Detector Considerations for Time-of-Flight in Positron Emission Tomography

Florian Bauer
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Florian Bauer
For my parents,
grandparents
and girlfriend.
Detector Considerations for Time-of-Flight in Positron Emission Tomography

Dissertation

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Siemens Molecular Imaging

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# Table of contents

Table of contents

List of publications

List of abbreviations

Sammanfattning

Abstract

1 Introduction

1.1 Positron Emission Tomography

1.2 Content overview

2 Nuclear Physics fundamentals

2.1 Beta decay

2.2 Positron Emitters

2.3 Photon interactions

2.3.1 Compton scattering:

2.3.2 Photoelectric absorption:

2.4 Radionuclides for PET

3 State of the art PET-scanners

3.1 The detector

3.2 The parallax error

4 Inorganic Scintillators for detection of gamma radiation

4.1 Scintillation process in crystals

4.2 Scintillator Properties

4.2.1 Density and effective Atomic number (Z_{eff})

4.2.2 Light output

4.2.3 Decay time

4.2.4 Afterglow

4.2.5 Optical properties

4.2.6 Mechanical properties and cost
Table of contents

5 Photodetectors ______________________________________________________________________ 26
   5.1 Photomultiplier Tubes ___________________________________________________________ 27
      5.1.1 Important performance parameters ___________________________________________ 28
      5.1.2 PMT types ___________________________________________________________________ 30
      5.1.3 The voltage-divider-network ________________________________________________ 32
      5.1.4 PMTs for PET and SPECT ____________________________________________________ 33
      5.1.5 Anode uniformity / Cathode uniformity __________________________________________ 36
   5.2 Micro-channel-plate PMT / Multi-channel plate ______________________________________ 39

6 Coincidence detection and electronic collimation _______________________________________ 42
   6.1 Time pick-off methods ___________________________________________________________ 43
      6.1.1 Leading edge timing ______________________________________________________________________ 44
      6.1.2 Cross-over timing for bipolar pulses _____________________________________________ 44
      6.1.3 Constant-fraction discrimination for unipolar pulses __________________________________________________________________________ 45

7 Image reconstruction __________________________________________________________________ 46
   7.1 Error sources and correction mechanisms _____________________________________________ 50
      7.1.1 Attenuation correction ________________________________________________________ 50
      7.1.2 Correction for random coincidences ____________________________________________ 51
      7.1.3 Scatter correction ____________________________________________________________________ 52
      7.1.4 Dead-time correction __________________________________________________________________ 52
      7.1.5 Normalization _________________________________________________________________________ 53

8 Time of Flight - PET __________________________________________________________________ 55
   8.1 Introduction to time-of-flight ______________________________________________________ 55
   8.2 FBP based TOF reconstruction ______________________________________________________________________ 56

9 Depth of interaction - PET ____________________________________________________________ 58
   9.1 Introduction to depth-of-interaction ________________________________________________ 58
   9.2 Pulse shape discrimination ____________________________________________________________________ 59

10 Summary of included publications ____________________________________________________ 61
    Publication I ___________________________________________________________________________ 61
    Publication II __________________________________________________________________________ 61
    Publication III _________________________________________________________________________ 62
    Publication IV _________________________________________________________________________ 62
    Publication V __________________________________________________________________________ 63
    Publication VI _________________________________________________________________________ 64
    Publication VII _________________________________________________________________________ 66

11 Conclusion and outlook __________________________________________________________________ 67

12 Bibliography _________________________________________________________________________ 69

13 Copyrights __________________________________________________________________________ 77

14 Publications _________________________________________________________________________ 79
List of publications

Publication I
Current and Future Use of LSO:Ce Scintillators in PET

Publication II
Timing Performance of Hi-Rez Detector for Time-of-Flight (TOF) PET

Publication III
Performance Study of the new Hamamatsu R9779 & Photonis XP20D0 fast 2” Photomultipliers

Publication IV
Dynode-timing method for PET block-detectors
Publication V
Evaluation of a Micro-Channel Plate PMT in PET

Publication VI
Measurements and Ray-Tracing Simulations of Light Spread in LSO Crystals

Publication VII
Depth of interaction with a 3-dimensional checkerboard arrangement LSO-LSO block
## List of abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>APD</td>
<td>Avalanche photodiode</td>
</tr>
<tr>
<td>BGO</td>
<td>Bismuth Germanate</td>
</tr>
<tr>
<td>CFD</td>
<td>Constant fraction discriminator</td>
</tr>
<tr>
<td>CT</td>
<td>Computer tomography</td>
</tr>
<tr>
<td>CZT</td>
<td>CdZnTe – Cadmium Zinc Telluride</td>
</tr>
<tr>
<td>DOI</td>
<td>Depth-of-interaction</td>
</tr>
<tr>
<td>ER</td>
<td>Energy resolution</td>
</tr>
<tr>
<td>FBP</td>
<td>Filtered back projection</td>
</tr>
<tr>
<td>FDG</td>
<td>Fluoro-deoxy-glucose</td>
</tr>
<tr>
<td>FOV</td>
<td>Field-of-view</td>
</tr>
<tr>
<td>FWHM</td>
<td>Full width at half maximum</td>
</tr>
<tr>
<td>GSO</td>
<td>Gadolinium-orthosilicate</td>
</tr>
<tr>
<td>HV</td>
<td>High voltage</td>
</tr>
<tr>
<td>IR</td>
<td>Iterative reconstruction</td>
</tr>
<tr>
<td>LED</td>
<td>Light emitting diode</td>
</tr>
<tr>
<td>LIDAR</td>
<td>Light-Imaging Detection and Ranging</td>
</tr>
<tr>
<td>LO</td>
<td>Light output</td>
</tr>
<tr>
<td>LOR</td>
<td>Line of response</td>
</tr>
<tr>
<td>LSO</td>
<td>Lutetium oxyorthosilicate</td>
</tr>
<tr>
<td>MCA</td>
<td>Multi-channel analyzer</td>
</tr>
<tr>
<td>MCP</td>
<td>Micro-channel-plate</td>
</tr>
<tr>
<td>MLEM</td>
<td>Maximum-likelihood expectation maximization</td>
</tr>
<tr>
<td>MRT</td>
<td>Magnet resonance tomography</td>
</tr>
<tr>
<td>NaI</td>
<td>Sodium-iodide</td>
</tr>
<tr>
<td>NECR</td>
<td>Noise-equivalent-count-rate</td>
</tr>
<tr>
<td>NIM</td>
<td>Nuclear instrumentation modules</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>OSEM</td>
<td>Ordered subset expectation maximization</td>
</tr>
<tr>
<td>PET</td>
<td>Positron-emission tomography</td>
</tr>
<tr>
<td>PHD</td>
<td>Pulse height discrimination</td>
</tr>
<tr>
<td>PHR</td>
<td>Pulse height resolution</td>
</tr>
<tr>
<td>PMT</td>
<td>Photomultiplier tube</td>
</tr>
<tr>
<td>PSD</td>
<td>Pulse shape discrimination</td>
</tr>
<tr>
<td>QE</td>
<td>Quantum efficiency</td>
</tr>
<tr>
<td>SCA</td>
<td>Single-channel analyzer</td>
</tr>
<tr>
<td>SiPMT</td>
<td>Silicon photomultiplier</td>
</tr>
<tr>
<td>SPECT</td>
<td>Single photon emission tomography</td>
</tr>
<tr>
<td>TAC</td>
<td>Time-to-amplitude converter</td>
</tr>
<tr>
<td>TOF</td>
<td>Time-of-flight</td>
</tr>
<tr>
<td>TR</td>
<td>Timing resolution</td>
</tr>
<tr>
<td>VDN</td>
<td>Voltage-divider network</td>
</tr>
</tbody>
</table>
Sammanfattning


Avhandlingen handlar om hur man kan förbättra gamma-detektorn genom att ge den "time-of-flight" egenskaper (TOF), som i sin tur leder till ökad känslighet och med det bättre bildkvalitet, snabbar registrering och/eller lägre dos.

Bildkvaliteten har genom åren förbättrats, men detta har inte i samma utsträckning gällt bilder från överviktiga patienter, beroende på strålningsens attenuering och spridning i den större volymen. Instrumentens begränsningar är fortfarande signifikanta för överviktiga patienter, men användning av "time-of-flight" information kan minska dessa begränsningar.

För att förbättra tidsupplösningen har vi undersökt nya snabba fotomultiplikatorer och ett nytt sätt att extrahera tidsinformationen genom att använda en summerad dynodsignal.

När man bygger nya blockdetektorer för PET är det viktigt att förstå ljusfördeelnsmekanismen i kristallblocken och hur man kontrollerar faktorer som påverkar ljusnivån. Därför är det viktigt att utföra optiska simuleringar och kunna uppstålla en modell för en (LSO) blockdetektor.

En annan väg att förbättra bildkvaliteten är att detektera gamma-absorptionernas position i djupled, ”depth-of-interaction” (DOI). Det visas att en flerlager (”phoswich”) detektor bestående av LSO med olika avklingningstider och TOF egenskaper kombinerar fördelarna med TOF och DOI, och maximerar den effektiva känslighetsförbättringen.
Abstract

Nuclear medicine enables physicians to perform functional imaging of the human body. The perfusion and metabolism of various organs and cells can be visualized by administering different radiopharmaceuticals. Improving the sensitivity and resolution of these methods is of great value in research and in clinical practice.

The gamma-detector is the very first link in the chain of components that constitute a positron-emission-tomograph (PET). It converts incoming radiation into optical light pulses, which are detected by photo multiplier tubes, converting the light into electric pulses, to be further processed by the acquisition electronics. The detector, along with fast acquisition electronics and fast reconstruction algorithms, is one of the main columns of nuclear imaging.

The focus of this work is to improve the front-end of the entire system – to give it time-of-flight capabilities, in order to further improve sensitivity and therefore image quality and to lower the dose exposure for the patient.

Image quality has improved over the years and improvements have benefited all patient images. But losses in image quality have been reported for heavy patients, due to increased attenuation, and due to more dispersed counts over a larger volume. Instrumentation limits are still quite significant in heavy patient images. The incorporation of time-of-flight (TOF) information promises to alleviate these limitations. Time of flight PET (TOF-PET) offers several advantages, such as lower dose exposure (while keeping the same scan time as for the standard delivery of activity), or shorter patient scan times without the dose reduction and a significant decrease in image noise.

In order to improve the timing resolution of the detector we have investigated new, fast photo-multipliers and a novel scheme to extract the event timing trigger from a detector by using the summed dynode signal. With this method it was found possible to improve the timing-resolution by 43 ps, which represents a 10% improvement, compared to the standard timing of the anode. The fast photo-multiplier tubes were tested for their uniformity and their timing resolution. Both photomultiplier tube samples were found suitable for their application in detectors with TOF capability.

When designing new PET detector blocks, it is important to have a detailed understanding of the light sharing mechanisms in the crystal arrays
and to control the factors that influence the overall light output. It was therefore necessary to perform optical simulations and to derive a model for an LSO block detector, based on a series of single-crystal light output measurements. These measurements were designed to yield information on the LSO bulk properties, the coupling interfaces properties and the reflector properties.

TOF represents one path to enhanced image quality. Another route is to detect the depth-of-interaction (DOI) of a gamma ray within a detector. Commonly, different scintillator materials with different decay times, light output and other differentiating factors, such as density, emission spectra, etc. are used for DOI detectors. It was effectively shown that a multi-layer phoswich detector comprised of LSO with different decay times and TOF capability, combining the benefits of TOF and DOI in one detector, thus maximizing the effective sensitivity gain.
1 Introduction

1.1 Positron Emission Tomography

Positron-Emission Tomography (PET) is a modern imaging technique in nuclear medicine providing quantitative 3D distribution of a radioactive tracer substance in the human body. Biologically active pharmaceuticals are being marked with short-lived positron emitters. An intravenous injection delivers these radioactive pharmaceutical tracers to the patient. The substance spreads and interacts, via the normal metabolic processes of living cells, within the body thus providing functional maps of those cells in which the tracers were absorbed. PET and SPECT (defined below) allow in vivo visualization of the metabolism at a cellular level. Functional information may to some extent be provided from magnet resonance tomography (MRT), but not from imaging modalities such as computer tomography (CT), planar X-ray tomography and ultra-sound imaging. The later modalities are best suited for anatomical imaging. Functional Magnetic Resonance Imaging (F-MRI) – a special type of MR scan – provides functional information by measuring the change in blood flow. This is done without radiation exposure but with poor temporal resolution.

PET is based on the emission of positrons and their annihilation with electrons while emitting two collinear gamma quanta. Opposing detectors are connected through coincidence electronics. By identifying which detector pair was activated within a defined time window, the preceding annihilation event is confined to a tube shaped region. This “electronic collimation” allows acquisition of parallel projections along many different angles. These projections can be reconstructed into a patient image, by back projection or iterative reconstruction algorithms. The PET image represents the distributed in-vivo biological assay of the injected activity in the entire observed volume. The process is illustrated in Figure 1.

A number of bio-tracers such as $^{11}$C, $^{15}$O, $^{13}$N and $^{18}$F are available to image and provide functional information. Functional information about an injected tracer is usually derived from dynamic studies, where the uptake of the tracer in the tissue is recorded as a function of time. When combined with time dependent arterial plasma information as the model input function, quantitative functional information can be determined.
Given that the cellular metabolic function in a tumor changes before the tumor starts to grow, nuclear medicine enables the physician to detect cancer at an early stage, before anatomical changes can be seen on a CT or MRT scan. Nuclear imaging has come to represent an important tool for treatment planning and monitoring in the field of oncology.

Single photon emission tomography or SPECT is another modality in the field of nuclear imaging. Here collimators are used to provide the detector with directional discrimination. However, the collimator limits the SPECT sensitivity significantly compared to PET. The collimator only allows photons following given trajectories towards the detector.

