered I-131 (half-life 8 days) and Co-60 (half-life 5.26 years).
Furthermore, this year Emilio Segre and Seaborg discovered Tc-99m the metastable (excited) Tc-99 isotope. The metastable isotope has a half-life of 6 hours and emit a γ-photon with energy 140 keV.
Tc–99m is an important isotope and is used in approximately 85 percent of diagnostic imaging procedures in nuclear medicine.
Berkeley – the birthplace of nuclear medicine

The key to nuclear medicine is the formation of suitable isotopes.

The development of nuclear accelerators – in particular the cyclotron – made it possible to enter the field of nuclear medicine.

Two scientists are of utmost importance for the construction of the first accelerators; Rolf Widerøe and Ernest Lawrence.

The development of the cyclotron and the beginning of nuclear medicine is closely connected to California and the Berkeley University. It all started when the oldest of the Lawrence brothers (Ernest) came to Berkeley in 1929. He became aware of the ideas included in the doctor degree of Rolf Widerøe. He used the ideas and invented the cyclotron.

In a linear accelerator charged particles are accelerated in tubes forming a straight line. Lawrence arranged this by letting the particles go in larger and larger circles within a box – kept in place by a magnetic field. The first cyclotron from 1931 was only 5 inches in diameter. However it could accelerate protons up to 80 keV. The development from this point was rapid and new isotopes were produced.

Ernest Lawrence is of Norwegian heritage (grandparents were from Norway). He was the father of the first cyclotrons constructed in Berkeley. He got the Nobel prize in 1939. The Radiation Laboratory in Berkeley are named after him. Furthermore, Lawrence Hall of Science above the UC campus is an exciting public science center with exciting hands-on experiences for learners of all ages.

Rolf Widerøe is Norwegian, born in Oslo. He was engaged in the construction of an accelerator, and published these ideas already in 1923 (21 years old). His name is connected to important accelerators for radiation therapy – such as the linear accelerator, the cyclotron and the betatron. He was behind the first high energy radiation source in Norway – the betatron from 1953 at The Radiumhospital.
A picture of the campus with its landmarks “Sather Gate” and “Sather Tower”. They are named after Peter Sather (born on Nedre Sæter farm in S-Odal, Norway). He was a banker and a trustee to CAL. The above picture is a model of a cyclotron – placed near the entrance of “Lawrence Hall of Science” in Berkeley.

The Berkeley University developed a number of accelerators and became the place where new isotopes were produced. The leading scientist in the production of new isotopes and elements was Glenn Seaborg.

**Glenn Seaborg**

(1912 – 1999)

Glenn Seaborg was a Swedish American (his mother was from Sweden). Seaborg was the principal or co-discoverer of ten elements: plutonium, americium, curium, berkelium, californium, einsteinium, fermium, mendelevium, nobelium and element 106, which was named seaborgium in his honor while he was still living. He also developed more than 100 atomic isotopes, like I-131 and Tc-99m which are important isotopes for medicine.

Seaborg was awarded the Nobel prize for Chemistry in 1951 together with another Berkeley scientist Edwin McMillan.
John Lawrence joined his brother Ernest in 1936, and started Donner Laboratory. He used for the first time a radioactive isotope in the treatment of a human disease (leukemia). The two brothers also treated successfully their mother. John Lawrence became known as the father of nuclear medicine and Donner laboratory is considered the birthplace of this field.

Hal Anger (also a Donner man) invented in 1958 the gamma-camera – also called Anger camera. He was awarded the first Cassen Prize in 1994 for his invention.

1958
Hal Anger (above) invented the “scintillation camera,” an imaging device that made it possible to conduct dynamic studies. This is also called “Anger camera” and consisted of a large flat scintillation crystal and a number of photomultipliers.

1959
Rosalyn Yalow and Solomon Berson developed radioimmunassay (RIA). They used I-131 labeled insulin to measure the reaction between an antigen and antibody. This technique is used widely to study other hormones in the body. Solomon Berson died in 1972. In 1977, Rosalyn Yalow was awarded the Nobel Prize in Medicine for their work.

1962
David Kuhl introduced emission tomography in 1962, leading to the first “computer tomography” which ultimately led to the development of the X-ray CT scanning as well as PET. He is recognized internationally as the “father” of PET scanning.
Some of the isotopes used in nuclear medicine

The use of radioactive isotopes in research and medicine can be divided in three groups.

