1 Introduction
The tomographic methods used in nuclear medicine are SPECT (described in chapter 2) and PET (chapter 3). Both SPECT and PET were introduced in the 1960's but it took quite long before they were established as part of clinical routine. In fact, while SPECT has been a standard tool in every nuclear medicine department for years, PET has not been available widely until the end of the 2010s. This has had mainly to do with the cost of PET cameras and limitations in the supply of radioisotopes suitable for PET.

2 Single Photon Emission Tomography (SPECT)
2.1 Introduction
Many gamma-cameras are able to perform Single Photon Emission Computed Tomography (SPECT, sometimes also called SPET). All it requires is that the camera can rotate around the patient or object of interest. With SPECT, it is possible to obtain tomographic images, i.e. “slices through the patient”.

Figure 1: Transversal slice through the brain acquired with SPECT. The image shows the distribution of $^{123}$I-FPCIT, a radioactively labelled substance that binds to Dopamine receptor sites. The basal ganglia have many of these sites and stand out clearly. Uptake of the tracer in the background is due to unspecific binding.

2.2 Projections
Imagine you let a gamma-camera rotate in small steps around a patient. Each two-dimensional image taken from a given angle would then correspond to the projection of photons emitted perpendicular to the detector. These projections are similar to those recorded with CT. However, a SPECT camera does not record the transmission
of X-rays, but the emission of photons from the object (a patient in medical imaging) into the direction of the camera (Figure 2).

![Series of 60 projection images (360° in 6° steps) acquired on a rotating gamma-camera. Each image is collected over 1 min and shows the count distribution of ⁹⁹mTc-labelled HMPAO in the head of a patient. HMPAO is a flow-tracer used for estimation of regional perfusion in the brain. Like in Figure 3, the s-axis is indicated by a dashed red line.](image)

For simplicity it is advantageous only to consider a single horizontal line in the projection images shown in Figure 2. With the projection reduced to a line the object is correspondingly reduced to a slice. The projection can be plotted as a profile as illustrated in Figure 3, middle panel.

The projection data of each slice along the axis of the gamma camera (i.e. the axis of rotation) is stored in an individual sinogram, where each row corresponds to one projection. Different rows represent different projection angles. A sinogram can be reconstructed into a tomogram (a slice), by using an algorithm called filtered back-projection (FBP). An animation illustrating the acquisition and reconstruction process can be downloaded from the web site.

Typical for the FBP algorithm are star-and streak artefacts as illustrated in Figure 4.

Gamma-cameras often employ more than one detector so that different projection angles are recorded simultaneously. A single detector thus only covers a part of a full circle.
Figure 3: Schematic illustration of a SPECT acquisition. The upper panel shows a single slice through the detector rotating around the chest of a patient. The detector records photons emitted along the direction of the black arrow. The projection data (number of recorded counts along the s-axis) at the current angle are shown in the middle panel. All measured projections over a 360° rotation (green arrow in upper panel) are collected in a sinogram (lower panel). Each horizontal line in the sinogram corresponds to a certain projection angle, \( \phi \). In the lower panel, the number of counts are coded in a greyscale “colour” table. The projection shown in the upper panels is marked by a thin blue line. Note, that the origin of the s-axis is the point closest to the axis of rotation.

Figure 4: Reconstructed object (left) and original object (right). Typical for the applied FBP algorithm are the “star” or “streak” artefacts, which also can be observed in the background.
2.3 The Filtered Back Projection in more detail
(This section can be left out without loss of continuity.)

Proving that the FBP indeed is the correct way to reconstruct the image slice from the projection data is somewhat more complicated than it may seem at first sight. Shortly, the sinogram represents a Radon transform of the object in the SPECT camera:

\[
P_{\phi}(s) = \iint_{\text{FOV}} \rho(x,y) \delta(x \cos \phi + y \sin \phi + s) dxdy
\]

where \(\rho(x,y)\) is the spatial distribution of the tracer in the field-of-view (FOV), limited by the distance between the rotational centre and the detector. \(P_{\phi}(s)\) is projection along angle \(\phi\) with \(s\) denoting the position along the detector surface. Thus, \(P_{\phi}\) represents a row in the sinogram, see also Figure 3.