Clinical PET imaging, almost exclusively performed with fluoro-deoxyglucose (FDG), is at present being used in three important areas of clinical diagnosis and management:

- Cancer diagnosis and management
- Cardiology and cardiac surgery
- Neurology and psychiatry.

An estimated 663,000 patient studies were performed using PET in Western Europe in 2008 [3]. These studies were performed by 399 providers using PET or PET/CT scanners. The majority of these studies were oncology studies, accounting for 94% of all PET studies in Europe. Less than 6% were cardiology studies. Neurological studies were mostly research related.
The idea to utilize time-of-flight information for positron-emission-tomography was proposed first in the 1960s (Anger 1966, Brownell et al 1969), but was quickly put aside due to the absence of fast scintillators, photo-multiplier tubes and electronics.

Time-of-flight PET experienced a renaissance in the 1980s, when the first systems were built with either CsF or BaF$_2$ (Ter-Pogossian et al 1982, Gariod et al 1982, Wong et al 1984, Lewellen et al 1988, Mazoyer et al 1990). Due to the available crystal material the early time-of-flight systems suffered from relatively low sensitivity compared to non-time-of-flight systems, which were based on BGO, having higher stopping power than CsF or BaF$_2$. Although the early time-of-flight systems delivered good timing resolution between 500 ps and 750 ps [4], they could not match the spatial resolution nor the sensitivity of BGO scanners, even with the effective gain in signal-to-noise ratio. Little attention has been paid to timing in PET since then due to the limitation of the slow BGO scintillators.

With the advent of LSO PET cameras, and the availability of new fast photo multiplier tubes and high speed electronics, efforts to improve PET by means of time-of-flight information have resumed.

1.2 Content overview

The first chapter of this thesis introduces positron emission tomography and gives some background information.

Chapter two briefly touches some fundamentals in nuclear physics, the basis of PET imaging physics.

The third chapter describes PET in general, focuses on the detector and describes the light-sharing principle.

Chapter four is dedicated to the scintillator, its properties and the special requirements for PET.

The photodetector, its working principle and its different manifestations are presented in chapter five.

The focus of the sixth chapter is on the electronics. Different trigger mechanisms and time pick-off methods are presented, to provide background information for the publications.

After the electronic pulses are digitized and preprocessed, the images are reconstructed. Different methods and correction steps are explained in chapter seven.

The time-of-flight method, which is the basis for publications II, III, V and VII, is addressed in chapter eight.

Another method to improve the sensitivity of a PET system – Depth-of-interaction – is explained in chapter nine, as background information for paper VII.

The different publications are presented in the appendix.
2 Nuclear Physics fundamentals

2.1 Beta decay

Beta particles are negatively or positively charged electrons that are emitted from the nucleus during a radioactive disintegration. The emitted beta particles have a continuous range of energies, up to a maximum value. In the case of electron emission, this process is referred to as "beta minus" ($\beta^-$) decay, while in the case of a positron emission it is called "beta plus" ($\beta^+$).

In $\beta^-$-decay, the weak interaction converts a neutron ($n$) into a proton ($p^+$) while emitting an electron ($e^-$) and an anti-neutrino ($\bar{\nu}_e$):

$$n \rightarrow p + e^- + \bar{\nu}_e \quad (1)$$

$\beta^-$-decay is energetically possible, if the mass of the daughter atom $M(A,Z+1)$ is less than the mass of its isobaric neighbor:

$$M(A,Z) > M(A,Z+1) \quad (2)$$

Here the mass of the entire atom is being considered, not just the mass of the nucleus. The rest-mass of the electron is also taken into account.

In the $\beta^+$-decay, a proton is converted into a neutron, a positron and a neutrino. Energetically, $\beta^+$-decay is possible when the following relationship between the masses of $M(A,Z)$ and $M(A,Z-1)$, the parent and daughter atoms respectively, is satisfied:

$$M(A,Z) > M(A,Z-1) + 2m_e \quad (3)$$

The creation of a positron and the existence of an excess electron in the parent atom are taken into account.
2.2 Positron Emitters

Positron emitters are nuclides whose nuclei contain a larger number of protons than stable isobars. $\beta^+$ decay only occurs inside nuclei when the value of the binding energy of the daughter nucleus is greater than that of the mother nucleus. The difference between these energies goes into the reaction of converting a proton into a neutron, a positron and a neutrino and kinetic energy. As the nuclides decay they emit a positron ($e^+$). One of the protons ($p$) in the nucleus converts into a neutron ($n$), which stays within the nucleus, while a positron ($e^+$ or $\beta^+$) and a neutrino ($\nu_e$) are emitted.

$$p \rightarrow n + e^+ + \nu_e$$  \hspace{1cm} (4)

The neutrino rarely interacts with matter and is therefore difficult (almost impossible) to detect. The positron is scattered by the surrounding atoms and loses its kinetic energy in those interactions. The positron interacts with surrounding nuclei as it is deflected from its original path by one of four types of interaction:

- **inelastic collisions** with atomic electrons, which is the predominant mechanism of loss of kinetic energy
- **elastic scattering** with atomic electrons, in which the positron is deflected, but energy and momentum are conserved
- **inelastic scattering** with a nucleus with deflection of the positron and often with the corresponding emission of Bremsstrahlung radiation
- **elastic scattering** with a nucleus in which the positron is deflected, but does not radiate any energy or transfer any energy to the nucleus.

When the positron has lost most of its kinetic energy it may either directly interact with an electron $e^-$ and annihilate or may enter into a short-lived hydrogen like state with the electron, positronium. The lifetime of the positronium is short ($\approx 10^{-10} \text{ s}$) [5] and the electron and positron annihilate into two gamma quanta. Due to the conservation of energy and momentum, the energy $E_\gamma$ of each of the two gamma quanta is 511 keV, with $m_e$ being the electron rest mass and $c$ being the speed of light.

$$E_\gamma = m_e \cdot c^2$$  \hspace{1cm} (5)

These two gamma quanta will be emitted in opposite directions, unless the annihilation occurs while the positron is still in motion, causing non-collinearity – a minute deviation from 180°. This holds true for most of the positron/electron annihilation, but there is a small possibility that not just
two but three quanta will be created. In this case the sum of the energy is still 1022 keV. The probability of a three quanta emission is small, and therefore does not have a significant effect on PET imaging. Figure 2 illustrates the positron emission and the following annihilation process.

![Diagram of nuclear reaction](image)

**Figure 2: Annihilation process**

2.3 Photon interactions

As photons pass through matter they interact with atoms. The type of interaction depends on the energy of the photons and the atomic number \( Z \) of the elements composing the matter. The energy range in the practice of nuclear medicine is between 50 keV and 550 keV, which is where Compton scattering is the dominant type of interaction in materials with low atomic numbers, such as human tissue \( (Z = 7.5) \). In materials with higher \( Z \), such as scintillator crystals \( (Z_{\text{eff}} = 66 \) for LSO) or lead \( (Z = 82) \) the photoelectric absorption is the dominating effect. Pair production only occurs with high photon energies above 1022 keV and is therefore not relevant in clinical nuclear medicine.

2.3.1 Compton scattering:

An incident photon interacts with an electron in the absorber material and transfers part of its energy, resulting in the creation of a recoil or Compton...
electron and a scattered gamma-ray photon. The energy of the two is divided depending on the scattering angle \( \Theta \) (Figure 3). The kinetic energy of the electron is increased while the photon changes direction and loses energy (frequency).

The energy of the scattered gamma-ray \( h\nu' \) in terms of the scattering angle \( \Theta \) is given by

\[
h\nu' = \frac{h\nu}{1 + \left( \frac{h\nu}{m_e} \right) (1 - \cos \Theta)}
\]

(6)

with \( m_e = m_0c^2 = 511 keV \) being the rest mass of the electron [6]. The energy of the Compton electron is therefore

\[
E_{e'} = h\nu - h\nu'
\]

(7)

2.3.2 Photoelectric absorption:

A low energy photon that has lost most of its energy through Compton interactions will eventually be absorbed by an atom. During the process an electron is ejected from one of its bound shells (Figure 4). The energy of the photoelectron \( E_{pe} \) is given by

\[
E_{pe} = E_p - E_b
\]

(8)

with \( E_p (=h\nu) \) being the photon energy and \( E_b \) the binding energy of the electron. The vacancy created by the ejected electron is filled by an electron from another shell, liberating the binding energy in form of an x-ray or an Auger electron [6].

The probability of photoelectric absorption increases rapidly with increasing atomic number of the absorber atom \((\sim Z^3)\), and decreases rapidly with increasing photon energy.
2.4 Radionuclides for PET

The nuclides used for PET scans are all positron emitters. The most commonly used radionuclides are produced in cyclotrons and listed in Table 1.

Table 1: List of most commonly used radionuclides in PET [7, 8]

<table>
<thead>
<tr>
<th>Radio-isotope</th>
<th>( E_{\beta_{\text{max}}} , [\text{MeV}] )</th>
<th>( t_{\frac{1}{2}} )</th>
<th>Daughter nuclei</th>
<th>Range in ( H_2O , [\text{mm}] )</th>
</tr>
</thead>
<tbody>
<tr>
<td>(^{11}\text{C} )</td>
<td>0.961</td>
<td>20.4 min</td>
<td>(^{11}\text{B} )</td>
<td>1.1</td>
</tr>
<tr>
<td>(^{13}\text{N} )</td>
<td>1.190</td>
<td>9.96 min</td>
<td>(^{13}\text{C} )</td>
<td>1.5</td>
</tr>
<tr>
<td>(^{15}\text{O} )</td>
<td>1.723</td>
<td>122.2 sec</td>
<td>(^{15}\text{N} )</td>
<td>2.5</td>
</tr>
<tr>
<td>(^{18}\text{F} )</td>
<td>0.635</td>
<td>110 min</td>
<td>(^{18}\text{O} )</td>
<td>0.6</td>
</tr>
<tr>
<td>(^{68}\text{Ga} ) (*)</td>
<td>1.89</td>
<td>68.3 min</td>
<td>(^{68}\text{Zn} )</td>
<td>2.9</td>
</tr>
<tr>
<td>(^{82}\text{Rb} ) (*)</td>
<td>3.35</td>
<td>1.25 min</td>
<td>(^{82}\text{Kr} )</td>
<td>5.9</td>
</tr>
</tbody>
</table>

* isotopes produced in a generator

Isotopic forms of Carbon, Nitrogen, Oxygen, Fluorine, Gadolinium and Rubidium permit incorporation of positron emitters into many biologically active compounds. This allows images of specific physiologic characteristics of an organ, like oxygen uptake or glucose metabolism. Other impure positron emitters, such as \(^{124}\text{I} \) an \(^{86}\text{Y} \) are also being investigated, primarily for radio-immunotherapy."[4] For applications that require longer half-lives in radionuclide therapy, \(^{76}\text{Br} \), \(^{52}\text{Fe} \), \(^{110m}\text{In} \) and \(^{134}\text{La} \) were studied as well [9]. A drawback when using these nuclides is the complication of quantitative PET due to the emission of gamma radiation in cascade with positrons, causing an increase in background radiation.
The short half-lives of $^{15}\text{O}$, $^{13}\text{N}$ and $^{11}\text{C}$ pose an obstacle for widespread clinical application on a large scale, since they require an on-site cyclotron and a rapid conversion from isotope to radiopharmaceutical. Due to these reasons, $^{18}\text{F}$ is a more convenient choice. It is, in fact, the established radionuclide for clinical PET, due to its good availability, ease of production and suitable half-life. Figure 5 shows the glucose (FDG) uptake in a human brain.

The high glucose metabolism of most tumors makes FDG a perfect tracer for oncology. Although its uptake is relatively unspecific, PET provides diagnostic results of high sensitivity and specificity.

Another attractive property of $^{18}\text{F}$ is its low $E_{\text{max}}$. This means that the difference between the measured positron annihilation distribution and the desired positron emission distribution is small (due to the short positron range). The non-collinearity is also reduced, improving the precision.

A list of common PET-radiopharmaceuticals and their physiologic application is given in Table 2.

---

Figure 5: Cerebral glucose metabolism [Biograph PET-CT] – 28 year old female with brain tumor diagnosed, presenting with speech difficulties and a seizure. **Image Findings:** large area of hypometabolism in left posterior temporal lobe. **Scan Protocol:** CT 130 kVp, 5 mm slices; PET 300 MBq FDG, 30 min p.i, 10 min scan time.
Table 2: Example of available PET-radiopharmaceuticals

<table>
<thead>
<tr>
<th>Radiopharmaceuticals</th>
<th>Physiologic imaging application</th>
</tr>
</thead>
<tbody>
<tr>
<td>[^{18}\text{F}]-fluorodeoxyglucose (FDG)</td>
<td>Cerebral and myocardial glucose metabolism and tumor localization</td>
</tr>
<tr>
<td>[^{15}\text{O}]_2</td>
<td>(Cerebral) oxygen metabolism and oxygen extraction</td>
</tr>
<tr>
<td>H_2 [^{15}\text{O}]</td>
<td>(Cerebral and myocardial) blood flow</td>
</tr>
<tr>
<td>C [^{15}\text{O}]</td>
<td>(Cerebral and myocardial) blood volume</td>
</tr>
<tr>
<td>[^{11}\text{C}]-N-methylspiperone</td>
<td>Cerebral dopamine receptor binding</td>
</tr>
<tr>
<td>[^{13}\text{N}]H_3</td>
<td>Myocardial blood flow</td>
</tr>
<tr>
<td>[^{11}\text{C}]-acetate</td>
<td>Myocardial metabolism</td>
</tr>
<tr>
<td>[^{82}\text{Rb}]Cl</td>
<td>Myocardial blood flow</td>
</tr>
</tbody>
</table>
3 State of the art PET-scanners

Conventional PET scanners are based on a circular configuration of the detectors around the patient. The detector ring is either fully or partially populated. In fully populated systems the rotation of the detector ring is seldom required, whereas it is a requirement for systems built of incomplete ring segments. The axial field-of-view (FOV) varies between 15 cm and 20 cm, the trans-axial FOV varies between 55 cm and 70 cm, depending on make and brand of the scanner. During an examination, the patient is moved along the scanner axis through the FOV. A whole body scan is taken in multiple steps, i.e. bed positions.