1. Isotopes used as tracers
A radioactive isotope attached to an important molecule can tell where it is. The radiation emitted yield the information. Isotopes emitting γ-rays are easily observed, but also pure β-emitters like H–3 (tritium) and C–14 can be used. Thus, Melvin Calvin used C–14 to the exploration of photosynthetic carbon dioxide reduction. He was awarded the Nobel prize in chemistry for 1961 for this work.

The Hershey – Chase experiment
A very well known experiment with radioactive tracers was the Hershey–Chase experiment from 1952. Alfred Hershey and Martha Chase used the isotopes P–32 (β-emitter with half-life 14 days) and S–35 (β-emitter with half-life 87 days). The first one was built into DNA in the virus T2 phage, whereas S–35 was built into the protein part of the virus. They studied how the virus infected E. Coli bacteria and could conclude that the genetic material which infects the bacteria is DNA.
Numerous experiments within biochemistry and biology use radioactive isotopes as tracers.

2. Isotopes in radiation therapy
In radiation therapy the purpose is to irradiate cancer cells to death and let the normal cells survive. Radium (Ra–226) was used from the beginning, both for teletherapy and as implants in brachytherapy. Radium was replaced by Co–60 and Ir–192 (see next chapter).

In later years new isotopes like At–211 (half-life 7.2 hours) have been used. Attached to compounds (monoclonal antibodies) the isotope can be transported to the the cancer cells. The isotope emits α-particles (energy 6.8 MeV) which have a short range and a high LET-value. We shall return to this in the next chapter.

3. Isotopes for diagnostic purposes
Several isotopes emitting γ-rays can, and have been used for diagnostic purposes. For example, I–131 will be accumulated in the thyroid and can via a gamma camera give information about sicknesses in the thyroid.

We have pointed out before that the isotope most often used for medical information is Tc–99m. Let us therefore give some details about the isotope – its formation and use.
Mo–99
In the figure below we have outlined how to make the isotope as well as the physical properties of it. We start with Mo–99, which is a fission product. The decay scheme for Mo–99 contains something new. Thus, after the β-particle emission the newly formed technetium isotope is in a so-called “meta-stable” state. This is designed by a “m” – like Tc–99m. The metastable state implies that the subsequent γ-emission is delayed. If we could isolate this metastable isotope it would be perfect for medical use, since the isotope would only emit a γ-photon with no contamination from β-particles.

Tc–99m
Decay scheme for Mo-99

Mo–99 67 h
 β-particle

Tc–99m 6 h
 140 keV

Tc–99 213 000 years

The decay of Mo–99 results in a metastable nucleus – denoted Tc–99m. The half-life is 6 hours.

Tc-99m is an excellent isotope for use in medical diagnostics. By emitting a γ-photon it ends up in Tc–99 which is radioactive with a half-life of 213 000 years.

Mo-99 is bound to aluminum-oxide. The half-life is 67 hours. The compound is rinsed with physiological saline, and the Tc-99m that has been formed follows the water – it is like “milking”.

The next step is to hook on this isotope to compounds that can bring it to particular places in the body that can be studied. More than 30 compounds based on Tc-99m have been made for imaging and functional studies of the brain, myocardium, thyroid, lungs, liver, gallbladder, kidneys, skeleton, blood and tumors.

Tc-99m emits γ-radiation with an energy of 140 keV, which readily escapes the body and is easily measurable. The distribution of the radioactivity in the body can be measured.

From a physicists point of view it is probably the technique developed to observe the distribution of radioactivity that is the most interesting – whereas from a medical point of view it is the diagnostic power that is the most interesting.

Ben Cassen and Hal Anger

The technique with the radioactive isotopes in medical diagnostics started in the 1950s when Benedict Cassen invented the rectilinear scanner and in 1958 with the γ-camera (or Anger camera). It was now possible to obtain a picture over the area of interest.

It can be mentioned that the “Society of Nuclear Medicine” every second year since 1994 give out a prize in honor of Benedict Cassen (The Benedict Cassen prize) for outstanding achievements in nuclear medicine.

The illustration to the right demonstrates the technique introduced by Benedict Cassen. He assembled the first automated scanning system that was comprised of a motor driven scintillation detector coupled to a relay printer. The scanner was used to image the thyroid glands with I-131. After the initial studies, it was an extensive use of the scanning system for thyroid imaging during the early 1950s. Cassen’s development of the rectilinear scanner was a defining event in the evolution of clinical nuclear medicine.

