Imaging properties of unconventional radionuclides in positron emission tomography

Lubberink, J.M.

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Imaging properties of unconventional radionuclides in Positron Emission Tomography

Mark Lubberink

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Abstract

Positron Emission Tomography (PET) is a medical imaging technique based on the principle of annihilation coincidence detection. An important property of PET is that the reconstructed image gives accurate spatial and quantitative information about the radioactivity distribution in the body. In clinical PET generally low energy pure positron emitters are used, such as $^{18}$F or $^{11}$C. The use of other radionuclides expands the range of possible PET investigations.

The goal of the work described in this thesis was to investigate the consequences of the use of $^{76}$Br, $^{83}$Sr and $^{52}$Fe on the imaging properties of PET. Besides the emission of high energy positrons these radionuclides also emit gamma radiation in their decay. Phantom studies were done to determine transaxial spatial resolution in different attenuation environments and to determine reconstructed scatter fraction in PET images, using these radionuclides. Results were compared to the imaging properties for $^{18}$F. $^{52}$Fe decays to $^{52}$Mn which also emits high energy positrons in its decay. A method is suggested to correct for the $^{52}$Mn fraction in PET images. The different detectors used in PET studies at Uppsala University PET Centre were cross-calibrated for the use of $^{76}$Br, $^{83}$Sr and $^{52}$Fe.

Transaxial spatial resolution ranged from 6.2 mm for $^{18}$F in 1 g/cm$^3$ material to 7.4 mm for $^{76}$Br in 1 g/cm$^3$ material. For both $^{18}$F and $^{83}$Sr spatial resolution improves for lower densities, whereas for $^{76}$Br and $^{52}$Fe/$^{52}$Mn spatial resolution worsens for lower densities. Reconstructed scatter fraction in the centre of the image was found to increase slightly for the use of these radionuclides. Conclusions are that the spatial resolution degrades little when using radionuclides emitting higher energy positrons and that quantification properties worsen for $^{76}$Br and $^{52}$Fe. Specific corrections may be applied for the use of $^{76}$Br, $^{83}$Sr or $^{52}$Fe in PET, and will have to be applied in 3D PET.
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1 Introduction

The discovery of X-rays by Wilhelm Röntgen in 1895 introduced radiation imaging methods in medical diagnostics. X-rays travel easily through the soft body tissue but are strongly attenuated by bone, so X-rays can produce detailed images of the skeleton and have proved to be invaluable in diagnostics leading to for example the resetting of broken bones. However, X-rays are not effective in differentiating between different types of soft body tissue and they produce a two dimensional image that gives no information on the depth of any revealed abnormalities inside the body.

A method to improve the X-ray image of a specific part of the body is to introduce a material with a high atomic number, such as barium or iodine, in that specific organ. Since the body contains a small amount of elements with high atomic number, the introduction of such a contrast medium results in a more detailed image.

The idea behind sectional imaging in X-ray computed tomography (CT) is to define a plane in the body and let X-rays pass through the body in one direction in this plane. By measuring the photon intensity after transmission, a projection of the attenuation in the chosen body plane is obtained. This procedure is repeated for the same plane at many viewing angles. By combining the projections at different angles an image of the plane can be made. This procedure can be repeated for as many planes as necessary, constructing a three-dimensional image.

In X-ray methods the radiation is transmitted through the body from an external source to an external detector. An alternative method is to use an internal source, a radionuclide, which emits radiation from inside the body to the detector. Radionuclide imaging involves the production of images of the distribution of radionuclide-labelled molecules inside the body to reveal the physiological functions of individual organs. One of the first applications of this technique, the introduction of $^{131}$I to investigate thyroid disease, was carried out in the late 1930's. Here also is the possibility of producing a two-dimensional projection, called planar scintigraphy, or the construction of a three dimensional image in emission computed tomography (ECT). The basic difference between ECT and CT is that ECT uses photons emitted inside the body, so one has to correct for photon attenuation in body tissues to determine the distribution of radioactivity inside the body.

Two forms of emission computed tomography can be mentioned. Single-photon emission computed tomography (SPECT) uses radioisotopes decaying only by photon emission. Positron emission tomography (PET) uses radioisotopes emitting a positron in their decay. The positron produces two photons in its annihilation, each with an energy of 511 keV, emitted simultaneously in opposite directions. An important feature of PET is the ability to quantify the radioactivity distribution of radionuclides in
the human body. A limitation of the spatial resolution in PET is the positron range in the body and
the finite size of detectors. This problem can vary depending on the kind of radionuclide being used.
Conventionally, radionuclides such as $^{11}$C, $^{15}$O and $^{18}$F, emitting positrons with relatively low
energies, decaying to stable isotopes and with short half-lives (minutes to a few hours) are used in
PET. Since a radionuclide can be traced in the body for approximately 3 times its half-life it can be
convenient to use radionuclides with half-lives longer than a few hours, such as $^{76}$Br or $^{83}$Sr. $^{76}$Br
emits high energy positrons (up to 4 MeV), accompanied by more than 100 different modes of
gamma radiation, which seems likely to worsen resolution and to increase background in the images.
Nuclides such as $^{52}$Fe, used to obtain information about a patient's iron metabolism, decay to
unstable isotopes also emitting positrons in their decay. The goal of this work was to investigate the
efficiency of the standard image correction methods for the use of these radionuclides and the
consequences of their use on PET imaging properties.

The physical foundations of PET are discussed in chapter 2. This chapter also deals with the physical
limitations of the PET-technique, the image reconstruction and necessary corrections. Also, the
decay properties of the different radionuclides used in this investigation are discussed. Chapters 3 to
6 describe the experiments. Chapter 3 discusses measurements of the range distribution of positrons
emitted by $^{76}$Br. Chapter 4 describes phantom studies carried out to investigate the spatial resolution
of PET with the use of different kinds of radionuclides as described above. Reconstructed scatter
fraction and a calibration of the different detectors used in PET studies at Uppsala University PET
Centre are also discussed. Chapter 5 discusses in vivo studies using $^{52}$Fe in PET and the consequences
of the iron decay to the also positron emitting $^{52}$Mn. A method to calculate the iron contribution in
PET images is suggested. In chapter 6 the consequences of the results from chapters 4 and 5 on
quantification using PET will be discussed. Chapter 7 states the conclusions that can be made from
the experiments.

Figure 1.1 - A GEMS 2096+ PET brain scanner at Uppsala University PET Centre. From: UUPC Internet
pages.
2 Positron Emission Tomography

This chapter deals with the foundations of PET. The physical principles, the positron decay and annihilation and the principles of a PET camera will be discussed first, followed by the image reconstruction and the necessary corrections to obtain a spatially and quantitatively accurate image. In the last paragraph of this chapter decay properties of radionuclides that are used in PET are discussed.

2.1 Foundations of PET

2.1.1 Positron decay and annihilation

In positron decay one proton in the nucleus is converted into a neutron, under the emission of a positron and a neutrino:

\[ ^{52}\text{Fe} \rightarrow ^{52}\text{Mn} + \beta^+ + \nu \]

The reaction energy that is released in this reaction is distributed between the positron and the neutrino, giving the positron a continuous energy distribution with as maximum energy the total decay energy (figure 2.1). The neutrino will leave a human body without any interactions. The positron will lose kinetic energy fast (circa $10^{-10}$ s) in repeated interactions with surrounding electrons and by emitting bremsstrahlung, which is generally emitted by a slowing down charged particle.

![Figure 2.1 - Typical energy distribution of positrons in positron decay. The maximum in the distribution lies at $E=Em/3$.](image)

Figure 2.2 shows the range of positrons in matter as a function of the kinetic energy of the positron. In chapter 3 the properties of some positron emitters used in PET will be discussed.
After losing its energy the positron and an electron will annihilate, generally producing two photons. Also one or three photon annihilations may occur, but can be neglected in living tissues. The two produced photons both have an energy of 511 keV and are emitted in almost exactly opposite directions. The maximum deviation from 180° of the angle between the two photons is 0.4°. This deviation is neglected in PET. The photons produced in the annihilation will interact in their way through the body. These interactions will be discussed in paragraph 2.2.

2.1.2 A positron emission tomograph

PET is based on the principle of annihilation coincidence detection [Phe75]. When a positron is emitted from a radionuclide inside the body, it will travel a short distance before annihilation. By detecting the two oppositely directed photons that are produced in the annihilation, a line is defined along which the annihilation event must have occurred.

Figure 2.3 shows the measuring principle of a 2-dimensional positron emission ring tomograph, which is the type used in the measurements described in chapters 4 and 5. Other types of PET systems, such as time-of-flight PET and double headed PET scintillation cameras with rotating position sensitive NaI(Tl) scintillation detectors are described in e.g. [Tre91] and [Paa85].
The basic unit of a PET system consists of two detectors in coincidence, a detector channel. In a ring tomograph (PET-camera) a number of rings of small scintillation detectors is used. Every detector is in coincidence with a row of detectors on the opposite side of its own ring (direct or true slice) and neighbouring rings (cross slices). Between the rings and blocks of detectors lead shields (septa) are placed which define the thickness of a slice and reduce the number of scattered and random coincidences (figure 2.5).

Figure 2.3 - Measuring principle of a positron emission tomograph. Two detectors register two photons in coincidence. The photons were emitted simultaneously in opposite directions after a positron decay and subsequent annihilation.

If one ring is made of N detectors and each detector is in coincidence with K other detectors in the same ring, N projections with each K/2 measuring points are obtained, where the angle between adjacent projections is $2\pi/N$. The sample interval can be increased by a movement of the detector rings, the centre of the rings following a circle which diameter is slightly larger than the diameter of one detector. This movement is called wobble motion. The movement is divided into a number of intervals and the measured data are ordered according to this. The wobble movement has to have a frequency high enough to be able to assume that the activity distribution is constant during one cycle [Wie89].

2-3
The detectors generally use bismuth germanate oxide (BGO) or NaI(Tl) scintillation crystals (see figure 2.4). In most cases BGO is used because of its higher intrinsic efficiency for 511 keV photons [Erl96]. In the first PET systems the detectors were composed of one crystal and one photomultiplier tube. The desire to use smaller detectors to improve spatial resolution has lead to the development of block detectors, consisting of a block of BGO cut into e.g. 4x4 elements and viewed by 4 photomultiplier tubes for element identification [Erl96]. Wobble motion is no longer necessary with the spatial resolution obtainable with these cameras.

Figure 2.4 - Basic processes in a scintillation detector. The scintillator material emits light after absorption of radiation. The intensity of the light is proportional to the amount of absorbed radiation. The photocathode releases photoelectrons, at most one per photon (usually the efficiency is of the order of 0.1) and these electrons are multiplied and accelerated in a PM tube. The pulse height is proportional to the radiation energy.