Early PET scanners had only a single ring of detectors. The acquisition of data and subsequent reconstruction was restricted to a single transverse plane (2D-reconstruction). State of the art scanners include multiple rings, essentially forming a cylinder of detectors, allowing coincidence events to be detected between all the rings as well as within rings.

3.1 The detector

In conventional PET systems detection of the two gamma quanta is achieved by scintillators which convert the radiation into light, and photomultipliers (PMT) which convert the light into electric pulses. The conversion of ionizing radiation into light pulses is called scintillation. Due to the fairly high energy of the gamma quanta – 511 keV– the scintillation crystals should be as dense as possible.

Early PET systems used Sodium-Iodide (NaI(Tl)) as scintillation material. Its relatively low density makes it less effective at stopping the high-energy 511-keV photons and its hygroscopic properties made handling complicated. Other types of crystals have since been developed for 511-keV imaging. They have higher densities and generally shorter decay times than NaI(Tl). Decay time is the time required for the radiation-excited atoms of the crystal lattice to return to their ground state (unexcited) with the emission of light photons. A shorter decay time is especially desirable for reducing the detector dead times and hence the system dead time.
Bismuth Germanate (BGO) proved to be a better scintillator than NaI(Tl), due to its higher stopping power (short mean free path length), i.e. its strong attenuation of 511 keV photons. BGO has a time resolution around ~ 6 ns full width at half maximum (FWHM) [10]. However, its long decay time (~300 ns) limits the count rate performance of PET scanners due to dead time issues and its low relative light output limits design options.

Gadolinium-orthosilicate (GSO) is also being used and investigated as scintillator for PET detector applications [11-14]. In recent years Lutetium oxyorthosilicate (LSO) has become the scintillator of choice, due to a higher light output, and significantly shorter decay time. LSO offers nearly the same stopping power as BGO, with the added benefit of a much shorter decay time and a 3-4 times higher light output.

Most PET systems use multiple PMTs coupled to the scintillator deriving the interaction position from their light distribution. A basic light sharing detector for gamma ray detection is made of four photomultiplier tubes, attached to the back of a scintillator crystal block [15]. By analyzing the weighted distribution of the light impinging on the four PMTs, it is possible to identify the pixel in which the gamma quantum is absorbed. The scintillator block is cut in a pattern at different depths to subdivide the scintillator into individual pixels, and to achieve optimal light distribution to the PMTs underneath. Newer detectors are completely pixelated, which means that the scintillator is fully cut into individual pixels with special reflective material taped on each side of the pixel, whereas in older systems the grooves are filled with white reflective powder. With the fully pixilated detector, it is necessary to place a light guide between the scintillator and the PMTs, which allows a certain amount of light-sharing. The slits between crystal subdivisions channel the low-energy scintillation photons through the light-guide toward the PMTs. The crystal is cut in such way that the PMTs and their associated electronics can determine the location where the photons entered the crystal (Figure 6). Figure 7 is a photograph of a detector block: a 13 x 13 LSO pixel matrix with a solid light-guide underneath. Localization of the site of interaction is achieved by measuring the light detected in each PMT; the closer the PMT is to the site of interaction, the stronger the signal generated by the PMT. This is referred to as Anger-logic [16]. Figure 8 shows photographs of a 13x13 pixel matrix on a light-guide, which is excited with a red LASER in different positions. The spreading of the light referred to as “light-sharing” is well visible. The reflector material on the sides of the individual pixels steer the distribution of the light. The size and thickness of the scintillation crystals (pixels) influence the sensitivity and spatial resolution of a scanner.

The weighted read-out of a block detector significantly reduces the necessary amount of read-out electronics compared to a one-to-one readout ratio. One problem of block detectors is that an event paralyzes the detector during the decay time of the crystal, before the next event can be processed. If two
gamma quanta hit the detector within a short time frame, and the first event is not processed, an exact localization of the second event is not possible. This effect is called “pile-up” and becomes worse with longer scintillator decay time and higher count rate. The pile-up effect is dependent on the activity applied to the patient.

50 – 60 mCi are a commonly applied activity of short-lived isotopes like $^{15}$O. The applied activity during an FDG scan ranges between 5 mCi to 12 mCi, depending on the weight of the patient.

![Figure 6: pixelated 13x13 detector block with 4 PMTs (A, B, C, D); left: view from top, right: side view on the detector](image)

![Figure 7: 13x13 LSO matrix with light guide](image)
The signals of four PMTs (A, B, C, D) from one detector (Figure 6) are summed (9), resulting in the total energy $E$. The x- and y-position of an event within the detector are computed with (10) and (11).

\[
E = A + B + C + D \tag{9}
\]

\[
X = \frac{(C + D)}{E} \tag{10}
\]

\[
Y = \frac{(B + D)}{E} \tag{11}
\]

Figure 9 shows a shielded detector assembly of four PMTs, and a properly prepared scintillator crystal.

Other detector designs are based on a continuous light guide [17] or multiple panel detectors [18, 19].
3.2 The parallax error

PET detector development is driven by the need for high sensitivity and improved spatial resolution. Since these two needs compete with one another, detector development is mostly an optimization process between the two parameters. Usually narrow and deep (long) scintillator crystals are used; however, this geometry results in degraded spatial resolution. This effect, known as parallax error or radial elongation, increases the uncertainty in the reconstructed location of the source; Thus producing a significantly elongated radial resolution. It is caused by the uncertainty of the location of the line-of-response (LOR) end-points between the crystals of two adjacent detectors. Photon penetration into the neighboring detectors of circular tomographs blurs PET images near the edge of the field of view.

The parallax error becomes more dominant as the source or annihilation point move outward from the isocenter of the detector ring, as shown in Figure 10. The parallax error is dominated by three factors: the diameter of the detector ring, its ratio to the diameter of the FOV and the depth (length) of the scintillator. Typically, annihilation points located at large radial distances from the scanners central axis, suffer from this parallax blurring.

Figure 10: Principle of the parallax effect: coincidence line and LOR of source a) are identical; coincidence lines of the two sources b) and c) would be assigned to the same LOR (--- -). With a three layer phoswich detector both LORs from b) and c) are located correctly (red and grey block).
4 Inorganic Scintillators for detection of gamma radiation

High energy physics and nuclear medicine use inorganic scintillator crystals with a high density and high effective atomic number \((Z_{\text{eff}})\), to efficiently detect ionizing radiation.

Semiconductor direct conversion detectors, such as a CdZnTe-detector (CZT) – so far – only play a role in the detection of fairly low energy gamma rays [20]. For the detection of 511 keV photons in PET imaging semiconductor detectors only play a subsidiary role, due to their low atomic number (~ 50) and low stopping power.

Among the diversity of the different scintillators, are several that match the requirements of PET imaging. The crucial parameters for PET are sufficient stopping power for 511 keV photons, short decay time, appropriate emission wavelength, high light output, and high intrinsic energy resolution.

4.1 Scintillation process in crystals

In general the scintillation process is the conversion of the energy of an incident gamma quant or particle into many light photons.

The scintillation process is a sequence of the following steps [21]:
1. Absorption of the ionizing radiation causing the creation of primary electrons and holes [Relaxation of the primary electrons and holes, causing production of secondary electrons, holes, photons \(\rightarrow\) Thermalization of low-energy secondary photons and other electronic excitations]
2. Energy transfer from the electron-hole pairs to luminescence centers and their excitation
3. Emission from luminescence centers.

In inorganic materials the scintillation mechanism depends on the energy states determined by the crystal lattice of the material. In doped crystals the scintillation mechanism depends on the activator and the energy states. In materials classified as insulators or semiconductors, only discrete energy bands are available to electrons. The width of the bands depends on interactions between atoms and ions in the lattice.
The last filled band is the valence band, in which the electrons are essentially bound to lattice sites. The first unfilled band is the conduction band, in which the electrons have enough energy to migrate throughout the crystal, exemplified in Figure 11. The intermediate band of energies – the forbidden band – is not allowed to be populated with electrons. Electrons in the valence band can absorb energy by interaction of the photo electron or Compton scatter electron with an atom. This results in the elevation of an electron from its ground state in the valence band across the band gap (EG) into the conduction band, leaving a hole in the normally filled valence band.

In a radiative transition, the electron returns to its ground state by releasing scintillation photons. Typical band gap widths are such that the resulting photon would be of such high energy that the emission is in the ultraviolet. To shift the emission wavelength in the visible range, which is more suited for the detection with PMTs, minute amounts of impurities called activators are added to a pure crystal, e.g. Thallium to pure Sodium-iodide (NaI:Tl), or Cerium to Lutetium oxyorthosilicate (LSO:Ce). Energy states within the forbidden band are created through which the electron can de-excite back to the valence band. An activator slightly raises the ground state above the valence band (Activator ground states) and lowers the activated states slightly below the conduction band (activator states – excited). The band gap has become narrower, so the energy difference is less than that of the full band gap and the de-excitation produces visible photons. The de-excitation sites are called luminescence or recombination centers.

![Figure 11: Scintillation process in the energy-band scheme of a scintillator crystal](image)

**4.2 Scintillator Properties**

A large number of different scintillation crystals exist for a variety of applications. Some important characteristics of scintillators used for PET are:

- Density and effective atomic number ($Z_{eff}$)
- Light output
4 Inorganic Scintillators for detection of gamma radiation

- Decay time
- Afterglow
- Optical properties
- Mechanical properties and cost

4.2.1 Density and effective Atomic number ($Z_{\text{eff}}$)

For efficient detection of gamma-rays, a material with a high density and high effective atomic number ($Z_{\text{eff}}$) is required. Materials of high density and high atomic number absorb the total energy of the gamma quanta more efficiently in a small volume, which allows the use of small scintillators, improving the spatial resolution of PET scanners. Inorganic scintillation crystals meet the requirements of high stopping power and optical transparency. Their densities ranging from $\sim 3 \text{ g/cm}^3$ to $9 \text{ g/cm}^3$ make them suitable to absorb gamma-rays. The density depends on the composition of the crystal and the crystalline structure.

4.2.2 Light output

Light output ($LO$) is a measure of how many photons ($N_{\text{ph}}$) are emitted from the scintillator per unit of absorbed energy ($E$), usually 1 MeV: $LO = \frac{N_{\text{ph}}}{E}$.

The number of photons reaching the photon detector depends on the following factors: crystal geometry, optical coupling, surface finish and reflector material around the scintillator. A crystal on a fairly small detector with a geometry much more long than wide significantly reduces the amount of photons impinging on the detector. The reflector material and the surface finish of the scintillator are very important, due to the isotropic distribution of the photons and the fact that most conversions occur in the upper part of the crystal. Since photoelectron statistics (or electron-hole pair statistics) play a key role in the accurate determination of the energy of the radiation, the use of scintillation materials with a high light output is preferred. The scintillator emission wavelength should be matched to the sensitivity of the photon detector.

4.2.3 Decay time

Scintillation light pulses are characterized by a fast increase of the intensity in time (pulse rise time) followed by an exponential decrease of the emission intensity.
The decay time of a scintillator is defined by the time after which the intensity of the light pulse has returned to $1/e$ of its maximum value. Most scintillators are characterized by more than one decay time and usually, the effective average decay time is mentioned. A typical example of a scintillator with well separated fast and slow components of the decay time is BaF$_2$. The decay time increases with wavelength [21], which is why ultraviolet emitting crystals tend to be fast, like e.g. BaF$_2$.

For PET, the ideal is a short decay time. This is especially true for high count rate applications, in order to collect all light quanta in a short time frame, contributing to the amplitude of the electric detector signal.

A short decay time is advantageous in most scintillator applications. One exception poses the phoswich detector, in which two scintillators are used [13, 22, 23] (Publication VII). One of which must have an appreciably slower decay time than the other, allowing crystal identification.

### 4.2.4 Afterglow

Afterglow is defined as the fraction of scintillation light still present for a certain time after the gamma absorption. A long-time luminescence of more than several microseconds up to hours or even days can occur. The origin of afterglow is phosphorescence caused by the release of carriers from the traps. Traps are formed by impurities and defects existing in the crystal, or created by radiation. The long duration afterglow can be a problem especially for high count rate applications. At high count rates phosphorescence tends to build up, caused by the overlap of many preceding pulses.

The purity of the raw material, crystal growth conditions, heat treatment and the activity dose influence the wavelength, decay time and afterglow characteristics of a scintillator.

### 4.2.5 Optical properties

The index of refraction of the scintillator is an optical characteristic that needs to be taken into account when selecting a photo sensor. The optical matching of scintillator and sensor is required; otherwise, part of the light will be reflected at the scintillator-detector interface and not be detected. Usually an optical silicone based compound is used to couple and match the photo detector to the scintillator.
4.2.6 Mechanical properties and cost

For use in PET the scintillator needs to be cut and finished in order to fit in a detector assembly. Ideally the crystal is mechanically stable, rigid and chemically inert, but easy to shape and process. Some scintillator crystals may easily crack or cleave under mechanical pressure, causing difficulties during processing, whereas others, like e.g. CsI, are more plastic and deform. Cleaving causes the material to break and crack along its natural cleavage planes. A typical example is GSO. The surfaces of the crystal may be polished for a specular reflection or roughened for a diffuse reflection.

Certain scintillation crystals are hygroscopic, like e.g. NaI(Tl) – the scintillator used in early PET systems. It has to be hermetically sealed in order to preserve its properties, which makes handling and processing more difficult, thus time consuming and costly. CsI and LaBr are other hygroscopic scintillators.