The task is now to retrieve the original spatial distribution, \(\rho(x,y)\) of radioactivity in the object under investigation. Considering \(S_{\phi}(\omega)\), the one-dimensional Fourier transform of \(P_{\phi}(s)\) (\(\omega\) being the reciprocal of \(s\)) and rotating \(\rho(x,y)\) by \(\phi\), it can be shown that:

\[
\rho(x, y) = \int \int S_{\phi}(\omega) e^{j2\pi(ux + vy)} dudv
\]

where \(u, v, \omega, \text{ and } \phi\) are related by

\[
\begin{align*}
u &= \omega \cos \phi \\
v &= \omega \sin \phi
\end{align*}
\]

Equation (2) is the sum of backprojections along angle \(\phi\) of the Fourier-transformed data in the sinogram. A backprojection simply "distributes" evenly the result of a projection back onto the original projected space, simply reverting the projection process without "inventing" any information about the original distribution along the projection line.

Coming back to equation (2) it is important to note that the sinogram is described in a rectangular coordinate system. Transforming to a polar coordinate system yields:

\[
\rho(x, y) = \int \int S_{\phi}(\omega) |\omega| e^{-j2\pi(s \cos \phi + y \sin \phi)} d\omega d\phi
\]
To reconstruct the object, each row of the sinogram is Fourier-transformed \((S_\phi(\omega))\), multiplied by a "ramp" filter, \(|\omega|\), and subsequently back-projected. It should be noted that a discrete approximation to the FBP, the so-called Riemann sum, is used. In addition, the integration over \(\omega\) is in reality constrained by the physical dimensions of the detector. The integration over \(\phi\) is often done from 0 to \(2\pi\) to minimise attenuation effects (see chapter 2.4). This means that the acquisition needs to be done over 360°.

On the internet, many web-sites discuss various aspects of the FBP algorithm. One I have used a lot is http://www.sv.vt.edu/xray_ct/parallel/Parallel_CT.html

2.4 Attenuation correction

A problem in SPECT is that the emitted photons are attenuated by the patient before they are detected by the camera. This means that there is a bias towards the outer structures of the object as the signal from these structures is not attenuated as much as signal from the inner structures.

In general, the attenuation of a photon beam \(I\) after distance \(r\) in a medium with linear absorption coefficient \(\mu(r)\) can be described by:

\[
I(r) = I_0 e^{-\mu(r)r}
\]  

(5)

Note that \(\mu(r)\) can vary in space. Only for homogeneous materials, \(\mu\) is independent of position. This simple case with a uniform \(\mu(r)\) in a phantom surrounded by air (\(\mu = 0\)) is illustrated in Figure 5.

![Figure 5: Image of a plastic phantom filled with a \(^{99m}\text{Tc}/\text{water solution}. The distribution of \(^{99m}\text{Tc}\) is uniform, as is the linear attenuation coefficient \(\mu\). The effect of attenuation is seen in the image, and also illustrated as vertical and horizontal profile through the centre. The recorded signal from the inner part of the phantom is lower than that from the edges which seem enhanced. The walls of the phantom are thin and can be neglected here.](image-url)
When scanning some organs, especially the brain, a post-hoc approach for correcting attenuation is used: Each slice of the head is approximately described as an ellipse. The matter inside the ellipse is modelled assuming uniform attenuation with a fixed value for $\mu$, e.g. $0.10$/cm ($\mu_{\text{water}}=0.15$/cm). Then, each pixel $i$ inside the ellipse is multiplied by a factor $e^{\mu \Delta x_i}$ depending on its average distance $\Delta x_i$ from the surface of the ellipse, seen over all projection angles.