Figure 2.5 - Background events: random coincidence (left) and scatter coincidence (right).
Before an image can be constructed, a number of corrections must be applied to the data obtained from a PET scanner. Corrections for variations in detector efficiency, dead-time effects, random coincidences, coincidences of scattered annihilation photons and attenuation have to be made (see figure 2.5). In the next two paragraphs first the image reconstruction and then the corrections will be discussed.

Apart from improving spatial resolution by the use of smaller detectors it is important to have optimal sensitivity, that is, a high ratio between the number of emitted positrons and registered true coincidences. Therefore septa can be removed, and instead of just using two-ring combinations for cross slices all ring combinations can be used. This requires 3-dimensional image reconstruction (see [Tow89], [Erl96]). A disadvantage of 3-dimensional PET is that although the sensitivity increases also the number of scattered and random coincidences increases.
2.2 Image reconstruction

The image can be reconstructed from the individual projections by analytical or iterative algebraic methods [Erf96]. The most common reconstruction technique in 2-dimensional PET is called filtered backprojection. If the object coordinates are \((x, y)\) and the projection coordinates \((r, \phi)\) (see figure 2.6), then the relationship between the two sets of coordinates is:

\[
\begin{align*}
    r &= x \cos \phi + y \sin \phi \\
    s &= -x \sin \phi + y \cos \phi
\end{align*}
\]  

with \(\phi\) the projection angle. The collection of parallel projections for all possible angles is called the Radon transform of the function \(f\). The principle of the image reconstruction is to obtain an inversion formula for the Radon transform.
The Radon transform is a projection of a 2D-function. The reverse operation to this projection is called backprojection:

\[ g(x, y) = \int_0^\pi p_\phi (r) d\phi \]  

The obtained result is a blurred version of the original function \( f \), not the inverse of the Radon transform. The basic idea of the image reconstruction is thus that given the projection \( p \), we want to estimate the original distribution \( f \). The most important property of the Radon transform is its relation to the Fourier transform with the so called central section theorem [Kina96]: the Fourier transform of a projection is a one-dimensional sample, at the same angle as the projection, through the centre of the two dimensional Fourier transform of the original function (see figure 2.5):

\[ P_\phi (v) = F(h, v) \bigg|_{x=0} \]  

where \( \phi \) is the projection angle and \( P_\phi (v) \) and \( F(h, v) \) are the Fourier transforms of \( p_\phi (r) \) and \( f(x, y) \), respectively. The filtered backprojection algorithm starts from the inverse 2D Fourier transform:

\[ f(x, y) = \iint F(h, v) e^{i2\pi(xu+yv)} du dv \]  

Changing to polar coordinates \((\rho, \phi)\), introducing \( r \) from equation (2.1) and changing integration limits because we only measure in the interval \([0, \pi)\) we obtain

\[ f(x, y) = \int_0^\pi \int_0^\infty F_p (\rho, \phi) \rho e^{i2\pi\rho \phi} d\rho d\phi \]  

where \( F_p \) is the representation of \( F \) in polar coordinates:

And with the central section theorem:

\[ f(x, y) = \int_0^\pi \left( \int_0^\infty P_\phi (\rho) \rho e^{i2\pi\rho \phi} d\rho \right) d\phi \]  

where \( P_\phi (\rho) \) is the Fourier transform of the projection \( p_\phi (r) \). The parallel projections are first individually filtered with the 'ramp filter' \( \rho \) and then backprojected to form the image. The high frequency part of the data is often dominated by noise and the ramp filter is therefore usually
combined with a low-pass filter. When this filtering step is also done in the frequency domain, the algorithm is called convolution and backprojection.

The convolution of two functions $f$ and $h$ gives a new function $g$ defined as:

$$g(x) = (f \otimes h)(x) = \int_{-\infty}^{\infty} f(s) h(x-s) \, ds$$  \hspace{1cm} 2.8

The convolution in spatial domain is equal to multiplication in frequency domain:

$$G(u) = F(u) H(u)$$  \hspace{1cm} 2.9

As mentioned before, the noise in a PET image is in the high frequency range, so a low pass filter is often used for smoothing of projections. An example is the often used Hanning filter:

$$A(\nu) = \begin{cases} 0.5 \left[ 1 + \cos \left( \frac{\pi |\nu|}{\nu_c} \right) \right], & |\nu| \leq \nu_c \\ 0, & |\nu| > \nu_c \end{cases}$$  \hspace{1cm} 2.10

where $A(\nu)$ is the amplitude at a spatial frequency $\nu$ and $\nu_c$, the cut-off frequency. Other frequently used filters in clinical PET are the Hamming filter [Web88] and ramp filter (see above).
2.3 Corrections

2.3.1 Random coincidences

A number of corrections have to be applied to the measured projections to obtain a spatially and quantitatively accurate image. First of all, the measured coincidence data have to be corrected for random (or chance, accidental) coincidences. Two photons are considered to have arrived simultaneously if, after detection of the first photon and subsequent opening of an electronic gate of length $2\tau$, the second photon is detected within this coincidence time window $2\tau$. If these two photons do not originate from the same annihilation then a random coincidence has occurred. This means that there is no possibility to distinguish between random and true coincidences. The time a photon travels through the body before reaching a detector is of the order of a nanosecond and considering the time resolution of the detector system and the electronics the minimum coincidence time window is of the order of $10$ ns [Wie89].

The number of random coincidences $R$ for a detector pair $(i,j)$ can be calculated from the single countrates $N_i$ and $N_j$:

$$R = 2\tau N_i N_j$$  \hspace{1cm} 2.11

where $2\tau$ is the coincidence time window [Voi95]. The true coincidence rate is in general smaller than $N_i$. Since the random fraction can never be reduced to zero, the random contribution to each detector pair is usually calculated during the measurement and subtracted before image reconstruction.

2.3.2 Scattered radiation

Annihilation photons interact with atomic electrons in the body either by photo-electric absorption or by Compton scattering. In body tissue and in the energy range of the annihilation photons Compton scattering plays the most important role and photo-electric absorption can be neglected [Oll96]. The possibility of Compton scattering is high: within 7 cm in body tissue every second annihilation photon undergoes scattering [Oll96]. When both annihilation photons are still detected in coincidence after one or both photons have been scattered, the origin of the photons, the location of the annihilation event, will be misinterpreted.
Compton scattering of the annihilation photons is strongly forward directed so the energy of the scattered photons will only differ slightly from the original energy of the annihilation photons:

\[
hv' = hv \left(1 + \frac{hv}{m_e c^2} (1 - \cos \theta) \right)^{-1}
\]

where \( \theta \) is the scattering angle, \( m_e c^2 \) is the rest mass of the electron (511 keV), and \( hv \) and \( hv' \) are the photon energies before and after scattering, respectively. The probability for Compton scattering can be calculated using the Klein-Nishina formula for the differential cross section per electron \([\text{Kra88}]\).

The distribution of scattered coincidences is such that it does not decrease the spatial resolution of the image, but it adds a background that influences quantitative measurements. Apart from septa, the influence of scattered radiation can be decreased by an increased ring diameter and an energy threshold. However, changing the geometry of PET cameras also influences the resolution and sensitivity of the system \([\text{Wie89}, \text{Ber82}]\).

The most common scintillator material in PET, BGO, has a low energy resolution at energies around 511 keV, which makes it impossible to discriminate these coincidences from unscattered coincidences by a narrow energy window. In PET cameras using NaI(Tl) as scintillator, which has a much better energy resolution at the energies involved, successful attempts to use an energy window have been made \([\text{Ols96}]\). Commonly a lower energy threshold of 200-300 keV is used.

The scattered radiation can be accounted for by correction algorithms in the image reconstruction software. The most common way of correcting for scattered radiation is the convolution-subtraction method \([\text{Ber82}]\).
The projection data in a PET-camera consists, after subtraction of random coincidences, of the following contributions:

\[ p_{\text{ohr}}(x) = p(x) + s(x) \]  

where \( p_{\text{ohr}}(x) \) is the observed projection data, \( p(x) \) the ideal projected activity distribution, \( s(x) \) the scatter distribution and \( x \) the position variable along the projection.

The projected scatter distribution \( s(x) \) is assumed to have the following form:

\[ s(x) = \int_{-D}^{D} p(t)f(x-t, t)dt \]  

where \( f(x, y) \) is the scatter distribution function giving the projected scatter amplitude at position \( x \) for a line source at position \( y \). The size of the field of view is 2D. Both \( x \) and \( y \) are projected positions. It is assumed that a change of the position of the source along the projection direction has no influence on \( S \). This assumption is not exactly true, as shown in [Ber82], but it is accurate enough.

The form of \( f(x, y) \) was determined experimentally in [Ber82], and can be described by:

\[ f(x, y) = A(y)\exp(-xa(y)) + C(y), \quad 0<y<x \]

or\[ 0>y>x \]  

\[ f(x, y) = A(y)\exp(-xa(y)), \quad \text{elsewhere} \]  

The constant \( C(y) \) increases with \( y \). The values of the parameters \( A(y) \) and \( a(y) \) depend on the projected position of the source and to some extent on the distribution of the scatter medium. The experimental observation gives the projection corrected for accidental coincidences \( P'_{\text{ohr}}(x) \). Using equation 2.7 a function \( h(x, y) \) should be found that gives the scatter distribution when operating on \( P_{\text{ohr}}(x) \):

\[ s(x) = \int_{-D}^{D} (p(t) + s(t))h(x-t, t)dt \]  

A function \( h(x, y) \) similar to \( f(x, y) \) is found to fulfill this very accurately. The parameters \( A(y), a(y) \) and \( C(y) \) can be determined from an experimental line source study. Once \( h(x, y) \) is determined, equation 2.16 gives the scatter distribution from any measured activity distribution. Using this method the amount of reconstructed scattered radiation can be reduced considerably in a very wide range of object configurations.
Another, simpler way to correct for scatter is to use a phantom uniformly filled with a radioactivity solution except for a thin region in the middle [Kar90]. The profile of the image of the radioactivity distribution in this phantom will show a dip in the middle and tails at the edges which should be zero in the absence of background events. A fit through the tails and the dip in the middle will give the background distribution. An advantage of this method is that random coincidences are also subtracted, although it is less exact than the above described convolution subtraction method.

2.3.3 Attenuation correction

One detector channel will view a strip across an object with a width determined by the size of the detectors. All photon pairs emitted within the solid angle defined by the detectors will have a probability of hitting the detectors and resulting in a valid event. However, the greatest probability is that they are scattered out of the detector channel by a Compton scattering process. The probability of not being scattered after a distance $x$ is:

$$N = N_0 \exp(-\mu x)$$ \hspace{1cm} 2.17

Where $N_0$ is the number of emitted photon pairs, $N$ the number of transmitted photon pairs and $\mu$ the linear attenuation coefficient.