In 1956, Kuhl and his colleagues developed a photographic attachment for the Cassen scanner that improved its sensitivity and resolution. With the development of organ-specific radio pharmaceuticals, a commercial model of this system was widely used during the late 1950s until the early 1970s to scan the major body organs. The decline of the rectilinear photoscanner began in 1973 with the advent of computed axial tomography.
**SPECT**

SPECT is short for Single Photon Emission Computed Tomography. As its name suggests (single photon emission), ordinary $\gamma$-ray emission is the source for the information.

The camera or detector rotates around the patient, and the detector will observe the tracer distribution for a variety of angles. After all these angles have been observed, it is possible to reconstruct a three-dimensional view of the isotope distribution within the body. A computer is used to apply a tomographic reconstruction algorithm to the multiple projections, yielding a 3-D dataset. This dataset may then be manipulated to show thin slices along any chosen axis of the body, similar to those obtained from other tomographic techniques, such as CT, PET and MR (or MRI).

**An example with Tc–99m**

In the example shown (to the right), Tc-99m was added to methylene-diphosphonate, which is absorbed by the bone-forming cells (the osteoblasts). The picture makes it possible to study diseases of the skeleton, such as bone cancer.

The doses to both the patient and the medical personnel are small. The strength of the source used for an examination is around a few hundred million Bq (MBq). In the present example 700 MBq was used.

*Courtesy of Arne Skretting, Norwegian Radium Hospital*
PET – Positron Emission Tomography

The development of positron imaging covered decades and included contributions from different scientists. The technique is based on artificially induced isotopes that emits positrons. In order to understand this we refer to chapter 2 where we discussed the different ways an unstable nucleus could attain a more stable state. We mentioned that in the ordinary $\beta$-decay, a neutron was transformed into a proton and an electron, which was emitted. This is a favorable reaction since the neutron mass is larger than the proton mass. The opposite reaction where a proton is transformed into a neutron is however, a more difficult process. We can however, attain this goal via two different routes: 1) electron capture and 2) positron emission.

For all natural isotopes, electron capture is the usual process – because the energy between the parent and daughter is less than $2m_e c^2$ ($m_e$ is the electron mass). However, for a number of artificially induced isotopes positron emission takes place.

The fate of the emitted positron is; after being slowed down, it will meet an electron, and then either annihilate directly, or form a short-lived “positronium atom”.

The final process is an annihilation where the mass of the two particles is transformed into $\gamma$-ray photons. Mainly two photons with equal energy, 511 keV, are formed. A very important point is that the photons fly off in opposite directions (see the illustration to the right). This annihilation process represents the basic physical principle for PET. We observe the two photons by detectors 180 degrees apart (coincidence measurements). We know from this observation that the annihilation process has taken place somewhere along the line shown in the illustration.

**PET:** We can determine the position of the radioactivity by coincidence measurements of photons with energy 511 keV. One coincidence observation yield a line whereas two or more observations in other directions give a point (or a small area) where the radioactivity has its origin. If we in addition have CT or MR measurements for body reference we can determine where in the body we find the radioactivity.

**PET can give us:**

1. Information on how tissue and organs functions on both the molecular and cell level.
2. PET is important to observe cancer – and in particular give information about metastases.
3. With PET it is possible to follow the effect of a treatment.
4. It is also possible to study changes in the brain that follows Alzheimer disease and epilepsy.
In PET we get information on metabolic changes on the cell level. Consequently, PET can to a larger extent observe cancer on an early level – when the changes are on the cellular level. For CT and MR malign changes can only be observed when the structure of the organs and tissue is changed.

**Positron and positronium**

In connection to positron emission – we have to mention the “atom” positronium. When the positron has lost its kinetic energy and meet an electron, it is a possibility that they will exist for a short moment almost like an atom (see illustration).

It can be mentioned that the first theoretical work on positronium was carried out by Aadne Ore in 1949. Ore was connected to the group of biophysics at the University of Oslo – in fact he was the one that started this group.

Positronium can be either orto-positronium (parallel spins) or para-positronium (opposite spin). Para-positronium has a lifetime of about 0.1 nanosecond, whereas ortho-positronium has a lifetime of about 140 nanoseconds. Para-positronium decays in two photons, both with energy 511 keV whereas orto-positronium decays in three photons (combined energy is 1.022 MeV).