Due to the ingredients of some scintillators, they may exhibit natural radioactivity. This requires special safety measures while machining the material and also causes an increased background level in the measurements. One has to evaluate whether the increased background level disturbs the outcome of measurements. Another important factor for scintillators used in PET is their large scale manufacturability. A scintillator may have perfect properties while not allowing growth of large boules, thus making it unsuitable for production.

Table 3 gives an overview of different scintillators and individual properties. The choice of scintillator material requires a compromise among factors like, density, stopping power, sufficient atomic number, decay time, light yield and cost.
Table 3: Properties of scintillators used for PET imaging [8, 21, 24]

<table>
<thead>
<tr>
<th>Scintillator</th>
<th>Density [g/cm$^2$]</th>
<th>$Z_{eff}$</th>
<th>Decay time</th>
<th>Light yield relative to NaI(Tl)</th>
<th>Light output</th>
<th>Wave length</th>
<th>Attenuation length (511 keV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$BaF_2$ (Barium-fluoride)</td>
<td>4.88</td>
<td>54</td>
<td>0.8 (25%) 630 (75%)</td>
<td>5 (fast) 16-20 (slow)</td>
<td>2500 (fast) 6500 (slow)</td>
<td>220 (fast) 310 (main)</td>
<td>~ 2.0</td>
</tr>
<tr>
<td>$BGO$ (Bismuth Germanate)</td>
<td>7.13</td>
<td>75</td>
<td>300</td>
<td>14</td>
<td>9000</td>
<td>480</td>
<td>1.05</td>
</tr>
<tr>
<td>$CsF$ (Cesium-fluoride)</td>
<td>4.64</td>
<td>53</td>
<td>3</td>
<td>8</td>
<td>2000 2500</td>
<td>390</td>
<td>2.69</td>
</tr>
<tr>
<td>$CsI(Tl)$ (Cesium-iodide)</td>
<td>4.51</td>
<td>52</td>
<td>1000</td>
<td>45 85</td>
<td>52,000 -59,000</td>
<td>540</td>
<td>2.43</td>
</tr>
<tr>
<td>$GSO$ (Gadolinium-orthosilicate)</td>
<td>6.71</td>
<td>59</td>
<td>60 600</td>
<td>20</td>
<td>8,000 -10,000</td>
<td>440</td>
<td>1.43</td>
</tr>
<tr>
<td>$LaBr$ (Lanthanum-bromide)</td>
<td>5.29</td>
<td>46.9</td>
<td>35</td>
<td></td>
<td>61,000</td>
<td>358 -387</td>
<td></td>
</tr>
<tr>
<td>$LSO$ (Lutetium oxyorthosilicate)</td>
<td>7.40</td>
<td>66</td>
<td>40</td>
<td>75</td>
<td>29,000</td>
<td>420</td>
<td>1.14</td>
</tr>
<tr>
<td>$LuAp$</td>
<td>8.34</td>
<td>64.9</td>
<td>18</td>
<td></td>
<td>17,000</td>
<td>360</td>
<td>1.1</td>
</tr>
<tr>
<td>$NaI(Tl)$ (Sodium-iodide)</td>
<td>3.67</td>
<td>51</td>
<td>230</td>
<td><strong>100</strong></td>
<td>38,000</td>
<td>415</td>
<td>2.56 3.05</td>
</tr>
<tr>
<td>$YAP$</td>
<td>5.37</td>
<td>5.55</td>
<td>30 / 10,000</td>
<td>40-50</td>
<td>18,000</td>
<td>370</td>
<td>5.55</td>
</tr>
<tr>
<td>$YSO$ (Yttrium-orthosilicate)</td>
<td>4.53</td>
<td>35</td>
<td>β 70; γ 82</td>
<td>26</td>
<td>10,000</td>
<td>420</td>
<td>2.58</td>
</tr>
<tr>
<td>EJ-200 Plastic *)</td>
<td>1.032</td>
<td>2.1</td>
<td></td>
<td></td>
<td>10,000</td>
<td>425</td>
<td></td>
</tr>
</tbody>
</table>

*) EJ-200 Plastic scintillator is used as reference for fast timing measurements
/ no reference values found
Photodetectors or light sensors can be generally classified by their operating principle in three major categories:

- external photoelectric effect,
- internal photoelectric effect and
- thermal photodetectors

The external photoelectric effect is a phenomenon in which electrons are emitted into a vacuum from the surface of a metal or a semiconductor, placed in an evacuated tube.

Photomultiplier tubes fall into this category and use the external photoelectric effect. They are superior in low-level light detection and response time. They represent the oldest and most reliable technique to measure low light levels, thus are widely used in medical equipment like PET and SPECT, analytical instruments and industrial measurement systems. A special representative of this group is the microchannel-plate PMT, which will be introduced in chapter 4.3, due to its outstanding timing resolution.

Solid-state light sensors, which can be subdivided in photoconductive and photovoltaic types, are based on the internal photoelectric effect. Photoelectrons are excited into the conduction band of a material. Photoconductive cells or photo resistors fall in the first group and are only mentioned for completeness, since they are not used in PET.

Photodiodes on the other hand, such as avalanche photodiodes (APDs), PIN-diodes and Silicon photomultipliers (SiPMTs), fall in the category of photovoltaic types. These types are becoming more and more important for PET. Up to now, their slow time response and – compared to PMTs – poor timing resolution made these photo detectors unsuitable for time-of-flight-PET. Grazioso [25] reported a timing resolution, of an APD with a 4mm x 4mm x 10mm LSO pixel in coincidence with a plastic scintillator coupled to a PMT, of 870 ps FWHM. SiPMTs on the other hand exhibit good timing resolution. Seifert [26] presented Si-PMT timing measurements at the 2009 IEEE Nuclear Science Symposium and Medical Imaging Conference, for LaBr and LYSO, with a timing resolution of 100 ps and 172 ps, respectively.

Thermal photodetectors do not depend on the wavelength of the light. At room temperature their sensitivity is low. Therefore, these devices are used
as temperature sensors, fire alarms and intrusion alarms. However, when cooled to temperatures below 1K the so called “Bolometer” is very sensitive. For the sub-millimeter wavelength range it is the most sensitive detector. Bolometers are used in astronomy and particle physics, and are directly sensitive to the energy deposited in the absorber. They can be used not only for ionizing particles and photons, but also for non-ionizing particles, for any sort of radiation. Due to their limitations, this type of detector is not used for PET applications.

In this section we will concentrate on photo detectors that are of relevance for Time-of-flight PET.

5.1 Photomultiplier Tubes

A photomultiplier tube is a vacuum tube with an entrance window (faceplate) coated with a thin photocathode layer and an electron multiplier, sealed in an evacuated glass tube. Figure 12 shows the drawing of a PMT and Figure 13 relates the drawing to a photograph of a PMT with its structures and labeled components.

An incoming scintillation photon enters the photomultiplier tube through the faceplate, deposits its energy in the photocathode, and excites the electrons in the photocathode coating. Depending on its energy, the photoelectrons can escape the surface potential, such that they are emitted into the vacuum (photoelectric effect). Under the presence of an electric field, the photoelectrons are accelerated and focused by the focusing electrode onto the first dynode, which is at a positive potential with respect to the photocathode. On impact onto the first dynode the photoelectrons are multiplied by means of secondary electron emission. This secondary emission is repeated at each of the following dynodes (stages), along an increasing potential cascade, resulting in a typical gain of $\sim 10^6$ for PET applications at the anode and last dynode [27] (Publication IV). The gain varies with high-voltage and the number of stages.

Head-on plano-plano or plano-concave photomultiplier tubes, as displayed in Figure 12 and Figure 13, with a multi-alkali photocathode and glass window, are most frequently used in PET applications.
5.1.1 Important performance parameters

There are several parameters that characterize the performance of photomultipliers, some general and some more specific and relevant for specialized uses.

*Energy resolution* is conventionally defined as the full width at half maximum (FWHM) divided by the location of the photo peak centroid. It is conventionally a dimensionless and unit-less number, expressed as a percentage. Energy resolution indicates the relation of the light output to the energy level of the entering gamma ray, and it usually varies with the energy.

*Quantum efficiency (QE)* is defined as the percentage of photons hitting a photosensitive surface that will produce an electron–hole pair. It is a measurement of the device's sensitivity. It is commonly measured at different wavelengths, in order to characterize a device's efficiency at each energy.
This characteristic, used to express the cathode sensitivity, is the ratio (12) of the number of photoelectrons emitted \( (n_{PE}) \) to the number of incident photons \( (n_P) \) hitting the photosensitive surface. It is usually specified for monochromatic light (light with a specific wave length). The wavelength is given by the scintillator. In most investigations for this thesis LSO was used, with a peak emission wavelength of \( \lambda = 420 \text{ nm} \). A typical QE value for PMTs used in PET is \(~27\%\) at peak. Special PMTs with a QE of \(~43\%\) \cite{28} are used in research systems as well \cite{29}.

\[
QE = \frac{n_{PE}}{n_P}
\]  

(12)

**Transit time** is the time interval between when a light pulse strikes the photocathode and when the corresponding current pulse is measured at the anode. The transit time varies depending on where the photocathode is illuminated \cite{30}. The transit time is inversely proportional to the square root of the supply voltage \cite{31, 32}. In PMTs with discrete dynodes, transit time widens due to the fact that the emission angle of the secondary electrons from the dynodes has a wide distribution.

Once the photoelectrons are emitted into the vacuum, they need to be focused on the first dynode by the electron-optical input system, which is done in some PMTs by a focusing electrode (Figure 12). Regardless of the initial velocity and of the point of origin on the photocathode, the maximum number of photoelectrons needs to be steered towards the first dynode with minimum variation in transit time. Transit time variations originate from differences in path length from different points on the cathode to the first dynode. These effects can be minimized by an increase of the electric field strength at the cathode surface. Minimum variation in transit time is especially important for fast-response PMTs. For that reason a higher voltage is often applied between the first two or three dynodes.

**Timing resolution** is defined as the FWHM of the probability distribution of the transit time fluctuations \cite{31, 32}.

**Dark current** flows in a PMT, even when operated completely in the dark. This current should be as small as possible, since it sets the limit for low level light detection. Dark current is caused by leakage currents between the anode and other electrodes inside the tube, thermionic emission from the photocathode and dynodes, environmental gamma rays and scintillation of the glass envelope.
5.1.2 PMT types

There are many different types of PMTs. They vary in mechanical structure and material, depending on their purpose. The dynode subassembly of a PMT is the section where the electrons are multiplied by means of secondary emission. The number of electrons increases from dynode to dynode along the cascading voltage. The dynode materials feature high secondary emission coefficients, such as insulators and semiconductors. Since the materials used for the dynode structure (AgMg, CuBe and NiAl) do not have sufficient secondary emission coefficients, they are coated with oxides like MgO, BeO and Al$_2$O$_3$ [33].

A variety of dynode structures are available, each featuring different time response, uniformity, current amplification and secondary-electron collection efficiency, depending on the structure and number of stages. An overview of the different types is given in Figure 14.

Figure 14: Dynode configurations: (a) venetian blind, (b) box, (c) linear focusing, (d) circular cage, (e) mesh and (f) foil [34]
The *venetian blind* type (Figure 14 a) is built of parallel strips, which are angled towards the PMT’s axis and stacked parallel to the cathode. It is suited for large diameter head-on PMTs.

*The box dynode* type (Figure 14 b) is widely used in head-on PMTs and features superior photo-electron collection efficiency and good uniformity at the cost of poor timing characteristics.

*Linear focusing dynodes* (Figure 14 c) are widely used in head-on PMTs. The design features progressive focusing of the electron paths through the multiplier stages, reducing the transit time variation between stages. This ensures fast timing response and requires well focusing input electron-optics on the first dynode. Therefore, the first dynodes are shaped and arranged differently than the later stages. Due to the linear arrangement, the focused dynodes and the highly focused input electron-optics this type is very sensitive to magnetic fields.

*Circular cage dynodes* (Figure 14 d) allow for a compact design, which is used in all side-on PMTs and some head-on types. Due to its compactness this design also features fast timing response.

*Mesh dynodes* (Figure 14 e) consist of parallel mesh planes of thin wire. Their collection efficiency from dynode to dynode is low. Two types exist: coarse and fine mesh types, both with excellent output linearity. They are very unsusceptible to magnetic fields of up to 1T, although the gain is reduced in fields of this magnitude. Position sensitive models exist, which comprise a cross wire or multi-anode. This type is also used in position sensitive multi-channel tubes, but at the cost of introduced cross-talk.

*Foil dynodes* (Figure 14 f) are built out of perforated metal foils with defined apertures. Their collection area is large and collection efficiency from dynode to dynode is comparable to that of venetian blind dynodes. They are also fairly unsusceptible to millitesla-level magnetic fields.

In a conventional PMT the spatial information about the light signal is lost. By using special cathode and dynode configurations retaining spatial information, it is possible to create position sensitive PMTs. The low crosstalk of foil dynodes allows them to be used in position sensitive multi-channel tubes in which all signals are read in parallel. Models with different sizes and spatial resolutions i.e. number of anodes are available. Multi-/ Micro channel plate PMTs (see Chapter 5.2) belong to the group of position sensitive PMTs.
5.1.3 The voltage-divider-network

Operating a photomultiplier tube requires a stable source of high voltage (usually in the range of one to two kV), and a voltage-divider-network or bleeder circuit that distributes an optimum voltage to each dynode.

The voltage divider network divides the high voltage and distributes voltage to each dynode independently to provide a proper voltage gradient between each dynode. PMTs can be operated with either negative or positive high voltage (HV). Figure 15 shows typical voltage divider networks, for positive and negative high voltage.