The two photons being emitted in opposite directions leads to the fact that the total attenuation of a photon pair is not dependent upon the position of annihilation but merely on the total length of the attenuation media transversed by the two photons. So not the distribution of the radionuclides has to be known but only the distribution of the attenuating media. If the total attenuation along a detector channel is known, the measured countrate $N$ is corrected for attenuation by:

$$N' = N \exp(\mu x)$$ \hspace{1cm} 2.18

with the same notations as above. The most common way of obtaining an attenuation correction is to perform a transmission scan of the object under study. This is done using either a ring source or a rod source rotating around the attenuating object. Other methods used for finding the right attenuation lengths range from a simple ellipse description of for example a head contour or the use of special contour finding algorithms to the use of a transmission CT scan to find the contour [Ber82], [Wie89].
2.3.4 Calibration and normalisation

After proper corrections the image reconstruction results in a proportionality between the radionuclide concentration in the object and the pixel values in the image. The proportional constant can be determined experimentally by a calibration procedure. This is usually done with the use of a phantom with carefully determined uniform radionuclide concentration. The phantom is scanned and the image reconstructed using the appropriate corrections.

Every detector channel has different characteristics due to differences in for example crystal light yield or photomultipliers. In the calibration process the detector channels are normalised. To decrease the influence of scatter, these measurements should be performed with for example rotating ring-shaped phantoms or a rotating line source to exclude inhomogenities. The countrate should be low to exclude dead-time effects and a sufficient amount of events must be measured in order to obtain good statistics. The in this way established correction factor for one detector pair, together with geometric factors, should be included in the image reconstruction model [Wie89], [Ber82], [Lit84].
2.4 Spatial resolution

The range of positrons in body tissue and the slight deviation from $180^\circ$ of the angle between the two annihilation photons set a physical limit to the spatial resolution obtainable in PET. This limit depends on the energy of the emitted positrons and on the surrounding tissue. As described in paragraph 2.1 another limit to the spatial resolution arises from the dimensions of the detectors used in the PET camera. This effect is much larger than the first two effects for most PET systems that are currently in use and for low-energy positron emitters.

An imaging system can be characterised by its response to a point source, the point response function (PRF) or point spread function (PSF). A method to determine the PSF is to scan very thin tubes of activity positioned perpendicular to the plane through a detector ring. By determining the centre of mass in the resulting image matrix, the centre of a point is found. The pixel values are then plotted against the distance from the centre of the point to the centre of the pixel. The full width at half maximum (FWHM) of this function represents the PSF. Other methods to determine the spatial resolution are the use of the line spread function or the edge response [Ber82]. The Fourier transform of the PRF is called the modulation transfer function (MTF). If the PRF is independent of position, and if noise is neglected, the response $g$ of an imaging system to an arbitrary input $f$ is given by:

$$ g = f \otimes h $$  \hspace{1cm} 2.19

or:

$$ G = FH $$  \hspace{1cm} 2.20

where $h$ is the PRF and $H$ the MTF, equation 2.21 in spatial domain and equation 2.22 in frequency domain [Web88], [Erl96].

Apart from the above described in-plane or transaxial spatial resolution the axial spatial resolution, the slice thickness, should be mentioned, which defines the response in the axial direction. The slice thickness depends on the size of the detectors in the axial direction. Since coincidences are recorded between adjacent rings the size of the septa and the distance between two rings will also effect the slice thickness. The slice thickness can be determined by the use of a point source, which is scanned at different position along the axis of the camera and at different distances from the axis. When the pixel values of the imaged object are plotted as a function of the position along the axis, the axial response curve is obtained. The FWHM of this curve determines the slice thickness. The slice thickness is different for true slices and cross slices and, as well as the transaxial spatial resolution, depends on the distance to the camera axis [Ber82], [Rot91], [Scand].
2.5 Radionuclides in PET - decay properties

Traditionally radionuclides that decay almost 100% by positron emission such as $^{11}$C, $^{15}$O and $^{18}$F have been used in PET. These nuclides can be coupled to certain molecules which transport in the body is of interest. The half-lives of these radionuclides are short, in the order of a few minutes to 2 hours. This means that their transport through the body can only be followed for a short time. The general rule is that radionuclides can be followed in the body during 3 times their half-life without exposing the patient to a too high radiation dose. This is one reason for the use of longer lived radionuclides. Another reason for the use of longer lived or not pure positron emitting radionuclides can be the kind of study one wants to do. Therefore also the radionuclides used in this study, $^{76}$Br, $^{83}$Sr and $^{52}$Fe, have become of interest to PET. Investigations of PET imaging properties of $^{124}$I were described in [Pen91]. The decay properties of these nuclides are not as ideal for PET as the properties of the radionuclides mentioned above.

Table 2.1 - Positron emitters, half-life and range

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Half-life</th>
<th>$\beta^+\text{energy (keV)}$</th>
<th>$\beta^+\text{range (cm)}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>average (max)</td>
<td>in 1 g/cm$^3$</td>
</tr>
<tr>
<td>$^{11}$C</td>
<td>20.5 min</td>
<td>386 (960)</td>
<td>0.5</td>
</tr>
<tr>
<td>$^{15}$O</td>
<td>2.03 min</td>
<td>735 (1732)</td>
<td>0.9</td>
</tr>
<tr>
<td>$^{18}$F</td>
<td>1.87 h</td>
<td>250 (633)</td>
<td>0.3</td>
</tr>
<tr>
<td>$^{52}$Fe</td>
<td>8.275 h</td>
<td>340 (804)</td>
<td>0.4</td>
</tr>
<tr>
<td>$^{52}$Mn</td>
<td>21.1 min</td>
<td>1174 (2633)</td>
<td>1.4</td>
</tr>
<tr>
<td>$^{76}$Br</td>
<td>16.2 h</td>
<td>1180 (3941)</td>
<td>1.7</td>
</tr>
<tr>
<td>$^{83}$Sr</td>
<td>32.4 h</td>
<td>496 (1234)</td>
<td>0.5</td>
</tr>
<tr>
<td>$^{124}$I</td>
<td>4.18 days</td>
<td>188 (2150)</td>
<td>1.1</td>
</tr>
</tbody>
</table>

The energy and abundance data in this chapter are extracted from the NUDAT database, version 31-1-1996, [Kins96]. In tables 2.2, 2.3, 2.4 and 2.5 the energies of positrons are written as "maximum (average)".
2.5.1 Bromine-76

Examples of the use of $^{76}$Br in PET can be found in [Löv96a] and [Löv96b]. $^{76}$Br has a half life is 16.2 hours, which makes it possible to follow it in the body for about 2 full days. It decays producing stable $^{76}$Se:

$$^{76}\text{Br} \rightarrow ^{76}\text{Se} + \beta^+ + \nu$$

Figure 2.7 gives a simplified decay scheme, in which only positron and gamma radiation with an abundance of over 1% is included. In total $^{76}$Br emits 16 different positrons and 116 different gammas in its decay, of which 18 have an abundance of over 1%. The abundance of gamma radiation with an energy higher than 300 keV, usually the threshold energy in PET measurements, is 192.5%, the total positron abundance is 55%. Figure 2.8 shows that most gammas are emitted in coincidence with a positron and other gammas.

![Figure 2.8 - Simplified $^{76}$Br decay scheme; only gamma's and positrons with an abundance higher than 1% are shown. Level energies are given in MeV. Gammas and positrons with an abundance higher than 5% are given in table 2.2.](image)

### Table 2.2 - $^{76}$Br decay

<table>
<thead>
<tr>
<th>Energy (keV)</th>
<th>Abundance (%)</th>
<th>Energy (keV)</th>
<th>Abundance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\gamma$</td>
<td>559.1</td>
<td>74</td>
<td>$\beta_1$</td>
</tr>
<tr>
<td>2</td>
<td>657.0</td>
<td>15.9</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>1853.7</td>
<td>14.7</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>1216.1</td>
<td>8.8</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>2950.5</td>
<td>7.4</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>2792.7</td>
<td>5.6</td>
<td></td>
</tr>
</tbody>
</table>
2.5.2 Strontium-83

The strontium isotope $^{89}\text{Sr}$ can be administered as a 'boneseeker' to treat bone tumours. This is a purely $\beta^-$-emitting radionuclide so little quantitative information can be obtained of its distribution inside a patient. If this therapeutic radionuclide is mixed with the positron emitting $^{83}\text{Sr}$, PET can be used to quantitatively observe the strontium distribution.

$^{83}\text{Sr}$ decays to stable $^{83}\text{Rb}$:

$$^{83}\text{Sr} \rightarrow ^{83}\text{Rb} + \beta^+ + \nu$$

Its half-life is 32.41 hours which means that it can be studied for 4 days. The maximum positron energy is 540 keV, which is less than the maximum positron energy in $^{11}\text{C}$ or $^{18}\text{F}$ decay, but it emits 141 different gamma's in its decay, of which 11 with an abundance of over 1%. The abundance of gamma radiation with energies higher than 300 keV is 73.8%, the total positron abundance is 23%.

A simplified decay scheme is given in figure 2.9. Table 2.3 lists the radiation energies.