Ore published the work in two articles; “Annihilation of Positrons in Gases” and “Ortho-Parapositronium conversion”.

Ore described the foundation of PET in the following way:

*In Norwegian:* “Atomet er en slags submikroskopisk dobbelt-stjerne, hvor de to partnere, et elektron og et positron, hvirvler om hverandre i en kortvarig dødsdans, som ender med materiell tilintengjørelse og et bluss av elektromagnetisk stråling.”

*In English:* “The atom is a submicroscopic double star. The two partners, the electron and the positron, is in a brief dance of death, which ends with material annihilation and a flare of electromagnetic radiation”

**The flare is the origin of PET**
Only artificial isotopes are positron emitters. Some possible isotopes are given in the table:

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Halflife</th>
</tr>
</thead>
<tbody>
<tr>
<td>C – 11</td>
<td>20.3 minutes</td>
</tr>
<tr>
<td>N – 13</td>
<td>10 minutes</td>
</tr>
<tr>
<td>O – 15</td>
<td>2.03 minutes</td>
</tr>
<tr>
<td>F – 18</td>
<td>109.8 minutes</td>
</tr>
</tbody>
</table>

The different isotopes have short half-lives which implies that the production and use has to take place quite close together. The isotopes must be hooked on special chemicals that can transport the positron emitter to places of interest.

C – 11 connected to acetate has been proposed as a tracer for prostate tumor cells. Also C – 11 connected to choline can be used.
F – 18 is so far the most used isotope in PET. Connected to deoxy-glucose (see illustration of the FDG-molecule) it is used to identify tumors by their increased rates of glucose metabolism compared to benign cells.

We have to mention that we also have isotopes with somewhat longer half-life. Thus, Zr-89 has a half-life of 3.27 days and I-124 has a half-life of 4.18 days.

The use of F-18

F-18 can be made in a cyclotron by irradiating O-18 enriched water with protons. The reaction can be written:

\[ ^{18}_{8}O + p = ^{18}_{9}F + n \]

After the production of F-18 we have to work fast since the half-life is only a couple of hours. If this isotope is used for detection of cancer it is hooked on to glucose (see illustration above of the FDG-molecule). We know that the active cancer cells need more sugar than other cells in the body. Therefore, we hook on F-18 to glucose – and the sugar molecule will transport F-18 to the active cells – the cancer cells.

An example

The patient is given F-18 (as FDG) in the blood. We wait for an hour before we start the measurement to let the FDG-molecules to find the cancer cells. When F-18 disintegrates it emit a positron with maximum energy 635 keV. The positron is slowed down within about 1 mm before annihilation. Photons with energy 511 keV are measured in coincidence by detectors 180 degrees from each other. No other radiation influence these measurements. The position for this radioactivity with regard to the body is determined by CT.

In the example below we have encircled a region which in CT was suspicious. In the right picture we see the results of PET. The PET activity is colored red. The suspicious region consists of rather active cells – cancer cells.
History

The first experiments to exploit positron-electron annihilation goes back to 1953 when Gordon Brownell at MIT constructs the first detector device. The first PET experiments were performed in 1974 by Michael E. Phelps, Edward Hoffman, and Michel M. Ter-Pogossian.

Michael E. Phelps  
(1939)

Edward Hoffman  
(1942 – 2004)

Michel M. Ter-Pogossian  
(1925 – 1996)

Alfred P. Wolf, Joanna S. Fowler and Tatsuo Ido developed F–18 fluorodeoxyglucose (FDG) – which is an important probe for glucose metabolism.

Brookhaven National Laboratory has been in the front for the development of PET. The leading scientists have been Al Wolf and Joanna Fowler.

Alfred Wolf  
(1923 – 1998)

Joanna Fowler
An example: PET used to study the effect of radiation

In the example below the isotope F–18 is bound to deoxyglucose (FDG) and used to localize tumors in a patient. Two different tumors were localized; a sarcoma in the right scapula (shoulder blade) and a lymphoma in the right axillary lymph. PET with F-18 shows both cancers – and CT is used to clearly localize where they are.

The cancers were treated by radiation and the result is seen on the series of pictures – the sarcoma to the left and the lymphoma to the right.

You see that the large sarcoma in the right scapula is radioresistant – independent of the radiation dose given. The lymphoma in the right axillary lymph is however radiosensitive and is eliminated after a dose of 40 Gy.