This is only a coarse approximation since $\mu$ differs markedly in bone, soft tissue and air (e.g. upper air ways and lungs), but it works remarkably well in tissue with relatively homogenous composition. The algorithm is often called Chang’s uniform attenuation correction, and is illustrated in Figure 6.

![Figure 6: Schematic presentation of Chang’s method: An attenuated image (left) is multiplied by a correction matrix (middle) to yield the attenuation-corrected image (right). Below each image, the profile through the centre point is plotted.](image)

Another, theoretically better method is obtaining a second set of images in the same geometric setting, where the attenuation coefficient in each voxel is measured. The classic approach is to use gamma-radiation from radioactive isotopes located in an external container (point or line source) as photon sources. The source is located such that the patient is in between source and detector, while obtaining data under a full $360^\circ$ rotation. The photons that are not attenuated are collected in the same way as the photons emitted from the radioactive tracers inside the patient. It is thus possible to measure the transmission and calculate an attenuation map. This map contains the value of $\mu$, in each position in the tomographic slice.

Depending on the manufacturer and model, the transmission scan is performed separately or simultaneously. In any case, the separation between emission and transmission photons is made on the basis of their energy. Emission counts are always present. (Remember that it often takes hours before a tracer is distributed. Therefore, it is not feasible to perform a transmission scan before administration of the tracer).
Modern scanners are often built together with a CT scanner and are then called hybrid systems. The CT part is either taken from a conventional CT scanner (thus useful for both attenuation correction and regular diagnostic CT imaging) or an X-ray tube/detector combination specifically designed for hybrid systems. The latter usually implies that it is possible to obtain data for attenuation correction with a relatively low radiation dose to the patient.

X-rays are polychromatic (50-150 KeV) while isotopes used in nuclear medicine are usually monochromatic (e.g. $^{99m}$Tc: 140 KeV) and this implies that the CT-data has to be converted to so-called $\mu$-maps (reflecting attenuation coefficients corresponding to the energy of the radioactive isotope) before being used for attenuation correction. Despite the similar energy range, the detector used for the emission radiation cannot be used for X-rays because of the enormous photon flux from an X-ray tube.

### 2.5 Scatter

Scattered radiation degrades SPECT images, just as it does planar images. There is no way to circumvent scatter, apart from removing unnecessary objects in the vicinity of the patient during acquisition. Scattered radiation has lost part of its original energy, thus it can be distinguished from unscattered radiation in terms of energy. The acceptance window settings (i.e. the “allowed energy interval”) reflect a compromise between reduction in scatter (unwanted photons) and reduction in sensitivity.

Scatter correction algorithms are important when dealing with more than one energy, e.g. in double-isotope investigations or when using radioactive transmission sources for attenuation correction. A discussion of these algorithms is also beyond the scope of this book.

Figure 7: Energy spectrum of a $^{133}$Ba transmission source in the presence of $^{99m}$Tc (emission). The green part of the spectrum is used for collecting “transmission photons” from Ba (356 keV±20%), whereas the red part (140 keV±10%) is used for “emission counts” from Tc. Additional windows can be used to estimate the contribution of scattered Ba-photons in the energy range of the Tc-window.
2.6 Advanced Reconstruction Methods

Correction for scatter and attenuation is best applied during the reconstruction, and not afterwards as a “post-hoc” method. However, as the correction for attenuation and scatter depends on the spatial distribution of the radioactive substances, the solutions are not separable, i.e. everything must be calculated at once. Therefore, iterative reconstruction methods like EM-ML and OS-EM are often used. A discussion of these methods is beyond the scope of this book.

2.7 Filtering

SPECT is very much constrained by the low signal-to-noise ratio. The Poisson statistics of the radioactive decay dominates the noise characteristics of the reconstructed data – and in fact, often the overall impression of the image. A property of the Poisson distribution is that the mean (expectation value) is equal to the variance, i.e. 100 counts in one pixel have a variance of 100 counts² and thus a standard deviation of 10 counts (10%) – plus the influence of all other noise sources.