![Simplified $^{83}\text{Sr}$ decay scheme](image)

**Table 2.3 - $^{83}\text{Sr}$ decay**

<table>
<thead>
<tr>
<th>Gamma (keV)</th>
<th>Abundance (%)</th>
<th>Energy (keV)</th>
<th>Abundance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>762.7</td>
<td>30</td>
<td>423.6</td>
<td>1.6</td>
</tr>
<tr>
<td>381.5</td>
<td>14</td>
<td>1160.0</td>
<td>1.5</td>
</tr>
<tr>
<td>418.5</td>
<td>4.4</td>
<td>1147.3</td>
<td>1.3</td>
</tr>
<tr>
<td>381.2</td>
<td>2.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>778.4</td>
<td>2.0</td>
<td>$\beta^+_1$</td>
<td>1234 (540)</td>
</tr>
<tr>
<td>1562.5</td>
<td>1.8</td>
<td>1192 (522)</td>
<td>9</td>
</tr>
<tr>
<td>389.4</td>
<td>1.7</td>
<td>810 (354)</td>
<td>2.9</td>
</tr>
<tr>
<td>423.6</td>
<td>1.6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Figure 2.9 - Simplified $^{83}\text{Sr}$ decay scheme; only gamma's and positrons with an abundance higher than 1% are shown. Left to right $\gamma$ numbers 6-11, 10-5, 1-4, 8-3-2, 7, and 9 and top to bottom $\beta^+$ numbers 3, 2 and 1 in table 3.3. Level energies are given in keV.*
2.5.3 Iron-52

Iron-52 decays to Manganese-52, also a positron-emitting radioisotope.

\[ ^{52}\text{Fe} \rightarrow ^{52}\text{Mn} + \beta^+ + \nu \]
\[ ^{52}\text{Mn} \rightarrow ^{52}\text{Cr} + \beta^+ + \nu \]

The \(^{52}\text{Fe}\) decay scheme (figure 2.10) is relatively simple. It emits only one positron, and the abundance of gammas with energy higher than 300 keV is 2.1\%. \(^{52}\text{Mn}\) emits many different gamma's as well as higher energy positrons in its decay. The decay scheme for \(^{52}\text{Mn}\) is given in figure 2.11. The half-lives are 8.275 hours for \(^{52}\text{Fe}\) and 21.1 minutes for \(^{52}\text{Mn}\), which introduces another problem in PET imaging: not only radiation originating from \(^{52}\text{Fe}\) decay is measured, but also radiation originating from \(^{52}\text{Mn}\) decay. This will be discussed further in chapter 5. Radiation energies for \(^{52}\text{Fe}\) and \(^{52}\text{Mn}\) are given in tables 2.4 and 2.5, respectively. \(^{52}\text{Mn}\) has two positron decay modes, one with a 5.59 days half-life and one with a 21.1 minutes half-life, of which only the last one is of importance. The 21.1 minutes \(^{52}\text{Mn}\) decay has an abundance of gammas with energies higher than 300 keV of 100.3\%.

![Figure 2.10 - Decay scheme \(^{52}\text{Fe}\). Level energies are given in MeV.](image)

<table>
<thead>
<tr>
<th>Table 3.4 - (^{52}\text{Fe}) decay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (keV)</td>
</tr>
<tr>
<td>(\gamma_1)</td>
</tr>
<tr>
<td>(\gamma_2)</td>
</tr>
<tr>
<td>(\gamma_3)</td>
</tr>
<tr>
<td>(\beta^+)</td>
</tr>
</tbody>
</table>
Figure 2.11 - Simplified $^{52}$Mn decay scheme; only gamma's and positrons with an abundance higher than 1% (21.1 minutes half-life) or 5% (5.59 days half-life) are shown. Level energies are given in MeV.

Table 2.5 - $^{52}$Mn decay
half-life 21.1 minutes

<table>
<thead>
<tr>
<th>Energy (keV)</th>
<th>Abundance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\gamma_2$</td>
<td>1434.1</td>
</tr>
<tr>
<td>6</td>
<td>377.7 (IT)</td>
</tr>
<tr>
<td>$\beta^+$</td>
<td>2633 (1174)</td>
</tr>
<tr>
<td></td>
<td>98.3</td>
</tr>
<tr>
<td></td>
<td>1.68</td>
</tr>
<tr>
<td></td>
<td>96.7</td>
</tr>
</tbody>
</table>
3 $^{76}$Br positron range

The range of positrons is one of the factors determining the spatial resolution in PET. In this chapter experiments to determine the combined range distribution of the positrons emitted by $^{76}$Br are described.

3.1 Introduction

As was said in chapter 2, one of the factors determining the spatial resolution in PET is the range of the positrons emitted by a radionuclide. $^{76}$Br emits 16 different positrons in its decay, each with a different energy distribution and maximum energy. The consequences of the use of $^{76}$Br on the spatial resolution in PET will depend on the shape of the range distribution.

A range distribution in a certain material can be obtained by measuring the number of positrons passing through a layer of this material, and by systematically increasing the thickness $d$ of this layer. The difference in the number of positrons $N_{i+1} - N_i$ that passed through the material after an increase in thickness is the amount of positrons with a range between $d$ and $d + \Delta d$. By measuring the amount of positrons passing through the material in one direction a positron range distribution can be calculated, assuming that the number of interactions of positrons in air is neglectable compared to the number of interactions in the absorbing material. A three-dimensional distribution is simply obtained by summation over all angles.

![Figure 3.1 - Positron absorption measurement. See text for explanation.](image)
Bacause of the low Z-value of their constituents plastic scintillators have virtually no cross section for photoelectric absorption, which is proportional to $Z^4$ [Kra88], and in thin plastic scintillators only a small fraction of all incident photons will undergo Compton scattering and lead to a light pulse. The fluorescent energy $L$ produced by a beta particle in a scintillator is approximately given by:

$$L = \int_0^d S \left( \frac{dE}{dx} \right) dx$$

with $S$ the normal scintillation efficiency, the incremental light output per unit of energy loss, $d$ the thickness of the scintillator material and $dE/dx$ the energy loss of the beta particle per unit path length [Kno79]. The energy loss per mm pathlength is for positrons emitted by $\text{Br}$ of the order of 10-100 keV in a material with a density of 1 g/cm$^3$. All positrons entering the scintillator will interact through Coulomb interactions and lead to pulse.

In the experiments described in the next paragraph, where a thin plastic scintillator is used as positron counter, we assume that the gamma radiation gives a constant background in the measured countrate.
3.2 Experiments

3.2.1 Experimental setup

To measure a positron range distribution the setup described in figure 3.2 was constructed. A scintillation detector (see figure 2.4) with a 0.1 mm thick plastic scintillator was used as counter. A sample of a positron emitting radionuclide absorbed in filter paper can be inserted between two polyethylene blocks. The blocks are 2 cm thick to prevent unnecessary exposure of the experimenter to beta-radiation. In the direction of the detector is a circular hole with a diameter of 0.5 cm. Between the PE blocks and the detector 1 to 20 slices of a plastic material with density 1.25 g/cm\(^3\) can be placed. The slices are 1 mm thick.

The output pulse of the detector is sent via an amplifier to a AD converter and a multi-channel analyzer (Personal Computer Analyzer, The Nucleus®).

![Diagram of the setup for the positron range measurements.](image)

Figure 3.2 - Schematic overview of the setup for the positron range measurements. The number of plastic slices can be varied between 1 and 20, creating a 1 to 20 mm thick attenuation layer for positrons. The output signal was amplified and the count rate was measured using a multi channel analyser.
3.2.2 Measurements

A 1 MBq sample of a $^{76}$Br solution was absorbed on a piece of filterpaper, dried, and inserted centrally between the two plastic blocks. The countrate was measured with 1 to 20 plastic slices inserted between source and detector, every time for 1 minute. The maximum positron range in a 1.25 g/cm$^3$ material is 1.4 cm, so the background was calculated as the average countrate with 15 to 20 slices inserted. Corrections were made for radioactive decay.

3.2.3 Results

Figure 3.3 shows the obtained positron range distribution of $^{76}$Br calculated for a 1 g/cm$^3$ material. The background was 1620 ± 16 counts per minute. The values in figure 3.3 have standard deviations given by Poisson statistics.

![Positron range Br-76](image)

Figure 3.3 - Measured positron range distribution for $^{76}$Br decay in a 1 g/cm$^3$ material.

The maximum range in the measured distribution is 1.65 cm, compared to the theoretical value of 1.7 cm in table 2.1. The countrates were low because of the low radioactivity of the sample, and the background relatively high. The shape of the distribution can be explained by the energy distribution of the positrons emitted by $^{76}$Br: most of the 16 different positrons have a maximum energy lower than 1 MeV and thus a range lower than 0.5 cm in a material with density 1 g/cm$^3$, and only two positrons have a maximum energy higher than 3 MeV and account for the larger range tail in the distribution.
This chapter described the measurements of in-plane spatial resolution and reconstructed scatter fractions of PET images. The measurements were done using different phantoms to simulate appropriate scatter and attenuation environments. Also, the cross-calibration of the different detectors used in normal PET practice is discussed.

4.1 Experimental setup

4.1.1 PET camera

The measurements described in this chapter were done with a GEMS 4092+ whole body camera (Scanditronix AB, Uppsala, Sweden) at Uppsala University PET Centre (UUPC). This camera consists of 8 rings each consisting of 512 BGO detector crystals organised in blocks of 4x4 detectors viewed by 4 photomultiplier tubes, producing 15 slices. Each detector is coupled in coincidence with 195 opposite detectors in the same ring and 195 detectors in adjacent rings. The camera has non-retractable septa to reduce effects of scattered annihilation radiation and random coincidences. The transaxial field of view (FOV) is 550 mm, the axial FOV is 103 mm. Wobble motion is possible. An energy threshold can be chosen to eliminate information from gamma radiation with energies below this threshold. In these experiments the energy threshold is set at 300 keV. The coincidence time window is 12 ns.

The nominal in-plane spatial resolution as well as the slice-thickness is 6 mm FWHM (stationary) or 5 mm FWHM (wobble) in the centre of the field of view (measured with a $^{18}$F line source in metal, [Scand]). Rota Kops et al. [Rot90] even find a resolution of 5.7 mm FWHM (stationary) in the centre of the field of view in the same type of camera, and a constant in-plane spatial resolution within a 7 cm radius from the centre of the FOV. The PET camera is linear up to a radioactivity of 20000 nCi/ml for a pure positron emitter dissolved in the calibration phantom (next paragraph) [Rot91].

A schematic overview of the data acquisition system and the PET camera is given in Appendix C. The image reconstruction software allows image formats of 128x128 or 256x256 pixels, and a minimum pixel size of 1x1 mm. The software contains corrections for normalisation of detector sensitivities, corrections for random coincidences obtained by single detector pair countrates, several attenuation correction methods, corrections for coincidences caused by scattered radiation according to the convolution subtraction method, dead time correction calculated from single and coincidence countrates, wobble speed variation correction and correction for defective detectors. Available filters are for example the Hanning and ramp filter (see paragraph 2.2).
In the measurements described below attenuation corrections were based on transmission measurements made with a rotating 6 mm diameter pin shaped $^{68}$Ga source. During emission scans this pin was removed. The PET camera's standard corrections were used which involve random corrections based on individual detector countrates, convolution subtraction scatter correction and the standard normalisation and dead time correction. Since in normal clinical practice no wobble motion is applied, these measurements were also done in the stationary mode.

4.1.2 Phantoms

In the experiments described in this chapter three different phantoms were used. For intercalibration of the PET camera and other detectors used in PET studies, a cylindrical polystyrene phantom with an inner diameter of 19.2 cm and a length of 17 cm was used.

The measurements of the reconstructed scatter fraction were done with a polystyrene cylinder (inner length 35 cm, inner diameter 19 cm) containing a polyethylene rod perpendicular to the cylinder axis with dimensions 19x4x4 cm. This phantom can be filled with an activity solution, the polyethylene rod providing a volume in the centre of which no true coincidences can be measured, allowing measurement of the reconstructed scatter fraction (figure 4.1). Figure 4.2 shows a transmission scan.