The images were taken before the start of radiotherapy (0 Gy), after 8 Gy (early treatment) and after 40 Gy (late treatment).

Courtesy of Eirik Malinen.
Magnetic resonance – MR (MRI)

Today we have other diagnostic methods in addition to, or often in combination with x-rays and radioactive isotopes. The methods in question are magnetic resonance and ultrasound. For these methods no ionizing radiation is involved and no absorbed or scattered photons are making the pictures.

What is MR?
The very first MR-picture on a human being was made 3. July 1977 by Raymond Damadian and co-workers in USA (left). The picture obtained was of poor quality and it took hours to obtain. However, in spite of this it was a sensation and a start of a technique that today is very important within medical diagnostics.

The field of magnetic resonance started in the 1940s. In 1944 the Russian physicist Yevgeny Zavoisky discovered electron paramagnetic resonance (ESR) and in 1946 Felix Bloch and Edward M. Purcell carried out the first nuclear spin experiments (NMR).

The pioneers of magnetic resonance
Magnetic resonance was developed in the 1940s – both electron spin resonance (ESR) and nuclear magnetic resonance (NMR). The Nobel prize in physics for 1952 was awarded to Bloch and Purcell for nuclear magnetic resonance.

The physics of magnetic resonance

In this book we are interested in the physical background for the different medical techniques rather than to the techniques themselves. Knowledge about x-rays and radioactive nuclides was important for the methods discussed so far. In the case of magnetic resonance (both ESR and NMR) the method is based on units with a magnetic moment. In the case of ESR it implies atoms or molecules with an unpaired electron (we have mentioned ESR in connection to dosimetry on page 80 – 83).

In the case of NMR the technique is based on atomic nuclei with spin – like protons (H-1), deuterons (H-2) , C-13, N-14, F-19, Na-23 and P-31. The general MR technique is based on protons in the water molecule.

Let us try to explain the background for magnetic resonance. Units with spin like the electron or proton have magnetic moments. In the case of the electron it can be written as:

\[
\vec{\mu}_e = g \beta \vec{S}
\]

Here \( \beta \) is the Bohr-magneton, \( S \) is the electron spin and “g“ is the spectroscopic splitting factor – which for free electrons is 2.0023. A similar expression is obtained for protons. This implies that we have a number of small magnets. If these small magnets are placed in a magnetic field \( B \), they will attain an energy which depends on the spin state. Thus, for electrons it is given as:

\[
E(m_s) = g \beta m_s B
\]

where \( m_s \) is the spin quantum number for the electron, which can have two values; +1/2 and -1/2. A figure would help in order to understand the resonance phenomenon.
The figure shows that all the small magnets have equal energy as long as the external magnetic field is zero. However, in a magnetic field the magnets will be oriented “with” or “against” the magnetic field. The two states have different energies – and the energy difference increases with the field B as shown. It is possible to induce transitions between the energy states by electromagnetic radiation. The condition for inducing transitions between the energy states is that the energy of the radiation (h\nu) is equal to the energy difference. A transition from the lower to the higher state yields an absorption. (A transition the other way yields an emission – i.e. the LASER condition).

The condition for an absorption can be written:

\[ h\nu = g_b B \quad \text{for electrons} \quad \text{and} \quad h\nu = g_N B_N \quad \text{for protons} \]

The figure indicates that we can have resonance at any given frequency as long as the magnetic field follows the resonance condition. We see that the resonance condition is the same for electrons and protons. However, it is a big difference since \( g_b \) for electrons is much larger than \( g_N B_N \) for protons. Thus, a magnetic field of 1 tesla (10 000 gauss) yield resonance for electrons at a frequency of 28 GHz (microwaves with wavelength 1 cm), whereas for protons the frequency is 42.6 MHz (in the radiofrequency region).

The electromagnetic radiation yields transitions in both directions with the same probability. Thus, if the populations of the two levels is equal, the net result would be nil – neither absorption, nor emission. The population of the states follows a Boltzmann distribution with the lowest level most populated. The difference increases with increasing magnetic field. This implies that we try to increase the magnetic field and for NMR it is normal to use fields of the order 1.5 tesla (and even up to 7 tesla).

In order to have a constant absorption, the difference in population must be kept. Two relaxation processes transfer spins to the lower state. Both processes are connected to changes in the proton spin. One process is “spin-lattice” relaxation and the other is “spin-spin” relaxation. The rates of the two processes are measured by the relaxation times \( T_1 \) and \( T_2 \).