Therefore, filtering of the data is essential in order to improve the signal-to-noise ratio. The idea with filtering is to remove high-frequency noise, assuming that the features that make up the image predominantly have low-frequency content. The most commonly used filter is a low-pass, Butterworth-filter. Its frequency response function is:

\[ H(f) = \frac{1}{1 + \left(\frac{f}{f_{\text{cutoff}}}\right)^N} \]  \hspace{1cm} (6)

where \( f_{\text{cutoff}} \) is the frequency where the magnitude of the transfer function has fallen to 50%. \( N \) is the order of the filter (i.e. the steepness of transition), see Figure 8. The filter parameters are very much dependent on the application and the organ of interest, but typical numbers are order=4 and cut-off=0.4.

Filtering can be done slice-by-slice or for the complete three-dimensional dataset. That means that the filter actually acts in two or three dimensions.
2.8 Corrections
SPECT requires very high quality gamma-cameras. The detection uniformity of each detector must be very high, the geometric centre of rotation well-defined and the projection direction of the collimators very precise. Otherwise systematic errors during angular sampling are introduced which result in various types of artefacts in the reconstructed images.

The typical spatial resolution of SPECT is just below 1 cm. However, this is very much dependent on the organ under investigation and the distance between the organ and the detector.

3 Positron Emission Tomography (PET)
The fundamental difference between Single Photon Emission Tomography and Positron Emission Tomography is that the former is based on detection of a single photon from a decay event whereas the latter detects two coinciding photons arising from an annihilation process after a positron decay.

A positron is the antimatter counterpart to an electron, having the same rest mass but opposite charge. Figure 9 illustrates the creation of a positron.
Figure 9: Simplified illustration of a positron decay. An excited nucleus removes energy by converting a proton (p⁺) into a neutron (n) and a positron (e⁺), also called β⁺-particle. Electrons (green) reside in their shells. Only relevant particles are mentioned here.

In biological tissue, a positron annihilates with an electron after travelling few millimetres, see Figure 10. Both particles are converted into energy in the form of two photons travelling along a line in opposite direction. The laws of conservation of mass and energy enforce this. This annihilation radiation can be detected with a PET camera. The energy of the photons is always 511 keV, corresponding to the rest mass of an electron (and positron).

Figure 10: Annihilation of an electron/positron pair into 2 photons

The detector system of a PET scanner consists of a few dozen detector rings with a total of several thousand individual crystals. (Each of these crystals can be regarded as a “mini-gamma-camera”.) The detection of a photon in a crystal starts an electronic coincidence circuit that tries to find a matching event on the opposite side of the detector ring with the chosen coincidence window, e.g. 10 ns, see Figure 11. In the case of no matching event, the primary event is discarded. If there is a matching event, the line-of-response (LOR) between the two crystals is recorded.

Strictly speaking, the annihilation photons are not necessarily emitted with an angle of exactly 180°. This is correct only in the centre-of-mass frame of reference of the electron-positron pair. In reality the difference is up to 0.5° which is negligible in this context.
As the reader may now have noticed by now, the term “positron emission tomography” is misleading: The detected particles are not emitted positrons but the annihilation photon pairs. Therefore, some people prefer to call PET for ART (“annihilation radiation tomography”).

In contrast to SPECT cameras, PET cameras do not employ collimators. The direction of the projection is determined by the coincidence logic. That is sometimes called “electronic collimation”. Note that while gamma cameras use NaI as detector material, PET cameras require other crystals with better stopping power. During the 1990s, BGO (bismuth germanate) was the standard crystal material for PET. During the last years, other detector materials like LSO (Luthetium-oxyorthosilicate) have become the material of choice. The great challenge is to develop detector materials that have high stopping power combined with high light output (counting statistics and efficiency), good energy resolution (reduction of scatter) and short decay time (short dead-time).