![Figure 4.1 - Transmission scan images of the resolution (left) and scatter phantom (right). The grey background in the images is normally black. The color scale is a measure of attenuation. The fact that the PE rod in the scatter phantom is not visible in the transmission scan shows that the photon attenuation in PE is equal to the attenuation in water.](image)

For the spatial resolution measurements a phantom consisting of four parts made from different materials was constructed, to provide different attenuation environments (figures 4.1, 4.2). The materials have densities of 0.15 (wood), 0.19 (bonded foam), 0.49 (wood) and 0.97 (polyethylene) g/cm$^3$, and dimensions of 8x8x12 cm$^3$ for the two highest density materials and 10x10x12 cm$^3$ for the lowest density materials. The lower density materials were included to simulate lung-tissue.
One single catheter (Terumo Radifocus SP-catheter, Terumo Corporation, Tokyo, Japan) with an inner diameter of circa 0.5 mm and a length of 130 cm was inserted through the middle of the four compartments of the phantom. Filling this catheter with a radioactive solution gives a line source with the same radioactivity concentration in the middle of each phantom part. The dimensions of the four compartments ensure that most positrons are stopped inside the compartment.

Scatter phantom

Resolution phantom

Figure 4.2 - Schematic description of the scatter phantom (top) and the phantom used in the resolution measurements. The four parts have densities (1) 0.19 g/cm³, (2) 0.49 g/cm³, (3) 0.15 g/cm³ and (4) 0.97 g/cm³.
4.1.3 Production of radionuclides

The radionuclides were produced at the Gustav Werner Cyclotron at The Svedberg Laboratory, Uppsala (maximum proton energy circa 180 MeV) or the Uppsala University PET Centre cyclotron (Scanditronix MC17, Scanditronix AB, Uppsala, Sweden, maximum proton energy 17 MeV), and the chemistry laboratory at UUPC or TSL.

The $^{18}$F was produced at Uppsala University PET Centre by the standard procedure, the $^{18}$O(p,n)$^{18}$F reaction in $^{18}$O-enriched H2O target material. The $^{76}$Br was produced via the $^{76}$Se(p,n)$^{76}$Br reaction with 16 MeV protons on $^{76}$Se-enriched Cu$_2$Se at the UUPC cyclotron. The procedure is described in [Löv96a]. $^{52}$Fe was produced via the Ni(p,xpxn)$^{52}$Fe reaction using 58 MeV protons on Ni metal at The Svedberg Laboratory [Tol94]. $^{85}$Sr was produced via the $^{85}$Rb(p,3n)$^{85}$Sr reaction using 22-32 MeV protons on natural RbCl at The Svedberg Laboratory [Tol95].

Figure 4.3 gives an overview of the different stages in the radionuclide preparation and PET study.

Figure 4.3 - Schematic overview of different stages in the radionuclide preparation and PET studies. The bold printed detectors were cross-calibrated.
4.2 Calibration

For each of the radionuclides used in the experiments a cross-calibration between the different detectors generally used in clinical PET (see figure 4.3) was performed.

**Ge-detector**
The activity of a radionuclide sample was first measured using a calibrated solid state Ge-detector (EG&G Ortec Gamma-X High-Purity Germanium detector). This detector is generally used to measure the activity of samples prepared at the TSL hotlab. The activity obtained using this detector was considered to be the exact radioactivity of the radionuclide sample. The Ge-detector was calibrated using a $^{152}$Eu source (Amersham International Limited, Amersham, England) of which the activity was known with an uncertainty of 2%. Efficiency curves as a function of gamma energy and distance to the detector were calculated. The efficiency values have a standard error of 3% and are listed in Appendix A.

**Ionisation chamber**
Consequently the activity of the sample was measured using the ionisation chamber normally used before administering samples in patient studies. This ionisation chamber is calibrated for the (almost) pure positron emitters that are used in standard clinical PET-practice, such as $^{11}$C and $^{18}$F.

**PET camera**
The radioactivity sample was injected in the calibration phantom filled with water, and mixed until a uniform distribution could be assumed. With the PET-camera the average radioactivity concentration was measured during a 10 minute emission scan. Attenuation correction was based on a 10 minute transmission scan. Standard corrections and a Hanning filter with filterwidth 4.2 mm were applied in the image reconstruction. For all radionuclides the average radioactivity per slice was uniform; the deviation from the average over all slices was maximum 1.5%.

**Well counters**
Then samples of the radionuclide solution were taken and the radioactivity measured in the well-type NaI(Tl) detectors commonly used for measuring activity in blood samples. Like the ion chamber, these counters are calibrated for the conventional radionuclides.

For each of the used radionuclides, correction factors for the activity measured in the different detectors and the PET camera were calculated. All measurements were repeated for three different amounts of radioactivity in the range 25-500 MeV to verify if the calibration factors were independent of radioactivity. Corrections were made to compensate for decay due to the time necessary during the calibration measurements. The calibration factors are given in Appendix B.
4.3 Spatial resolution

4.3.1 Measurements

The phantom was placed in the centre of the field of view of the PET camera, so the line sources were located at a distance of circa 6 cm from and parallel to the camera axis. This way the line sources are viewed as point sources in the measurement planes. A 10 minute transmission scan was made using the rotating $^{68}$Ga rod-source to obtain an attenuation correction. After this the catheter was filled with radioactive solution. Emission data were collected for 10 or 20 minutes, depending on the level of radioactivity of the solution, to obtain sufficient measuring statistics.

The images were reconstructed using a ramp filter with a filter width of 1 mm to obtain an image of 256x256 pixels and a pixel size of 1x1 mm$^2$. The ramp filter is commonly used in resolution measurements [Rot90], [Lit83].

4.3.2 Results

Figure 4.4 shows the reconstructed images for $^{18}$F and $^{76}$Br.

Figure 4.4 - PET images of the spatial resolution phantom studies, $^{18}$F (left) and $^{76}$Br (right) in a direct slice. The grey background in the images is normally black. The color scale is a measure of radioactivity concentration.

The images were analysed by placing concentric regions of interest around the centre of the peak, calculating the mean radioactivity concentration in these ROI's, and plotting these values as a function of the radius.
Figures 4.5, 4.6, 4.7 and 4.8 give the point spread functions for \(^{18}\text{F}\), \(^{85}\text{Sr}\), \(^{76}\text{Br}\) and \(^{52}\text{Fe}\), respectively, in all four materials in the resolution phantom, for direct slices (the results in cross slices are not significantly different).
Figure 4.7 - Point spread functions for $^{76}$Br in a direct slice in 0.97 g/cm$^3$ (squares), 0.49 g/cm$^3$ (diamonds), 0.19 g/cm$^3$ (triangles) and 0.15 g/cm$^3$ (circles) materials.

Figure 4.8 - Point spread functions for $^{52}$Fe and $^{52}$Mn in equilibrium in a direct slice in 0.97 g/cm$^3$ (squares), 0.49 g/cm$^3$ (diamonds), 0.19 g/cm$^3$ (triangles) and 0.15 g/cm$^3$ (circles) materials.

Table 4.1 lists the calculated values of the PET camera's in-plane spatial resolution (in mm FWHM) for the four used radionuclides in the four materials. Table 4.2 lists the full width at tenth maximum (FWTM) values. These values were calculated by a least squares fit of a sum of two Gaussian functions to the obtained radioactivity concentration profiles.
Table 4.1 - In-plane spatial resolution

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Density</th>
<th>0.97 gcm(^{-3})</th>
<th>0.49 gcm(^{-3})</th>
<th>0.19 gcm(^{-3})</th>
<th>0.15 gcm(^{-3})</th>
</tr>
</thead>
<tbody>
<tr>
<td>(^{18})F</td>
<td>6.2</td>
<td>6.4</td>
<td>6.3</td>
<td>6.4</td>
<td></td>
</tr>
<tr>
<td>(^{76})Br</td>
<td>7.4</td>
<td>7.3</td>
<td>6.9</td>
<td>6.8</td>
<td></td>
</tr>
<tr>
<td>(^{52})Fe/(^{52})Mn</td>
<td>7.0</td>
<td>6.9</td>
<td>6.7</td>
<td>6.6</td>
<td></td>
</tr>
<tr>
<td>(^{85})Sr</td>
<td>6.3</td>
<td>6.6</td>
<td>6.7</td>
<td>6.6</td>
<td></td>
</tr>
</tbody>
</table>

resolution in mm FWHM, standard deviations 0.2 mm

Table 4.2 - Full width at tenth maximum

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Density</th>
<th>0.97 gcm(^{-3})</th>
<th>0.49 gcm(^{-3})</th>
<th>0.19 gcm(^{-3})</th>
<th>0.15 gcm(^{-3})</th>
</tr>
</thead>
<tbody>
<tr>
<td>(^{18})F</td>
<td>11.5</td>
<td>11.9</td>
<td>12.0</td>
<td>12.1</td>
<td></td>
</tr>
<tr>
<td>(^{76})Br</td>
<td>16.6</td>
<td>18.2</td>
<td>18.0</td>
<td>16.1</td>
<td></td>
</tr>
<tr>
<td>(^{52})Fe/(^{52})Mn</td>
<td>14.4</td>
<td>16.1</td>
<td>15.7</td>
<td>15.4</td>
<td></td>
</tr>
<tr>
<td>(^{85})Sr</td>
<td>12.2</td>
<td>13.5</td>
<td>15.3</td>
<td>14.9</td>
<td></td>
</tr>
</tbody>
</table>

FWTM in mm, standard deviations 0.5 mm

4.3.3 Discussion

In most literature point spread functions are being described by Gaussian functions. This gives a good fit as long as the range of emitted positrons is low. However for most of the measurements described in this chapter it was not possible to fit a Gaussian curve to the data since a fit to all the points in the measured peak does not give a good estimation and a fit to only the highest part of the measured peak will result in a Gaussian function with a too low FWHM. The spatial resolution was also calculated using a dedicated Scanditronix computer program which fits a single Gaussian curve to a profile through the data and the resolutions found in these calculations were usually somewhat worse (less than 0.5 mm FWHM). For this reason a sum of two Gaussians was fit to the measured data:

\[ A(r) = C_1e^{-\lambda_1r^2} + C_2e^{-\lambda_2r^2} \]  

with \( A \) the radioactivity contribution, \( r \) the distance to the centre of the peak and \( C_1, C_2, \lambda_1 \) and \( \lambda_2 \) the parameters of the Gaussian curves.
One of the parts of the right side of the equation could be seen as caused by the contribution of the spread caused by the finite resolution of the PET camera, the other as the contribution caused by the distribution of the positron range. This leads in all cases to a fit with a R-square value larger than 0.998.