In case of positive HV, the cathode is at ground potential and the anode at high potential. Therefore, no additional insulation is required. Magnetic shields and additional screens are also tied to ground. Operation with positive HV requires the use of a coupling capacitor at the anode, in order to protect the signal processing equipment from high voltage. At high count rates this coupling capacitor can cause base-line shift, not allowing the base line to return to its true zero level, which must be compensated for with additional circuitry.

If negative HV is applied, the cathode is at high negative potential and the anode at ground potential. The glass envelope is therefore at negative high potential, requiring insulation if the PMT is operated close to metal parts, as it is in a block detector. Negative HV is required for continuous flux measurements, since DC components of the signal cannot pass the coupling capacitor required for positive HV. The use of negative HV does not require a
baseline restoration circuit, which reduces the complexity of the measuring circuit and improves performance. If lime glass is used for the face plate negative HV causes a strong voltage gradient across the glass, which degrades, and eventually destroys the device. PMTs with quartz glass face plates do not exhibit this problem. The use of positive HV allows both types of PMT’s to be used. Lime glass units tend to be cheaper to produce.

The voltage divider network is adapted for each PMT type individually and depends on the performance requirements, such as gain, linearity, timing, stability, etc.

The gain of a typical photomultiplier tube is extremely high ($\sim 10^3 - 10^7$) compared to a transistor amplifier ($\sim 20 - 200$). The noise of a PMT is very low, but it is very sensitive to variations in the high voltage. If the output stability of a photomultiplier should be maintained within one percent, the power supply stability must be maintained within 0.1%. The characteristics of a photomultiplier may also vary with external magnetic fields, ambient temperature, humidity, and mechanical stress applied to the tube.

The output of a photomultiplier tube can be processed like a constant current source. At very low light levels, like PET, the photoelectron counting method is used. The output pulses from the photomultiplier tubes are amplified and only pulses with amplitudes higher than the preset discrimination pulse height are counted. This method allows detection of discrete output pulses from the PMT and accurate timing. It is the most effective technique to detect very low light levels. Analog methods are mainly used at comparatively high light levels.

5.1.4 PMTs for PET and SPECT

Special applications like PET and SPECT have their own requirements for PMTs, structural as well as functional. Some different PMTs used in PET applications are shown in Figure 16. PMTs and are commonly used PMTs in block detectors. The large 2” (52 mm) PMTs ( and ) are mostly being used in special detector designs, such as continuous light-guide designs or quadrant sharing designs [35, 36]. Larger PMTs allow a higher pixel per PMT ratio, which helps reduce cost, but has the trade off of increased dead time, due to pile-up events, mentioned earlier.

PMTs are tailored to interface with scintillation crystals to count the scintillation events, detect the pulse height and their arrival time.
5 Photodetectors

Figure 16: Photograph of various PMTs used in PET scanners

Description to Figure 16:
① 19mm round tube, 10 stages, linear focusing dynodes
② 1” round tube, 10 stages, linear focusing dynodes
③ 2” square tube, 9 stages, box dynodes
④ 2” square tube, 10 stages, hybrid of box dynodes front end and linear focusing dynodes

The spectral sensitivity of a PMT is determined by the type of glass and the material used as photocathode layer. For short wavelengths the glass is the limiting factor, where as the photo emission threshold of the cathode material sets the limit for long wavelengths. Commonly used glasses for PET applications are borosilicate and lime glass with cut-off wavelengths between 250 and 300 nm. In rare cases (BaF$_2$ as scintillator), quartz glass is used due to its transparency in the UV range (190 nm).

Bialkali compositions are commonly used as coating material for the photocathode, since their spectral sensitivity matches the emission spectra of the scintillators used in PET (NaI and LSO; details are listed in Table 3). Tubes with bialkali cathodes are also known to have low dark currents.

Generally important requirements of PMTs for use in PET and SPECT applications are:
- High energy resolution
- Good quantum efficiency (QE)
- Fast transit time, and transit time uniformity
- Good timing resolution
- Uniform current amplification across the cathode (Anode / cathode uniformity)
- High stability in gain drift (Long term stability)
- Low susceptibility in magnetic fields
For time-of-flight PET, additional requirements become important such as a fast time response, which is determined by the transit time, and the transit time difference.

**Transit time variations**
For TOF-PET applications it is important that the transit time variation among different PMTs and across the photo-cathode of each individual PMT is very small, due to the fact that these differences diminish the accuracy of the position resolution.

**Timing resolution**
The timing resolution is an important characteristic of PMTs, especially for time-of-flight measurements, since it directly affects the position resolution in TOF-PET systems. The timing resolution is defined as the FWHM of the probability distribution of the transit time fluctuations [31, 32].

Figure 17 shows the diagram of a fast / slow measurement system for precision timing resolution. A radioactive source is placed between two opposing PMTs, both equipped with scintillators (in these studies plastic or LSO were used), and emits pairs of gamma-rays in opposing directions. Commonly used sources for PET experiments are $^{22}$Na, $^{68}$Ge or $^{60}$Co.

“Fast” refers to the timing part (Figure 17 - gray background) of the system: The anode output of one PMT is connected to a constant fraction discriminator (CFD) (see 6.1.3 Constant-fraction discrimination) which delivers a timing trigger pulse, which is directly connected to the start channel of the time-to-amplitude converter (TAC). The output of the second PMT is also connected to a CFD, but its signal is delayed before it is fed into the stop channel of the TAC so that it always arrives after the start. The TAC delivers a signal whose amplitude is proportional to the time difference between the start and the stop channel. The TAC output is digitized and histogrammed by a multi-channel analyzer (MCA).

The “slow” part refers the two branches on the side used for energy discrimination. The dynode output of each PMT is fed via a pre-amplifier in an amplifier, then into a single-channel analyzer (SCA). The SCAs allow setting an upper and lower threshold for an energy window around the energy peak of interest – for PET applications 511 keV. The energy window is commonly set from 425 keV to 650 keV. The output of the SCAs is connected to a coincidence unit, which is basically a logic AND. The coincidence unit in turn is connected to the gate input of the MCA, triggering an acquisition of the TAC signal only if the events fall within the allowed energy window.

The resulting timing spectrum displays the statistical fluctuation of the signals reaching the TAC. Causes for this fluctuation are 1) the transit time spread of the PMT, 2) the scintillators used, 3) the applied high voltage to some extent, and 4) the voltage-divider network. The timing resolution is
proportional to the square root of the scintillator decay time $\tau$ and inversely proportional to the square root of the number of photo-electrons per pulse (per ns) [37], as well as to the square root of the supply voltage [38].

The combined coincidence timing resolution (TR) is the square root of the summed squares of the transit time spread ($\tau_1$ and $\tau_2$) from both detectors.

$$TR = \sqrt{(\tau_1)^2 + (\tau_2)^2} \quad (13)$$

5.1.5 Anode uniformity / Cathode uniformity

Cathode uniformity is the variation of the output signal with regards to the position of illumination on the photo cathode. This means that the output signal varies depending on where the photo cathode is illuminated. The variation is mapped by scanning a narrow light beam across the surface of the cathode, while recording the output current. To map the anode uniformity the PMT is operated normally with a standard voltage divider network. Cathode uniformity is measured in the same way, but with the PMT operated as a diode. [31, 32] Cathode and anode uniformity both depend very much on the wavelength of the incident light. In our case only the peak wavelength of the scintillator is of particular interest, which in the case of LSO is $\lambda = 420$ nm. The uniformity is an important parameter for PET, be-
cause the position detection accuracy directly relates to the uniformity of the PMT.

Figure 18 shows a diagram of the anode and cathode uniformity test system. Figure 19 gives an example of an anode scan of two Hamamatsu R9779 PMTs, analyzed in further detail by Bauer et al in [39] (Publication III). A light emitting diode (LED) is encapsulated in a black plastic shell with a neutral density filter and a pin-hole (0.5 mm diameter) in the front, which serves as an aperture. The enclosure with the LED is mounted on a computer controlled X-Y-stage. The motorized X-Y-stage moves the LED with its case across the entire front-window of the PMT, which is situated face to face with the aperture. Both, PMT and LED are driven by external power supplies. The anode signal is connected to an amplifier, in order to convert the anode current to a voltage (1V / 1μA). The voltage signal is digitized by a PC based data acquisition system.

![Figure 18: Test system for anode / cathode sensitivity](image)
Long-term gain stability

One noted attribute of photomultiplier tubes is that they exhibit increasing and decreasing gain drift. A set of PMTs changes gain such that equal numbers would be higher and lower than their starting anode currents after a period of tens to hundreds of hours. It is an observable fact that the rate of divergence of the ensemble decreases with time. It was empirically determined, that PMT drift rates increase as the cube root of anode current. [40]

$$Drift \approx \sqrt[3]{I_{Anode}}$$

Behavior in magnetic fields

PMTs are sensitive to the presence of external magnetic and electrostatic fields. These fields may deflect electrons from their normal path between dynodes and cause a gain loss. Tubes designed for scintillation counting are generally very sensitive to magnetic fields because of the relatively long path
from the cathode to the first dynode. Magnetic fields may reduce the anode current by 50% or more compared to the “no-field” value [41]. For this reason it is necessary to use a magnetic or electric shield that protects the tube from such disturbing environmental factors. µ-metal\(^1\) provides good protection against electromagnetic radiation.

### 5.2 Micro-channel-plate PMT / Multi-channel plate

Micro-channel-plate (MCP) PMTs are PMTs in which the standard dynodes are replaced by a multi-channel plate. An MCP is built of a large number of glass capillaries (channels), bundled in parallel and formed in the shape of a thin disk. Both sides of the disc are metalized to provide parallel electrical connections to all channels. The glass capillaries have a microscopic diameter of ~ 2 to 25 µm. Their inner wall is coated to have the appropriate electrical resistance and secondary emissive properties. With a potential difference (~ 800 to 1400 V) across each plate, each channel or capillary acts as an independent continuous dynode electron multiplier, based on the electron avalanche principle. Figure 20 shows the cross section of a single channel of a multi-channel plate with its principle of electron amplification and how two multi-channel plates are stacked for higher gain.

![Figure 20: Schematic construction of an MCP with its principle of photo electron multiplication and the arrangement of two multi-channel plates to a two stage MCP with chevron-stack, as used in [42] (Publication V)](image)

\(^1\) µ-metal: special metal used for magnetic shielding; is an alloy of Iron, Nickel, Molybdenum, Copper and others
Just as for a conventional PMT, an incoming scintillation photon enters the photomultiplier tube through the front window, deposits its energy in the photocathode, excites the electrons in the photocathode coating and photoelectrons are emitted. The primary electron hits the inner wall of a channel and secondary electrons are emitted. The voltage differential $V_D$ across the capillary accelerates the secondary electrons, which impinge on the channel wall again, where more electrons are emitted [31]. The electrons undergo this process along the entire length of the channel wall, where a large number of electrons is released and captured by one or multiple anodes, depending on type and design. A single multi-channel plate has a gain of $\sim 10^4$. Collisions of electrons with residual gas particles in the PMT cause ionization. Positive ions are accelerated towards the entrance. If they strike the photo cathode or the channel wall near the channel entrance they will produce many secondary electrons that will multiply, eventually causing saturation – an effect called ion feedback.

Higher gain can be obtained by cascading multi-channel plates. The plates can be stacked with the channels straight, normal to the front window, or arranged so that the channels form a chevron pattern (Figure 20), reducing noise created by ion feedback [44].

One electron entering the channel can give rise to as many as $10^8$ electrons at the output, depending on parameters like number of plates, the potential across the channel (voltage drop per unit length of the channel) and its length / diameter ratio [32]. The plate thickness is determined by mechanical and electrical considerations. Thicker plates are more robust and allow operation at higher voltage resulting in higher gain, but at the cost of increased transit time caused by a longer path length.
Due to the difference in design from conventional PMTs with discrete dynodes, MCPs feature a compact size, but high gain. Thanks to multiple anodes the devices are position sensitive with a high spatial resolution. The short electron amplification path provides very fast response time, a short transit time and makes the device fairly unsusceptible to magnetic fields. Common applications include Cherenkov counters [45, 46], fluorescence microscopy, high-speed applications such as LIDAR\(^2\) (Light-Imaging Detection and Ranging) and possibly future use in medical imaging.

The device used in [42] \((Publication \, V)\) has 64 anodes \((8 \times 8)\) for an active area of 51 mm x 51 mm. The front window is a fused silica window with a bi-alkali photo cathode coating. Figure 21 b) shows a photograph of the device under investigation.

Saturation occurs, when the output signal is no longer proportional to the incident light intensity. In MCP-PMTs saturation is caused by space charge effects in the multi-channel plate and perturbed potential distribution. For detection of low current pulses (e.g. photon counting) saturation might be desirable, since gain fluctuations are reduced during saturation [32].

The resistance of an MCP is of the magnitude of \(\sim 10 \, M\Omega \) to \(100 \, M\Omega\), which represents the limiting factor for the strip current (see Figure 20: \(I_{\text{strip}}\)) through the MCP. As a result, the output current saturates with increasing input current. The main reason is the drop in electric field intensity due to variations of the potential distribution at the output of the MCP.

Transit time

In PMTs with discrete dynodes transit time widens, due to the fact that the emission angles of the secondary electrons from the dynodes have a broad distribution. MCP PMTs have a much narrower distribution in transit time, due to the multi-channel plate. The transit time spread is much improved also, due to the parallel electric field between cathode, MCP and dynode. The close proximity of \(\sim 2 \, \text{mm}\) of photo cathode to MCP and the strong electric field between them reduces the effects of the emission angle from the photo cathode significantly [31]. Transit time depends on the channel diameter; thus, smaller channel diameter results in decreased path length across the channel, thus in shorter transit times. Thicker plates and therefore longer channels allow operation at higher voltage resulting in higher gain, bringing the disadvantage of increased transit time, caused by the longer path lengths.