We have seen above that the x-ray picture is a shadow of the electron density. In the case of MR the picture depends on the proton density as well as on the two relaxation times \( T_1 \) and \( T_2 \). It appears that these relaxation times changes when going from normal to pathological tissue – and this can be used in diagnostics.

**How is a picture made?**

A part of the body is placed in a strong magnetic field. The resonance condition gives the connection between field and frequency. It is therefore easy to understand that it is possible to fulfill the resonance condition for a small volume element. However, it is a long way from a volume element to a picture – and the question is: How is it possible to go from a point (a tiny volume element) to construct a whole picture?

The first solution of this came when Paul Lautubur tried out his ideas in the early 1970s. He introduced magnetic field gradients and by analysis of the characteristics of the emitted radio waves, he was able to determine their origin. This made it possible to build up images of structures. In 1973
he demonstrated how it was possible to see the difference between tubes filled with water from an environment of heavy water. These very first experiments showed that one could use a set of simple linear gradients, oriented in three dimensions and slowly build up a picture. Peter Mansfield showed how the radio signals could be mathematically analyzed, which made it possible to develop a useful imaging technique.

One of the major practical difficulties encountered with the early MRI, was the time it took to acquire the data. Line-scanning, for example, took typically 10–20 min. The breakthrough came in 1977 when Mansfield introduced the echo-planar imaging. This snap-shot technique meant that in principle complete two-dimensional images could be achieved in extremely short times like 20 – 50 ms.

A modern MR scanner has coils in three directions (see illustration below). They modify the magnetic field at very particular points and work in conjunction with the RF pulses to produce the picture. They are rapidly turned on and off (which causes that banging noise), and the gradient magnets allow the scanner to image the body in slices. The transverse (or axial, or x-y) planes slice you from top to bottom; the coronal (x-z) plane slice you lengthwise from front to back; and the sagittal (y-z) planes slice you lengthwise from side to side. However, the x, y and z gradients can be used in combination to generate image slices that are in any direction, which is one of the great strengths of MR as a diagnostic tool.

An illustration of the field gradient coils. They usually give off a banging noise.

(Illustration taken from Internett)
The Nobel prize in Physiology or Medicine for 2003 was given to the field of MR. The winners were Paul Lauterbur and Peter Mansfield for their contribution.

Lauterbur introduced magnetic field gradients, which made it possible to obtain a picture. Mansfield showed how the radio signals can be mathematically analyzed, and thus made the image possible. He also discovered how fast imaging could be possible by developing the MR protocol called echo-planar imaging. Echo-planar imaging allows T$_2$-weighted images to be collected many times faster than previously possible. It also has made functional magnetic resonance imaging (fMRI) feasible.

In connection with this Nobel prize it is quite easy to understand that Raymond Damadian who obtained the very first MR-picture was disappointed and expressed this in several newspapers. Damadian and coworkers also discovered in 1971 that some malignant tissue, obtained from implanted tumors removed from rats, had longer NMR relaxation times than many normal tissues.

The technique has been further developed in several ways. In 1991 Richard Ernst was awarded the Nobel prize in chemistry for the introduction of Fourier transform and pulse techniques in NMR spectroscopy, thereby improving the sensitivity of the technique tenfold or even hundredfold. Furthermore, functional MR have been available for some years.

In order to attain better resolution MR machines with larger magnetic field have been available. There are different MR machines that use field strengths of 3 and 4 tesla, – and research machines with 9.4 tesla and even 15 tesla.
MR pictures and use in medicine

Most MR scanners in the hospitals are using 1.5 tesla magnets. The electromagnets consist of a solenoid cooled down to about 4 K by liquid helium. At such temperatures superconduction is attained and it is possible to send large currents through the solenoid and thus get the large magnetic fields required.

MR can be used to study all different organs in the body. For parts of the body with bones it is difficult to use x-rays to study the tissue around – because the bones absorb the x-rays much more than the tissue. In these cases MR is very valuable. It has been used to study details in the brain and spine. Brain sicknesses results in changes in the water content which can be visualized in MR. Thus, only a difference in water content of 1 percent can be detected. Multiple Sclerosis (MS) can be studied and followed by MR. The sickness give infections to brain and spine and with MR it is possible to localize this, and observe the effect of a treatment.