As expected, the FWHM increases with decreasing density of the scattering material for $^{18}\text{F}$ and $^{85}\text{Sr}$. A lower density leads to a larger spread (larger FWHM and FWTM) in the point spread function, and a slightly lower peak, since the total peak activity is the same for all four peaks. The total peak activity has been calculated by drawing a circular ROI with a radius of 3 cm around the peak centre. The total radioactivity within this ROI was found to be approximately equal for all four peaks (see chapter 6), like expected. The increase in FWHM in lower density materials can be explained by the larger positron ranges in these materials.

For $^{76}\text{Br}$ and $^{52}\text{Fe}/^{52}\text{Mn}$ the opposite correlation between resolution and density was found. For these two radionuclides the maximum peak activity decreases rapidly with decreasing density, and the spread in the PSF is larger, resulting in an FWTM between 16 mm and 20 mm (density 0.15 g/cm$^3$). The normalised plots in figures 4.9 to 4.11 show these effects clearly.

![Normalised PSF Br-76 and F-18](image)

*Figure 4.9 - Normalised point spread function for $^{18}\text{F}$ (solid line 1 g/cm$^3$ and dashed line 0.2 g/cm$^3$) and $^{76}\text{Br}$ (dotted line 1 g/cm$^3$ and lines-dots 0.2 g/cm$^3$)*
With the above mentioned Scanditronix computer program the resolutions were calculated by fitting a single Gaussian curve to a horizontal and a vertical profile. No systematic differences between the horizontal and vertical resolution were found.

During the transmission scans the catheter was filled with air. To verify that this did not lead to different results a transmission scan with the catheter filled with water was made, resembling the situation during an emission scan. No differences were found.
An explanation for the unexpected improvement of resolution in lower density materials might lie in the shape of the energy distribution of the positrons emitted by $^{76}$Br and $^{52}$Mn ($^{52}$Fe only emits low energy positrons like $^{18}$F, so the effect here is caused by $^{52}$Mn positrons). For lower densities, most of the positrons will have a short range, but there will be a relatively large fraction having a large range, only contributing to a larger spread in the low part of the PSF, but not influencing the FWHM. For increasing densities, these positrons will also be stopped within a short distance, leading to a smaller spread in the lower part of the PSF and a larger FWHM.

As mentioned in chapter 2, the spatial resolution is also characterised by the modulation transfer function (MTF). Figure 4.12 gives the MTF for $^{76}$Br and $^{18}$F in materials of 0.19 and 0.97 g/cm$^3$.

![Modulation Transfer Functions](image)

**Figure 4.12** - Modulation transfer functions (MTF) for (right) $^{18}$F in 0.97 g/cm$^3$, (middle) $^{76}$Br in 0.97 g/cm$^3$ and (left) $^{76}$Br in 0.19 g/cm$^3$.

Clearly, the MTF decreases faster at low spatial frequencies for $^{76}$Br, and the cut-off frequency is the highest for $^{18}$F in 0.97 g/cm$^3$, as would be expected because of the smaller FWHM of the point spread function. The spatial frequency at which the MTF is 0.1 is 1.1 cm$^{-1}$ for $^{76}$Br in 0.97 g/cm$^3$, and 1.4 cm$^{-1}$ for $^{18}$F in 0.97 g/cm$^3$. The MTF for $^{76}$Br in high and low density materials cross at a spatial frequency of 0.64 cm$^{-1}$, which is also expected from the PSF's.
4.4 Reconstructed scatter fraction

4.4.1 Measurements

The scatter phantom was filled with water and positioned central in the field of view of the PET camera, with the polyethylene rod vertical in the image plane, the axes of PET camera and cylinder coinciding. A 10 minute transmission scan using the rotating $^{68}$Ga rod source was made to obtain the attenuation correction. The radioactive solution was added to the water and mixed properly, until a uniform distribution of the radioactivity in the water could be assumed. A 10 to 20 minute emission scan was made.

The images were reconstructed using a Hanning filter with filter width 4.2 mm, image size 128x128 pixels and pixel size 2x2 mm$^2$ which is also used in standard clinical PET imaging and the standard scatter correction for pure positron emitters.

Average horizontal activity profiles over a 2 cm wide area across the polyethylene rod were calculated. The mean radioactivity in the central 1 cm wide part (over the whole length) of the polyethylene rod was calculated and divided by the mean radioactivity as measured in the radioactivity solution. Only the central 1 cm has been chosen to exclude annihilation photons from high energy positrons annihilated inside the rod. The in this way obtained ratio is a measure of the amount of reconstructed scattered coincidences.

4.4.2 Results

Figure 4.13 shows two reconstructed PET images.

![PET images from the scatter phantom studies with $^{18}$F (left) and $^{37}$Br (right). The grey background in the images is normally black. Note: the radioactivity concentrations are not the same.](image-url)
Figure 4.14 to 4.17 show the obtained normalised radioactivity profiles for $^{18}$F, $^{76}$Br, $^{52}$Fe and $^{83}$Sr. Table 4.3 lists the ratios of the measured radioactivity in the centre of the polyethylene rod to the measured radioactivity in the radionuclide solution for both direct and cross slices. Data are normalised by dividing by the average radioactivity concentration measured in the radionuclide solution.
Normalized radioactivity profile Fe-52

Figure 4.16 - Normalised radioactivity profiles of the polyethylene rod in the scatter phantom filled with a solution of $^{52}\text{Fe}/^{52}\text{Mn}$ in equilibrium.

Normalized radioactivity profile Sr-83

Figure 4.17 - Normalised radioactivity profiles of the polyethylene rod in the scatter phantom filled with a solution of $^{83}\text{Sr}$.

Table 4.3 - Reconstructed scatter fractions

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Reconstructed scatter fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{18}\text{F}$</td>
<td>1.3 %</td>
</tr>
<tr>
<td>$^{76}\text{Br}$</td>
<td>4.8 %</td>
</tr>
<tr>
<td>$^{52}\text{Fe}/^{52}\text{Mn}$</td>
<td>4.0 %</td>
</tr>
<tr>
<td>$^{83}\text{Sr}$</td>
<td>1.7 %</td>
</tr>
</tbody>
</table>

standard deviations: ± 1
4.4.3 Discussion

The scatter reduction algorithm reduces the reconstructed scatter fraction in the centre of the FOV to 1.3% for $^{18}$F. For the other radionuclides the scatter reduction is less effective, although the amount of scattered radiation in the final image is still only 4.8% for $^{76}$Br. No significant differences between the reconstructed scatter fractions in cross slices and in direct slices was found. The central 1x19 cm$^2$ part of the PE rod was divided into 5 parts of 1x4.8 cm$^2$ to determine if there was a proportionality between reconstructed scatter fraction and distance to the centre of the image. No significant difference between centre and edge was found.

Background

The background in PET projection data originates mainly from:

1. coincidences of scattered annihilation photons originating from the annihilation,
2. coincidences of scattered and unscattered annihilation photons not originating from the same decay process,
3. coincidences of gammas (not annihilation photons) not originating from the same decay process,
4. coincidences of (scattered) annihilation photons with gammas emitted in coincidence with the annihilated positron (figure 4.19) and
5. coincidences caused by gammas emitted in coincidence from the same nucleus (figure 4.19).

![Figure 4.19 - Coincidence of two gammas emitted in coincidence (left) and coincidence of a gamma emitted simultaneously with a positron. One of the annihilation photons is scattered out of the detector plane (right).](image)

In case of a pure positron emitter such as $^{18}$F, only the first two types of coincidences occur. The standard correction for random coincidences accounts for the second type of background coincidences. The scatter correction algorithm corrects for circa 80% (the scatter contribution before correction is usually around 5%, [Rot91], in the same PET camera) of the scattered coincidences.
In case of $^{76}$Br, $^{52}$Fe and $^{85}$Sr, also the last three types of background radiation occur. The third type is accounted for by the random correction, but the last two types are not accounted for by the standard corrections. The amounts of these coincidences depend on the decay scheme of a radionuclide. These occur more frequently for $^{76}$Br with its 116 different gamma’s and 16 different positrons. Further, the standard scatter correction is determined for the use of pure positron emitters with a zero positron range. This scatter correction may be less effective for non-zero positron ranges which is another explanation for the increase in reconstructed scatter fraction.

**2D versus 3D PET**

The probability $P_T$ that two annihilation photons that both don’t undergo scattering are detected as a true coincidence in a direct slice is proportional to the solid angle of the detector ring:

$$P_T \approx \frac{D}{2R}$$

where $D$ is the detector dimension (the width of the ring) and $R$ the radius of the detector ring. The probability of detection in a cross slice is approximately twice as high. The probability $P_{\gamma\gamma}$ for a pair of gammas emitted simultaneously to be detected in coincidence in a direct slice or the probability $P_{\gamma T}$ for a triple coincidence of two annihilation photons and a gamma emitted in coincidence with a positron are:

$$P_{\gamma\gamma} = P_{\gamma T} \sim P_T^2$$

since the gammas are not emitted under opposite angles, and again twice that probability for cross slices. If one of two annihilation photons is scattered, the probability of the two photons still to be detected in coincidence is in a direct slice equal to:

$$P_{\gamma\gamma} = P_T^2 P_C$$

where $P_C$ is the probability that a photon after scattering will still reach a detector in the same detector ring, which is determined by the Compton cross section (see paragraph 2.3) and the location of the scatter event. The possibility of reaching a neighbouring ring is decreased by the use of septa, which also reduce the effects of random coincidences because only photons moving roughly in the plane of a detector ring can be detected.

In 3-dimensional PET septa are absent and coincidences between all detector rings are registrated. This means that the solid angle for true coincidences increases by more than a factor $8/3$ for an 8-ring PET camera. The probability for scattered annihilation photons to be detected in coincidence increases more because of the removal of the septa. The probability for two-gamma and triple coincidences increases by a more than factor $64/9$. 

4-17
Assuming that an accurate 3D scatter correction will remove the scattered coincidences, the effect of the gamma-gamma coincidences and triple coincidences compared to the number of true coincidences will be more than 3 times as high as in 2D PET. This shows that a dedicated correction will be necessary in 3D PET.
5 $^{52}$Fe in vivo measurements

In this chapter, quantification of in-vivo measurements of $^{52}$Fe kinetics using PET is discussed. A method is suggested to correct for the contribution of $^{52}$Mn decay in PET images.