\(^2\) LIDAR - optical remote sensing technology which measures properties of scattered light to find range and/or other information of a distant target [source: http://en.wikipedia.org/wiki/LIDAR]
6 Coincidence detection and electronic collimation

In a PET camera, each gamma-detector generates a timed pulse when it registers an incident photon. These pulses are then combined in coincidence circuitry. If one pulse falls within the others coincidence time-window, they are coincident. The width of the time window of 4-10ns depends on the scintillator material, PMT response and the electronics. A conceptualized diagram of this process is shown in Figure 22.

![Diagram of Coincidence Detection](image)

*Figure 22: Coincidence detection in a PET camera.*

The amplitudes (V₁ and V₂) of the signals from detector A and B (Figure 22) may be different, due to varying gains of the photodetectors or partial deposition of 511keV in the detector. When the detector signals cross a certain fixed fraction (Tr₁ and Tr₂) of their individual amplitudes, the trigger
unit (see Chapter 6.1) generates narrow trigger pulses (with width $\tau$), i.e.
signal A and B, respectively. These pulses are combined in coincidence cir-
cuity. If the signals A and signal B occur within a time interval $\tau$, they are
registered as coincident events, independent which detector triggered first. In
other words, if signal B occurs within the $2\tau$ coincidence window around
signal A, a valid coincidence event is registered.

For detectors with poor timing resolution due to a slower scintillator or
PMTs with a slower response, a larger coincidence window is needed to
detect most of the valid coincidence events. Newer scintillators, such as LSO
permit a width of the coincidence window of less than 8 ns. The hardware
coincidence window width is usually set to twice the coincidence timing
FWHM, to achieve high efficiency for true events. It cannot be made smaller
than $\sim 4$ ns, as this is the time-of-flight (TOF) difference across the detector
ring and would result in valid events near the edge of the FOV being re-
jected. If the coincidence window is too small, true coincidences are lost, if
it is too large the system saturates with random coincidences. Random coin-
cidences or “randoms” are coincidences between two uncorrelated events,
randomly occurring in the coincidence time window and thus being regis-
tered as being coincident.

Electronic collimation refers to the fact that positional information is ob-
tained from the LOR virtually connecting the two detectors which registered
the coincident event. Electronic collimation has two advantages compared to
physical collimation: improved sensitivity and improved uniformity of the
point source response function. When a physical collimator is used, as is in
Single Photon Emission Tomography (SPECT) applications, directional
information is obtained by only accepting photons that are normal or nearly
normal to the collimator face. Using electronic collimation, these photons
are accepted within a much larger solid angle. This results in a significant
increase in sensitivity.

6.1 Time pick-off methods

In many applications it is important to know the exact arrival time of a
particle. For this purpose time pick-off units or trigger units are used. These
devices generate a logic pulse based on the conditions at their input and the
input signal. The leading edge of the logic pulse indicates when the event
occurred. The accurate time of arrival is especially important for systems
whose design is based on the time-of flight principle, like TOF-PET. Which
degree of accuracy in timing is obtainable depends on the detector and the
electronics used to process the signals from the detector.
Three methods are commonly used for time pick-off: 1) leading edge timing, 2) cross-over timing and 3) constant fraction discrimination. A brief introduction to the different time pick-off methods follows.

The constant-fraction discriminator is the method most commonly used in PET systems.

6.1.1 Leading edge timing

The leading edge trigger mechanism is very direct. Once an input signal crosses a fixed threshold level, a trigger signal is generated. Timing errors can arise from *time walk* (Figure 23 a) or *time jitter* (Figure 23 b).

Pulses of similar shape but different amplitude cause trigger signals at different times, due to a dependence of signal peak height and trigger time. This effect is referred to as *time walk*. A change in the shape of the pulse may also cause walk. A noisy signal can cause early or less often late trigger signals, which leads to an increased uncertainty in the timing measurement. This effect is called *time jitter*.

If the amplitude range of the input signals is fairly narrow leading edge timing gives an exact event timing trigger.

![Figure 23: influence of a) time walk and b) time jitter on the leading edge trigger mechanism](image)

6.1.2 Cross-over timing for bipolar pulses

Cross-over timing allows the extraction of an event timing trigger from a wide range of pulse amplitudes. It reduces timing uncertainty caused by am-
amplitude walk. The cross-over timing method requires a bipolar signal and the signals to be of constant shape and rise-time. The trigger point is always at the zero crossing point of the bipolar signal, independent of variations in the amplitude.

6.1.3 Constant-fraction discrimination for unipolar pulses

A constant fraction discriminator (CFD) produces an output signal a fixed time after the leading edge of the input pulse reaches a constant fraction of the amplitude. The CFD does not require a bipolar input pulse. Identical rise times and pulse shapes permit triggering not on a fixed threshold but on a constant fraction of the total peak height, yielding trigger times independent of pulse amplitude [47, 48]. Figure 24 shows a diagram of the steps finally leading to the output signal. The input signal (1), commonly an anode or dynode pulse from a PMT with Amplitude V – possibly amplified, is split. One component is multiplied with fraction $f$ to attenuate the signal to the desired timing fraction (2). The input signal is delayed by a time $t_d$ and inverted (3). These two components (2 and 3) are then summed, to produce a bipolar waveform (4). The point of the zero-crossing is independent of the pulse amplitude. The circuit will trigger the output pulse at a time defined by the fractional trigger level of the original input pulse.

![Diagram of constant-fraction discrimination](image)

*Figure 24: principle of operation of a constant-fraction discrimination unit*
The basic reconstruction algorithm for PET is – similarly to CT – the filtered back projection, which is here used to obtain cross-sectional images of the distribution of a radiopharmaceutical within patients. PET measures pairs of gamma quanta that result from annihilation events. The virtual line between the two crystals that detect those gamma quanta is called a Line-of-Response (LOR). The sum of events that are collected in one LOR is proportional to the line-integral through the activity distribution along this LOR. The LORs can be organized into parallel sets, which can also be regarded as 1-dimensional projections.

In 1917 the mathematician J. Radon wrote the article "Über die Bestimmung von Funktionen durch ihre Integralwerte längs gewisser Mannigfaltigkeiten" [49], which approximately 50 years later became important in the field of tomographic imaging. It describes the radon-transformation, which defines how 1-dimensional projections can be derived from 2-dimensional function. Its inverse is used to reconstruct images from computed tomography scans [50].

Figure 25: Line integral along LOR through object tracer distribution \( f(x,y) \)
\[ p(s, \Theta) = \int_{-\infty}^{\infty} f((s \cdot \cos \Theta - u \cdot \sin \Theta),(s \cdot \sin \Theta + u \cdot \cos \Theta)) \, du \quad (15) \]

\( p(s, \Theta) \) is the radon-transform (projection) of the tracer distribution – the two-dimensional function \( f(x,y) \) in Figure 25. It allows to describe any integrable function \( f(x,y) \) by means of all straight line-integrals over the defined area of \( f(x,y) \). The Radon transform data is commonly referred to as a *sino-gram*, because the Radon transform of a delta function is the characteristic function of the graph of a sine wave, where the amplitude of the wave is the distance of the delta function to the center of the projection. The graphic plot of a Radon transform of a number of small objects appears consequently as a number of blurred sine waves with different amplitudes and phases.

With one-dimensional projections of an object taken at an infinite number of angles, it is possible to perfectly reconstruct the original object [50]. To get the original function back one can use the inverse Radon transform. Equation (16) describes the backprojection operation, i.e. when each point is assigned the sum of all projection lines passing through it. Applying backprojection after a projection does not bring the function back. The result is a smeared image. However, this effect is avoided by filtering the 1-dimensional projections before the backprojection by using a suitable backprojection filter, hence the name: the *filtered back projection* (FBP) algorithm. Figure 26 illustrates the reconstruction chain.

\[ \hat{f}(x, y) = \int_{0}^{\pi} p_{f}((x \cdot \cos \Theta + y \cdot \sin \Theta), \Theta) \, d\Theta \quad (16) \]

The projection data is transformed into frequency space (FFT). Then the ramp filter is applied – which is now a simple multiplication instead of a folding operation. Then the filtered projection is transformed back into image space (iFFT) and then back projected. The inverse Radon transform proves to be sensitive to noisy data, due to the fact that the ramp filter amplifies high-frequency components. Modifications to the ramp filter can be used in order to reduce this effect. The Hanning filter is commonly used, besides others.

The image quality is very much dependent on the number of detected events [2], i.e. sensitive to statistical noise.
Besides analytical methods based on the inversion of the Radon transform, algebraic methods have proven to be superior with regards to different aspects. FBP is still the standard to which other algorithms like algebra based methods are being compared against, such as iterative reconstruction methods. Maximum-likelihood expectation maximization (MLEM) and Ordered Subset Expectation Maximization (OSEM) [2] fall in the category of iterative reconstruction methods.

*Iterative reconstruction* is a method or group of algorithms used to reconstruct 2D and 3D images from the projections of an object. This technique is different from the FBP method, described earlier. The benefit of iterative reconstruction methods is that they are less sensitive to noisy data, allow better modeling of the physical processes such as point spread functions and beta range. Correction mechanisms e.g. attenuation and scatter can be integrated into the iterative optimization. While FBP is a strictly planar method, iterative methods can be extended to 3D geometries.

The MLEM reconstruction is based on explicit modeling of the Poisson-distribution of the detected events, as well as the noise. The goal of the iterative reconstruction is to find an image that “fits” to a measured sinogram, i.e.
to find the image with the maximum likelihood that the sinogram of the image would look like the one that was measured. Finding the maximum likelihood is done by a statistical optimization method – the “expectation maximization”, which is an iterative method. MLEM therefore means “using the method of expectation maximization to find an image where the likelihood is maximized that the sinogram is identical to the measured sinogram”

The measured data are considered to be samples from a set of random variables, whose probability density functions are related to the activity distribution within the object, according to a mathematical model of the detection mechanism. The model is used to calculate the probability that any initial distribution density in the object could have produced the measured data. In the set of all possible images, which represent a potential object distribution, the image with the highest probability is the maximum likelihood estimate of the original object. A homogenous start image is forward-projected into a sinogram, which is compared to the acquired sinogram data by dividing the measured data by the projected data. The quotient, which still is a sinogram, is back-projected into an image. This gives the correction matrix, with which the initial image is multiplied. This new image is normalized by dividing it by the back-projection of a sinogram that is 1 everywhere. The resulting image is the start value for the next iteration. The process usually terminates, once a certain number of iterations are executed. This number is determined by heuristic methods: the convergence behavior of the EM algorithm is studied by measuring recovery coefficients with phantom data of known activity.

Model-based iterative approaches to image reconstruction in PET and SPECT allow good noise handling and accurate system response modeling under consideration of system parameters [51]. IR features improved image quality for low statistics data compared to FBP but at the cost of longer computation time. IR methods have a computation time that is significantly longer than analytical methods, since iterative methods require one forward- and one backprojection for every iteration, and a number of iterations before they achieve convergence, whereas FBP consists only of a simple filter operation and a single backprojection.

For these reasons, FBP initially remained the reconstruction method of choice in clinical PET even after the introduction of iterative methods. Due to today’s availability of fast computers and efficient implementations (see OSEM) the IR methods are now widely being used in clinical applications.

Ordered Subset Expectation Maximization [52] is an accelerated version of the MLEM algorithm for PET reconstruction, sufficiently fast for clinical application. It improves the speed of previous MLEM algorithms, by dividing the set of projections into independent ordered subsets.
A forward-and backprojection cycle are then performed on the first subset. Even though a small number of measured data is being considered, the result gives a good estimate of the activity distribution. The next subset is reconstructed based on the first estimate, improving computation time by reducing the number of iterations and time until it converges. The one-time use of all subsets corresponds to one OSEM iteration. As long as the number of subsets does not become too large, and the number of subsets is not too small, respectively, OSEM reduces the number of iterations necessary to reach a certain convergence point, by a factor corresponding to the number of subsets [2]. If the number of subsets is too large, the projection data within a subset is not sufficient to create a reasonable estimate of the image – and therefore the algorithm will not converge. Heuristics are used to determine the minimum number of required projections in a subset (i.e. the maximum number of subsets to use).

7.1 Error sources and correction mechanisms

7.1.1 Attenuation correction

The consequence of attenuation is that less photons are detected from deeper structures in the body than from tissues near the body surface. Reconstruction of a uniform source will demonstrate that counts are low towards the centre. The number of coincidences lost due to attenuation depends on tissue density and thickness and in the region of the head is approximately 75-80% and in the chest region above 95% [2]. The attenuation coefficients along the LORs can be determined with a transmission scan.

In older scanners a line source (commonly $^{68}$Ge) is rotated around the patient and the number of photons per coincidence channel registered. A correction factor for the attenuation can be calculated by comparing the transmission data with data from a blank scan – a transmission scan without attenuating medium present [53].

The disadvantage of this method is the additional scan time during which the patient should stay motionless and the additional radiation exposure of the patient. Another problem is that statistical noise in the transmission scan is added to the PET-data.

Alternatively the attenuation coefficient can be determined by X-ray CT scan [54]. The alignment of the PET and CT images might be problematic in older systems. Newer systems incorporate both, PET and CT integrated in one system, which allows for the exact alignment of the images. The advantages of a CT scan are that it takes less time (30s) compared to a transmission scan with a PET system, which takes several minutes, it has higher reso-
Image reconstruction, less noise, and better tissue density differentiation. The difference in energies of the CT and the PET makes the conversion of the measured attenuation coefficient from the CT energy (typically 120-140 keV) to the PET energy (511 keV) necessary. The converted image is called a μ-map, which is forward projected into attenuation correction factors. Every LOR in the emission data is multiplied with the attenuation correction factors for this LOR.

In certain cases (brain scan) it may be possible to use a calculated attenuation correction [55] instead of performing a separate measurement, although a correct modeling of the attenuation of the head is difficult and therefore quality of this attenuation correction is quite limited.

7.1.2 Correction for random coincidences

To obtain quantitative data in PET it is necessary to estimate and subtract the random coincidences from the measured data in each LOR to yield the sum of the true and scattered coincidences.