Modern PET cameras normally have a few dozen detector rings resulting in an axial field-of-view (FOV) of 15-20 cm. The radial FOV is usually about 50-60 cm. When coincidence events between different detector rings are recorded as well, the acquisition method is called “3D-PET”. Recording only coincidence events within one ring (as in Figure 11) is called “2D-PET”. In 2D-PET, collimating septa are inserted between the detector rings to reduce unwanted cross-talk. (The difference between these septa and collimators in gamma-cameras is that septa only separate slices.) 3D-PET is about five times more sensitive that 2D-PET, but more susceptible to scattered radiation and radiation sources outside the FOV. Modern PET cameras do not to support 2D-PET any more, and offer solutions for the drawbacks of 3D-PET. The typical spatial resolution of a PET camera is below 5 mm in all directions.
Ultimately, the resolution in PET is limited by the distance the positron travels away from the decaying nucleus to the point of annihilation.

The reconstruction of the collected coincidence data into an image is very similar to SPECT and CT. As the geometry of the detector ring is fixed, each detector-pair (i.e. each LOR) corresponds to a certain projection angle in SPECT. Instead of sampling all projection angles one by one, all angles are sampled in parallel at the same time. Detected coincidence events (i.e. a detector-pair has recorded coinciding photons) are distributed (“sorted”) into an array (the sinogram) according to the LOR of that event which again corresponds to a projection angle. This can be done on-line in real-time or off-line after the acquisition. The resulting sinogram is reconstructed as described above for SPECT cameras. Iterative reconstruction algorithms are available as well and widely used.

As in SPECT, the problem of photon attenuation can be solved by recording an additional transmission image. In “conventional” PET cameras this is achieved by rotating a radioactive line source (often $^{68}$Ge or $^{137}$Cs) around the patient and counting the photons transmitted through the patient and those detected close to the source. Modern hybrid PET/CT have replaced these systems and employ a CT image for estimation of photon attenuation. While CT yield much better images (virtually noise free), some scaling of the attenuation coefficients is required, as photon attenuation in tissue varies considerably between 120 keV (photon energy in CT) and 511 keV. The CT images can subsequently also used for image fusion, accurate anatomic localisation of PET findings and – if acquired with the correct parameters – for diagnosis.

Traditionally, PET systems were installed in research institutions with nearby facilities for isotope production. There were various demands on PET images, one of them being that PET should be a quantitative method, i.e. that the pixel data in PET could be calibrated to reflect radioactivity concentration in tissue. This requires accurate attenuation and scatter correction and both were possible even with limited computing power. Most important in this context is the fact that the main obstacle, attenuation correction, is separable from solving the problem of reconstruction of emission images. The two types of images can be calculated separately and independently. This is because the attenuation along a LOR does not depend on the location of the annihilation event. (This is easy to see – make a drawing and write down the probability for detecting both photons.) PET has been a quantitative method ever since meaning that pixel data in PET usually has units of Bq/ml.
The most widely used isotope for PET is $^{18}$F with a half-life of about 110 minutes – sufficiently long to allow production with a cyclotron, subsequent synthesis of labelled radiopharmaceuticals, and finally delivery to PET sites without cyclotron of their own. $^{18}$F is usually produced for the synthesis of $^{18}$F-FDG, a glucose analogue that allows for mapping glucose metabolism in patients. Major applications are diagnosis, staging, and treatment evaluation of cancer. Another $^{18}$F-labelled radiopharmaceutical is $^{18}$F-NaF, a bone-seeking agent used for detecting skeletal abnormalities. The uptake of $^{18}$F-NaF in bone reflects blood flow and bone remodelling (Fig. 12). The clinical use of $^{18}$F-NaF is expected to grow considerably over the next years.

![3D-rendering of a fused PET/CT dataset. $^{18}$F-NaF PET and CT were acquired in a single session on a combined PET/CT system less than one hour after tracer administration. Note the $^{18}$F-NaF uptake in the spine and hips compared to the low uptake in the skull and bones of the limbs. $^{18}$F-NaF is excreted through the bladder.](image)

4 **Suggestions for further reading**