Contrast compounds
It is also possible to introduce contrast media in MR. We can mention the element gadolinium (Gd). This is a Lanthanide element (atomic number 64) that is paramagnetic and has the effect that it strongly decrease the T1 relaxation times of the tissues.
Also several vanadyl compounds are used as contrast agents for MR. These compounds are taken up by, and accumulate in, glycolytically active cells, such as rapidly dividing tumor cells. The resulting MR images have excellent resolution and contrast. These compounds also bind to albumin in the blood, allowing for the assessment of blood volume at tumor sites prior to cellular uptake (similar to imaging with gadolinium), a valuable diagnostic indicator and tool for treatment response in its surroundings.
Diagnostic ultrasound

Ultrasound is sound waves with a frequency above the limit for human hearing – about 20 kHz. For medical use the frequency is in the region from 2 – 40 MHz.

Formation of ultrasound

In 1880 Pierre Curie and his brother Jacques discovered that certain crystals (the so-called piezoelectric crystals) can produce a pulse of mechanical energy (sound pulse) by electrically exciting the crystal. Furthermore, the crystals can produce a pulse of electrical energy by mechanically exciting the crystal. This ultrasound physics principle is called the piezoelectric effect (pressure electricity). Crystalline materials with piezoelectric properties are quartz crystals, piezoelectric ceramics such as barium titanate or lead zirconate titanate.

A device that converts one form of energy into another is called a “transducer” – and they can be used for production and detection of diagnostic ultrasound.

We are not going into more details about the equipment here, but it is possible to use ultrasound technique to produce pictures of the inside of the body. Since ultrasound images are captured in real-time, they can show the structure and movement of the body’s internal organs, as well as blood flowing through the blood vessels. Ultrasound imaging is a noninvasive medical test that helps physicians diagnose and treat medical conditions.

A short history

The origin of the technology goes back to the Curies, who first discovered the piezoelectric effect. Attempts to use ultrasound for medical purposes started in the 1940s when they used a continuous ultrasonic emitter to obtain images from a patient’s brain. During the war it was a rapid development within ultrasound. They generated pulsed echoes and developed Sonar and Radar. A spin-off from Sonar is ultrasound medical imaging.

The use of Ultrasonics in the field of medicine had nonetheless started initially with it’s applications in therapy rather than diagnosis, utilising it’s heating and disruptive effects on animal tissues. An excellent review of the history of ultrasound can be found in the following address:

http://www.ob-ultrasound.net/history1.html

A short description of the technique

In the clinical use of ultrasound a transmitter produce a short pulse of electrical oscillations (2 – 10 MHz). The transducer converts this to a pulse of mechanical vibrations. The transducer is coupled to the body by a gel and the pulse of ultrasound goes into the soft tissue (speed of about 1500 m per second). The transducer will then sense the reflected, weaker pulses of ultrasound and transform them back into electrical signals. These echoes from different organs are amplified and processed by the receiver and sent to the computer, which keeps track of the return times and amplitudes.
A new pulse is produced and sent off in a slightly different direction (pulse repetition frequency is in the range 2 – 10 kHz). The data from all these pulses are treated by the computer and yield a CT-like image in “real time”. You can see how arms and legs of a fetus move, or see the heart valve open and close.

A lot of technology is involved in the different parts of the ultrasound technique. However, it is not the purpose of this book to go into details in this field.

Let us shortly mention that the transducer, that transmits and receives the ultrasound energy into and from the body is a key component. It is built up of hundreds of transducers in order to take a high resolution real-time scan. The many transducers create a wavefront and the angle of the wavefront can be altered by firing the transducers one after another. By changing the angle of the wavefront, a three-dimensional image can be built up over a large area.

**Doppler ultrasound**

The velocity of the blood can be measured by the Doppler effect – i.e. the change in ultrasound frequency. If the ultrasound frequency is 5 MHz and the blood velocity is 20 cm s\(^{-1}\), the change in frequency is 1274 Hz if we look along the bloodvessel (the frequency shift changes with \(\cos \phi\) to the viewing angle) – and can easily be measured.

**Side effects**

Current evidence indicates that diagnostic ultrasound is safe even when used to visualize the embryo or fetus. In this connection we would like to mention that research in the beginning of 1980s showed that use of clinical ultrasound equipment could result in water radicals (H. and OH.). Furthermore, in work with cells in culture exposed to ultrasound resulted in damage (similar to those known from ionizing radiation).