The coincidence time window, in which two gamma quanta are recognized as a pair, needs to have a minimum width, determined by the time a photon needs to travel from the annihilation point to the detector. In theory this would be 2-4 ns for whole-body PET systems, depending on the bore diameter. In reality the coincidence time window is set with regards to the properties of the scintillator, the PMTs and the electronics. For BGO-systems it is between 10-20 ns (ECAT EXACT 12ns; HR+ 12ns), and less for systems with LSO (currently 4.5ns). Even though random coincidences originate from two different but nearly simultaneous annihilation processes, they also fall in the coincidence window and are therefore registered by the system as coincidence event. Random coincidences can also be caused by activity outside the FOV. For example during the examination of the abdomen the accumulated activity in the bladder – even though located outside the FOV – causes an increase in random events.

One method to estimate the number of randoms ($N_{random}$) is based on the single count rates ($N_i$ and $N_j$) of the detector pair on a particular LOR with and the width of the coincidence time window ($2\tau$) [2].

$$N_{random} = 2\tau \cdot N_i \cdot N_j$$  \hspace{1cm} (17)

Another method for estimating the randoms rate in a particular LOR is the delayed coincidence channel method. The signal from one of two coincident detectors is delayed by a time $\tau_2$ significantly greater than the coincidence resolving time of the circuitry ($\tau_2 \gg \tau$). Thus, no true coincidences are de-
tected and the remaining recorded coincidences therefore are randoms, which need to be subtracted from the acquired data.

7.1.3 Scatter correction

On the path through the tissue the gamma quanta interact with electrons of surrounding tissue. Through Compton scattering the photon changes its direction with some loss in energy and eventually hits a different detector than it would have, without being scattered. If two scattered quanta occur within the coincidence resolving time, they will be detected as coincident.

The path length from deep brain tissue is approximately 7 cm. Depending on the detector system, up to 50% of the photons are scattered during a brain examination. The energy loss in the process is so small that scattered photons are not sufficiently filtered by increasing the lower energy threshold, without significantly reducing the scanner sensitivity [56], depending on the energy resolution. The purpose of the energy window in a PET system is to reduce the number of these scattered events that are detected. However, there are still many photon pairs that have undergone scatter but remain energetic enough that they fall within the energy window. Those will be measured in the wrong LOR and therefore would later cause artifacts during reconstruction. Complex computations are necessary to estimate the scattered fraction of photons left with higher energies, in order to subsequently subtract these from the measured data.

One common method is to first reconstruct the activity distribution based on the uncorrected data. The scatter distribution is subsequently simulated, based on the tissue density data from the attenuation image ($\mu$-map) and the activity distribution from the uncorrected image. The simulated scatter can then be subtracted from the measured activity distribution data for correction.

7.1.4 Dead-time correction

After the detection of a gamma-photon the detector is paralyzed for a certain amount of time, before the next event can be detected. The recovery time required before another event can be detected is called detector dead-time. It depends on the decay-time of the scintillator, the processing time of the electronics and very much on the activity. The dead time is set by the detector reset time, which is a constant. The amount of dead time is related to the activity since the detector is dead during the reset time. Radioactive decay is of random nature, which is why there is always a probability that true events are lost because they happen too quickly in sequence. Commonly multiple detectors are connected to a single coincidence unit, thus increasing the probability of coincidences falling into the dead-time of the system. So
when one event is detected by one of those detectors, the complete subsystem goes into deadtime, increasing the number of events that cannot be detected because of deadtime.

To correct for dead-time, the losses are modeled as a combination of paralyzable and non-paralyzable components. The parameters for the model are acquired by measurements of a decaying source. A phantom with a known high activity is measured. Only a fraction of the events are recorded, the rest is lost due to dead-time. With the decay of the activity, the difference between real events and the measured counts becomes smaller, because the system is less paralyzed. The initial activity and the half-life of the used isotope are known and used to calculate the theoretical decay curve — which then can be compared to the measured decay curve. The difference leads to a deadtime correction factor for a certain activity, i.e. how many events were not detected due to deadtime Models to correct for dead-time have been investigated by Daube-Witherspoon [57] and Eriksson [58].

A problem especially of block-detector systems is event mis-positioning at high count-rates due to pulse pile-up [59], which can lead to image artifacts if the normalization measurements are carried out at significantly different count-rates compared to the emission measurements.

7.1.5 Normalization

In a PET system the sensitivity may not be uniform for all LORs. Reasons for the variation in sensitivity are variations in detector efficiencies, geometric effects, variation in PMT gains (which may change over time) and variation in light-output among crystals [60, 61]. For quantitative and artifact-free images, these variations need to be compensated for before the reconstruction. The process of correcting for these effects is referred to as normalization. The LOR specific correction factors are referred to as normalization coefficients [62].

The sensitivity of a particular LOR is affected by the angle at which it faces the detectors, by the geometry of the camera and the LOR position. To obtain a full set of normalization coefficients a uniform phantom is scanned, in order to illuminate every possible LOR. This approach is known as direct normalization. Normalization coefficients can change over time (likely due to PMT drift) and should therefore be remeasured as part of routine quality control.

Direct normalization uses either a planar or a rotating source (usually $^{68}$Ge), to illuminate all possible LORs. After correction for non-uniform radial illumination, the normalization coefficients are estimated inverse proportional to the counts in each LOR [62].

Another normalization method is known as component-based normalization [63]. These model based normalization procedures are complex and involve the sequential estimation of multiple components contributing to the
sensitivity differences. Typically, the protocol involves the measurement of a uniform cylindrical phantom to calculate crystal efficiencies, and a rotating rod-source (nothing in the FOV) to calculate geometric effects. In both cases the activity of the source is fairly low to avoid dead-time effects, with the disadvantage of long scan times of several hours to ensure good counting statistics.

Correction and normalization mechanisms can be applied before or after the FBP based reconstruction. The use of iterative reconstruction methods allows implementing corrections directly into the reconstruction process.
8 Time of Flight - PET

8.1 Introduction to time-of-flight

Good timing resolution can help not just to reduce the number of random coincidences, but also to estimate the point of annihilation between the two detectors by measuring the difference in arrival times of the two coincident photons. To facilitate measurement of this extremely short time fraction an extremely fast scintillator is needed. Earlier systems were built with Barium-Fluoride (BaF2) [64], while currently developed systems are based on LSO.

![Figure 27: Depiction of the time-of-flight concept](image)

Point A in Figure 27 marks the point of an annihilation event, which occurs offset from the center by distance d. The center marks the half-way point between the two detectors D₁ and D₂. Photon $\gamma_1$ travels the distance \( AD_1 = r - d \) and photon $\gamma_2$ travels the distance \( AD_2 = r + d \) before they enter the detector D₁ and D₂, respectively. Photon $\gamma_2$ travels the extra distance \((r + d) - (r - d) = 2d\) relative to photon $\gamma_1$. The photons are traveling with the speed of light \(c = 3 \cdot 10^8\) m/s. Time-of-flight PET is based on the accurate measurement with high speed electronics of the time difference (\(\Delta t\)) between the two coincident detectors due to the different distances the photons travel [65]. Using the speed of light this path length difference can be calculated with \(2d = \Delta t \cdot c\).

A timing resolution better than 500 ps is desirable [10] for several reasons. This would allow for narrowing of the coincidence time window,
which decreases the random count rate, as the number of randoms linearly depends on the width of the coincidence window \((2\tau)\). The lower limit for the width of the coincidence window is \(~4\text{–}5\) ns, to be able to record all LORs within a \(~70\) cm transaxial FOV.

The major advantage of TOF information is noise reduction. In large patients of e.g. 40 cm diameter, a 500 ps timing resolution results in a TOF-gain in signal to noise ratio of

\[
\text{gain}_{\text{TOF}} = \frac{40\text{cm}}{c \cdot 500\text{ps} / 2} = 5.3
\]

This can be viewed as a certain image quality, obtained with a certain number of counts can now be obtained with 5.3 times less counts. This may be used to lower the radiation dose to the patient, while keeping image quality constant, or to improve the image quality by administering the same dose as on a non TOF system.

The use of TOF data in the reconstruction helps to reduce the noise variance. In normal image reconstruction methods the coincidence events in the projections are back projected in the entire image plane. Instead of projecting the same count number along the whole LOR, the TOF info gives the likelihood that the event occurred at a certain position along the LOR. This likelihood has a Gaussian distribution. [66].

A TR \(< 500\) ps would also reduce the axial blurring, since TOF would allow for the determination of the correct axial plane of origin for each event. Another benefit of such good timing resolution would be the reduction of the total scan time, due to the fact that transmission and emission scans could be performed simultaneously; although, this argument has become obsolete due to the fact that most currently available PET scanners are combined PET-CT systems, like the Siemens Biograph and mCT (molecular CT) or Philips Gemini.

### 8.2 FBP based TOF reconstruction

TOF information literally adds a new dimension to the data set compared to conventional PET systems. The size of the projection data is multiplied by the number of TOF segments (time bins) per LOR.

The datum consists of the locations of the two detector elements which detect the 511 keV photon pair and the time difference between their arrivals. This time difference corresponds to a position along the LOR, but the measurement error implies an uncertainty in the positioning. Therefore not every pixel along that LOR is incremented by the same amount during back-projection. Each pixel is incremented by an amount proportional to the probability that the annihilation occurred at that section along the LOR. This
amount is given by the measured time difference and the timing resolution. The backprojection introduces some blurring. Its width depends on the timing resolution.

Coincidence events only contribute to those pixels that are within a certain distance to the correct pixel. The distance is consistent with the timing resolution, i.e. time bin. Therefore, the statistical fluctuations from the measurement data contribute to a much smaller number of image pixels. Therefore, reconstruction algorithms utilizing TOF information reduce the statistical noise.

Compared to regular filtered back projection reconstruction two extra steps are needed to utilize the additional timing information provided by a TOF system.

The acquired sinogram data are filtered, using the TOF information. The filter function is convoluted with a Gaussian distribution, whose full width at half maximum is the timing resolution of the PET-system. The new TOF-filter is applied for all TOF bins. With the inverse Fourier transform the data are then transformed back into spatial domain and then back projected for all time bins. Figure 28 shows a flow chart for the reconstruction process based on the filtered back projection with TOF-data.

Today, most image reconstructions are performed with more advanced iterative algorithms, as described earlier in chapter 7 Image reconstruction.

![Figure 28: Reconstruction process for TOF data](image)
9.1 Introduction to depth-of-interaction

The measured position of energy deposition is projected to the entrance face of the detector. For photons that enter the detector at oblique angles, this projected position can produce significant deviations from the real position, leading to a blurring of the reconstructed image (as mentioned in Chapter 3.2 The parallax error). Typically, annihilation points located at large radial distances from the scanners central axis, suffer from this parallax blurring.

To separate the interdependence of sensitivity and parallax error, it is required to measure the depth-of-interaction within the crystal. This problem is addressed by using depth-of-interaction (DOI) information from e.g. multi-layer phoswich detectors, while maintaining high sensitivity. Two practically feasible methods are used for the DOI-measurement: The first technique is based on two photon detectors, at both ends of the scintillator [67, 68]. The physical principle is that the relative number of photons reaching either detector is a function of the photons depth of interaction within the scintillator. The photon detector at the front end, facing the patient, has to be very thin; therefore, only PIN-photodiodes or APDs are applicable.

The second method is a phoswich (PHOSphor sandWICH) [69] detector, comprised of layers of different scintillators on top of each other. The depth of the interaction is measured by the identification of each layer in the phoswich detector. The scintillator layers have to have a significant separation in decay-time or light-output, in order to identify them by pulse shape discrimination (PSD) or pulse height discrimination (PHD). The idea of PSD in combination with a phoswich detector was first used in space applications [70, 71], later it was used for in-vivo counting [72] and then in PET [73, 74].

The optical coupling between the individual scintillator layers is very important, for the transmission of the scintillation photons to the photon detector.
9.2 Pulse shape discrimination

In a standard PET system, the amplitude of a pulse is the information of interest. But a pulse contains more information than just the amplitude, e.g. its shape and the point in time when it occurred. Most shape differences are caused by the differences in the time profile of the current produced at the detector by a radiation interaction [75].

A common method to detect the differences in pulse shapes is the crossover method. The pulse is passed through a shaping network, resulting in a bipolar pulse. The time at which the pulse crosses zero in theory does not depend on pulse amplitude, but instead is a function of the pulse shape and rise time. The time interval between the beginning of the pulse and the zero crossover point is an indication for the difference in pulse shape before the shaping network [76]. A Timing Filter Amplifier was used to shape (differentiate and integrate) the signal. Figure 29 shows the test system. The time difference is measured between a CFD set as low as possible at the beginning of the pulse and a second trigger that senses the crossover point. A TAC converts the time difference into a pulse-amplitude, which is digitized by a National Instruments 6110 Data Acquisition card (Figure 30). Based on this pulse the crystal is identified by its decay time and thus, the layer in which it occurred. Through an identification of the different decay times of the scintillators the layer and thus the depth of the interaction is determined. The scintillators are chosen to have different decay times so that the shape of the output pulse of the PMT is dependent on the relative contribution of scintillation light from the different scintillators. Figure 30 shows the spectrum from a TAC, used for PSD. The crystals have a separation in decay time of ~12ns.
Figure 29: Basic test system for depth of interaction based on pulse shape discrimination

![Diagram of a basic test system for depth of interaction based on pulse shape discrimination.]

Figure 30: PSD spectrum of two scintillators with two different decay times (peaks) and a decay time difference of ~12 ns between the peaks; upper right: Shaped pulses from LSO:Ce (~30 ns) and LSO:Ce,Ca (~47 ns) going in two CFDs, the difference in decay time of 12.9 ns shows in the two zero crossing points, visible in red (cursor marks).
Publication I

*Current and Future Use of LSO:Ce Scintillators in PET*

This paper gives an overview over the refinements and developments of LSO as a scintillator for PET, especially with regards to its applicability in TOF-PET. It briefly describes the history of LSO and puts its properties in relation to other scintillators.