5.1 Introduction

In paragraph 3.1.3, the $^{52}$Fe decay was discussed. $^{52}$Fe decays by emission of positrons to $^{52}$Mn, which then, also by positron emission, decays to stable $^{52}$Cr:

$$
^{52}\text{Fe} \rightarrow ^{52}\text{Mn} + \beta^+ + \nu \\
^{52}\text{Mn} \rightarrow ^{52}\text{Cr} + \beta^+ + \nu
$$

Intravenous iron administration, for example in the form of iron sucrose, is a common therapy for anaemia. Since iron preparations at high concentrations are toxic and some patients have a poor utilisation of the administered iron, it is important to study the detailed kinetics of different iron preparations and to optimise the iron uptake in the red bone marrow [Lun96]. As was mentioned in chapter 3, PET can be used for this purpose by administering $^{52}$Fe-labeled iron preparations. A problem that arises is that PET will measure the combined distribution of $^{52}$Fe and $^{52}$Mn.

Immediately after administration, $^{52}$Fe and $^{52}$Mn will be freely circulating in the blood and will have different kinetics. They are removed from the blood at different rates. In organs like the bone marrow, where the iron is trapped intercellularly [Bes97], $^{52}$Fe and $^{52}$Mn are in equilibrium due to the longer half life of $^{52}$Fe. In blood there is supposed to be a balance between production by $^{52}$Fe decay and biological removal of $^{52}$Mn. The goal of the experiments described in this chapter is to find a method to determine the ratio of $^{52}$Mn and $^{52}$Fe in the blood at different times after the intravenous injection of an equilibrium sample $^{52}$Fe/$^{52}$Mn. In this way, a correction factor for subtraction of $^{52}$Mn radioactivity in the blood from the measured radioactivity in PET-images can be obtained.

The activity of $^{52}$Fe radioactivity is given by:

$$
A_{Fe,t} = A_{Fe,0} \exp(-\lambda_{Fe} t)
$$  5.1

where $A_{Fe,0}$ is the activity of the sample at time $t=0$, and $\lambda_{Fe}$ is the decay constant of $^{52}$Fe.
The activity of $^{52}$Mn as decay product in the $^{52}$Fe decay:

$$A_{Me} = \frac{\lambda_{Me}}{\lambda_{Me} - \lambda_{Y}} A_{Y}^m \left[ \exp(-\lambda_{Y} t) - \exp(-\lambda_{Me} t) \right]$$  \hspace{1cm} (5.2)

where and $\lambda_{Me}$ is the decay constants of $^{52}$Mn. The decay constant is:

$$\lambda = \frac{\ln 2}{t_{1/2}}$$  \hspace{1cm} (5.3)

with $t_{1/2}$ the radioactive half-life of a radionuclide.

A combined gamma spectrum of $^{52}$Fe and $^{52}$Mn is shown in figure 5.1.

![Fe-52/Mn-52 gamma spectrum](image)

*Figure 5.1 - $^{52}$Fe-$^{52}$Mn gamma spectrum measured in a well counter. Peak energies are given in keV (*: summation peak).*

$^{52}$Fe has two peaks besides the 511 keV annihilation photons: 168.7 and 378.7 keV. Above a certain energy, there is no gamma radiation from $^{52}$Fe decay, whereas the $^{52}$Mn spectrum continues to higher energies. This part of the combined spectrum can be used to obtain information about the amount of $^{52}$Mn in a blood sample.

The amount of $^{52}$Mn can be divided into two parts: one part that was in the blood at the time of the collection of the blood sample, and one part produced by $^{52}$Fe decay after the taking of the blood sample. The radioactivity of the first part is given by equation 5.2, the radioactivity of the second part by equation 5.1 for $^{52}$Mn.
The amount of the total measured radioactivity originating from $^{52}\text{Mn}$ is described by:

$$A_{\text{Mn}} = A_{\text{Mn}}^0 \exp(-\lambda_{\text{Mn}} t) + \frac{\lambda_{\text{Mn}}}{\lambda_{\text{Mn}} - \lambda_{\text{Fe}}} A_{\text{Fe}}^0 \left[ \exp(-\lambda_{\text{Fe}} t) - \exp(-\lambda_{\text{Mn}} t) \right]$$  \hspace{1cm} 5.4

which can be written as:

$$A_{\text{Mn}} \exp(\lambda_{\text{Mn}} t) = A_{\text{Fe}}^0 \frac{\lambda_{\text{Mn}}}{\lambda_{\text{Mn}} - \lambda_{\text{Fe}}} \left[ \exp(-\lambda_{\text{Fe}} t) - \exp(-\lambda_{\text{Mn}} t) \right] \exp(\lambda_{\text{Mn}} t) + A_{\text{Mn}}^0$$  \hspace{1cm} 5.5

The radioactivity of both $^{52}\text{Mn}$ and $^{52}\text{Fe}$ at time $t=0$ can be calculated by measuring $A_{\text{Mn}}$ during a certain time and fitting equation 5.3 to the data, provided the measured radioactivity is only originating from $^{52}\text{Mn}$.
5.2 Experiments

5.2.1 Measurements

In a number of patient studies, blood samples were taken at regular times after the injection of $^{52}$Fe/$^{52}$Mn (in equilibrium) in a patient.

In the analysis of the blood samples, only countrates from gamma radiation with energies between 1400 and 1700 keV were included in the calculations. This radiation is supposed to be originating only from $^{52}$Mn decay. Countrates were measured with a well-type detector and the Personal Computer Analyzer (The Nucleus®) program.

5.2.2 Results

Figure 5.3 shows an example of the radioactivity of a blood sample containing $^{52}$Fe and $^{52}$Mn in time after the collection of the sample.

![Graph](image)

Figure 5.3 - Number of counts per minute in a region of interest between 1400 and 1700 keV as a function of the time after the taking of the blood sample. Patient study, 1 hour after the $^{52}$Fe injection. The solid line is a least squares fit of equation 5.5 to the data points. Data were corrected for dead-time.

Table 5.1 summarises the results of the patient studies.
Table 5.1 - results patient studies

<table>
<thead>
<tr>
<th>Date</th>
<th>Time after injection</th>
<th>Ratio $^{52}$Mn/$^{52}$Fe activity in blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>960312</td>
<td>1 h</td>
<td>$0.21 \pm 0.04$</td>
</tr>
<tr>
<td>960410</td>
<td>20 min</td>
<td>$0.25 \pm 0.02$</td>
</tr>
<tr>
<td></td>
<td>3 h</td>
<td>$0.29 \pm 0.02$</td>
</tr>
<tr>
<td>960423</td>
<td>1 h</td>
<td>$0.26 \pm 0.04$</td>
</tr>
<tr>
<td>960507</td>
<td>1 h</td>
<td>$0.21 \pm 0.01$</td>
</tr>
<tr>
<td></td>
<td>5 h</td>
<td>$0.14 \pm 0.01$</td>
</tr>
<tr>
<td>961016</td>
<td>1 h</td>
<td>$0.31 \pm 0.01$</td>
</tr>
</tbody>
</table>

5.2.3 Discussion

For accurate determination of the true $^{52}$Fe contribution in a PET image the $^{52}$Fe/$^{52}$Mn ratio should be calculated by continuously collecting and measuring blood samples in an automatic system. For convenience reasons an average correction factor can be calculated. The results as shown in table 3.1 give an average ratio of $0.24 \pm 0.06$. After correcting for positron abundances this means that the radioactivity concentration in a PET image has to be multiplied by a factor 0.7 to obtain an approximate $^{52}$Fe radioactivity concentration.

The assumption that there is no radiation in the 1400-1700 keV energy region originating from $^{52}$Fe decay can be proved in a better way by measuring the countrate in this energy region during a certain time immediately after production of pure $^{52}$Fe. The countrate in this energy region should then be accurately described by equation 5.2.

Since no pure $^{52}$Fe was available, the method used to calculate the $^{52}$Mn/$^{52}$Fe ratio was verified as follows. If the calculated $^{52}$Mn/$^{52}$Fe ratios of two samples taken from the same patient after different times are $R_1$ and $R_2$, and the sums of the number of counts in the energy range 1400-1700 keV of the normalised spectra of the samples are $S_1$ and $S_2$, then:

$$\frac{S_1}{S_2} \approx \frac{R_1}{R_2} \quad 5.6$$

should be an equality if there is no $^{52}$Fe decay radiation in the 1400-1700 keV region. This has been calculated for the 960410 patient.
Figure 5.3 - Normalised spectra of the blood samples taken 20 min (solid line) and 3 hours (dotted line) after administration of the iron. The spectra were measured 7.5 minutes after collecting of the sample. For peak energies see figure 5.1.

The ratio $S_1/S_2$ was found to be 0.94. From table 5.1 we would expect a value of $0.87 \pm 0.09$. The ratio of the sums of the number of counts in the energy region 0-1000 keV was found to be 1.01. The result was verified by doing the same procedure with two samples of the 960507 patient. Here, a ratio of $1.6 \pm 0.2$ was found and $1.5 \pm 0.1$ was expected from table 5.1. A correction for the amount of radiation originating from decay of $^{52}$Mn produced by $^{52}$Fe decay after collection of the sample will lead to a lower value of the found ratios, and brings them into better agreement with the values expected from table 5.1.
6 Quantification

In this chapter the consequences of the results described in chapters 4 and 5 on the accuracy of quantification in PET will be discussed.

Quantification of in vivo radioactivity concentrations in PET is usually done by defining a region of interest (ROI) in a PET image, and calculating the average radioactivity concentration per pixel in that ROI. PET images for clinical use are commonly filtered with a 4.2 mm Hanning filter, which leads to a slightly worse resolution [Rot91], and have a pixel size of 2x2 mm. It is important to define a ROI that has a large distance to major variations in radioactivity concentrations to obtain a reliable average radioactivity concentration.

Figures 6.1 to 6.4 give the integrated point spread functions for the radionuclides used in the phantom studies. The figures show the fraction of the total peak radioactivity inside a circle with a given radius.

![Integrated PSF; F-18; direct slice](image)

*Figure 6.1 - Integrated point spread functions for $^{18}$F in a direct slice, in 0.97 g/cm$^3$ (solid line), 0.49 g/cm$^3$ (dashed line), 0.19 g/cm$^3$ (dotted line) and 0.15 g/cm$^3$ (dash-dot) materials.*
Figure 6.2 - Integrated point spread functions for $^{76}$Br in a direct slice, in 0.97 g/cm$^3$ (solid line), 0.49 g/cm$^3$ (dashed line), 0.19 g/cm$^3$ (dotted line) and 0.15 g/cm$^3$ (dashes-dots) materials.