This implies that if you believe in the LNT-hypothesis where even the smallest radiation dose is deleterious we have a problem and a possible side effect.

May be we should not overdue obstetric ultrasound.
Radiation doses in medicine

Each time you are examined by radiation you attain a small radiation dose. The doses from medical use add to the background dose.

In the figure to the right is given the world average use of radiation for medical imaging. It has been a rapid increase since the 1940s. New techniques and methods have been added with the result that the total dose (the collective dose) has increased.

Since the 1950s it has been a goal to keep the doses for each examination as low as possible – in order to prevent any deleterious effects of radiation.

It may be of interest to attain some information about the radiation exposure from diagnostic medical examinations. For this purpose UNSCEAR have collected a lot of information from all different sources around the world. The Committee concluded that medical applications are the largest man-made source of radiation exposure for the world’s population. The doses are in general small and are justified by the benefits of accurate diagnosis of possible disease conditions.

The 2000 UNSCEAR report conclude that the world average effective annual dose per capita from medical use is 0.4 mGy (or mSv). The variation from one country to another is large, approximately from 0.05 to 1.3 mGy.

For Norway the annual dose level is now assumed to be 1.1 mGy.

How to observe annual doses?

The dose given in each type of examination has been observed and calculated. Thus, the absorbed dose to each organ or tissue of the body have been obtained. This implies that the effective doses to patients undergoing different types of medical diagnostic have been obtained. Multiplied with the number of examinations yield an effective collective dose in the LNT terminology. From this per capita annual doses can be obtained by averaging the collective doses over the entire population (including non-exposed individuals).

This procedure yield a world average of 0.4 mSv and for countries like Norway an annual dose per capita of 1.1 mSv.
Will this dose give deleterious effects?

There is no direct evidence that diagnostic use of radiation ever causing any harm to the public. It is evident that the dose to certain groups of patients may be relatively large, for example for a number of patients with tuberculosis where chest fluoroscopy was used through 2 – 5 years. Significant doses has also been the result after the use of thorotrast in the period 1930 – 1950.

However, the collective dose to the public (1.1 mSv to Norwegians) is only a figure that shows the standard of health care and can not be used to calculate deleterious effects. Some people like the most devoted supporter of the LNT-hypothesis would disagree with this view. According to this hypothesis it is possible to claim that about 250 fatal cancers per year would be the result for Norway with a population of 4.7 million. Do not believe it!

We mentioned two exceptions from the genral positive picture. The old use of Thorotrast and the use of fluoroscopy in combination the the pneumatorax treatment for tuberculosis. Let us explore this in some more detail.

Thorotrast

Thorotrast was widely used from 1930 – 1950. It is in the form of thorium dioxide colloid. Thorotrast is retained by the reticuloendothelial system, with a biological half-life of several hundred years, so that such patients suffer lifetime exposure to internal radiation. Some of the decay products, principally the radium isotopes Ra–228 and Ra–224, escape from the colloidal particles and deposit in the skeleton.

The doses involving α-particles may be rather large. The biological end-points include liver cancer and leukemia and it can be concluded that Thorotrast increased the carcinogenic risk.

Tuberculosis and chest fluoroscopy

In the period 1930 – 1960 a large number of patients with tuberculosis were treated by pneumathorax – air was filled in the cavity of the chest and the lung was forced to collapse. The aim of the treatment was to give the lung an opportunity to rest.

In order to control the air filling the patient was x-rayed both before and after the filling and fluoroscopy was the method. A treatment could last for a number of years and consequently the number of x-ray examinations could be up to 100 and more. This resulted in a rather large dose to the breasts.

A number of TB-patients have been followed up in order to observe deleterious effects such as breast cancer for women. The results are not easy to understand – see next page.
A Canadian study looked at breast cancer mortality rates for women who had fluoroscopic examinations for tuberculosis, between 1932 and 1952. The results are given in the figure below.

We have several comments with regard to this figure. First of all the dose determination is highly uncertain – can probably vary by a factor 2. Second, no information exists about the doses received in the time elapsed since the last examination – i.e. background variation.

Despite of these weak points, the data show a surprising decrease in cancer for those who received low doses (34 percent and 16 percent at the dose points of about 15 and 25 centi-Gray).

The picture shows a typical examination from about 1940. The lungs are examined both before and after air is filled. This is done in order to control the collapse of the lung – as shown in the illustration.