Based on the findings that LSO is not utilized to its full potential with regards to the timing properties an effort was made to improve the detector timing resolution, with new photomultipliers. In order to get a start point we evaluated the current LSO based detector from the Siemens Hi-Rez PET system.

Adjusting a coincidence timing system requires careful adjustment of the trigger threshold and choice of delay line for the CFDs.

*Contribution of the author:*
The author performed the timing measurements for this publication.

Publication II

*Timing Performance of Hi-Rez Detector for Time-of-Flight (TOF) PET*

Research for this publication started in order to find out what the standard detector of the Siemens HI-REZ PET system is capable of with regards to timing performance. Two HI-REZ detectors were operated in coincidence in bench-top experiments. Measurements were performed with standard nuclear instrumentation modules (NIM). As part of the detector evaluation the type of PMTs used was also tested individually for their timing capabilities, with respect to transit time and timing resolution.
To get comparable results for the mapping of the PMT response, the positioning of the scintillator was of utmost importance.

**Contribution of the author:**
The timing resolution of the reference PMT used in the experiments was measured by the author, as well as the mapping of the PMT response.

**Publication III**

*Performance Study of the new Hamamatsu R9779 & Photonis XP20D0 fast 2” Photomultipliers*

This paper was written as a summary to the investigation of two newly introduced 2” (51 mm) diameter Hamamatsu and Photonis PMTs for their potential application in TOF-PET. We investigated, if these PMTs could deliver a timing resolution necessary for TOF-PET, the uniformity of the timing resolution across the cathode, as well as the anode uniformity. We investigated these parameters in a small number of samples.

**Contribution of the author:**
The author planned and performed the measurements, the data analysis and wrote the publication.

**Publication IV**

*Dynode-timing method for PET block-detectors*

The idea for this publication emerged from discussions about whether it would be possible to extract the timing signal from detectors in a faster and more cost effective way, than commonly done from the anode. Typically, PET systems based on the block detector design use the summed anode signal of the block detector as an event timing-trigger, which requires a summing amplifier, adding noise to the signal and cost to the design. The utilization of the dynode signal in multi PMT detectors makes the use of summing amplifiers for the anode signals obsolete, since the dynodes are simply tied together [77]. The output from the last dynode is suitable for timing measurements, since it is synchronous with the anode output and with a faster rise time than the anode output [32]. Bengtson and Moszyński [78] and de Vries and Kelling [79] reported, that the extraction of the event timing trigger from the dynode results in improved timing resolution compared to the standard...
event timing trigger of the anode signal. This could make the circuit performance faster, simpler and cheaper than the usage of summing amplifier circuits. We found an improvement of $\sim 10\%$.

For the first evaluation of the dynode timing method we used single PMTs, since the test system is less complicated than block detector measurements. An important aspect of the measurements was to keep the CFD settings on a similar level, on both, the anode and dynode signals, to ensure a fair comparison.

**Contribution of the author:**
The author participated in the design of the circuit, planned and performed the measurements, analyzed the data and wrote the publication.

Publication V
**Evaluation of a Micro-Channel Plate PMT in PET**
Paper V was presented at the 2006 IEEE MIC/NSS conference. It is available as conference record.

Initial interest to use MCPs in PET was raised by the fast response time MCPs are known for. Their domain is usually in high energy physics, especially mass-spectroscopy, based on time-of-flight measurements.

Earlier generation MCPs were current limited, caused by their high resistance, and therefore not suited for their use in PET detectors especially with LSO, due to its high light output. Recently Burle introduced a new MCP which is capable of handling a higher current. With the new generation MCP, the hope is to be able to utilize a large piece of LSO up to the size of an entire block, without causing saturation of the channel plate.

Initial tests were performed with a pulsed LASER. The Burle 85011 MCP exhibited a timing resolution of 33 ps. The output of the laser had to be adjusted to the same light output level of a 4mm x 4mm x 20mm LSO pixel. Encouraged by these results tests were performed using LSO pixels. Unfortunately the timing resolution suffered dramatically. More tests were planned to find the reason for this discrepancy. However, the project was stopped before this could be done.

The difficulty in the measurement was the exact positioning of the PMT relative to the laser. For that purpose a mounting fixture and a mask were designed, which allowed accurate positioning of the MCP and made the laser
visible on the glass front window. For the timing measurements the system had to be carefully calibrated. For that purpose we used an Ortec 462 Time Calibrator module. It generates pulses on the start and stop channel of the TAC, at a preset amplitude with a preset time interval between the pulses, generating a timing spectrum of which the pulse spacing is known. The delay line of the CFD had to be carefully chosen, not to deteriorate the pulses and to obtain optimum timing performance.

**Contribution of the author:**
The author incorporated the pulsed laser in test system and developed the voltage divider network. Measurements, data analysis and presentation of the results were made by the author.

Publication VI

**Measurements and Ray-Tracing Simulations of Light Spread in LSO Crystals**

Recent developments in positron emission tomography (PET) have shown three major trends: 1) a move towards higher spatial resolution by utilizing block detectors with smaller scintillator pixels [13, 19, 80], 2) detectors with faster timing resolution for use in time-of-flight systems [10, 30, 81] and 3) the use of silicon-based photo detectors for compatibility with magnetic fields in combined MR/PET detectors [82, 83]. When designing new PET detector blocks for such applications, it is important to have a detailed understanding of the light sharing mechanisms in the crystal arrays and to control the factors that influence the overall light output. The light distribution between the pixels not only determines the accuracy of the crystal identification and spatial resolution, but the overall light output is also critical due to the strong influence of photon statistics on energy resolution and timing.

In this paper we report on measurements of the absolute light output from LSO crystals for irradiation with 511 keV gamma rays as a function of interaction position, reflector arrangement, detector coupling geometry and optical coupling to an adjacent crystal.

The light output for this series of geometrical configurations is simulated with the ZEMAX ray-tracing software. By fine-tuning the optical parameters of the bulk and at the interfaces, a model is obtained which yields good agreement with experimental data for all configurations. The resulting parameter set is applied to calculate the light distribution in a 12x12 crystal block detector. A comparison of measured and calculated block position profiles shows good agreement, demonstrating the potential of the simula-
tion model to predict block detector performance data and provide guidelines for future array designs.

The aim of this work is to derive an optical model for an LSO based block detector, where the crystals are separated by air gaps and by reflector partitions in selected locations.

The entire work hinges on the accurate measurement of the single photo electron peak. Single electron pulse height response was measured for the R8619 PMT at −1250V without crystal while keeping the spectroscopy amplifier gain at a very high value. The PMT output signal was fed to a Tennelec TC 145 pre-amplifier which was connected a Tennelec TC 241 linear amplifier, which, in turn, was fed into an Ortec 855 Dual spectroscopy amplifier. Its signal was then digitized with a Multi-channel analyzer.

To be independent from random single photo electrons, we used a pulsed laser, which is attenuated to single photon level with an aperture and multiple neutral density filters in the beam path. The trigger signal from the laser was connected to the gate channel of the MCA, so that the system only recorded counts when the laser actually fired. The position of the single photo electron peak centroid, combined with the total gain of the amplifier chain, is taken as measure for the number of photons detected. The amplifier chain mentioned afore was used since each amplifier had been tested for linearity independently.

After the centroid of the single electron spectrum was determined, the test crystal was optically coupled to the R8619 PMT. Then, the gain of the spectroscopy amplifier was set to a relatively low value so that the energy spectrum for the Na-22 source can be seen with the LSO crystal. Assuming that the amplifier chain and the PMT response are linear, one can estimate the total number of photoelectrons collected from the LSO crystal.

Contribution of the author:
The idea for this research project was developed together with Debora Henseler at Siemens, Erlangen. The development of the measurement system and the data analysis as base for the simulations were performed by the author. The simulations were performed by Debora Henseler. The publication was shared between Debora Henseler and the author.
Publication VII

Depth of interaction with a 3-dimensional checkerboard arrangement
LSO-LSO block

(This paper is currently submitted for review to IEEE Transactions on Medical Imaging)

In order to improve image quality in PET different routes are being pursued such as fast timing resolution for time-of-flight PET, higher spatial resolution by the use of smaller scintillator pixels and the use of depth-of-interaction information. The detection of the depth-of-interaction (DOI) of a gamma ray within a detector, deploying pulse shape discrimination (PSD), has been used to increase sensitivity and spatial resolution, especially at the edge of the FOV. The DOI information is used to reduce the parallax error; thus improving spatial resolution.

Commonly, different scintillator materials with different decay times and light output and other differentiating factors, such as density, emission spectra, etc. are used for DOI detectors.

We present a multi-layer phoswich detector comprised of LSO with different decay times in the range from 30 ns to 47 ns. The difference in decay times is achieved by co-doping LSO:Ce with Ca, resulting in short decay times of ~30ns [84].

The use of a cut light guide allows the use of fast Hamamatsu R9800 PMTs, giving the opportunity of designing a potential DOI detector replacement for current detectors. We were able to identify each pixel in the different detector layers and thus, to determine the depth of the photon interaction and achieve good timing resolution, necessary for TOF information.

This paper shows that it is possible to combine the advantages from DOI- and TOF- information.

The preparation of the scintillator pixels was quite elaborate. The fast pixels had to be etched, to be able to distinguish between the two types. Every pixel had to be taped with reflector material on the sides. The difficulty in the electronics adjustment was to find the optimum integration and differentiation time on the fast timing amplifier, to get the best separation of the decay time spectrum, so that a discrimination threshold could be applied. The software for the discrimination on the pulse shape second order discrimination on the light output was developed by the author.

Contribution of the author:

The idea for this research project was developed together with Mehmet Aykac and is based on a patent [85]. The author built the scintillator block, planned and performed the measurements, developed the software and wrote the paper.
11 Conclusion and outlook

The aim of this work was to improve the first link in the chain of components of a PET system – the detector, so that it may be given time-of-flight capabilities to improve signal to noise ratio and therefore image quality and lower the dose exposure for the patient.

The examination of the scintillator for its capabilities with regards to timing performance was the first step. We found LSO to be a viable scintillator with high density and atomic number for the detection efficiency demanded by clinical PET as well as fast rise time, short decay time, and high light output needed for time-of-flight.

Based on the results from the LSO, we examined the limitations of the existing detectors and their potential for improvements. The average coincidence timing resolution of a non-TOF detector was measured to be 733 ps at its operating voltage. An increase in high voltage of the PMTs improved this value to 642 ps. Although the increase in high voltage was not the final solution, because the gain specification was exceeded, it showed the potential of the detector design. To utilize the scintillator to its full potential, we found fast new PMTs, taking advantage of the fast rise- and decay times of LSO to a much higher degree.

Now the electronics moved into the focus of our efforts. We investigated a new dynode-timing technique optimized for PET block detectors. It allows utilization of dynode signals from multiple PMTs, operated with negative high-voltage, providing an event-timing trigger without deteriorating the anode signal. The timing-resolution improved 10%, by 43 ps compared to the standard anode timing. The improved timing is accompanied by the easy extraction of an event-timing trigger, especially for multi-PMT detector assemblies. Potential further improvements might be possible by moving the CFD closer to the detector. This would reduce the amount of cabling, while improving signal quality and shorten the time the signals take to travel to the CFD.

After improving the hardware we were able to find a simulation model, based on single crystal measurements, to describe the light spread in single LSO crystals, as well as in entire block arrangements. This will be a valuable tool for future detector developments, saving time in the laboratory and costly experiments.

With the use of LSO only, we were able to build a detector, capable of delivering depth-of-interaction data. Due to the fast rise time of the scintillator
and the use of fast PMTs, the DOI detector even delivers TOF performance, combining two methods for sensitivity and thus image improvements.

**Outlook:**
A promising candidate for further improvements would be to include the CFD on the voltage divider network. This measure would shorten the cables; hence, improve signal quality and therefore further improve the timing. The next step to further improve timing would be to digitize the PMT signals right after the PMT, on the voltage divider network.

In the future more and more solid state photo detectors, such as APDs and SiPMs will be used in PET. At present, systems with APDs are entering the market, in MR/PET systems. Their timing resolution in the nanosecond range is not suitable for TOF PET. Silicon photo multipliers on the other hand show good sub-nanosecond timing resolution, thus are promising candidates for future TOF-PET systems.

To achieve sub-centimeter position resolution a timing resolution of less than 50 ps is necessary. We were able to achieve a timing resolution below 250 ps with highly optimized single crystal measurements in the laboratory. On commercial scale a system timing resolution at ~500 ps is currently realistic.

Recent research activities, presented at the 2009 IEEE Nuclear Science Symposium and Medical Imaging Conference, regarding Si-PMTs show a very good timing resolution below 200 ps with LYSO and LaBr, which makes these devices interesting candidates for future TOF-PET and multi-modality MR/PET systems, due to the insusceptibility to magnetic fields.

Time of flight was recently implemented by two leading manufacturers of PET systems, bringing the benefits of increased sensitivity, shorter scan times and improved image resolution to the patient.


[9] M. Lubberink, “Quantitative imaging with PET - Performance and Applications of \textsuperscript{76}Br, \textsuperscript{52}Fe, \textsuperscript{110m}In and \textsuperscript{134}La,” Doctoral thesis, Department of Oncology, Radiology and Clinical Immunology, Uppsala University, Uppsala, 2001.


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Publication I
Current and Future Use of LSO:Ce Scintillators in PET

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Timing Performance of Hi-Rez Detector for Time-of-Flight (TOF) PET

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Performance Study of the new Hamamatsu R9779 & Photonis XP20D0 fast 2” Photomultipliers

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Depth of interaction with a 3-dimensional checkerboard arrangement LSO-LSO block