Figure 6.3 - Integrated point spread functions for $^{52}$Fe/$^{52}$Mn in a direct slice, in 0.97 g/cm$^3$ (solid line), 0.49 g/cm$^3$ (dashed line), 0.19 g/cm$^3$ (dotted line) and 0.15 g/cm$^3$ (dashes-dots) materials.

Figure 6.1 shows that for $^{18}$F, the peak radioactivity is confined inside a circle with a 1 cm radius in the image, in all density materials. For $^{83}$Sr (figure 6.4) in lower density materials only 75% of the peak radioactivity is inside a circle in the image with a radius of 1 cm around the centre of a peak, for $^{52}$Fe (figure 6.3) about 50% and for $^{76}$Br (figure 6.2) less than 50%.
Some curves in figures 6.1 to 6.4 keep increasing for radiiuses larger than the maximum positron range. This is caused by the reconstructed scatter in the image outside the line source peaks. For each nuclide, the total amount of radioactivity in the 4 peaks, determined by placing a ROI with a radius equal to the maximum positron range around the peaks and calculating the total radioactivity in this ROI, is within 10% deviation from average the same in all parts of the line source. Differences can be caused by variations in catheter diameter or radioactivity concentration in the catheter.

Many parts of the body have densities of around 1 g/cm³, so quantification of ⁷⁶Br, ⁵²Fe/⁵²Mn or ⁸³Sr will result in slightly less accurate results than quantification of ¹⁸F. However in small structures, the measured radioactivity will be lower than the true radioactivity due to the spread in the point response function. In lung tumours, where the tumour density is circa 1 g/cm³ and the density of the surrounding tissue circa 0.3 g/cm³, more caution is necessary. If the radioactivity concentration in a small lung tumour is calculated using a ROI almost as large as the tumour the concentration will be underestimated.

Furthermore, the increased amount of reconstructed scatter as calculated in paragraph 4.4 should be subtracted. As was discussed in chapter 5, an extra correction factor has to be applied to blood radioactivity concentrations in PET images using ⁵²Fe to correct for ⁵²Mn radioactivity.
7 Conclusions

In the preceding chapters experiments have been described that were done to investigate the effects of the use of unconventional radionuclides on PET imaging and quantification properties. In this chapter the conclusions are summarised and a number of recommendations for further research are given.

In-plane spatial resolution

• In-plane spatial resolution in the centre of the field of view, measured using a line source in a 1 g/cm³ surrounding material, was found to be 6.2±0.2 mm (¹⁸F), 6.3±0.2 mm (⁸³Sr), 7.0±0.2 mm (⁵²Fe/⁵²Mn in equilibrium) and 7.4±0.2 mm using ⁷⁶Br as positron emitting radionuclide.
• In-plane spatial resolution increases for decreasing density of the surrounding material for ¹⁸F and ⁸³Sr, to 6.4±0.2 mm and 6.6±0.2 mm, respectively, in 0.15 g/cm³ surrounding material.
• In-plane spatial resolution decreases for decreasing density of the surrounding material for ⁷⁶Br and ⁵²Fe/⁵²Mn, to 6.8±0.2 mm and 6.6±0.2 mm, respectively, in 0.15 g/cm³ surrounding material. This effect is caused by the shape of the energy distribution of the positrons emitted by these radionuclides.

Reconstructed scatter fraction

• The reconstructed scatter fraction in the centre of the field of view was found to be 1.3% for ¹⁸F, 1.7% using ⁸³Sr, 4.0% with ⁵²Fe/⁵²Mn and 4.8% for ⁷⁶Br.
• The increase in reconstructed scatter fraction is caused by a less effective functioning of the scatter correction mechanism for other radionuclides than ¹⁸F and by influence of coincidences of simultaneously emitted gammas and gammas emitted in coincidence with positrons.

Quantification

• The use of radionuclides emitting positrons with relatively large energies can lead to underestimation of the radioactivity concentrations in small structures, especially for lower density tissues.
• Corrections for the amount of ⁵²Mn in quantitative in vivo PET measurements after administration of ⁵²Fe can be made by measuring the gamma spectra of blood samples for a certain time after taking of the sample and calculating the ⁵²Mn/⁵²Fe ratio in blood.
Recommendations

• The current corrections in the image reconstruction appear to work fairly well for other than pure positron emitters. The significantly increased reconstructed scatter fraction for $^{80}$Br and $^{52}$Fe/$^{52}$Mn may be corrected for by a dedicated scatter correction. In 3-dimensional PET the effects of gammas emitted in coincidence in the decay and triple coincidences, caused by gammas emitted in coincidence with positrons, will be more prominent because of the absence of septa and the use of all detector rings in coincidence. Specific corrections will have to be applied to reduce these effects.

• More radionuclides than the ones discussed in this study are currently in use in PET. Some of these nuclides also emit high energy positrons, such as $^{86}$Y which is used to follow the uptake of $^{99}$Y. Also for these radionuclides a cross calibration between the different detectors will have to be made.

• The method used to obtain the $^{52}$Mn/$^{52}$Fe ratio in blood is elaborate; it may be possible to incorporate this in the automatic system used to follow radioactivity in blood samples during PET studies at Uppsala University PET Centre. However, further investigations to the iron and manganese metabolism is necessary to be able to quantify radioactivity concentrations in different organs apart from the blood. Experiments that were done recently in this field are described in [Bes97].
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Mark.
Appendices
Appendix A

Efficiency of Ge-detector

Efficiency x 1000000 as a function of energy and distance, 1-7-1996

<table>
<thead>
<tr>
<th>Energy (keV)</th>
<th>50 cm</th>
<th>100 cm</th>
<th>150 cm</th>
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<th>250 cm</th>
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<td>36.39</td>
<td>20.94</td>
<td>13.76</td>
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<td>29.58</td>
<td>16.63</td>
<td>10.72</td>
</tr>
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<td>24.78</td>
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</tbody>
</table>

Errors: ca. 3%.
Appendix B

PET cross calibration

$^{76}\text{Br}$

*Activity of 1.0 MBq measured with absolute calibrated Ge-detector corresponds to:*

<table>
<thead>
<tr>
<th></th>
<th>Value(s)</th>
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<tbody>
<tr>
<td>ion-chamber ($^{11}\text{C}$)</td>
<td>2.56 MBq</td>
</tr>
<tr>
<td>PET-camera</td>
<td>0.69 MBq</td>
</tr>
<tr>
<td>well-counters</td>
<td>3.01 MBq</td>
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</tbody>
</table>

*1.0 MBq in PET-camera corresponds to:*

<table>
<thead>
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<th></th>
<th>Value(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>total activity</td>
<td>1.44 MBq</td>
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<tr>
<td>ion-chamber ($^{11}\text{C}$)</td>
<td>3.65 MBq</td>
</tr>
<tr>
<td>well-counters</td>
<td>2.09 MBq</td>
</tr>
</tbody>
</table>

*1.0 nCi/cc in PET-camera corresponds to:*

<table>
<thead>
<tr>
<th></th>
<th>Value(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>total activity</td>
<td>53 Bq</td>
</tr>
<tr>
<td>ion-chamber ($^{11}\text{C}$)</td>
<td>135 Bq</td>
</tr>
<tr>
<td>well-counters</td>
<td>160 Bq</td>
</tr>
</tbody>
</table>

$1 \text{nCi} = 37 \text{Bq}$

errors ca. 5%
$^{52}$Fe

Activity of 1,0 MBq ($^{52}$Fe) measured with absolute calibrated Ge-detector corresponds to:

- ion-chamber ($^{11}$C) 3,16 MBq ($^{52}$Fe$^{52}$Mn)
- PET-camera 1,63 MBq ($^{52}$Fe$^{52}$Mn)
- well-counters 2,62 2,57 2,54 2,62 MBq ($^{52}$Fe$^{52}$Mn)

1,0 MBq in PET-camera corresponds to:

- total activity 0,61 MBq (only $^{52}$Fe)
- ion-chamber ($^{11}$C) 1,93 MBq ($^{52}$Fe$^{52}$Mn)
- well-counters 1,60 1,57 1,55 1,60 MBq ($^{52}$Fe$^{52}$Mn)

1,0 nCi/cc in PET-camera corresponds to:

- total activity 22,6 Bq (only $^{52}$Fe)
- ion-chamber ($^{11}$C) 71,4 Bq ($^{52}$Fe$^{52}$Mn)
- well-counters 59,2 58,1 57,4 59,2 Bq/cc ($^{52}$Fe$^{52}$Mn)

1 nCi = 37 Bq
errors ca. 5%
Activity of 1,0 MBq measured with absolute calibrated Ge-detector corresponds to:

<table>
<thead>
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<th>Detector Type</th>
<th>Activity (MBq)</th>
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</thead>
<tbody>
<tr>
<td>Ion-chamber ((^{11})C)</td>
<td>1,35 MBq</td>
</tr>
<tr>
<td>PET-camera</td>
<td>0,36 MBq</td>
</tr>
<tr>
<td>Well-counters</td>
<td>-</td>
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</table>

1,0 MBq in PET-camera corresponds to:

<table>
<thead>
<tr>
<th>Detector Type</th>
<th>Activity (MBq)</th>
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</thead>
<tbody>
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<td>Total activity</td>
<td>2,74 MBq</td>
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<tr>
<td>Ion-chamber ((^{11})C)</td>
<td>3,70 MBq</td>
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<td>Well-counters</td>
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</table>

1,0 nCi/cc in PET-camera corresponds to:

<table>
<thead>
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<th>Activity (Bq)</th>
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<tbody>
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<tr>
<td>Ion-chamber ((^{11})C)</td>
<td>137 Bq</td>
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<tr>
<td>Well-counters</td>
<td>-</td>
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</tbody>
</table>

1 nCi = 37 Bq
errors ca. 5%
Appendix C

PET camera data acquisition system

from: Scanditronix technical specification PC-4096-15WB high resolution whole-body positron camera system, Scanditronix AB, Uppsala, Sweden.
Technology Assessment

This graduation work has been carried out at the Division of Biomedical Radiation Sciences, Faculty of Medicine, at Uppsala University in Uppsala, Sweden. One of the areas of competence of this group is dosimetry using Positron Emission Tomography. The applications of this medical imaging technique require the development of radionuclides as tracers, labelling techniques, and the development of camera equipment such as detectors and electronics.

Positron Emission Tomography gives the possibility to follow and quantify the distribution of radionuclides inside the body, and by labelling these nuclides to chemicals of which the kinetics are of interest, the technique can be used to evaluate effects of pharmaceuticals, to follow processes in the body and thus investigate certain disorders, and to evaluate different forms of radiation therapy against tumours. The use of the unconventional radionuclides which imaging properties were discussed in this thesis expands the range of possible applications of positron emission tomography.